DISSERTATION

# CHIRAL KETONE-CATALYZED ASYMMETRIC EPOXIDATION OF *CIS*-OLEFINS

Submitted by

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In partial fulfillment of the requirements

For the Degree of Doctor of Philosophy

Colorado State University

Fort Collins, Colorado

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WE HEREBY RECOMMEND THAT THE DISSERTATION PREPARED UNDER OUR SUPERVISION BY CHRISTOPHER PATRICK BURKE ENTITLED CHIRAL KETONE-CATALYZED ASYMMETRIC EPOXIDATION OF *CIS*-OLEFINS BE ACCEPTED AS FULFILLING IN PART REQUIREMENTS FOR THE DEGREE OF DOCTOR OF PHILOSOPHY.

Committee on Graduate Work

Prof. Delphi Chatterjee

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# ABSTRACT OF DISSERTATION

# CHIRAL KETONE-CATALYZED ASYMMETRIC EPOXIDATION OF *CIS*-OLEFINS

Epoxides are invaluable intermediates in organic synthesis and are present in many biologically active compounds. As such, there is great interest in the synthesis of chiral non-racemic epoxides. One of the most convenient methods for their synthesis is the catalytic asymmetric epoxidation of olefins, and much work has been done in this area. Our group has been interested in epoxidation of unfunctionalized olefins using chiral dioxiranes generated from chiral ketones and Oxone or other oxidant.

Glucose-derived chiral ketones have been employed in the epoxidation of conjugated dienes to synthesize vinyl *cis*-epoxides with high chemo- and enantioselectivity. The reactions are stereospecific in that *cis*-olefins yielded only *cis*-epoxides with no isomerization observed. It was shown that a conjugating olefin is an effective directing group for the asymmetric epoxidation of unfunctionalized olefins with chiral ketone catalysts. The enantioselectivity of the reaction is highly dependent on the substitution pattern of the diene with *cis/trans*-dienes being the most effective. With this methodology a variety of synthetically useful enantioenriched vinyl epoxides are now readily accessible.

An effective system for the asymmetric epoxidation of conjugated *cis*-enynes has been developed using glucose-derived chiral ketones and Oxone as oxidant. The reactions are highly chemoselective and stereoselective and are stereospecific. In

addition to the directing effect of the alkyne, hydrophobic interactions between the catalyst and substrate play an important role in stereodifferentiation. These insights will be useful for expansion of this methodology to other substrate classes, the prediction of the stereochemical outcome of a given reaction, and the design of new ketone catalysts.

A method for the asymmetric epoxidation of *cis*-olefins using glucose-derived oxazolidinone-containing chiral ketones with $H_2O_2$ as stoichiometric oxidant has been developed. Use of $H_2O_2$ as oxidant rather than Oxone allows for use of less solvent and salts, and eliminates the need for slow addition of oxidant. A variety of olefins can be epoxidized with good yields and ee's. The reactions are operationally simple, and in most cases give results similar to those obtained with Oxone.

The scope of the ketone-catalyzed asymmetric epoxidation reaction has been expanded to include several types of unconjugated *cis*-olefins. With this system it is possible to use substituent polarity as an effective method of stereodifferentiation between two prochiral faces of an olefin. Allylic oxygen functionality also provides a mechanism for stereodifferentiation, although further experimentation is needed to define this mechanism clearly. This study opens up a whole new avenue of potential for this system that is yet unexplored and will be valuable for further studies and designing new ketone catalysts in the future.

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# CHAPTER ONE

# RECENT DEVELOPMENTS IN THE APPLICATIONS OF OXONE (POTASSIUM PEROXYMONOSULFATE) IN ORGANIC SYNTHESIS

## 1.A. INTRODUCTION

Oxone (potassium peroxymonosulfate) is a stable, convenient inorganic oxidant that is widely used in organic synthesis and other areas of chemistry and industry. As such, there are numerous reports of a wide variety of applications of Oxone in organic synthesis. This topic has been reviewed in the past,[1] so this review will focus on the most important developments reported in the literature since 1992.

## 1.B. MODIFICATION OF OXONE

[1] Crandall, J. K. in *Encyclopedia of Reagents for Organic Synthesis* **1992**, 4265-4269.

Since Oxone is a triple salt (2 $KHSO_5 \cdot KHSO_4 \cdot K_2SO_4$), only about 50% per mole is active oxidant. A convenient method for the preparation of pure $KHSO_5 \cdot H_2O$ on a large scale has been developed which allows for significant reduction in the physical amount of oxidizing agent needed for a reaction.[2] One of the main drawbacks of using Oxone is that aqueous/alcoholic or at least biphasic reaction conditions are usually necessary. To circumvent this issue several organic-soluble forms of Oxone have been developed including tetra-*n*-butylammonium peroxymonosulfate (*n*-$Bu_4NHSO_5$), [3] tetraphenylphosphonium peroxymonosulfate ($Ph_4PHSO_5$), [4] and benzyltriphenyl-phosphonium peroxymonosulfate ($BnPh_3PHSO_5$).[5] These oxidants can be used under anhydrous conditions, and in many cases show similar reactivity to Oxone. A study has been done comparing the activity of these different oxidants in the oxidation of benzaldehyde, *trans*-stilbene, triphenylphosphine, thioanisole and phenylboronic acid.[2]

## 1.C. KETONES, ALDEHYDES, ESTERS, AND ALCOHOLS

The well-known Baeyer-Villiger oxidation of ketones by Oxone has been exploited in a variety of reactions. This protocol has been used with $KHSO_5$ for cleavage

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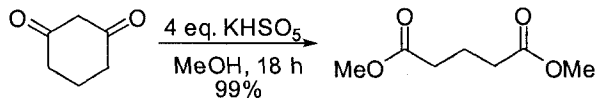
[2] Travis, B. R.; Ciaramitaro, B. P.; Borhan, B. *Eur. J. Org. Chem.* **2002**, 3429-3434.

[3] Trost, B. M.; Braslau, R. *J. Org. Chem.* **1988**, *53*, 532-537.

[4] Campestrini, S.; Di Furia, F.; Labat. G.; Novello, F. *J. Chem. Soc., Perkin Trans. 2* **1994**, 2175-2180.

[5] (a) Hajipour, A. R.; Mallakpour, S. E.; Adibi, H. *Chem. Lett.* **2000**, 460-461. (b) Bullman Page, P. C.; Barros, D.; Buckley, B. R.; Ardakani, A.; Marples, B. A. *J. Org. Chem.* **2004**, *69*, 3595-3597.

of α- and β-dicarbonyl compounds to esters and acids (Eq. 1.1, 1.2).[6] This process is simpler, cheaper, and milder than the commonly used haloform reaction.



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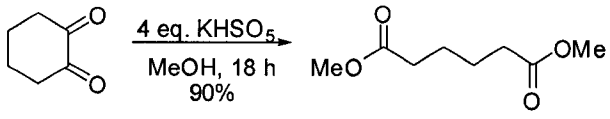
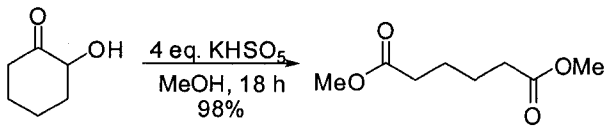


**(1.2)**

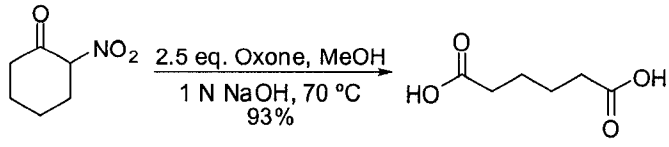
α-Hydroxy and α-nitroketones are oxidatively cleaved by Oxone in a similar manner to yield the corresponding esters and acids (Eq. 1.3, 1.4).[6,7] α-Nitroketones can be cleaved to dicarboxylic acids or dicarboxylic acid monomethyl esters depending on reaction conditions. It is proposed that in the case of α-hydroxy ketones, Bayer-Villiger oxidation is followed by oxidation of the resulting aldehyde to give the diacid/ester.



**(1.3)**

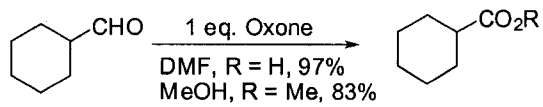
[6] (a) Yan, J.; Travis, B. R.; Borhan, B. *J. Org. Chem.* **2004**, *69,* 9299-9302. (b) Ashford, S. W.; Grega, K. C. *J. Org. Chem.* **2001**, *66*, 1523-1524.

[7] Ballini, R.; Curini, M.; Epifano, F.; Marcotullio, M. C.; Rosati, O. *Synlett* **1998**, 1049-1050.




**(1.4)**

Oxone has recently also been more thoroughly studied as reagent for the oxidation of aldehydes.[8] Aryl and aliphatic aldehydes can be efficiently converted directly to acids or esters depending on choice of solvent (Eq. 1.5).[8b] They can also be converted to nitriles in one pot by reaction with hydroxylamine on alumina with microwave irradiation (Eq. 1.6).[9] Aromatic aldehydes can be converted to aldoximes by the action of ethylene diamine and Oxone in water (Eq. 1.7).[10] The exact mechanism is unknown, but imine intermediates are likely.

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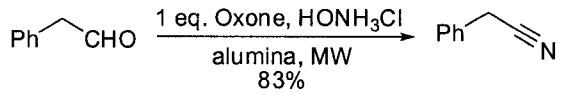


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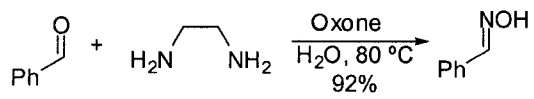


**(1.7)**

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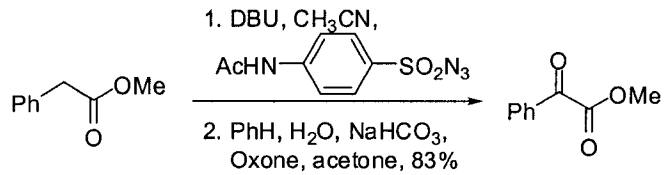
[8] (a) Webb, K. S.; Ruszkay, J. S. *Tetrahedron* **1998**, *54,* 401-410. (b) Travis, B. R.; Sivakumar, M.; Hollist, G. O.; Borhan, B. *Org. Lett* **2003**, *5,* 1031-1034.

[9] Bose, D. S.; Narsaiah, A. V. *Tetrahedron Lett.* **1998**, *39,* 6533-6534.

[10] Xia, J.-J.; Wang, G.-W. *Molecules* **2007**, *12*, 231-236.

α-Aryl esters can be oxidized to aryl α-keto esters by diazotization at the benzylic position followed by oxidation of the diazo group to the ketone with dimethyldioxirane (Eq. 1.8).[11]




**(1.8)**

Oxone oxidizes metal complexes including tris[(2-oxazolinyl)phenolato] manganese (III) which, in conjunction with *n*-$Bu_4NBr$, is an effective oxidant for aromatic and primary and secondary aliphatic alcohols (Figure 1.1).[12]

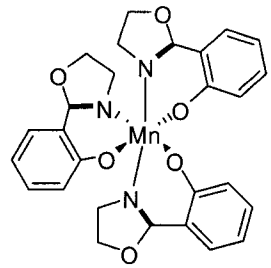
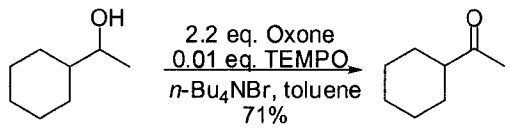



**Figure 1.1** tris[(2-oxazolinyl)phenolato] manganese(III)

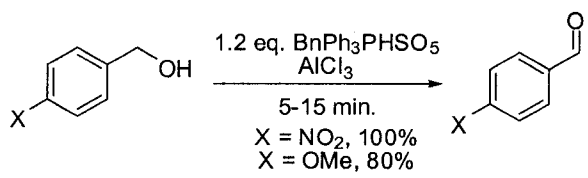
[11] Ma, M.; Li, C.; Peng, L.; Xie, F.; Zhang, X.; Wang, J. *Tetrahedron Lett.* **2005**, *46*, 3927-3929.

[12] Bagherzadeh, M. *Tetrahedron Lett.* **2003**, *44*, 8943-8945.

Additionally, Oxone is a suitable stoichiometric oxidant for alcohol oxidations with TEMPO and *n*-$Bu_4NBr$ even in aprotic solvents (Eq. 1.9).[13] Aliphatic and electron-rich benzylic alcohols give lower yields than electron-neutral benzylic alcohols in this case. A simple combination of Oxone and NaBr can also oxidize benzylic alcohols to aldehydes and ketones.[14] Once again, electron-rich benzylic alcohols gave lower yields; in this case it is due to competing halogenation of the aromatic ring. $BnPh_3PHSO_5$ has been used with $AlCl_3$ to oxidize benzylic and allylic alcohols under aprotic solvent-free conditions (Eq. 1.10).[15] This protocol gives good yields for both electron-poor and electron-rich primary and secondary benzylic alcohols.




**(1.9)**




**(1.10)**

Oxone has also been used to generate *o*-iodoxybenzoic acid (IBX) *in situ* for the oxidation of primary and secondary alcohols to aldehydes or carboxylic acids and ketones

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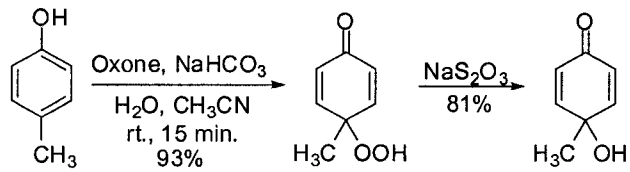
[13] Bolm, C.; Magnus, A. S.; Hildebrand, J. P. *Org. Lett.* **2000**, *2,* 1173-1175.

[14] Koo, B.-S.; Lee, C. K.; Lee, K.-J. *Synth. Commun.* **2002**, *32,* 2115-2123.

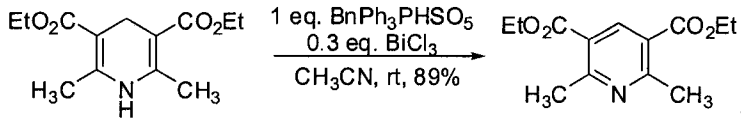
[15] Hajipour, A. R.; Mallakpour, S.; Adibi, H. *Chem. Lett.* **2000**, 460-461.

respectively in good yields.[16] A system using Oxone and catalytic amount of NaCl has also been reported to oxidize primary alcohols to symmetric esters and secondary alcohols to ketones.[17]

Phenols can be oxidatively dearomatized to *p*-peroxyquinols and *p*-quinols in one pot using Oxone as a source of singlet oxygen (Eq. 1.11).[18] Hantzsch 1,4-dihydropyridines can be oxidatively aromatized using benzyltriphenylphosphonium peroxymonosulfate with $BiCl_3$ (Eq. 1.12).[19]



**(1.11)**



**(1.12)**

## 1.D. ALKENES, ALKYNES, ARENES, AND ALKANES

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[16] (a) Thottumkara, A. P.; Bowsher, M. S.; Vinod, T. K. *Org. Lett.*, **2005**, *7*, 2933-2936. (b) Schulze, A.; Giannis, A. *Synthesis* **2006**, 257-260.

[17] Schulze, A.; Pagona, G.; Giannis, A. *Synth. Comm.* **2006**, *36*, 1147-1156.

[18] Carreño, C. M.; González-López, M.; Urbano, A. *Angew. Chem. Int. Ed.* **2006**, *45*, 2737-2741.

[19] Adibi, H.; Hajipour, A. R. *Bioorg. Med. Chem. Lett.* **2007**, *17*, 1008-1012.

One of the most common applications of Oxone in organic synthesis is the *in situ* formation of dioxiranes from ketones. Dioxirane chemistry has grown significantly in recent years—particularly in the area of enantioselective epoxidation, and a wide variety of chiral ketones has been designed for this purpose.[20] Notably, ketones **1-5** and **1-6** (Figure 1.2), derived from fructose and glucose respectively, have been shown to be effective catalysts for enantioselective epoxidations of a variety of *trans*-, trisubstituted, conjugated *cis*-, and terminal olefins with Oxone as primary oxidant (Eq. 1.13 and 1.14).[20b,c,21,22]

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[20] (a) Denmark, S. E.; Wu, Z. *Synlett.* **1999**, 847-859. (b) Frohn, M.; Shi, Y. *Synthesis* **2000**, 1979-2000. (c) Shi, Y. *Acc. Chem. Res.* **2004**, *37*, 488-496. (d) Yang, D. *Acc. Chem. Res.* **2004**, *37*, 497-505. (d) Curci, R.; Fiorentino, M.; Serio, M. R. *J. Chem. Soc., Chem. Commun.* **1984**, 155-156. (e) Yang, D.; Tang, Y.-C.; Wong, M.-K.; Zheng, J.-H.; Cheung, K.-K. *J. Am. Chem. Soc.* **1996**, *118*, 491-492. (f) Yang, D.; Wang, X.-C.; Wong, M.-K.; Yip, Y.-C.; Tang, M.-W. *J. Am. Chem. Soc.* **1996**, *118*, 11311-11312. (g) Yang, D.; Wong, M.-K.; Yip, Y.-C.; Wang, X.-C.; Tang, M.-W.; Zheng, J.-H.; Cheung, K.-K. *J. Am. Chem. Soc.* **1998**, *120*, 5943-5952. (h) Denmark, S. E.; Wu, Z.; Crudden, C. M.; Matsuhashi, H. *J. Org. Chem.* **1997**, *62*, 8288-8289. (i) Denmark, S. E.; Matsuhashi, H. *J. Org. Chem.* **2002**, *67;* 3479-3486. (j) Stearman, C. J.; Behar, V. *Tetrahedron Lett.* **2002**, *43*, 1943-1946. (k) Denmark, S. E.; Forbes, D. C.; Hays, D. S.; DePue, J. S.; Wilde, R. G. *J. Org. Chem.* **1995**, *60*, 1391-1407. (l) (m) Bortolini, O.; Gantin, G.; Fogagnolo, M.; Mari, L. *Tetrahedron* **2006**, *62*, 4482-4490. (n) Armstrong, A.; Tsuchiya, T. *Tetrahedron* **2006**, *62*, 257-263.

[21] (a) Tu, Y.; Wang, Z.-X.; Shi, Y. *J. Am. Chem. Soc.* **1996**, *118*, 9806-9807. (b) Wang, Z.-X.; Tu, Y.; Frohn, M.; Zhang, J.-R.; Shi, Y. *J. Am. Chem. Soc.* **1997**, *119*, 11224-11235. (c) Shu, L.; Shi, Y. *Tetrahedron Lett.* **2004**, *45*, 8115-8117.

[22] (a) Tian, H.; She, X.; Shu, L.; Yu, H.; Shi, Y. *J. Am. Chem. Soc.* **2000**, *122*, 11551-11552. (b) Tian, H.; She, X.; Yu, H.; Shu, L.; Shi, Y. *J. Org. Chem.* **2002**, *67*, 2435-2446. (c) Shen, Y.-S.; Wang, B.; Shi, Y. *Angew. Chem. Int. Ed.* **2006**, *45*, 1429-1432. (d) Wang, B.; Shen, Y.-S.; Shi, Y. *J. Org. Chem.* **2006**, *71*, 9519-9521. (e) Tian, H. T.; She, X.; Xu, J.; Shi, Y. *Org. Lett.* **2001**, *3*, 1929-1931. (f) Goeddel, D.; Shu, L.; Yuan, Y.; Wong, O. A.; Wang, B.; Shi, Y. *J. Org. Chem.* **2006**, *71*, 1715-1717. (g) Burke, C. P.; Shi, Y. *Angew. Chem. Int. Ed.* **2006**, *45*, 4475-4478.

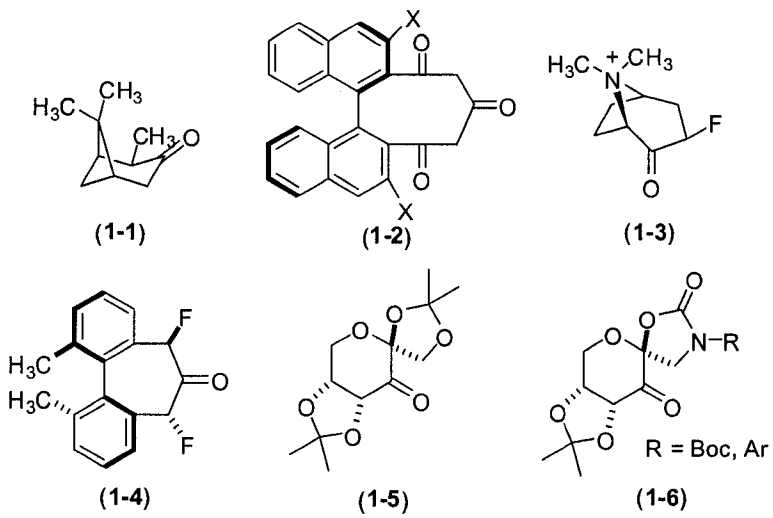
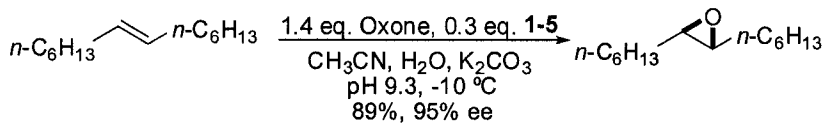
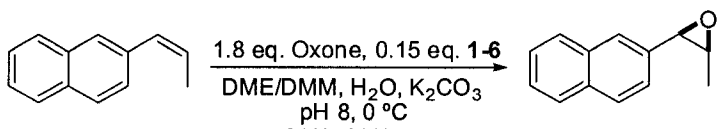



**Figure 1.2**



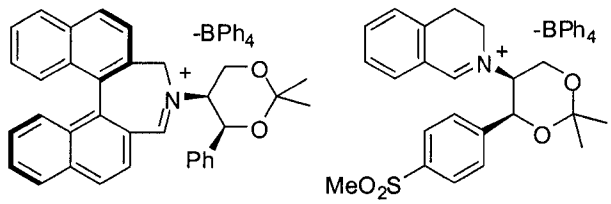

**(1.13)**




**(1.14)**

Oxone and its derivatives have also been used with chiral iminium salts and imines to form enantiomerically enriched epoxides. The scope and enantioselectivity of epoxidation with chiral iminium salts with Oxone and $Ph_4PHSO_5$ have made progress

during recent years.[5a,23] Chiral iminium salts **1-7** and **1-8** (Figure 1.3) have been particularly successful for some olefins (Eq. 1.15, 1.16).[24]

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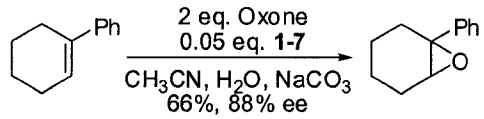


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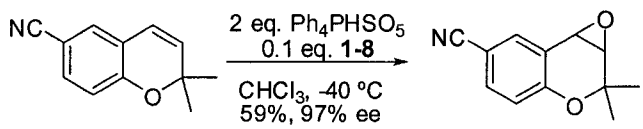


**(1.16)**

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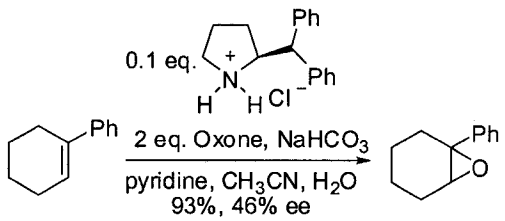
[23] (a) Aggarwal, V. K.; Wang, M. F. *Chem. Commun.* **1996**, 191-192. (b) Bullman Page, P. C.; Rassias, G. A.; Bethell, D.; Schilling, M. B. *J. Org. Chem.* **1998**, *63*, 2774-2777. (c) Minakata, S.; Takemiya, A.; Nakamura, K.; Ryu, I.; Komatsu, M. *Synlett.* **2000**, *12*, 1810-1812. (d) Wong, M.-K.; Ho, L.-M.; Zheng, Y.-S.; Ho, C.-Y.; Yang, D. *Org. Lett.* **2001**, *16*, 2587-2590. (e) Armstrong, A.; Ahmed, G.; Garnett, I.; Goacolou, K.; Wailes, J. S. *Tetrahedron* **1999**, *55*, 2341-2352. (f) Bullman Page, P. C.; Buckley, B. R.; Rassias, G. A.; Blackler, A. J. *Eur. J. Org. Chem.* **2006**, 803-813.

[24] (a) Bullman Page, P. C.; Buckley, B. R.; Blackler, A. J. *Org. Lett.* **2004**, *6*, 1543-1546. (b) Bullman Page, P. C.; Buckley, B. R.; Heaney, H.; Blackler, A. J. *Org. Lett.* **2005**, *7*, 375-377. (c) Bullman Page, P. C.; Buckley, B. R.; Barros, D.; Blackler, A. J.; Heaney, H.; Marples, B. A. *Tetrahedron* **2006**, *62*, 6607-6613.

Amine-catalyzed epoxidation is a relatively new area, and the active species is thought to be an ammonium peroxymonosulfate salt which acts as a phase transfer catalyst and undergoes electrophilic attack by an olefin.[25] Primary allylic amines have been regioselectively and diastereoselectively epoxidized in an intramolecular fashion using this methodology.[26] This is particularly useful since the use of a nitrogen protecting group is unnecessary. Use of chiral secondary and tertiary amines as catalysts has given rise to enantiomerically enriched epoxides (Eq. 1.17).[25]




**(1.17)**

Oxone in conjunction with $OsO_4$ cleaves alkenes to ketones or carboxylic acids (Eq. 1.18).[27] This protocol has the advantage over traditional methods in that there is no need for intermediate 1,2-diols. This methodology has been exploited in the direct

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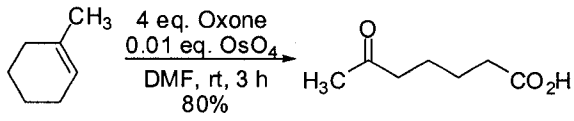
[25] (a) Armstrong, A. *Angew. Chem. Int. Ed.* **2004**, *43*, 1460-1462. (b) Aggarwal, V. K.; Lopin, C.; Sandrinelli, F. *J. Am. Chem. Soc.* **2003**, *125*, 7596-7601. (c) Ho, C.-Y.; Chen, Y.-C.; Wong, M.-K.; Yang, D. *J. Org. Chem.* **2005**, *70*, 898-906. (d) Gonçalves, M.-H.; Martinez, A.; Grass, S.; Bullman Page, P. C.; Lacour, J. *Tetrahedron Lett.* **2006**, *47*, 5297-5301.

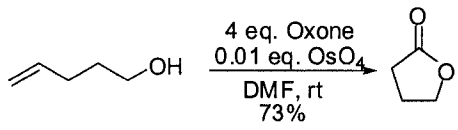
[26] Aggarwal, V. K.; Fang, G. Y. *Chem. Comm.* **2005**, 3448-3450

[27] Travis, B. R.; Narayan, R. S.; Borhan, B. *J. Am. Chem. Soc.* **2002**, *124*, 3824-3825.

synthesis of lactones from alkenols (Eq. 1.19) and tetrahydrofuran-diols from 1,4-dienes as well.[28]




**(1.18)**




**(1.19)**

When used in conjunction with $RuCl_3$, Oxone cleaves alkenes to aldehydes in high yields (Eq. 1.20).[29] This methodology is less effective for aliphatic olefins, and $NaIO_4$ is suggested as an alternate oxidant in those cases. The same combination with more Oxone and less water oxidizes alkenes to α-hydroxy ketones (Eq. 1.21).[30] The reaction is fairly regioselective depending on the electronic properties of the substrate. The hydroxy group usually ends up next to the more electron-withdrawing substituent. 1,2-Diols, which are possible intermediates/by-products in the above keto-hydroxylation, are also oxidized under the same conditions to α-hydroxy ketones, and enantiopurity of the starting material is preserved during the reaction (Eq. 1.22).[31]

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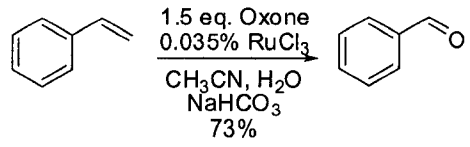
[28] (a) Schomaker, J. M.; Travis, B. R.; Borhan, B. *Org. Lett.* **2003**, *5*, 3089-3092. (b) Travis, B.; Borhan, B. *Tetrahedron Lett.* **2001**, *42*, 7741-7745.

[29] Yang, D.; Zhang, C. *J. Org. Chem.* **2001**, *66*, 4814-4818.

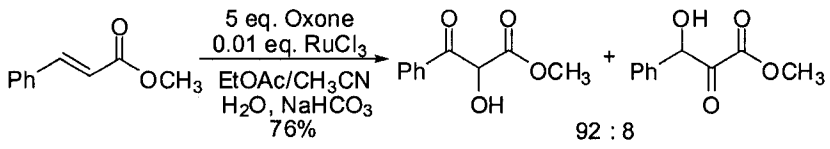
[30] (a) Plietker, B. *J. Org. Chem.* **2003**, *68*, 7123-7125. (b) Plietker, B. *J. Org. Chem.* **2004**, *69*, 8287-8296.

[31] Plietker, B. *Org. Lett.* **2004**, *6*, 289-291.

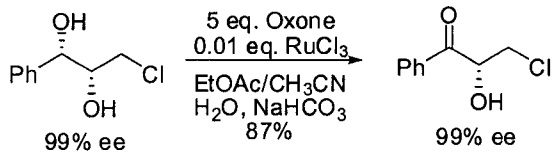
β-Alkoxy alcohols are obtained from the treatment of olefins with Oxone in the presence of alcohols. This process likely occurs via epoxidation followed by alcoholysis, although formation of intermediate epoxides was not detected.[32] Oxone in aqueous acetone has been shown to dihydroxylate various 1,2-glycals in one step in moderate to good yields.[33]




**(1.20)**




**(1.21)**




**(1.22)**

Oxone in conjunction with $RuO_2$ cleaves alkynes to carboxylic acids.[34] Both internal and terminal alkynes are cleaved in short reaction times with high yields (Eq. 1.23), and intermediate 1,2-diketones are proposed.

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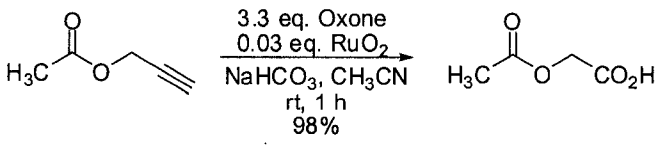
[32] Le Bras, J.; Chatterjee, D.; Muzart, J. *Tetrahedron Lett.* **2005**, *46*, 4741-4743.

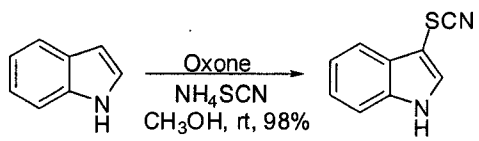
[33] Rani, S.; Vankar, Y. D. *Tetrahedron Lett.* **2003**, *44*, 907-909.

[34] Yang, D.; Chen, F.; Dong, Z.-M.; Zhang, D.-W. *J. Org. Chem.* **2004**, *69*, 2221-2223.

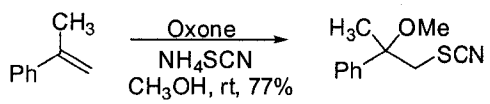
Nitrogen-containing aromatic and heteroaromatic compounds undergo regioselective thiocyanation using ammonium thiocyanate and Oxone (Eq. 1.24).[35] When olefins are subjected to these same conditions, methoxy thiocyanation is observed (Eq. 1.25).[36]




**(1.23)**




**(1.24)**




**(1.25)**

Dioxiranes generated from Oxone have recently been shown to undergo C-H insertion reactions with activated and unactivated C-H bonds. This strategy has been used in an intramolecular fashion for the oxidation of hydrocarbons (Eq. 1.26) and steroids.[37] Fructose-derived ketone **1-5** has also been used for this purpose in an

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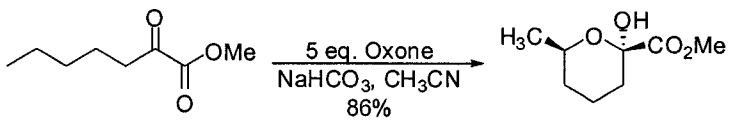
[35] Wu, G.; Liu, Q.; Shen, Y.; Wu, W.; Wu, L. *Tetrahedron Lett.* **2005**, *46*, 5831-5834.

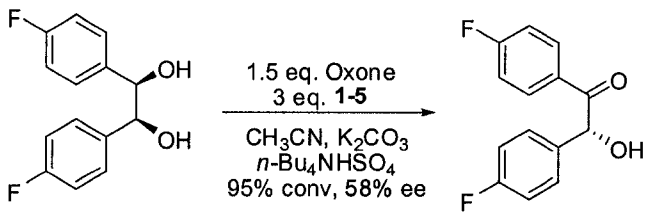
[36] Wu, G.; Wu, W.; Li, R. Shen Y.; Wu, L. *Chem. Lett.* **2007**, *36*, 188-189.

[37] (a) Yang, D.; Wong, M.-K.; Wang, X.-C.; Tang, Y.-C. *J. Am. Chem. Soc.* **1998**, *120*, 6611-6612. (b) Wong, M.-K.; Chung, N.-W.; He, L.; Wang, X.-C.; Yan, Z.; Tang, Y.-C.; Yang, D. *J. Org. Chem.* **2003**, *68*, 6321-6328.

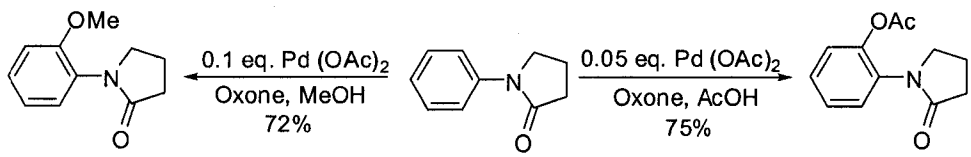
intermolecular reaction for the desymmetrization and kinetic resolution of 1,2-diols to α-hydroxy ketones (Eq. 1.27).[38] Aromatic and aliphatic C-H bonds have been oxygenated using Pd(II) with Oxone as primary oxidant and MeOH or AcOH (Eq. 1.28).[39] Oxone/Pd(II) has also been used for highly regioselective oxidative biaryl coupling (Eq. 1.29).[40] There is a report of the direct oxidation of hydrocarbons to ketones and lactones by Mn-porphyrin complexes with Oxone.[41]




**(1.26)**




**(1.27)**




**(1.28)**

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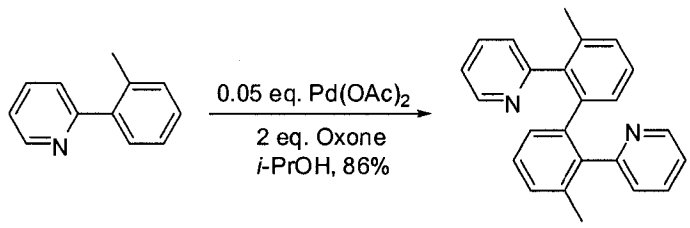
[38] (a) Adam, W.; Saha-Moller, C. R.; Zhao, C.-G. *Tetrahedron: Asymmetry* **1998**, *9*, 4117-4122. (b) Adam, W.; Saha-Moller, C. R.; Zhao, C.-G. *J. Org. Chem.* **1999**, *64*, 7492-7497.

[39] Desai, L. V.; Malik, H. A.; Sanford, M. S. *Org. Lett.* **2006**, *8*, 1141-1144.

[40] Hull, K. L.; Lanni, E. L.; Sanford, M. S. *J. Am. Chem. Soc.* **2006**, *128*, 14047-14049.

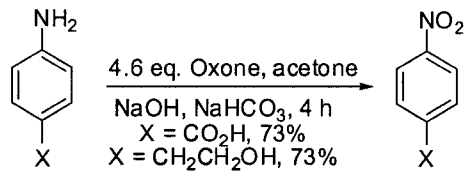
[41] Cammarota, L.; Campestrini, S.; Carrieri, M.; Di Furia, F.; Ghiotti, P. *J. Mol. Catal. A.* **1999**, *137*, 155-160.



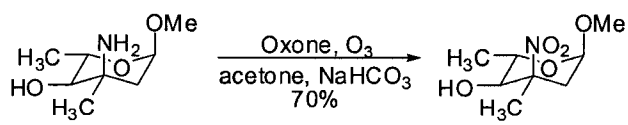

**(1.29)**

## 1.E. NITROGEN COMPOUNDS

Previous methods for oxidizing anilines to nitro compounds with Oxone/acetone were ineffective with carboxylic acid and alcohol-containing systems.[42] A new method using Oxone and acetone under aqueous conditions allows for the oxidation of carboxylic and alcoholic anilines as well (Eq. 1.30).[43] In this case the reaction occurred in the absence of acetone, but yields were significantly reduced. The combination of Oxone and ozone has been used to oxidize amino sugars to nitro sugars as well (Eq. 1.31).[44]




**(1.30)**




**(1.31)**

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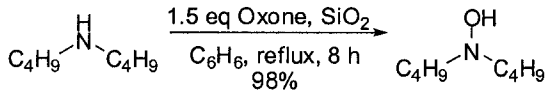
[42] Zabrowski, D. L.; Moormann, A. E.; Beck, K. R. J. *Tetrahedron Lett.* **1988**, *29*, 4501-4504.

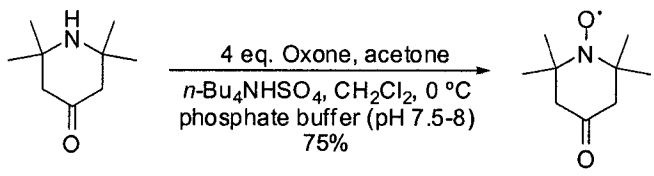
[43] Webb, K. S.; Seneviratne, V. *Tetrahedron Lett.* **1995**, *36*, 2377-2378.

[44] Noecker, L.; Giuliano, R. M.; Cooney, M.; Boyko, W.; Zajac Jr., W. W. *J. Carbohydr. Chem.* **2002**, *21*, 539-544.

Oxone adsorbed on silica gel or alumina is a very effective oxidant for the selective oxidation of primary and secondary amines to hydroxyl amines without over oxidation. These reactions can even be accomplished under solvent-free conditions and with very short reaction times with heating or microwave irradiation (Eq. 1.32).[45] Pyridine and trialkyl amines were also readily oxidized to their *N*-oxides. It is suggested that the hydroxyl amines are protected from over oxidation because of their strong adsorption to the silica gel or alumina surface. The Oxone/acetone system is also very effective for the formation of nitroxides from secondary amines without α-hydrogens (Eq. 1.33).[46]



**(1.32)**

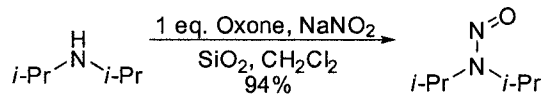


**(1.33)**

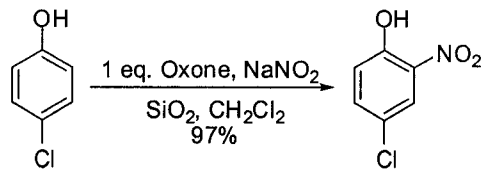
[45] Fields, J. D.; Kropp, P. J. *J. Org. Chem.* **2000**, *65*, 5937-5941.

[46] Brik, M. E. *Tetrahedron Lett.* **1995**, *36*, 5519-5522.

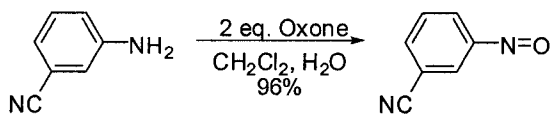
Because of Oxone's acidic nature, *N*-nitrosation of secondary amines is possible with the use of sodium nitrite in the presence of wet $SiO_2$ (Eq. 1.34).[47] Nitrophenols can be obtained via nitrosation-oxidation of phenols under similar conditions (Eq. 1.35).[48] Use of Oxone for these reactions eliminates the need for strong acids to generate $NO^+$ unlike traditional methods. Nitrosoarenes can also be prepared by oxidation of anilines with Oxone (Eq. 1.36).[49]



**(1.34)**



**(1.35)**



**(1.36)**

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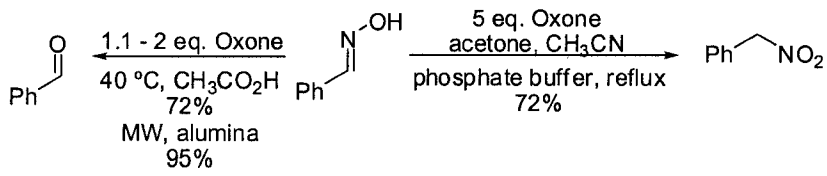
[47] Zolfigol, M. A.; Bagherzadeh, M.; Choghamarani, A. G.; Keypour, H.; Salehzadeh, S. *Synth. Commun.* **2001**, *31*, 1161-1166.

[48] Zolfigol, M. A.; Bagherzadeh, M.; Madrakian, E.; Ghaemi, E.; Taquian-Nasab, A. *J. Chem. Research (S)* **2001**, 140-142.

[49] Priewisch, B.; Rück-Braun, K. *J. Org. Chem.* **2005**, *70*, 2350-2352.

Oximes can be converted to their corresponding nitro compounds with Oxone in refluxing acetonitrile (Eq. 1.37).[50] They can also be cleaved to their parent carbonyl compounds by Oxone in conjunction with glacial acetic acid, or silica gel/alumina and microwave irradiation (Eq. 1.37).[51] In contrast to the result shown in Eq. 1.7, ketoximes and aldoximes are both converted to carbonyl compounds in high yields using the microwave and alumina procedure. Several of the above transformations are highlighted in the oxidative decarboxylation of α-amino acids to form ketones and carboxylic acids.[52]




**(1.37)**

Aldoximes can be converted to isothiocyanates in a convenient one-pot procedure with Oxone and HCl based on a procedure for synthesizing hydroximoyl chlorides.[53] The reaction presumably proceeds through an oxathiazoline that decomposes to give the isothiocyanate (Eq. 1.38).

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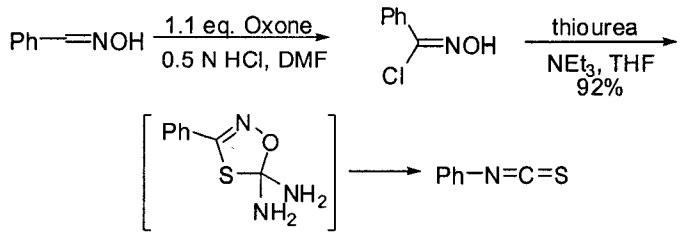
[50] Bose, D. S.; Vanajatha, G. *Synth.Commun.* **1998**, *28*, 4531-4535.

[51] (a) Bose, D. S.; Srinivas, P. *Synth. Commun.* **1997**, *27*, 3835-3838. (b) Bose, D. S.; Narsaiah, A. V.; Lakshminarayana, V. *Synth. Commun.* **2000**, *30*, 3121-3125. (c) Bigdeli, M. A.; Nikje, M. M. A.; Heravi, M. M. *Phosphorus, Sulfur, Silicon* **2002**, *177*, 15-18.

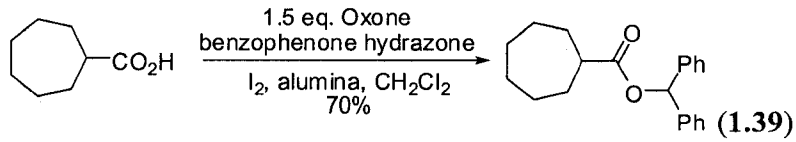
[52] Paradkar, V. M.; Latham, T. B.; Demko, D. M. *Synlett.* **1993**, 1059-1060.

[53] (a) Kim, J. N.; Ryu, E. K. *J. Org. Chem.* **1992**, *57*, 6649-6650. (b) Kim, J. N.; Jung, K. S.; Lee, H. J.; Son, J. S. *Tetrahedron Lett.* **1997**, *38*, 1597-1598.




**(1.38)**

An interesting method for the protection of carboxylic acids as diphenylmethyl esters in high yield using Oxone and benzophenone hydrazone has been reported (Eq. 1.39).[54] Various aromatic tosylhydrazones can also be cleaved to carbonyl compounds by Oxone/acetone (Eq. 1.40).[55] It is proposed that cleavage occurs via collapse of an oxaziridine intermediate. $BnPh_3PHSO_5$ has been used with $BiCl_3$ to regenerate carbonyl compounds from oximes, phenylhydrazones, 2,4-dinitrophenylhydrazones, and semicarbazones under non-aqueous conditions.[56] Yields are generally very good, and it is also possible to oxidize alcohols to ketones under these conditions without affecting any of the above mentioned carbonyl derivatives. Likewise, Oxone is useful for the conversion of nitro groups into carbonyl compounds (Nef reaction) in the presence of aqueous base (Eq. 1.41).[57]

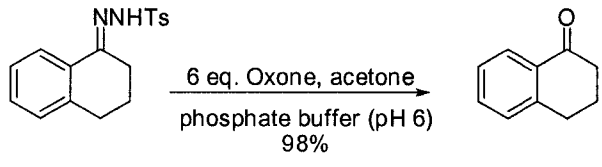



**(1.39)**

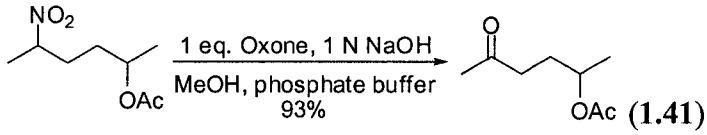
[54] Curini, M.; Rosati, O.; Pisani, E. *Tetrahedron Lett.* **1997**, *38*, 1239-1240.

[55] Jung, J. C.; Kim, K. S.; Kim, Y. H. *Synth. Commun.* **1992**, *22*, 1583-1587.

[56] Hajipour, A. R.; Mallakpour, S. E.; Baltork, I. M.; Adibi, H. *Synth. Commun.* **2001**, *31*, 3401-3409.

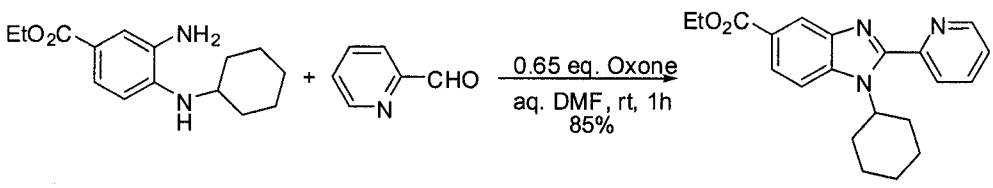



**(1.40)**




**(1.41)**

Benzimidazoles can be synthesized in one step by condensing 1,2-phenylenediamines and aldehydes in the presence of Oxone (Eq. 1.42).[58] The reaction gives good selectivity and tolerates electron-rich and electron-poor phenylenediamines as well as a wide variety of aromatic and aliphatic aldehydes.

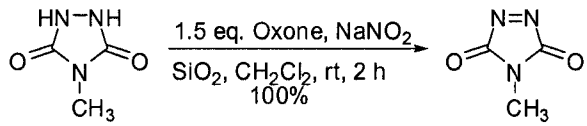



**(1.42)**

[57] Ceccherelli, P.; Curini, M.; Marcotullio, M. C.; Epifano, F.; Rosati, O. *Synth. Commun.* **1998**, *28,* 3057-3064.

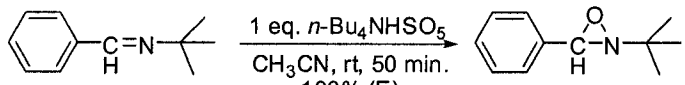
[58] Beaulieu, P. L.; Haché, B.; von Moos, E. *Synthesis* **2003**, 1683-1692.

Urazoles are oxidized to triazolinediones when subjected to Oxone and $NaNO_2$ (Eq. 1.43).[59] These compounds, which have typically been difficult to synthesize and purify, are relatively easily made in high yields and purity by this procedure.




**(1.43)**

Oxaziridines, which have previously been produced from reaction of imines with Oxone,[60] have recently been made in excellent yields with *n*-$Bu_4NHSO_5$ in acetonitrile (Eq. 1.44).[61] The reactions are generally E-selective. However, as the size of the group on nitrogen decreases, more Z-isomer is produced. Effects of solvent and Lewis acids on the E/Z selectivity and rate of reaction were studied as well.




**(1.44)**

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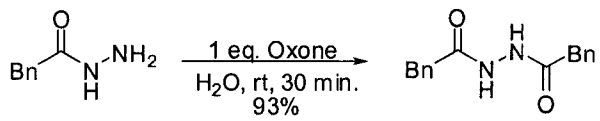
[59] Zolfigol, M. A.; Bagherzadeh, M.; Chehardoli, G.; Mallakpour, S. E. *Synth. Commun.* **2001**, *31*, 1149-1154.

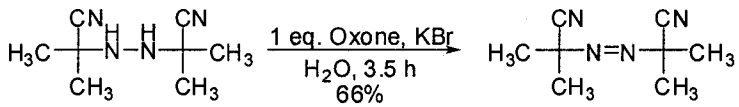
[60] (a) Davis, F. A.; Chattopadhyay, S.; Towson, J. C.; Lal, S.; Reddy, T. *J. Org. Chem.* **1988**, *53*, 2087-2089. (b) Davis, F. A.; Weismiller, M. C.; Murphy, C. K.; Reddy, R. T.; Chen, B. C. *J. Org. Chem.* **1992**, *57*, 7274-7285.

[61] Mohajer, D.; Iranpoor, N.; Rezaeifard, A. *Tetrahedron Lett.* **2004**, *45*, 631-634.

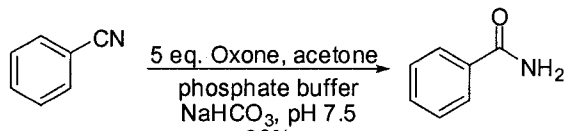
Acylhydrazides are oxidized to *N,N'*-diacylhydrazines in high yields with aqueous Oxone (Eq. 1.45) although only aromatic hydrazides were effective.[62] The oxidation of alkylcyanohydrazines to azo-*bis* nitriles can be done with an Oxone/KBr system (Eq. 1.46).[63] Nitriles can also be hydrolyzed to amides in moderate to good yields with Oxone/acetone (Eq. 1.47).[64]




**(1.45)**




**(1.46)**




**(1.47)**

## 1.F. SULFUR COMPOUNDS

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[62] Kulkarni, P.P.; Kadam, A. J.; Desai, U.V.; Mane, R. B.; Wadgaonkar, P. P. *J. Chem. Research (S)* **2000**, 184-185.

[63] Tamhankar, B.V.; Desai, U. V.; Mane, R. B.; Kulkarni, P. P.; Wadgaonkar, P. P. *Synth. Commun.* **2002**, *32*, 3643-3646.

[64] Bose, D. S.; Baquer, S. M. *Synth. Commun.* **1997**, *27*, 3119-3123.

A convenient procedure for high yielding oxidation of sulfides to either sulfoxides or sulfones using aqueous acetone and Oxone has been reported (Eq. 1.48) and has been used to produce SK&F 107310 (Figure 1.4) in kilogram quantities.[65] Selectivity is attained by controlling stoichiometry and reaction temperature. Sulfides and sulfoxides can be oxidized in high yields to sulfones, and disulfides can be oxidized to thiosulfonates by tetrabutylammonium peroxymonosulfate with imidazole and a Mn(III)-porphyrin catalyst.[66] Various disulfides can be enantioselectively oxidized to thiosulfinates with Oxone and ketone **1-5** (Eq. 1.49).[67,68] The highest enantioselectivities were obtained when the disulfides were sterically bulky. Many of these same transformations have also been accomplished with good yield and selectivity on silica gel and alumina. The role of the surfaces has been investigated, and it was found that Oxone is activated by dispersal on the surface of the adsorbent allowing greater contact with the substrate.[69] Mechanistic studies of sulfide oxidation and thioester hydrolysis by Oxone have also been performed.[70] In addition, oxidation of glycosyl sulfides to glycosyl sulfoxides has been accomplished with Oxone on silica gel.[71]

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[65] Webb, K. S. *Tetrahedron Lett.* **1994**, *35*, 3457-3460.

[66] Iranpoor, N.; Mohajer, D.; Rezaeifard, A.-R. *Tetrahedron Lett.* **2004**, *45*, 3811-3815.

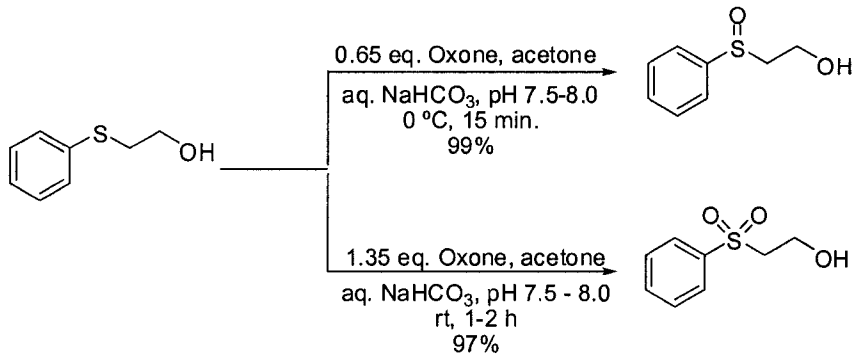
[67] Colonna, S.; Pironti, V.; Drabowicz, J.; Brebion, F.; Fensterbank, L.; Malacria, M. *Eur. J. Org. Chem.* **2005**, 1727-1730.

[68] Khiar, N.; Mallouk, S.; Valdivia, V.; Bougrin, K.; Soufiaoui, M.; Fernández, I. *Org. Lett.* **2007**, *9*, 1255-1258.

[69] Kropp, P. J.; Breton, G. W.; Fields, J. D.; Tung, J. C.; Loomis, B. R. *J. Am. Chem. Soc.* **2000**, *122*, 4280-4285.

[70] Bunton, C. A.; Foroudian, H. J.; Kumar, A. *J. Chem. Soc., Perkin Trans. 2* **1995**, 33-39.

[71] Chen, M.-Y.; Patkar, L. N.; Chen, H.-T.; Lin, C.-C. *Carbohydr. Res.* **2003**, *338*, 1327-1332.




**(1.48)**

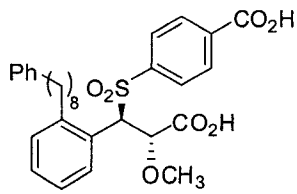
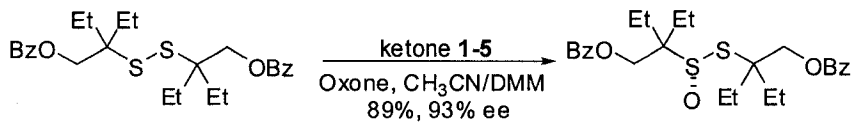



**Figure 1.4** SK&F 107310




**(1.49)**

Episulfides can be oxidized to episulfones with Oxone and 1,1,1-trifluoroacetone without considerable episulfoxide formation in many cases (Eq. 1.50).[72] Sulfides and thiols can be selectively oxidized to sulfoxides and disulfides respectively with the use of $BnPh_3PHSO_5$ in anhydrous aprotic solvents or solvent free conditions (Eq. 1.51).[73]

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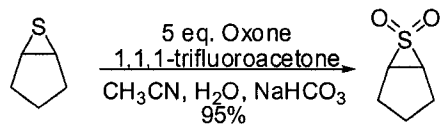
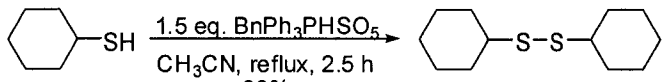
[72] Johnson, P.; Taylor, R. J. K. *Tetrahedron Lett.* **1997**, *38*, 5873-5876.

[73] (a) Hajipour, A. R.; Mallakpour, S. E.; Adibi, H. *J. Org. Chem.* **2002**, *67*, 8666-8668. (b) Hajipour, A. R.; Mallakpour, S. E.; Adibi, H. *Phosphorus, Sulfur, Silicon* **2002**, *177*, 2277-2284.

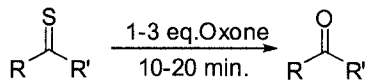



**(1.50)**




**(1.51)**

A variety of thiocarbonyl compounds including thioamides, thioureas, and thionoesters are converted to their corresponding carbonyl compounds in good yield by simply grinding them with solid Oxone with a mortar and pestle (Eq. 1.52).[74] Thioketones remained unchanged under the reaction conditions.



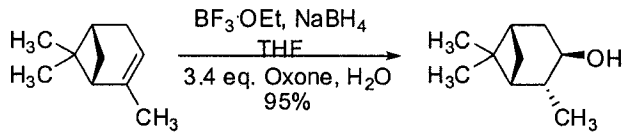

| R | R' | Yield |
|---|---|---|
| Me | NMePh | 95% |
| $NH_2$ | NHPh | 85% |
| Ph | OEt | 80% |

**(1.52)**

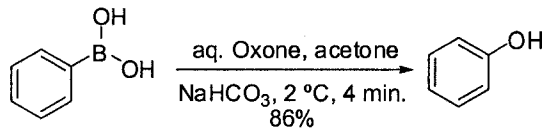
## 1.G. BORON, PHOSPHORUS, AND SELENIUM COMPOUNDS

[74] Baltork, I. M.; Sadeghi, M. M.; Esmayilpour, K. *Synth. Commun.* **2003**, *33*, 953-959.

Oxone has been used to oxidize carbon-boron bonds during the work-up of hydroboration reactions to obtain high yields of the resultant alcohols (Eq. 1.53).[75] Aqueous Oxone/acetone oxidizes electron-poor and electron-rich aromatic and aliphatic boronic acids and esters to the corresponding alcohols rapidly and efficiently (Eq. 1.54).[76] A one-pot procedure for the synthesis of *meta*-substituted phenols from benzenes has been developed, and a similar strategy has been devised for the synthesis of Boc-oxindoles from Boc-indoles.[77]




**(1.53)**




**(1.54)**

Phosphorus (III), phosphothio-, and phosphoseleno- compounds are oxidized by Oxone in THF/MeOH to produce phosphono- compounds with predominant retention of

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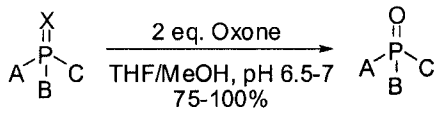
[75] Ripin, D. H. B.; Cai, W.; Brenek, S. J. *Tetrahedron Lett.* **2000**, *41*, 5817-5819.

[76] Webb, K. S.; Levy, D. *Tetrahedron Lett.* **1995**, *36*, 5117-5118.

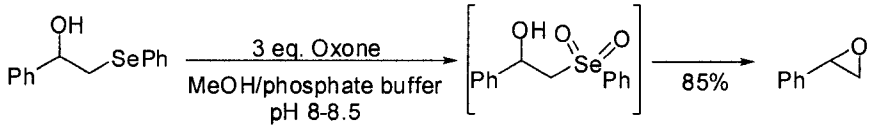
[77] (a) Maleczka Jr., R. E.; Shi, F.; Holmes, D.; Smith III, M. R. *J. Am. Chem. Soc.* **2003**, *125*, 7792-7793. (b) Vazquez, E.; Payack, J. F. *Tetrahedron Lett.* **2004**, *45*, 6549-6550.

configuration at phosphorus (Eq. 1.55).[78] Thioalkyl or amino groups attached to phosphorus are unaffected.




**(1.55)**

Selenides can be oxidized directly to selenones with methanolic buffered Oxone solutions under mild conditions. Selenones can be isolated directly, or if a nucleophile is present, they are displaced giving the substitution product (Eq. 1.56).[79] Some α-sulfonyl selenides can be oxidized to selenolesters with Oxone in MeOH or THF.[80]




**(1.56)**

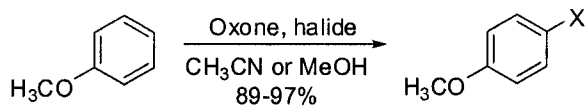
## 1.H. HALIDES

[78] Woźniak, L. A.; Stec, W. J. *Tetrahedron Lett.* **1999**, *40*, 2637-2640.

[79] Ceccherelli, P.; Curini, M.; Epifano, F.; Marcotullio, M. C.; Rosati, O. *J. Org. Chem.* **1995**, *60*, 8412-8413.

[80] Yi, J. S.; Kim, K. *J. Chem. Soc., Perkin Trans. 1* **1999**, 71-76.

Oxone oxidizes halides to form electrophilic halogens *in situ* for a variety of halogenation reactions. Use of *in situ* generated halogens is advantageous because it obviates the need for storage and handling of dangerous chlorine/bromine and keeps these compounds at low concentrations during reaction. Electron-rich aromatic compounds undergo predominantly *para-* halogenation with Oxone and KX or $NH_4I$ (Eq. 1.57).[81] Significant amounts of *ortho-* halogenated products are sometimes observed. Phenols can also be halogenated in high yields and selectivity with $BnPh_3PHSO_5$ and KI or KBr.[82]



**(1.57)**

Conjugated enones and simple alkenes also undergo halogenation with chlorine or bromine generated from Oxone and the corresponding sodium halide or hydrohalic

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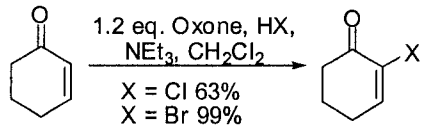
[81] (a) Tamhankar, B. V.; Desai, U. V.; Mane, R. B.; Wadgaonkar, P. P.; Bedekar, A. V. *Synth. Commun.* **2001**, *31*, 2021-2027. (b) Narender, N.; Srinivasu, P.; Kulkarni, S. J.; Raghavan, K. V. *Synth. Commun.* **2002**, *32*, 279-286. (c) Narender, N.; Srinivasu, P.; Prasad, M. R.; Kulkarni, S. J.; Raghavan, K. V. *Synth. Commun.* **2002**, *32*, 2313-2318. (d) Narender, N.; Srinivasu, P.; Kulkarni, S. J.; Raghavan, K. V. *Synth. Commun.* **2002**, *32*, 2319-2324. (e) Mohan, K. V. V. K.; Narender, N.; Kulkarni, S. J. *Tetrahedron Lett.* **2004**, *45*, 8015-8018.

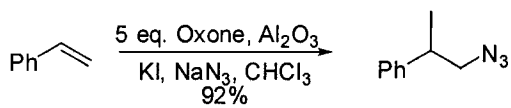
[82] (a) Hajipour, A. R.; Adibi, H. *J. Chem. Res.* **2004**, 294-295. (b) Adibi, H.; Hajipour, A. R.; Hashemi, M. *Tetrahedron Lett.* **2007**, *48*, 1255-1259.

acid.[83] In the case of enones, the addition product can be treated with base to give conjugated vinyl halides (Eq. 1.58).




**(1.58)**

A variety of alkenes undergo azidoiodination with sodium azide, potassium iodide, and Oxone on wet alumina to give azido-iodo compounds regioselectively in high yield (Eq. 1.59).[84] These compounds are useful precursors to vinyl azides, amines, and aziridines and are typically synthesized with more expensive and exotic reagents. Similar methodology has been used in the iodolactonization and iodoetherification of unsaturated carboxylic acids and alcohols to make five and six-membered lactones, tetrahydrofurans and tetrahydropyrans (Eq. 1.60).[85] *N*-Tosyl lactams have also been synthesized with Oxone and KI and alumina via a similar procedure.[86]




**(1.59)**

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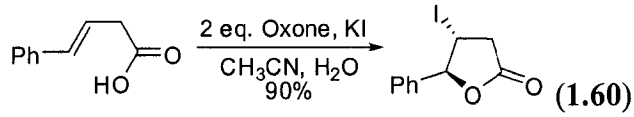
[83] (a) Dieter, R. K.; Nice, L. E.; Velu, S. E. *Tetrahedron Lett.* **1996**, *37*, 2377-2380. (b) Kim, K.-M.; Park, I.-H. *Synthesis* **2004**, 2641-2644.

[84] (a)Curini, M.; Epifano, F.; Marcotullio, M. C.; Rosati, O. *Tetrahedron Lett.* **2002**, *43*, 1201-1203. (b) Rawal, G. K.; Rani, S.; Madhusudanan, K. P.; Vankar, Y. D. *Synthesis* **2007**, 294-298.

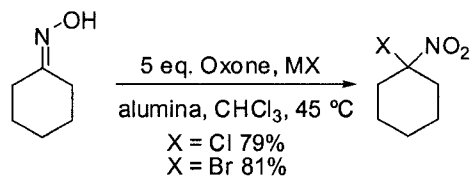
[85] Curini, M.; Epifano, F.; Marcotullio, M. C.; Montanari, F. *Synlett.* **2004**, 368-370.

[86] Marctullio, M. C.; Campagna, V.; Sternativo, S.; Costantino, F.; Curini, M. *Synthesis* **2006**, 2760-2766.



**(1.60)**

*gem*-Halo-nitro compounds can be prepared in one step from oximes with Oxone supported on wet basic alumina and NaCl or KBr (Eq. 1.61).[87] Use of basic alumina is essential in this case due to oxidative deprotection of the oximes to ketones when neutral alumina is used.



**(1.61)**

Halodecarboxylation of aromatic α,β-unsaturated carboxylic acids (Hunsdiecker reaction) to make β-halo-styrenes has been accomplished with Oxone and sodium halide (Eq. 1.62). [88] Bromodecarbonylation and bromodecarboxylation of electron-rich benzaldehydes and benzoic acids has also been observed.[89]

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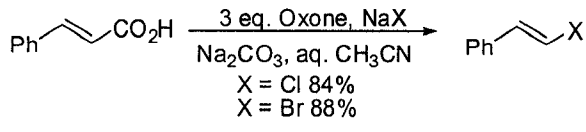
[87] (a) Ceccherelli, P.; Curini, M.; Epifano, F.; Marcotullio, M. C.; Rosati, O. *Tetrahedron Lett.* **1998**, *39*, 4385-4386. (b) Curini, M.; Epifano, F.; Marcotullio, M. C.; Rosati, O.; Rossi, M. *Tetrahedron* **1999**, *55*, 6211-62

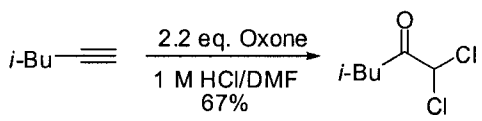
[88] You, H.-W.; Lee, K.-J. *Synlett.* **2001**, 105-107.

[89] Koo, B.-S.; Kim, E.-H.; Lee, K.-J. *Synth. Commun.* **2002**, *32*, 2275-2286.

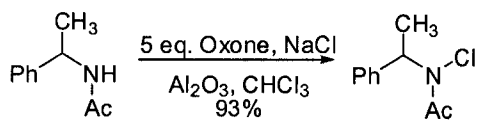



**(1.62)**

Aromatic methyl ketones can be halogenated at the α-position with Oxone and sodium halide; however competing halogenation of the aromatic ring is significant.[90] α,α-Dichloroketones can be synthesized from alkynes by reaction with Oxone in HCl/DMF (Eq. 1.63).[91] Oxone consistently gave better results than MCPBA for this transformation. Reaction of amides and carbamates with Oxone on wet alumina and NaCl gives *N*-chlorinated products in high yields (Eq. 1.64).[92]




**(1.63)**




**(1.64)**

## 1.I. PROTECTING GROUP REMOVAL

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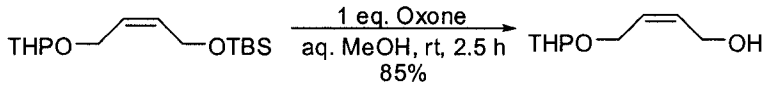
[90] Kim, E.-H.; Koo, B.-S.; Song, C. E.; Lee, K. J. *Synth. Commun.* **2001**, *31*, 3627-3632.

[91] Kim, K. K.; Kim, J. N.; Kim, K. M.; Kim, H. R.; Ryu, E. K. *Chem. Lett.* **1992**, 603-604.

[92] Curini, M.; Epifano, F.; Marcotullio, M. C.; Rosati, O.; Tsadjout, A. *Synlett.* **2000**, 813-814.

Several types of alcohol and carbonyl protecting groups can be removed with solutions of Oxone. Deprotection with Oxone offers a mild alternative to traditional methods which often require harshly acidic or basic conditions. Primary alkyl and phenolic TBS ethers are cleaved with aqueous methanolic Oxone (Eq. 1.65).[93] Primary alkyl TBS ethers are much more labile and thus can be cleaved in the presence of phenolic TBS ethers by limiting the reaction time. Secondary and tertiary TBS ethers and TBDPS ethers are unaffected. When the reactions were carried out in the absence of Oxone with solutions of HCl and HF adjusted to the same pH as the Oxone solution, no cleavage was observed for any type of TBS ether after 2.5-3 h suggesting that Oxone's deprotective ability is not due solely to its acidic nature.




**(1.65)**

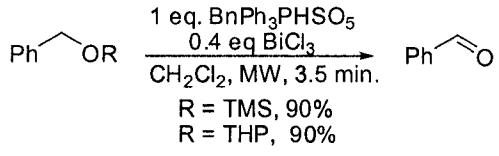
Oxone in refluxing acetonitrile cleaves TMS and THP ethers to alcohols and acetals to carbonyls.[94] In contrast, $BnPh_3PHSO_5$ has been used to oxidatively cleave TMS and THP ethers and ethylene acetals to carbonyl compounds under microwave irradiation with $BiCl_3$ (Eq. 1.66, 1.67).[95] No over oxidation products were observed with

[93] Sabitha, G.; Syamala, M.; Yadav, J. S. *Org. Lett.* **1999**, *1*, 1701-1703.

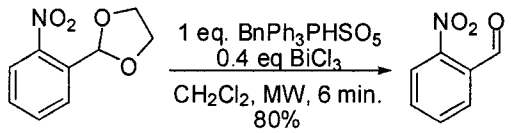
[94] Baltork, I. M.; Amini, M. K.; Farshidipoor, S. *Bull. Chem. Soc. Jpn.* **2000**, *73*, 2775-2778.

[95] Hajipour, A. R.; Mallakpour, S. E.; Baltork, I. M.; Adibi, H. *Synth. Commun.* **2001**, *31*, 1625-1631.

this method. Oxone on alumina has also been used to cleave ketals to diols and carbonyl compounds under solvent-free conditions with microwave irradiation.[96]

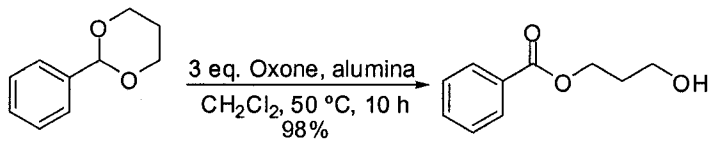



**(1.66)**




**(1.67)**

Cleavage of acetals to esters (Eq. 1.68) as well as cleavage of THP ethers with Oxone on wet alumina has also been reported.[97] THP ethers gave mainly the deprotected alcohols along with significant amounts of esterified products.



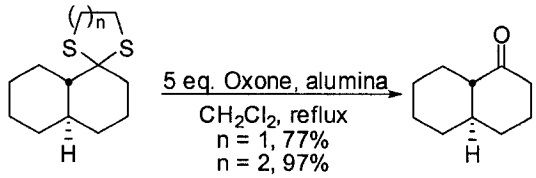

**(1.68)**

1,3-Dithiolanes and 1,3-dithianes can also be cleaved by Oxone on wet alumina or by Oxone-KBr to give the parent carbonyl compounds in high yields (Eq. 1.69).[98] The

[96] Bose, D. S.; Jayalakshmi, B.; Narsaiah, A. V. *Synthesis* **2000**, 67-68.

[97] Curini, M.; Epifano, F.; Marcotullio, M. C.; Rosati, O. *Synlett.* **1999**, 777-779.

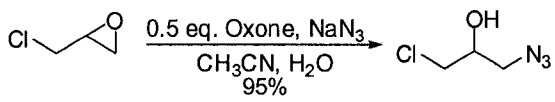
combination of $BnPh_3PHSO_5$ and $BiCl_3$ has also been applied successfully to the deprotection of 1,3-dithiolanes and 1,3-dithianes under non-aqueous conditions.[99]




**(1.69)**

## 1.J. MISCELLANEOUS

Ring opening of a variety of epoxides and aziridines with $NaN_3$ in the presence of Oxone in high yields has been accomplished (Eq. 1.70).[100] The specific role of Oxone is unclear; however no ring opening takes place in its absence. It is suggested that the results are due to Oxone's acidic nature.




**(1.70)**

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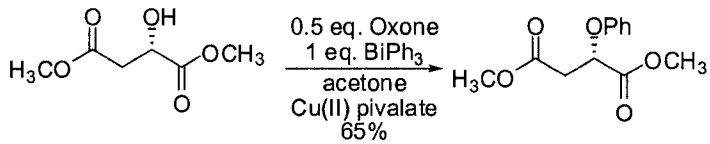
[98] (a) Ceccherelli, P.; Curini, M.; Marcotullio, M. C.; Epifano, F.; Rosati, O. *Synlett.* **1996**, 767-768. (b) Desai, U. V.; Pore, D. M.; Tamhankar, B. V.; Jadav, S. A.; Wadgaonkar, P. P. *Tetrahedron Lett.* **2006**, *47*, 8559-8561.

[99] Hajipour, A. R.; Mallakpour, S. E.; Baltork, I. M.; Adibi, H. *Phosphorus, Sulfur, Silicon* **2002**, *177*, 2805-2811.

[100] Sabitha, G. Babu, R. S.; Reddy, M. S. K.; Yadav, J. S. *Synthesis* **2002**, 2254-2258.

Oxone has been used with triarylbismuth and copper salts to effect aryl transfer reactions.[101] Aryl groups can be transferred to alcohols to make phenyl ethers (Eq. 1.71), however, two coordination sites on the substrate are necessary.




**(1.71)**

## 1.K. CONCLUSION

In summary, Oxone is a convenient oxidant for many functional groups including carbonyls, alcohols, unsaturated C-C bonds, many nitrogen-containing functional groups, sulfur, boron, phosphorous, selenium, halides, and is capable of removing a number of protecting groups. The number of applications of Oxone in organic synthesis has increased significantly in recent years and will undoubtedly continue to do so in the future.

[101] Sheppard, G. S. *Synlett.* **2002**, 1207-1210.

# CHAPTER TWO

# CATALYTIC ASYMMETRIC EPOXIDATION OF *CIS*-OLEFINS AND AN IMPROVED SYNTHESIS OF A KETONE CATALYST FOR THE ASYMMETRIC EPOXIDATION OF OLEFINS

## 2.A. INTRODUCTION

Epoxides are invaluable intermediates in organic synthesis and are present in many biologically active compounds. As such, there is great interest in the synthesis of chiral non-racemic epoxides.[102] One of the most convenient methods for their synthesis is catalytic asymmetric epoxidation of olefins, and much work has been done in this area. Great progress has been made in the area of asymmetric epoxidation of allylic and homoallylic alcohols where coordination of a chiral catalyst to the substrate results in

[102] *Aziridines and Epoxides in Organic Synthesis*; Yudin, A. K. Ed.; Wiley-VCH: Weinheim, 2006.

high enantiomeric excess for a wide variety of these olefin substrates.[103] Great progress has also been made in the area of asymmetric epoxidation of unfunctionalized olefins where non-bonded interactions between the catalyst and substrate determine the stereochemical outcome of the reaction.[104]

## 2.B. CATALYTIC ASYMMETRIC EPOXIDATION OF *CIS*-OLEFINS

Among the different classes of unfunctionalized olefins, asymmetric epoxidation of *cis*-olefins has received a substantial amount of attention using various different methods but still remains a very challenging problem. Allylic alcohols of all kinds have been epoxidized using Sharpless' method, and *cis*-allylic alcohols are epoxidized with varying degrees of success depending on the non-alcohol substituent (Scheme 2.1).[103a,b] Generally, the ee's are in the 80-95% range; however, higher ee's can often be attained through recrystallization.

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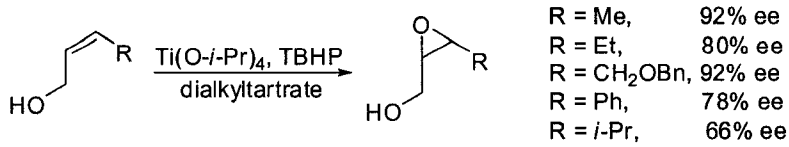
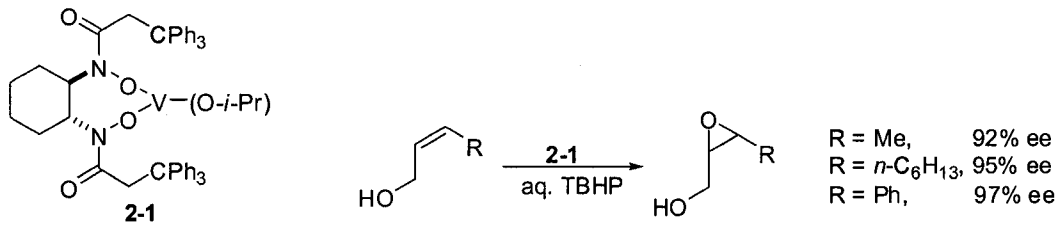
[103] (a) Johnson, R.A.; Sharpless, K.B. In *Catalytic Asymmetric Synthesis, 2nd Ed.*; Ojima, I. Ed.; Wiley-VCH: New York, 2000; Chapter 6A. (b) Katsuki, T.; Martin, V.S. *Org. React.* **1996**, *48*, 1-299. (c) Zhang, W.; Basak, A.; Kosugi, Y.; Hoshino, Y.; Yamamoto, H. *Angew. Chem. Int. Ed.* **2005**, *44*, 4389-4391. (d) Zhang, W.; Yamamoto, H. *J. Am. Chem. Soc.* **2007**, *129*, 286-287.

[104] For leading references see: (a) Jacobsen, E. N. in *Catalytic Asymmetric Synthesis*; Ojima, I. Ed.; VCH: New York, 1993; Chapter 4.2. (b) Katsuki, T. in *Catalytic Asymmetric Synthesis, 2nd Ed.*; Ojima, I. Ed.; Wiley-VCH: New York, 2000; Chapter 6B. (c) Nakata, K.; Takeda, T. Mihara, J.; Hamada, T.; Irie, R.; Katsuki, T. *Chem. Eur. J.* **2001**, *7*, 3776-3782. (d) Sawada, Y.; Matsumoto, K.; Kondo, S.; Watanabe, H, Ozawa, T.; Suzuki, K.; Saito, B.; Katsuki, T. *Angew. Chem. Int. Ed.* **2006**, *45*, 3478-3480.

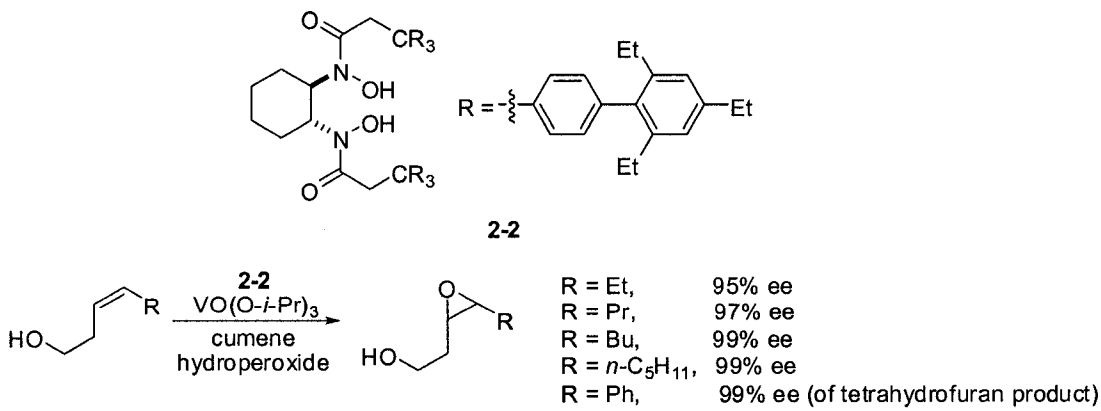



**Scheme 2.1**

Yamamoto et al. have also recently reported an effective method for asymmetric epoxidation of allylic alcohols (including *cis*-) using chiral vanadium complexes (Scheme 2.2).[103c] They then extended this methodology to homoallylic alcohols which are also very effective substrates with this system (Scheme 2.3).[103d]

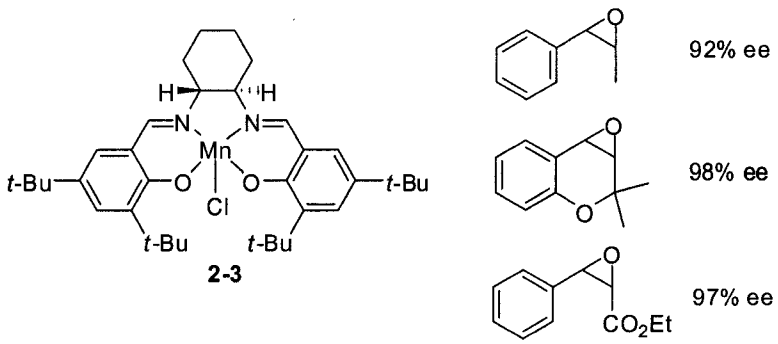



**Scheme 2.2**

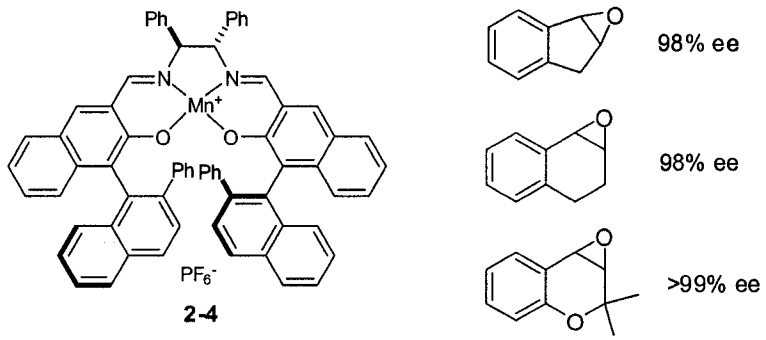



**Scheme 2.3**

A number of metal-ligand complexes in conjunction with stoichiometric oxidants have been used for the asymmetric epoxidation of unfunctionalized *cis*-olefins. Of these, salen-type complexes of Mn, Ru, and Ti have seen the most success and have been used to epoxidize a variety of conjugated *cis*-olefins (Schemes 2.4-2.7).[104] More recently, chiral bishydroxamic acid complexes of Mo have been reported for effective asymmetric epoxidation of non-alcohol containing conjugated *cis*-olefins (Scheme 2.8).[105]

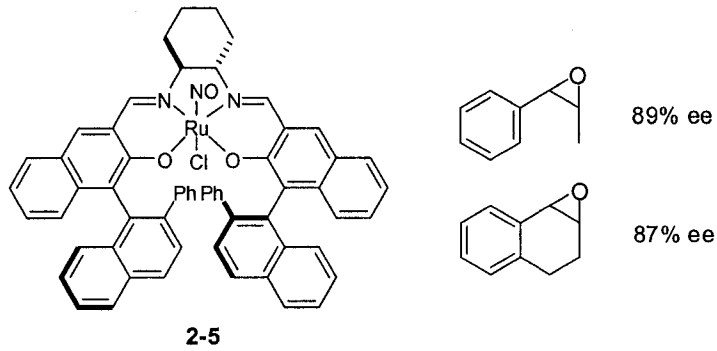



**Scheme 2.4**



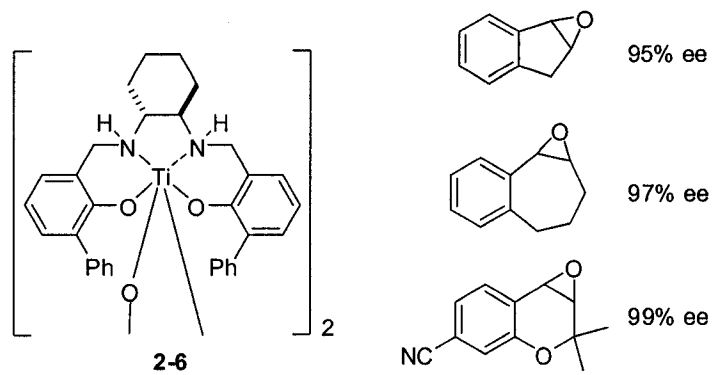

**Scheme 2.5**

[105] Barlan, A. U.; Basak, A.; Yamamoto, H. *Angew. Chem. Int. Ed.* **2006**, *45*, 5849-5852.



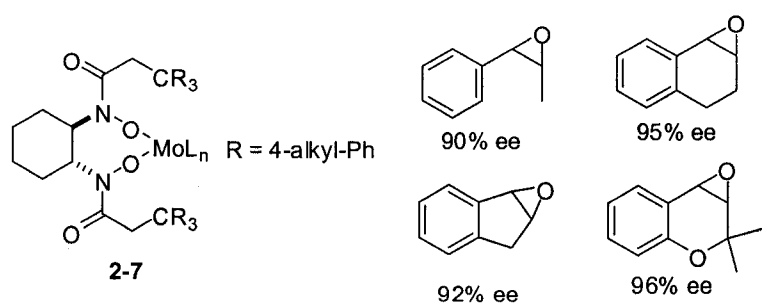

2-5

**Scheme 2.6**




2-6

**Scheme 2.7**

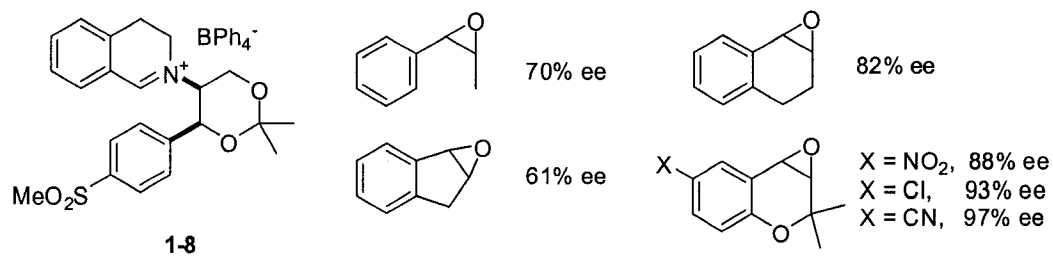



2-7

**Scheme 2.8**

Non-metal or organocatalytic asymmetric epoxidations have also been extensively studied. Much research has been done on the epoxidation of *cis*-olefins with chiral

oxaziridinium salts which are usually generated from iminium salts and peroxymonosulfate as discussed earlier. The highest ee's are generally obtained with 6-substituted-2,2-dimethylchromenes (Scheme 2.9).[106]



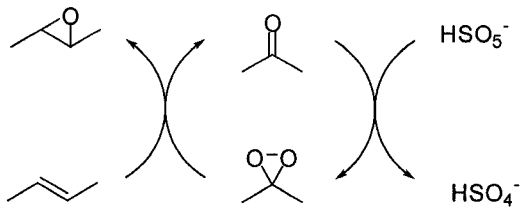

**Scheme 2.9**

Chiral dioxiranes are a class of organic oxidant that has been studied in great depth for the asymmetric epoxidation of olefins.[107] Dioxiranes are generated from ketones by the action of an oxidant such as Oxone (potassium peroxymonosulfate). Use of a chiral ketone, then, might be expected to give enantioenriched epoxide products, and after the epoxidation the ketone is regenerated making only a catalytic amount of ketone necessary in principle (Scheme 2.10).

---

[106] For leading references see: (a) Bullman Page, P. C.; Buckley, B. R.; Blackler, A. J. *Org. Lett.* **2004**, *6*, 1543-1546. (b) Bullman Page, P. C.; Buckley, B. R.; Heaney, H.; Blackler, A. J. *Org. Lett.* **2005**, *7*, 375-377.

[107] For leading reviews on chiral dioxirane-mediated asymmetric epoxidation see: (a) Frohn, M.; Shi, Y. *Synthesis* **2000**, 1979-2000. (b) Shi, Y. *Acc. Chem. Res.* **2004**, *37*, 488-496. (c) Yang, D. *Acc. Chem. Res.* **2004**, *37*, 497-505.




**Scheme 2.10**

The two extreme transition state geometries for epoxidation of olefins with dioxiranes are spiro and planar (Figure 2.1). In a spiro transition state the plane of the dioxirane is orthogonal to the plane of the olefin. In a planar transition state the plane of the dioxirane is in the same plane as the olefin. All other factors being equal, spiro transition states are favored over planar transition states due to secondary orbital overlap between the olefin $\pi^*$ and the dioxirane n orbitals.[108]

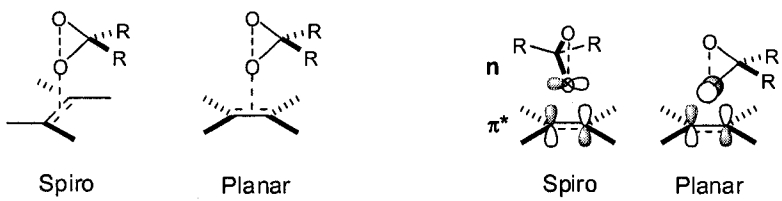



**Figure 2.1**

Many chiral ketones have been investigated, but ketone **1-5** in particular, reported by our group and synthesized in two steps from D-fructose, has been shown to give very

[108] For leading references on the mechanism of dioxirane epoxidations see: (a) Baumstark, A. L.; Vasquez, P. C. *J. Org. Chem.* **1988**, *53*, 3437-3439. (b) Houk, K. N.; Liu, J.; DeMello, N. C.; Condroski, K. R. *J. Am. Chem. Soc.* **1997**, *119*, 10147-10152.

high enantioselectivity for the epoxidation of *trans*- and trisubstituted olefins.[107,109] *cis*-Olefins, however, are ineffective substrates with this ketone (Figure 2.2).

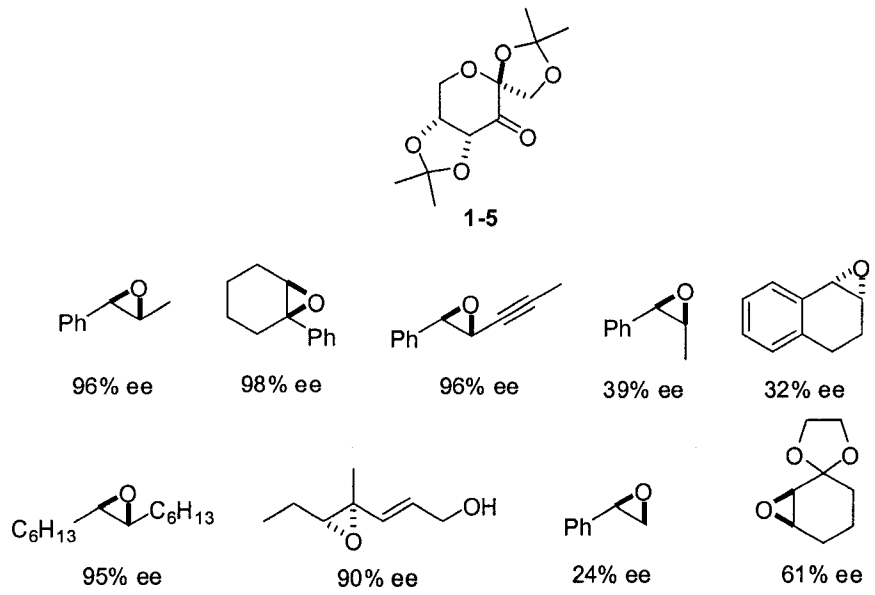



**Figure 2.2**

The results of epoxidation with ketone **1-5** can be rationalized using the transition state analysis below (Figure 2.3). Figure 2.3 shows the most plausible transition states that lead to the observed products. Transition states **B-G** are disfavored due to unfavorable steric interactions. That leaves spiro **A** and planar **H**, which give opposite enantiomers of epoxide, as the most likely contributors to the observed ratio of enantiomers. High ee is obtained because of the preference for spiro over planar transition states.

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[109] Wang, Z.-X.; Tu, Y.; Frohn, M.; Zhang, J.-R.; Shi, Y. *J. Am. Chem. Soc.* **1997**, *119*, 11224-11235.

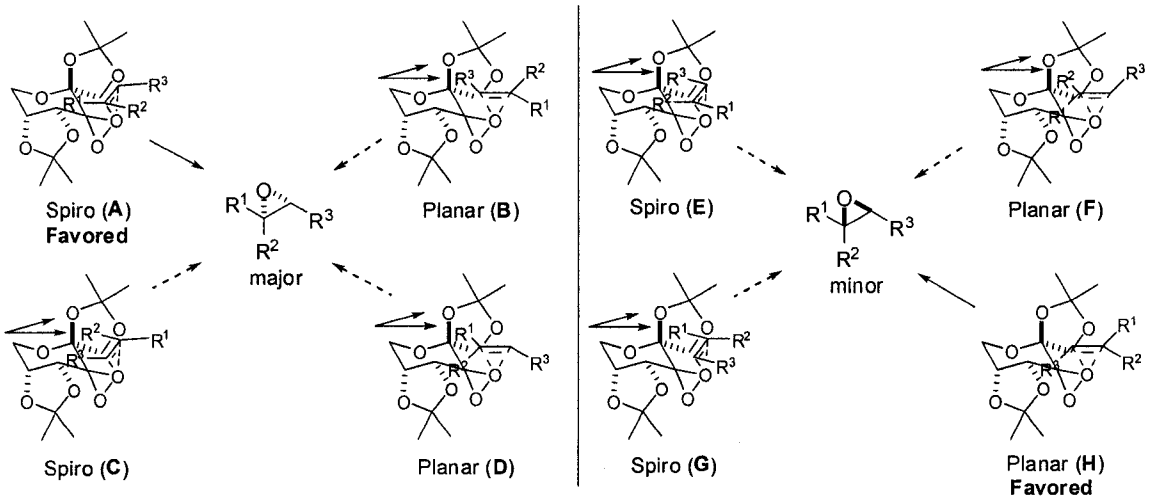



**Figure 2.3**

For *cis*-olefins, the most likely transition states with **1-5** are spiro **I** and spiro **J** (Figure 2.4). The low ee observed indicates that this ketone is not able to significantly differentiate between the two substituents on these olefins.

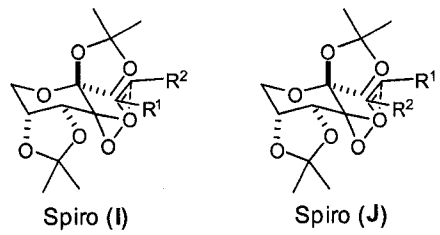



**Figure 2.4**

Ketone **2-8**, synthesized in six steps from D-glucose, was reported by our group in 2000, and it is effective for the epoxidation of a variety of conjugated *cis*-olefins (Figure 2.5).[110]

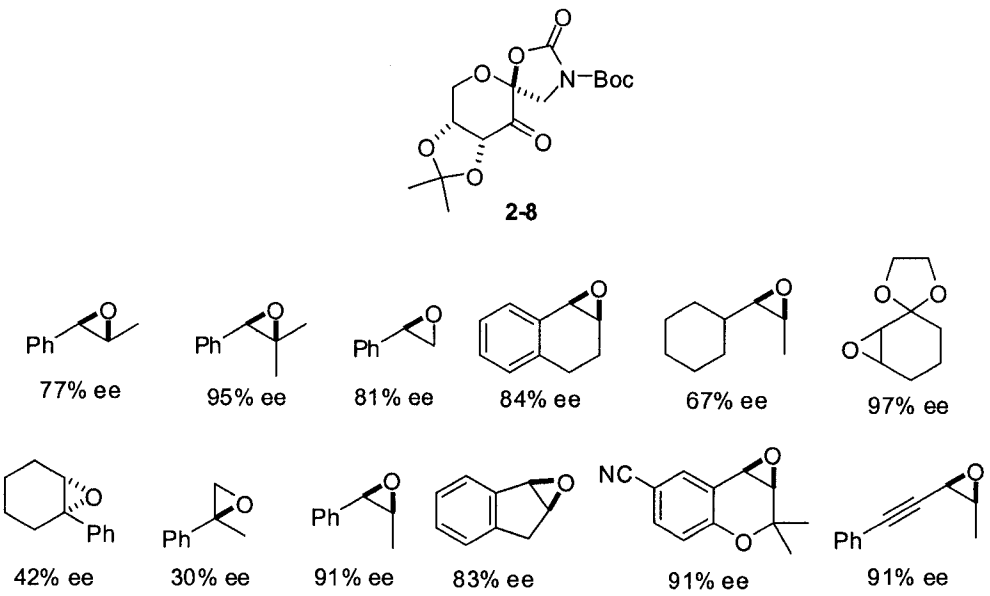



**Figure 2.5**

The two most likely transition states for *cis*-olefins in this case are spiro **K** and spiro **L** (Figure 2.6). The configuration of the major products indicates that spiro **K**, where the $R_\pi$ group is proximal to the oxazolidinone of the ketone, is favored, and the high ee for these substrates shows that ketone **2-8** is capable of significantly differentiating groups with $\pi$ systems from those without in the transition state.

---

[110] (a) Tian, H.; She, X.; Shu, L.; Yu, H.; Shi, Y. *J. Am. Chem. Soc.* **2000**, *122*, 11551-11552. (b) Tian, H.; She, X.; Yu, H.; Shu, L.; Shi, Y. *J. Org. Chem.* **2002**, *67*, 2435-2446.

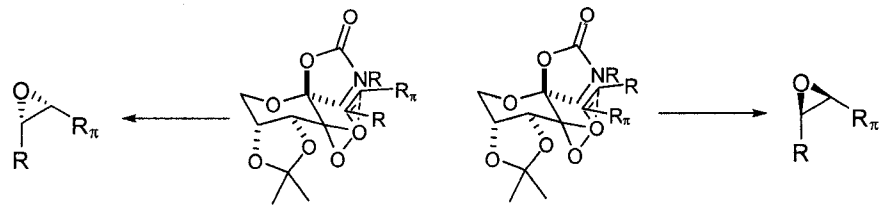



**Figure 2.6**

The reason for the apparent attraction between π systems and the oxazolidinone of the ketone is intriguing but unclear. One possibility is that there is an attractive π–π interaction or Van der Waals interaction between the $R_\pi$ group of the olefin and the oxazolidinone of the ketone. Another possibility is that there is an attraction between the π system on the olefin and a partial or transient positive charge on the oxazolidinone. It could also be that there is a repulsion between the electrons of the π system and the electrons of the fused ketal of the catalyst which would disfavor spiro transition state **L** (Figure 2.6).

In 2005 Singleton and coworkers proposed an additional factor that may contribute to the observed enantioselectivity with **2-8**. They discovered through calculations and kinetic isotope effects that conjugated olefins go through asynchronous transition states during epoxidation where the forming C-O bond α to the $R_\pi$ group is longer than the C-O bond β to the $R_\pi$ group (Figure 2.7).[111] The net result is that

[111] Singleton, D. A.; Wang, Z. *J. Am. Chem. Soc.* **2005**, *127*, 6679-6685.

asynchronicity disfavors transition state **N** relative to **M** due to the steric repulsion of an olefinic hydrogen with the oxygen of the oxazolidinone ring (Figure 2.7).

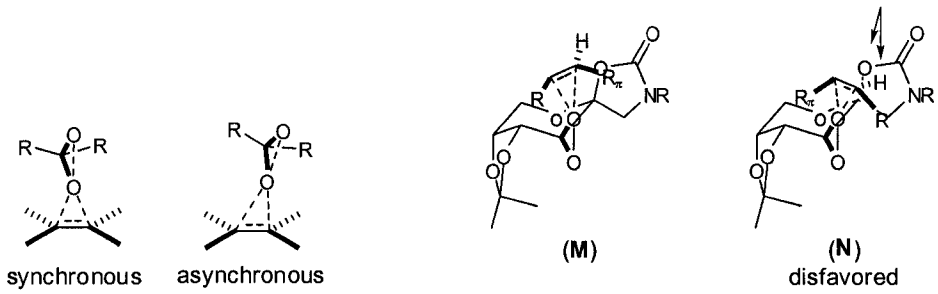
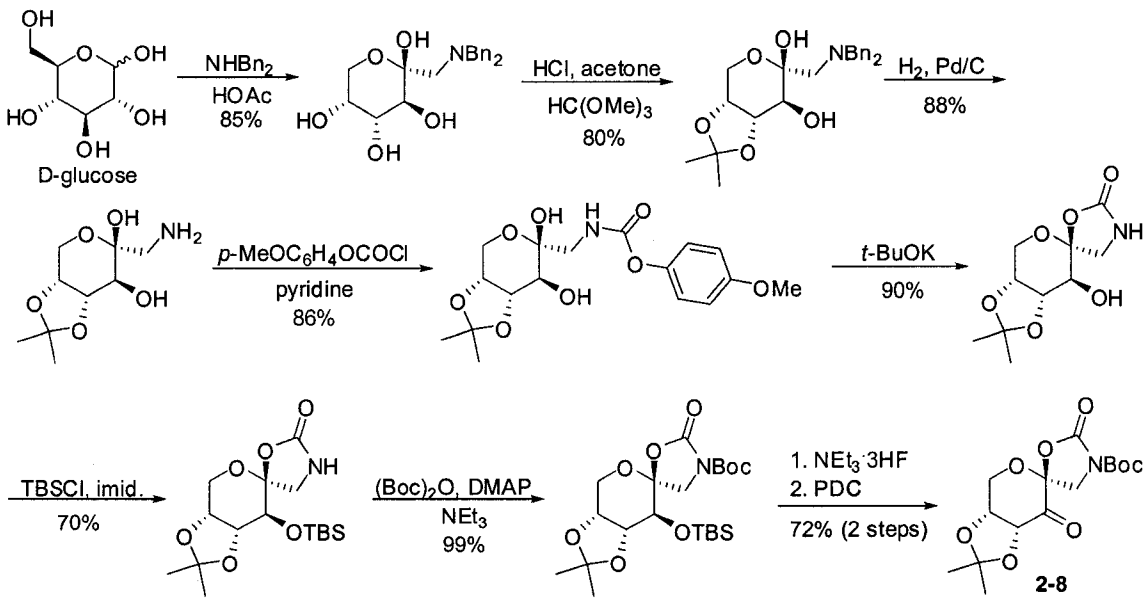



**Figure 2.7**

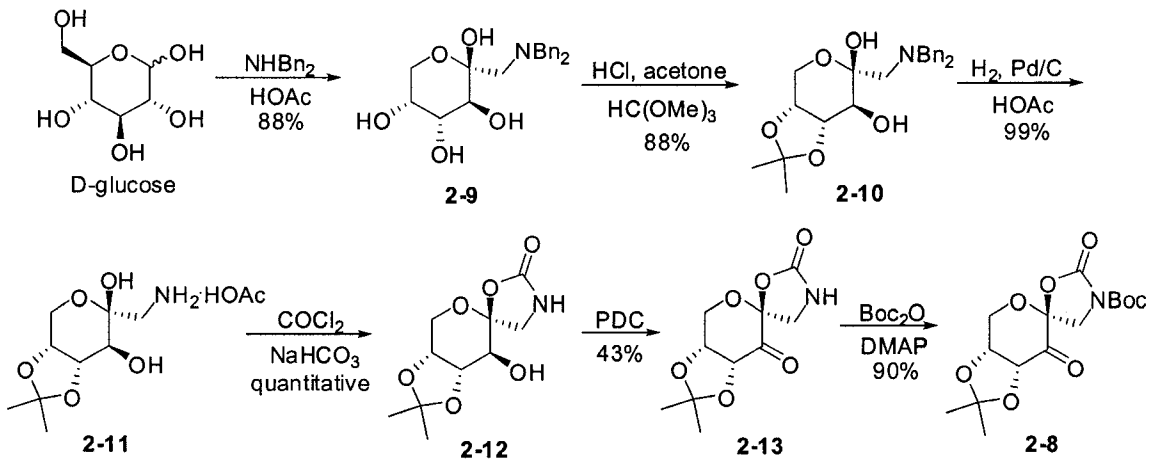
## 2.C. IMPROVED SYNTHESIS OF A KETONE CATALYST FOR THE ASYMMETRIC EPOXIDATION OF OLEFINS

Whatever the cause, the ability of ketone **2-8** to differentiate between π systems and aliphatic groups on *cis*-olefins makes it potentially very synthetically useful, and we undertook full exploration of the ketone's scope. In order to accomplish this, a large amount of ketone was necessary and therefore a simple, reliable, and large-scale synthesis was desired. The original synthesis of ketone **2-8** took nine steps and included a two-step carbamate installation, the installation and removal of a protecting group, and several chromatographic purifications (Scheme 2.11).[110]




**Scheme 2.11** Original synthesis of **2-8**

Along with Dr. Lianhe Shu, Dr. Yumei Shen, and Mr. David Goeddel, the synthesis of **2-8** was significantly shortened and improved (Scheme 2.12). To begin with, the yield of the reductive debenzylation of the amine was improved, and carbamate **2-12** was installed in one step with the use of a phosgene/$NaHCO_3$ cyclization. Oxidation of alcohol **2-12** to the ketone before Boc protection of the amine avoided use of the alcohol protecting group. This new route along with several procedural improvements allowed for the synthesis of **2-8** in six steps on a multi-gram scale in about a week.




**Scheme 2.12** Improved synthesis of **2-8**

## 2.D. CONCLUSION

Asymmetric epoxidation of unfunctionalized olefins is a very important and challenging problem. Chiral ketone-catalyzed epoxidation has been shown to be a viable method for the asymmetric epoxidation of a variety of *trans*-, trisubstituted, and conjugated *cis*-olefins. With an improved synthesis of ketone **2-8** further study to expand the scope of this reaction is now greatly facilitated.

## 2.E. EXPERIMENTAL

**1-Dibenzylamino-1-deoxy-D-fructose (2-9) (CPB-0140).**[112] To a suspension of D-glucose (63.2 g, 350 mmol) and $Bn_2NH$ (67.8 g, 350 mmol) in absolute ethanol (400 mL) was added HOAc (61.0 mL, 1050 mmol). Upon refluxing (the temperature of the oil bath was not allowed to rise above 90 °C) for 3 h, the reaction mixture was cooled to 0 °C and filtered with suction. The resulting filter cake was washed thoroughly with ethanol until white and was dried under vacuum to give 1-dibenzylamino-1-deoxy-D-fructose as a white solid (111 g, 88%).

**(2-10) (CPB-0118).** To a suspension of 1-dibenzylamino-1-deoxy-D-fructose (**2-9**) (26.9 g, 75.0 mmol) and trimethylorthoformate (35.0 mL, 320.0 mmol) in acetone (700 mL) at 0 °C under $N_2$ was added concentrated hydrochloric acid (9.0 mL, 108.0 mmol). Upon vigorous stirring at 0 °C for about 1.5 h, the reaction mixture was quenched with $NH_4OH$ (12 mL), filtered through a pad of silica gel with suction to remove $NH_4Cl$, and washed with additional acetone. The resulting solution was concentrated to about 50 mL, diluted with hexanes-EtOAc (3:2, 400 mL), and allowed to stand in the freezer for about 3 h to precipitate most of the unreacted starting material. The mixture was then filtered through a second pad of silica gel with suction to remove the remaining starting material dissolved in the solution, and the pad was washed with hexanes-EtOAc (3:2, 200 mL).

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[112] Hodge, J. E.; Fisher, B. E. *Methods Carbohydr. Chem.* **1963**, *2*, 99.

The filtrate was concentrated and dried under vacuum overnight to give compound **2-10** as a pale yellow oil (26.4 g, 88%).

**(2-11) (CPB-0143).** A solution of the above oil (20.0 g, ca. 50.0 mmol) in absolute ethanol (270 mL) was degassed and purged with $N_2$ three times. After AcOH (3.8 mL, 66 mmol) and 10% Pd/C (4.3 g) were added, the reaction mixture was degassed and filled with $H_2$ three times. Upon stirring at room temperature under $H_2$ to completion as judged by TLC (about 4.5 h), the reaction mixture was filtered through a short pad of Celite to remove the catalyst. The filtrate was then concentrated at room temperature and dried under vacuum to give compound **2-11** as a brown glassy solid (13.91 g, crude yield 99%), which was used directly in the next step without further purification (the product must be dried under vacuum to remove any remaining EtOH, which will otherwise consume phosgene in the next step).

**(2-12) (CPB-0208).** To a suspension of the above compound (5.7 g, 21.0 mmol) and $NaHCO_3$ (10.0 g, 120.0 mmol) in $CH_2Cl_2$ (100 mL) was added dropwise a solution of 20% phosgene in toluene (15.3 mL, 29.0 mmol) at 0 °C under $N_2$ with vigorous stirring over 30 min. The reaction mixture was stirred at room temperature to completion as judged by TLC (about 6 h). After the flask was opened to air, MeOH (33 mL) was added dropwise at room temperature with vigorous stirring over 30 min. After an additional 30 min. of stirring, the mixture was flushed through a short column of silica gel and washed with additional methanol until the brown liquid no longer came off the column (it is

important not to wash with too much methanol in order to prevent excess salts from passing through the silica gel). The resulting solution was concentrated and dried under vacuum to give the crude alcohol **2-12** as a light brown solid (5.56 g, crude quantitative yield) (the product must be dried under vacuum to remove any remaining MeOH, which will otherwise consume PDC in the next step).

**(2-13) (CPB-0208).** To a solution of the above alcohol (6.13 g, ca. 25.0 mmol) in dry $CH_2Cl_2$ (125 mL) were added 3 Å MS (unactivated) (23 g), PDC (14.1 g, 37.5 mmol), and acetic acid (4 drops). Upon stirring at room temperature to completion as judged by TLC (about 5 h), the reaction mixture was filtered through a short column of silica gel and washed with EtOAc-hexane (3:1). The filtrate was concentrated, dried under vacuum, and recrystallized using hexane-$CH_2Cl_2$ (3:1) to afford ketone **2-13** as a white solid (2.64 g, 43% overall yield from compound **2-11**): IR (film) 3378, 3319, 1759, 1731 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) 5.48 (brs, 1H), 4.82 (d, $J$ = 5.4 Hz, 1H), 4.64-4.53 (m, 2H), 4.32 (d, $J$ = 10.7 Hz, 1H), 4.23 (d, $J$ = 13.5 Hz, 1H), 3.38 (dd, $J$ = 10.7, 0.6 Hz, 1H), 1.46 (s, 3H), 1.42 (s, 3H); $^{13}C$ NMR (75 MHz, $CDCl_3$) 195.1, 155.9, 111.1, 102.8, 77.6, 75.6, 61.2, 45.4, 27.3, 26.2.

**(2-8) (CPB-0213).** To a solution of the above ketone **2-13** (3.28 g, 13.5 mmol) and $(Boc)_2O$ (3.53 g, 16.2 mmol) in freshly distilled THF (40 mL) was added DMAP (0.017 g, 0.14 mmol). Upon stirring under $N_2$ at room temperature until completion as judged by TLC (about 15-20 min), the reaction mixture was *immediately* quenched with oxalic acid

(0.012 g, 0.14 mmol), and *immediately* flushed through a prepacked column of silica gel, and washed with hexanes-EtOAc (dried over $K_2CO_3$) (1:1, 53 mL). The solution was concentrated, and the residue began to crystallize. Hot hexanes-ether (3:1, 33 mL) was added to the solid, and the resulting suspension was stirred for 10 min without further heating. The suspension was then filtered with suction and washed with cold hexanes-ether (3:1, 24 mL). Ketone **2-8** was obtained as a white solid (4.16 g, 90% yield): IR (film) 3446 (hydrate), 1823, 1756, 1731 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) 4.79 (d, $J$ = 5.6 Hz, 1H), 4.61 (dd, $J$ = 5.6, 1.8 Hz, 1H), 4.56 (d, $J$ = 11.6 Hz, 1H), 4.51 (dd, $J$ = 13.6, 1.8 Hz, 1H), 4.23 (d, $J$ = 13.6 Hz, 1H), 3.71 (d, $J$ = 11.6 Hz, 1H), 1.53 (s, 9H), 1.45 (s, 3H), 1.41 (s, 3H); $^{13}C$ NMR (75 MHz, $CDCl_3$) 194.7, 148.8, 148.4, 111.3, 98.9, 85.0, 77.4, 75.5, 61.3, 48.5, 28.1, 27.3, 26.1.

# CHAPTER THREE

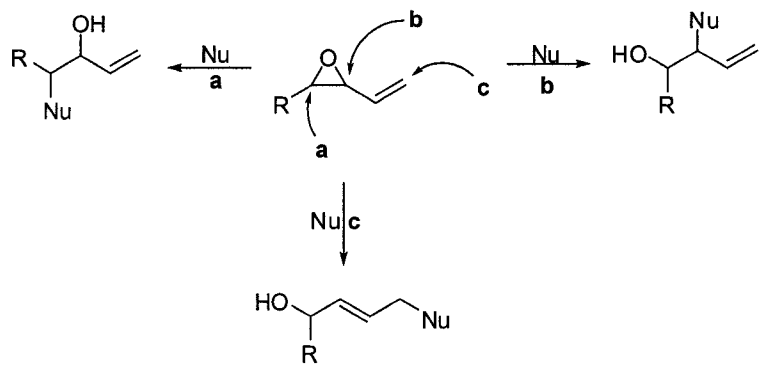
# CATALYTIC ASYMMETRIC REGIO- AND ENANTIOSELECTIVE EPOXIDATION OF CONJUGATED DIENES: SYNTHESIS OF OPTICALLY ACTIVE VINYL *CIS*-EPOXIDES

## 3.A. INTRODUCTION AND BACKGROUND

Enantioenriched vinyl epoxides are very valuable synthetic intermediates capable of undergoing a variety of useful synthetic transformations.[113] They are most often utilized in ring-opening reactions with a variety of nucleophiles. Three possible pathways for reaction with nucleophiles can be envisioned (Scheme 3.1). Path **a** involves nucleophilic attack at the homoallylic site to give an allylic alcohol product, but is only observed in rare instances where steric bulk at the other sites prohibits attack at those positions. Nucleophilic addition to the allylic position (path **b**) is common with "hard"

[113] Oloffson, B.; Somfai, P. in *Aziridines and Epoxides in Organic Synthesis*; Yudin, A. K. Ed.; Wiley-VCH: Weinheim, 2006; Chapter 9.

nucleophiles and gives homoallylic alcohol products. Path **b** is generally favored over path **a** due to the alkenyl group's steric smallness and its ability to stabilize developing positive charge in the transition state. "Soft" nucleophiles usually add to the olefin in an $S_N2'$ fashion (path **c**) to give allylic alcohols as products.




**Scheme 3.1**

Several methods for the direct $S_N2$-type addition of various nucleophiles to vinyl epoxides have been developed. Vinyl epoxides undergo attack at the allylic position by heteroatom nucleophiles such as ammonium hydroxide or by primary amines in the presence of LiOTf (Scheme 3.2).[114,115] Alcohols will also open vinyl epoxides in this fashion in the presence of Lewis acids such as $BF_3{\cdot}OEt_2$ (Scheme 3.2).[116] Nicolaou et al.

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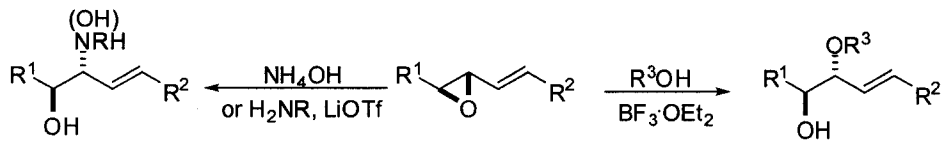
[114] (a) Olofsson, B.; Somfai, P. *J. Org. Chem.* **2002**, *67*, 8574-8583. (b) Lindström, U. M.; Olofsson, B.; Somfai, P. *Tetrahedron Lett.* **1999**, *40*, 9273-9276. (c) Lindström, U. M.; Franckowiak, R.; Pinault, N.; Somfai, P. *Tetrahedron Lett.* **1997**, *38*, 2027-2030. (d) Lindström, U. M.; Somfai, P. *Synthesis*, **1998**, 109-117.

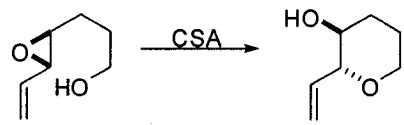
[115] Tang, M.; Pyne, S. G. *J. Org. Chem.* **2003**, *68*, 7818-7824.

[116] Prestat, G.; Baylon, C.; Heck, M.-P.; Mioskowski, C. *Tetrahedron Lett.* **2000**, *41*, 3829-3831.

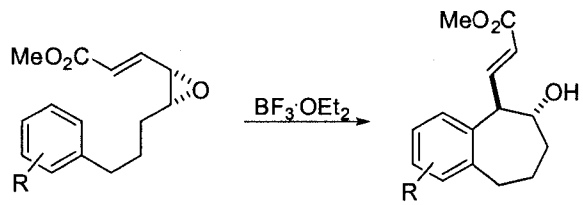
have developed a very useful method for tetrahydropyran synthesis via acid-catalyzed intramolecular opening of hydroxy vinyl epoxides.[117] The preferred mode of attack at the allylic position is taken advantage of in order to activate 6-endo epoxide opening over the typically favored 5-exo opening (Scheme 3.3). This principle has also been used for 7-endo Friedel-Crafts type cyclizations (Scheme 3.4).[118]




**Scheme 3.2**




**Scheme 3.3**

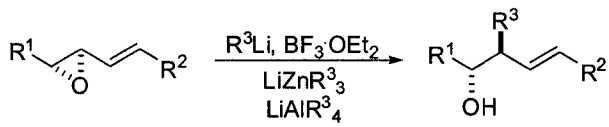



**Scheme 3.4**

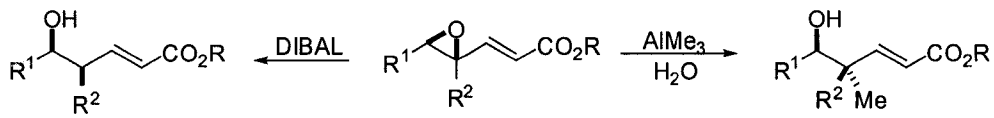
[117] (a) Nicolaou, K. C.; Prasad, C. V. C.; Somers, P. K.; Hwang, C.-K. *J. Am. Chem. Soc.* **1989**, *111*, 5330-5334. (b) Matsukura, H.; Morimoto, M.; Koshino, H.; Nakata, T. *Tetrahedron Lett.* **1997**, *38*, 5545-5548.

[118] Nagumo, S.; Miyoshi, I.; Akita, H.; Kawahara, N. *Tetrahedron Lett.* **2002**, *43*, 2223-2226.

Addition of organometallic nucleophiles to the allylic postion of vinyl epoxides has also been well-studied. Alkyl lithium reagents in the presence of $BF_3{\cdot}OEt_2$ as well as trialkylzincates and tetraalkylaluminates are effective nucleophiles (Scheme 3.5).[119,120] DIBAL and trimethyl aluminum also add a hydride or methyl group respectively to the allylic position of epoxy vinyl esters (Scheme 3.6).[121,122] Finally, allylstannanes in the presence of $BF_3{\cdot}OEt_2$ react with vinyl epoxides primarily at the allylic position to give homoallylic alcohols as products (Scheme 3.7).[123]




**Scheme 3.5**




**Scheme 3.6**

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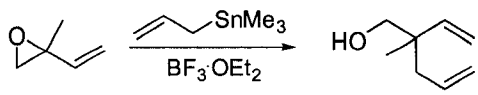
[119] Alexakis, A.; Vranken, E.; Mangeney, P.; Chemla, F. *J. Chem. Soc., Perkin Trans. 1* **2000**, 3352-3353.

[120] Equey, O.; Vranken, E.; Alexakis, A. *Eur. J. Org. Chem.* **2004**, 2151-2159.

[121] (a) Nicolaou, K. C.; Uenishi, J. *J. Chem. Soc., Chem. Commun.* **1982**, 1292-1293. (b) Nicolaou, K. C.; Daines, R. A.; Uenishi, J.; Li, W. S.; Papahatjis, D. P.; Chakraborty, T. K. *J. Am. Chem. Soc.* **1988**, *110*, 4672-4685.

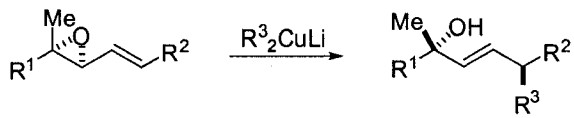
[122] (a) Miyashita, M.; Hoshino, M.; Yoshikoshi, A. *J. Org. Chem.* **1991**, *56*, 6483-6485. (b) Ishibashi, N.; Miyazawa, M.; Miyashita, M. *Tetrahedron Lett.* **1998**, *39*, 3775-3778. (c) Miyazawa, M.; Matsuoka, E.; Sasaki, S.; Oonuma, S.; Maruyama, K.; Miyashita, M. *Chem. Lett.* **1998**, 109-110.

[123] Naruta, Y.; Maruyama, K. *Chem. Lett.* **1987**, 963-966.

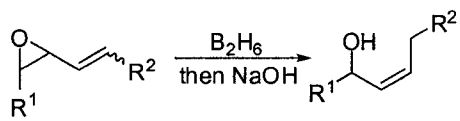



**Scheme 3.7**

A variety of nucleophiles add in $S_N2'$ fashion directly to vinyl epoxides. In this respect, organocopper reagents, including but not limited to dialkylcuprates, have garnered the most attention.[124] Typically, the nucleophiles attack *anti* to the epoxide, and selectivity for 1,4-addition over 1,2-addition is high (Scheme 3.8).[125] Conjugate hydride reduction can be accomplished with diborane followed by basic hydrolysis to give exclusively the *cis*-olefin regardless of the olefin geometry (Scheme 3.9).[126]




**Scheme 3.8**




**Scheme 3.9**

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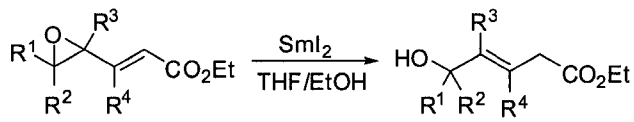
[124] Marshall, J. A.; *Chem. Rev.* **1989**, *89*, 1503-1511.

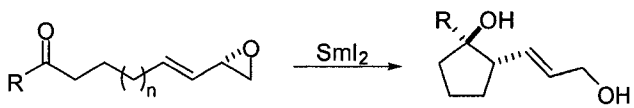
[125] (a) Marshall, J. A.; Trometer, J. D.; Blough, B. E.; Crute, T. D. *J. Org. Chem.* **1988**, *53*, 4274-4282. (b) Marshall, J. A.; Trometer, J. D.; Cleary, D. G. *Tetrahedron* **1989**, *45*, 391-402. (c) Marshall, J. A.; Trometer, J. D. *Tetrahedron Lett.* **1987**, *28*, 4985-4988.

[126] Zaidlewicz, M.; Uzarewicz, A.; Sarnowski, R. *Synthesis* **1979**, 62-64.

Formal conjugate hydride addition to a range of epoxy vinyl esters has also been reported using $SmI_2$ (Scheme 3.10).[127] $SmI_2$-mediated ketyl-olefin coupling has also been employed in intramolecular cyclization reactions which tend to occur through the $S_N2'$ pathway (Scheme 3.11).[128]




**Scheme 3.10**




**Scheme 3.11**

Vinyl epoxides have also been used extensively as allylic electrophiles in π-allyl chemistry. In this reaction manifold a metal, usually Pd(0), adds conjugate to the vinyl epoxide resulting in an $S_N2'$ opening of the epoxide to give an alkoxy π -allyl metal complex. Nucleophiles can then add to either of two positions in the complex to regenerate Pd(0) and give the 1,2- or 1,4-addition product (Scheme 3.12).

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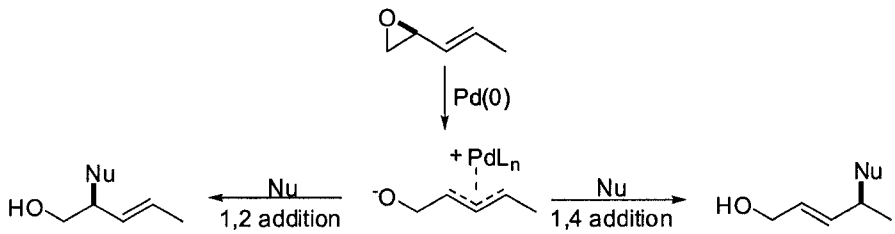
[127] Molander, G. A.; La Belle, B. E.; Hahn, G. *J. Org.Chem.* **1986**, *51*, 5259-5264.

[128] Molander, G. A.; Shakya, S. R. *J. Org. Chem.* **1996**, *61*, 5885-5894.




**Scheme 3.12**

Usually, nucleophiles add in 1,4-fashion to π-allyl complexes of vinyl epoxides, but several strategies have been developed for 1,2-addition. Subjecting the alkoxy π-allyl Pd complex to a $CO_2$ atmosphere results in formation of the cyclic carbonate in a formal *cis*-dihydroxylation reaction (Scheme 3.13).[129] Likewise, alkoxy π-allyl Pd complexes formed in the presence of boronic acids and isocyanates give cyclic boronic esters and oxazolidinones in formal dihydroxylations and aminohydroxylations respectively (Scheme 3.13).[130,131] Formal 1,2-hydride addition can also be accomplished via a slightly different mechanism when the π-allyl Pd complex is formed in the presence of formic acid (Scheme 3.14).[132] Finally, a Rh-catalyzed 1,2-addition of alcohols and aromatic amines to vinyl epoxides has been developed (Scheme 3.15).[133] In this case nucleophiles add with net inversion of stereochemistry. A π-allyl complex mechanism is postulated although definitive proof of the role Rh plays awaits further study.

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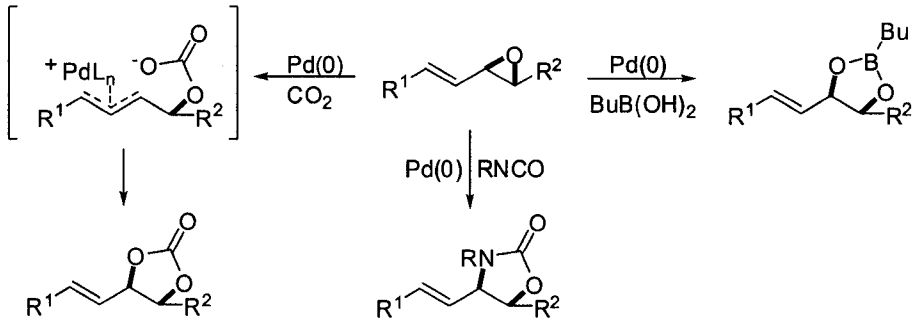
[129] (a) Trost, B. M.; Angle, S. R. *J. Am. Chem. Soc.* **1985**, *107*, 6123-6124. (b) Fujinami, T.; Suzuki, T.; Kamiya, M.; Fukuzawa, S.-i.; Sakai, S. *Chem. Lett.* **1985**, 199-200.

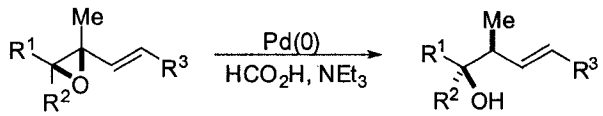
[130] Hirai, A.; Yu, X.-Q. Tonooka, T.; Miyashita, M. **2003**, 2482-2483.

[131] Trost, B. M.; Sudhakar, A. R. *J. Am. Chem. Soc.* **1987**, *109*, 3792-3794.

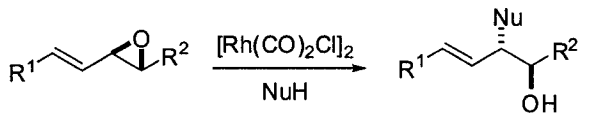
[132] (a) Tsuji, J.; Mandai, T. *Synthesis* **1996**, 1-24. (b) Oshima, M.; Yamazaki, H.; Shimizu, I.; Nisar, M.; Tsuji, J. *J. Am Chem. Soc.* **1989**, *111*, 6280-6287.



**Scheme 3.13**



**Scheme 3.14**



**Scheme 3.15**

A range of nucleophiles has been used in Pd-catalyzed 1,4-additions to vinyl epoxides, and they most commonly add with net retention of stereochemistry due to double inversion.[134,135] One particularly useful application of this methodology is in

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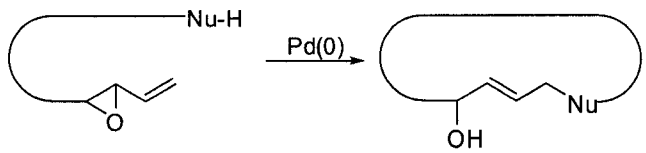
[133] Fagnou, K.; Lautens, M. *Org. Lett.* **2000**, *2*, 2319-2321.

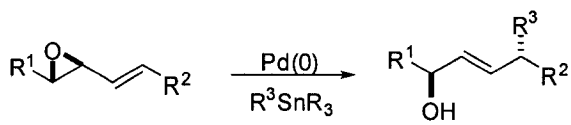
[134] Godleski, S. A. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Semmelhack, M. F. Eds.; Pergamon Press: Oxford, 1991; Vol. 4, Chapter 3.3.

[135] (a) Trost, B. M.; Molander, G. A. *J. Am. Chem. Soc.* **1981**, *103*, 5969-5972. (b) Elliot, M. R.; Dhimane, A.-L.; Malacria, M. *Tetrahedron Lett.* **1998**, *39*, 8849-8852. (c) Pettersson-Fasth, H.; Riesinger, S. W.; Bäckvall, J.-E. *J. Org. Chem.* **1995**, *60*, 6091-6096.

macrocyclization reactions. An array of medium to large-sized rings has been formed including several in syntheses of natural products (Scheme 3.16).[136] Vinyl epoxide-derived π-allyl Pd complexes have also been used for cross coupling with vinyl and aryl stannanes to give formal 1,4-addition products with net inversion of stereochemistry (Scheme 3.17).[137]




**Scheme 3.16**




**Scheme 3.17**

Vinyl epoxides also undergo several rearrangements.[138] Lewis acid catalysis has been employed to give ketones and aldehydes via 1,2-shifts depending on the migratory ability of the groups involved (Scheme 3.18).[139] There are also reports of tandem epoxide rearrangement/aldehyde addition by organometallic reagents such as allyl indium

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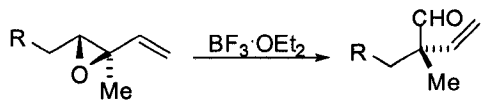
[136] Trost, B. M. *Angew. Chem. Int. Ed.* **1989**, *28*, 1173-1192.

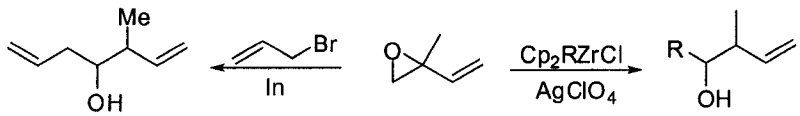
[137] Echavarren, A. M.; Tueting, D. R.; Stille, J. K. *J. Am. Chem. Soc.* **1988**, *110*, 4039-4041.

[138] Hudlicky, T.; Reed, J. W. in *Comprehensive Organic Synthesis* Trost, B. M.; Fleming, I. Eds.; Pergamon: Oxford, 1991, Vol. 5, 899-970.

and alkyl zirconium reagents (Scheme 3.19).[140,141] Treatment of silicon-substituted vinyl epoxides with Pd(0) gives α-trialkylsilyl-β,γ-unsaturated aldehydes with complete transfer of chirality (Scheme 3.20).[142] Finally, vinyl epoxides also undergo various thermal rearrangements.[138] For example, dihydrofurans can be obtained by thermal rearrangement of vinyl epoxides as in Scheme 3.21.[143]




**Scheme 3.18**




**Scheme 3.19**

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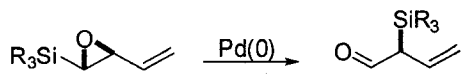
[139] (a) Jung, M. E.; D'Amico, D. C. *J. Am. Chem. Soc.* **1995**, *117*, 7379-7388. (b) Jung, M. E.; Anderson, K. L. *Tetrahedron Lett.* **1997**, *38*, 2605-2608.

[140] Oh, B. K.; Cha, J. H.; Cho, Y. S.; Choi, K. I.; Koh, H. Y.; Chang, M. H.; Pae, A. N. *Tetrahedron Lett.* **2003**, *44*, 2911-2913.

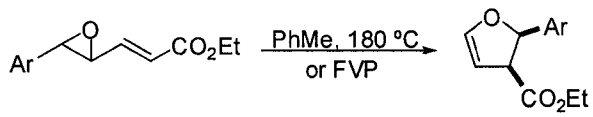
[141] Wipf, P.; Xu, W. *J. Org. Chem.* **1993**, *58*, 825-826.

[142] Le Bideau, F.; Gilloir, G.; Nilsson, Y.; Aubert, C.; Malacria, M. *Tetrahedron Lett.* **1996**, *52*, 7487-7510.

[143] Aldous, D. J.; Dalençon, A. J.; Steel, P. G. *Org. Lett.* **2002**, *4*, 1159-1162.



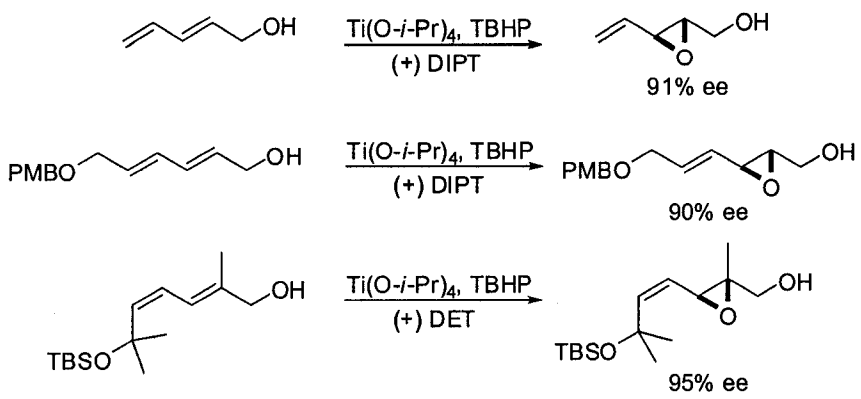

**Scheme 3.20**




**Scheme 3.21**

Because optically active vinyl epoxides are so useful, much effort has been directed toward their synthesis. Of the methods for their synthesis, asymmetric epoxidation of conjugated dienes is among the most convenient since there are many straightforward techniques for accessing these compounds. The Sharpless epoxidation has been used to epoxidize many conjugated allylic dienols with high enantioselectivity, but stoichiometric conditions are sometimes necessary to overcome problems of low reactivity (Scheme 3.22).[113,114a,144]

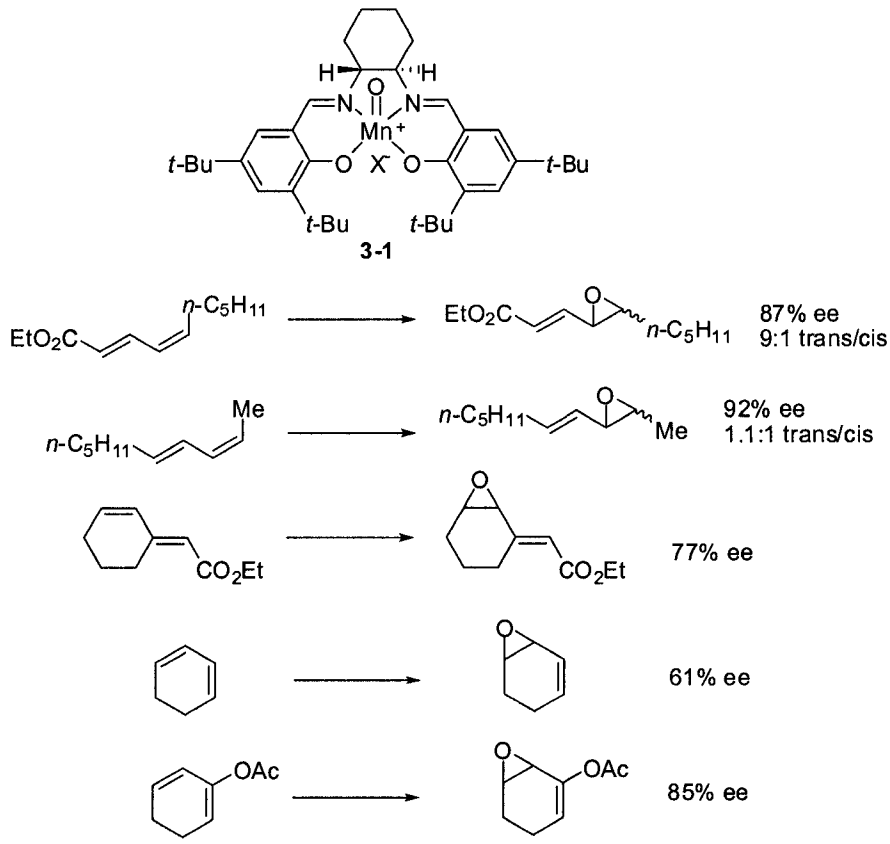
[144] (a) Wershofen, S.; Scharf, H.-D. *Synthesis* **1988**, 854-858. (b) Martín, D. D.; Marcos, I. S.; Basabe, P.; Romero, R. E.; Moro, R. F.; Lumeras, W.; Rodríguez, L.; Urones, J. G. *Synthesis* **2001**, 1013-1022.



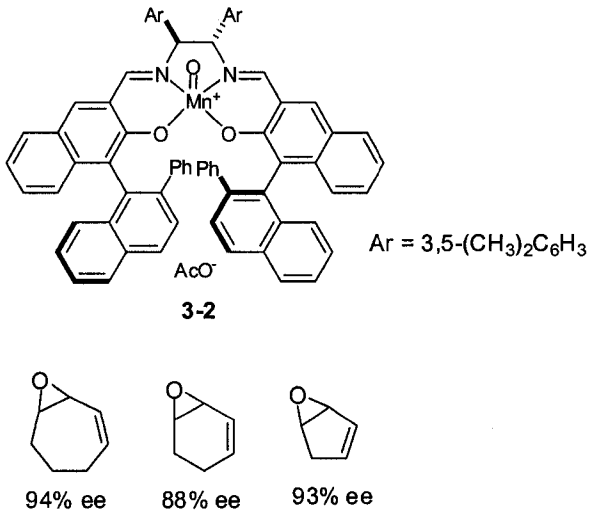

**Scheme 3.22**

Chiral Mn-salen complexes have also been applied to the epoxidation of conjugated dienes.[145] The most effective substrates are *cis/trans* or *cis*/E dienes, and epoxidation proceeds predominantly at the *cis*-olefin with high enantioselectivity (Scheme 3.23, 3.24). For acyclic dienes, vinyl *trans*-epoxides are obtained as the major products. This observation has been attributed to isomerization of a radical intermediate during oxygen transfer (Scheme 3.25).

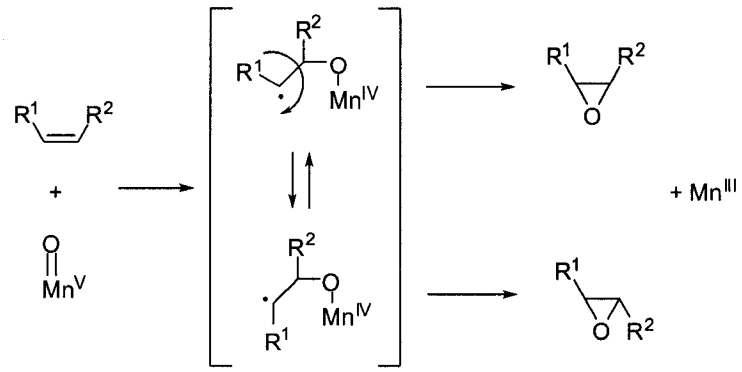
[145] (a) Lee, N. H.; Jacobsen, E. N. *Tetrahedron Lett.* **1991**, *32*, 6533-6536. (b) Chang, S.; Lee, N. H.; Jacobsen, E. N. *J. Org. Chem.* **1993**, *58*, 6939-6941. (c) Chang, S.; Heid, R. M.; Jacobsen, E. N. *Tetrahedron Lett.* **1994**, *35*, 669-672. (d) Zhang, W.; Lee, N. H.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1994**, *116*, 425-426. (e) Hamada, T.; Irie, R.; Katsuki, T. *Synlett* **1994**, 479-481. (f) Mikame, D.; Hamada, T.; Irie, R.; Katsuki, T. *Synlett* **1995**, 827-828. (g) Hentemann, M. F.; Fuchs, P. L. *Tetrahedron Lett.* **1997**, *38*, 5615-5618. (h) Rasmussen, K. G.; Thomsen, D. S.; Jørgensen, K. A. *J. Chem. Soc., Perkin Trans. 1* **1995**, 2009-2017.




**Scheme 3.23**




**Scheme 3.24**



**Scheme 3.25**

Ketone **1-5** has also been applied to the asymmetric epoxidation of conjugated dienes and is very effective for the synthesis of optically active vinyl *trans*- and trisubstituted epoxides.[146] In epoxidations with this catalyst, the more electron-rich olefin of the diene system is epoxidized preferentially (Scheme 3.26).

Despite all these efforts, an efficient synthesis of optically active vinyl *cis*-epoxides is still an unsolved problem and is highly desirable. As discussed before, ketone **2-8** is effective for the epoxidation of a variety of conjugated *cis*-olefins.[147] We then began an intensive study on the epoxidation of conjugated dienes with ketone **2-8** with the goal of expanding the ketone's scope to these olefins as well as furthering our understanding of this ketone's origin of enantioselectivity for conjugated *cis*-olefins.

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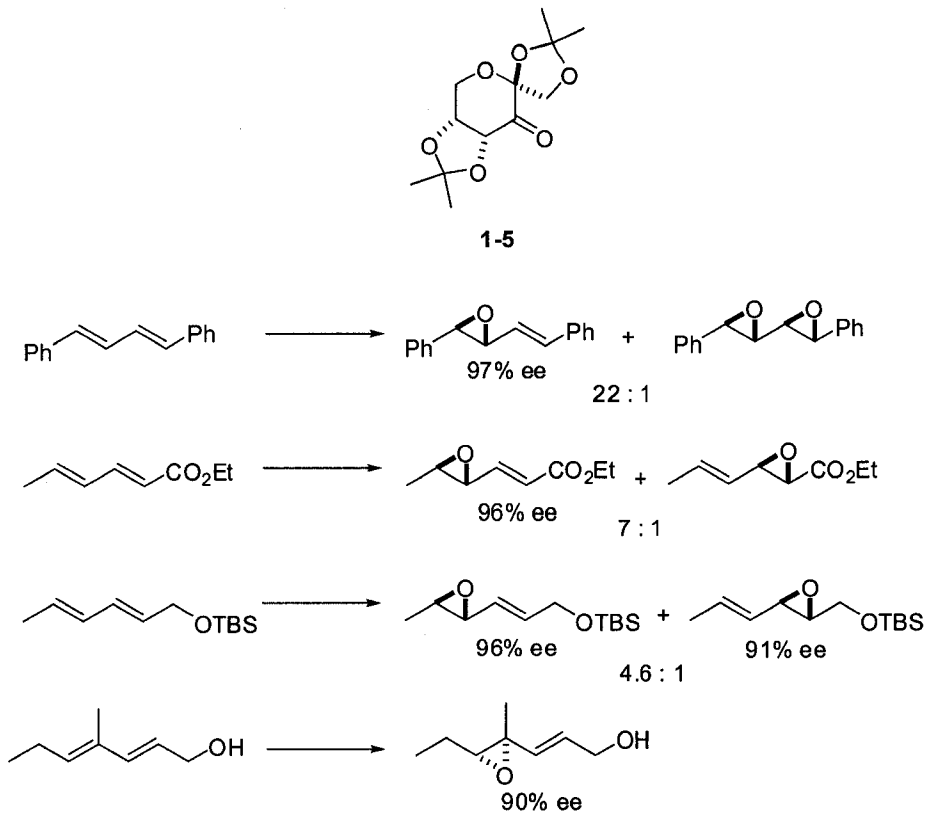
[146] Frohn, M.; Dalkiewicz, M.; Tu, Y.; Wang, Z.-X.; Shi, Y. *J. Org. Chem.* **1998**, *63*, 2948-2953.

[147] (a) Tian, H.; She, X.; Shu, L.; Yu, H.; Shi, Y. *J. Am. Chem. Soc.* **2000**, *122*, 11551-11552. (b) Tian, H.; She, X.; Yu, H.; Shu, L.; Shi, Y. *J. Org. Chem.* **2002**, *67*, 2435-2446.



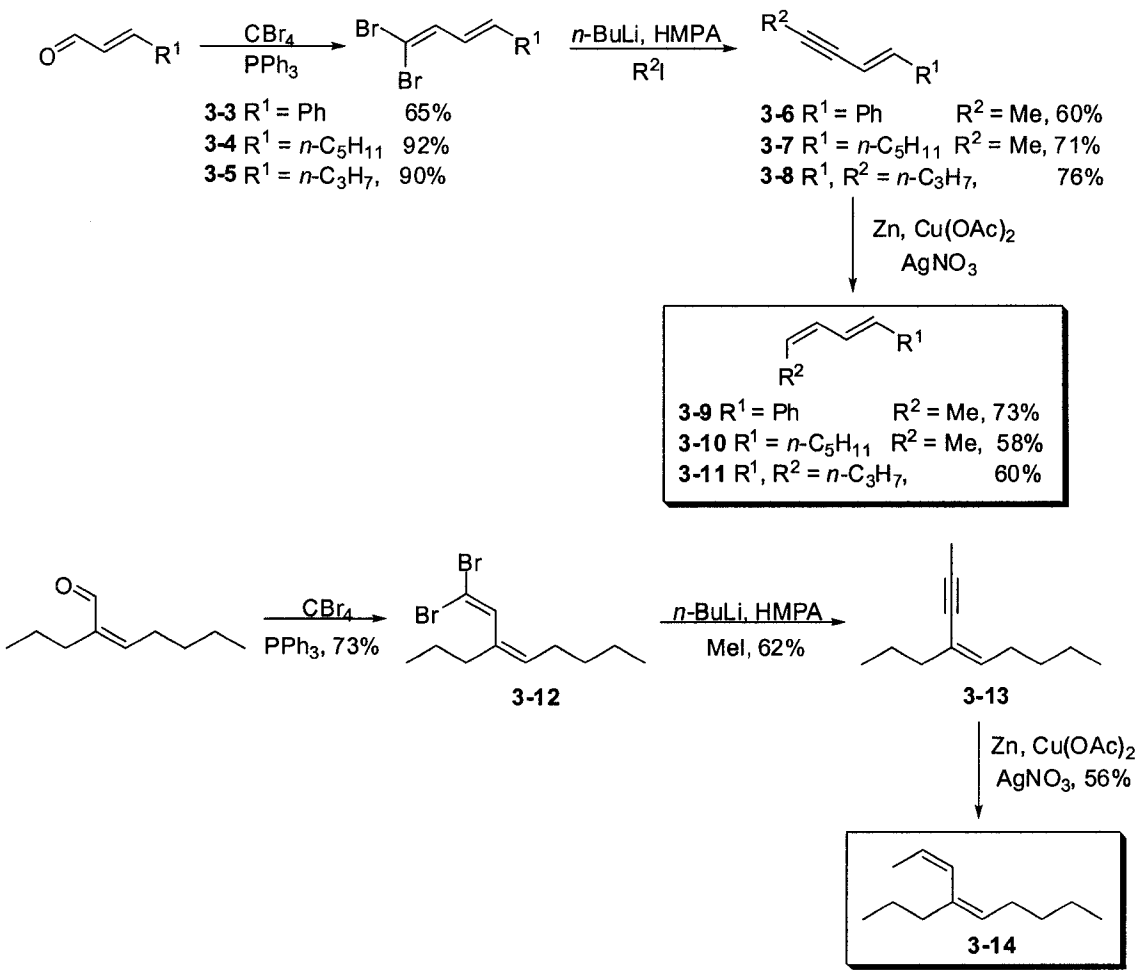

**Scheme 3.26**

## 3.B. RESULTS AND DISCUSSION

### 3.B.i. Substrate Synthesis

Very few of the conjugated dienes used for this study were commercially available so a variety of conjugated dienes with varying geometries and hydrophobic and electronic properties were synthesized. **3-9** – **3-11** were synthesized starting with

dibromoolefination of the requisite unsaturated aldehydes.[148] Reaction of the dibromoolefins with *n*-BuLi followed by trapping of the alkynyl anions with alkyl iodides gave enynes **3-6 – 3-8**.[148] The conjugated enynes were then stereospecifically reduced to the *cis/trans* dienes with activated Zn.[149] **3-14** was also made using this same sequence of reactions (Scheme 3.27).

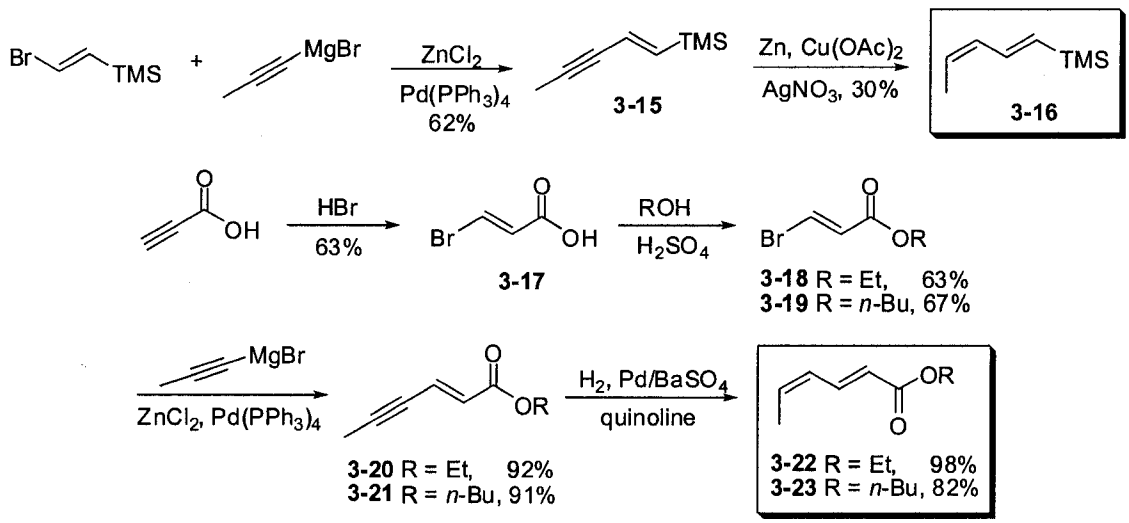



**Scheme 3.27**

[148] Wang, Z.-X.; Cao, G.-A.; Shi, Y. *J. Org. Chem.* **1999**, *64*, 7646-7650.

[149] Boland, W.; Schroer, N.; Sieler, C. *Helv. Chim. Acta*, **1987**, 1025-1040.

**3-16** was synthesized by activated Zn reduction of **3-15** which was accessed from a Pd-catalyzed coupling of propynyl magnesium bromide and *trans*-bromovinyltrimethylsilane.[150] Treatment of propiolic acid with HBr gave **3-17** which was esterified and coupled with propynyl magnesium bromide as before.[151] Enynes **3-20** and **3-21** were then partially hydrogenated giving conjugated diene esters **3-22** and **3-23**. Diene **3-26** was synthesized in an analogous manner except that Sonogashira coupling was used instead of Negishi-type coupling to make enyne **3-25** (Scheme 3.28).[152]

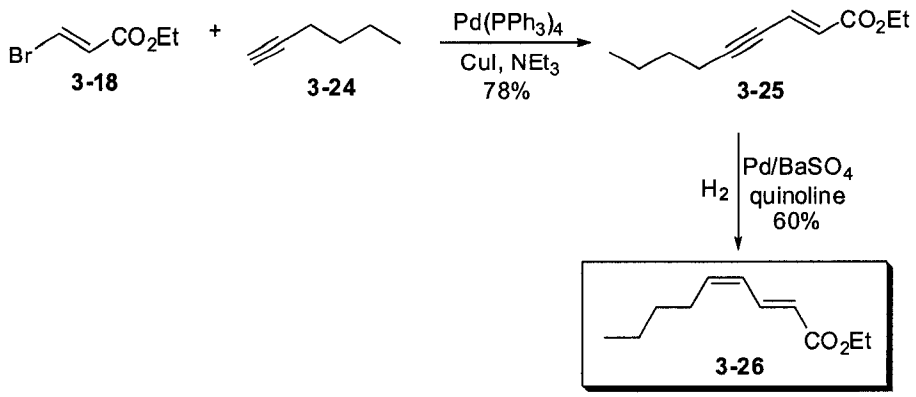



**Scheme 3.28**

[150] Bellina, F.; Biagetti, M.; Carpita, A.; Rossi, R. *Tetrahedron*, **2001**, *57*, 2857-2870.

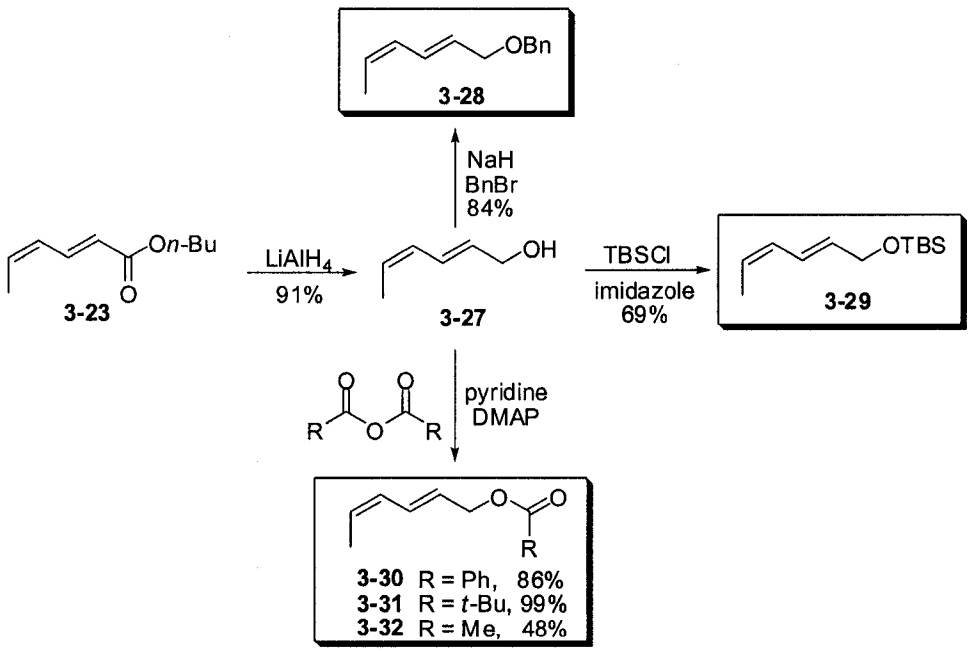
[151] Just, G.; Oullet, R. *Can. J. Chem.* **1976**, *54*, 2925-2934.

[152] Bellina, F.; Carpita, A.; Corradi, C.; Rossi, R. *Synth. Commun.* **1996**, *26*, 3297-3316.



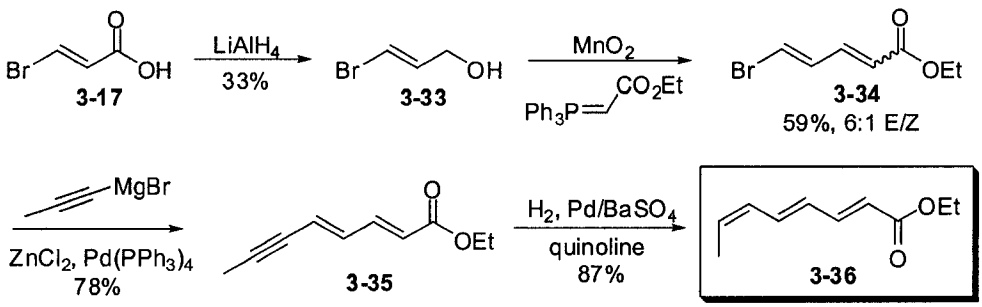

**Scheme 3.28 (continued)**

Diene ester **3-23** was reduced with $LiAlH_4$ to give alcohol **3-27**. This alcohol was then protected as the benzyl and TBS ethers, and benzoyl, pivaloyl, and acetyl esters to give **3-28 – 3-32** (Scheme 3.29).




**Scheme 3.29**

Conjugated triene **3-36** was synthesized starting with $LiAlH_4$ reduction of **3-17** to give alcohol **3-33** which was elaborated to ester **3-34** via *in situ* oxidation/Wittig reaction.[153] Coupling with propynyl magnesium bromide and partial reduction as before gave **3-36** in good yield (Scheme 3.30).




**Scheme 3.30**

Sonogashira coupling of iodide **3-37**[154] with 4-pentyn-1-ol gave enyne **3-38** which was reduced to *cis/trans* diene **3-39** with activated Zn.[155] Likewise, Sonogashira coupling of **3-40**[156] with 6-heptynoic acid gave **3-41** which was reduced to hydroxy acid **3-42**. This was then subjected to Yamaguchi macrolactonization conditions to efficiently

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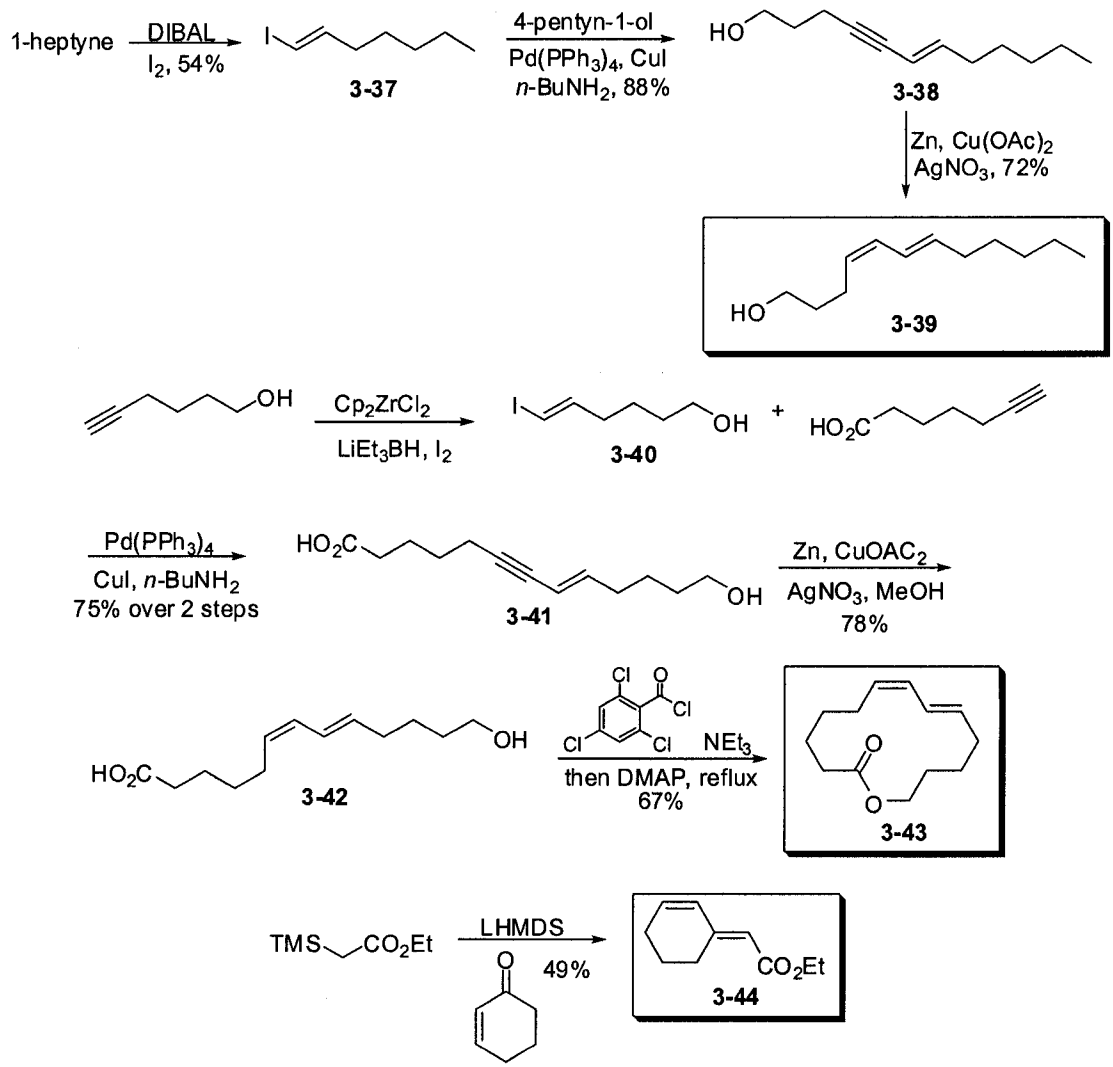
[153] Wei, X,; Taylor, R. J. K.; *J. Org. Chem.* **2000**, *65*, 616-620.

[154] Zweifel, G.; Whitney, C. C. *J. Am. Chem. Soc.* **1967**, *89*, 2753-2754.

[155] Ratovelomana, V.; Linstrumelle, G. *Synth. Commun.* **1981**, *11*, 917-923.

[156] Lipshutz, B. H.; Keil, R.; Ellsworth, E. L. *Tetrahedron Lett.* **1990**, *31*, 7257-7260.

give macrocyclic diene **3-43**.[157] **3-44** was obtained through Peterson olefination of 2-cyclohexen-1-one with ethyltrimethylsilyl acetate (Scheme 3.31).[158]




**Scheme 3.31**

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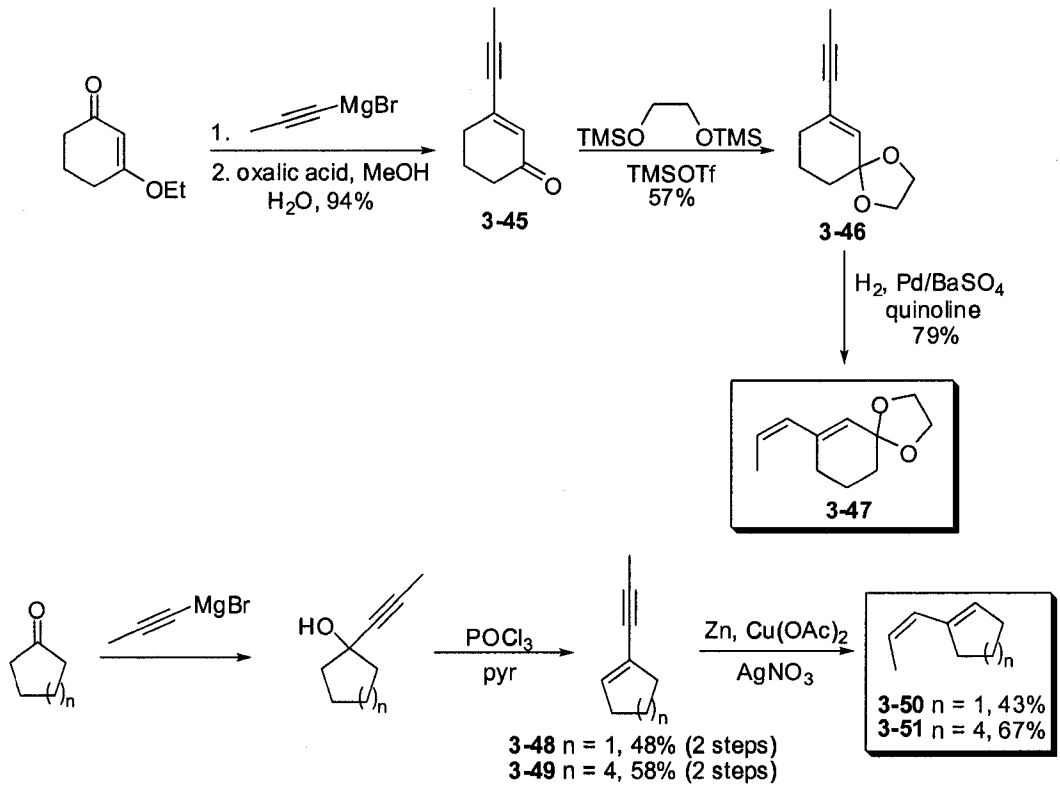
[157] Inanaga, J.; Hirata, K.; Saeki, H.; Katsuki, T.; Yamaguchi, M. *Bull. Chem. Soc. Jpn.* **1979**, *52*, 1989-1993.

[158] Shimoji, K.; Taguchi, H.; Oshima, K.; Yamamoto, H.; Nozaki, H. *J. Am. Chem. Soc.* **1974**, *96*, 1620-1621.

Synthesis of diene ketal **3-47** began with addition of propynyl magnesium bromide to 3-ethoxy-2-cyclohexen-1-one followed by acid catalyzed dehydration/hydrolysis to give ketone **3-45**.[159] The ketone was then masked as the ketal and the alkyne was partially hydrogenated to give diene **3-47**.[160] Dienes **3-50,** and **3-51** were synthesized through a similar sequence starting with addition of propynyl magnesium bromide to the requisite cyclic ketones. Dehydration with $POCl_3$/pyridine gave the conjugated enynes which were reduced with activated Zn to give dienes **3-50** and **3-51** (Scheme 3.32).

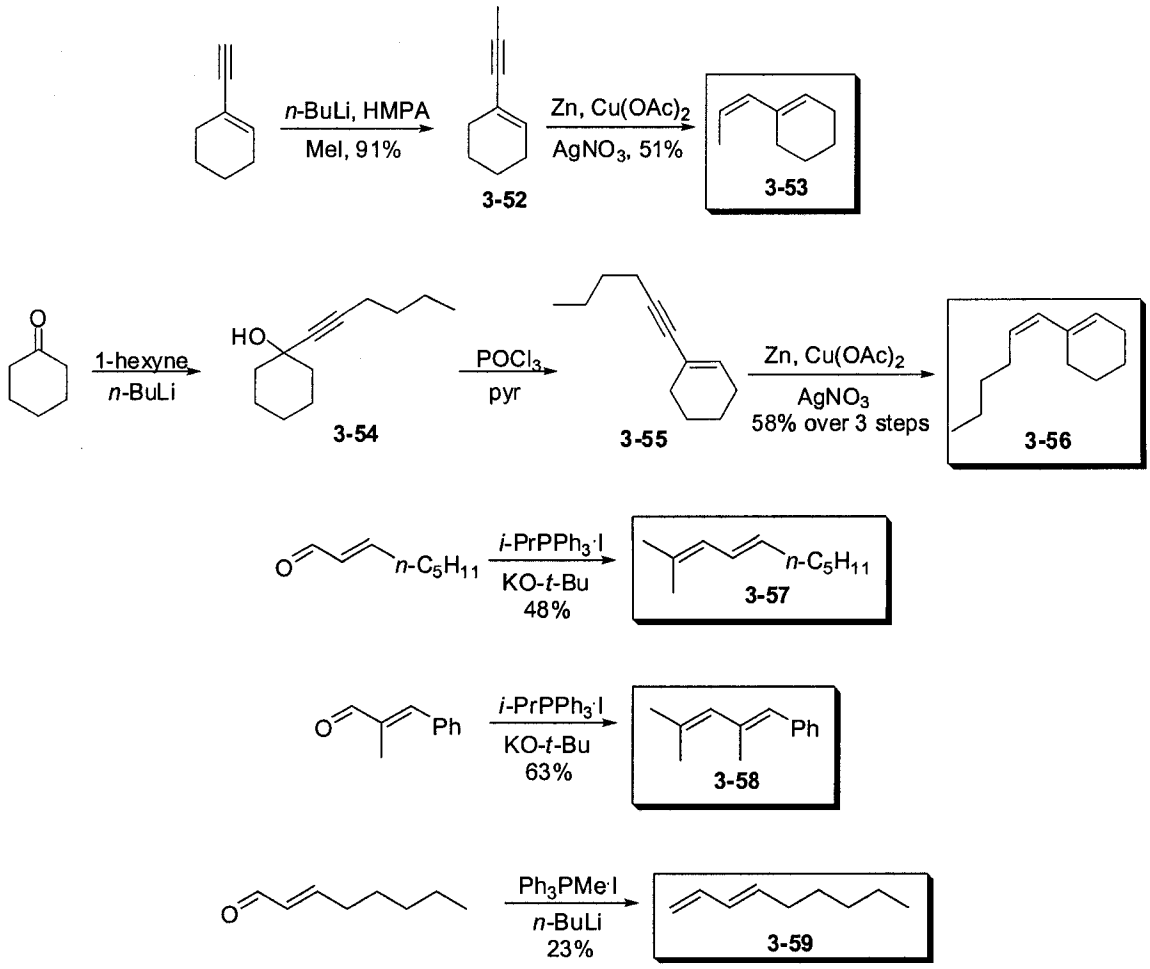



**Scheme 3.32**

[159] Rathjen, H.-J.; Margaretha, P.; Wolff, S.; Agosta, W.C. *J. Am. Chem. Soc.* **1991**, *113*, 3904-3909.

[160] Tsunoda, T.; Suzuki, M.; Noyori, R. *Tetrahedron Lett.* **1980**, *21*, 1357-1358.

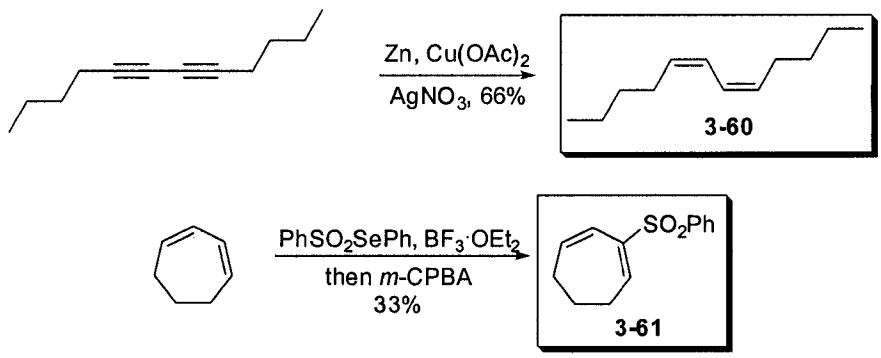
Diene **3-53** was made by methylation of commercially available ethynyl cyclohexene followed by activated Zn reduction.[161] **3-56** was made analogously to **3-50** and **3-51** except that hexynyl lithium was used for the addition to the ketone rather than the alkynyl Grignard reagent. **3-57** – **3-59** were synthesized via simple Wittig reactions of the requisite aldehydes with the requisite phosphonium salts (Scheme 3.33).




**Scheme 3.33**

[161] Wang, Z.-X.; Cao, G.-A.; Shi, Y. *J. Org. Chem.* **1999**, *64*, 7646-7650.

**3-60** was accessed through activated Zn reduction of commercially available 5,7-dodecadiyne, and **3-61** was made by one-pot selenosulfonation/oxidation of 1,3-cycloheptadiene (Scheme 3.34).[162]




**Scheme 3.34**

### 3.B.ii. Asymmetric Epoxidation of Conjugated Dienes

While study on the epoxidation of conjugated dienes was just getting underway, several *N*-aryl-substituted ketones synthesized in four steps from D-glucose were developed in our labs, and some of these were incorporated into the study (Figure 3.1) (Note: **3-66** was developed later than **3-62** -**3-65** and so only the latest substrates studied were screened with it). Study began with screening different ketone catalysts for epoxidation of **3-3**. To our delight, high enantiomeric excess and conversion was

[162] Bäckvall, J.-E.; Nájera, C; Yus, M. *Tetrahedron Lett.* **1988**, *29*, 1445-1448.

obtained with all ketones screened. For this substrate, ketones **3-62** and **3-63** gave the best results (Table 3.1).

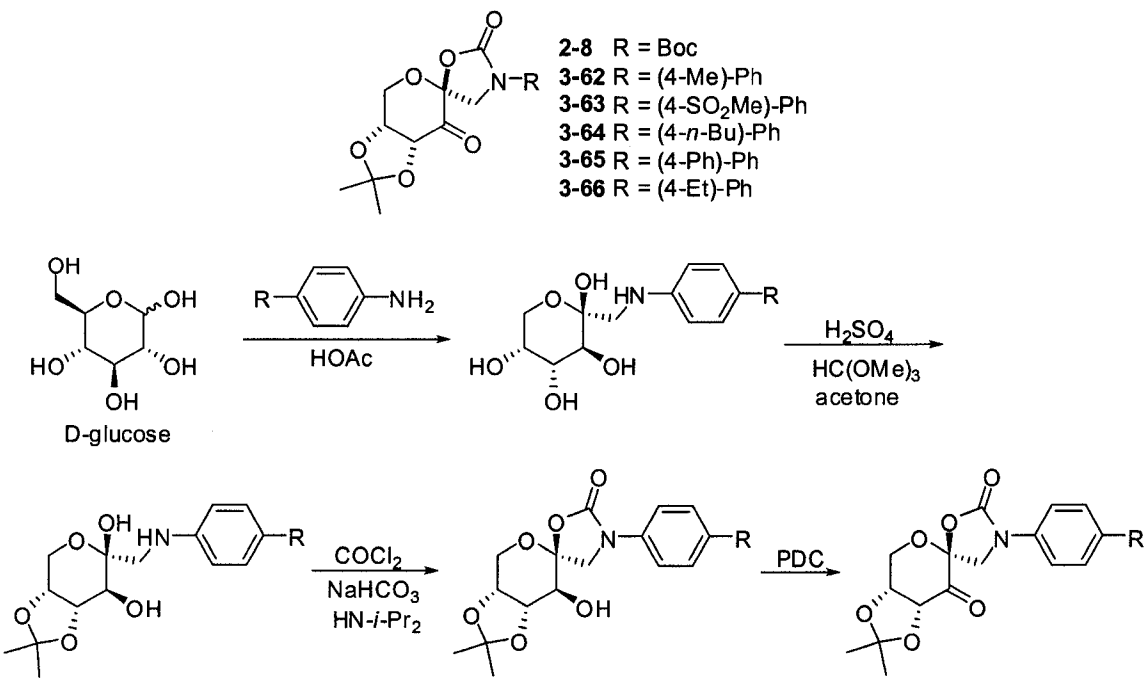
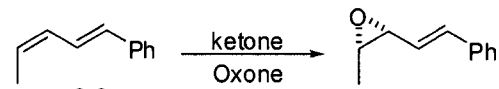



**Figure 3.1** Synthesis of *N*-aryl ketones

**Table 3.1.**[a]




**3-3**

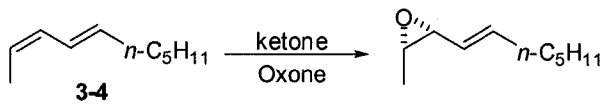
| Entry | ketone [R] | conv. (%)[b] | ee (%)[c] |
|---|---|---|---|
| 1 | **2-8** [Boc] | 84[d,e,f] | 81 |
| 2 | **3-62** [(4-Me)-Ph] | >95 | 85 |
| 3 | **3-63** [(4-$SO_2$Me)-Ph] | >95 | 86 |
| 4 | **3-64** [(4-*n*-Bu)-Ph] | 65[d] | 80 |
| 5 | **3-65** [(4-Ph)-Ph] | 85 | 73 |

[a] Unless stated otherwise, reactions were carried out with diene (1.0 eq.), catalyst (0.10 eq.), Oxone (1.6 eq.), and $K_2CO_3$ (6.7 eq.) in DME/DMM (3:1, v/v) and buffer (0.1 M $K_2CO_3$-AcOH in 4 x $10^{-4}$ M aq. EDTA, pH 9.3) (1.5:1, v/v). Oxone and $K_2CO_3$ were added separately and simultaneously over 4 h at -10 °C. [b] The conversion was determined by $^1$H NMR of the crude reaction mixture. [c]

Enantioselectivity was determined by chiral HPLC (Chiralcel OJ column). [d] 0.15 eq. catalyst used. [e] 3.8 eq. $K_2CO_3$ and buffer (0.1 M $K_2CO_3$-AcOH in 4 x $10^{-4}$ M aq. EDTA, pH 8.0) were used. [f] A 3:1 mixture of *cis*-monoepoxide and bisepoxide was obtained.

Initial epoxidation of **3-4** with a variety of ketones showed that ketone **3-64** gave highest ee (Table 3.2). From these and other preliminary results we weren't able to definitively identify a single "best" ketone, so we screened every substrate with this same assortment of ketones. The results in Tables 3.3 and 3.4 represent the optimized results of epoxidation with the best ketone for each substrate.

**Table 3.2.**[a]




**3-4**

| Entry | ketone [R] | ee (%)[b] |
|---|---|---|
| 1 | **2-8** [Boc] | 77[c,d] |
| 2 | **3-62** [(4-Me)-Ph] | 78[e] |
| 3 | **3-63** [(4-$SO_2$Me)-Ph] | 84[f] |
| 4 | **3-64** [(4-*n*-Bu)-Ph] | 88[d] |
| 5 | **3-65** [(4-Ph)-Ph] | 81[g] |

[a] Unless stated otherwise, reactions were carried out with diene (1.0 eq.), catalyst (0.10-0.30 eq.), Oxone (1.6 eq.), and $K_2CO_3$ (6.7 eq.) in DME/DMM (3:1, v/v) and buffer (0.1 M $K_2CO_3$-AcOH in 4 x $10^{-4}$ M aq. EDTA, pH 9.3) (1.5:1, v/v). Oxone and $K_2CO_3$ were added separately and simultaneously over 4 h at -10 °C. [b] Enantioselectivity was determined by chiral GC (Chiraldex B-DM column) of the crude reaction mixture. [c] 3.8 eq. $K_2CO_3$ and buffer (0.1 M $K_2CO_3$-AcOH in 4 x $10^{-4}$ M aq. EDTA, pH 8.0) were used. [d] 0.15 eq. catalyst used. [e] 0.30 eq. catalyst used. [f] 0.10 eq. catalyst used. [g] 0.25 eq. catalyst used.

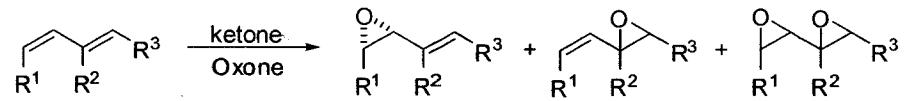
As Tables 3.3 and 3.4 show, a variety of conjugated dienes were effective substrates under the epoxidation conditions. The reactions were generally clean as judged by $^1$H NMR of the crude reaction mixtures, and the reactions were stereospecific in that *cis*-alkenes yielded only *cis*-epoxides with no isomerization observed. The low isolated yield compared with the conversion in some cases was due to the high sensitivity of vinyl epoxides toward flash column chromatography using silica gel.

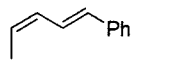
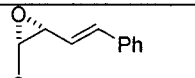
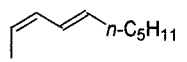
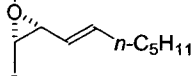
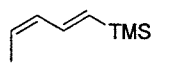
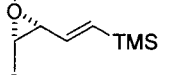
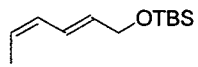
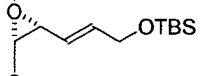
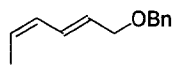
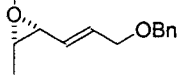
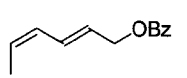
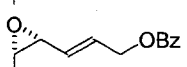
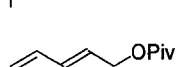
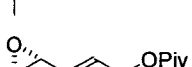
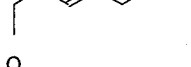
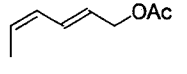
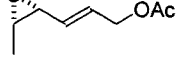
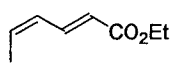
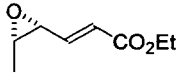
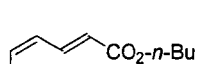
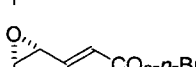
Several trends in reactivity were observed. Regioselectivity for the epoxidation is dependent on the type of diene. For *cis/trans*-dienes it was found that the *cis*-olefins are epoxidized preferentially with high regioselectivity (Table 3.3, entries 1-13, 15). Epoxides derived from *trans*-olefin epoxidation were observed in only a few cases (Table 3.3, entries 11, 15). This was not unexpected, as dioxiranes are known to epoxidize *cis*-olefins ca. 7-9 times faster than *trans*-olefins.[163] Conjugated triene **3-36** (Table 3.3, entry 14) also proved to be an effective substrate.

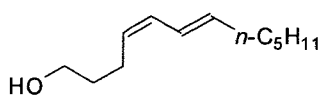
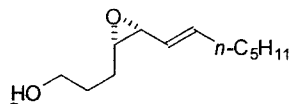
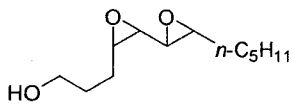
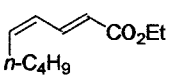
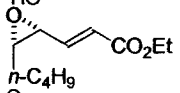
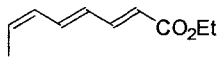
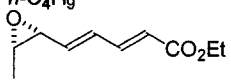
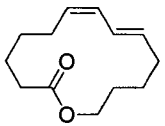
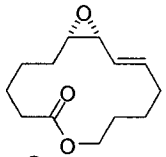
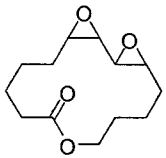
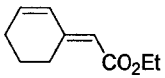
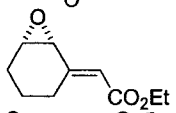
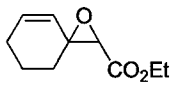
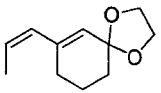
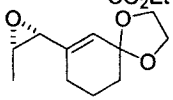
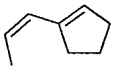
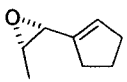
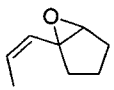
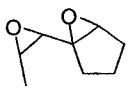
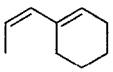
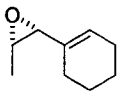
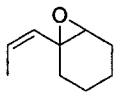
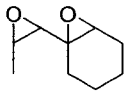
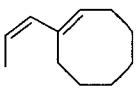
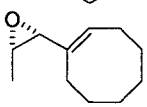
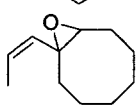
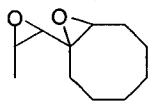
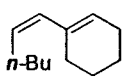
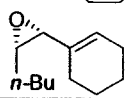
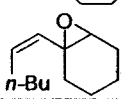
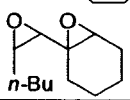
As expected, *cis*/trisubstituted dienes show competition for epoxidation between the two olefins (Table 3.3, entries 16-21; Table 3.4, entry 6). The degree of trisubstituted olefin epoxidation varies depending on the steric and electronic properties of the diene. If the trisubstituted olefin is deactivated electronically and/or sterically, *cis*-olefin epoxidation is favored (Table 3.3, entries 16, 17; Table 3.4, entry 7). Dienes

[163] Baumstark, A. L.; Vasquez, P. C. *J. Org. Chem.* **1988**, *53*, 3437-3439.

**Table 3.3.** Asymmetric Epoxidation of Conjugated *cis*/*E* Dienes[a]



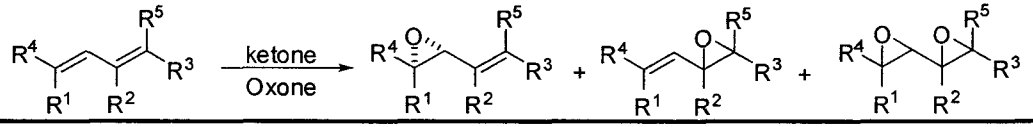

| Entry | Diene | Epoxides | Ketone [R] | Ratio[b] | Yield (conv.) (%)[c,d] | ee(%)[e] |
|---|---|---|---|---|---|---|
| 1 |  |  | **3-62** [(4-Me)-Ph] | | 66 (>95)[f,g] | 85[h] |
| 2 |  |  | **3-64** [(4-*n*-Bu)-Ph] | | 47 (89)[i,j,k] | 89[h] |
| 3 |  |  | **3-65** [(4-Ph)-Ph] | | 58 (100)[f,k] | 92[l] |
| 4 |  |  | **3-65** [(4-Ph)-Ph] | | 64 (85)[m,j,k] | 90[n] |
| 5 |  |  | **3-65** [(4-Ph)-Ph] | | 62 (98) | 90[n] |
| 6 |  |  | **3-65** [(4-Ph)-Ph] | | 64 (89)[k] | 89[n] |
| 7 |  |  | **3-65** [(4-Ph)-Ph] | | 51 (66)[j,k] | 84[n] |
| 8 |  |  | **3-62** [(4-Me)-Ph] | | 74 (100) | 84[n] |
| 9 |  |  | **3-62** **[(4-Me)-Ph]** | | 64 (99) | 94[n] |
| 10 |  |  | **3-65** [(4-Ph)-Ph] | | 65 (91)[k] | 96[n] |
| 11 |  |   | **3-65** [(4-Ph)-Ph] | 12:1 | 66 (88)[j,o] | 76[n] |

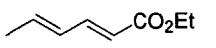
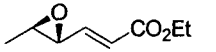
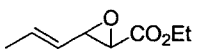
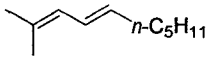
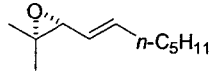
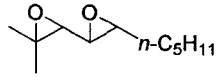
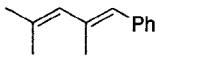
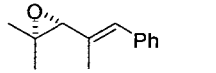
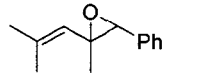
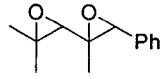
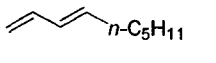
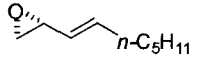
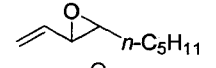
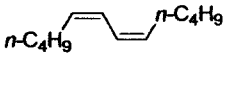
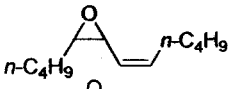
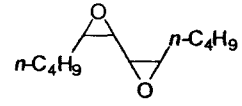
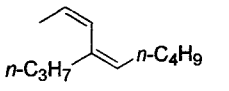
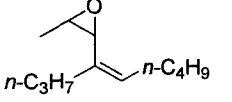
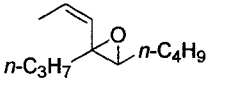
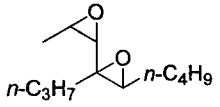
| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 12 |  |  |  | **3-64** [(4-*n*-Bu)-Ph] | 10:1 | 80 (>95)[f,k,p] | 89[q] |
| 13 |  |  | | **3-62** [(4-Me)-Ph] | | 35 (54)[j,m,q,r] | 85[n] |
| 14 |  |  | | **3-62** [(4-Me)-Ph] | | 74 (99) | 94[n] |
| 15 |  |  |  | **3-66** [(4-Et)-Ph] | 10:1 | 61 (93)[f,k,s] | 75[h] |
| 16 |  |  |  | **3-62** [(4-Me)-Ph] | 3.3:1 | 67 (>95)[f,t] | 91[u,33b] |
| 17 |  |  | | **2-8** [Boc] | | 61 (100)[k,v] | 93[n,w] |
| 18 |  |  |  |  | **3-62** [(4-Me)-Ph] | 1:5:5 | 48 (100)[t,x] | >99[n,w] |
| 19 |  |  |  |  | **3-62** [(4-Me)-Ph] | 1:1:1.6 | 42 (94)[t,x] | 98[n,w] |
| 20 |  |  |  |  | **3-62** [(4-Me)-Ph] | 1:3:1 | 78 (99)[k,t,x] | 95[n,w] |
| 21 |  |  |  |  | **3-65** [(4-Ph)-Ph] | 1:1:1 | 57 (85)[k,t] | 87[n,w] |

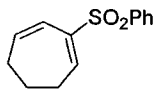
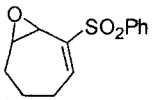
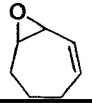
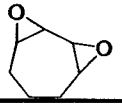
[a] Unless stated otherwise, all reactions were carried out at -10 °C with diene (1 eq.), catalyst (0.25 eq.), Oxone (1.6 eq.), and $K_2CO_3$ (6.7 eq.) in DME/DMM (3:1) and buffer (0.1 M $K_2CO_3$-AcOH in 4 x $10^{-4}$ aq EDTA, pH 9.3) (1.5:1, v/v). Oxone and $K_2CO_3$ were added separately and simultaneously over 4 h. [b] The product ratios were determined by GC and/or $^1$H NMR of the crude reaction mixtures. [c] Unless stated otherwise, the conversions were determined by GC of the crude reaction mixtures. [d] Unless stated otherwise, the yield is for the *cis*-epoxide. [e] ee is for the *cis*-epoxide. [f] The conversion was determined by $^1$H NMR of the

crude reaction mixture. [g] 0.10 eq. catalyst used. [h] Enantioselectivity was determined by chiral HPLC (Chiralcel OJ column). [i] 0.20 eq. catalyst used. [j] 2.4 eq. Oxone and 10.1 eq. $K_2CO_3$ were used. [k] Oxone and $K_2CO_3$ were added over 8 h. [l] Enantioselectivity was determined by chiral shift $^1H$ NMR with Eu(hfc)$_3$. [m] 0.30 eq. of catalyst used. [n] Enantioselectivity was determined by Chiral GC (Chiraldex B-DM column). [o] Oxone and $K_2CO_3$ were added over 10 h. [p] 0.96 eq. Oxone and 4.0 eq. $K_2CO_3$ were used. [q] The reaction was carried out at 0 °C. [r] Oxone and $K_2CO_3$ were added over 12 h. [s] 1.1 eq. Oxone and 4.6 eq. $K_2CO_3$ were used. [t] Yield of mixture of monoepoxides. [u] Enantioselectivity was determined by chiral HPLC (Chiralcel OD column). [v] 1.8 eq. Oxone and 4.0 eq. $K_2CO_3$ were used. [w] ee of the *cis*-epoxide increased with conversion. [x] 0.15 eq. catalyst used.

**Table 3.4.** Asymmetric Epoxidation of Miscellaneous Conjugated Dienes[a]




| Entry | Diene | Epoxides | | | Ketone (R) | Ratio[b] | Yield (conv.) (%)[c,d] | ee (%)[e] |
|---|---|---|---|---|---|---|---|---|
| 1 |  |  |  | | **3-62** [(4-Me)-Ph] | 6.7:1 | 51 (93)[f,g,n] | 75[i,34] |
| 2 |  |  |  | | **3-66** [(4-Et)-Ph] | 3.3:1 | 59 (92)[g,h] | 71[i] |
| 3 |  |  |  |  | **3-66** [(4-Et)-Ph] | 1:0.8:0.7 | 25 (>95)[h,j] | >99[k,l] |
| 4 |  |  |  | | **3-64** [(4-*n*-Bu)-Ph] | 6:1 | 68 (98)[h,m] | 64[i] |
| 5 |  |  |  | | **3-65 [(4-Ph)-Ph]** | 8:1 | 41 (66)[f,n] | 28[i,o] |
| 6 |  |  |  |  | **3-64** [(4-*n*-Bu)-Ph] | 4:6:1 | 20 (92)[f,n,p,q] | 58[i] |

| | | | | | | |
|---|---|---|---|---|---|---|
| 7 |  |  | **3-62** [(4-Me)-Ph] | | 66 (87)[j] | 83[r,33g] |
| 8 |  |   | **3-62** [(4-Me)-Ph] | 3:1 | 53 (>95)[j,s,t] | ~50[r,u,33c,f,] |

[a] Unless stated otherwise, all reactions were carried out at -10 °C with diene (1 eq.), catalyst (0.25 eq.), Oxone (1.6 eq.), and $K_2CO_3$ (6.7 eq.) in DME/DMM (3:1) and buffer (0.1 M $K_2CO_3$-AcOH in 4 x $10^{-4}$ aq EDTA, pH 9.3) (1.5:1, v/v). Oxone and $K_2CO_3$ were added separately and simultaneously over 4 h. [b] The product ratios were determined by GC and/or $^1$H NMR of the crude reaction mixtures. [c] Unless stated otherwise, the conversions were determined by GC of the crude reaction mixtures. [d] Unless stated otherwise, the yield is for the major product. [e] The ee is for the major product. [f] 0.30 eq. catalyst used. [g] The reaction was carried out at 0 °C. [h] Oxone and $K_2CO_3$ were added over 8 h. [i] Enantioselectivity was determined by chiral GC (Chiraldex B-DM column). [j] The conversion was determined by $^1$H NMR of the crude reaction mixture. [k] Enantioselectivity was determined by chiral HPLC (Chiralcel OD column). [l] ee of the major product increased with conversion. [m] DME was used as solvent. [n] Oxone and $K_2CO_3$ were added over 10 h. [o] ee of the monoepoxide decreased with conversion. [p] 2.4 eq. Oxone and 10.1 eq. $K_2CO_3$ were used. [q] Yield of mixture of monoepoxides. [r] Enantioselectivity was determined by $^1$H NMR with Eu(hfc)$_3$. [s] 0.20 eq. catalyst used. [t] 1.1 eq. Oxone and 4.6 eq. $K_2CO_3$ were used. [u] Enantioselectivity could not be determined with great accuracy due to poor resolution of enantiomer peaks in the $^1$H NMR spectrum with Eu(hfc)$_3$.

with other substitution patterns were also examined (Table 3.4), and the trends in reactivity are similar to those above.

In many cases, no further epoxidation of vinyl *cis*-epoxides was found, presumably due to the deactivation of the olefin by the epoxide. However, in some cases, particularly for *cis*/trisubstituted dienes, bisepoxide products were observed (Table 3.3, entries 12, 17, 18-21). In these cases kinetic resolution becomes a possibility as one enantiomer of the monoepoxide could undergo subsequent epoxidation at a faster rate than the other. If the minor enantiomer of the monoepoxide undergoes the subsequent epoxidation at a faster rate, an increase in ee of the monoepoxide is observed as conversion increases, and if the major enantiomer of monoepoxide undergoes subsequent epoxidation at a faster rate, a decrease in ee of the monoepoxide is observed as conversion increases.[164] Significant change in ee of the major monoepoxide product with conversion was observed for entries 17-21 (Table 3.3) and entry 3 (Table 3.4). In all these cases the ee increased with increasing conversion. Although the ee increased with conversion for entry 17 (Table 3.3), no bisepoxide could be isolated or observed in the $^1$H NMR of the crude reaction mixture. The reason for this is unclear, but it could be attributed to instability of the bisepoxide under the reaction conditions.

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[164] For leading references on kinetic resolution, see: (a) Kagan, H. B.; Fiaud, J. C. *Top. Stereochem.* **1988**, *18*, 249-330. (b) Martin, V. S.; Woodard, S. S.; Katsuki, T. Yamada, Y.; Ikeda, M.; Sharpless, K. B. *J. Am. Chem. Soc.* **1981**, *103*, 6237-6240.

The enantioselectivity of the epoxidation depends significantly on the substituents ($R^1$-$R^5$) on the dienes and can be rationalized by examining the transition states involved (Figure 3.2). Changing the group on the 4-position of the aromatic ring of the catalyst also has a significant effect on ee. This is likely due to additional interactions (possibly hydrophobic in nature) between this group and the substrate in the transition state. The highest enantioselectivities are obtained for *cis/E*-dienes where $R^1 = CH_3$ (Table 3.3, entries 1-10, 13-14, 17-21). More hydrophobic $R^1$ substituents result in lower ee presumably because increased hydrophobic interactions between the catalyst and substrate increase the contribution of competing spiro transition state **B** (Figure 3.2) (Table 3.3, entries 11, 13). Conversely, transition state **A** could be further favored by increasing the hydrophilicity of $R^1$ and/or increasing the hydrophobicity of $R^3$ (Table 3.3, entry 12).

Enantioselectivity also greatly depends on the geometry of the conjugating olefin. Ee's are typically high when the olefin is of *E* geometry. However, conjugating olefins of *Z* geometry result in poor enantioselectivities (Table 3.4, entries 5, 6). This is likely due to disfavoring of spiro transition state **C** because of steric repulsion (Figure 3.2, other substituents omitted for clarity). When the diene is locked into an s-*cis* conformation as in the case of 1,3-cycloheptadiene (Table 3.4, entry 8) the ee is low. However, the presence of a conjugated group at the 2-position of the diene greatly increases the enantioselectivity (Table 3.4, entry 7).

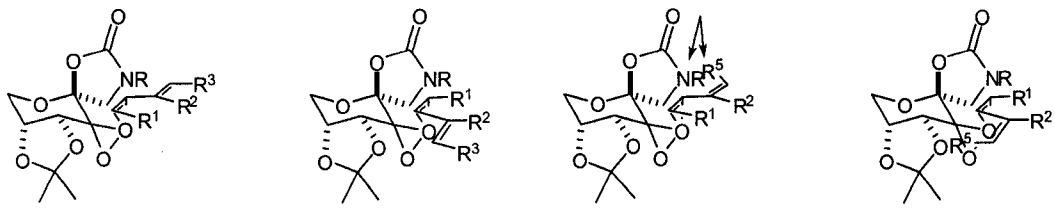


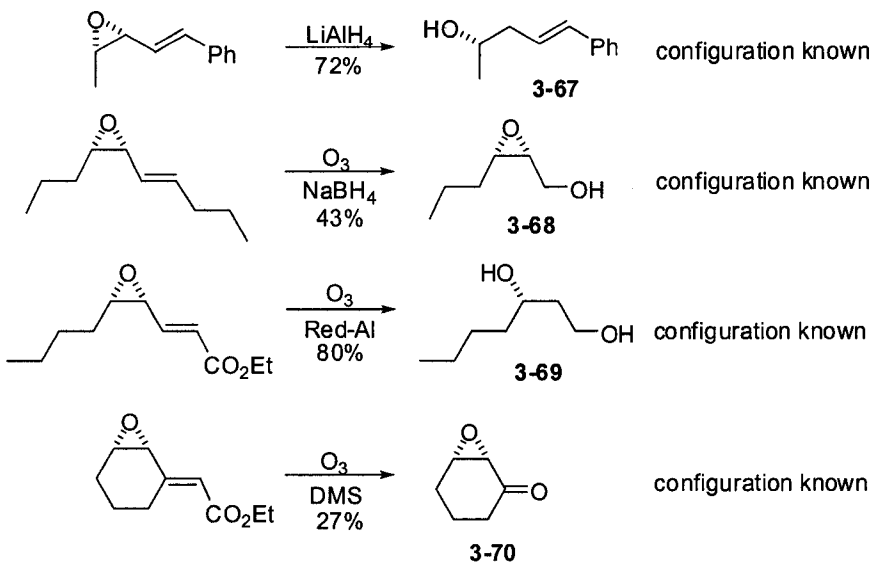

**Figure 3.2**

Ethyl sorbate, like most *trans*-olefins with the oxazolidinone-containing catalysts, gives only moderate enantioselectivity (Table 3.4, entry 1) as does terminal olefin **3-59** (Table 3.4, entry 4). Trisubstituted/*trans*-diene **3-57** is also a poor substrate (Table 3.4, entry 2). This was unexpected since this type of substitution on styrenyl substrates usually results in high ee.[147] Trisubstituted/trisubstituted-diene **3-58** gives very high ee (likely due to kinetic resolution), but regioselectivity and yield are low (Table 3.4, entry 3).

The stereochemistry of the epoxides shown in Tables 3.3 and 3.4 is assigned based on spiro transition state **A** (Figure 3.2). To further validate this model and the assigned stereochemistry, the absolute configuration of four representative examples was determined by converting the epoxides to compounds of known configuration and comparing the optical rotations (Scheme 3.35). The epoxide from Table 3.3, entry 1 was opened with $LiAlH_4$ to give known homoallylic alcohol **3-67**.[165] The epoxide from Table 3.3, entry 11 was ozonolyzed and the resulting aldehyde was reduced to give known

[165] Hayashi, T.; Konishi, M.; Kumada, M. *J. Org. Chem.* **1983**, *48*, 281-282.

epoxy alcohol **3-68**.[166] The epoxide from Table 3.3, entry 13 was ozonolyzed followed by reduction with Red-Al to give known diol **3-69**.[167] Finally, the epoxide from Table 3.3, entry 13 was ozonolyzed to give 2,3-epoxycyclohexanone (**3-70**).[168] The results in all four cases support the initial assignment based on the spiro transition state **A** model.




**Scheme 3.35**

## 3.C. CONCLUSION

In conclusion, a conjugating olefin is an effective directing group for the asymmetric epoxidation of unfunctionalized olefins with chiral ketone catalysts. A

[166] Mori, K.; Nakazono, Y. *Tetrahedron* **1986**, *42*, 6459-6464.

[167] Taber, D.F.; Deker, P.B.; Silverberg, L.J. *J. Org. Chem.* **1992**, *57*, 5990-5994.

[168] Aoki, M.; Seebach, D. *Helv. Chim. Act.* **2001**, *84*, 187-207.

variety of conjugated dienes can be epoxidized with high selectivity using glucose-derived catalysts **2-8**, and **3-62** – **3-66** and Oxone as oxidant making this an efficient synthesis of vinyl *cis*-epoxides from conjugated dienes. The enantioselectivity of the reaction is highly dependent on the substitution pattern of the diene system with *cis/trans*-dienes being the most effective. With this methodology a variety of synthetically useful enantioenriched vinyl epoxides are now readily accessible.

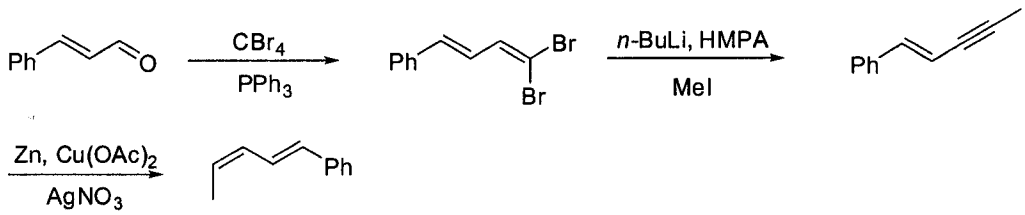
## 3.D. EXPERIMENTAL

**General Methods.** All commercially available reagents were used without further purification. All glassware used for epoxidation was carefully washed with soap and water to be free of any trace metals which catalyze the decomposition of Oxone. Column chromatography was performed with silica gel (200-400 mesh). Melting points are uncorrected.

**Representative Asymmetric Epoxidation Procedure (Table 3.3, entry 9).** To a solution of 2-*trans*,4-*cis*-ethyl-hexa-2,4-dienoate (**3-22**) (0.07 g, 0.5 mmol) and ketone **3-62** (0.042 g, 0.126 mmol) in DME-DMM (3:1, v/v) (7.5 mL) were added buffer (0.1 M $K_2CO_3$-AcOH in 4 x $10^{-4}$ M aqueous EDTA, buffer pH = 9.3) (5 mL) and $Bu_4NHSO_4$ (0.0075 g, 0.02 mmol) with stirring. After the mixture was cooled to about -10 °C (bath temperature) via a NaCl-ice bath, a solution of Oxone (0.20 M in 4 x $10^{-4}$ M aqueous

EDTA, 4 mL) (0.49 g, 0.80 mmol) and $K_2CO_3$ (0.84 M in 4 x $10^{-4}$ M aqueous EDTA, 4 mL) (0.46 g, 3.36 mmol) were added dropwise simultaneously and separately over 4 h via syringe pump. The reaction was then quenched with the addition petroleum ether and extracted with pet. ether. The combined organic layers were washed with water, brine, dried ($Na_2SO_4$), filtered, concentrated, and purified by flash chromatography [the silica gel was buffered with 1% $Et_3N$ in pet. ether; pet.ether/ether (1/0 to 19/1, v/v) was used as eluent] to give the *cis*-epoxide as a colorless oil (0.050 g, 64% yield, 94% ee).

**(Table 3.3, entry 1)**




***trans*-1,1-Dibromo-4-phenyl-1,3-butadiene (3-3) (CPB-0514).** The title compound was prepared according to a literature procedure.[148] Carbon tetrabromide (47.8 g, 144.0 mmol) and triphenylphosphine (75.5 g, 288 mmol) were dissolved in 600 mL $CH_2Cl_2$ and the mixture was cooled to 0 °C. *trans*-Cinnamaldehyde (11.5 g, 87.0 mmol) was then added and the mixture was stirred for 45 min at 0 °C. The mixture was then concentrated under vacuum and the yellow residue was triturated repeatedly with petroleum ether. The pet. ether solution was decanted and concentrated and then purified by column chromatography (pet. ether) to give 16.4 g (65%) of the title compound as a white solid:

IR (NaCl): 3015, 1416, 961, $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 7.44 (m, 2H), 7.31 (m, 3H), 7.09 (d, $J$ = 9.3 Hz, 1H), 6.76 (d, $J$ = 9.3 Hz, 1H), 6.72 (s, 1H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 137.3, 136.5, 135.9, 129.0, 128.8, 127.1, 125.4, 91.5.

***trans*-1-Phenyl-1-penten-3-yne (3-6) (CPB-0444).** The title compound was prepared according to a literature procedure.[148] *trans*-1,1-Dibromo-4-phenyl-1,3-butadiene (**3-3**) (CPB-0514) (4.0 g, 13.9 mmol) was dissolved in THF (80 mL) and the solution was dropped to -78 °C. *n*-BuLi (2.2 M, 13.0 mL, 28.0 mmol) was then added and the mixture was stirred for 1 h at -78 °C and then 2 h at rt. HMPA (2.5 g, 14.0 mmol), and MeI (2.2 g, 15.3 mmol) were then added and the mixture was stirred for an additional 6 h at rt. The reaction was then quenched by addition of water (30 mL). The aqueous layer was extracted with pet. ether, and the combined organic extracts were washed with brine, dried over $Na_2SO_4$, filtered, and concentrated under vacuum. The mixture was then purified by flash column chromatography (100% pet. ether) to yield a colorless oil (1.3 g, 60%): IR (NaCl): 2217, 1491, 1448, $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 7.39-7.24 (m, 5H), 6.88 (d, $J$ = 16.5 Hz, 1H), 6.14 (dq, $J$ = 16.5, 2.1 Hz, 1H), 2.03 (d, $J$ = 2.1 Hz, 3H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 140.3, 136.7, 128.9, 128.5, 126.3, 109.0, 88.5, 79.1, 4.8.

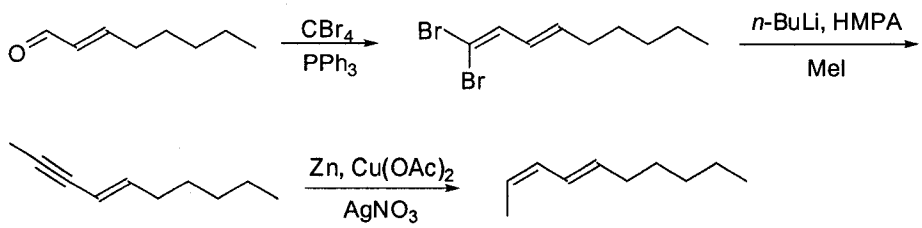
**(1-*trans*,3-*cis*)-1-Phenyl-1,3-pentadiene (3-9) (CPB-0449).** The enyne was reduced according to the procedure of Boland et al.[149] Argon was passed through a stirred suspension of Zn dust (25.9 g, 396.2 mmol) in water (134 mL) for 15 min., and then $Cu(OAc)_2 \cdot H_2O$ (2.59 g, 12.95 mmol) was added and stirring continued for another 15 min.

Then $AgNO_3$ (2.7 g, 16.0 mmol) was added and the suspension was stirred for another 30 min. The metal was then collected by vacuum filtration and washed on the filter with water (2 x 30 mL), MeOH (2 x 30 mL), acetone (2 x 30 mL), and ether (2 x 30 mL) successively. The Zn was then transferred into 1:1 $H_2O$/MeOH (v/v) (100 mL) and to this was added a solution of *trans*-1-phenyl-1-penten-3-yne (**3-6**) (CPB-0444) (1.3 g, 8.4 mmol)in MeOH (53 mL). The mixture was stirred at 50 °C for 24 hr. It was then cooled to rt and sat. aq. $NH_4Cl$ (50 mL) was added and the solution was stirred vigorously for 10 min. The metal was then removed by filtration through a pad of silica gel and the filter was washed with ether. The filtrate was then washed with sat. aq. $NH_4Cl$, and the aqueous layer was extracted with ether. The organic layers were then washed with brine, dried ($Na_2SO_4$), filtered, and concentrated. The crude product was purified by column chromatography (pet. ether) to give 0.96 g (73%) of the desired product as a colorless oil: IR (NaCl): 1488, 1448, 1407, $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 7.50-7.20 (m, 5H), 7.11 (dd, $J$ = 15.6, 10.8 Hz, 1H), 6.53 (d, $J$ = 15.6 Hz, 1H), 6.20 (td, $J$ = 10.8, 1.8, 1H), (dq, $J$ = 10.8, 7.2 Hz, 1H), 1.87 (dd, $J$ = 7.2, 1.8 Hz, 3H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 137.8, 132.0, 129.7, 128.7, 127.5, 127.3, 126.4, 124.3, 14.0.

**Epoxide (CPB-2021).** 85% ee $[\alpha]^{25}_D$ = -54.4 (*c* 0.27, $CHCl_3$); Colorless oil; IR (NaCl): 1494, 1450, $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 7.43-7.24 (m, 5H), 6.80 (d, $J$ = 15.8 Hz, 1H), 6.07 (dd, $J$ = 15.8, 7.5 Hz, 1H), 3.58 (dd, $J$ = 7.5, 4.2 Hz, 1H), 3.35-3.28 (m, 1H),

1.36 (d, $J$ = 5.7 Hz, 3H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 136.5, 135.7, 128.9, 128.2, 126.7, 123.8, 57.6, 55.3, 13.7. Anal. Calcd. for $C_{11}H_{12}O$: C, 82.46; H, 7.55. Found: C, 82.67; H, 7.69.

**(Table 3.3, entry 2)**




***trans*-1,1-Dibromo-1,3-nonadiene (3-4) (CPB-0529).** The title compound was prepared according to the same procedure used for *trans*-1,1-dibromo-4-phenyl-1,3-butadiene (**3-3**) (CPB-0514) above (92%). Colorless oil; IR (NaCl): 1769, 1637, 1465 cm$^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$) δ 6.90 (d, $J$ = 9.9 Hz, 1H), 6.08 (ddt, $J$ = 15.3, 9.9, 1.2 Hz, 1H), 5.91 (dt, $J$ = 15.3, 6.9 Hz, 1H), 2.02 (qd, $J$ = 6.9, 0.9, Hz, 2H), 1.39-1.17 (m, 6H), 0.82 (t, $J$ = 6.6 Hz, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 139.9, 137.4, 127.3, 88.5, 33.2, 31.6, 28.7, 22.7, 14.2.

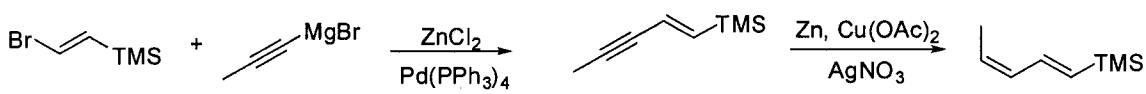
***trans*-4-Decen-2-yne (3-7) (CPB-0532).** The title compound was prepared according to the same procedure used for *trans*-1-phenyl-1-penten-3-yne (**3-6**) (CPB-0444) above (71%). Colorless oil; IR (NaCl): 2225, 1466, 1378 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) δ 6.06 (dt, $J$ = 16.0, 6.8 Hz, 1H), 5.43 (dq, $J$ = 16.0, 2.0 Hz, 1H), 2.07 (q, $J$ = 6.8 Hz, 2H),

1.93 (d, $J$ = 2.0 Hz, 3H), 1.39-1.26 (m, 6H), 0.89 (t, $J$ = 6.4 Hz, 3H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 143.8, 109.2, 84.2, 78.7, 33.1, 31.5, 28.7, 22.7, 14.2, 4.4.

**(2-*cis*,4-*trans*)-2,4-Decadiene (3-10) (CPB-0537).** The title compound was prepared according to the same procedure used for (1-*trans*,3-*cis*)-1-phenyl-1,3-pentadiene (**3-9**) (CPB-0449) above (58%). Colorless oil; IR (NaCl): 1458 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) δ 6.34 (dd, $J$ = 15.2, 11.2 Hz, 1H), 5.98 (t, $J$ = 10.6 Hz, 1H), 5.68 (dt, $J$ = 15.2, 7.2 Hz, 2H), 5.39 (dq, $J$ = 10.6, 7.0 Hz, 1H), 2.12 (q, $J$ = 7.2 Hz, 2H), 1.74 (d, $J$ = 7.0 Hz, 3H), 1.44-1.24 (m, 6H), 0.90 (t, $J$ = 6.4 Hz, 3H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 134.9, 129.8, 125.5, 124.1, 33.1, 31.7, 29.3, 22.8, 14.3, 13.5.

**Epoxide (CPB-0549).** 90 % ee $[\alpha]^{25}_D$ = -23.6 (*c* 0.37, $CHCl_3$); Colorless oil; IR (NaCl): 1458, 1388 cm$^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$) δ 5.94 (dt, $J$ = 15.3, 6.9 Hz, 1H), 5.31 (ddt, $J$ = 15.3, 8.1, 1.5 Hz, 1H), 3.36 (dd, $J$ = 8.1, 4.5 Hz, 1H), 3.24-3.16 (m, 1H), 2.09 (qd, $J$ = 6.6, 1.5 Hz, 2H), 1.44-1.24 (m, 6H), 1.30 (d, $J$ = 5.4 Hz, 3H) 0.90 (t, $J$ = 6.9 Hz, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 138.6, 123.9, 57.5, 54.7, 32.8, 31.5, 28.9, 22.7, 14.3, 13.7. Anal. Calcd. for $C_{10}H_{18}O$: C, 77.87; H, 11.76. Found: C, 77.76; H, 11.69.

**(Table 3.3, entry 3)**

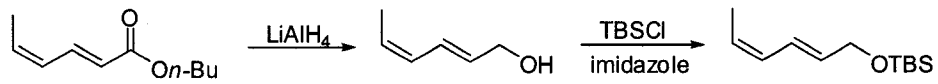


***trans*-1-Trimethylsilyl-1-penten-3-yne (3-15) (CPB-1121).** The title compound was prepared based on a literature procedure.[150] Propynyl magnesium bromide (0.5 M in THF, 116 mL, 58.0 mmol) was added to a slurry of dry $ZnCl_2$ (4.0 g, 29.1 mmol) in 58 mL THF at 0 °C. After 15 min. *trans*-bromovinyltrimethylsilane (3.9 g, 21.7 mmol) in 5.8 mL THF and $Pd(Ph_3)_4$ (1.3 g, 1.2 mmol) were added sequentially and the mixture was allowed to stir at rt for 20 h. The mixture was then poured into sat. $NH_4Cl$ and was extracted with petroleum ether. The combined organic extracts were then washed with brine, dried over $Na_2SO_4$ and concentrated. The residue was purified by column chromatography (petroleum ether) to give 1.86 g (62%) of the title compound as a colorless oil: IR (NaCl): 2217, 1573, 1249 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 6.33 (d, $J$ = 19.2 Hz, 1H), 5.91 (dq, $J$ = 19.2, 2.0 Hz, 1H), 1.96 (d, $J$ = 2.0 Hz, 3H), 0.08 (s, 9H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 144.0, 124.1, 86.8, 80.4, 4.5, -1.4.

**(1-*trans*,3-*cis*)-1-Trimethylsilyl-1,3-pentadiene (3-16) (CPB-1137).** The diene was prepared by activated zinc reduction of *trans*-1-trimethylsilyl-1-penten-3-yne (3-x) (CPB-1121) according to the same procedure used for (1-*trans*,3-*cis*)-1-phenyl-1,3-pentadiene (**3-9**) (CPB-0449) (30%). Colorless oil: IR (NaCl): 1573, 1247 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 6.86 (ddd, $J$ = 18.3, 10.5, 1.2 Hz, 1H), 6.04 (tq, $J$ = 10.5, 1.8 Hz, 1H), 5.85 (d, $J$ = 18.3 Hz, 1H), 5.30 (dq, $J$ = 10.5, 7.2 Hz, 1H), 1.81 (dd, $J$ = 7.2, 1.8 Hz, 3H), 0.11 (s, 9H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 138.9, 133.7, 132.5, 127.1, 13.9, -0.9.

**Epoxide (CPB-1237).** 90% ee $[\alpha]^{25}_{D}$ = -67.8 (*c* 0.27, $CHCl_3$); Colorless oil; IR (NaCl): 1353, 1249 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 6.19 (d, *J* = 18.9 Hz, 1H), 5.87 (dd, *J* = 18.9, 6.9 Hz, 1H), 3.40 (dd, *J* = 6.9, 4.4 Hz, 1H), 3.22 (dd, *J* = 5.4, 4.4 Hz, 1H), 1.29 (d, *J* = 5.4 Hz, 1H), 0.09 (s, 9H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 139.7, 137.8, 59.0, 55.0, 13.5, -1.2. HRMS Calcd. for $C_8H_{15}OSi$ (M -1): 155.0892. Found: 155.0890.

**(Table 3.3, entry 4)**




**(2-*trans*,4-*cis*)-2,4-Hexadien-1-ol (3-27) (CPB-0948).** A solution of (2-*trans*,4-*cis*)-*n*-butyl-hexa-2,4-dienoate (**3-23**) (CPB-0943) (1.96 g, 11.65 mmol) in 40 mL $Et_2O$ was added slowly to a stirred mixture of $LiAlH_4$ (0.47 g, 12.31 mmol) in 80 mL dry $Et_2O$ under Ar at 0 °C. It was allowed to warm to rt and was stirred overnight. It was then quenched at 0 °C by addition of $H_2O$. The solid was removed by filtration, and the filtrate was washed with $NaHCO_3$, brine, dried ($Na_2SO_4$), and concentrated. The residue was then purified by column chromatography (pet. ether:$Et_2O$ 4:1) to give 1.04 g (91%) of the title compound as a colorless oil: IR (NaCl): 3334 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 6.58 (ddd, *J* = 15.4, 11.2, 1.2 Hz, 1H), 6.03 (t, *J* = 10.8 Hz, 1H), 5.83 (dt, *J* = 15.4, 6.0 Hz, 1H), 5.55 (dq, *J* = 10.8, 7.2 Hz, 1H), 4.23 (t, *J* = 6.0 Hz, 2H), 2.62 (brs, 1H),

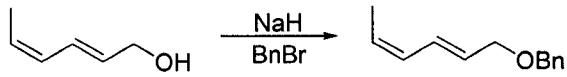
1.78 (dd, $J$ = 7.2, 1.6 Hz, 3H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 131.6, 128.7, 127.4, 126.8, 63.8, 13.6.

**(2-*trans*,4-*cis*)-1-(*t*-Butyldimethylsiloxy)-2,4-hexadiene (3-29) (CPB-1005).** (2-*trans*,4-*cis*)-2,4-Hexadien-1-ol (**3-27**) (CPB-0948) (0.1 g, 1.0 mmol) was dissolved in $CH_2Cl_2$ (4 mL) and imidazole (0.14 g, 2.1 mmol) was added at 0 °C. The mixture was stirred until homogeneous and then TBSCl (0.20 g, 1.3 mmol) was added. The mixture was allowed to warm to rt and was stirred for 24 h. It was then poured into sat. $NH_4Cl$, washed with water, brine, dried ($Na_2SO_4$) and concentrated. The crude oil was then purified by column chromatography (pet. ether) to give 0.13 g (69%) of the title compound as a colorless oil: IR (NaCl): 1472 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) δ 6.56 (ddq, $J$ = 15.2, 10.8, 1.2 Hz, 1H), 6.03 (td, $J$ = 10.8, 1.6 Hz, 1H), 5.74 (dt, $J$ = 15.2, 5.0 Hz, 1H), 5.49 (dq, $J$ = 10.8, 7.2 Hz, 1H), 4.25 (d, $J$ = 5.0 Hz, 2H), 1.76 (dd, $J$ = 7.2, 1.2 Hz, 3H), 0.93 (s, 9H), 0.09 (s, 6H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 132.3, 129.0, 126.2, 125.1, 63.9, 26.2, 18.6, 13.5, -5.0.

**Epoxide (CPB-1033).** 90% ee $[\alpha]^{25}_D$ = -19.8 (*c* 0.61, $CHCl_3$); Colorless oil; IR (NaCl): 1472, 1255 cm$^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$) δ 6.02 (dt, $J$ = 15.3, 4.5 Hz, 1H), 5.60 (ddt, $J$ = 15.3, 7.8, 1.8 Hz, 1H), 4.23 (dd, $J$ = 4.5, 1.8 Hz, 2H), 3.43 (dd, $J$ = 7.8, 4.2 Hz, 1H), 3.22 (qd, $J$ = 5.4, 4.2 Hz, 1H), 1.29 (d, $J$ = 5.4 Hz, 3H), 0.92 (s, 9H), 0.08 (s, 6H); $^{13}$C

NMR (75 MHz, $CDCl_3$) δ 136.3, 123.9, 63.2, 56.9, 54.7, 26.1, 18.6, 13.6, -5.1. HRMS Calcd. for $C_{12}H_{24}O_2Si$ (M +): 228.1546. Found: 228.1546.

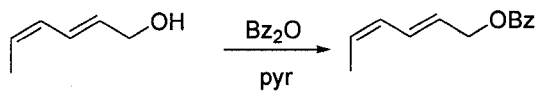
**(Table 3.3, entry 5)**




**(2-*trans*,4-*cis*)-1-Benzyloxy-2,4-hexadiene (3-28) (CPB-1030).** To a dry flask was added NaH (60% in mineral oil, 0.223g, 5.57 mmol). The mineral oil was then removed by washing with petroleum ether. To this was added THF (4 mL) and the mixture was cooled to 0 °C. (2-*trans*,4-*cis*)-2,4-Hexadien-1-ol (**3-27**) (CPB-0948) (0.50 g, 5.1 mmol) in 4 mL THF was then added and the mixture was allowed to warm to rt. Benzylbromide (0.88 g, 5.12 mmol) was then added and the mixture was allowed to stir overnight. The reaction was quenched by addition of $H_2O$. It was then extracted with $Et_2O$, washed with brine, dried ($Na_2SO_4$), concentrated, and purified by column chromatography (pet. ether.) to give 0.81 g (84%) of the title compound as a colorless oil: IR (NaCl): 1454, 1107 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 7.37-7.28 (m, 5H), 6.59 (ddd, $J$ = 15.3, 11.1, 1.2 Hz, 1H), 6.04 (td, $J$ = 10.8, 1.5 Hz, 1H), 5.79 (dt, $J$ =15.3, 6.0, Hz, 1H,), 5.55, (dq, $J$ = 10.8, 7.2 Hz, 1H), 4.54 (s, 2H), 4.10 (d, $J$ = 6.0 Hz, 2H), 1.77 (dd, $J$ = 7.2, 1.8 Hz, 3H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 138.6, 129.2, 128.9, 128.6, 128.3, 128.0, 127.8, 127.2, 72.3, 70.9, 13.6.

**Epoxide (CPB-1045).** 90% ee $[\alpha]^{25}_{D}$ = -12.6 (*c* 2.33, $CHCl_3$); Colorless oil; IR (NaCl): 1454, 1364, 1099 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.38-7.28 (m, 5H), 6.06 (dt, *J* = 15.6, 5.6 Hz, 1H), 5.64 (ddt, *J* = 15.6, 7.6, 1.6 Hz 1H), 4.54 (s, 2H), 4.08 (dd, J = 5.6, 1.6 Hz, 2H), 3.44 (dd, *J* = 7.6, 4.4 Hz, 1H), 3.23 (qd, *J* = 5.6, 4.4 Hz, 1H), 1.30 (d, *J* = 5.6 Hz, 3H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 138.3, 133.3, 128.6, 128.0, 127.9, 127.2, 72.5, 70.1, 56.7, 54.7, 13.6. Anal. Calcd. for $C_{13}H_{16}O_2$: C, 76.44; H, 7.90. Found: C, 76.69; H, 7.71.

**(Table 3.3, entry 6)**

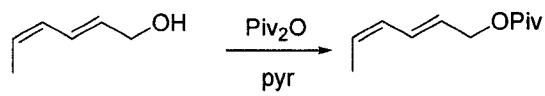



**(2-*trans*,4-*cis*)-1-Benzoyloxy-2,4-hexadiene (3-30) (CPB-1050).** (2-*trans*,4-*cis*)-2,4-Hexadien-1-ol (**3-27**) (CPB-0948) (0.75 g, 7.64 mmol) was dissolved in $CH_2Cl_2$ (38 mL). Benzoic anhydride (3.46 g, 15.3 mmol), pyridine (1.55 mL, 19.0 mmol), and DMAP (0.047 g, 0.388 mmol) were added in single portions and the mixture was stirred overnight at rt. The reaction was then quenched by addition of sat. aq. $NH_4Cl$ and was extracted with pet. ether. The combined organic extracts were washed with $H_2O$, brine, dried ($Na_2SO_4$), and concentrated. The residue was then purified by column chromatography (pet. ether) to give 1.33 g (86%) of the title compound as a colorless oil: IR (NaCl): 1720, 1269, 1112 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 8.10-8.04 (m, 2H), 7.60-7.54 (m, 1H), 7.48-7.42 (m, 2H), 6.71 (ddd, *J* = 15.2, 11.2, 0.8 Hz, 1H), 6.06 (td, *J* = 11.2, 1.6, Hz, 1H), 5.87 (dt, *J* = 15.2, 6.8 Hz, 1H), 5.60 (dq, *J* = 10.8, 7.2 Hz, 1H), 4.89 (d,

$J$ = 6.4, Hz, 2H), 1.80 (dd, $J$ = 7.2, 1.6 Hz, 3H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 166.6, 133.1, 130.5, 129.9, 129.8, 128.6, 128.4, 126.2, 65.7, 13.7.

**Epoxide (CPB-1113).** 89% ee $[\alpha]^{25}_D$ = -19.8 (*c* 1.0, $CHCl_3$); Colorless oil; IR (NaCl): 1720, 1272, 1111 $cm^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, $J$ = 7.2 Hz, 2H), 7.58 (t, $J$ = 7.6 Hz, 1H), 7.46 (t, $J$ = 7.6 Hz, 2H), 6.14 (dt, $J$ = 15.6, 6.0 Hz, 1H), 5.76 (dd, $J$ = 15.6, 7.2 Hz, 1H), 4.88 (d, $J$ = 5.6 Hz, 2H), 3.45 (dd, $J$ = 7.2, 4.4 Hz, 1H), 3.25 (m, 1H), 1.31 (d, $J$ = 5.6 Hz, 3H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 166.4, 133.3, 130.4, 130.2, 139.8, 128.8, 128.6, 64.6, 56.4, 54.8, 13.5. Anal. Calcd. for $C_{13}H_{14}O_3$: C, 71.54; H, 6.47. Found: C, 71.70; H, 6.62.

**(Table 3.3, entry 7)**

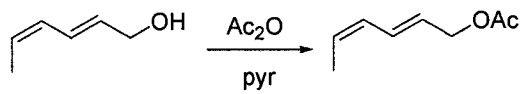



**(2-*trans*,4-*cis*)-1-Pivaloyloxy-2,4-hexadiene (3-31) (CPB-1103).** (2-*trans*,4-*cis*)-2,4-Hexadien-1-ol (**3-27**) (CPB-0948) (0.75 g, 7.64 mmol) was dissolved in $CH_2Cl_2$ (38 mL). Pivalic anhydride (2.85 g, 15.3 mmol), pyridine (1.6 mL, 19.0 mmol), and DMAP (0.047 g, 0.388 mmol) were added in single portions and the mixture was stirred overnight. The reaction was quenched by addition of sat. aq. $NH_4Cl$, and extracted with pet. ether. The combined organic extracts were washed with $H_2O$, brine, dried ($Na_2SO_4$), and concentrated. The residue was then purified by column chromatography (pet. ether) to

give a mixture of the title compound and pivalic anhydride as a coloress oil (1.38 g, 99%, impure): IR (NaCl): 1741, 1480, 1152 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 6.59 (dd, $J$ = 15.2, 11.2 Hz, 1H), 6.02 (t, $J$ = 10.8 Hz, 1H), 5.73 (dt, $J$ = 15.2, 6.4 Hz, 1H), 5.57 (dq, $J$ = 10.8, 7.2 Hz, 1H), 4.62 (d, $J$ = 6.4 Hz, 2H), 1.78 (d, $J$ = 7.2 Hz, 3H), 1.22 (s, 9H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 178.5, 128.9, 128.5, 128.0, 126.6, 65.0, 39.0, 27.4, 13.6

**Epoxide (CPB-1116).** Colorless oil; 84% ee $[\alpha]^{25}_D$ = -25.4 (*c* 0.9, $CHCl_3$); IR (NaCl): 1732, 1282, 1152 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 6.00 (dt, $J$ = 15.3 5.7 Hz, 1H), 5.63 (ddt, $J$ = 15.3, 6.9, 1.2 Hz, 1H), 4.60 (dd, $J$ = 5.7, 1.2 Hz, 2H), 3.42 (dd, $J$ = 6.9, 4.2 Hz, 1H), 3.22 (qd, $J$ = 5.4, 4.2 Hz, 1H), 1.28 (d, $J$ = 5.4 Hz, 3H), 1.22 (s, 9H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 178.3, 130.8, 127.9, 64.0, 56.4, 54.7, 39.0, 27.4, 13.4. Anal. Calcd. for $C_{11}H_{16}O_3$: C, ; H, . Found: C, ; H, .

**(Table 3.3, entry 8)**

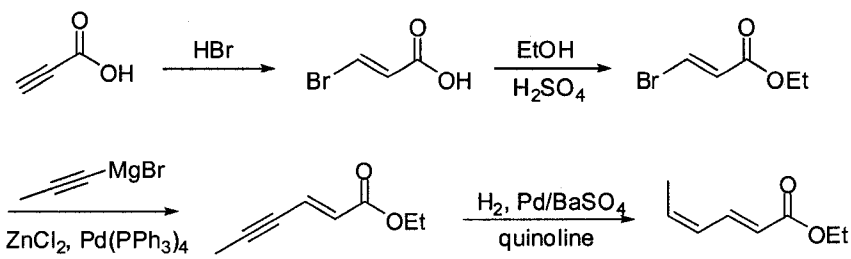



**(2-*trans*,4-*cis*)-1-Acetyloxy-hexadiene (3-32) (CPB-1016).** (2-*trans*,4-*cis*)-2,4-Hexadien-1-ol (3-27) (CPB-0948) (0.29 g, 2.95 mmol) was dissolved in $CH_2Cl_2$ (15 mL). Acetic anhydride (0.6 g, 5.9 mmol), pyridine (0.6 mL, 7.38 mmol), and DMAP (0.02 g, 0.15 mmol) were added in single portions and the mixture was stirred overnight. It was then quenched by addition of sat. aq. $NH_4Cl$, and extracted with pet. ether. The

combined organic extracts were washed with $H_2O$, brine, dried ($Na_2SO_4$), and concentrated. The residue was then purified by column chromatography (pet. ether) to give 0.20 g (48%) of the title compound as a colorless oil: IR (NaCl): 1743, 1238, 1024 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 6.61 (ddd, $J$ = 15.2, 10.8, 1.6 Hz, 1H), 6.02 (td, $J$ = 10.8, 1.6 Hz, 1H), 5.74 (dt, $J$ = 15.2, 6.8 Hz, 1H), 5.59 (dq, $J$ = 10.8, 7.2 Hz, 1H), 6.63 (d, $J$ = 6.4 Hz, 2H), 2.08 (s, 3H), 1.78 (dd, $J$ = 7.2, 1.6 Hz, 3H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 168.0, 129.8, 128.4, 126.1, 65.2, 21.2, 13.7.

**Epoxide (CPB-1027).** 84% ee $[\alpha]^{25}_D$ = -11.7 (*c* 1.5, $CHCl_3$); Colorless oil; IR (NaCl): 1740, 1243, 1028 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 6.01 (dt, $J$ = 15.6, 6.0 Hz, 1H), 5.66 (dd, $J$ = 15.6, 7.2 Hz, 1H), 4.62 (d, $J$ = 6.0 Hz, 2H), 3.42 (dd, $J$ = 7.2, 4.2 Hz, 1H), 3.23 (qd, $J$ = 5.1, 4.2 Hz, 1H), 2.09 (s, 3H), 1.29 (d, $J$ = 5.1 Hz, 3H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 170.9, 130.4, 128.7, 64.2, 56.4, 54.8, 21.1, 13.5. Anal. Calcd. for $C_8H_{12}O_3$: C, 61.52; H, 7.74. Found: C, 61.52; H, 7.80.

**(Table 3.3, entry 9)**



***trans*-β-Bromoacrylic acid (3-17) (CPB-0826).** The acid was prepared according to literature procedure.[151] Propiolic acid (10.0 g, 143 mmol) and HBr (50% aq., 40 mL) were stirred at 100 °C for 2 h. The mixture was then allowed to cool to rt and was left to stand overnight. The resulting crystals were then collected by vacuum filtration while washing with cold $H_2O$ giving 13.7 g (63%) of the title compound as a beige solid: $^1$H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, $J$ = 14 Hz, 1H), 6.55 (d, $J$ = 14 Hz, 1H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 169.7, 130.4, 128.6.

***trans*-Ethyl-β-Bromoacrylate (3-18) (CPB-0839).** *trans*-β-Bromoacrylic acid (**3-17**) (CPB-0826) (6.6 g, 44.0 mmol) was dissolved in 65 mL absolute ethanol and $H_2SO_4$ (0.4 mL) was added. The mixture was refluxed for 24 h and cooled to rt. It was then diluted with $Et_2O$ and poured into sat. $NaHCO_3$. The aqueous layers were then extracted with $Et_2O$ and the combined organic layers were washed with water, brine, dried ($Na_2SO_4$) and concentrated. The crude oil was then purified by column chromatography (petroleum ether) to give 4.73 g (60%) of the title compound as a colorless oil: IR (NaCl): 1723, 1607 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.60 (d, $J$ = 14.0 Hz, 1H), 6.53 (d, $J$ = 14.0 Hz, 1H), 4.22 (q, $J$ = 6.8 Hz, 2H), 1.30 (t, $J$ = 6.8 Hz, 3H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 164.3, 129.1, 126.8, 61.2, 14.4.

***trans*-Ethylhex-2-en-4-ynoate (3-20) (CPB-0916).** The synthesis of the enyne was adapted from a literature procedure.[152] Propynyl magnesium bromide (0.5 M in THF, 53

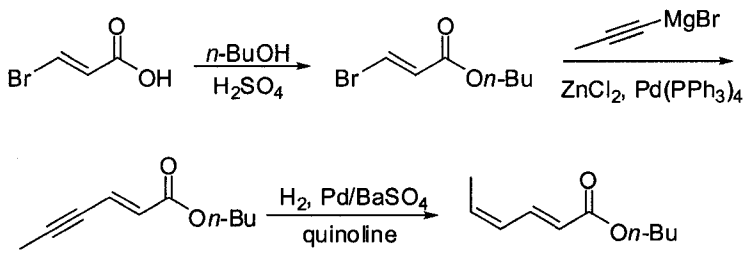
mL, 26.5 mmol) was added to a slurry of dry $ZnCl_2$ (1.8 g, 13.2 mmol) in 27 mL THF at 0 °C. After 15 min. *trans*-ethyl-β-bromoacrylate (**3-18**) (CPB-0839) (1.8 g, 10.0 mmol) in 2.7 mL THF and $Pd(Ph_3)_4$ (0.61 g, 0.53 mmol) were added sequentially, and the mixture was allowed to stir at rt for 20 h. The mixture was then poured into sat. aq. $NH_4Cl$ and was extracted with $Et_2O$. The combined organic extracts were then washed with brine and dried over $Na_2SO_4$ and concentrated. The residue was purified by column chromatography (pet. ether to 9:1 pet. ether:$Et_2O$) to give 1.26 g (92%) of the title compound as a colorless oil: IR (NaCl): 2223, 1716, 1622 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 6.73 (dq, $J$ = 16.0, 2.8 Hz, 1H), 6.14 (d, $J$ = 16.0 Hz, 1H), 4.21 (q, $J$ = 7.2 Hz, 2H), 2.03 (d, $J$ = 2.8 Hz, 3H), 1.23 (t, $J$ = 7.2 Hz, 3H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 166.4, 129.6, 126.3, 96.4, 77.3, 60.8, 14.4, 5.0.

**(2-*trans*,4-*cis*)-Ethyl-hexa-2,4-dienoate (3-22) (CPB-0907).** *trans*-Ethylhex-2-en-4-ynoate (**3-20**) (CPB-0916) (0.09 g, 0.65 mmol) was dissolved in 17 mL 1-hexene/EtOAc (1:1). The solution was degassed with Ar and 5% $Pd/BaSO_4$ (0.069 g) and quinoline (0.84 g, 6.5 mmol) was added. The Ar in the flask was then replaced with $H_2$. The reaction was then stirred under $H_2$ atmosphere (balloon) and was followed closely by GC. The reaction was stopped by filtration through a plug of silica gel when the starting material disappeared. The product was purified by column chromatography (pet. ether) to give 0.09 g (98%) of the title compound as a colorless oil: IR (NaCl): 1715, 1270, 1179, 1133 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 7.64 (dd, $J$ = 15.2, 11.6 Hz, 1H), 6.16 (tq,

$J$ = 10.4, 1.2 Hz, 1H), 5.95 (dq, $J$ = 10.4, 7.2 Hz, 1H), 5.87 (d, $J$ = 15.2 Hz, 1H), 4.22 (q, $J$ = 7.2 Hz, 2H), 1.90 (dd, $J$ = 7.2, 1.2 Hz, 3H), 1.31 (t, $J$ = 7.2 Hz, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 167.6, 139.4, 135.9, 127.6, 121.3, 60.5, 14.5, 14.3.

**Epoxide (CPB-0932).** 94% ee $[\alpha]^{25}_D$ = -50.8 (*c* 0.45, $CHCl_3$); Colorless oil; IR (NaCl): 1720, 1308 cm$^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$) δ 6.80 (dd, $J$ = 15.6, 6.6 Hz, 1H), 6.13 (dd, $J$ = 15.6, 0.9 Hz), 4.22 (q, $J$ = 7.2 Hz, 2H), 3.52 (ddd, $J$ = 6.6, 4.2, 0.9 Hz, 1H), 3.32 (qd, $J$ = 5.4, 4.5 Hz, 1H), 1.30 (t, $J$ = 7.2 Hz, 3H)1.30 (d, $J$ = 5.4 Hz, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 165.8, 142.0, 125.6, 60.8, 55.6, 55.5, 14.4, 13.4. Anal. Calcd. for $C_8H_{12}O_3$: C, 61.52; H, 7.74. Found: C, 61.73; H, 7.60.

**(Table 3.3, entry 10)**




***trans-n*-Butyl-β-bromoacrylate (3-19) (CPB-0935).** The ester was prepared according to the procedure for *trans*-ethyl-β-bromoacrylate (**3-18**) (CPB-0839) as described above (67%). Colorless oil; IR (NaCl): 1723, 1607, 1230 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.60 (d, $J$ = 14.0 Hz, 1H), 6.53 (d, $J$ = 14.0 Hz, 1H), 4.16 (t, $J$ = 6.8 Hz, 2H), 1.65 (quint,

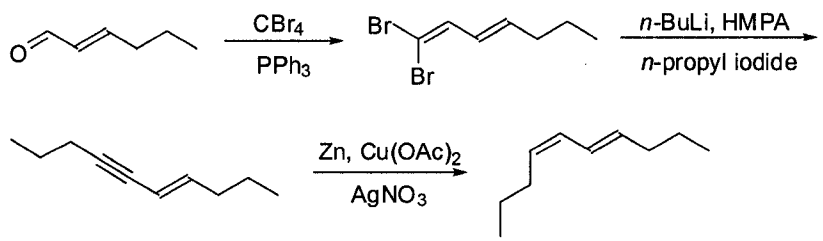
$J$ = 7.2, Hz, 2H), 1.41 (sextet, $J$ = 7.2 Hz, 2H), 0.95 (t, $J$ = 7.2 Hz, 3H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 164.4, 129.1, 126.7, 65.1, 30.8, 19.3, 13.9.

***trans-n*-Butylhex-2-en-4-ynoate (3-21) (CPB-0942).** The enyne was prepared analogously to *trans*-ethylhex-2-en-4-ynoate (**3-20**) (CPB-0916) as discussed above (91%). Colorless oil; IR (NaCl): 2222, 1716, 1622 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) δ 6.73 (dq, $J$ = 16.0, 2.4 Hz, 1H), 6.15 (d, $J$ =16.0 Hz, 1H), 4.16 (t, $J$ = 6.8 Hz, 2H), 2.03 (d, $J$ = 2.4 Hz, 3H), 1.65 (quint., $J$ = 6.8 Hz, 2H), 1.41 (sextet, $J$ = 7.2 Hz, 2H), 0.95 (t, $J$ = 7.2 Hz, 3H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 166.5, 129.7, 126.2, 96.4, 77.3, 64.7, 30.9, 19.4, 13.9, 5.0.

**(2-*trans*,4-*cis*)-*n*-Butyl-hexa-2,4-dienoate (3-23) (CPB-0943).** The diene was prepared by partial hydrogenation of *trans-n*-butylhex-2-en-4-ynoate (**3-21**) (CPB-0942) at 0 °C as described for (2-*trans*,4-*cis*)-ethyl-hexa-2,4-dienoate (**3-22**) (CPB-0907) above (82%). Colorless oil; IR (NaCl): 1716, 1638, 1270 cm$^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$) δ 7.64 (dd, $J$ = 11.7, 15.0 Hz, 1H), 6.16 (t, $J$ = 11.7 Hz, 1H), 6.00-5.90 (m, 1H), 5.88 (d, $J$ = 15.0 Hz, 1H), 4.17 (t, $J$ = 6.9 Hz, 2H), 1.98 (dd, $J$ = 7.2, 1.8 Hz, 3H), 1.70-1.60 (m, 2H), 1.50-1.38 (m, 2H), 0.96 (t, $J$ = 7.2 Hz, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 167.7, 139.4, 135.9, 127.6, 121.3, 64.4, 31.0, 19.4, 14.3, 14.0.

**Epoxide (CPB-1011).** 96% ee $[\alpha]^{25}_{D}$ = -84.0 (*c* 0.13, $CHCl_3$); Colorless oil; IR (NaCl): 1721, 1657, 1251 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 6.80 (dd, *J* = 15.6, 6.4 Hz, 1H), 6.14 (d, *J* = 15.6 Hz, 1H), 4.20-4.14 (m, 2H), 3.54-3.50 (m, 1H), 3.32 (qd, *J* = 5.6, 4.8 Hz, 1H), 1.66 (quint, *J* = 7.2 Hz, 2H), 1.40 (sextet, *J* = 7.2 Hz, 2H), 1.30 (d, *J* = 5.6 Hz, 3H), 0.95 (t, *J* = 7.2 Hz, 3H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 165.9, 141.9, 125.7, 64.7, 55.6, 55.5, 30.9, 19.4, 13.9, 13.4. Anal. Calcd. for $C_{10}H_{16}O_3$: C, 65.19 ; H, 8.75. Found: C, 65.38; H, 8.93.

**(Table 3.3, entry 11)**




***trans*-1,1-Dibromo-1,3-heptadiene (3-5) (CPB-0433).** The title compound was prepared according to the same procedure used for *trans*-1,1-dibromo-4-phenyl-1,3-butadiene (**3-3**) (CPB-0514) as discussed above (90%). Yellow oil; IR (NaCl): 1767, 1463, $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) 6.89 (d, *J* = 9.8 Hz, 1H), 6.05 (ddt, *J* = 15.2, 9.8, 1.6 Hz, 1H), 5.87 (dt, *J* = 15.2, 7.2 Hz, 1H ), 2.07 (qd, *J* = 7.2, 1.6 Hz, 2H), 1.46-1.36 (m,

1H), 0.91 (t, $J$ = 7.2 Hz, 3H); δ $^{13}$C NMR (101 MHz, $CDCl_3$) δ 139.5, 137.4, 127.5, 88.6, 35.2, 22.2, 13.9.

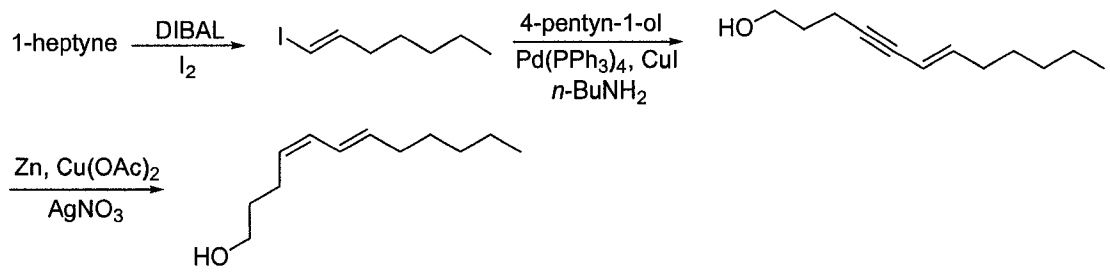
***trans*-Dec-4-en-6-yne (3-8) (CPB-0546).** The title compound was prepared according to the same procedure used for *trans*-1-phenyl-1-penten-3-yne (**3-6**) (CPB-0444) above (76%). Colorless oil; IR (NaCl): 2220, 1463 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) δ 6.06 (dt, $J$ = 15.6, 7.2 Hz, 1H), 5.45 (dquint, $J$ = 15.6, 2.0 Hz, 1H), 2.27 (td, $J$ = 7.2, 2.0 Hz, 2H), 2.05 (qd, $J$ = 6.9, 2.0 Hz, 2H), 1.60-1.51 (m, 2H), 1.46-1.37 (m, 2H), 1.00 (t, $J$ = 7.2 Hz, 3H), 0.95 (t, $J$ = 7.2 Hz, 3H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 143.4, 110.2, 88.7, 79.5, 35.2, 22.5, 22.3, 21.6, 13.83, 13.76.

**(4-*trans*,6-*cis*)-4,6-Decadiene (3-11) (CPB-0606).** The title compound was prepared according to the same procedure used for (1-*trans*,3-*cis*)-1-phenyl-1,3-pentadiene (**3-9**) (CPB-0449) above (60%). Colorless oil; IR (NaCl): 1464, cm$^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$) δ 6.30 (dd, $J$ = 15, 10.8 Hz, 1H), 5.96 (t, $J$ = 10.8 Hz, 1H), 5.65 (dt, $J$ = 15, 6.9 Hz, 1H), 5.30 (dt, $J$ = 10.8, 7.5 Hz, 1H), 2.20-2.00 (m, 4H), 1.50-1.15 (m, 4H), 1.00-0.80 (m, 6H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 134.6, 130.1, 129.0, 126.0, 35.2, 29.9, 23.1, 22.8, 14.0, 13.9.

**Epoxide (CPB-0635).** 78% ee $[\alpha]^{25}_D$= -18.3 (*c* 0.42, $CHCl_3$); Colorless oil; IR (NaCl): 1465, 1380 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) δ 5.89 (dt, $J$ = 15.6, 6.8 Hz, 1H), 5.26 (m, 1H), 3.33 (dd, $J$ = 8.4, 4.4 Hz, 1H), 3.02 (m, 1H), 2.03 (dt, $J$ = 8.0, 6.8 Hz, 2H), 1.56-1.35

(m, 6H), 0.92 (t, $J$ = 7.2 Hz, 3H), 0.87 (t, $J$ = 7.2 Hz, 3H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 138.1, 124.5, 58.9, 57.4, 34.9, 30.2, 22.4, 19.9, 14.2, 13.8. Anal. Calcd. for $C_{10}H_{18}O$: C, 77.87; H, 11.76. Found: C, 77.86; H, 11.82.

**(Table 3.3, entry 12)**




***trans*-1-Iodo-1-heptene (3-37) (CPB-2503).** The title compound was prepared according to a literature procedure.[154] To a solution of 1-heptyne (9.6 g, 100 mmol) in 20 mL hexanes was added diisobutyl aluminum hydride (1.5 M in toluene, 66.7 mL, 100 mmol) with stirring slowly at rt. The reaction mixture was then heated at 50 °C for 2 h. Most of the solvent was then distilled off and 40 mL THF was added to the residue. This mixture was cooled to -78 °C and then $I_2$ (25.4 g, 100 mmol) in 40 mL THF was added with stirring at -78 °C. The mixture was allowed to gradually warm to rt and then 20% aq. $H_2SO_4$ was slowly added until gas evolution ceased. The mixture was then poured into 20% aq. $H_2SO_4$/ice mixture and was extracted with hexanes. The combined organic extracts were then washed with sat. aq. $Na_2S_2O_3$, sat. aq. $NaHCO_3$, brine, dried ($Na_2SO_4$), and concentrated. The residue was then distilled (bp 65-67 °C @ 4mmHg) to yield 12.1 g

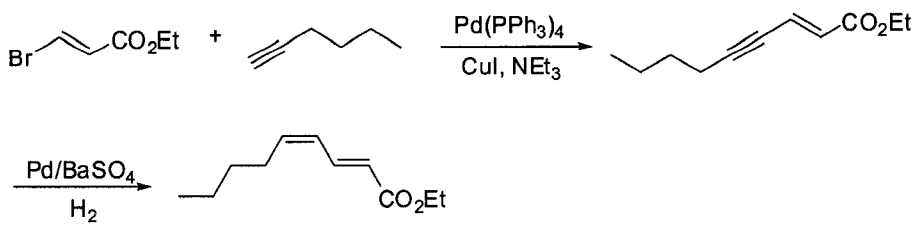
(54%) of the title compound as a colorless oil: IR (NaCl): 2927, 1606, 1465, 940 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 6.52 (dt, $J$ = 14.0, 6.8 Hz, 1H), 5.98 (dt, $J$ = 14.0, 1.2 Hz, 1H), 2.05 (qd, $J$ = 7.2, 1.2 Hz, 2H), 1.44-1.22 (m, 6H), 0.89 (t, $J$ = 7.2 Hz, 3H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 147.0, 74.5, 36.2, 31.3, 28.2, 22.6, 14.2.

***trans*-Dodec-6-en-4-yn-1-ol (3-38) (CPB-2507).** The enyne was prepared based on an adapted literature procedure.[155] $Pd(PPh_3)_4$ (0.38 g, 0.325 mmol) was added at rt to a solution of *trans*-1-iodo-1-heptene (**3-37**) (CPB-2503) (3.39 g, 15.1 mmol) in benzene (16 mL) under Ar and was stirred for 45 min. A solution of 4-pentyn-1-ol (0.64 g, 7.56 mmol) in *n*-$BuNH_2$ (8 mL, 80 mmol) was then added followed by CuI (0.24 g, 1.24 mmol). After stirring overnight at rt $Et_2O$ (20 mL) was added and the mixture was poured into sat. aq. $NH_4Cl$ and was extracted with more $Et_2O$. The combined organic extracts were washed with sat. aq. $NH_4Cl$, $H_2O$, brine, dried ($Na_2SO_4$), and filtered. The residue was then concentrated and purified by column (1:1 hexanes/$Et_2O$) to give 1.20 g (88%) of the title compound as a yellow oil: IR (NaCl): 3344, 2218, 1059 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 6.07 (dt, $J$ = 15.8, 7.0 Hz, 1H), 5.45 (dquint., $J$ = 15.8, 1.8 Hz, 1H), 3.77 (td, $J$ = 6.2, 5.6 Hz, 2H), 2.43 (td, $J$ = 7.0, 2.0 Hz, 2H), 2.08 (qd, $J$ = 7.6, 1.2 Hz, 2H), 1.79 (quint, $J$ = 6.4 Hz, 1H), 1.54-1.49 (m, 1H), 1.42-1.21 (m, 6H), 0.89 (t, $J$ = 6.8 Hz, 3H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 144.2, 109.7, 87.7, 80.1, 62.1, 33.2, 31.6, 31.5, 28.7, 22.7, 16.2, 14.2.

**(4-*cis*,6-*trans*)-4,6-Dodecadien-1-ol (3-39) (CPB-2508).** Prepared via activated zinc reduction of *trans*-dodec-6-en-4-yn-1-ol (**3-38**) (CPB-2507) according to the same procedure used for (1-*trans*,3-*cis*)-1-phenyl-1,3-pentadiene (**3-9**) (CPB-0449) as discussed above with the following exceptions: twice the usual amount of activated zinc was used, and the reaction took 42 h to complete (72%). Colorless oil; IR (NaCl): 3333, 1456, 1059 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 6.32 (ddd, $J$ = 14.8, 10.8, 1.2 Hz, 1H), 5.99 (t, $J$ = 10.8 Hz, 1H), 5.69 (dt, $J$ = 14.8, 7.2 Hz, 1H), 5.31 (dt, 10.8, 7.6 Hz, 1H), 3.67 (t, $J$ = 6.4 Hz, 2H), 2.27 (q, $J$ = 7.6 Hz, 2H), 2.10 (q, J = 6.8 Hz, 2H) 1.67 (quint., 7.2 Hz, 2H), 1.48-1.25 (m, 6H), 0.90 (t, $J$ = 7.2 Hz, 3H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 135.6, 129.6, 128.9, 125.5, 62.7, 33.1, 32.7, 31.6, 29.3, 24.2, 22.7, 14.3.

**Epoxide (CPB-2514).** 89% ee $[\alpha]^{25}_D$ = -16.0 (*c*, 0.74 $CHCl_3$); Colorless oil; IR (NaCl): 3420, 1456, 1062 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 5.96 (dt, $J$ = 15.2, 6.8 Hz, 1H), 5.32 (ddt, $J$ = 15.2, 8.0, 1.2 Hz, 1H), 3.77-3.64 (m, 2H), 3.42 (dd, $J$ = 8.0, 4.4 Hz, 1H), 3.12-3.07 (m, 1H), 2.09 (qd, $J$ = 6.8, 1.2 Hz, 2H), 1.82-1.58 (m, 4H), 1.44-1.24 (m, 6H), 0.89 (t, $J$ = 7.2 Hz, 3H); $^{13}C$ NMR (100 MHz, $CDCl_3$) δ 138.8, 123.9, 62.6, 58.8, 57.7, 32.8, 31.5, 29.7, 28.9, 24.8, 22.7, 14.3. HRMS calcd. for $C_{12}H_{22}O_2$ (M + 1): 199.1698; Found: 199.1699.

**(Table 3.3, entry 13)**



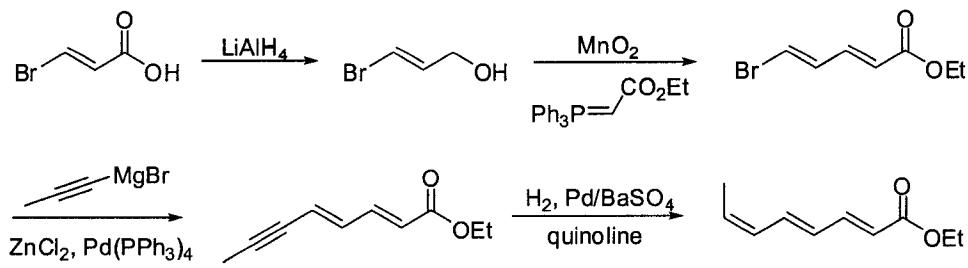

***trans*-Ethylnon-2-en-4-ynoate (3-25) (CPB-1048).** The title compound was prepared base on a literature method.[152] *trans*-Ethyl-β-bromoacrylate (**3-18**) (CPB-0839) (4.0 g, 22.4 mmol) and 1-hexyne (2.1 g, 25.6 mmol), were sequentially added to a suspension of $Pd(PPh_3)_4$ (1.3 g, 1.1 mmol), CuI (0.64 g, 3.4 mmol), and $Et_3N$ (8.7 g, 85.3 mmol) in benzene (52 mL) at 0 °C. The mixture was allowed to warm to rt and was stirred overnight. It was then diluted with petroleum ether and poured, into sat. aq. $NH_4Cl$. The $H_2O$ layer was extracted with petroleum ether and the organic layers were washed with $H_2O$, brine, dried ($Na_2SO_4$) and concentrated. The residue was then purified by column chromatography (pet. ether to 9:1 pet. ether:$Et_2O$) to give 3.14 g (78%) of the title compound as a yellow oil: IR (NaCl): 2215, 1717, 1621, 1301, 1157 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 6.75 (dt, $J$ = 15.9, 2.1 Hz, 1H), 6.15 (d, $J$ = 15.9 Hz, 1H), 4.21 (q, $J$ = 7.2 Hz, 2H), 2.38 (td, $J$ = 6.9, 2.1 Hz, 2H), 1.58-1.39 (m, 4H), 1.30 (t, $J$ = 7.2 Hz, 3H), 0.93 (t, $J$ = 7.2 Hz, 3H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 166.4, 129.5, 126.3, 101.0, 78.1, 60.8, 30.6, 22.2, 19.7, 14.4, 13.8.

**(2-*trans*,4-*cis*)-Ethyl-2,4-nonadieneoate (3-26) (CPB-1104).** *trans*-Ethylnon-2-en-4-ynoate (**3-25**) (CPB-1048) (1.0 g, 5.6 mmol) was dissolved in 136 mL 1-hexene/EtOAc

(1:1, v/v). The solution was degassed with Ar and 5% $Pd/BaSO_4$ (0.59 g, 0.28 mmol) and quinoline (6.6 mL, 56.0 mmol) was added. The Ar in the flask was then replaced with $H_2$. The reaction was stirred under $H_2$ (balloon) and was followed closely by GC. The reaction was stopped by filtration through a plug of silica gel when the starting material had disappeared. The product was purified by column chromatography (pet. ether to 9:1 pet. ether:$Et_2O$). An inseparable mixture of the desired diene (0.92 g, ~60%) and a monounsaturated overreduction product was obtained as a colorless oil: IR (NaCl): 1717, 1637, 1269, 1176 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.62 (ddd, $J$ = 15.2, 11.6, 0.8 Hz, 1H), 6.13 (t, $J$ = 11.6 Hz, 1H), 5.89-5.79 (m, 2H), 4.22 (q, $J$ = 7.2 Hz, 2H), 2.32 (q, $J$ = 7.6 Hz, 2H), 1.48-1.27 (m, 7H), 0.91 (t, $J$ = 7.2 Hz, 3H).

**Epoxide (CPB-1115).** 85% ee $[\alpha]^{25}_D$ = -25.9 (*c* 0.70, $CHCl_3$); Colorless oil; IR (NaCl): 1720, 1656 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 6.82 (dd, $J$ = 16.0, 6.8 Hz, 1H), 6.13 (d, $J$ = 16.0 Hz, 1H), 4.22 (q, $J$ = 6.8 Hz, 2H), 3.52 (dd, $J$ = 6.8, 4.4 Hz, 1H), 3.22-3.16 (m, 1H), 1.62-1.22 (m, 6H), 1.31 (t, 7.2 Hz, 3H), 0.92 (t, $J$ = 7.2 Hz 3H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 165.8, 142.3, 125.5, 60.8, 60.0, 55.4, 28.6, 27.5, 22.6, 14.4, 14.2. Anal. Calcd. for $C_{11}H_{18}O_3$: C, 66.64 ; H, 9.15. Found: C, 66.60; H, 9.00.

**(Table 3.3, entry 14)**




***trans*-3-Bromo-2-propen-1-ol (3-33) (CPB-0830).** The alcohol was prepared according to a literature procedure.[153] A solution of *trans*-β-bromoacrylic acid (**3-17**) (CPB-0826) (8.45 g, 56.0 mmol) in 46 mL $Et_2O$ was added dropwise to a stirred mixture of $LiAlH_4$ in 170 mL $Et_2O$ under Ar at 0 °C. The mixture was allowed to warm to rt and was stirred overnight. The reaction was then quenched at 0 °C by addition of 0.24 mL $H_2O$, 0.24 mL 15% aq. NaOH, and 7.2 mL $H_2O$ sequentially. It was then filtered through Celite and the filtrate was washed with $NaHCO_3$, brine, dried ($Na_2SO_4$), and concentrated to give 2.52 g (33%) of the title compound as a beige oil: IR (NaCl): 3333, 1622 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 6.38 (m, 2H) 4.14 (m, 2H), 1.57 (s, 1H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 136.7, 108.1, 63.2.

***trans,trans*-Ethyl-5-bromo-penta-2,4-dienoate (3-34) (CPB-0846).** The ester was prepared according to a literature procedure.[153] To a solution of *trans*-3-bromo-2-propen-1-ol (**3-33**) (CPB-0830) (2.52 g, 18.4 mmol) in 552 mL $CH_2Cl_2$ was added $MnO_2$ (16.0 g, 184 mmol) and (carbethoxymethylene)triphenylphosphorane (7.67 g, 22.0 mmol) with stirring under Ar at rt. The mixture was stirred for 24 h at rt and then the solvent was

removed. The residue was repeatedly triturated with pet. ether and the pet. ether solution was concentrated. The residue was purified by column (pet. ether to 95:5 pet. ether/$Et_2O$) to give 1.85 g of the desired product and 0.38 g of the product as a mixture of geometrical isomers (59% total, colorless oils). About a 6:1 E/Z ratio was observed, but the geometrical isomers could be mostly separated during column chromatography: IR (NaCl): 1713, 1631 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 7.17 (dd, $J$ = 15.3, 10.2 Hz, 1H), 6.90-6.74 (m, 2H), 5.93 (d, $J$ = 15.3 Hz, 1H), 4.22 (q, $J$ = 7.2 Hz, 2H), 1.31 (t, $J$ = 7.5 Hz, 3H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 166.7, 141.2, 135.6, 122.5, 117.9, 60.8, 14.4.

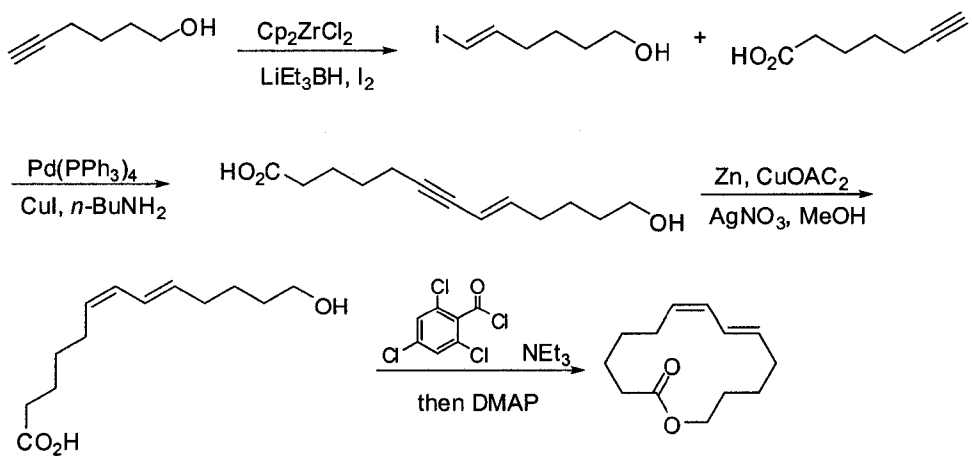
***trans,trans*-Ethyl-octa-2,4-dien-6-ynoate (3-35) (CPB-0911).** The dienyne was prepared analogously to *trans*-ethylhex-2-en-4-ynoate (**3-20**) (CPB-0916) as discussed above (78%). Yellow oil; IR (NaCl): 2216, 1713, 1625 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.25 (dd, $J$ = 15.2, 11.2 Hz, 1H), 6.58 (dd, $J$ = 15.2, 11.2 Hz, 1H), 5.93 (m, 2H), 4.20 (q, $J$ = 7.2 Hz, 2H), 2.02 (d, $J$ = 2.4 Hz, 3H), 1.30 (t, $J$ = 7.2 Hz, 3H) ; $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 166.9, 143.5, 137.9, 122.5, 120.5, 93.6, 78.9, 60.7, 14.5, 4.9.

**(2-*trans*,4-*trans*,6-*cis*)-Ethyl-octa-2,4,6-trienoate (3-36) (CPB-0930).** The triene was synthesized by partial hydrogenation of *trans,trans*-ethyl-octa-2,4-dien-6-ynoate (**3-35**) (CPB-0911) as described for (2-*trans*,4-*cis*)-ethyl-hexa-2,4-dienoate (**3-22**) (CPB-0907) except that the reaction was run at 0 °C (87%). White solid; IR (NaCl): 1712, 1617, 1140 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 7.37 (dd, $J$ = 15.3, 11.4, 1H), 6.88 (dd, $J$ = 14.7,

11.4 Hz, 1H), 6.30 (dd, $J$ = 14.7, 11.4 Hz, 1H) 6.12 (td, $J$ = 10.8, 1.5 Hz, 1H), 5.87 (d, $J$ = 15.3 Hz, 1H), 5.77 (dq, $J$ = 10.5, 7.2 Hz, 1H), 4.21 (q, $J$ = 7.14 Hz, 2H), 1.84 (dd, $J$ = 7.2, 1.8 Hz, 3H), 1.31 (t, $J$ = 7.2 Hz, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 167.4, 145.0, 135.8, 131.9, 129.8, 129.1, 120.8, 60.5, 14.5, 14.0.

**Epoxide (CPB-0940).** 94% ee $[\alpha]^{25}_D$ = -41.2 (*c* 1.7, $CHCl_3$); Colorless oil; IR (NaCl): 1713, 1643, 1232, 1136 $cm^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$) δ 7.29 (dd, $J$ = 15.3, 11.1 Hz, 1H), 6.52 (dd, $J$ = 15.0, 11.1 Hz, 1H), 5.96 (dd, $J$ = 15.6, 6.9 Hz, 1H), 5.93 (d, $J$ = 15.9 Hz, 1H), 4.21 (q, $J$ = 7.2 Hz, 2H), 3.48 (dd, $J$ = 6.9, 4.5 Hz, 1H), 3.29 (qd., $J$ = 5.4, 4.5 Hz, 1H), 1.30 (t, $J$ = 7.2 Hz, 3H), 1.29 (d, $J$ = 5.4 Hz, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 167.0, 143.0, 136.1, 132.8, 122.4, 60.6, 56.5, 55.6, 14.5, 13.5. HRMS Calcd. for $C_{10}H_{14}O_3$ (M +): 182.0943. Found: 182.0940.

**(Table 3.3, entry 15)**



***trans*-6-Iodohex-5-en-1-ol (3-40) (CPB-3013).** The title compound was prepared according to a literature procedure.[156] To 5-hexyn-1-ol (5.0 g, 51 mmol) was added $LiEt_3BH$ (1.0 M in THF, 51 mL, 51 mmol) slowly at 0 °C with stirring. To a separate flask was added $Cp_2ZrCl_2$ (29.8 g, 102 mmol) and 430 mL THF. To this solution was added $LiEt_3BH$ (1.0 M in THF, 102 mL, 102 mmol) slowly at rt with stirring. The mixture was stirred shielded from light for 1 h at rt after which time the 5-hexyn-1-ol solution from above was added via cannula. After stirring at rt for about 20 min the mixture became a clear yellow solution, and $I_2$ (28.7 g, 113 mmol) was added. After stirring for another 20 min at rt the mixture was poured into sat. aq. $NaHCO_3$. The phases were separated and the aqueous phase was extracted with $Et_2O$. The combined organic phases were then washed with sat. aq. $Na_2S_2O_3$, water, brine, dried ($Na_2SO_4$), filtered, and concentrated to give a quantitative yield of the title compound as a yellow oil which was taken on to the next step without further purification: IR (NaCl): 3338, 1456, 1333, 1065, 949 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 6.49 (dt, $J$ = 14.4, 7.2 Hz, 1H), 5.98 (d, $J$ = 14.4 Hz, 1H), 3.62 (q, $J$ = 6.0 Hz, 2H), 2.07 (q, $J$ = 7.2 Hz, 2H), 1.61-1.36 (m, 4H), 1.24 (t, $J$ = 5.2 Hz, 1H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 146.4, 75.0, 62.8, 35.9, 32.1, 24.7.

***trans*-13-Hydroxytridec-8-en-6-ynoic acid (3-41) (CPB-3030).** The title compound was prepared according to the same procedure used for *trans*-dodec-6-en-4-yn-1-ol (**3-38**)

(CPB-2507). To a solution of *trans*-6-iodohex-5-en-1-ol (**3-40**) (CPB-3013) (5.11 g, 22.6 mmol) in 24 mL benzene was added $Pd(PPh_3)_4$ (0.57 g, 0.49 mmol) and 6-heptynoic acid at rt with stirring. *n*-Butylamine (11.2 ml) and CuI (0.34 g, 1.8 mmol) were then added sequentially and the mixture was stirred at rt overnight. The solvent was then evaporated and the residue was dissolved in EtOAc. The solution was then washed with 10% aq. HCl until the organic phase became acidic. The organic phase was then washed with water, brine, dried ($Na_2SO_4$), filtered and concentrated. The residue was purified by column (1:1 hexanes/$Et_2O$ to $Et_2O$) to give 1.89 g (75%) of the title compound as a brown solid which was taken on to the next step directly. Relatively pure material was obtained by recrystallization of the product from $CH_2Cl_2$/hexanes giving a beige solid: IR (NaCl): 3338, 2215, 1694 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.28-6.20 (brs, 2H), 6.04 (dt, $J$ = 15.6, 7.2 Hz, 1H), 5.46 (d, $J$ = 15.6 Hz, 1H), 3.65 (t, 6.8 Hz, 2H), 2.38 (t, $J$ = 7.2 Hz, 2H), 2.32 (td, $J$ = 6.8, 1.6 Hz, 2H), 2.12 (q, $J$ = 6.8 Hz, 2H), 1.80-1.70 (m, 2H), 1.58 (quint, 7.2 Hz, 4H), 1.51-1.41 (m, 2H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 179.4, 143.2, 110.3, 88.2, 79.7, 62.8, 33.7, 32.8, 32.1, 28.2, 25.1, 24.0, 19.2.

**(6-*cis*-8-*trans*)-13-Hydroxytrideca-6,8-dienoic acid (3-42) (CPB-3033).** The diene was prepared by activated Zn reduction of *trans*-13-hydroxytridec-8-en-6-ynoic acid (**3-41**) (CPB-3030) according to the procedure used for (1-*trans*,3-*cis*)-1-phenyl-1,3-pentadiene (**3-9**) (CPB-0449) as described previously but with 142 eq. Zn instead of 50 eq. Also, the filtrate was acidified to ~pH 2 by addition of 1M HCl after filtration. No other

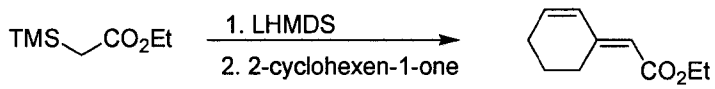
purification was done. Yield (78%) Yellow oil; IR (NaCl): 3331, 1709, 1457, 1410 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 6.30 (dd, $J$ = 15.2, 10.8 Hz, 1 H), 5.97 (t, $J$ = 10.8 Hz, 1H), 5.66 (dt, $J$ = 15.2, 7.0 Hz, 1H), 5.30 (dt, $J$ = 10.8, 7.6, Hz, 1H), 3.66 (t, $J$ = 6.4 Hz, 2H), 2.36 (t, 7.4 Hz, 2H), 2.22-2.10 (m, 4H), 1.69-1.40 (m, 8H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 178.7, 134.4, 129.5, 129.4, 126.2, 63.1, 33.9, 32.6, 32.2, 29.2, 27.4, 25.5, 24.5.

**7-*cis*-9-*trans*-Oxacyclotetradeca-7,9-dien-2-one (3-43) (CPB-3035).** The title compound was prepared based on a literature procedure.[157] To a solution of (6-*cis*-8-*trans*)-13-hydroxytrideca-6,8-dienoic acid (**3-42**) (CPB-3033) (1.48 g, 6.54 mmol) and triethylamine (1.0 mL, 7.2 mmol) in 65 mL THF was added 2,4,6-trichlorobenzoylchloride (1.60 g, 6.54 mmol). The mixture was stirred at rt for 2 h and was then filtered through a cotton plug to remove triethylammonium chloride while washing with $Et_2O$. The solvents were then removed and the residue was dissolved in 2335 mL toluene. This solution was then added to a refluxing solution of DMAP (3.42 g, 28.0 mmol) in 467 mL toluene over 8 h via addition funnel. After the addition was complete the solvent was removed and the residue was dissolved in $Et_2O$ and was washed with 3% aq. HCl, water, sat. aq. $NaHCO_3$, water, brine, dried ($Na_2SO_4$), and concentrated. The residue was then purified by column (95:5 to 80:20 hexanes/$Et_2O$) to yield 0.90 g (67%) of the title compound as a white solid: mp 56-58 °C; IR (NaCl): 1732, 1462 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 6.43-6.34 (m, 1H), 6.03 (t, $J$ = 10.2 Hz, 1H), 5.67 (dt, $J$ = 15.6, 5.2 Hz, 1H), 5.49 (dt, $J$ = 10.2, 8.4 Hz, 1H), 4.19 (t, $J$ = 4.8 Hz, 2H), 2.44 (t, $J$ = 6.8

Hz, 2H), 2.22 (q, $J$ = 5.2 Hz, 2H), 2.14 (q, $J$ = 8.4 Hz, 2H), 1.81-1.68 (m, 4H), 1.65-1.57 (m, 2H), 1.47-1.38 (m, 2H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 173.9, 132.0, 130.0, 129.0, 125.1, 64.6, 32.5, 29.8, 28.1, 27.8, 25.4, 24.1, 23.7.

**Epoxide (CPB-3041).** 75% ee $[\alpha]_D^{25}$ = -44.5 (*c* 0.58, $CHCl_3$); White solid; mp: 52-54 °C; IR (NaCl): 1724, 1456 $cm^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) δ 5.94 (dt, 15.6, 6.4 Hz, 1H), 5.40 (dd, $J$ = 15.6, 7.2 Hz, 1H), 4.67 (dt, $J$ = 10.8, 3.6 Hz, 1H), 3.64 (quint, 5.2 Hz, 1H), 3.40 (dd, $J$ = 7.2, 4.4 Hz, 1H), 3.07 (quint, $J$ = 4.4 Hz, 1H), 2.43-2.24 (m, 3H), 2.02-1.94 (m, 1H), 1.92-1.76 (m, 2H), 1.68-1.42 (m, 6H), 1.38-1.24 (m, 2H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 173.6, 136.2, 124.9, 64.3, 58.3, 56.3, 33.2, 30.0, 27.8, 27.4, 25.9, 24.8, 23.8. HRMS Calcd for $C_{13}H_{20}O_3$: 225.1491. Found: 225.1489.

**(Table 3.3, entry 16)**

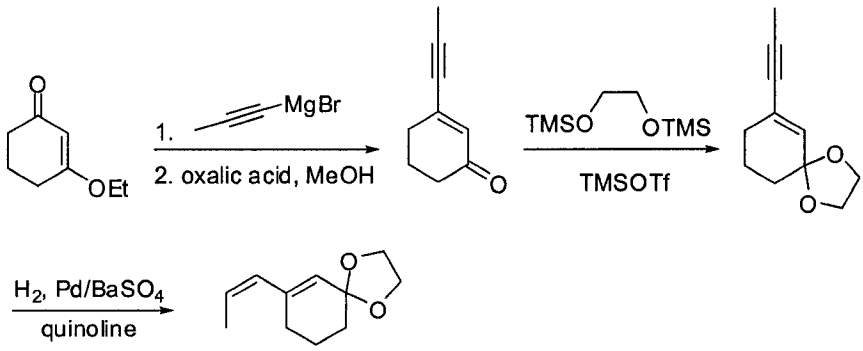



**(*E*)-Carbethoxymethylidenecyclohex-2-ene (3-44) (CPB-0321).** The title compound was prepared based on an adapted literature procedure.[158] To a solution of lithium bistrimethylsilylamide (1M in THF) (50 mL, 50.0 mmol) in 200 mL THF at -78 °C was slowly added ethyltrimethylsilylacetate (8.0 g, 50.0 mmol), and the solution was stirred for 15 minutes. 2-Cyclohexen-1-one (2.1 g 22.0 mmol) in THF (40 ml) was added dropwise and the mixture was stirred at -78 °C for one hour followed by an hour at -25 °C,

and 10 hours at rt (the rxn was followed by TLC, Hex/AcOEt 7:1). The reaction was then quenched with sat. aq. $NH_4Cl$, the aqueous layer was extracted with ether, and the combined organic phases were dried ($Na_2SO_4$) and concentrated. The yellow oil was then distilled (bp 90-94 °C at 4mm Hg) to give 1.8 g (49%) of the title compound, exclusively as the *E* isomer as confirmed by NOE, as a colorless oil: IR (NaCl): 1709, 1624, 1604 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 6.20 (dt, $J$ = 9.3, 3.9 Hz, 1H), 6.10 (dt, $J$ = 9.3, 1.8 Hz, 1H), 5.56 (s, 1H), 4.14 (q, $J$ = 7.2 Hz, 2H), 2.96 (m, 2H), 2.19 (m, 2H), 1.72 (m, 2H), 1.27 (t, $J$ = 7.2 Hz, 3H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 167.27, 154.01, 138.03, 130.39, 115.12, 59.82, 26.69, 25.96, 22.12, 14.73.

**Epoxide (CPB-1203).** Colorless oil; IR (NaCl): 1643, 1443, 1382 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 6.00 (s, 1H), 4.16 (q, $J$ = 7.2 Hz, 2H), 3.46 (m, 1H), 3.34 (d, $J$ = 4.2 Hz, 1H), 2.94 (ddd, $J$ = 17.7, 5.1, 4.8 Hz, 1H), 2.58-2.46 (m, 1H), 2.18-2.08 (m, 1H), 1.87-1.77 (m, 1H), 1.70-1.56 (m, 1H), 1.52-1.41 (m, 1H), 1.28 (t, $J$ = 6.9 Hz, 3H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 165.6, 154.4, 121.1, 60.2, 56.0, 54.8, 25.4, 23.9, 17.7, 14.6. Anal. Calcd. for $C_{10}H_{14}O_3$: C, 65.91; H, 7.74. Found: C, 66.14; H, 7.74.

**(Table 3.3, entry 17)**




**3-Prop-1-ynyl-cyclohexen-2-one (3-45) (CPB-0704).** This compound was prepared according to known literature procedure.[159] To a flame-dried flask was added propynyl magnesium bromide (0.5 M in THF, 56 mL, 28.0 mmol) under Ar. To this was added 3-ethoxycyclohexen-2-one (3.5 g, 25 mmol) in 5 mL THF dropwise with stirring. The mixture was heated to reflux and was stirred for 30 min. It was then cooled to rt and poured into cold sat. aq. $NH_4Cl$ (30 mL). It was then extracted with $Et_2O$, dried ($Na_2SO_4$), and concentrated yielding a pale yellow solid. This solid was then dissolved in MeOH and 4 mL sat. aq. oxalic acid was added and the mixture was stirred at rt for 2 h. The MeOH was then evaporated and the residue was dissolved in $CH_2Cl_2$ (20 mL). It was washed with water, brine, dried ($Na_2SO_4$), and concentrated. The residue was purified by column chromatography (9:1 pet. ether:$Et_2O$ ) to give 3.14 g (94%) of the title compound as a yellow oil: IR (NaCl): 2225, 1668, 1590 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 6.14 (s, 1H), 2.44-2.37 (m, 4H), 2.06 (s, 3H), 2.01 (quint., $J$ = 6.0 Hz, 2H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 199.3, 144.8, 132.2, 98.0, 79.8, 37.5, 31.0, 22.8, 5.1.

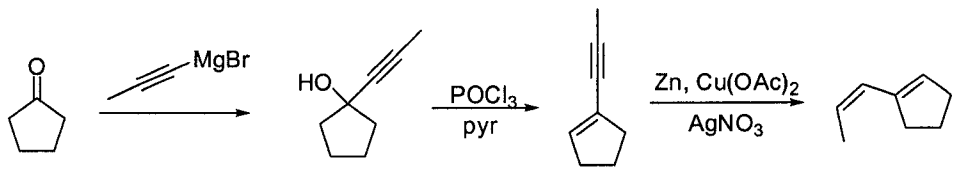
**7-Prop-1-ynyl-1,4-dioxa-spiro[4.5]dec-6-ene (3-46) (CPB-0713).** This compound was prepared based on a literature procedure.[160] To a stirred solution of TMSOTf (0.028 g, 0.125 mmol) in 2.5 mL $CH_2Cl_2$ at -78 °C was added 1,2-bistrimethylsiloxy ethane (10.32 g, 50 mmol) and 3-prop-1-ynyl-cyclohexen-2-one (**3-45**) (CPB-0704) successively with stirring under Ar. After 20 h the reaction was quenched by addition of pyridine (2 drops). The mixture was then poured into sat. aq. $NaHCO_3$ and was extracted with $Et_2O$. The combined organic fractions were dried ($Na_2SO_4$), filtered, and concentrated. The residue was purified by column (pet. ether to 9:1 pet. ether/$Et_2O$) to give 2.53 g (57%) of the title compound as a colorless oil: IR (NaCl): 2225, 1633 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 5.80 (s, 1H), 4.02-3.40 (m, 4H), 2.16-2.10 (m, 2H), 1.95 (s, 3H), 1.81-1.76 (m, 4H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 131.3, 126.8, 105.9, 86.6, 80.1, 64.8, 33.2, 29.8, 20.9, 4.5.

***cis*-7-Prop-1-enyl-1,4-dioxa-spiro[4.5]dec-6-ene (3-47) (CPB-0716):** To a solution of 7-prop-1-ynyl-1,4-dioxa-spiro[4.5]dec-6-ene (**3-46**) (CPB-0713) (0.15 g, 0.84 mmol) in acetone (11 mL) was added 1-hexene (11 mL) and quinoline (1.08 g, 8.40 mmol). Air was removed from the system and replaced with Ar, and then Pd/$BaSO_4$ (5%, 0.089 g, 0.042 mmol) was added. The Ar was removed and replaced with $H_2$ and the mixture was stirred vigorously while being followed closely by GC. After five minutes all of the starting material had reacted. The mixture was then filtered through a pad of celite. The remaining solution was concentrated and purified by column chromatography (the silica

gel was buffered with 1% $Et_3N$, petroleum ether to 9:1 petroleum ether/$Et_2O$) to give 0.12 g (79%) of the title compound as a colorless oil: IR (NaCl): 1439, 1177 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 5.78 (d, $J$ = 11.6 Hz, 1H), 5.61-5.52 (m, 1H), 5.48 (s, 1H), 4.06-3.94 (m, 4H), 2.20-2.14 (m, 2H), 1.86-1.80 (m, 7H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 140.9, 131.1, 126.8, 125.9, 106.8, 64.7, 33.4, 29.3, 21.3, 15.2.

**Epoxide (CPB-0743).** 93% ee $[\alpha]^{25}_D$ = -30.0 (*c* 0.73, $CHCl_3$); Colorless oil; IR (NaCl): 1181, 1088 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 5.58 (s, 1H), 4.40-3.92 (m, 4H), 3.35 (d, $J$ = 4.0 Hz, 1H), 3.22-3.16 (m, 1H), 2.14-1.76 (m, 6H), 1.18 (d, $J$ = 5.2 Hz, 3H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 138.0, 124.0, 106.0, 64.8, 64.7, 57.7, 54.4, 34.0, 26.3, 21.0, 12.5. Anal. Calcd. for $C_{11}H_{16}O_3$: C, 67.32; H, 8.22. Found: C, 67.44; H, 8.12.

**(Table 3.3, entry 18)**




**1-Prop-1-ynylcyclopentanol (CPB-0722).** To a flame-dried flask was added 1-propynylmagnesium bromide (0.5 M in THF, 108 mL, 54.0 mmol) under Ar. To this cyclopentanone (4.0 g, 48.0 mmol) in 10 mL THF was added slowly with stirring. The mixture was refluxed for 30 min. and then cooled to rt at which point it was poured into sat. aq. $NH_4Cl$. It was then extracted with ether, dried, and concentrated to yield 6.19 g

(quantitative, crude) of the title compound as a yellow oil. The compound was taken on to the next step without further purification: IR (NaCl): 3377, 2242 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 3.80-3.70 (m, 1H), 1.92-1.68 (m, 11 H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 83.3, 79.3, 74.9, 42.6, 23.6, 3.8.

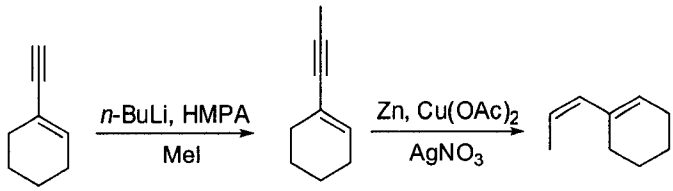
**1-Prop-1-ynyl-cyclopentene (3-48) (CPB-0726).** The enyne was prepared according to the same procedure used for 1-hex-1-ynyl-cyclohexene (**3-55**) (CPB-0711) below (48%). Colorless oil; IR (NaCl): 1443 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 5.94 (s, 1H), 2.41 (m, 4H), 1.98 (s, 3H), 1.89 (quint., $J$ = 7.8 Hz, 2H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 136.2, 125.2, 87.0, 36.7, 33.2, 23.5, 4.6.

***cis*-1-Prop-1-enylcyclopentene (3-50) (CPB-0729).** The diene was prepared via activated zinc reduction of 1-prop-1-ynyl-cyclopentene (**3-48**) (CPB-0726) according to the same procedure used for (1-*trans*,3-*cis*)-1-phenyl-1,3-pentadiene (**3-9**) (CPB-0449) (43%). Colorless oil: IR (NaCl): 1444 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 6.04 (d, $J$ = 11.7 Hz, 1H), 5.67 (s, 1H), 5.46 (dq, $J$ = 11.7, 7.5 Hz, 1H), 2.64-2.56 (m, 2H), 2.42-2.32 (m, 2H), 1.92 (quint., $J$ = 7.8 Hz, 2H), 1.84 (d, $J$ = 7.5 Hz, 3H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 141.9, 131.2, 126.6, 125.1, 35.4, 32.3, 24.2, 15.1.

**Monoepoxides (mixture) (CPB-0801).** Colorless oil; $^1H$ NMR (400 MHz, $CDCl_3$) δ 5.64 (m, 3H), 3.45 (m, 1H), 3.41 (s, 1H), 3.19 (m, 1H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ

129.3, 128.4, 126.1, 65.5, 64.7, 55.7, 54.7. HRMS Calcd. for $C_8H_{12}O$ (M + 1): 124.0888. Found: 124.0891.

**(Table 3.3, entry 19)**

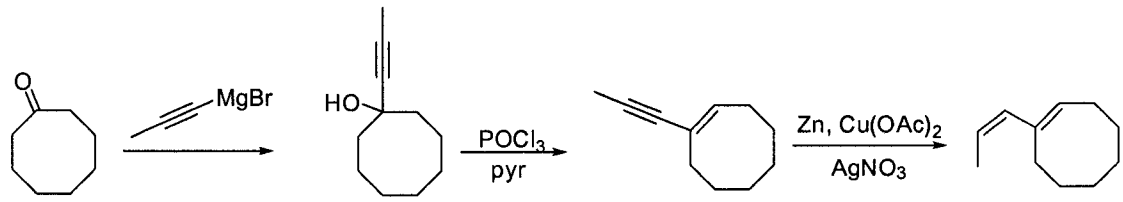



**1-Prop-1-ynyl-cyclohexene (3-52) (CPB-0609).** A solution of 1-ethynylcyclohexene (4.0 g, 37.7 mmol) in THF (40 ml) was cooled to -78 °C and *n*-BuLi (2.2M, 17.3 mL, 38.0 mmol), was added slowly. After stirring for 15 min at -78 °C and 1 h at 0 °C, HMPA (13.7 mL) and iodomethane (6.5 g, 45.6 mmol) were added sequentially. The mixture was stirred for 3 h at 0 °C and overnight at rt. It was then quenched by addition of water, extracted with petroleum ether, washed with water, brine, dried ($Na_2SO_4$), filtered and concentrated. The compound was then purified by column chromatography (pet. ether) to give 4.1 g (91%) of the title compound as a pale yellow oil: IR (NaCl): 2230, 1436 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.02 (s, 1H), 3.3.14-3.04 (m, 4H), 2.95 (s, 3H), 2.67-2.54 (m, 4H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 133.4, 121.2, 82.9, 81.7, 29.7, 25.8, 22.6, 21.8, 4.4.

***cis*-1-Prop-1-enyl-cyclohexene (3-53) (CPB-0612).** This compound was prepared via activated Zn reduction of 1-prop-1-ynyl-cyclohexene (**3-52**) (CPB-0609) according to the same procedure used for (1-*trans*,3-*cis*)-1-phenyl-1,3-pentadiene (**3-9**) (CPB-0449) (51%). Colorless oil; IR (NaCl): 1467 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 5.76 (d, $J$ = 11.4 Hz, 1H), 5.64 (s, 1H), 5.46-5.34 (m, 1H), 2.22-2.08 (m, 4H), 1.81 (dd, $J$ = 6.9, 1.8 Hz, 3H), 1.70-1.56 (m, 4H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 135.6, 132.9, 127.5, 123.4, 29.3, 25.8, 23.2, 22.4.

**Monoepoxides (mixture) (CPB-1327).** Colorless oil; IR (NaCl): 1438 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 5.62 (m, 1H), 3.28 (m, 1H), 3.18-3.10 (m, 1H), 2.10-1.58 (m, 8H), 1.16 (d, $J$ = 5.4 Hz, 3H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 131.3, 123.7, 58. 8, 54.4, 26.3, 24. 8, 22.8, 22.6, 12.5. Anal. Calcd. for $C_9H_{14}O$: C, 78.21; H, 10.21. Found: C, 78.12; H, 10.49.

**(Table 3.3, entry 20)**




**1-Prop-1-ynylcyclooctanol (CPB-0724).** The title compound was prepared according to the same procedure used for 1-prop-1-ynylcyclopentanol (CPB-0722) above (96%, crude).

Yellow oil; IR (NaCl): 3284, 2916, 2853, 2236, 1446, 1047, 982 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 1.98-1.86 (m, 4H), 1.85 (s, 3H), 1.73-1.42 (m, 11H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 84.2, 79.2, 71.7, 38.7, 28.2, 24.7, 22.4, 3.8.

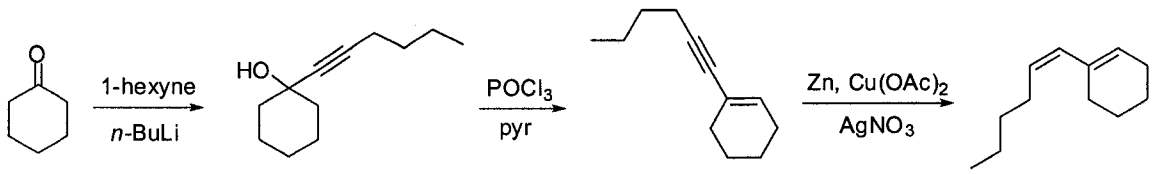
**1-Prop-1-ynylcyclooctene (3-49) (CPB-0727).** The title compound was prepared according to the same procedure used for 1-prop-1-ynyl-cyclopentene (**3-48**) (CPB-0726) (58%). Colorless oil; IR (NaCl): 2925, 2851, 1466, 1446, 902, 845 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 5.96 (t, $J$ = 8.4 Hz, 1H), 2.27 (m, 2H), 2.15 (m, 2H), 1.94 (s, 3H), 1.60 (m, 2H), 1.49 (m, 6H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 136.2, 124.3, 82.4, 82.4, 82.3, 30.4, 30.0, 29.9, 28.7, 27.1, 26.7, 26.1, 4.5.

***cis*-1-Prop-1-enylcyclooctene (3-51) (CPB-0730).** The diene was prepared via activated zinc reduction of 1-prop-1-ynylcyclooctene (**3-49**) (CPB-0727) according to the same procedure used for (1-*trans*,3-*cis*)-1-phenyl-1,3-pentadiene (**3-9**) (CPB-0449) (67%). Colorless oil; IR (NaCl): 3007, 2924, 2850, 1447, 854, 716 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 5.78 (d, $J$ = 11.7 Hz, 1H), 5.6 (t, $J$ = 8.1 Hz, 1H), 5.47 (dq, $J$ = 11.7, 7.2 Hz, 1H), 2.30-2.16 (m, 4H), 1.83 (dd, $J$ = 6.9, 1.8 Hz, 3H), 1.52 (m, 8H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 138.0, 132.6, 129.8, 123.9, 30.3, 29.1, 28.9, 27.0, 26.9, 26.4, 14.9.

**Monoepoxides (mixture) (CPB-0809).** Colorless oil; IR (NaCl): 2926, 2856, 1448 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 5.67-5.53 (m, 3H), 3.36 (d, $J$ = 4Hz, 1H), 2.84 (dd, $J$ = 4.4,

10 Hz, 1H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 129.6, 128.4, 126.1, 62.2, 61.2, 59.0, 55.1. HRMS Calcd. for $C_{11}H_{18}O$ (M + 1): 166.1358. Found: 166.1355.

**(Table 3.3, entry 21)**




**1-Hex-1-ynyl-cyclohexanol (3-54) (CPB-0710).** 1-Hexyne (4.9 g, 60.0 mmol) was dissolved in THF (100 mL) and dropped to -78 °C. *n*-BuLi (2.2 M in THF, 30 mL, 66.0 mmol) was then added and the mixture was stirred for 1 h. Cyclohexanone (6.48 g, 66.0 mmol) was then added and the mixture was stirred for 3 h at -78 °C and 1 h at rt. The reaction was then quenched by addition of water, extracted with ether, washed with water, brine, dried ($Na_2SO_4$), and concentrated yielding 13.3 g (quantitative, crude) of the title compound as a colorless oil . The product was taken on to the next step without further purification: IR (NaCl): 3363, 2235 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 2.22 (t, $J$ = 6.8 Hz, 2H), 1.86 (m, 4H), 16.7 (m, 2H), 1.58-1.39 (m, 8H), 0.92 (t, $J$ = 7.2 Hz, 3H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 84.1, 69.0, 68.2, 40.5, 31.1, 25.5, 23.7, 22.1, 18.5, 13.8.

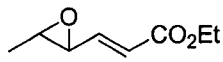
**1-Hex-1-ynyl-cyclohexene (3-55) (CPB-0711).** To a stirred solution of pyridine (2.6 mL) and 1-hex-1-ynyl-cyclohexanol (**3-54**) (CPB-0710) (5.0 g, 27.7 mmol) was added

dropwise a solution of $POCl_3$ (4.3 g, 27.7 mmol) in pyridine (2.6 mL). The flask became warm and a white precipitate formed. The mixture was then stirred at 90 °C for 45 min. It was then cooled and water (23 mL) was slowly added. The mixture was then extracted with petroleum ether (3 x 15 mL), washed with 1 M HCl (20 ml), saturated aq. $NaHCO_3$, (3 x 15 mL), brine (3 x 15 mL) and dried ($Na_2SO_4$). It was then concentrated yielding 4.49 g (99%, crude) of the title compound as a pale yellow oil. The product was taken on to the next step without further purification: IR (NaCl): 2223 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 6.02 (m, 1H), 3.60 (m, 2H), 2.40-2.26 (m, 2H) 2.20-2.05 (m, 2H), 2.00-1.90 (m, 2H) 1.64-1.40 (m, 6H), 0.90 (m, 3H); $^{13}C$ NMR (100 MHz, $CDCl_3$) δ 133.4, 121.3, 87.6, 82.5, 44.4, 31.3, 29.9, 25.8, 22.6, 21.8, 19.2, 13.9.

***cis*-1-Hex-1-enyl-cyclohexene (3-56) (CPB-0715).** The diene was synthesized via activated Zn reduction of 1-hex-1-ynyl-cyclohexene (**3-55**) (CPB-0711) according to the same procedure used for (1-*trans*,3-*cis*)-1-phenyl-1,3-pentadiene (**3-9**) (CPB-0449) as previously discussed (58%). Colorless oil; IR (NaCl): 1448 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 5.74 (d, $J$ = 12.0 Hz, 1H), 5.63 (s, 1H), 5.28 (dt, $J$ = 12.0, 7.6 Hz, 1H), 2.30-2.20 (m, 2H), 2.20-2.08 (m, 4H), 1.68-1.56 (m, 4H), 1.42-1.28 (m, 4H), 0.96-0.86 (m, 3H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 135.7, 131.8, 130.0, 127.3, 32.8, 29.3, 28.9, 25.9, 23.2, 22.6, 22.4, 14.2.

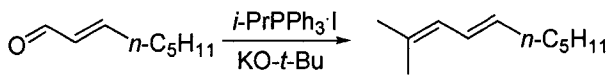
**Monoepoxides (mixture) (CPB-0813).** Colorless oil; IR (NaCl): 1457 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 5.59 (m, 2H), 5.41 (dt, $J$ = 11.1, 7.2 Hz, 1H), 3.28 (m, 1H), 3.08 (s, 1H), 3.01 (q, $J$ = 5.7 Hz, 1H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 132.9, 130.3, 123.5, 117.6, 60.1, 58.9, 58.7. Anal. Calcd. for $C_{12}H_{20}O$: C, 79.94; H, 11.18. Found: C, 79.90; H, 11.12.

**(Table 3.4, entry 1)**




**Epoxide (CPB-2734).** 75% ee $[\alpha]_D^{25}$ = +5.2 (*c* 0.65, $CHCl_3$); Colorless oil; IR (NaCl): 1722, 1656, 1303 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 6.67 (dd, $J$ = 15.6, 7.0 Hz, 1H), 6.13 (d, $J$ = 15.6 Hz, 1H), 4.20 (q, $J$ = 7.2 Hz, 2H), 3.18 (dd, $J$ = 7.0, 1.8 Hz, 1H), 2.98 (qd $J$ = 5.2, 1.8 Hz, 1H), 1.39 (d, 5.2 Hz, 3H), 1.29 (t, $J$ = 7.2 Hz, 3H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 165.9, 144.9, 123.9, 60.8, 57.6, 57.5, 17.7, 14.4.

**(Table 3.4, entry 2)**

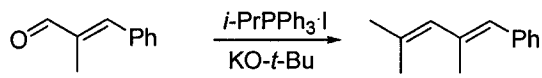



***trans*-2-Methyl-2,4-decadiene (3-57) (CPB-2816).** To a stirring slurry of isopropyltriphenylphosphonium bromide (7.00 g, 16.0 mmol) in 79 mL THF was added potassium *t*-butoxide (1.82 g, 16.2 mmol) and 18-crown-6 (0.15 g, 0.55 mmol) at rt.

After 30 min. *trans*-2-octenal (1.90 g, 15.1 mmol) was added and the mixture was stirred overnight. The solvent was then removed and the sludge that remained was repeatedly triturated with hexanes. The combined hexanes were then concentrated and the residue was purified by column (hexanes) to yield 1.20 g (48%) of the title compound as a colorless oil: IR (NaCl): 1450, 1377, 957 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 6.22 (dd, $J$ = 15.0, 10.8 Hz, 1H), 5.79 (d, $J$ = 10.8 Hz, 1H), 5.56 (dt, $J$ = 15.0, 7.2 Hz, 1H), 2.07 (q, 7.2 Hz, 2H), 1.75 (s, 3H), 1.74 (s, 3H), 1.43-1.23 (m, 6H), 0.89 (t, $J$ = 6.8 Hz, 3H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 132.9, 132.4, 126.8, 125.3, 33.1, 31.7, 29.5, 26.1, 22.8, 18.4, 14.3.

**Epoxide (CPB-2835).** 77% ee $[\alpha]_D^{25}$ = +2.66 (*c* 1.2, $CHCl_3$); Colorless oil; IR (NaCl): 1456, 1377 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 5.91 (dt, $J$ = 15.4, 6.8 Hz, 1H), 5.32 (ddt, $J$ = 15.4, 8.0, 1.4 Hz, 1H), 3.17 (d, $J$ = 8.0 Hz, 1H), 2.08 (qd, $J$ = 6.8, 1.2 Hz, 2H), 1.43-1.24 (m, 6H), 1.35 (s, 3H), 1.29 (s, 3H), 0.89 (t, $J$ = 7.2 Hz, 3H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 138.1, 125.2, 64.7, 60.3, 32.8, 31.6, 28.9, 24.9, 22.7, 19.2, 14.3. Anal. Calcd for $C_{12}H_{22}O$: C, 78.51; H, 11.98. Found: C, 78.32; H, 11.87.

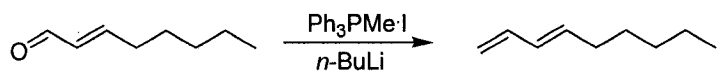
**(Table 3.4, entry 3)**



**(*E*)-2,4-Dimethyl-1-phenyl-1,3-pentadiene (3-58) (CPB-2732B).** The substrate was prepared from 2-methyl-*trans*-cinnamaldehyde by the same method as *trans*-2-methyl-2,4-decadiene (**3-57**) (CPB-2816) above (63%). Colorless oil; IR (NaCl): 1599, 1442, 698 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.35-7.24 (m, 4H), 7.22-7.16 (m, 1H), 6.31 (brs, 1H), 5.79 (brs, 1H), 1.97 (d, $J$ = 0.8 Hz, 3H), 1.87 (d, $J$ = 0.8 Hz, 3H), 1.83 (d, $J$ = 0.8 Hz, 3H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 138.6, 136.0, 134.3, 129.8, 129.2, 128.6, 128.3, 126.3, 27.2, 20.0, 19.2.

**Epoxide (CPB-2834).** > 99% ee $[\alpha]_D^{25}$ = -125.4 (*c* 0.59, $CHCl_3$); Colorless oil; IR (NaCl): 1600, 1447, 1377 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.36-7.19 (m, 5H), 6.44 (s, 1H), 3.30 (s, 1H), 1.93 (s, 3H), 1.45 (s, 3H), 1.23 (s, 3H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 137.5, 132.6, 129.1, 128.4, 126.6, 125.8, 67.2, 61.1, 25.0, 17.7, 16.1. HRMS Calcd for $C_{13}H_{16}O$: 188.1201, . Found: 188.1204 .

**(Table 3.4, entry 4)**

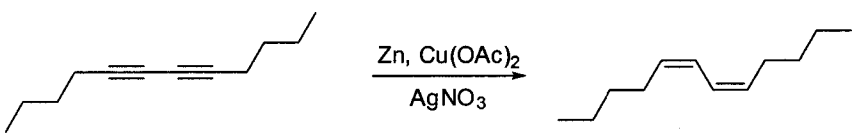



***trans*-1,2-Nonadiene (3-59) (CPB-1004).** Triphenylmethylphosphonium iodide (5.0 g, 12.3 mmol) was dissolved in THF (60mL) and dropped to -78 °C. To this was added *n*-BuLi (2.20 M in hexane, 5.6 mL, 12.3 mmol). The mixture was stirred for 30 min. and then *trans*-2-octenal (1.44 g, 11.43 mmol) in THF (30 mL) was added. The mixture was

stirred for 1 h at -78 °C and was then brought to rt and stirred overnight. The reaction was then quenched by addition of sat. aq. $NH_4Cl$. It was extracted with petroleum ether, dried ($Na_2SO_4$), and concentrated. The crude oil was then purified by column chromatography (petroleum ether) to give 0.33 g (23%) of the desired compound as a colorless volatile oil: IR (NaCl): 1002, 896 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 6.32 (dt, $J$ = 16.8, 10.4 Hz, 1H), 6.05 (dd, $J$ = 15.2, 10.8 Hz, 1H), 5.72 (dt, $J$ = 15.2, 6.8 Hz, 1H), 5.09 (d, $J$ = 16.8 Hz, 1H), 4.96 (d, $J$ = 10 Hz, 1H), 2.08 (q, $J$ = 7.2 Hz, 2H), 1.40 (quint., $J$ = 7.2 Hz, 2H), 1.38-1.24 (m, 4H), 0.90 (t, $J$ = 7.2 Hz, 3H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 137.6, 135.9, 131.0, 114.8, 32.8, 31.6, 29.1, 22.8, 14.3.

**Epoxide (CPB-1021).** 64% ee $[\alpha]^{25}_D$ = 1.5 (*c* 0.54, $CHCl_3$); Colorless oil; IR (NaCl): 1467 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 5.97 (dt, $J$ = 15.6, 6.6 Hz, 1H), 5.14 (ddt, $J$ = 15.3, 8.1, 1.5 Hz, 1H), 3.33 (m, 1H), 2.95 (dd, $J$ = 5.1, 4.2 Hz, 1H), 2.66 (dd, $J$ = 5.1, 2.7 Hz, 1H), 2.06 (q, $J$ = 6.6 Hz, 1H), 1.42-1.20 (m, 6H), 0.90 (t, 3H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 137.7, 127.6, 52.8, 49.1, 32.5, 31.5, 28.8, 22.7, 14.2. HRMS Calcd. for $C_9H_{16}O$ (M +): 140.1201. Found: 140.1197.

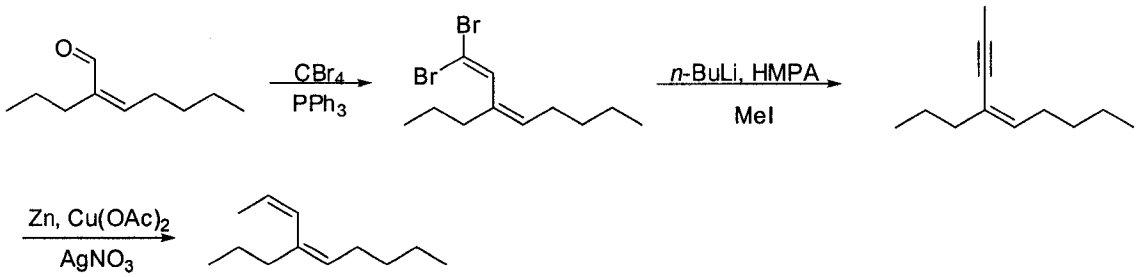
**(Table 3.4, entry 5)**



***cis,cis*-5,7-dodecadiene (3-60) (CPB-8024).** The diene was prepared by activated zinc reduction of 5,7-dodecadiyne according to the same procedure used for (1-*trans*,3-*cis*)-1-phenyl-1,3-pentadiene (**3-9**) (CPB-0449) (66%). Colorless oil; IR (NaCl): 1466 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 6.26 (m, 2H), 5.46 (m, 2H) 2.19 (q, $J$ = 6.8 Hz, 4 H), 1.42-1.30 (m, 8H), 0.91 (t, $J$ = 7.2 Hz, 6H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 132.3, 123.8, 32.0, 27.4, 22.6, 14.2.

**Epoxide (CPB-0908).** 26% ee $[\alpha]^{25}_D$= -0.1 (*c* 0.25, $CHCl_3$); Colorless oil; IR (NaCl): 1466 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 5.76 (m, 1H), 5.21 (m, 1H), 3.64 (m, 1H), 3.07 (m, 1H), 2.21 (m, 2H), 1.61-1.29 (m, 10H), 0.94-0.84 (m, 6H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 137.7, 124.0, 58.9, 53.0, 31.9, 28.7, 28.2, 27.7, 22.8, 22.5, 14.2, 14.1. HRMS Calcd. for $C_{12}H_{22}O$ (M +): 182.1671. Found: 182.1666.

**(Table 3.4, entry 6)**




**(*Z*)-1,1-Dibromo-3-propyl-1,3-octadiene (3-12) (CPB-0504).** The title compound was prepared according to the same procedure used for *trans*-1,1-dibromo-4-phenyl-1,3-

butadiene (**3-3**) (CPB-0514) above (73%). Yellow oil; IR (NaCl): 1465 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 6.80 (s, 1H), 5.64 (t, $J$ = 7.6 Hz, 1H), 2.13 (t, $J$ = 7.6 Hz, 2H), 2.05 (q, $J$ = 7.2 Hz, 2H), 1.40-1.26 (m, 6H), 0.92-0.80 (m, 6H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 140.3, 135.9, 136.1, 87.0, 31.6, 31.2, 27.9, 22.6, 22.2, 14.2, 14.0.

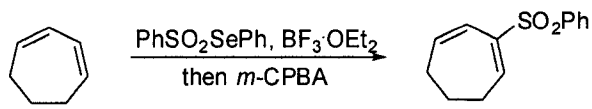
**(*Z*)-4-Propyl-4-nonen-2-yne (3-13) (CPB-0509).** The title compound was prepared according to the same procedure used for *trans*-1-phenyl-1-penten-3-yne (**3-6**) (CPB-0444) above (62%). Pale yellow oil; IR (NaCl): 2959, 2227, 1465 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 5.76 (t, $J$ = 7.2 Hz, 1H), 2.14-2.00 (m, 4H), 1.93 (s, 3H), 1.59-1.44 (m, 2H), 1.38-1.20 (m, 4H), 0.98-0.78 (m, 6H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 137.1, 123.4, 82.4, 82.0, 33.1, 31.8, 28.1, 22.5, 21.8, 14.1, 13.9, 4.3.

**(2-*cis*,4-*Z*)-4-Propyl-2,4-nonadiene (3-14) (CPB-0512).** The title compound was prepared via activated Zn reduction according to the same procedure used for (1-*trans*,3-*cis*)-1-phenyl-1,3-pentadiene (**3-9**) (CPB-0449) above (56%). Colorless oil; IR (NaCl): 1465 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 5.77 (d, $J$ = 11.6 Hz, 1H), 5.52-5.44 (m, 1H), 5.32 (t, $J$ = 7.2 Hz, 1H), 2.16-2.00 (m, 4H), 1.76 (dd, $J$ = 7.2 , 2.0 Hz, 3H), 1.44-1.34 (m, 6H), 0.96-0.80 (m, 6H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 136.3, 133.1, 130.3, 124.3, 32.8, 32.4, 27.9, 22.7, 22.0, 14.7, 14.3, 14.2.

**Epoxide (CPB-0627).** 58% ee $[\alpha]^{25}_D$= -45.0 (*c* 0.16, $CHCl_3$); Colorless oil; IR (NaCl): 1466 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 5.34 (t, $J$ = 7.6 Hz, 1H), 3.53 (d, $J$ = 4.4 Hz,

1H), 3.16 (quint, $J$ = 5.2 Hz, 1H), 2.18-2.00 (m, 4H), 1.40-1.26 (m, 6H), 1.13 (d, $J$ = 5.6 Hz, 3H), 0.98-0.86 (m, 6H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 131.8, 127.2, 59.0, 55.1, 32.2, 31.4, 27.1, 22.6, 21.9, 14.5, 14.2, 12.5. Anal. Calcd. for $C_{12}H_{22}O$: C, 79.06; H, 12.16. Found: C, 79.27; H, 12.38.

**(Table 3.4, entry 7)**




***Se*-Phenyl benzeneselenolsulfonate (CPB-1325).** The title compound was prepared according to a literature procedure.[169] A solution of benzene sulfonyl hydrazide (3.44 g, 20 mmol) in 130 ml $CH_2Cl_2$. was added over 15 min to a suspension of benzeneseleninic acid (3.78 g, 20 mmol) in $CH_2Cl_2$ (70 mL) and the reaction was stirred overnight. The yellow solution was then evaporated to dryness and the residue was recrystallized from MeOH. 4.13 g (69%) of the title compound as a yellow powder was obtained.

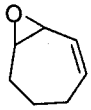
**2-Phenylsulfonyl-1,3-cycloheptadiene (3-61) (CPB-1326).** The diene was synthesized according to a literature procedure.[162] To a solution of 1,3-cycloheptadiene (1.11 g, 11.78 mmol) and $PhSO_2SePh$ (CPB-1325) (3.5 g, 11.78 mmol) in $CH_2Cl_2$ (120 mL) was added $BF_3{\cdot}OEt_2$ (0.60 mL, 4.73 mmol) at rt. The mixture was then stirred for 17 h at rt.

[169] Back, T.G.; Collins, S. *Tetrahedron Lett.* **1980**, 2213-2214.

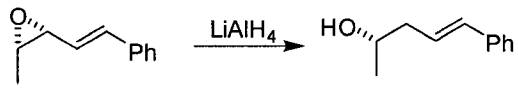
A solution of *m*-CPBA (5.98 g, 29.45 mmol) in 120 mL $CH_2Cl_2$ was then added and the mixture was stirred for 15 min. the organic phase was then washed with 5% aq. $NaHCO_3$ and dried ($Na_2SO_4$) and concentrated. The yellow residue was then purified by column chromatography (1:1 pet. ether:$Et_2O$) and recrystallized from $Et_2O$/hexanes to yield 0.911 g (33%) of the title compound as a white solid: IR (NaCl): 2929, 1446, 1303, 1149 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.87, (m, 2H), 7.60 (m, 1H), 7.53 (m, 2H), 7.29 (t, $J$ = 5.6 Hz, 1H), 6.04 (m, 2H), 2.57 (q, $J$ = 5.6 Hz, 2H), 2.33 (m, 2H), 1.86 (quint., $J$ = 6.0 Hz 2H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 142.2, 140.4, 139.5, 138.3, 133.2, 129.3, 128.1, 119.4, 31.4, 30.9, 24.9.

**Epoxide (CPB-1329).** 83% ee $[\alpha]^{25}_D$ = +44.2 (*c* 3.24, $CHCl_3$); White solid; IR (NaCl): 2935, 1648, 1446, 1304, 1150, 1088 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.92 (m, 2H), 7.64 (m, 1H), 7.57 (m, 2H), 7.41 (ddd, $J$ = 7.2, 3.2, 1.2 Hz, 1H), 3.72 (dd, $J$ = 4.4, 1.2 Hz, 1H), 3.45 (m, 1H), 2.57 (m, 1H), 2.28 (m, 1H), 2.18-2.03 (m, 2H), 1.67-1.60 (m, 2H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 146.9, 140.0, 138.9, 133.6, 129.4, 128.2, 59.8, 51.4, 30.9, 29.2, 21.2.

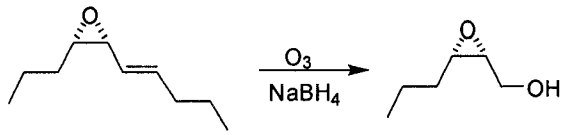
**(Table 3.4, entry 8)**



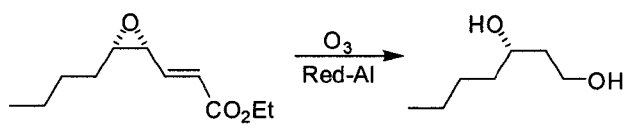
**Cycloheptadiene oxide (CPB-1247).** $[\alpha]^{25}_D$ = -73.3 (*c* 0.06, $CHCl_3$); Colorless oil; IR (NaCl): 1436 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 5.92 (m, 1H), 5.79 (m, 1H), 3.44 (m, 1H), 3.24 (t, *J* = 4.8 Hz, 1H), 2.27 (m, 2H), 2.01 (m, 2H), 1.64 (m, 2H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 138.7, 124.0, 60.9, 53.8, 31.6, 30.0, 22.3.



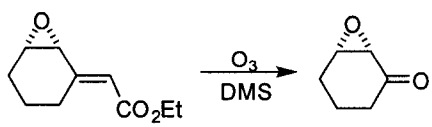

**(S)-*trans*-5-Phenyl-4-penten-2-ol (3-67) (CPB-0629).** $LiAlH_4$ (0.02 g, 0.51 mmol) was added to a flame-dried flask under Ar. To this was added 1.5 mL THF at rt followed by vinyl epoxide (85% ee, 0.05 g, 0.29 mmol) in 0.50 mL THF slowly via syringe. The mixture was allowed to stir at rt for 3 h at which point it was quenched with $H_2O$. It was then extracted with $Et_2O$ and the combined organic extracts were washed with brine, dried ($Na_2SO_4$), filtered, and concentrated. The residue was purified by column chromatography (9:1 pet. ether:$Et_2O$) to yield 0.04 g (72%) of the title compound as a colorless oil: $[\alpha]^{25}_D$ = +18.3 (*c* 1.38, $CCl_4$); Lit. 64% ee $[\alpha]^{20}_D$ = +14.2 (c 1.6, $CCl_4$);[165] IR (NaCl): 3359, 1449, $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 7.41-7.19 (m, 5H), 6.50 (d, *J* = 15.9 Hz, 1H), 6.24 (dt, *J* = 15.9, 6.9 Hz, 1H), 4.02-3.88 (m, 1H), 2.49-2.29 (m 2H), 1.61 (d, *J* = 4.2 Hz, 1H), 1.27 (d, *J* = 6.3 Hz, 3H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 137.4, 133.4, 128.7, 127.5, 126.4, 126.3, 67.6, 43.1, 23.1.




**(2R,3S)-2,3-Epoxy-1-hexanol (3-68) (CPB-1321).** A solution of vinyl epoxide (55% ee, 0.06 g, 0.30 mmol) in $CH_2Cl_2$ (7 mL) was prepared and cooled to -78 °C. Ozone was then bubbled through the solution until a blue color persisted, and then ozone was removed. After the blue color disappeared $NaBH_4$ (0.06 g, 1.5 mmol) in 7 mL MeOH was added slowly and the mixture was stirred at -78 °C for 2 h and then at rt for 4 h. The solution was then diluted with $CH_2Cl_2$, washed with water, brine, dried ($Na_2SO_4$), and concentrated. The residue was then purified by column chromatography (pet. ether:$Et_2O$ 1:1) to yield 0.015 g (43%) of the title compound as a colorless oil: $[\alpha]^{25}_D$ = +1.33 (*c* 0.75, $CHCl_3$); Lit. 80% ee $[\alpha]^{23.5}_D$ = +4.9 (c 2.02, $CHCl_3$);[166] IR (NaCl): 3415, 1465, 1043 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 3.87 (ddd, *J* = 11.7, 7.2, 4.5 Hz, 1H), 3.69 (ddd, *J* = 11.7, 6.9, 4.5 Hz, 1H), 3.17 (dt, *J* = 7.2, 4.5 Hz, 1H) 3.06 (m, 1H), 2.83 (brs, 1H), 1.60-1.43 (m, 4H), 0.99 (t, *J* = 6.9 Hz); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 14.1, 20.2, 30.2, 56.9, 57.4, 61.2.



**(S)-1,3-Heptanediol (3-69) (CPB-1320).** A solution of vinyl epoxide (85% ee, 0.07 g, 0.35 mmol) in $CH_2Cl_2$ (7 mL) was prepared and cooled to -78 °C. Ozone was then bubbled through the solution until a blue color persisted, and then ozone was removed. After the blue color disappeared Red-Al (65% in toluene, 0.54 mL, 1.8 mmol) was added slowly and the mixture was stirred at -78 °C for 2 h and then at rt for 4 h. The solution was then diluted with $CH_2Cl_2$, washed with water, brine, dried ($Na_2SO_4$), and concentrated. Upon analysis it became apparent that 2,3-epoxy-1-heptanol had been isolated. The crude epoxy alcohol in 9 mL $CH_2Cl_2$ was then resubjected to Red-Al (65% in toluene, 0.84 mL, 2.59 mmol) and was stirred until the reaction had completed as judged by TLC. The mixture was then diluted with $CH_2Cl_2$, quenched with water, washed with brine, dried ($Na_2SO_4$), and concentrated. It was then purified by column chromatography (2:1 to 1:1 pet. ether:$Et_2O$) to give 0.04 g (80%) of a colorless oil: $[\alpha]^{25}_D$ = +3.4 (*c* 1.85, EtOH); Lit. 98% ee $[\alpha]_D$ = +9.6 (*c* 5.0, EtOH);[167] IR (NaCl): 3345, 1466, 1054 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 3.87 (m, 3H), 2.71 (dd, *J* = 6.0, 4.5 Hz, 1H), 2.62 (d, *J* = 3.9 Hz, 1H), 1.71 (m, 2H), 1.52-1.30 (m, 6H), 0.91 (t, 6.9 Hz, 3H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 72.6, 62.1, 38.4, 37.7, 27.9, 22.9, 14.3.



**(S,S)-2,3-Epoxycyclohexanone (3-70) (CPB-1314).** A solution of epoxy ester (90% ee, 0.06 g, 0.33 mmol) in $CH_2Cl_2$ (5 mL) was prepared and cooled to -78 °C. Ozone was then bubbled through the solution until a blue color persisted, and then flow of ozone was stopped. After the blue color disappeared $Me_2S$ (0.1 mL) was added dropwise and the mixture was stirred at -78 °C for 2 h and then at rt for 4 h. The yellow solution was then diluted with $CH_2Cl_2$, washed with water, brine, dried ($Na_2SO_4$), and concentrated. The residue was then purified by column chromatography (2:1 pet. ether:$Et_2O$) to yield 0.01 g (27%) of the title compound as a colorless oil: $[\alpha]^{25}_D$ = -144.2 (*c* 0.48, MeOH); Lit. (R,R) isomer 75% ee $[\alpha]^{25}_D$ = +90.5 (*c* 0.60, MeOH);[168] IR (NaCl): 1712 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 3.60 (m, 1H), 3.23 (d, *J* = 3.9 Hz, 1H), 2.56 (dt, *J* = 16.8, 4.5 Hz, 1H) 2.26 (m, 1H), 2.15-1.87 (m, 3H), 1.68 (m, 1H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 206.2, 56.2, 55.4, 36.6, 23.1, 17.2.

# CHAPTER FOUR

# CATALYTIC ASYMMETRIC EPOXIDATION OF CONJUGATED *CIS*-ENYNES

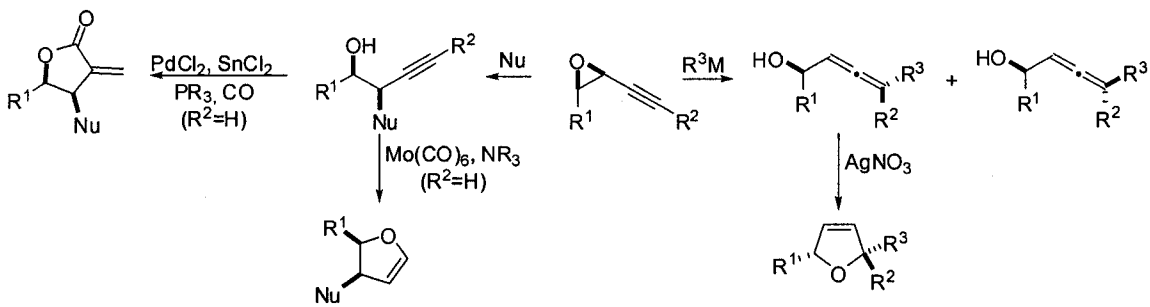
## 4.A. INTRODUCTION AND BACKGROUND

Like vinyl epoxides, chiral alkynyloxiranes (propargyl epoxides) are very valuable synthetic intermediates capable of undergoing a variety of useful ring-opening reactions. They can be opened selectively by nucleophiles directly at the propargyl position to give homopropargylic alcohols, which themselves undergo a variety of useful reactions,[170,171] or can be opened via attack on the alkyne in an $S_N2'$ fashion to give

[170] (a) Bernard, N.; Chemla, F.; Normant, J.F. *Tetrahedron Lett.* **1998**, *39*, 6715. (b) Mukai, C.; Ikeda, Y.; Sugimoto, Y-i.; Hanaoka, M. *Tetrahedron Lett.* **1994**, *35*, 2183-2186. (c) Mukai, C.; Ikeda, Y.; Sugimoto, Y-i.; Hanaoka, M. *Tetrahedron Lett.* **1994**, *35*, 2179-2182.

[171] (a) Murray, T. F.; Samsel, E. G.; Varma, V.; Norton, J. R. *J. Am. Chem. Soc.* **1981**, *103*, 7520-7528. (b) McDonald, F. E.; Gleason, M. M. *J. Am. Chem. Soc.* **1996**, *118*, 6648-6659.

allenyl alcohols which are also valuable compounds (Scheme 4.1).[172,173] Pd(0) will also add to the alkyne in $S_N2'$ manner to give the metalated allene. These species can then do classical palladium chemistry such as CO insertion and cross coupling (Scheme 4.2).[174] Propargyl epoxides can also be metalated at the propargyl position, and the resulting oxiranyl anions are capable of trapping various electrophiles (Scheme 4.3).[175] On top of this, there are many propargyl epoxide-containing natural products including antifeedant epoxypolyynes **4-1** and **4-2** as well as the dienediyne family of antitumor antibiotics such as neocarzinostatin (**4-3**) to name a few (Figure 4.1).[176,177]




**Scheme 4.1**

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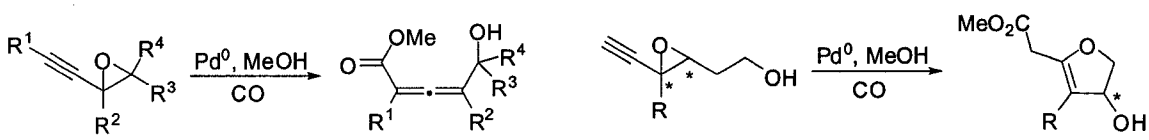
[172] (a) Alexakis, A.; Marek, I.; Mangeney, P.; Normant, J. F. *Tetrahedron* **1991**, *47*, 1677-1696. (b) Marshall, J. A.; Tang, Y. *J. Org. Chem.* **1994**, *59*, 1457-1464. (c) Aurrecoechea, J. M.; Alonso, E.; Solay, M. *Tetrahedron* **1998**, *54*, 3833-3850. (d) Aurrecoechea, J. M.; Solay, M. *Tetrahedron Lett.* **1995**, *36*, 2501-2504.

[173] (a) Aurrecoechea, J. M.; Solay, M. *Tetrahedron* **1998**, *54*, 3851-3856. (b) Marshall, J. A.; Pinney, K. G. *J. Org. Chem.* **1993**, *58*, 71807184.

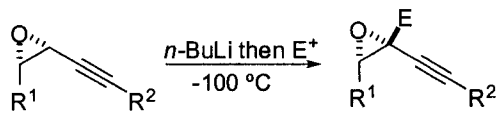
[174] (a) Piotti, M. E.; Alper, H. *J. Org. Chem.* **1997**, *62*, 8484-8489. (b) Minami, I.; Yuhara, M.; Watanabe, H.; Tsuji, J. *J. Organomet. Chem.* **1987**, *334*, 225-242.

[175] Klein, S.; Zhang, J. H.; Holler, M.; Weibel, J.-M.; Pale, P. *Tetrahedron* **2003**, *59*, 9793-9802.

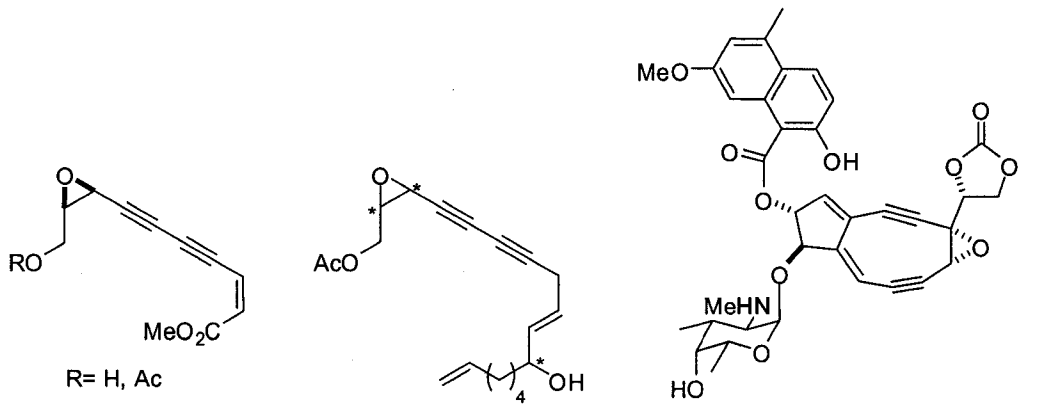
[176] For leading references on epoxypolyynes see: (a) Grandjean, D.; Chuche, J.; *Tetrahedron* **1993**, *49*, 5225-5236. (b) Rose, A. F.; Butt, B. A.; Jermy, T. *Phytochemistry* **1980**, *19*, 563-566. (c) Bohlmann, F.; Zdero, C.; Robinson, H.; King, R. M. *Phytochemistry* **1979**, *18*, 563-1519. (d) Bohlmann, F.; Gerke, T.; King, R. M.; Robinson, H. *Liebigs Ann. Chem.* **1983**, 714-716.



**Scheme 4.2**



**Scheme 4.3**



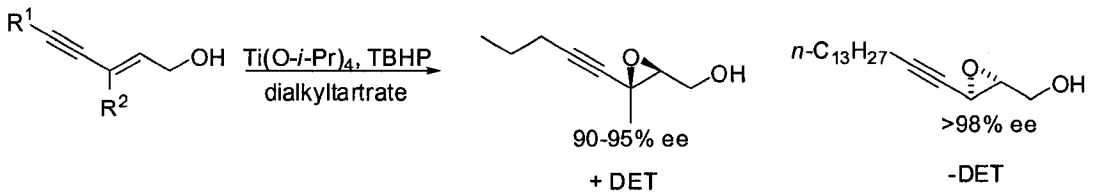
**4-1** **4-2** **4-3,** Neocarzinostatin Chromophore

**Figure 4.1** Propargyl epoxide-containing natural products.

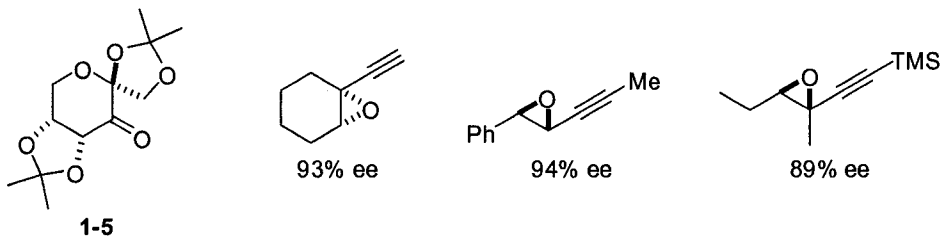
One of the most convenient methods for the synthesis of enantioenriched propargyl epoxides is asymmetric epoxidation of conjugated enynes since conjugated

[177] For a leading reference on neocarzinostatin see: Myers, A. G.; Hammond, M.; Wu, Y.; Xiang, J.-N.; Harrington, P. M.; Kuo, E. Y. *J. Am. Chem. Soc.* **1996**, *118*, 10006-10007.

enynes are readily prepared by a variety of methods.[178] Naturally, the Sharpless epoxidation has been used with success on enynes containing allylic hydroxyl functionality (Scheme 4.4).[179] Ketone **1-5** was investigated for the epoxidation of *trans*- and trisubstituted enynes and is very effective for these substrates (Scheme 4.5).[180]




**Scheme 4.4**



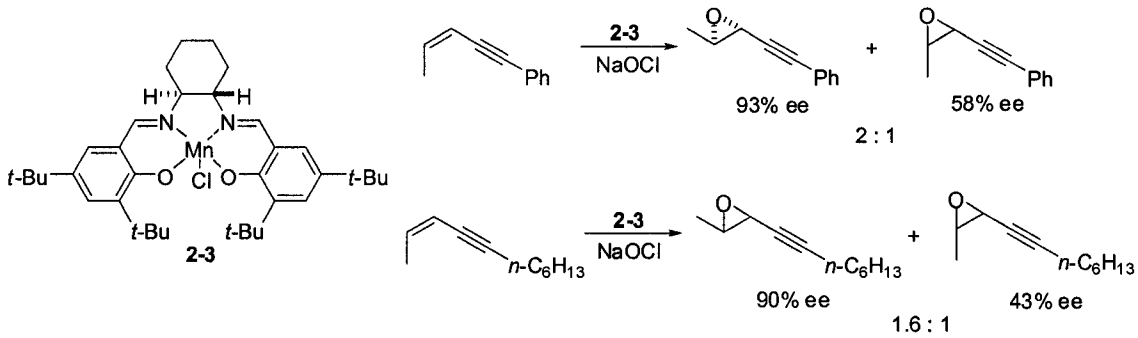

**Scheme 4.5**

[178] For leading references on the synthesis of conjugated enynes see: (a) Doucet, H.; Hierso, J.-C. *Angew. Chem. Int. Ed.* **2007**, *46*, 834-871. (b) Ikeda, S.-i.; Kondo, K.; Sato, Y. *J. Org. Chem.* **1996**, *61*, 8248-8255. (c) Manai, T.; Tsujiguchi, Y.; Matsuoka, S; Tsuji, J. *Tetrahedron Lett.* **1993**, *34*, 7615-7618.

[179] (a) Johnson, R.A.; Sharpless, K.B. In *Catalytic Asymmetric Synthesis*; Ojima, I. Ed.; VCH: New York, 1993; Chapter 4.1. (b) Katsuki, T.; Martin, V.S. *Org. React.* **1996**, *48*, 1-299.

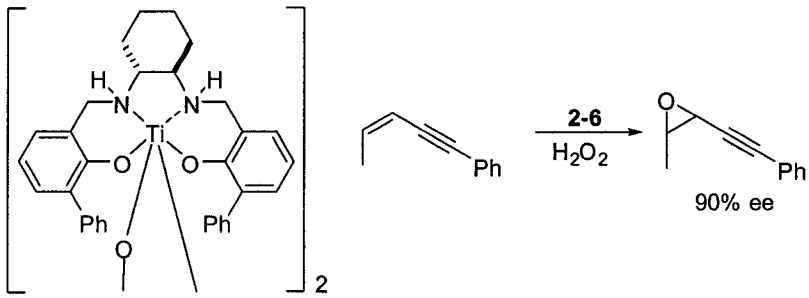
[180] Wang, Z.-X.; Cao, G.-A.; Shi, Y. *J. Org. Chem.* **1999**, *64*, 7646-7650.

Metal-catalyzed asymmetric epoxidation of *cis*-enynes using salen-type ligands has also been reported.[181] With the popular Mn-salen catalysts, isomerization due to radical intermediates results in predominantly *trans*- epoxides from *cis*-olefins (Scheme 4.6). Recently, the epoxidation of *cis*-1-phenylpent-3-en-1-yne in 90% ee with no isomerization was reported using dimeric Ti-salan complex **2-6** (Scheme 4.7) (no other examples were reported).[181g] However, there is still a need for a reliable and general method for epoxidation of conjugated *cis*-enynes.



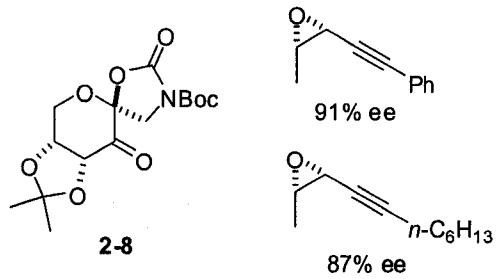

**Scheme 4.6**

[181] (a) Lee, N. H.; Jacobsen, E. N. *Tetrahedron Lett.* **1991**, *32*, 6533-6536. (b) Zhang, W.; Lee, N. H.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1994**, *116*, 425-426. (c) Hamada, T.; Irie, R.; Katsuki, T. *Synlett* **1994**, 479-481. (d) Sasaki, H.; Irie, R.; Hamada, T.; Suzuki, K.; Katsuki, T. *Tetrahedron* **1994**, *50*, 11827-11838. (e) Matsumoto, K.; Sawada, Y.; Saito, B.; Sakai, K.; Katsuki, T. *Angew. Chem. Int. Ed.* **2005**, *44*, 4935-4939. (f) Shitama, H.; Katsuki, T. *Tetrahedron Lett.* **2006**, *47*, 3203-3207. (g) Sawada, Y.; Matsumoto, K.; Kondo, S.; Watanabe, H, Ozawa, T.; Suzuki, K.; Saito, B.; Katsuki, T. *Angew. Chem. Int. Ed.* **2006**, *45*, 3478-3480. (h) Egami, H.; Irie, R.; Sakai, K, Katsuki, T. *Chem. Lett.* **2007**, *36*, 46-47.




**Scheme 4.7**

Epoxidation of phenylpent-3-en-1-yne and *cis*-undec-2-en-4-yne was reported by our group using ketone **2-8**,[182] and 91% and 87% ee were obtained respectively with no *trans*-epoxide formation observed (Scheme 4.8). With these promising results and the readily available *N*-aryl-substituted ketones in hand, a more in-depth study of the epoxidation of conjugated *cis*-enynes was undertaken.



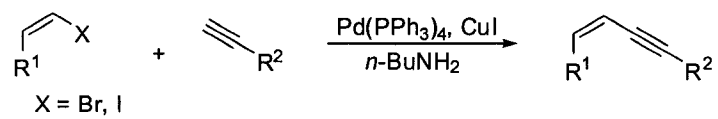

**Scheme 4.8**

## 4.B. RESULTS AND DISCUSSION

[182] (a) Tian, H.; She, X.; Shu, L.; Yu, H.; Shi, Y. *J. Am. Chem. Soc.* **2000**, *122*, 11551-11552. (b) Tian, H.; She, X.; Yu, H.; Shu, L.; Shi, Y. *J. Org. Chem.* **2002**, *67*, 2435-2446.

### 4.B.i. Substrate Synthesis

A variety of conjugated *cis*-enynes with different steric, electronic, and hydrophilic properties were synthesized. Although not commercially available, most of the enynes used for this study were synthesized in 1-3 steps from readily available starting materials in good yields. Enynes **4-4 - 4-9** were obtained in one step via Sonogashira coupling from commercially available *cis*-1-bromo-1-propene and terminal alkynes (Scheme 4.9).[183] For enynes **4-10 – 4-17**, the *cis*-vinyl iodide was synthesized from the requisite terminal alkyne via iodination and diimide reduction.[184,185]




| | | | | | | | |
|---|---|---|---|---|---|---|---|
| **4-4** | $R^1$ = Me | $R^2$ = Ph, | 87% | **4-11** | $R^1$ = $n$-$C_4H_9$ | $R^2$ = $n$-$C_6H_{13}$, | 49% |
| **4-5** | $R^1$ = Me | $R^2$ = $n$-$C_6H_{13}$, | 82% | **4-12** | $R^1$ = $(CH_2)_4OH$ | $R^2$ = TMS, | 62% |
| **4-6** | $R^1$ = Me | $R^2$ = $CH_2OH$, | 56% | **4-13** | $R^1$ = $(CH_2)_4OH$ | $R^2$ = $n$-$C_4H_9$, | 63% |
| **4-7** | $R^1$ = Me | $R^2$ = $CH_2OTBS$, | 61% | **4-14** | $R^1$ = $n$-$C_4H_9$ | $R^2$ = $(CH_2)_4OH$, | 71% |
| **4-8** | $R^1$ = Me | $R^2$ = $C(CH_3)_2OH$, | 85% | **4-15** | $R^1$ = $CH_2OH$ | $R^2$ = $n$-$C_6H_{13}$, | 85% |
| **4-9** | $R^1$ = Me | $R^2$ = $(CH_2)_3OH$, | 77% | **4-16** | $R^1$ = $(CH_2)_2OH$ | $R^2$ = $n$-$C_6H_{13}$, | 83% |
| **4-10** | $R^1$ = $n$-$C_4H_9$ | $R^2$ = Ph, | 76% | | | | |

**Scheme 4.9**

[183] Ratovelomana, V.; Linstrumelle, G. *Synth. Commun.* **1981**, *11*, 917-923.

[184] Dieck, H.A.; Heck, R.F. *J. Org. Chem.* **1975**, *40*, 1083-1090.

[185] Denmark, S.E.; Yang, S.-M. *J. Am. Chem. Soc.* **2002**, *124*, 2102-2103.

Enynes **4-17 – 4-18** were synthesized by a slightly different procedure from vinyl halides and trimethylsilylacetylene.[186] Enynes **4-19** and **4-20** were synthesized from **4-6** by benzoylation and benzylation of the alcohol respectively. Negishi coupling using the zinc salt of ethyl propiolate was used to synthesize **4-21** and **4-22**.[187] In the case of **4-23**, the free alcohol on the vinyl iodide was first protected as the TBS ether before Negishi coupling and was later removed. **4-24** was synthesized from **4-12** by removal of the TMS group with methanolic potassium carbonate. Carboxylic acid-containing enyne **4-26** was synthesized by Sonogashira coupling of *cis*-5-iodopent-4-en-1-ol and 1-octyne followed by oxidation of alcohol **4-25** to the acid with PDC in DMF.[188] Dibenzoate enyne **4-28** was synthesized by Sonogashira coupling of the requisite alcohols followed by benzoylation. Macrocyclic enyne **4-31** was obtained from the ruthenium catalyzed head-to-tail coupling of diyne **4-29**.[189] Finally, ene-triyne **4-35** was synthesized by Cadiot-Chodkiewicz coupling to give **4-33** followed by liberation of the terminal diyne and Sonogashira coupling (Scheme 4.10).[190]

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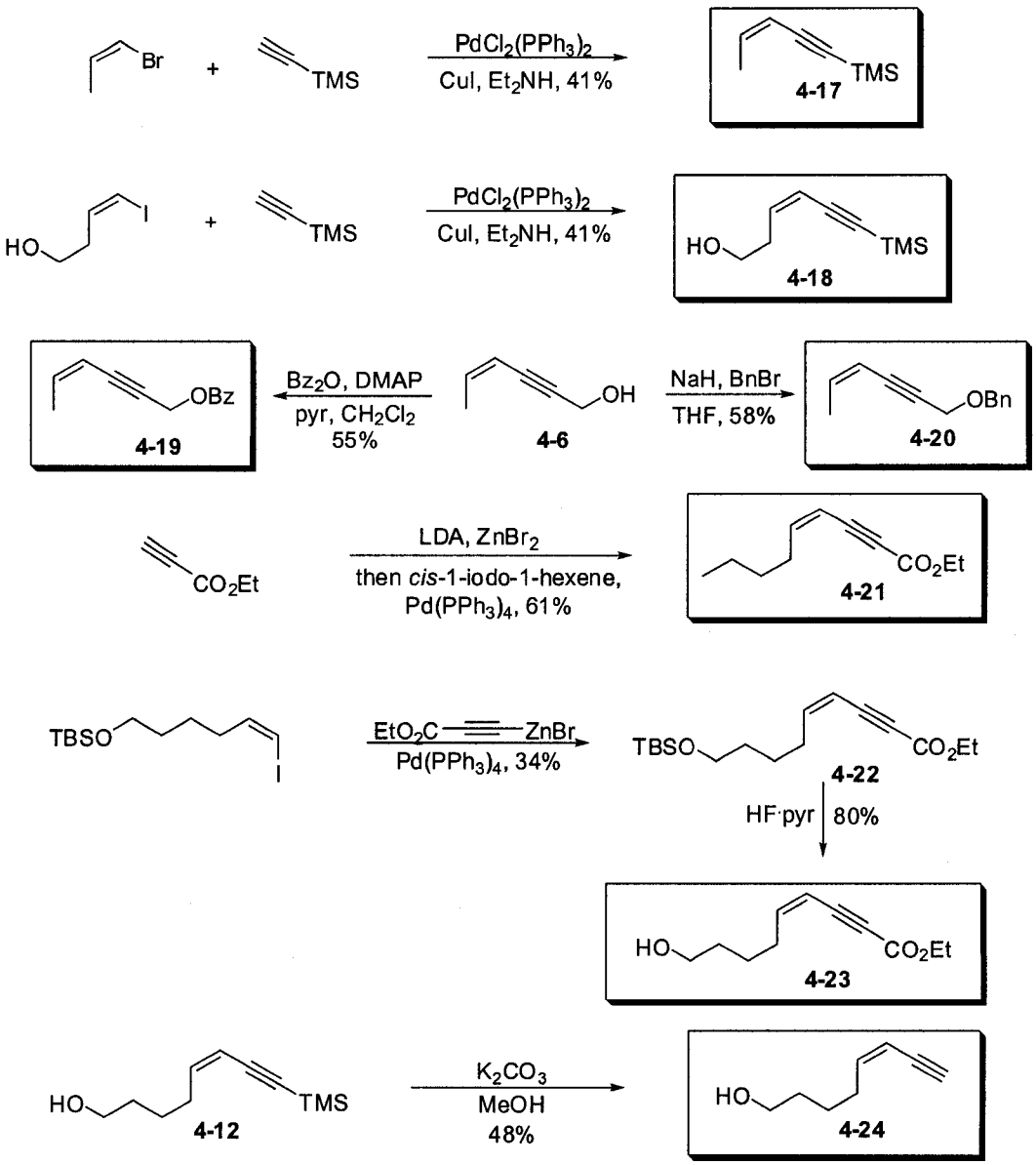
[186] Marshall, J.A.; Bourbeau, M.P. *Org. Lett.* **2002**, *4*, 3931-3934.

[187] Negishi, E.; Qian, M.; Zeng, F.; Anastasia, L.; Babinski, D. *Org. Lett.* **2003**, *5*, 1597-1600.

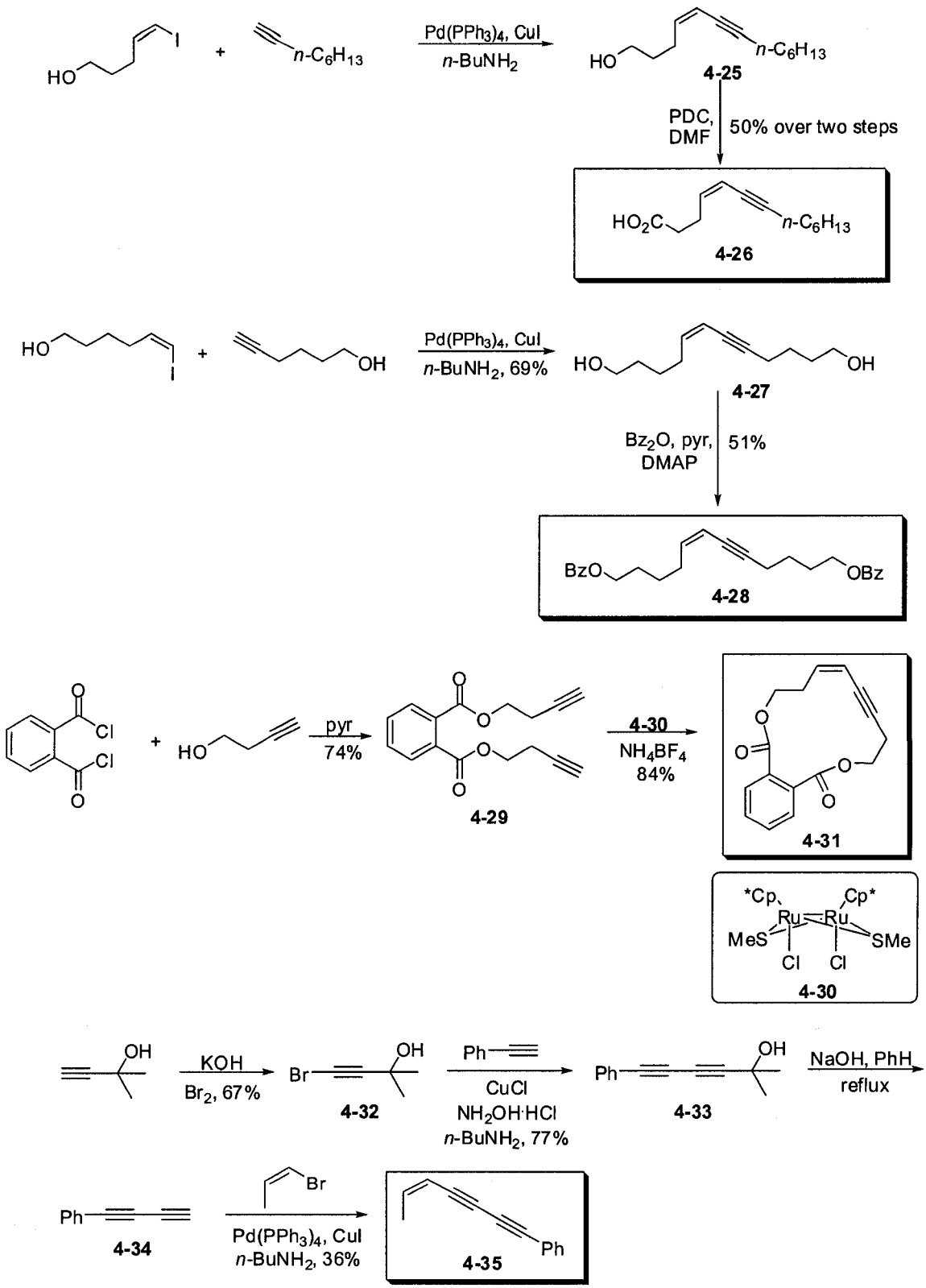
[188] Corey, E. J.; Schmidt, G. *Tetrahedron Lett.* **1979**, 399-402.

[189] Nishibayashi, Y.; Yamanashi, M.; Wakiji, I.; Hidai, M. *Angew. Chem. Int. Ed.* **2000**, *39*, 2909-2911.

[190] (a) Dabdoub, M.J.; Baroni, A.C.M.; Lenardão, E.J.; Gianeti, T.R.; Hurtado, G. *Tetrahedron* **2001**, *57*, 4271-4276. (b) Jiang, M. X.-W.; Rawat, M.; Wulff, W.D. *J. Am. Chem. Soc.* **2004**, *126*, 5970-5971.

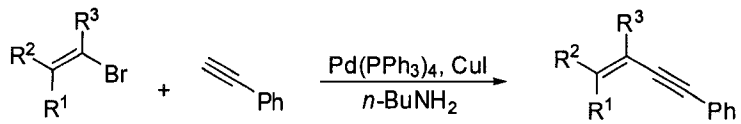



**Scheme 4.10**




**Scheme 4.10 (continued)**

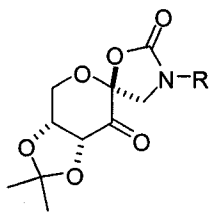
In addition to the conjugated *cis*-enynes above, a few enynes (**4-36 – 4-38**) with different olefin substitution patterns were synthesized via Sonogashira coupling (Scheme 4.11).




| | | | |
|---|---|---|---|
| **4-36** $R^1$ = Me | $R^2$ = Me | $R^3$ = H, | 79% |
| **4-37** $R^1$ = H | $R^2$ = Me | $R^3$ = H, | 84% |
| **4-38** $R^1$ = H | $R^2$ = Me | $R^3$ = Me, | 75% |

**Scheme 4.11**

### 4.B.ii. Asymmetric Epoxidation of Conjugated Enynes



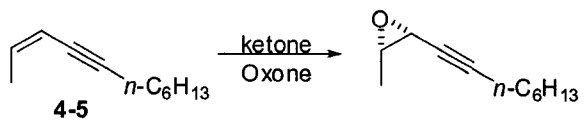

**3-62** R = (4-Me)-Ph
**3-63** R = (4-$SO_2$Me)-Ph
**3-64** R = (4-*n*-Bu)-Ph
**3-65** R = (4-Ph)-Ph
**3-66** R = (4-Et)-Ph
**4-39** R = (4-*t*-Bu)-Ph

**Figure 4.2**

Ketones **3-62 – 3-66** and **4-39** (Figure 4.2) developed in our labs were screened for epoxidation efficacy using *cis*-undec-2-en-4-yne (**4-5**) as substrate (Table 4.1). All gave higher enantiomeric excess than ketone **2-8**. Ketones **3-62** and **3-66** (Table 4.1, entries 1 and 2) were generally as effective as the others screened, and since they are the

most inexpensive to make and the most plentiful in our labs, they were chosen for use during further study.

**Table 4.1**[a]




**4-5**

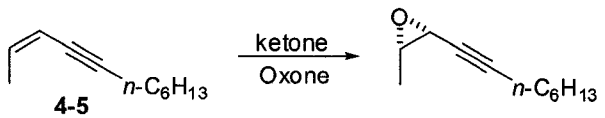
| Entry | ketone [R] | conv. (%)[b] | ee (%)[c] |
|---|---|---|---|
| 1 | **3-62** [(4-Me)-Ph] | 56 | 93 |
| 2 | **3-63** [(4-$SO_2$Me)-Ph] | 11 | 92 |
| 3 | **3-64** [(4-*n*-Bu)-Ph] | 68 | 94 |
| 4 | **3-65** [(4-Ph)-Ph] | 51 | 88 |
| 5 | **3-66** [(4-Et)-Ph] | 43 | 94 |
| 6 | **4-39** [(4-*t*-Bu)-Ph] | 26 | 95 |

[a] Reactions were carried out with enyne (1.0 eq.), catalyst (0.25 eq.), Oxone (1.6 eq.), and $K_2CO_3$ (6.7 eq.) in DME and buffer (0.1 M $K_2CO_3$-AcOH in 4 x $10^{-4}$ M aq. EDTA, pH 9.3) (1.5:1, v/v). Oxone and $K_2CO_3$ were added separately and simultaneously over 4 h at 0 °C. [b] The conversion was determined by GC of the crude reaction mixture. [c] Enantioselectivity was determined by GC (Chiraldex B-DM column) of the crude reaction mixture.

The reaction was further optimized by varying the reaction time, solvent, solvent/buffer ratio, and amount of Oxone (Table 4.2). Straight DME gave higher conversions than DME/DMM mixtures without sacrificing ee (Table 4.2, entries 1-3). It was found that for particularly unreactive substrates such as **4-5** (likely due to its poor solubility in the reaction mixture), the use of dioxane as solvent significantly increased conversion but gave lower ee. Increasing the ratio of solvent to buffer from 3:2 to 2:1 (v/v) (Table 4.2, entry 5 vs 6) and increasing the amount of Oxone (with a concomitant increase in $K_2CO_3$) (Table 4.2, entry 1 vs 4) also increases the conversion—sometimes

with an additional slight drop in ee. Addition of Oxone over longer periods of time increased conversion as well. Of all these measures to increase conversion, the use of dioxane is the most detrimental to enantioselectivity and should be used as a last resort.

**Table 4.2**[a]




**4-5**

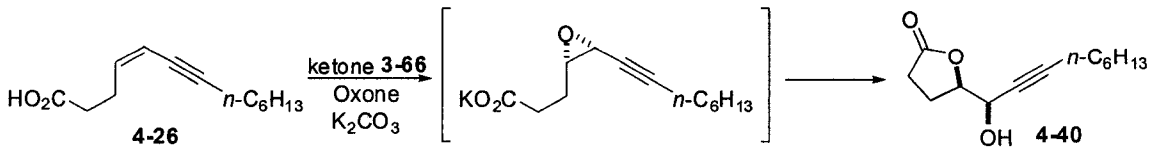
| Entry | ketone [R] | time (h) | solvent | solv:buffer (v/v) | eq. Oxone | conv. (%)[b] | ee (%)[c] |
|---|---|---|---|---|---|---|---|
| 1 | **3-62** [(4-Me)-Ph] | 4 | DME:DMM (3:1) | 3:2 | 1.6 | 27 | 93 |
| 2 | **3-62** [(4-Me)-Ph] | 4 | DME:DMM (5:1) | 3:2 | 1.6 | 27 | 93 |
| 3 | **3-62** [(4-Me)-Ph] | 4 | DME | 3:2 | 1.6 | 56 | 93 |
| 4 | **3-62** [(4-Me)-Ph] | 4 | DME:DMM (3:1) | 3:2 | 2.4 | 38 | 93 |
| 5 | **3-62** [(4-Me)-Ph] | 8 | DME | 3:2 | 2.4 | 77 | nd |
| 6 | **3-62** [(4-Me)-Ph] | 8 | DME | 2:1 | 2.4 | 85 | 92 |
| 7 | **3-66** [(4-Et)-Ph] | 12 | DME | 3:2 | 2.4 | 66 | 94 |
| 8 | **3-66** [(4-Et)-Ph] | 12 | dioxane | 3:2 | 1.6 | 85 | 91 |
| 9 | **3-66** [(4-Et)-Ph] | 12 | dioxane | 2:1 | 2.4 | 95 | 90 |

[a] Reactions were carried out with enyne (1.0 eq.), catalyst (0.25 eq.), Oxone (amount indicated), and $K_2CO_3$ (6.7 or 10.1 eq.) in DME and buffer (0.1 M $K_2CO_3$-AcOH in 4 x $10^{-4}$ M aq. EDTA, pH 9.3). Oxone and $K_2CO_3$ were added separately and simultaneously over the time indicated at 0 °C. [b] The conversion was determined by GC of the crude reaction mixture. [c] Enantioselectivity was determined by GC (Chiraldex B-DM column) of the crude reaction mixture.

With optimized conditions in hand, the epoxidation of other substrates was examined (Table 4.3). The data in Table 4.3 are the result of the best conditions for each substrate using the most effective ketone. As shown in the table, a variety of *cis*-enynes can be epoxidized with high enantioselectivity and good yield. The reactions were generally clean as judged by $^1$H NMR of the crude reaction mixtures, and, as was the case

with conjugated dienes, the reactions are stereospecific in that *cis*-enynes yield only *cis*-epoxides with no isomerization observed.

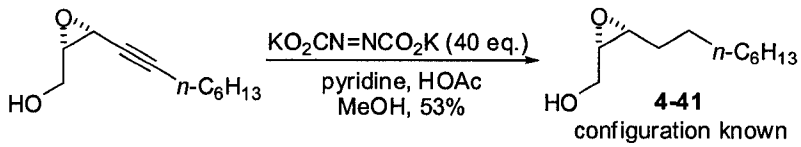
The substituents on the enynes ($R^1$ and $R^2$) have a significant effect on enantioselectivity. As with conjugated dienes, substrates where $R^1 = CH_3$ give higher ee's than analogous substrates with longer alkyl groups (Table 4.3, entries 1, 2, 10, and 11). More generally, substrates in which the polarity of the $R^1$ substituent is greater than that of the $R^2$ substituent give the highest enantioselectivities. This is particularly apparent when entries 17 (80% ee) and 18 (90% ee) are compared (Table 4.3). Biasing the system even more leads to higher enantioselectivity for allylic and homoallylic alcohols (97% ee) (Table 4.3, entries 19 and 20). Entry 22 with identical $R^1$ and $R^2$ groups gives 84% ee. In this case, any substituent effects should be nullified, thus giving an idea of the directing ability of the alkyne itself. When $R^2$ = TMS high enantioselectivities are observed, but yields are low due to cleavage of the TMS group under the reaction conditions (Table 4.3, entries 3, 14-15). In the case of entry 21, the epoxide is opened *in situ* to give lactone **4-40** as the product (Scheme 4.12). Macrocyclic enyne **4-31** and enediyne **4-35** and are also effective substrates in this system (entries 23-24). Electron-poor substrates such as **4-21** and **4-23** (entries 12-13) or very non-polar substrates such as **4-10** and **4-11** (entries 10 and 11) show markedly decreased reactivity (Table 4.3).




**Scheme 4.12**

Enynes **4-36** – **4-38** (Table 4.3, entries 25-27) were epoxidized in order to study the effect of different substitution patterns on enantioselectivity. For **4-36** (entry 25) the ee is very high (94%). This is fortuitous since ketone **1-5** is generally ineffective for this type of substrate.[191] Indeed, ketone **1-5** gives only 55% ee for epoxidation of this olefin.

The absolute configurations of the epoxides in entries 1 and 2 were determined to be (3R, 4S) and (2S, 3R) respectively by comparing their optical rotations with those previously determined.[182] For entry 11, the configuration was determined to be (2S, 3R) by reducing the alkyne with a large excess of diimide to known saturated epoxy alcohol (**4-41**) and comparing the optical rotation with the reported value (Scheme 4.13).[185,192]




**Scheme 4.13**

**Table 4.3.** Asymmetric Epoxidation of Conjugated Enynes[a]

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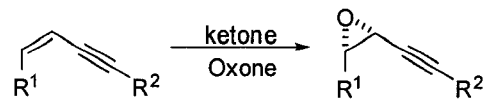
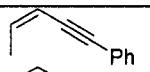
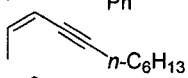
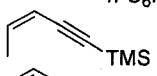
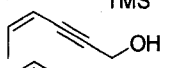
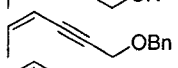
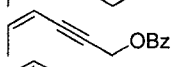
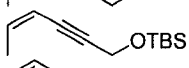
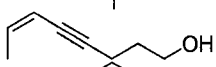
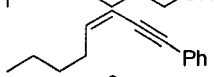
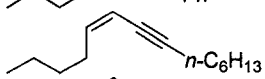
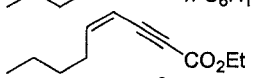
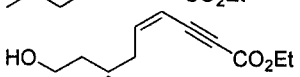
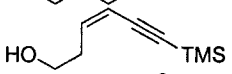
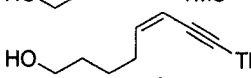
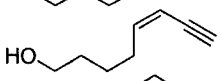
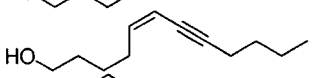
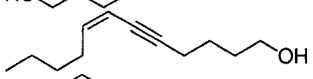
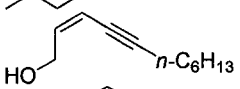
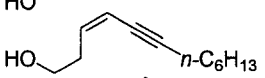
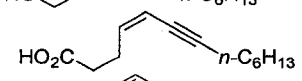
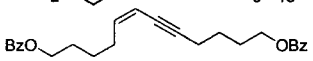
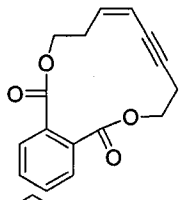
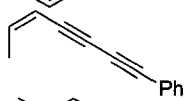
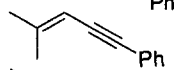
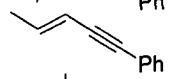
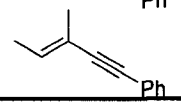
[191] Wang, Z.-X.; Tu, Y.; Frohn, M.; Zhang, J.-R.; Shi, Y. *J. Am. Chem. Soc.* **1997**, *119*, 11224-11235.

[192] Gao, Y.; Hanson, R. M.; Klunder, J. M.; Ko, S. Y.; Masamune, H.; Sharpless, K. B. *J. Am. Chem. Soc.* **1987**, *109*, 5765.




| Entry | Enyne | ketone [R] | T (°C) | t (h) | Yield (conv.) (%)[b] | ee (%) |
|---|---|---|---|---|---|---|
| 1 |  | **3-66** [(4-Et)-Ph] | -10 | 8 | 78 (100)[c,d] | 93[e,181a,c-h,182] |
| 2 |  | **3-66** [(4-Et)-Ph] | 0 | 12 | 84 (95)[f,g,h] | 90[i,181a,b,182] |
| 3 |  | **3-66** [(4-Et)-Ph] | 0 | 4 | 29 (88)[f,g] | 90[i] |
| 4 |  | **3-62** [(4-Me)-Ph] | -10 | 8 | 52 (100) | 85[i] |
| 5 |  | **3-66** [(4-Et)-Ph] | 0 | 12 | 67 (91) | 92[i] |
| 6 |  | **3-62** [(4-Me)-Ph] | 0 | 8 | 67 (90)[j] | 89[i] |
| 7 |  | **3-62** [(4-Me)-Ph] | 0 | 12 | 49 (68)[f,g,h] | 89[i] |
| 8 |  | **3-66** [(4-Et)-Ph] | -10 | 8 | 77 (99) | 80[i] |
| 9 |  | **3-62** [(4-Me)-Ph] | -10 | 8 | 83 (100) | 88[k] |
| 10 |  | **3-62** [(4-Me)-Ph] | 0 | 12 | 52 (70)[f,g,h] | 84[i] |
| 11 |  | **3-62** [(4-Me)-Ph] | 0 | 12 | nd (33)[f] | nd |
| 12 |  | **3-66** [(4-Et)-Ph] | 0 | 8 | (0)[g,h,j] | |
| 13 |  | **3-62** [(4-Me)-Ph] | 0 | 4 | nd (14)[f] | nd |
| 14 |  | **3-66** [(4-Et)-Ph] | 0 | 4 | 46 (80)[f,g] | 94[i,193] |
| 15 |  | **3-62** [(4-Me)-Ph] | 0 | 4 | 52 (82)[f,g] | 87[i] |
| 16 |  | **3-62** [(4-Me)-Ph] | 0 | 8 | 59 (92) | 80[i] |
| 17 |  | **3-62** [(4-Me)-Ph] | -10 | 8 | 70 (97) | 90[l] |
| 18 |  | **3-62** [(4-Me)-Ph] | -10 | 8 | 64 (100)[c] | 80[e] |
| 19 |  | **3-62** [(4-Me)-Ph] | -10 | 8 | 68 (92) | 97[i] |
| 20 |  | **3-66** [(4-Et)-Ph] | -10 | 8 | 66 (96) | 97[i] |
| 21 |  | **3-66** [(4-Et)-Ph] | -10 | 12[m] | 61 (nd) | 96[e] |
| 22 |  | **3-66** [(4-Et)-Ph] | 0 | 12 | 47 (67)[f,g,h] | 83[e] |

[193] Mukai, C.; Sugimoto, Y-i.; Ikeda, Y.; Hanaoka, M. *Chem. Commun.* **1994**, 1161-1162.

| | | | | | | |
|---|---|---|---|---|---|---|
| 23 |  | **3-66** [(4-Et)-Ph] | 0 | 12 | 54 (100)[c,f,g,n] | 87[e] |
| 24 |  | **3-62** [(4-Me)-Ph] | 0 | 8 | 76 (86)[c,g,n] | 93[e] |
| 25 |  | **3-66** [(4-Et)-Ph] | -10 | 8 | 71 (88) | 94[i,194] |
| 26 |  | **3-66** [(4-Et)-Ph] | 0 | 12 | 46 (86)[h] | 74[i] |
| 27 |  | **3-66** [(4-Et)-Ph] | 0 | 8 | 75 (99) | 40[i] |

[a] Unless otherwise stated, all reactions were carried out with enyne (1.0 eq.), catalyst (0.25 eq.), Oxone (1.6 eq.), and $K_2CO_3$ (6.7 eq.) in DME and buffer (0.1 M $K_2CO_3$-AcOH in 4 x $10^{-4}$ M aq. EDTA, pH 9.3) (1.5:1, v/v). Oxone and $K_2CO_3$ were added separately and simultaneously over the time and temperature specified. [b] Unless stated otherwise the conversion was determined by GC of the crude reaction mixture. [c] The conversion was determined by $^1$H NMR of the crude reaction mixture. [d] 0.20 eq. catalyst used [e] Enantioselectivity was determined by chiral HPLC (Chiralcel OD column). [f] with dioxane as solvent. [g] solvent-buffer (2:1, v/v). [h] 2.4 eq. Oxone/10.1 eq. $K_2CO_3$ were used. [i] Enantioselectivity was determined by Chiral GC (Chiraldex B-DM column). For entry 16, the ee was determined using the corresponding acetate. [j] with DME/dioxane (1:1, v/v) as solvent. [k] Enantioselectivity was determined using the corresponding benzoate by chiral HPLC (Chiralpak AD column). [l] Enantioselectivity was determined by chiral HPLC (Chiralcel OJ column). [m] Oxone was added over 8 h, and then the mixture was allowed to stir for an additional 4 h at 0 °C. [n] 0.30 eq. catalyst used.

The two major competing transition states for this system are likely spiro **A** and spiro **B** (Figure 4.3), and the previous observations can be rationalized based on this model. The configurations (*vide infra*) and high enantiomeric excess of the epoxides show that spiro **A** is greatly favored over spiro **B**. The stereochemistry of the remaining epoxides in Table 4.3, with the exception of entry 27, is tentatively assigned based on this model. Additionally, the results indicate that spiro **A** is further favored by increasing the polarity of $R^1$ with respect to $R^2$ or decreasing the polarity of $R^2$ with respect to $R^1$. A

[194] Nakata, K.; Takeda, T. Mihara, J.; Hamada, T.; Irie, R.; Katsuki, T. *Chem. Eur. J.* **2001**, *7*, 3776-3782.

probable explanation for this is that there exist additional hydrophobic interactions between the enyne substituents and catalyst (likely the *N*-aryl group). The reactions are conducted in an aqueous medium, so it's possible that a non-polar substituent on the olefin would prefer to orient itself next to the greasy *N*-aryl group on the oxazolidinone of the catalyst during the transition state.

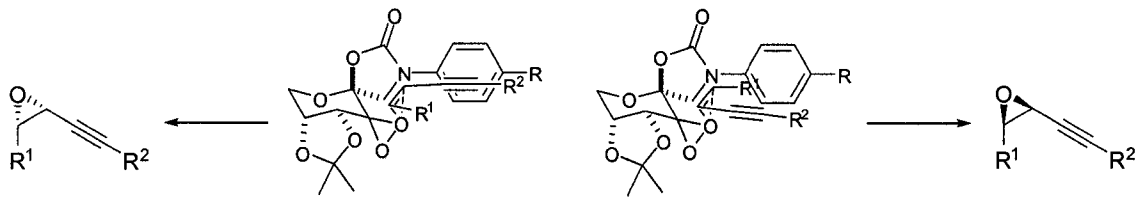



**Figure 4.3**

The results of entries 25-27 (Table 4.3) can also be rationalized using this model. In the case of entry 25, competing spiro transition state **D** is likely further disfavored due to steric repulsion between the methyl group *trans*- to the alkyne and the oxazolidinone resulting in higher ee than for entry 1 (Figure 4.4). In the case of entry 26, like other *trans*-olefins with the oxazolidinone-containing ketones, enantioselectivity suffers due to competition from planar transition state **F** (Figure 4.5). And finally, for entry 27, the enantioselectivity is low because spiro transition state **G** is disfavored due to steric repulsion between the methyl group α– to the alkyne and the oxazolidinone (Figure 4.6).

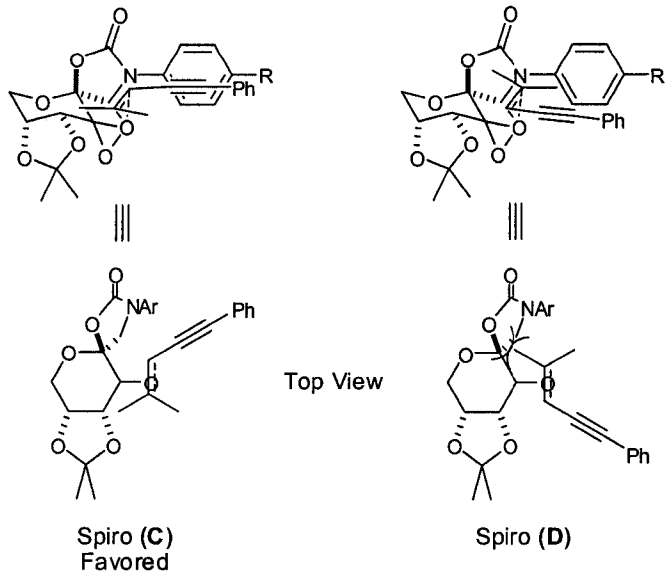



**Figure 4.4**

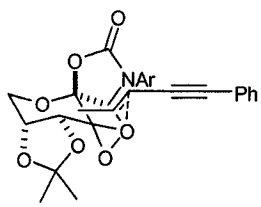
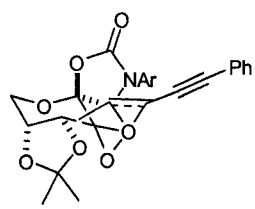



**Figure 4.5**



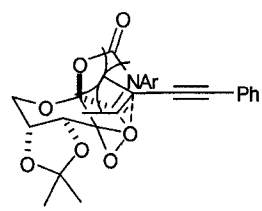




**Figure 4.6**

## 4.C. CONCLUSION

An effective system for the asymmetric epoxidation of conjugated *cis*-enynes has been developed using chiral ketones **3-62**, **3-66** and Oxone as oxidant. The reactions are highly stereo- and chemoselective and are stereospecific. In addition to the directing effect of the alkyne, hydrophobic interactions play an important role in stereodifferentiation. The increase in ee observed for **4-4** and **4-5** with ketones **3-62** and

**3-66** vs **2-8** is likely due to these ketones' increased ability to provide hydrophobic interactions. These insights will be useful for expansion of this methodology to other substrate classes, the prediction of the stereochemical outcome of a given reaction, and the design of new ketone catalysts in the future.

## 4.D. EXPERIMENTAL

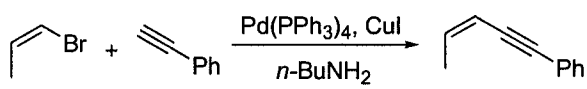
**General Methods.** All commercially available reagents were used without further purification. All glassware used for epoxidation was carefully washed with soap and water to be free of any trace metals which catalyze the decomposition of Oxone. Column chromatography was performed with silica gel (200-400 mesh) which was buffered with 1% $NEt_3$ (v/v). Melting points are uncorrected.

**General procedure for Sonogashira coupling.** Unless otherwise stated the enynes were prepared according to the following general procedure.[183] $Pd(PPh_3)_4$ (0.60 g, 0.50 mmol) was added at rt to a solution of vinyl halide (23.4 mmol) in benzene (25 mL) under Ar and was stirred for 45 min. A solution of alkyne (11.7 mmol) in *n*-$BuNH_2$ (12 mL, 120 mmol) was then added followed by CuI (0.35 g, 1.91 mmol). The reaction is exothermic, so the flask was kept in a cool water bath for the first 10 min. After stirring overnight at rt, petroleum ether (or $Et_2O$) (50 mL) was added and the mixture was poured into sat. aq. $NH_4Cl$ and was extracted with more petroleum ether. The combined organic extracts

were washed with sat. aq. $NH_4Cl$, $H_2O$, brine, dried ($Na_2SO_4$), and filtered. The residue was then concentrated and purified by column chromatography (pet. ether to 1:1 pet. ether:$Et_2O$).

**Representative Asymmetric Epoxidation Procedure (Table 4.3, entry 1).** To a solution of *cis*-1-phenyl-3-penten-1-yne **4-4** (0.071 g, 0.5 mmol) and ketone **3-66** (0.035 g, 0.10 mmol) in DME (7.5 mL) were added buffer (0.1 M $K_2CO_3$-AcOH in 4 x $10^{-4}$ M aq. EDTA, pH = 9.3) (5.0 mL) and $Bu_4NHSO_4$ (0.0075 g, 0.02 mmol) with stirring. After the mixture was cooled to -10 °C (bath temperature) via NaCl-ice bath, solutions of Oxone (0.20 M in 4 x $10^{-4}$ M aqueous EDTA, 4 mL) (0.49 g, 0.80 mmol) and $K_2CO_3$ (0.84 M in 4 x $10^{-4}$ M aqueous EDTA, 4 mL) (0.46 g, 3.36 mmol) were added dropwise separately and simultaneously over a period of 8 h via syringe pump. The reaction was then quenched with the addition petroleum ether and extracted with petroleum ether. The combined organic layers were washed with water, brine, dried ($Na_2SO_4$), filtered, concentrated, and purified by flash chromatography [the silica gel was buffered with 1% $Et_3N$ in petroleum ether; petroleum ether-ether was used as eluent] to give the *cis*-epoxide as a colorless oil (0.062 g, 78% yield, 93% ee).

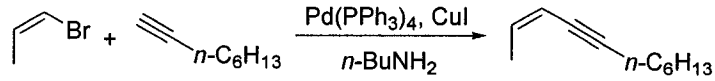
**(Table 4.3, entry 1)**



***cis*-1-Phenylpent-3-en-1-yne (4-4) (CPB-1346).** The enyne was prepared via Sonogashira coupling of *cis*-1-bromo-1-propene and phenylacetylene (87%). Colorless oil; IR (NaCl): 3027, 1490, $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 7.49-7.43 (m, 2H), 7.35-7.29 (m, 3H), 6.06 (dq, $J$ = 10.8, 6.9. Hz, 1H), 5.71 (dq, $J$ = 10.8, 1.5 Hz, 1H), 1.98 (dd, $J$ = 6.9, 1.5 Hz, 3H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 138.9, 131.6, 128.5, 128.2, 123.9, 110.2, 94.1, 86.4, 16.3.

**Epoxide (CPB-1440).** Colorless oil; 93% ee $[\alpha]^{25}_D$ = -40.3 (*c* 0.65, $CHCl_3$); IR (NaCl): 2227, 1490, 1349 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.49-7.45 (m, 2H), 7.35-7.30 (m, 3H), 3.65 (d, $J$ = 4.0 Hz, 1H), 3.27 (qd, $J$ = 5.2, 4.0 Hz, 1H), 1.51 (d, $J$ = 5.2 Hz, 3H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 132.1, 128.9, 128.5, 122.3, 85.5, 84.3, 54.7, 46.1, 15.0.

**(Table 4.3, entry 2)**

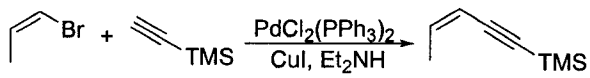



***cis*-Undec-2-en-4-yne (4-5) (CPB-1403).** The enyne was prepared via Sonogashira coupling of *cis*-1-bromo-1-propene and 1-hexyne (82%). Colorless oil; IR (NaCl): 2931, $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 5.89 (dq, $J$ = 10.6, 6.8 Hz, 1H), 5.50-5.45 (m, 1H), 2.35 (td, $J$ = 7.2, 2.0 Hz, 2H), 1.86 (dd, $J$ = 6.8, 1.6 Hz, 3H), 1.60-1.51 (m, 2H), 1.46-1.38

(m, 2H), 1.35-1.27 (m, 4H), 0.90 (t, $J$ = 7.2 Hz, 3H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 137.1, 110.6, 95.3, 77.3, 31.6, 29.1, 28.8, 22.8, 19.8, 15.9, 14.3.

**Epoxide (CPB-1726).** Colorless oil; 90% ee $[\alpha]^{25}_D$ = -34.2 (c 0.37, $CHCl_3$); IR (NaCl): 2240, 1456, 1349 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) δ 3.40 (dt, $J$ = 4.0, 1.6 Hz, 1H), 3.11 (qd, $J$ = 5.2, 4.0 Hz, 1H), 2.20 (td, $J$ = 7.2, 1.6 Hz, 2H), 1.53-1.47 (m, 2H), 1.42-1.22 (m, 6H), 1.40 (d, $J$ = 5.2 Hz, 3H), 0.88 (t, $J$ = 7.2 Hz, 3H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 86.8, 75.1, 54.1, 46.0, 31.5, 28.64, 28.60, 22.7, 19.0, 14.8, 14.2.

**(Table 4.3, entry 3)**

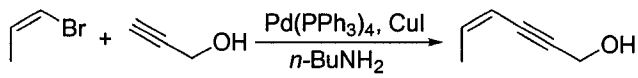



***cis*-1-Trimethylsilylpent-3-en-1-yne (4-17) (CPB-0917).** The enynye was prepared via Sonogashira coupling using a slightly different procedure.[186] *cis*-1-Bromopropene (3.0 g, 24.8 mmol) was taken up in $Et_2NH$ (25 mL). To this was added $PdCl_2(PPh_3)_4$ (0.23 g, 0.32 mmol), CuI (1.18 g, 6.2 mmol), and trimethylsilylacetylene (2.44 g, 24.8 mmol) at 0 °C under Ar. After 2 h the mixture was diluted with $Et_2O$, washed with water, brine, dried ($Na_2SO_4$), filtered, and concentrated. The crude oil was purified by column (pet. ether) to yield 3.43 g (41%) of a colorless volatile oil: IR (NaCl): 2152, 1251 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) δ 6.00 (dq, $J$ = 10.8, 6.8 Hz, 1H), 5.52 (dq, $J$ = 10.8, 1.6 Hz,

1H), 1.90 (dd, $J$ = 6.8, 1.6 Hz, 3H), 0.21 (s, 9H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 140.3, 110.3, 102.1, 99.2, 16.3, 0.3.

**Epoxide (CPB-1737).** Colorless oil; 90% ee $[\alpha]^{25}_D$ = -49.1 (*c* 0.11, $CHCl_3$); IR (NaCl): 2174, 1345, 1251 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) δ 3.42 (d, $J$ = 4.0 Hz, 1H), 3.16 (qd, $J$ = 5.4, 4.0 Hz, 1H), 1.40 (d, $J$ = 5.4 Hz, 3H), 0.19 (s, 9H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 100.5, 91.4, 54.4, 45.8, 14.8, -0.1. Anal. Calcd. for $C_8H_{14}OSi$: C, 62.28; H, 9.15. Found: C, 62.42; H, 9.02.

**(Table 4.3, entry 4)**

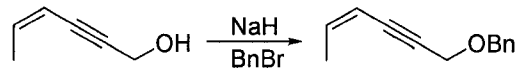



***cis*-Hex-4-en-2-yn-1-ol (4-6) (CPB-1503).** The enyne was prepared via Sonogashira coupling of *cis*-1-bromo-1-propene and propargyl alcohol (56%). Yellow oil; IR (NaCl): 3334, 2199, 1363, 1011 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) δ 6.01 (dq, $J$ = 10.8, 6.8 Hz, 1H), 5.54-5.48 (m, 1H), 4.44 (d, $J$ = 2.4 Hz, 2H), 1.88 (dd, $J$ = 6.8, 1.6 Hz, 3H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 139.5, 109.5, 91.9, 82.6, 51.9, 16.2.

**Epoxide (CPB-1538).** Colorless oil; 85% ee $[\alpha]^{25}_D$ = -52.3 (*c* 0.43, $CHCl_3$); IR (NaCl): 3383, 1350, 1025 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) δ 4.32 (d, $J$ = 1.6 Hz, 2H), 3.47 (dt, $J$ = 4.0, 1.6 Hz, 1H), 3.19 (qd, $J$ = 5.2, 4.0 Hz, 1H), 1.78 (s, 1H), 1.43 (d, $J$ = 5.2 Hz, 3H);

$^{13}C$ NMR (101 MHz, $CDCl_3$) δ 84.0, 80.9, 54.3, 51.3, 45.6, 14.9. Anal. Calcd. for $C_6H_8O_2$: C, 64.27; H, 7.19. Found: C, 64.50; H, 7.31.

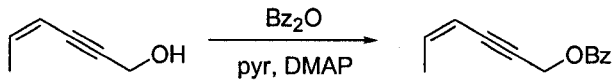
**(Table 4.3, entry 5)**




***cis*-1-Benzyloxyhex-4-en-2-yne (4-20) (CPB-1513).** Sodium hydride (0.45 g of a 60% dispersion in mineral oil, 11.2 mmol) was placed in a flask under Ar and the mineral oil was removed with pet. ether. THF (16 mL) was then added and the mixture was dropped to 0 °C. *cis*-Hex-4-en-2-yn-1-ol (**4-6**) (CPB-1503) (0.98g, 10.19 mmol) was then added with stirring and the mixture was warmed to rt over about 0.5 hr. Benzylbromide (1.75 g, 10.25 mmol was added and the mixture was allowed to stir overnight. The reaction was then quenched by addition of water and the mixture was extracted with $Et_2O$. The combined organic phases were washed with brine, dried ($Na_2SO_4$), filtered and concentrated. The residue was purified by column (pet. ether) to yield 1.10 g (58%) of the title compound as a colorless oil: IR (NaCl): 1355, 1088 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.41-7.28 (m, 5H), 6.03 (dq, $J$ = 10.8, 6.8 Hz, 1H), 5.58-5.53 (m, 1H), 4.65 (s, 2H), 4.36 (d, $J$ = 2.0 Hz, 2H), 1.91 (dd, $J$ = 6.8, 2.0 Hz, 3H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 139.4, 137.8, 128.6, 128.3, 128.0, 109.7, 89.7, 83.4, 71.6, 58.1, 16.2.

**Epoxide (CPB-1542).** Colorless oil; 92% ee $[\alpha]^{25}_{D}$ = -34.8 (*c* 0.31, $CHCl_3$); IR (NaCl): 1348, 1074 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.38-7.28 (m, 5H), 4.61 (s, 2H), 4.24 (d, *J* = 1.6 Hz, 2H), 3.50 (dt, *J* = 4.0, 1.6 Hz, 1H), 3.20 (qd, *J* = 5.6, 4.0 Hz, 1H), 1.46 (d, *J* = 5.6 Hz, 3H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 137.4, 128.7, 128.3, 128.2, 81.7, 71.8, 57.5, 54.2, 45.6, 15.0. Anal. Calcd. for $C_{13}H_{14}O_2$: C, 77.20; H, 6.98. Found: C, 77.42; H, 6.70.

**(Table 4.3, entry 6)**

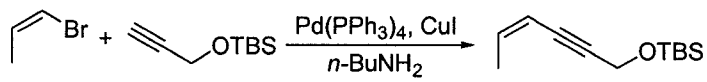



***cis*-Benzoyloxyhex-4-en-2-yne (4-19) (CPB-1507).** *cis*-Hex-4-en-2-yn-1-ol (**4-6**) (CPB-1503) (0.90 g, 9.36 mmol) was dissolved in 48 mL $CH_2Cl_2$. Benzoic anhydride (4.24 g, 18.72 mmol), pyridine (1.9 mL, 23.4 mmol) and DMAP (0.06 g, 0.48 mmol) were then added in single portions and the mixture was stirred at rt overnight. Sat. aq. $NH_4Cl$ (50 ml) was then added and the aqueous layer was extracted with $CH_2Cl_2$. The combined organic phases were washed with water, brine, dried ($Na_2SO_4$), filtered and concentrated. The residue was purified by column (pet. ether) to yield 1.03 g (55%) of the title compound as a colorless oil: IR (NaCl): 2211, 1724, 1268 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 8.11-8.08 (m, 2H), 7.61-7.56 (m, 1H), 7.48-7.44 (m, 2H), 6.06 (dq, *J* = 11.2, 6.8 Hz, 1H), 5.57-5.50 (m, 1H), 5.10 (d, *J* = 2.0 Hz, 2H), 1.89 (dd, *J* = 6.8, 1.6 Hz, 3H);

$^{13}$C NMR (101 MHz, $CDCl_3$) δ 166.1, 140.4, 133.4, 130.0, 129.9, 128.6, 109.4, 87.6, 83.6, 53.7, 16.3.

**Epoxide (CPB-1648).** Colorless oil; 89% ee $[\alpha]^{25}_D$ = -49.2 (*c* 0.38, $CHCl_3$); IR (NaCl): 1726, 1270 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) δ 8.10-8.06 (m, 2H), 7.70-7.57 (m, 1H), 7.49-7.44 (m, 2H), 4.98 (d, *J* = 1.4 Hz, 2H), 3.48 (dt, *J* = 4.0, 1.6 Hz, 1H), 3.23-3.16 (m, 1H), 1.45 (d, *J* = 5.2 Hz, 3H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 166.0, 133.6, 130.0, 129.6, 128.7, 82.1, 79.7, 54.3, 52.8, 45.5, 14.9. Anal. Calcd. for $C_{13}H_{12}O_3$: C, 72.21; H, 5.59. Found: C, 72.36; H, 5.70.

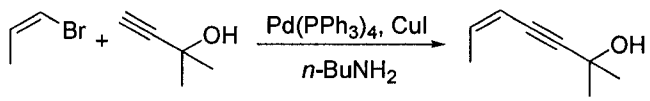
**(Table 4.3, entry 7)**




***cis*-1-*t*-Butyldimethylsiloxyhex-4-en-2-yne (4-7) (CPB-1349).** The enyne was prepared via Sonogashira coupling of *cis*-1-bromo-1-propene and *t*-butyldimethyl-(2-propynyloxy)-silane with propargyl alcohol (61%). Colorless oil; IR (NaCl): 1088 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) δ 5.98 (dq, *J* = 10.8, 6.8 Hz, 1H), 5.53-5.48 (m, 1H), 4.88 (d, *J* = 1.6 Hz, 2H), 1.88 (dd, *J* = 6.8, 1.6 Hz, 3H), 0.93 (s, 9H), 0.14 (s, 6H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 138.8, 109.9, 92.5, 81.7, 52.5, 26.1, 18.5, 16.1, -4.9.

**Epoxide (CPB-1724).** Colorless oil; 89% ee $[\alpha]^{25}_{D}$ = -40.0 (*c* 0.11, $CHCl_3$); IR (NaCl): 1472, 1083 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 4.36 (d, *J* = 1.6 Hz, 2H), 3.46 (dt, *J* = 4.0, 1.6 Hz, 1H), 3.17 (qd, *J* = 4.8, 4.0 Hz, 1H), 1.43 (d, *J* = 4.8 Hz, 3H), 0.92 (s, 9H), 0.13 (s, 6H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 84.5, 79.9, 54.3, 51.9, 45.7, 26.0, 18.5, 15.0, -4.9. Anal. Calcd. for $C_{12}H_{22}O_2Si$: C, 63.66; H, 9.80. Found: C, 63.47; H, 9.79.

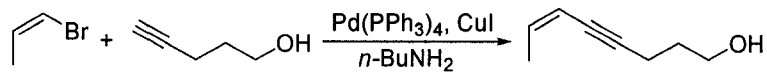
**(Table 4.3, entry 8)**




***cis*-2-Methylhept-5-en-3-yn-2-ol (4-8) (CPB-1525).** The enyne was prepared via Sonogashira coupling of *cis*-1-bromo-1-propene and 2-methyl-3-butyn-2-ol (85%). Yellow oil; IR (NaCl): 3356, 2215, 1363, 1165 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 5.98 (dq, *J* = 10.8, 6.8 Hz, 1H), 5.49 (dq, *J* = 10.8, 1.6 Hz, 1H), 1.87 (dd, *J* = 6.8, 1.6 Hz, 3H), 1.57 (s, 6H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 138.9, 109.7, 98.6, 79.0, 65.9, 31.8, 16.1.

**Epoxide (CPB-1541).** Colorless oil; 80% ee $[\alpha]_D^{25}$ = -38.5 (*c* 0.28, $CHCl_3$); IR (NaCl): 3416, 2241, 1349, 1169 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 3.42 (d, *J* = 4.4 Hz, 1H), 3.20-3.14 (m, 1H), 1.94 (s, 1H), 1.54 (s, 6H), 1.42 (d, *J* = 4.8 Hz, 3H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 90.4, 65.4, 54.2, 45.6, 31.5, 14.9. Anal. Calcd. for $C_8H_{12}O_2$: C, 68.54; H, 8.63. Found: C, 68.33; H, 8.75.

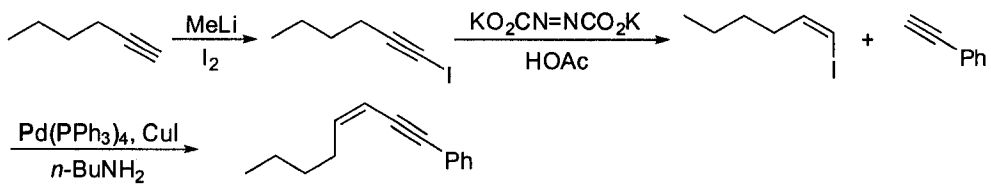
**(Table 4.3, entry 9)**




***cis*-Oct-6-en-4-yn-1-ol (4-9) (CPB-1508).** The enyne was prepared via Sonogashira coupling of *cis*-1-bromo-1-propene and 2-methyl-3-butyn-2-ol (77%). Yellow oil; IR (NaCl): 3346, 1435, 1055 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 5.89 (dq, $J$ = 10.8, 6.8 Hz, 1H), 5.45 (m, 1H), 3.77 (t, $J$ = 6.4 Hz, 2H), 2.47 (td, $J$ = 6.8, 2.4 Hz, 2H), 1.83 (dd, $J$ = 6.8, 1.6 Hz, 3H), 1.81-1.78 (m, 3H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 137.4, 110.3, 94.0, 77.8, 61.8, 31.6, 16.2, 15.9.

**Epoxide (CPB-1534).** Colorless oil; 92 % ee $[\alpha]^{25}_D$ = -27.9 (*c* 2.33, $CHCl_3$); IR (NaCl): 3384, 2241, 1350, 1055 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 3.76 (q, $J$ = 6.0 Hz, 2H), 3.42 (dt, $J$ = 4.0, 2.0 Hz, 1H), 3.14 (qd, $J$ = 5.6, 4.0 Hz, 1H), 2.38 (td, $J$ = 7.2, 2.0 Hz, 2H), 1.79 (quint., $J$ = 6.0 Hz, 2H), 1.42 (d, $J$ = 5.6 Hz, 3H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 85.9, 75.7, 61.7, 54.2, 46.0, 31.3, 15.5, 14.9. Anal. Calcd. for $C_8H_{12}O_2$: C, 68.54; H, 8.63. Found: C, 68.37; H, 8.68.

**(Table 4.3, entry 10)**




**1-Iodo-1-hexyne (CPB-1409).** The title compound was prepared according to a literature procedure:[184] 1-Hexyne (36.0 g, 0.44 mol) in 200 mL $Et_2O$ was placed in a flask equipped with stir bar and reflux condenser. The system was flushed with Ar and MeLi (1.6 M in $Et_2O$, 313 mL, 0.5 mol) was added at 0 °C. The ice bath was then removed and the mixture was stirred at rt for 1 h and then dropped to -78 °C. $I_2$ (127.0 g, 0.5 mmol) was then added and the mixture was allowed to warm to rt over 2 h and the was stirred at rt overnight. Water (200 mL) was then added and the mixture was poured into 300 mL water. The phases were separated and the aqueous phase was extracted with $Et_2O$. The combined organic phases were then washed with sat. aq. $Na_2S_2O_3$, brine, dried ($Na_2SO_4$), filtered, and concentrated. The residue was then distilled (bp 40-43 °C at 3 mmHg) to yield 76.48 g (84%) of the title compound as a colorless oil: IR (NaCl): 1465 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 2.37 (t, $J$ = 6.8 Hz, 2H), 1.56-1.37 (m, 4H), 0.92 (t, $J$ = 7.6 Hz, 3H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 95.0, 30.8, 22.1, 20.7, 13.8, -7.5.

***cis*-1-Iodo-1-hexene (CPB-1413).** The title compound was prepared according to a literature procedure:[184] Azodicarbonamide (180.0 g, 1.54 mol) was added over a period of 30 min to 40% aq. KOH (540 mL) at 0 °C with stirring in a 2 L flask. After the

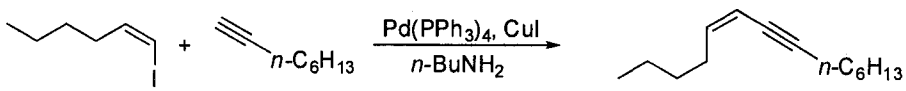
addition was complete the mixture was stirred for 45 min at 0 °C and was then filtered. The solid was washed on the filter with 500 mL cold MeOH. The bright yellow potassium azodicarboxylate was then placed into a 2 L flask containing MeOH (800 mL ) and 1-iodo-1-hexyne (CPB-1409) (38 g, 0.18 mol) and equipped with reflux condenser and addition funnel. The mixture was stirred at rt while a solution of acetic acid (150 mL) in MeOH (400 mL) was slowly added via addition funnel at such a rate so as to maintain a gentle reflux. After the addition was complete the colorless mixture was poured into 500 mL water and was extracted with pet. ether. The combined organic phases were then washed with water, brine, dried ($Na_2SO_4$), filtered and concentrated. The residue was then dissolved in 150 mL *n*-butylamine and was allowed to stand for 2 h at rt in order to remove any iodohexane that had been formed. Pet. ether was then added and the solution was washed with water, 10% aq. HCl, water, dried ($Na_2SO_4$), filtered, and concentrated to yield 13.1 g (35%) of the desired compound as a colorless oil: IR (NaCl): 1278 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 6.20-6.14 (m, 2H), 2.18-2.12 (m, 2H), 1.45-1.33 (m, 4H), 0.93 (t, $J$ = 7.2, Hz, 3H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 141.7, 82.3, 34.6, 30.3, 22.4, 14.2.

***cis*-1-Phenyloct-3-en-1-yne (4-10) (CPB-1416).** The enyne was prepared via Sonogashira coupling of *cis*-1-iodo-1-hexene (CPB-1413) and phenylacetylene (76%). Colorless oil; IR (NaCl): 1466 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.36-7.32 (m, 2H), 7.25-7.19 (m, 3H), 5.89 (dt, $J$ = 10.8, 7.6 Hz, 1H), 5.58 (dt, $J$ = 10.8, 1.2 Hz, 1H), 2.32

(qd, $J$ = 7.6, 1.2 Hz, 2H), 1.38-1.26 (m, 4H), 0.85 (t, $J$ = 7.2 Hz, 3H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 144.6, 131.6, 128.5, 128.2, 123.9, 109.2, 93.6, 86.7, 31.2, 30.3, 22.5, 14.1.

**Epoxide (CPB-1711).** Colorless oil; 84% ee $[\alpha]^{25}_D$ = -3.6 (*c* 0.42, $CHCl_3$); IR (NaCl): 2227, 1491 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.48-7.44 (m, 2H), 7.36-7.29 (m, 3H), 3.66 (d, $J$ = 4.4 Hz, 1H), 3.14 (td, $J$ = 6.0, 4.4 Hz, 1H), 1.87-1.72 (m, 2H), 1.59-1.40 (m, 4H), 0.96 (t, $J$ = 7.2 Hz, 3H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 132.1, 128.9, 122.4, 85.4, 84.5, 58.9, 45.9, 29.4, 28.3, 22.7, 14.3. Anal. Calcd. for $C_{14}H_{16}O$: C, 83.96; H, 8.05. Found: C, 84.04; H, 7.78.

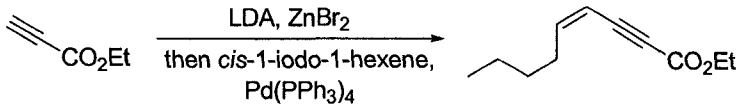
**(Table 4.3, entry 11)**




***cis*-Tetradec-5-en-7-yne (4-11) (CPB-1418).** The enyne was prepared via Sonogashira coupling of *cis*-1-iodo-1-hexene (CPB-1413) and 1-octyne (49%). Colorless oil; IR (NaCl): 1489 cm$^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$) δ 5.82 (dt, $J$ = 10.5, 7.5 Hz, 1H), 5.48-5.40 (m, 1H), 2.40-2.24 (m, 4H), 1.60-1.50 (m, 2H), 1.50-1.24 (m, 10H), 0.98-0.84 (m, 6H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 142.8, 109.5, 94.7, 81.3, 31.6, 31.3, 29.9, 29.1, 28.8, 22.8, 22.5, 19.8, 14.3.

**Epoxide (CPB-1707).** Colorless oil; IR (NaCl): 2239, 1467 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 3.42 (dt, $J$ = 4.0, 1.6 Hz, 1H), 3.00 (td, $J$ = 6.0, 4.0 Hz, 1H), 2.26-2.21 (m, 2H), 1.78-1.61 (m, 2H), 1.55-1.24 (m, 12H), 0.97-0.88 (m, 6H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 86.8, 75.3, 58.3, 45.8, 31.5, 29.2, 28.7, 28.6, 28.3, 22.8, 19.0, 14.3, 14.2. Anal. Calcd. for $C_{14}H_{24}O$: C, 80.71; H, 11.61. Found: C, 80.77; H, 11.69.

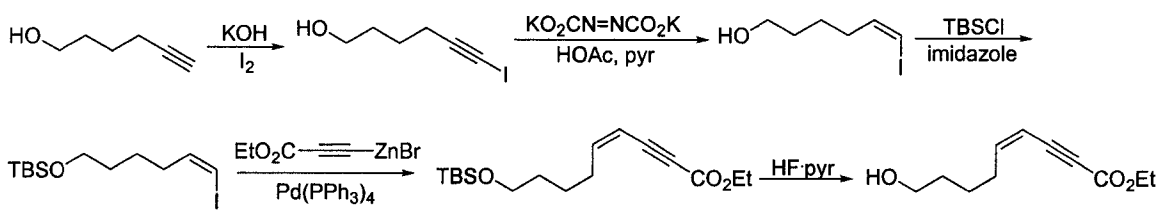
**(Table 4.3, entry 12)**




***cis*-Ethylnon-4-en-2-ynoate (4-21) (CPB-1446).** The enyne was prepared according to to a literature procedure.[187] To a solution of *N,N*-diisopropylamine (0.34 mL, 2.4 mmol) in THF (5 mL) was added *n*-BuLi (1.6 M in hexane, 1.5 mL, 2.4 mmol) at 0 °C under Ar. After stirring for 30 min, ethyl propiolate (0.235 g, 2.4 mmol) in THF (1mL) was added to the LDA solution via cannula at -78 °C. The mixture was stirred at -78 °C for 30 min and then a solution of anhydrous $ZnBr_2$ (0.54g, 2.4 mmol) in THF (2 mL) was added via cannula at -78 °C and the mixture was warmed to 0 °C over 30 min. *cis*-1-Iodo-1-hexene (CPB-1413) (0.42g, 2.0 mmol) and $Pd(PPh_3)_4$ (0.07 g, 0.06 mmol) in 2 mL THF were then added via cannula at 0 °C and the mixture was stirred at rt overnight. The mixture was then diluted with $Et_2O$, washed with sat. aq. $NH_4Cl$, sat. aq. $NaHCO_3$, dried

($Na_2SO_4$), filtered, and concentrated. The residue was purified by column (pet. ether to 95:5 pet. ether:$Et_2O$) to yield 0.22 g (61%) of the enyne as a yellow oil: IR (NaCl): 2209, 1712, 1263 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 6.25 (dt, $J$ = 10.8, 7.6 Hz, 1H), 5.55 (dt, $J$ = 10.8, 1.2 Hz, 1H), 4.26 (q, $J$ = 7.2 Hz, 2H), 2.39 (qd, $J$ = 7.2, 1.2 Hz, 2H), 1.45-1.30 (m, 4H), 1.33 (t, $J$ = 7.2 Hz, 3H), 0.93 (t, $J$ = 7.2 Hz, 3H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 154.4, 151.7, 106.7, 84.9, 83.6, 62.1, 30.92, 30.88, 22.4, 14.3, 14.1.

**(Table 4.3, entry 13)**




**6-Iodo-5-hexyn-1-ol (CPB-1549).** The title compound was prepared according to a literature procedure (46%):[185] To a solution of 5-hexyn-1-ol (14.5 g, 147 mmol) in 150 mL MeOH was added a solution of KOH (20.7 g, 369 mmol) in 30 mL water at 0 °C. After stirring for 10 min, $I_2$ (41.2 g, 162 mmol) was added in one portion and the mixture was warmed to rt. After being stirred at rt for 3 h, the mixture was diluted with water and the aqueous layer was extracted with $Et_2O$. The combined organic layers were concentrated to give a brown residue. This residue was then dissolved in $CH_2Cl_2$ and was washed with sat. aq. $Na_2S_2O_3$, brine, dried ($Na_2SO_4$), and concentrated. The residue was then purified by column (1:1 pet. ether:$Et_2O$) to give 15.2 g (46%) of the title compound

as a yellow oil: IR (NaCl): 3306, 2184, 1063 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 3.68 (t, $J$ = 6.4 Hz, 2H), 2.42 (t, $J$ = 6.4 Hz, 2H), 1.74-1.57 (m, 4H), 1.45 (s, 1H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 94.5, 62.6, 31.9, 25.0, 20.8, -6.7.

***cis*-6-Iodo-5-hexen-1-ol (CPB-1604).** The title compound was prepared according to a literature procedure:[185] To a solution of 6-iodo-5-hexyn-1-ol (CPB-1549) (15.2 g, 67.9 mmol) in 110 mL MeOH was added pyridine (32.3 g, 408 mmol), and potassium azodicarboxylate (1413) (8.0 g, 40.8 mmol) with stirring at rt. Acetic acid (25.7 g, 428 mmol) was then added by syringe pump over 10 h. During the addition of acetic acid additional potassium azodicarboxylate (8.0 g, 40.8 mmol) was added at 2 h, 4 h, 6 h, and 8 h (40 g, 204 mmol total). After complete addition of acetic acid, the mixture was poured into a 1 L flask with 150 mL $Et_2O$. 1.0 M aq. HCl (450 mL) was then added very slowly. The aqueous phase was then extracted with $Et_2O$ and the combined organic layers were concentrated. The residue was dissolved in $Et_2O$ and was washed with 1.0 M aq. HCl, sat. aq. $NaHCO_3$, brine, dried ($Na_2SO_4$), filtered and concentrated. The residue was then dissolved in *n*-butylamine (15 mL) and was stirred overnight at rt to remove any over reduction product. The mixture was then dissolved in $Et_2O$ and was washed with 1.0 M aq. HCl, sat. aq. $NaHCO_3$, brine, dried ($Na_2SO_4$), filtered and concentrated. The residue was then purified by column (1:1 pet. ether:$Et_2O$) to give 9.94 g (65%) of the title compound as a colorless oil: IR (NaCl): 3329, 1274, 1065 $cm^{-1}$; $^1H$ NMR (400 MHz,

$CDCl_3$) δ 6.24-6.15 (m, 2H), 3.68 (t, $J$ = 6.4 Hz, 2H), 2.19 (q, $J$ = 7.2 Hz, 2H), 1.65-1.48 (m, 4H), 1.36 (s, 1H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 141.2, 82.9, 62.9, 34.6, 32.3, 24.4.

***cis*-6-Iodo-1-*t*-butyldimethylsiloxy-hex-5-ene (CPB-1619).** To a solution of *cis*-6-iodo-5-hexen-1-ol (15.4 g, 68.3 mmol) in 270 ml $CH_2Cl_2$ was added imidazole (9.79 g, 144 mmol) at rt with stirring. After the imidazole had completely dissolved *t*-butyldimethylchlorosilane (13.4 g, 89.0 mmol) was added. The mixture was stirred overnight at rt in the dark and was then poured into water (200 mL). The phases were separated and the organic phase was washed with sat. aq. $NH_4Cl$, water, brine, dried ($Na_2SO_4$), filtered, and concentrated. The residue was purified by column (pet. ether) to give 19.7 g (85%) of the title compound as a colorless oil: IR (NaCl): 1471, 1255, 1105 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 6.22-6.14 (m, 2H), 3.63 (t, $J$ = 6.0 Hz, 2H), 2.17 (q, $J$ = 6.7 Hz, 2H), 1.64-1.45 (m, 4H), 0.90 (s, 9H), 0.06 (s, 6H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 141.5, 82.6, 63.1, 34.6, 32.4, 26.2, 24.5, 18.6, -5.0.

***cis*-Ethyl-9-*t*-butyldimethylsiloxynon-4-en-2-ynoate (4-22) (CPB-1621).** The enyne was prepared according to the procedure used above to prepare *cis*-ethyl-4-nonen-2-ynoate (CPB-1446) (34%). Brown oil; IR (NaCl): 2209, 1709, 1259, 1101 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 6.25 (dt, $J$ = 10.8, 7.6 Hz, 1H), 5.70 (dt, $J$ = 10.8, 1.6 Hz, 1H), 4.26 (q, $J$ = 6.8 Hz, 2H), 3.63 (t, $J$ = 6.2 Hz, 2H), 2.41 (qd, $J$ = 7.6, 1.6 Hz, 2H), 1.58-1.48 (m, 4H), 1.33, (t, $J$ = 6.8 Hz, 3H), 0.90 (s, 9H), 0.06 (s, 6H); $^{13}C$ NMR (101 MHz,

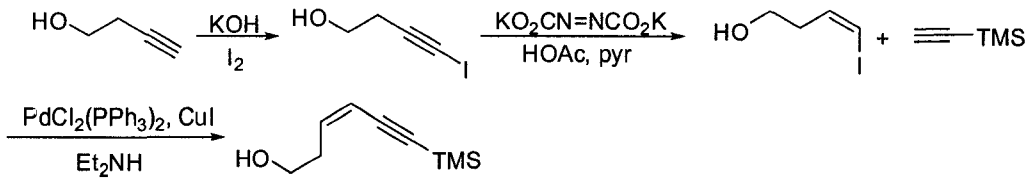
$CDCl_3$) δ 154.3, 151.3, 106.9, 85.0, 83.4, 63.0, 62.1, 32.4, 30.9, 26.2, 25.1, 18.6, 14.3, -5.1.

***cis*-Ethyl-9-hydroxy-non-4-en-2-ynoate (4-23) (CPB-1638).** (Z)-Ethyl-9-*t*-butyldimethylsiloxynon-4-en-2-ynoate (**4-22**) (CPB-1621) (2.0 g, 6.4 mmol) was dissolved in 130 mL THF with stirring. The mixture was cooled to 0 °C and HF·pyridine complex (7.73 mL) was added. The mixture was stirred for 0.5 h and then the ice bath was removed. When the starting material had disappeared by TLC the mixture was recooled to 0 °C, diluted with 100 mL $Et_2O$, and washed with sat. aq. $NaHCO_3$. The organic layer was then washed with water, brine, dried ($Na_2SO_4$), filtered, and concentrated. The residue was purified by column (1:1 pet. ether:$Et_2O$ to $Et_2O$) to yield 1.01 g (80%) of the title compound as a pale yellow oil: IR (NaCl): 3378, 2208, 1708, 1262 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 6.27 (dt, $J$ = 10.8, 7.6 Hz, 1H), 5.60-5.56 (m, 1H), 4.26 (q, $J$ = 7.2 Hz, 2H), 3.72-3.64 (m, 2H), 2.42 (qd, $J$ = 7.6, 1.6 Hz, 2H), 1.66-1.49(m, 4H), 1.33 (t, $J$ = 7.2 Hz, 3H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 154.3, 151.0, 107.2, 85.0, 83.4, 62.7, 62.2, 32.2, 30.7, 24.9, 14.3.

**Epoxide (CPB-1630).** Colorless oil; IR (NaCl): 3392, 2240, 1714, 1269 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 4.26 (q, $J$ = 7.2 Hz, 2H), 3.70 (t, $J$ = 6.0 Hz, 2H), 3.53 (d, $J$ = 4.2, Hz, 1H), 3.16 (td, $J$ = 6.0, 4.2 Hz, 1H), 1.80-1.58 (m, 6H), 1.44 (s, 1H), 1.33 (t, 7.2 Hz,

3H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 153.1, 82.3, 76.8, 62.7, 62.6, 58.7, 44.4, 32.4, 29.4, 22.4, 14.2.

**(Table 4.3, entry 14)**



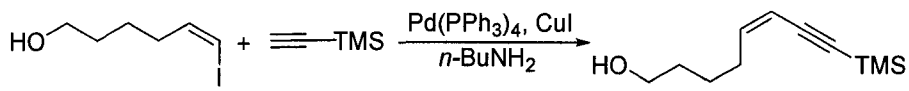

**4-Iodo-3-butyn-1-ol (CPB-0413).** The title compound was prepared according to the procedure used above to prepare 6-iodo-5-hexyn-1-ol (CPB-1549) (73%). Yellow oil; IR (NaCl): 3356, 2184, 1048 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 3.74 (t, $J$ = 6.4 Hz, 2H), 2.64 (t, $J$ = 6.4 Hz, 2H), 1.83 (s, 1H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 91.4, 61.2, 25.3, -4.2.

***cis*-4-Iodo-3-buten-1-ol (CPB-0415).** The title compound was prepared according to the procedure used above to prepare *cis*-6-iodo-5-hexen-1-ol (CPB-1604) (49%). Colorless oil; IR (NaCl): 3331, 1610, 1045 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 6.37 (d, $J$ = 7.2 Hz, 1H), 6.28 (q, $J$ = 7.0 Hz, 1H), 3.75 (t, $J$ = 6.6 Hz, 2H), 2.44 (qd, $J$ = 6.6, 0.9 Hz, 2H), 1.43 (s, 1H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 137.8, 85.1, 61.2, 38.3.

***cis*-6-Trimethylsilylhex-3-en-5-yn-1-ol (4-18) (CPB-0418).** The enyne was prepared via Sonogashira coupling of *cis*-4-iodo-3-buten-1-ol (CPB-0415) and trimethylsilylacetylene according to the same procedure used for *cis*-1-trimethylsilylpent-3-en-1-yne (**4-6**) (CPB-0917) (80%). Colorless oil: IR (NaCl): 3344, 2149, 1250 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 5.97 (dt, $J$ = 10.8, 7.2 Hz, 1H), 5.59 (d, $J$ = 10.8 Hz, 1H), 3.71 (t, $J$ = 6.8 Hz, 2H), 2.58 (dt, $J$ = 7.2, 6.8 Hz, 2H), 1.36 (s, 1H), 0.17 (s, 9H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 141.0, 111.9, 101.8, 99.7, 62.0, 34.0, 0.0.

**Epoxide (CPB-1618).** Colorless oil; 94% ee $[\alpha]^{25}_D$ = -41.6 (*c* 0.91, $CHCl_3$); IR (NaCl): 3404, 2173, 1251, 1047 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 3.90 (td, $J$ = 6.0, 1.6 Hz, 2H), 3.48 (d, $J$ = 4.0, 1H), 3.26-3.22 (m, 1H), 2.08-1.92 (m, 2H), 0.19 (s, 9H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 100.3, 92.0, 60.2, 56.2, 45.2, 32.5, -0.1. Anal. Calcd. for $C_9H_{16}O_2Si$: C, 58.65; H, 8.75. Found: C, 58.90; H, 8.90.

**(Table 4.3, entry 15)**

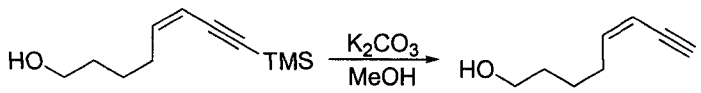



***cis*-8-Trimethylsilyloct-5-en-7-yn-1-ol (4-12) (CPB-1609).** The enyne was prepared via Sonogashira coupling of *cis*-6-iodo-5-hexen-1-ol (CPB-1604) and trimethylsilylacetylene (62%). Yellow oil; IR (NaCl): 3346, 2150, 1250 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 5.95 (dt, $J$ = 10.8, 7.6 Hz, 1H), 5.51 (dt, $J$ = 10.8, 1.6 Hz, 1H), 3.68 (t, $J$ = 6.4 Hz, 2H),

2.37 (qd, $J$ = 7.6, 1.6 Hz, 2H), 1.66-1.47 (m, 4H), 1.36 (s, 1H), 0.21 (s, 9H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 145.1, 109.8, 102.2, 99.0, 62.9, 32.3, 30.1, 25.0, 0.2.

**Epoxide (CPB-1703).** Colorless oil; 87% ee $[\alpha]^{25}_D$ = -20.6 (*c* 0.35, $CHCl_3$); IR (NaCl): 3383, 2176, 1251 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) δ 3.69 (q, $J$ = 6.4 Hz, 2H), 3.43 (d, $J$ = 4.0 Hz, 1H), 3.04 (td, $J$ = 6.0, 4.0 Hz, 1H), 1.83-1.56 (m, 6H), 0.19 (s, 9H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 100.5, 91.5, 62.9, 58.3, 45.5, 32.6, 29.2, 22.3, -0.1. Anal. Calcd. for $C_{11}H_{20}O_2Si$: C, 62.21; H, 9.49. Found: C, 62.20; H, 9.41.

**(Table 4.3, entry 16)**

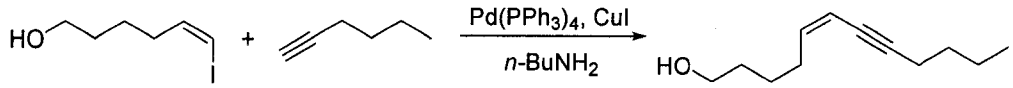



***cis*-Oct-5-en-7-yn-1-ol (4-24) (CPB-1715).** *cis*-8-Trimethylsilyloct-5-en-7-yn-1-ol (**4-12**) (CPB-1609 ) (0.71 g, 3.37 mmol) was treated at rt with saturated methanolic $K_2CO_3$ solution (10.6 mL) and stirred until complete as judged by TLC. The mixture was then extracted with $Et_2O$, and the combined organic layers were washed with brine, dried ($Na_2SO_4$), filtered and concentrated. The residue was purified by column (1:2 pet. ether:$Et_2O$) to yield 0.42 g (48%) of the title compound as a colorless oil: IR (NaCl): 3289, 2096, 1066 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) δ 6.01 (dt, $J$ = 10.8, 7.2 Hz, 1H), 5.50-5.46 (m, 1H), 3.68 (t, $J$ = 6.0 Hz, 2H), 3.09 (d, $J$ = 2.0 Hz, 1H), 2.38 (qd, $J$ = 7.2, 1.2

Hz, 2H), 1.66-1.58 (m, 2H), 1.56-1.47 (m, 2H), 1.40 (s, 1H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 145.8, 108.7, 81.6, 80.7, 62.9, 32.3, 30.1, 25.1.

**Epoxide (CPB-1727).** Colorless oil; 80% ee $[\alpha]^{25}_D$ = -40.0 (*c* 0.12, $CHCl_3$); IR (NaCl):3382, 3291, 2120 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 3.69 (t, *J* = 6.0 Hz, 2H), 3.43 (dd, *J* = 4.0 1.8 Hz, 1H), 3.05 (td, *J* = 6.0, 4.0 Hz, 1H), 2.36 (d, *J* = 1.8 Hz, 1H), 1.82-1.56 (m, 6H), 1.42 (s, 1H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 79.1, 73.9, 62.8, 57.9, 44.9, 32.5, 29.1, 22.4. Anal. Calcd. for $C_8H_{12}O_2$: C, 68.54; H, 8.63. Found: C, 68.38; H, 8.39.

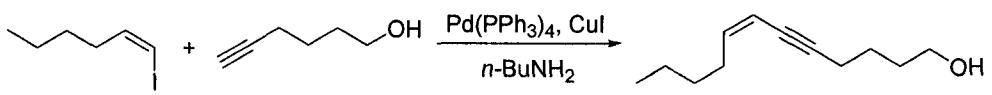
**(Table 4.3, entry 17)**




***cis*-Dodec-5-en-7-yn-1-ol (4-13) (CPB-1640).** The enyne was prepared via Sonogashira coupling of *cis*-6-iodo-5-hexen-1-ol (CPB-1604) and 1-hexyne (63%). Orange oil; IR (NaCl): 3333, 2210, 1458, 1061 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 5.81 (dt, *J* = 10.8, 7.4 Hz, 1H), 5.49-5.44 (m, 1H), 3.67 (t, *J* = 6.6 Hz, 2H), 2.37-2.30 (m, 4H), 1.66-1.28 (m, 8H), 0.93 (t, *J* = 7.2 Hz, 3H) ; $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 142.1, 110.1, 94.9, 77.4, 63.0, 32.4, 31.2, 29.8, 25.2, 22.2, 19.4, 13.8.

**Epoxide (CPB-1650).** Colorless oil; 91% ee $[\alpha]^{25}_{D}$ = -8.2 (*c* 0.65, $CHCl_3$); IR (NaCl): 3358, 2239, 1458 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 3.69 (q, *J* = 6.0 Hz, 2H), 3.43 (dt, *J* = 4.0, 1.6 Hz, 2H), 3.00 (td, *J* = 6.0, 4.0 Hz, 1H), 2.23 (td, *J* = 6.8, 1.6 Hz, 2H), 1.81-1.28 (m, 10H), 0.91 (t, *J* = 7.2 Hz, 3H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 86.9, 75.1, 62.9, 58.1, 45.8, 32.6, 30.7, 29.2, 22.4, 22.1, 18.7, 13.8. Anal. Calcd. for $C_{12}H_{20}O_2$: C, 73.43; H, 10.27. Found: C, 73.14; H, 10.15.

**(Table 4.3, entry 18)**

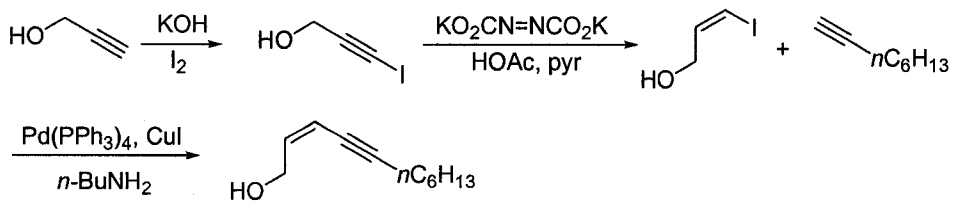



***cis*-Dodec-7-en-5-yn-1-ol (4-14) (CPB-1706).** The enyne was prepared via Sonogashira coupling of *cis*-1-iodo-1-hexene (CPB-1413) and 5-hexyn-1-ol (71%). Orange oil; IR (NaCl): 3344, 2213, 1721, 1061 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 5.83 (dt, *J* = 10.8, 7.2 Hz, 1H), 5.46-5.41 (m, 1H), 3.70 (t, *J* = 6.2 Hz, 2H), 2.40 (td, *J* = 6.8, 2.0 Hz, 2H), 2.30 (q, *J* = 7.2 Hz, 2H), 1.76-1.60 (m, 4H), 1.43-1.32 (m, 4H), 0.92 (t, *J* = 6.8, Hz, 3H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 143.1, 109.4, 94.0, 78.0, 62.7, 32.1, 31.2, 30.0, 25.3, 22.5, 19.5, 14.1.

**Epoxide (CPB-2029).** Colorless oil; 80% ee $[\alpha]^{25}_{D}$ = -14.1 (*c* 0.26, $CHCl_3$); IR (NaCl): 3385, 2240, 1457, 1061 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 3.68 (t, *J* = 6.4 Hz, 2H), 3.42 (dt, *J* = 4.4, 2.0 Hz, 1H), 3.00 (td, *J* = 6.0, 4.4 Hz, 1H), 2.29 (td, *J* = 6.8, 2.0 Hz, 2H),

1.77-1.36 (m, 10H), 1.26 (s, 1H), 0.94 (t, $J$ = 7.2 Hz, 3H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 86.2, 75.7, 62.6, 58.3, 45.7, 32.0, 29.2, 28.3, 24.9, 22.7, 18.8, 14.2. Anal. Calcd. for $C_{12}H_{20}O_2$: C, 73.43; H, 10.27. Found: C, 73.19; H, 10.26.

**(Table 4.3, entry 19)**



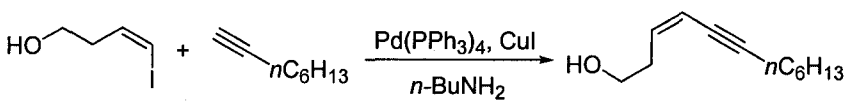

**3-Iodo-2-propyn-1-ol (CPB-1713).** The title compound was prepared according to the procedure used above to prepare 6-iodo-5-hexyn-1-ol (CPB-1549) (71%). Yellow oil; IR (NaCl): 3333, 2187, 1035 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) δ 4.43 s (2H), 1.67 (s, 1H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 92.7, 52.8, 2.9.

***cis*-3-Iodo-2-propen-1-ol (CPB-1714).** The title compound was prepared according to the procedure used above to prepare *cis*-6-iodo-5-hexen-1-ol (CPB-1604) (17%). Colorless oil; IR (NaCl): 3319, 1608, 1278 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) δ 6.50 (dt, $J$ = 7.6, 5.6 Hz, 1H), 6.37 (dt, $J$ = 7.6, 1.6 Hz, 1H), 4.26 (dd, $J$ = 5.6, 1.6 Hz, 2H), 1.69 (s, 1H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 140.2, 82.9, 66.0.

***cis*-Undec-2-en-4-yn-1-ol (4-15) (CPB-1717).** The enyne was prepared via Sonogashira coupling of *cis*-3-iodo-2-propen-1-ol (CPB-1714) and 1-octyne (85%). Orange oil; IR (NaCl): 3326, 2216, 1020 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 6.01 (dt, $J$ = 11.0, 6.4 Hz, 1H), 5.61-5.56 (m, 1H), 4.40 (dd, $J$ = 6.4, 1.2 Hz, 2H), 2.34 (td, $J$ = 6.8, 2.0 Hz, 2H), 1.63 (s, 1H), 1.58-1.51 (m, 2H), 1.44-1.26 (m, 6H), 0.90 (t, $J$ = 7.2 Hz, 3H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 140.0, 111.5, 97.1, 76.4, 61.2, 31.5, 28.9, 28.8, 22.8, 19.7, 14.2.

**Epoxide (CPB-1719).** Colorless oil; 97% ee $[\alpha]^{25}_D$ = -41.4 (*c* 0.22, $CHCl_3$); IR (NaCl): 3416, 2234, 1044 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 3.98-3.95 (m, 1H), 3.88-3.82 (m, 1H), 3.54 (dt, $J$ = 4.4, 1.6 Hz, 1H), 3.26 (td, $J$ = 6.0, 4.4 Hz, 1H), 2.22 (td, $J$ = 7.2, 1.6 Hz, 2H), 1.70 (s, 1H), 1.52 (quint., $J$ = 7.2 Hz, 2H), 1.44-1.24 (m, 6H), 0.90 (t, $J$ = 6.8 Hz, 3H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 87.7, 74.3, 62.4, 57.4, 44.9, 31.5, 28.7, 28.5, 22.7, 19.0, 14.2. Anal. Calcd. for $C_{11}H_{18}O_2$: C, 72.49; H, 9.95. Found: C, 71.26; H, 9.68.

**(Table 4.3, entry 20)**

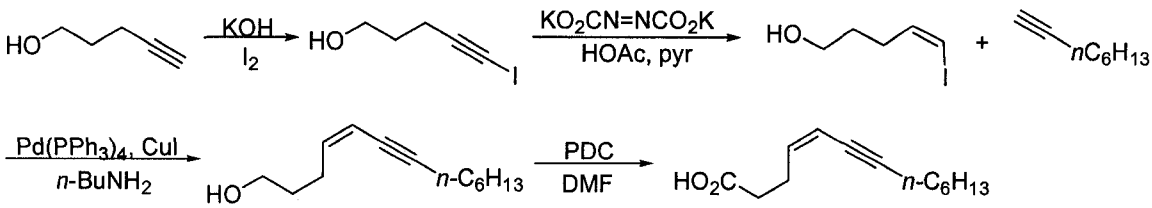



***cis*-Dodec-3-en-5-yn-1-ol (4-16) (CPB-1722).** The enyne was prepared via Sonogashira coupling of *cis*-4-iodo-3-buten-1-ol (CPB-0415) and 1-octyne (83%). Orange oil; IR (NaCl): 3330, 2217, 1048 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 5.87 (dt, $J$ = 10.8, 7.2 Hz,

1H), 5.64-5.58 (m, 1H), 3.73 (q, $J$ = 6.0 Hz, 2H), 2.58 (qd, $J$ = 6.4, 1.2 Hz, 2H), 2.34 (td, $J$ = 7.2, 2.0 Hz, 2H), 1.59-1.51 (m, 2H), 1.45-1.27 (m, 6H), 0.90 (t, $J$ = 7.2 Hz, 3H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 137.9, 112.5, 95.6, 62.2, 33.8, 31.5, 29.0, 28.8, 22.8, 19.7, 14.3.

**Epoxide (CPB-1725).** Colorless oil; 97% ee $[\alpha]^{25}_D$ = -36.8 (*c* 0.37, $CHCl_3$); IR (NaCl): 3418, 2237, 1051 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) δ 3.92-3.88 (m, 2H), 3.48 (dt, $J$ = 6.0, 1.6 Hz, 1H), 3.23-3.19 (m, 1H), 2.23 (td, $J$ = 7.2, 1.6 Hz, 2H), 2.06-1.91 (m, 2H), 1.62-1.24 (m, 10 H,) 0.90 (t, $J$ = 7.2 Hz, 3H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 87.5, 75.0, 60.4, 56.0, 45.4, 32.5, 31.5, 28.7, 28.6, 22.7, 19.0, 14.2. Anal. Calcd. for $C_{12}H_{20}O_2$: C, 73.43; H, 10.27. Found: C, 73.19; H, 10.07.

**(Table 4.3, entry 21)**




**5-Iodo-4-pentyn-1-ol (CPB-2543).** The title compound was prepared according to the procedure used above to prepare 6-iodo-5-hexyn-1-ol (CPB-1549) (79%). Yellow oil; IR (NaCl):3341, 2184, 1430 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) δ 3.76 (t, $J$ = 6.2 Hz, 2H),

2.51 (t, $J$ = 7.0 Hz, 2H), 1.82-1.76 (m, 2H), 1.45 (brs , 1H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 94.0, 61.7, 31.3, 17.6, -6.2.

***cis*-5-Iodo-4-penten-1-ol (CPB-2548).** The title compound was prepared according to the procedure used above to prepare *cis*-6-iodo-5-hexen-1-ol (CPB-1604) (50%). Yellow oil; IR (NaCl): 3330, 1609 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) δ 6.26-6.18 (m, 2H), 3.69 (t, $J$ = 6.4 Hz, 2H), 2.30-2.23 (m, 2H), 1.72 (quint., $J$ = 7.2 Hz, 2H), 1.42 (s, 1H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 140.8, 83.3, 62.3, 31.4, 31.0.

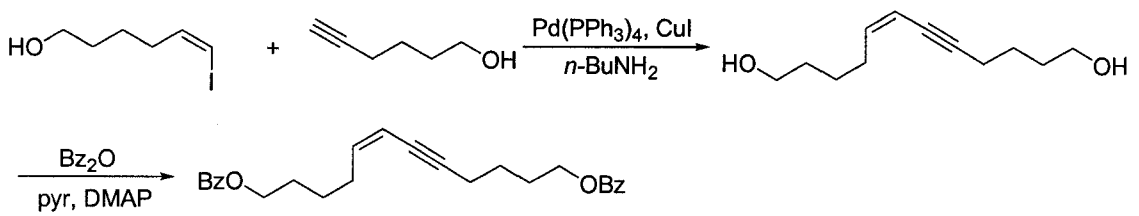
***cis*-Tridec-4-en-6-yn-1-ol (4-25) (CPB-2604).** The enyne was prepared via Sonogashira coupling of *cis*-5-iodo-4-penten-1-ol (CPB-2548) and 1-octyne with no purification. Colorless oil; IR (NaCl): 3340, 2211, 1456 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) δ 5.83 (dt, $J$ = 10.4, 7.2 Hz, 1H), 5.51 (m, 1H), 3.67 (t, $J$ = 6.4 Hz, 2H), 2.40 (q, $J$ = 7.2 Hz, 2H), 2.34 (td, $J$ = 7.2 2.0 Hz, 2H), 1.69 (quint. $J$ = 6.8 Hz, 2H), 1.55 (quint., $J$ = 7.6 Hz, 2H), 1.45-1.37 (m, 2H), 1.37-1.24 (m, 4H), 0.90 (t, $J$ = 6.8 Hz, 3H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 141.4, 110.6, 95.4, 94.6, 62.3, 31.7, 31.6, 29.0, 28.8, 26.3, 22.8, 19.7, 14.3.

***cis*-Tridec-4-en-6-ynoic acid (4-26) (CPB-2605).** The title compound was prepared according to the method of Corey et al:[188] PDC (26.5 g, 70.4 mmol) was added to a solution of *cis*-tridec-4-en-6-yn-1-ol (CPB-2604) (3.7 g, 21.3 mmol) in 57 mL DMF at rt and the mixture was stirred overnight. The brown mixture was then poured into 400 mL

water and was then extracted with $Et_2O$. The combined organic extracts were then filtered through a plug of silica gel and concentrated to yield a pink oil which was purified by column (7:1 hexanes:$Et_2O$ to $Et_2O$) to yield 2.21 g (50% over two steps) of the title compound as a colorless oil: IR (NaCl): 2215, 1712 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 11.14 (brs, 1H), 5.84 (dt, $J$ = 10.8, 7.2 Hz, 1H), 5.52 (m, 1H), 2.62 (q, $J$ = 7.2 Hz, 2H), 2.49 (m, 2H), 2.35 (td, $J$ = 6.8, 2.0 Hz, 2H), 1.55 (quint., $J$ = 7.6 Hz, 2H), 1.46-1.36 (m, 2H), 1.36-1.24 (m, 4H), 0.90 (t, $J$ = 7.2 Hz, 3H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 178.9, 139.4, 111.5, 96.1, 33.3, 31.6, 29.0, 28.8, 25.3, 22.8, 19.8, 14.3.

**5-(1-Hydroxynon-2-ynyl)-dihydrofuran-2-one (4-39) (CPB-2624).** Colorless oil; 96% ee $[\alpha]_D^{25}$ = -19.3 (*c* 0.29, $CHCl_3$); IR (NaCl): 3427, 2233, 1778 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 4.56 (ddd, $J$ = 7.6, 6.0, 5.6 Hz, 1H), 4.46 (m, 1H), 2.70-2.50 (m, 2H), 2.40-2.30 (m, 1H), 2.26-2.14 (m, 4H), 1.56-1.47 (m, 2H), 1.42-1.23 (m, 6H), 0.90 (t, $J$ = 7.2 Hz, 1H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 177.0, 88.6, 81.9, 76.3, 65.2, 31.5, 28.7, 28.5, 28.4, 23.6, 22.7, 18.9, 14.3. Anal. Calcd for $C_{13}H_{20}O_3$: C, 69.61; H, 8.99. Found: C, 69.39; H, 9.16.

**(Table 4.3, entry 22)**



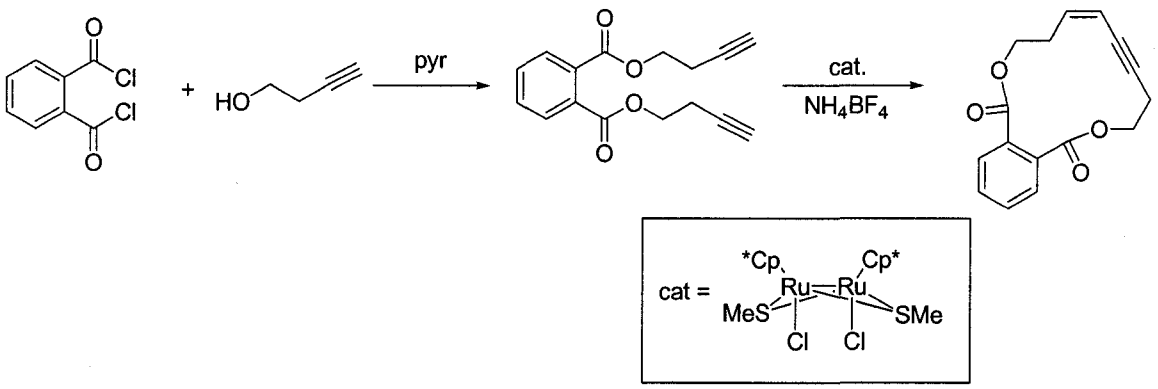
***cis*-1,12-Hydroxydodec-5-en-7-yne (4-27) (CPB-1609).** The enyne was prepared via Sonogashira coupling of *cis*-6-iodo-5-hexen-1-ol (CPB-1604) and 5-hexyn-1-ol (69%). Yellow oil; IR (NaCl): 3343, 2210, 1432, 1062 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 5.83(dt, $J$ = 10.8, 7.6 Hz, 1H), 5.49-5.45 (m, 1H), 3.70 (t, $J$ = 6.4 Hz, 2H), 3.68 (t, $J$ = 6.4 Hz, 2H), 2.40 (td, $J$ = 6.8, 2.0 Hz, 2H) 2.33 (qd, $J$ = 7.6, 1.2 Hz, 2H), 1.78-1.47 (m, 8H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 142.4, 110.0, 94.3, 78.0, 62.8, 62.7, 32.2, 32.1, 29.8, 25.3, 25.1, 19.5.

***cis*-1,12-Dibenzoyloxydodec-5-en-7-yne (4-28) (CPB-1647).** To a solution of *cis*-1,12-hydroydodec-5-en-7-yne (**4-27**) (CPB-1609) (0.90 g, 4.6 mmol) in 25 mL $CH_2Cl_2$ was added benzoic anhydride (4.2 g, 18.4 mmol), pyridine (1.8 g, 23 mmol), and DMAP (0.06 g, 0.5 mol) with stirring at rt. The mixture was stirred overnight and was then quenched with sat. aq. $NH_4Cl$ and extracted with pet. ether. The combined organic phases were washed with water, brine, dried ($Na_2SO_4$), filtered, and concentrated. The residue was then purified by column (9:1 pet. ether:$Et_2O$) to yield 0.94 g (51%) of the title compound as a colorless oil: IR (NaCl): 1719, 1274 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 8.06-8.03 (m, 4H), 7.60-7.53 (m, 2H), 7.47-7.41 (m, 4H), 5.84 (dt, $J$ = 10.8, 7.6 Hz, 1H), 5.52-5.47 (m, 1H), 4.36 (t, $J$ = 6.4 Hz, 2H), 4.34 (t, $J$ = 6.4 Hz, 2H), 2.44 (td, $J$ = 6.8, 2.4 Hz, 2H), 2.38 (qd, $J$ = 7.6, 1.2 Hz, 2H), 1.96-1.88 (m, 2H), 1.83-1.68 (m, 4H), 1.62-1.54 (m, 2H);

$^{13}C$ NMR (101 MHz, $CDCl_3$) δ 166.9, 166.8, 142.1, 133.09, 133.05, 130.7, 130.6, 129.8, 128.6, 110.2, 94.2, 78.0, 65.0, 64.7, 29.8, 28.4, 28.2, 25.7, 25.5, 19.5.

**Epoxide (CPB-1716).** Colorless oil; 83% ee $[\alpha]^{25}_D$ = -6.2 (*c* 0.28, $CHCl_3$); IR (NaCl): 2239, 1717, 1275 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 8.07-8.03 (m, 3H), 7.59-7.53 (m, 2H), 7.47-7.42 (m, 3H), 4.35 (t, *J* = 6.4 2H), 4.34 (t, *J* = 6.4 Hz, 2H), 3.45 (dt, *J* = 4.0, 1.6 Hz, 1H), 3.04 (td, *J* = 6.0, 4.0 Hz, 1H), 2.32 (td, *J* = 7.2, 1.6 Hz, 2H), 1.92-1.62 (m, 10H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 166.84, 166.80, 133.1, 130.6, 130.5, 129.8, 128.6, 86.1, 75.8, 64.9, 64.6, 58.0, 45.6, 29.2, 28.7, 28.1, 25.3, 22.9, 18.7. Anal. Calcd. for $C_{26}H_{28}O_4$: C, 74.26; H, 6.71 . Found: C, 74.35; H, 6.46.

**(Table 4.3, entry 23)**




**[Cp*ClRu(μ$_2$SMe)$_2$RuCp*Cl] (4-30) (CPB-2618).** The catalyst was prepared according to a literature procedure.[190] To a suspension of biscyclopentadienyl ruthenium dichloride (1.0 g, 1.63 mmol) in 17.4 mL THF was added (methylthio)trimethylsilane (0.49 g) under

Ar with stirring at rt. The mixture was stirred at rt for 24 h and was then filtered. The crude crystalline product was then recrystallized from $CH_2Cl_2$ giving 0.51 g (49%) of brown crystals. Note: the product is air stable and should be stored at rt.

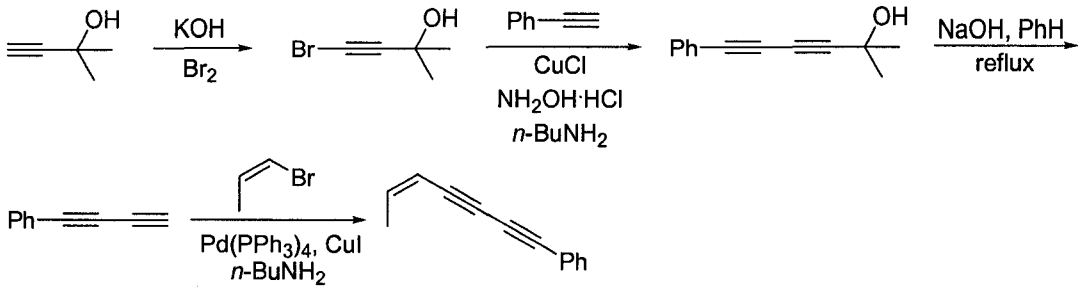
**Phthalic acid dibut-3-ynyl ester (4-29) (CPB-2716).** Phthaloyl dichloride (5.1 g, 25.0 mmol), 3-butyn-1-ol (3.4 g, 48 mmol), and pyridine (7.6 g, 96 mmol) were dissolved in $CH_2Cl_2$ (250 mL) at 0 °C with stirring. The mixture was allowed to gradually warm to rt and was stirred overnight. The mixture was then poured into sat. aq. $NH_4Cl$ and the aq. phase was extracted with $CH_2Cl_2$. The combined organic phases were then washed with water, brine, dried ($Na_2SO_4$), filtered and concentrated. The residue was purified by column (1:1 hexanes:$Et_2O$) yielding 5.0 g (74%) of the title compound as a colorless syrup: IR (NaCl): 3293, 2122, 1728 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.78-7.74 (m, 2H), 7.59-7.53 (m, 2H), 4.43 (t, $J$ = 6.8 Hz, 4H), 2.66 (td, $J$ = 6.8, 2.8 Hz, 4H), 2.04 (t, $J$ = 2.8 Hz, 2H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 167.4, 132.0, 131.5, 129.3, 80.1, 70.3, 63.4, 19.1.

**Enyne (4-31) (CPB-2735).** The enyne was prepared according to a literature procedure.[189] $NH_4BF_4$ (0.036 g, 0.342 mmol) and phthalic acid dibut-3-ynyl ester (**4-29**) (CPB-2716) (0.465 g, 1.72 mmol) were added to a solution of catalyst (0.218 g, 0.342 mmol) in dry MeOH. The reaction was followed by GC and was stirred at 60 °C for 24 h after which time an additional 0.12 g (0.188 mmol) of catalyst (**4-30**) (CPB-2618) was

added. After 48 h more, an additional 0.19 g (0.298 mmol) of catalyst was added. After stirring for 120 h total, the solvent was removed and the residue was purified by column (1:1 hexanes:$Et_2O$) to yield 0.389 g (84%) of the title compound as white crystals: mp 108-109 °C; IR (NaCl): 2215, 1717, 1275, 1133cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.77-7.68 (m, 2H), 7.55-7.50 (m, 2H), 5.91(dt, $J$ = 10.4, 8.0 Hz, 1H), 5.54 (d, $J$ = 10.4 Hz, 1H), 4.54 (t, $J$ = 5.2 Hz, 2H), 4.41 (t, $J$ = 5.6 Hz, 2H), 2.82-2.72 (m, 4H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 168.4, 167.2, 138.9, 133.0, 132.5, 131.3, 131.2, 129.5, 129.0, 112.6, 90.4, 79.2, 65.1, 62.9, 29.9, 20.6.

**Epoxide (CPB-2810).** Colorless oil; 87% ee $[\alpha]_D^{25}$ = -87.1 (*c* 0.86, $CHCl_3$); IR (NaCl): 2245, 1728, 1293, 1129 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.79-7.71 (m, 2H), 7.60-7.53 (m, 2H), 4.84-4.76 (m, 1H), 4.73 (dt, $J$ = 11.2, 4.0 Hz, 1H), 4.28 (td, $J$ = 11.2, 3.2 Hz, 1H), 4.17 (ddd, $J$ = 10.4, 4.8, 3.2 Hz, 1H), 3.44-3.42 (m, 1H), 3.11 (ddd, $J$ = 10.0, 4.0, 1.6 Hz, 1H), 2.82-2.72 (m, 1H), 2.59 (dt, $J$ = 17.6, 2.8 Hz, 1H), 2.34-2.26 (m, 1H), 2.23-2.11 (m, 1H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 168.5, 166.9, 132.9, 132.1, 131.5, 131.3, 129.6, 129.1, 82.9, 77.1, 63.3, 62.3, 56.9, 46.3, 28.3, 20.1. Anal. Calcd for $C_{16}H_{14}O_5$: C, 67.13; H, 4.93. Found: C, 67.36; H, 5.05.

**(Table 4.3, entry 24)**




**4-Bromo-2-methyl-3-butyn-2-ol (4-32) (CPB-2606).** The title compound was prepared according to a literature procedure:[190] A solution of KOH (89.2 g, 1.59 mmol) in 350 ml water was cooled to 0 °C. $Br_2$ (33.9 g, 200 mmol) was then added and the mixture was stirred at 0 °C for 10 min. 2-Methyl-3-butyn-2-ol (23.2 g, 276 mmol) in 40 mL hexanes was then added dropwise at 0 °C. After the addition was complete the mixture was stirred at 0 °C for 30 min. $Et_2O$ (200 mL) was then added and the layers were separated the aqueous layer was extracted with $Et_2O$ and the combined organic layers were washed with water, brine, dried ($Na_2SO_4$), filtered, and concentrated. The residue was then purified by distillation (bp. 66-68 °C at 13 mmHg) to give 30.3 g (67%) of the title compound as a colorless oil: IR (NaCl): 3350, 2214 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 2.00 (s, 1), 1.53 (s, 6H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 84.7, 66.5, 43.0, 31.4.

**2-Methyl-6-phenyl-3,5-hexadiyn-2-ol (4-33) (CPB-2607).** The title compound was prepared according to a literature procedure:[190] Phenylacetylene (2.72 g, 26.6 mmol), *n*-butlyamine (31 mL), CuCl (0.05 g, 0.5 mmol), and hydroxylamine hydrochloride (0.14 g, 2.01 mmol) were combined and stirred at 0 °C under Ar. 4-Bromo-2-methyl-3-butyn-2-

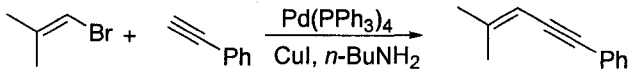
ol (**4-32**) (CPB-2606) (3.0 g, 22.2 mmol) was then added slowly to the yellow solution. The mixture was stirred at 0 °C for 5 h and was then extracted with $Et_2O$. The combined organic fractions were then washed with water, brine, dried ($Na_2SO_4$), and concentrated. The residue was purified by column (1:1 hexanes:$Et_2O$) to yield 3.16 g (77%) of the title compound as a white solid: IR (NaCl): 3352, 2359, 2237 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.52-7.46 (m, 2H), 7.40-7.30 (m, 3H), 2.08 (s, 1H), 1.59 (s, 6H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 132.7, 129.5, 128.6, 121.7, 86.9, 79.0, 73.3, 67.3, 66.0, 31.3.

***cis*-1-Phenylhept-4-en-1,3-diyne (4-35) (CPB-2611).** Powdered NaOH (0.66 g, 16.4 mmol) and 2-methyl-6-phenyl-3,5-hexadiyn-2-ol (**4-33**) (CPB-2607) (2.73 g, 14.8 mmol) were added to 29 mL of toluene and the mixture was refluxed under Ar until the starting material had disappeared by TLC (~ 1h). The brown mixture was then cooled to rt, filtered through a pad of silica gel (the filter was washed with 1:1 hexanes/$Et_2O$). The filtrate was concentrated to give a yellow oil. *cis*-1-Bromo-1-propene (3.6 g, 29.6 mmol) and $Pd(PPh_3)_4$ (0.76 g, 0.66 mmol) were then added to a flask with 33 mL of benzene. A solution of crude terminal diyne from above in 15 mL *n*-$BuNH_2$ (150 mmol) was then added to the benzene solution along with CuI (0.46 g, 2.4 mmol). The mixture was stirred at rt under Ar overnight, and then hexane (50 mL) was added. The mixture was poured into sat. aq. $NH_4Cl$ and washed with sat. aq. $NH_4Cl$, $H_2O$, brine, dried ($Na_2SO_4$), filtered, and concentrated. The residue was purified by column (hexanes) to give 0.88 g (36%) of a the title compound as a colorless oil: IR (NaCl): 2214, 2149, 1490 $cm^{-1}$; $^1H$

NMR (400 MHz, $CDCl_3$) ) δ 7.54-7.46 (m, 2H), 7.41-7.30 (m, 3H), 6.20 (dq, $J$ = 10.8, 6.8 Hz, 1H), 5.61 (dd, $J$ = 10.8, 0.8 Hz, 1H), 1.97 (dd, $J$ = 6.8, 0.8 Hz, 3H; $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 143.3, 132.6, 129.3, 128.6, 122.2, 109.3, 81.9, 79.0, 78.2, 74.2, 16.8.

**Epoxide (CPB-2647).** Colorless oil; 93% ee $[\alpha]_D^{25}$ = -48.4 (*c* 0.25, $CHCl_3$); IR (NaCl): 2232 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.53-7.48 (m, 2H), 7.42-7.31 (m, 3H), 3.57 (d, $J$ = 4.0 Hz, 1H), 3.25 (qd, $J$ = 5.2, 4.0 Hz, 1H), 1.49 (d, $J$ = 5.2 Hz, 3H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 132.9, 129.7, 128.7, 121.4, 78.01, 77.96, 73.5, 70.1, 55.1, 46.0, 15.2. Anal. Calcd for $C_{13}H_{10}O$: C, 85.69; H, 5.53. Found: C, 85.44; H, 5.45.

**(Table 4.3, entry 25)**

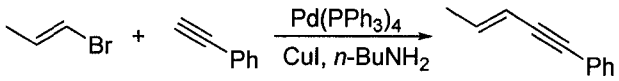



**4-Methyl-1-phenylpent-3-en-1-yne (4-36) (CPB-2845).** The enyne was prepared via Sonogashira coupling of 1-bromo-2-methylpropene and phenylacetylene (79%). Colorless oil; IR (NaCl): 2197, 1489 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.45-7.40 (m, 2H), 7.33-7.24 (m, 3H), 5.48 (s, 1H), 1.98 (s, 3H), 1.87 (s, 3H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 149.2, 131.5, 128.5, 127.9, 124.2, 105.4, 91.6, 87.9, 25.2, 21.4.

**Epoxide (CPB-2914).** Colorless oil; 94% ee $[\alpha]_D^{25}$ = +3.56 (*c* 0.59, $CHCl_3$); IR (NaCl): 2221, 1490 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.47-7.43 (m, 2H), 7.36-7.28 (m, 3H),

3.44 (s, 1H), 1.52 (s, 3H), 1.41 (s, 3H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 132.1, 128.9, 128.5, 122.5, 85.5, 85.2, 61.2, 52.5, 23.7, 20.6. Anal. Calcd for $C_{12}H_{13}O$: C, 83.69; H, 7.02. Found: C, 83.80; H, 7.00.

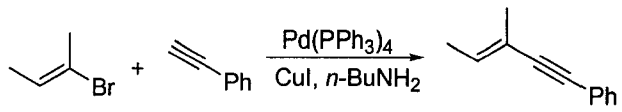
**(Table 4.3, entry 26)**




***trans*-1-Phenyl-pent-3-en-1-yne (4-37) (CPB-2833).** The enyne was prepared via Sonogashira coupling of *trans*-1-bromopropene and phenylacetylene (84%). Colorless oil; IR (NaCl): 2200, 1596, 1489 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.45-7.39 (m, 2H), 7.33-7.27 (m, 2H), 6.25 (dq, $J$ = 15.6, 6.8 Hz, 1H), 5.72 (dq, $J$ = 15.6, 1.6 Hz, 1H), 1.85 (dd, $J$ = 6.8, 1.6 Hz, 3H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 140.1, 131.6, 128.5, 128.1, 123.8, 111.0, 88.4, 87.9, 19.0.

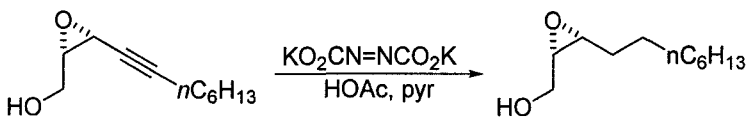
**Epoxide (CPB-2917).** Colorless oil; 74% ee $[\alpha]_D^{25}$ = -3.61 (*c* 0.31, $CHCl_3$); IR (NaCl): 2229, 1490 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.46-7.42 (m, 2H), 7.34-7.27 (m, 3H), 3.31-3.24 (m, 2H), 1.40 (d, $J$ = 4.8 Hz, 3H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 132.1, 128.9, 128.5, 122.3, 86.0, 83.7, 57.2, 46.9, 17.6.

**(Table 4.3, entry 27)**




**(E)-1-Phenyl-3-methylpent-3-en-1-yne (4-38) (CPB-2932).** The enyne was prepared via Sonogashira coupling of (E)-2-bromo-2-butene and phenylacetylene (75%). Colorless oil; IR (NaCl): 2204, 1596, 1493 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.46-7.40 (m, 2H), 7.34-7.24 (m, 3H), 6.03 (qd, $J$ = 7.2, 1.4 Hz, 1H), 1.88 (t, $J$ = 1.2 Hz, 3H), 1.74 (dd, $J$ = 7.2, 1.4 Hz, 3H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 133.1, 131.6, 128.4, 127.9, 124.0, 118.8, 92.8, 85.9, 17.2, 14.4.

**Epoxide (CPB-2938).** Colorless oil; 40% ee $[\alpha]_D^{25}$ = -7.57 (*c* 0.37, $CHCl_3$); IR (NaCl): 2220, 1491 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.46-7.41 (m, 2H), 7.33-7.27 (m, 3H), 3.37 (q, $J$ = 5.6 Hz, 1H), 1.59 (s, 3H), 1.37 (d, $J$ = 5.6 Hz, 3H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 132.1, 128.7, 128.5, 122.5, 90.1, 81.9, 61.1, 51.5, 18.5, 13.9. Anal. Calcd for $C_{12}H_{12}O$: C, 83.69; H, 7.02. Found: C, 83.50; H, 7.05.




**(2S,3R)-2,3-Epoxyundecan-1-ol (4-41) (CPB-1838).** The enyne was reduced according to a modification of Denmark's procedure.[185] To a solution of propargyl epoxide (96% ee, 0.096 g, 0.53 mmol) in MeOH (4 mL) and pyridine (0.86 mL) was added potassium

azodicarboxylate (1.03 g, 5.3 mmol) at rt at the beginning and every 12 h until 4.12 g (21.2 mmol) had been added. At the same time acetic acid (2.57 mL, 44.52 mmol, in 5 mL MeOH) was added over 60 h via syringe pump. The reaction was then diluted with $Et_2O$ and washed with water until no more gas bubbles evolved. The aqueous phase was then extracted with $Et_2O$ and the combined organic phases were washed with sat. aq. $CuSO_4$, $H_2O$, brine, dried ($Na_2SO_4$), filtered and concentrated. The residue was purified by column (1:1 pet. ether:$Et_2O$) to yield 0.05 g (53%) of the saturated epoxide as a white solid: $[\alpha]_D^{25}$ = -2.7 (*c* 0.37, $CHCl_3$); lit. $[\alpha]_D^{25}$ = -3.5 (*c* 1.3, $CHCl_3$) (>80% ee)[192]; IR (NaCl): 3297, 1469 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 3.92-3.82 (m, 1H), 3.73-3.64 (m, 1H), 3.16 (dt, *J* = 7.2, 4.0 Hz, 1H), 3.08-3.02 (m, 1H), 1.66 (s, 1H), 1.62-1.22 (m, 14H), 0.89 (t, *J* = 6.8 Hz, 1H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 61.2, 57.6, 57.0, 32.1, 29.7, 29.6, 29.4, 28.2, 26.9, 22.9, 14.3.

# CHAPTER FIVE

# KETONE-CATALYZED ASYMMETRIC EPOXIDATION OF *CIS*-OLEFINS USING HYDROGEN PEROXIDE AS PRIMARY OXIDANT

## 5.A. INTRODUCTION

Chiral dioxiranes have proven to be valuable agents for the asymmetric epoxidation of olefins.[195] As previously discussed, they are typically prepared by the action of Oxone (potassium peroxymonosulfate) on a ketone. Recent studies from our group have shown that hydrogen peroxide ($H_2O_2$) coupled with a nitrile activator presents a viable method for the formation of dioxiranes from ketones and the subsequent epoxidation of olefins.[196] The active oxidant for formation of the dioxirane in this case is

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[195] For leading reviews on chiral ketone catalyzed asymmetric epoxidations see: (a) Denmark, S.E.; Wu, Z. *Synlett* **1999**, 847-859. (b) Frohn, M.; Shi, Y. *Synthesis* **2000**, 1979-2000. (c) Shi, Y. *Acc. Chem. Res.* **2004**, *37*, 488-496. (d) Yang, D. *Acc. Chem. Res.* **2004**, *37*, 497-505.

[196] (a) Shu, L.; Shi, Y. *J. Org. Chem.* **2000**, *65*, 8807-8810. (b) Shu, L.; Shi, Y. *Tetrahedron Lett.* **1999**, *40*, 8721-8724. (c) Shu, L.; Shi, Y. *Tetrahedron* **2001**, *57*, 5213-5218. (d) Li, W.; Fuchs, P. L. *Org. Lett.* **2003**, *5*, 2853-2856.

likely a peroxyimidic acid (**5-1**) (Scheme 5.1).[197] $H_2O_2$ is a very useful oxidant because of its high active oxygen content and the fact that its reduction product is water.[198] In addition, ketone-catalyzed epoxidation reactions with $H_2O_2$ require less solvent and salts than those with Oxone, and slow addition of oxidant is unnecessary. An effective method for epoxidation with $H_2O_2$ and ketone **1-5** (Figure 5.1), an effective catalyst for the epoxidation of unfunctionalized *trans*- and trisubstituted olefins,[195b,c] has been developed.[196b,c] Recently, our group has reported that glucose-derived ketones **2-8, 3-62,** and **3-66** (Figure 5.1) are effective catalysts for epoxidation of conjugated aromatic *cis*-olefins,[199] styrenes,[200] certain trisubstituted and tetrasubstituted olefins,[201] conjugated *cis*-dienes, as well as conjugated *cis*-enynes. We then began an investigation to see whether the $H_2O_2$ methodology could be extended to these ketones as well.

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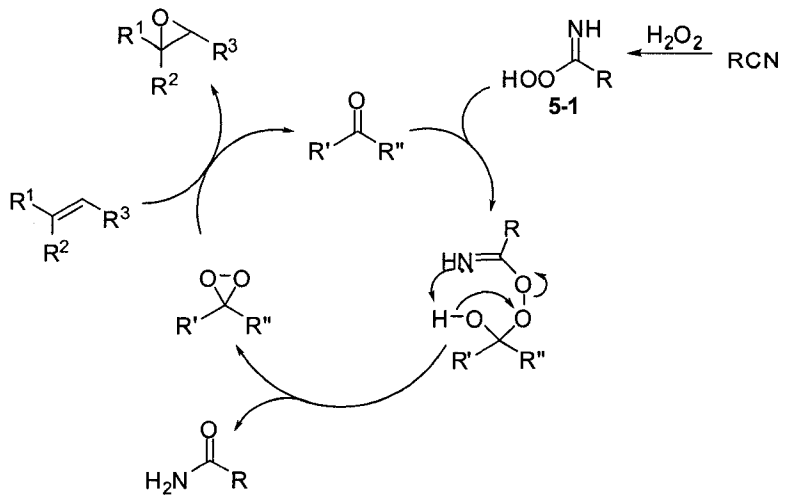
[197] For leading references on epoxidation using $H_2O_2$ and RCN, see: (a) Payne, G. B.; Deming, P. H.; Williams, P. H. *J. Org. Chem.* **1961**, *26*, 651-659. (b) Payne, G. B. *Tetrahedron* **1962**, *18*, 763-765. (c) McIsaac, Jr. J. E.; Ball, R. E.; Behrman, E. J. *J. Org. Chem.* **1971**, *36*, 3048-3050. (d) Bach, R. D.; Knight, J. W. *Org. Synth.* **1981**, *60*, 63. (e) Arias, L. A.; Adkins, S.; Nagel, C. J.; Bach, R. D. *J. Org. Chem.* **1983**, *48*, 888-890.

[198] For a general reference on oxidation with hydrogen peroxide see: Strukul, G. *Catalytic Oxidations with Hydrogen Peroxide as Oxidant*; Kluwer Academic Publishers: New York, 1992.

[199] (a) Tian, H.; She, X.; Shu, L.; Yu, H.; Shi, Y. *J. Am. Chem. Soc.* **2000**, *122*, 11551-11552. (b) Tian, H.; She, X.; Yu, H.; Shu, L.; Shi, Y. *J. Org. Chem.* **2002**, *67*, 2435-2446. (c) Shu, L.; Wang, P.; Gan, Y.; Shi, Y. *Org. Lett.* **2003**, *5*, 293-295. (d) Shu, L.; Shi, Y. *Tetrahedron Lett.* **2004**, *45*, 8115-8117. (e) Wong, O. A.; Shi, Y. *J. Org. Chem.* **2006**, *71*, 3973-3976.

[200] (a) Tian, H.; She, X.; Xu, J.; Shi, Y. *Org. Lett.* **2001**, *3*, 1929-1931. (b) Goeddel, D.; Shu, L.; Yuan, Y.; Wong, O. A.; Wang, B.; Shi, Y. *J. Org. Chem.* **2006**, *71*, 1715-1717.

[201] (a) Shen, Y.-M.; Wang, B.; Shi, Y. *Angew. Chem. Int. Ed.* **2006**, *45*, 1429-1432. (b) Shen, Y.-M.; Wang, B.; Shi, Y. *Tetrahedron Lett.* **2006**, *47*, 5455-5458. (c) Wang, B.; Shen, Y-M.; Shi, Y. *J. Org. Chem.* **2006**, *71*, 9519-9521.



**Scheme 5.1**

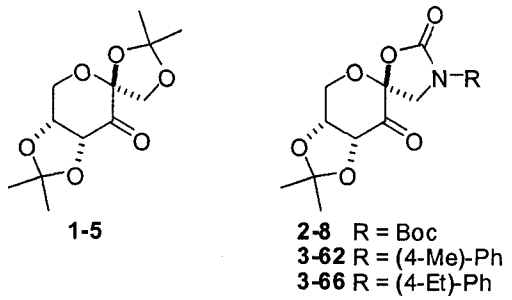



**Figure 5.1**

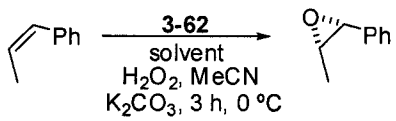
## 5.B. RESULTS AND DISCUSSION

Much of the preliminary work on this project was done by Dr. Lianhe Shu. Early in the study it became apparent that ketone **2-8** would not be useful under these conditions because of rapid decomposition.[202] Ketones **3-62** and **3-66** are more readily

[202] For facile hydrolysis of oxazolidinones using LiOOH see: Evans, D. A.; Britton, T. C.; Ellman, J. A. *Tetrahedron Lett.* **1987**, *28*, 6141-6144.

available and were more robust under the reaction conditions than **2-8**, so further study was conducted with these catalysts. *cis*-β-Methylstyrene was chosen as a test substrate for initial investigations. The optimum conditions for ketone **1** with $H_2O_2$ and acetonitrile as solvent gave poor enantioselectivity with ketone **3-62** (~50% ee). Dr. Shu then reduced the amount of acetonitrile to 7.6 eq. and screened a range of solvents with ketone **3-62** (Table 5.1).

**Table 5.1**[a]

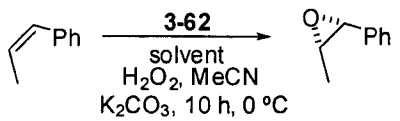



| Entry | solvent | conv. (%)[b] | ee (%)[c] |
|---|---|---|---|
| 1 | DME | 28 | 68 |
| 2 | DMM | 27 | 66 |
| 3 | DME/DMM (1:1) | 28 | 65 |
| 4 | $CH_2Cl_2$ | 6 | 52 |
| 5 | $CH_2Cl_2$/EtOH (1:1) | 54 | 57 |
| 6 | $CH_2Cl_2$/EtOH (2:1) | 28 | 54 |
| 7 | *n*-BuOH | 60 | 73 |
| 8 | $C_6H_6$ | 13 | 69 |
| 9 | PhMe | 13 | 68 |
| 10 | $C_6H_6$/EtOH (1:1) | 37 | 68 |
| 11 | PhMe/EtOH (1:1) | 14 | 69 |
| 12 | $C_6H_6$/*n*-BuOH (1:1) | 47 | 71 |
| 13 | PhMe/*n*-BuOH (1:1) | 23 | 70 |
| 14 | $C_6H_6$/*n*-BuOH (1:6.5) | 57 | 72 |
| 15 | dioxane | 35[d,e] | 70[f] |

[a] Unless stated otherwise, all reactions were performed by Dr. Lianhe Shu. Reactions were run with olefin (0.5 mmol), ketone **3-62** (0.025 mmol), acetonitrile (0.20 mL, 3.8 mmol), solvent (0.75 mL), aq. 0.6 M $K_2CO_3$ in 4 x $10^{-4}$ M aq. EDTA (0.75 mL), and 30% $H_2O_2$ (0.20 mL, 2.0 mmol) at 0 °C for 3 h. [b] Conversion was determined by $^1$H NMR of the crude reaction mixture. [c] Enantioselectivity was determined by chiral GC (Chiraldex B-DM column). [d] 0.10 mL (1.9 mmol) MeCN was used. [e] The reaction time was 4 h. [f] Reaction was done by the author.

Of the solvents screened, *n*-BuOH gave the best results after 3 h. Dr. Shu then screened several other alcohols as solvents (Table 5.2). None performed better than *n*-BuOH, so this was chosen for further study.

**Table 5.2**[a]




| Entry | solvent | conv (%)[b] | ee (%)[c] |
|---|---|---|---|
| 1 | MeOH | 32 | 21 |
| 2 | EtOH | 67 | 47 |
| 3 | *n*-PrOH | 90 | 69 |
| 4 | *i*-PrOH | 92 | 70 |
| 5 | *n*-BuOH | 100 | 74 |
| 6 | *t*-BuOH | 97 | 74 |
| 7 | *i*-$PrCH_2CH_2OH$ | 100 | 73 |

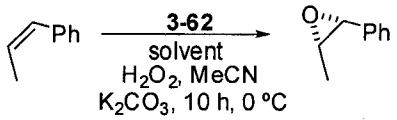
[a] All reactions were performed by Dr. Lianhe Shu. Reactions were run with olefin (0.5 mmol), ketone **3-62** (0.025 mmol), acetonitrile (0.20 mL, 3.8 mmol), solvent (0.75 mL), aq. 0.6 M $K_2CO_3$ in 4 x $10^{-4}$ M aq. EDTA (0.75 mL), and 30% $H_2O_2$ (0.20 mL, 2.0 mmol) at 0 °C for 10 h. [b] Conversion was determined by $^1H$ NMR of the crude reaction mixture. [c] Enantioselectivity was determined by chiral GC (Chiraldex B-DM column).

From this point forward, all work was performed by the author. Dr. Shu had shown that, for *cis*-β-methylstyrene, 0.84 M $K_2CO_3$ was beneficial for conversion during a 4 h reaction time, and less acetonitrile was beneficial for enantioselectivity. *n*-BuOH was then screened along with several co-solvents using 3.8 eq. acetonitrile and 0.84 M $K_2CO_3$. *n*-BuOH and *n*-BuOH/*t*-BuOH (1:1, v/v) performed best after 10 h (Table 5.3).

The conversion with *n*-BuOH alone under these conditions was lower relative to the result in Table 5.2, but the ee increased.

Now that we had promising solvents, we examined concentration of $K_2CO_3$ in more detail to further optimize the reaction (Table 5.4). Use of propionitrile was also examined, as Dr. Shu had shown in preliminary studies that this nitrile was also effective in the reaction. The amount of $H_2O_2$ was reduced to three equivalents because this was shown to give higher enantioselectivity. Acetonitrile and propionitrile gave similar results, and 0.30 M aq. $K_2CO_3$ gave the highest conversion under these conditions. *n*-BuOH and *n*-BuOH/*t*-BuOH (1:1, v/v) gave very similar ee with *n*-BuOH giving slightly higher conversion, so *n*-BuOH was chosen for further study.

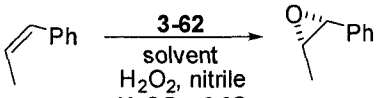
**Table 5.3**[a]




| Entry | solvent (v/v) | conv. (%)[b] | ee (%)[c] |
|---|---|---|---|
| 1 | *n*-BuOH | 55 | 78 |
| 2 | *n*-BuOH/dioxane (1:1) | 34 | 74 |
| 3 | *n*-BuOH/$CH_2Cl_2$ (1:1) | 76 | 66 |
| 4 | *n*-BuOH/DME (1:1) | 33 | 74 |
| 5 | *n*-BuOH/DMM (1:1) | 38 | 78 |
| 6 | *n*-BuOH/*t*-BuOH (1:1) | 60 | 78 |

[a]Reactions were run with olefin (0.5 mmol), ketone **3-62** (0.025 mmol), acetonitrile (0.10 mL, 1.9 mmol), solvent (1.5 mL), aq. 0.84 M $K_2CO_3$ in 4 x $10^{-4}$ M aq. EDTA (1.5 mL), and 30% $H_2O_2$ (0.20 mL, 2.0 mmol) at 0 °C for 10 h. [b] Conversion was determined by $^1H$ NMR of the crude reaction mixture. [c] Enantioselectivity was determined by chiral GC (Chiraldex B-DM column).

**Table 5.4.**[a]




| Entry | solvent | nitrile[b] | $[K_2CO_3]$ (M) | 4 h | | 10 h | |
|---|---|---|---|---|---|---|---|
| | | | | conv. (%)[c] | ee (%)[d] | conv. (%)[c] | ee (%)[d] |
| 1 | *n*-BuOH | MeCN | 0.30 | 38 | 78 | 63 | 79 |
| 2 | *n*-BuOH | MeCN | 0.60 | 32 | 79 | 58 | 79 |
| 3 | *n*-BuOH | MeCN | 0.80 | 50 | 80 | 50 | 80 |
| 4 | *n*-BuOH | EtCN | 0.10 | 27 | 79 | 42 | 80 |
| 5 | *n*-BuOH | EtCN | 0.30 | 35 | 80 | 62 | 80 |
| 6 | *n*-BuOH | EtCN | 0.60 | 31 | 80 | 57 | 79 |
| 7 | *n*-BuOH | EtCN | 0.80 | 28 | 79 | 56 | 79 |
| 8 | *n*-BuOH | EtCN | 0.84 | 30 | 79 | 42 | 79 |
| 9 | *n*-BuOH/*t*-BuOH (1:1) | EtCN | 0.30 | 32 | 81 | 54 | 80 |
| 10 | *n*-BuOH/*t*-BuOH (1:1) | EtCN | 0.60 | 34 | 80 | 53 | 81 |
| 11 | *n*-BuOH/*t*-BuOH (1:1) | EtCN | 0.80 | 28 | 81 | 41 | 80 |

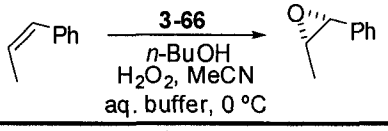
[a] Reactions were run with olefin (1.0 mmol), ketone **3-62** (0.05 mmol), nitrile (3-3.8 mmol), solvent (3 mL), aq. $K_2CO_3$ in 4 x $10^{-4}$ M aq. EDTA (3 mL), and 30% $H_2O_2$ (0.30 mL, 3.0 mmol) at 0 °C for 10 h. Aliquots were removed after 4 h for conversion determination. [b] 3.8 mmol MeCN and 3.0 mmol EtCN were used. [c] Conversion was determined by GC of the crude reaction mixture. [d] Enantioselectivity was determined by chiral GC (Chiraldex B-DM column).

During the investigation, NMR studies showed that the ketone catalysts were susceptible to decomposition under the basic reaction conditions (3.0 M $K_2CO_3$ ~ pH 11.5). At such a high pH, α-deprotonation of the ketones occurs, leading to the subsequent elimination of acetone. It is also possible that the oxazolidinone is gradually hydrolyzed over time, perhaps due to the nucleophilic action of peroxide anion.[202]

We found that ketone **3-66** usually gave better overall results than **3-62**, so it was used in further studies. A detailed pH study was then undertaken with ketone **3-66** using a range of lower pH buffers in hopes of extending the lifetime of the catalyst under the

reaction conditions. The trend clearly showed that higher pH was better for conversion despite the ketone decomposition (Table 5.5). The major consequence of this is that relatively unreactive olefins are difficult to drive to full conversion because the ketone decomposition process(es) are competing with epoxidation.

**Table 5.5**[a]



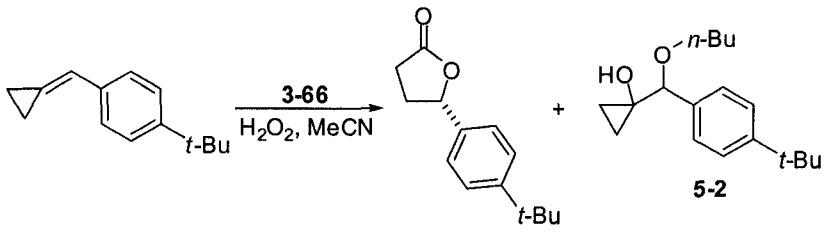

| Buffer pH | 10 h | | 24 h | |
|---|---|---|---|---|
| | conv. (%)[b] | ee (%)[c] | conv. (%)[b] | ee (%)[c] |
| 8.0 | 4 | nd | 12 | 79 |
| 8.5 | 4 | 80 | 15 | 80 |
| 9.0 | 11 | 80 | 22 | 80 |
| 9.5 | 21 | 81 | 42 | 80 |
| 10.0 | 47 | 81 | 79 | 80 |
| 10.5 | 55 | 81 | 77 | 82 |
| 11.0 | 72 | 81 | 93 | 81 |

[a] Reactions were run with olefin (1.0 mmol), ketone **3-66** (0.05 mmol), acetonitrile (3.8 mmol), *n*-BuOH (3 mL), buffer (0.30 M $K_2CO_3$-AcOH in 4 x $10^{-4}$ M aq. EDTA, pH indicated) (3 mL), and 30% $H_2O_2$ (3.0 mmol) at 0 °C for 24 h. Aliquots were removed after 10 h for conversion determination. [b] Conversion was determined by GC of the crude reaction mixture. [c] Enantioselectivity was determined by chiral GC (Chiraldex B-DM column).

After more investigation it was found that 3.8 eq. acetonitrile along with 3 eq. $H_2O_2$ in 1:1 *n*-BuOH/0.30 M aq. $K_2CO_3$ gave the best overall results for a number of substrates.[203] We then investigated a variety of olefin types with this set of conditions (Table 5.6). All the olefins used were commercially available or had previously been

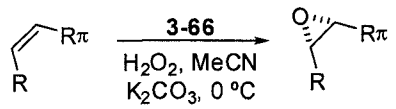
[203] Under these conditions, 28% conversion and 78% ee were obtained for *cis*-β-methylstyrene with 10 mol% ketone **2-8**.

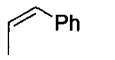
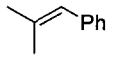
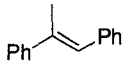
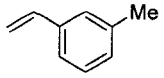
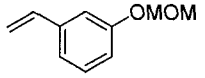
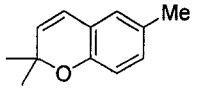
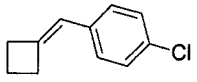
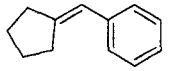
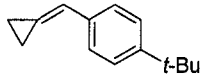
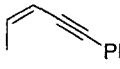
made for other projects within the group. For many substrates including aromatic *cis*-olefins (entries 1, and 6), trisubstituted olefins (entries 2, 3, 7-9), styrenes (entries 4, and 5), conjugated *cis*-enynes (entries 10 and 11), and conjugated dienes (entries 12-14) this protocol is a suitable alternative to the Oxone protocol. In most cases ee's are within a few percent of, if not as high as the corresponding ee's with Oxone as oxidant. The drop in enantioselectivity observed in some cases is likely due to a solvent effect since the asymmetric induction of ketone **3-66** is largely attributed to electronic and hydrophobic effects which are solvent-dependent.[195c,199-201] The largest drop in enantioselectivity was observed for the epoxidation of conjugated dienes (Table 5.6, entries 12-14). For entry 9, the yield is low due to the formation of a significant amount of ring-opened product **5-2** in addition to the expected aryl-lactone (Scheme 5.2).




**Scheme 5.2**

**Table 5.6** Asymmetric Epoxidation of Olefins with $H_2O_2$ as Primary Oxidant[a]




| Entry | Substrate | time (h) | Yield (conv.)(%)[b] | ee (%) | config.[c] |
|---|---|---|---|---|---|
| 1 |  | 24 | 83 (99)[d] | 82[e] | (-)(1R,2S)[199a-d,204] |
| 2 |  | 24 | 82 (96)[f] | 92[e] | (+)[199a,b,205] |
| 3 |  | 24 | 78 (90)[g] | 88[h] | (+)(R,R)[205a] |
| 4 |  | 24 | 93 (100) | 83[e] | (-)[200b,206] |
| 5 |  | 30 | 83 (94)[g] | 80[h] | (-) |
| 6 |  | 24 | 89 (100)[g] | 91[h] | (+)[199e] |
| 7 |  | 24 | 92 (93) | 96[e] | (+)(R)[201a] |
| 8 |  | 24 | 72 (100) | 90[e] | (+) |
| 9 |  | 24 | 28 (100)[g] | 86[h,i] | (-)[201c] |
| 10 |  | 48 | 77 (91)[g] | 88[h] | (-)(2S,3R)[199a,b,207] |

[204] (a) Witkop, B.; Foltz, C. M. *J. Am. Chem. Soc.* **1957**, *79*, 197-201. (b) Zhang, W.; Loebach, J. L.; Wilson, S. R.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1990**, *112*, 2801-2803.

[205] (a) Wang, Z.-X.; Tu, Y.; Frohn, M.; Zhang, J.-R.; Shi, Y. *J. Am. Chem. Soc.* **1997**, *119*, 11224-11235. (b) Brandes, B. D.; Jacobsen, E. N. *J. Org. Chem.* **1994**, *59*, 4378-4380.

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[207] (a) Lee, N. H.; Jacobsen, E. N. *Tetrahedron Lett.* **1991**, *32*, 6533-6536. (b) Hamada, T.; Irie, R.; Katsuki, T. *Synlett* **1994**, 479-481. (c) Sasaki, H.; Irie, R.; Hamada, T.; Suzuki, K.; Katsuki, T. *Tetrahedron* **1994**, *50*, 11827-11838. (d) Matsumoto, K.; Sawada, Y.; Saito, B.; Sakai, K.; Katsuki, T. *Angew. Chem. Int. Ed.* **2005**, *44*, 4935-4939. (e) Shitama, H.; Katsuki, T. *Tetrahedron Lett.* **2006**, *47*, 3203-3207. (f) Sawada, Y.; Matsumoto, K.; Kondo, S.; Watanabe, H.; Ozawa, T.; Suzuki, K.; Saito, B.; Katsuki, T. *Angew. Chem. Int. Ed.* **2006**, *45*, 3478-3480. (g) Egami, H.; Irie, R.; Sakai, K.; Katsuki, T. *Chem. Lett.* **2007**, *36*, 46-47.

| | | | | | |
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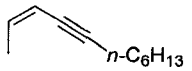
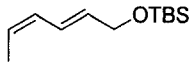
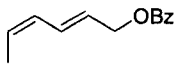
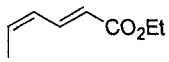
| 11 |  | 48 | 65 (91)[j] | 90[e] | (-)(2S,3R)[199a,b,207a,b] |
| 12 |  | 24 | 61 (100) | 82[e] | (-) |
| 13 |  | 24 | 74 (100) | 80[e] | (-) |
| 14 |  | 48 | nd (44)[i] | 89[e] | (-) |

[a] Unless stated otherwise, the reactions were carried out with olefin (1.0 mmol), ketone **3-66** (0.25 mmol), $CH_3CN$ (0.20 mL, 3.8 mmol), *n*-BuOH (3.0 mL), 0.30 M $K_2CO_3$ in 4 x $10^{-4}$ M aq. EDTA (3.0 mL), and 30% $H_2O_2$ (0.30 mL, 3.0 mmol) at 0 °C for the time indicated. [b] Unless stated otherwise, the conversion was determined by GC of the crude reaction mixture. [c] Absolute configurations were determined by comparing the measured optical rotations to those reported. [d] 0.10 mmol ketone used. [e] Enantioselectivity was determined by chiral GC (Chiraldex B-DM column). [f] 0.15 mmol ketone used. [g] Conversion was determined by $^1H$ NMR of the crude reaction mixture. [h] Enantioselectivity was determined by chiral HPLC (Chiralcel OD column). [i] Yield of aryl-lactone product. [j] 0.30 mmol ketone used.

## 5.C. CONCLUSION

In summary, a method for the asymmetric epoxidation of *cis*-olefins using chiral ketones with $H_2O_2$ as stoichiometric oxidant has been described. A variety of olefins can be epoxidized with good yields and ee's. Use of $H_2O_2$ allows for use of less solvent and salts, and eliminates the need for slow addition of oxidant. The reactions are operationally simple, and in most cases give results similar to those obtained with Oxone.

## 5.D. EXPERIMENTAL

**General Methods.** Hydrogen peroxide ($H_2O_2$) is potentially explosive, although no incidents occurred by our experience. Care must be taken in handling this compound. In the epoxidation reaction, EDTA is used to minimize the decomposition of $H_2O_2$ catalyzed by any trace metals. Freshly purchased $H_2O_2$ was used in this study. It was found that vigorous stirring is crucial for epoxidation efficiency—particularly for very non-polar substrates.

**Representative procedure for asymmetric epoxidation (Table 5.6, entry 2).** 2-Methyl-1-phenyl-1-propene (0.135 g, 1.00 mmol), ketone **3-66** (0.051 g, 0.15 mmol), *n*-BuOH (3.0 mL), and $CH_3CN$ (0.20 mL, 3.8 mmol) were mixed and cooled to 0 °C. 0.30 M aq. $K_2CO_3$ in 4 x $10^{-4}$ M aq. EDTA (3.0 mL) was then added followed by $H_2O_2$ (30%, 0.30 mL, 3.0 mmol) with vigorous stirring. The mixture was stirred vigorously at 0 °C for 24 h and was then poured into petroleum ether and extracted with pet. ether. The combined organic layers were washed with water, sat. aq. $Na_2S_2O_4$, dried ($Na_2SO_4$), filtered, concentrated, and purified by flash chromatography [silica gel was buffered with 1% $Et_3N$ in pet. ether; pet. ether was used as eluent] to give 2,2-dimethyl-3-phenyloxirane as a colorless oil (0.121 g, 82% yield, 92% ee).

**(Table 5.6, entry 1)**

**(CPB-1916).** Colorless oil; 82% ee $[\alpha]_D^{25}$ = -40.0 (*c* 0.77, $CHCl_3$); $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.40-7.28 (m, 5H), 4.07 (d, *J* = 4.4 Hz, 1H), 3.39-3.32 (m, 1H), 1.10 (d *J* = 5.2 Hz, 3H).

**(Table 5.6, entry 2)**

**(CPB-1913).** Colorless oil; 92% ee $[\alpha]_D^{25}$ = +38.3 (*c* 0.85, $C_6H_6$); $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.40-7.28 (m, 5H), 3.87 (s, 1H), 1.49 (s, 3H), 1.08 (s, 3H).

**(Table 5.6, entry 3)**

**(CPB-1923).** Colorless oil; 88% ee $[\alpha]_D^{25}$ = +99.3 (*c* 0.46, EtOH); $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.50-7.36 (m, 10H), 3.98 (s, 1H), 1.48 (s, 3H).

**(Table 5.6, entry 4)**

**(CPB-1917).** Colorless oil; 83% ee $[\alpha]_D^{25}$ = -17.3 (*c* 0.60, $CHCl_3$); $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.28-7.23 (m, 1H), 7.14-7.08 (m, 3H), 3.84 (dd, *J* = 4.2, 2.8 Hz, 1H), 3.14 (dd, *J* = 5.6, 4.2 Hz, 1H), 2.81 (dd, *J* = 5.6, 2.8 Hz, 1H), 2.35 (s, 3H).

**(Table 5.6, entry 5)**

**(CPB-1919).** Colorless oil; 80% ee $[\alpha]_D^{25}$ = -13.8 (*c* 0.48, $CHCl_3$); IR (NaCl) 1587, 1152 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.30-7.24 (m, 1H), 7.01-6.92 (m, 3H), 5.18 (m, 2H), 3.84 (dd, *J* = 4.2, 2.8 Hz, 1H), 3.48 (s, 3H), 3.14 (dd, *J* = 5.6, 4.2 Hz, 1H), 2.79 (dd,

$J$ = 5.6, 2.8 Hz, 1H); $^{13}C$ NMR (100 MHz, $CDCl_3$) δ 157.5, 139.6, 129.9, 119.2, 11.63, 113.4, 94.6, 56.3, 52.5, 51.4. Anal. Calcd. For $C_{10}H_{12}O_3$: C, 66.65; H, 6.71; Found: C, 66.90; H, 6.94.

**(Table 5.6, entry 6)**

**(CPB-2018).** White solid; 91% ee $[\alpha]_D^{25}$ = +14.8 (*c* 1.80, $CHCl_3$); $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.15-7.14 (m, 1H), 7.05-7.02 (m, 1H), 6.70 (d, $J$ = 8.4 Hz, 1H), 3.86 (d, $J$ = 4.2 Hz, 1H), 3.48 (d, $J$ = 4.2 Hz, 1H), 2.29 (s, 3H), 1.57 (s, 3H), 1.24 (s, 3H).

**(Table 5.6, entry 7)**

**(CPB-1921).** Colorless oil; 96% ee $[\alpha]_D^{25}$ = +106.9 (*c* 1.38, $CHCl_3$); $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.34-7.31 (m, 2H), 7.13-7.10 (m, 2H), 3.83 (s, 1H), 2.67-2.57 (m, 1H), 2.51-2.36 (m, 2H), 1.99-1.83 (m, 2H), 1.76-1.60 (m, 1H).

**(Table 5.6, entry 8)**

**(CPB-1925b).** Colorless oil; 90% ee $[\alpha]_D^{25}$ = +52.4 (*c* 0.67, $CHCl_3$); IR (NaCl) 1604, 1497, 1455 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.38-7.26 (m, 5H), 4.02 (s, 1H), 2.10-1.40 (m, 8H); $^{13}C$ NMR (100 MHz, $CDCl_3$) δ 137.4, 128.3, 127.7, 126.4, 72.8, 63.5, 34.2, 28.6, 25.5, 25.4. Anal. Calcd. For $C_{12}H_{14}O$: C, 82.72; H, 8.10; Found: C, 82.56, H, 7.99.

**(Table 5.6, entry 9)**

**(CPB-1928a).** Colorless oil; 86% ee $[\alpha]_D^{25}$ = -25.8 (*c* 0.12, $CHCl_3$); $^1H$ NMR (300 MHz, $CDCl_3$) δ 7.44-7.41 (m, 2H), 7.30-7.27 (m, 2H), 5.13 (dd, *J* = 8.1, 6.3 Hz, 1H), 2.70-2.60 (m, 3H), 2.27-2.17 (m, 1H) 1.34 (s, 9H).

**(5-2) Ring-opened product.** Colorless oil; IR (NaCl): 3443, 2961, 1093 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.36-7.28 (m, 2H), 7.26-7.16 (m, 2H), 4.28 (s, 1H), 3.45-3.30 (m, 2H), 2.51 (s, 1H), 1.60-1.50 (m, 2H), 1.52-1.20 (m, 11H), 0.88 (t, *J* = 6.8 Hz, 3H), 0.60-0.45 (m, 4H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 150.8, 136.0, 127.4, 125.3, 85.0, 69.5, 58.6, 34.8, 32.2, 31.6, 20.0, 14.2, 11.6, 10.1.

**(Table 5.6, entry 10)**

**(CPB-1924).** Colorless oil; 88% ee $[\alpha]_D^{25}$ = -34.8 (*c* 0.43, $CHCl_3$); $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.48-7.45 (m, 2H), 7.35-7.30 (m, 3H), 3.65 (d, *J* = 4.4 Hz, 1H), 3.27 (qd, *J* = 5.2, 4.4 Hz, 1H), 1.51 (d, *J* = 5.2 Hz, 3H).

**(Table 5.6, entry 11)**

**(CPB-1937).** Colorless oil; 90% ee $[\alpha]_D^{25}$ = -31.2 (*c* 0.41, $CHCl_3$); $^1H$ NMR (400 MHz, $CDCl_3$) δ 3.42 (dt, *J* = 4.4, 1.6 Hz, 1H), 3.13 (qd, *J* = 5.2 4.4 Hz, 1H), 2.22 (td, *J* = 7.2, 1.6 Hz, 2H), 1.53-1.47 (m, 2H), 1.42-1.22 (m, 8H), 1.40 (d, *J* = 5.2 Hz, 3H), 0.89 (t, *J* = 7.2 Hz, 3H).

**(Table 5.6, entry 12)**

**(CPB-1934b).** Colorless oil; 82% ee $[\alpha]_D^{25}$ = -19.1 (*c* 0.33, $CHCl_3$); $^1H$ NMR (400 MHz, $CDCl_3$) δ 6.02 (dt, *J* = 15.4, 4.4 Hz, 1H), 5.60 (ddt, *J* = 15.4, 7.6, 1.7 Hz, 1H), 4.22 (dd, *J* = 4.4, 1.7 Hz, 2H), 3.43 (dd, *J* = 7.6, 4.0 Hz, 1H), 3.22 (quint, *J* = 5.4 Hz, 1H), 1.29 (d, *J* = 5.4 Hz, 3H), 0.91 (s, 9H), 0.07 (s, 6H).

**(Table 5.6, entry 13)**

**(CPB-1934a).** Colorless oil; 80% ee $[\alpha]_D^{25}$ = -18.8 (*c* 0.35, $CHCl_3$); $^1H$ NMR (400 MHz, $CDCl_3$) δ 8.07 (d, *J* = 7.2 Hz, 2H), 7.58 (t, *J* = 7.6 Hz, 1H), 7.46 (t, *J* = 7.6 Hz, 2H), 6.14 (dt, *J* = 15.6, 6.0 Hz, 1H), 5.76 (dd, *J* = 15.6, 7.2 Hz, 1H), 4.88 (d, *J* = 5.6 Hz, 2H), 3.45 (dd, *J* = 7.2, 4.4 Hz, 1H), 3.25 (quint, *J* = 5.6 Hz, 1H), 1.31 (d, *J* = 5.6 Hz, 3H).

**(Table 5.6, entry 14)**

**(CPB-1922).** Colorless oil; 89% ee; $^1H$ NMR (300 MHz, $CDCl_3$) δ 6.80 (dd, *J* = 15.6, 6.6 Hz, 1H), 6.13 (dd, *J* = 15.9, 0.9 Hz), 4.22 (q, *J* = 7.2 Hz, 2H), 3.52 (ddd, *J* = 6.6, 4.2, 0.9 Hz, 1H), 3.32 (quint., *J* = 5.4 Hz, 1H), 1.30 (m, 6H).

# CHAPTER SIX

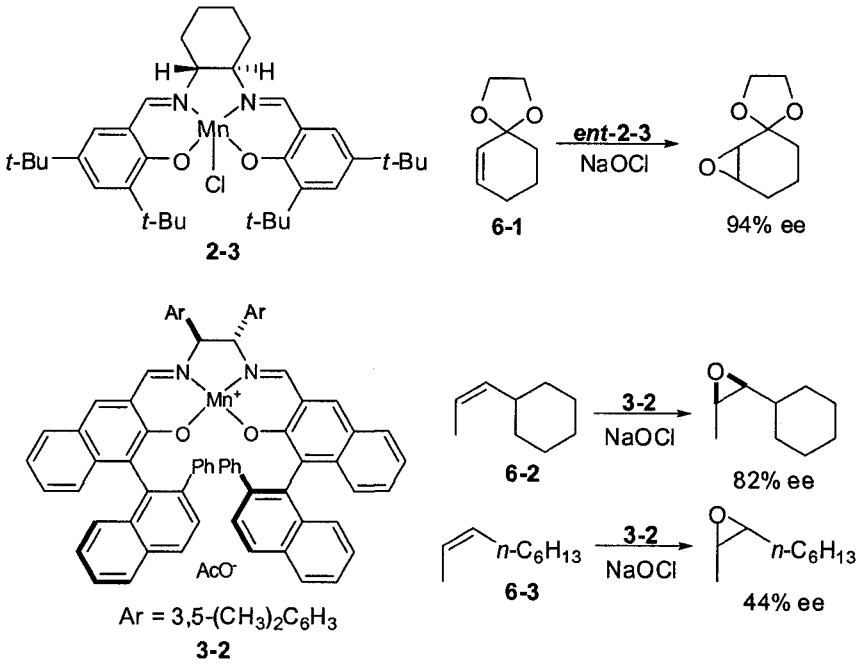
# CATALYTIC ASYMMETRIC EPOXIDATION OF UNCONJUGATED *CIS*-OLEFINS

## 6.A. INTRODUCTION AND BACKGROUND

As previously discussed, there has been a substantial amount of work done in the area of asymmetric epoxidation of *cis*-olefins both by our group and by others. However, nearly all of this work has targeted *conjugated cis*-olefins. *cis*-Olefins have a high degree of symmetry, so effective differentiation between the two prochiral faces is often difficult. With conjugated *cis*-olefins one substituent is sterically and electronically significantly different than the other making these effective substrates. For unconjugated *cis*-olefins some other method of stereodifferentiation must be employed.

There have been very few reports of asymmetric epoxidation of unconjugated *cis*-olefins indicating the level of difficulty that this problem poses. Mn-salen complex **2-3**

has been used to epoxidize **6-1** in 94% ee,[208] and **3-2** has been used to epoxidize **6-2** and **6-3** in 82% and 44% ee respectively (Scheme 6.1).[209]




**Scheme 6.1**

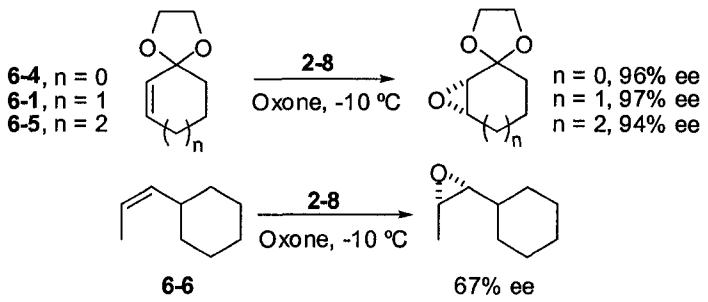
Epoxidation of cyclic enone acetals **6-1**, **6-4**, and **6-5** by ketone **2-8** in very high ee was reported by our group in 2000.[210] **6-6** was also examined and gave 67% ee (Scheme 6.2). In order to elucidate the reason for the high asymmetric induction with olefins **6-1**, **6-4**, and **6-5**, and to further expand the scope of the asymmetric epoxidation

[208] Jacobsen, E. N.; Zhang, W.; Muci, A. R.; Ecker, J. R.; Deng, L. *J. Am. Chem. Soc.* **1991**, *113*, 7063-7064.

[209] Mikame, D.; Hamada, T.; Irie, R.; Katsuki, T. *Synlett* **1995**, 827-828.

[210] (a) Tian, H.; She, X.; Shu, L.; Yu, H.; Shi, Y. *J. Am. Chem. Soc.* **2000**, *122*, 11551-11552. (b) Tian, H.; She, X.; Yu, H.; Shu, L.; Shi, Y. *J. Org. Chem.* **2002**, *67*, 2435-2446.

of *cis*-olefins using the knowledge gained in the previous studies, we undertook the investigation of asymmetric epoxidation of a variety of unconjugated olefins.




**Scheme 6.2**

## 6.B. RESULTS AND DISCUSSION

### 6.B.i. Substrate Synthesis

Some of the olefins used for this study are commercially available (Figure 6.1), but others had to be synthesized (Scheme 6.3). Olefin **6-3** was prepared simply by partial hydrogenation of 2-nonyne. **6-11** was prepared by oxidation of commercially available *cis*-4-decen-1-ol with PDC in DMF.[211] Allylic ether **6-12** was synthesized by methylation of *cis*-2-nonen-1-ol (**6-7**). Aromatic ethers **6-15** and **6-16** were made by $S_N2$

[211] Corey, E.J.; Schmidt, G. *Tetrahedron Lett.* **1979**, *20*, 399-402.

reactions of *p*-flurophenol and *p*-cresol on 1-bromo-2-butyne followed by partial hydrogenation of the alkynes to the corresponding *cis*-alkenes.[212] **6-19**, the all-carbon analog of **6-16**, was prepared by reduction of *p*-tolylacetic acid with $LiAlH_4$ followed by conversion of alcohol **6-17** to bromide **6-18**.[213] Nickel-catalyzed coupling of the corresponding Grignard reagent with *cis*-1-bromo-1-propene gave **6-19** in good yield.[214] Acetal **6-21** was synthesized starting with acetalization of 2-octynal.[215] Partial hydrogenation of alkyne **6-20** then gave desired olefin **6-21** in high yield. Reaction of propynyl magnesium bromide with heptanoyl chloride gave ketone **6-32** which was then ketalized to give **6-23**.[216,217] Ketal **6-24** was then synthesized by partial hydrogenation of the alkyne as before. Spirocyclic compound **6-28**, the all carbon analog of **6-1**, was prepared starting with a pinacol coupling of cyclopentanone to give diol **6-25**.[218] Lewis acid-catalyzed pinacol rearrangement of **6-25** furnished ketone **6-26** which was converted to tosylhydrazone **6-27**.[219,220] Shapiro reaction then furnished **6-28** in moderate yield.[221]

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[221] Yamazaki, M.; Shibasaki, M.; Ikegami, S. *Chem. Lett.* **1981**, 1245-1248.

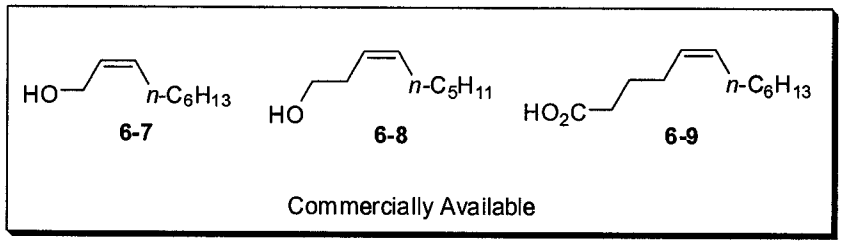
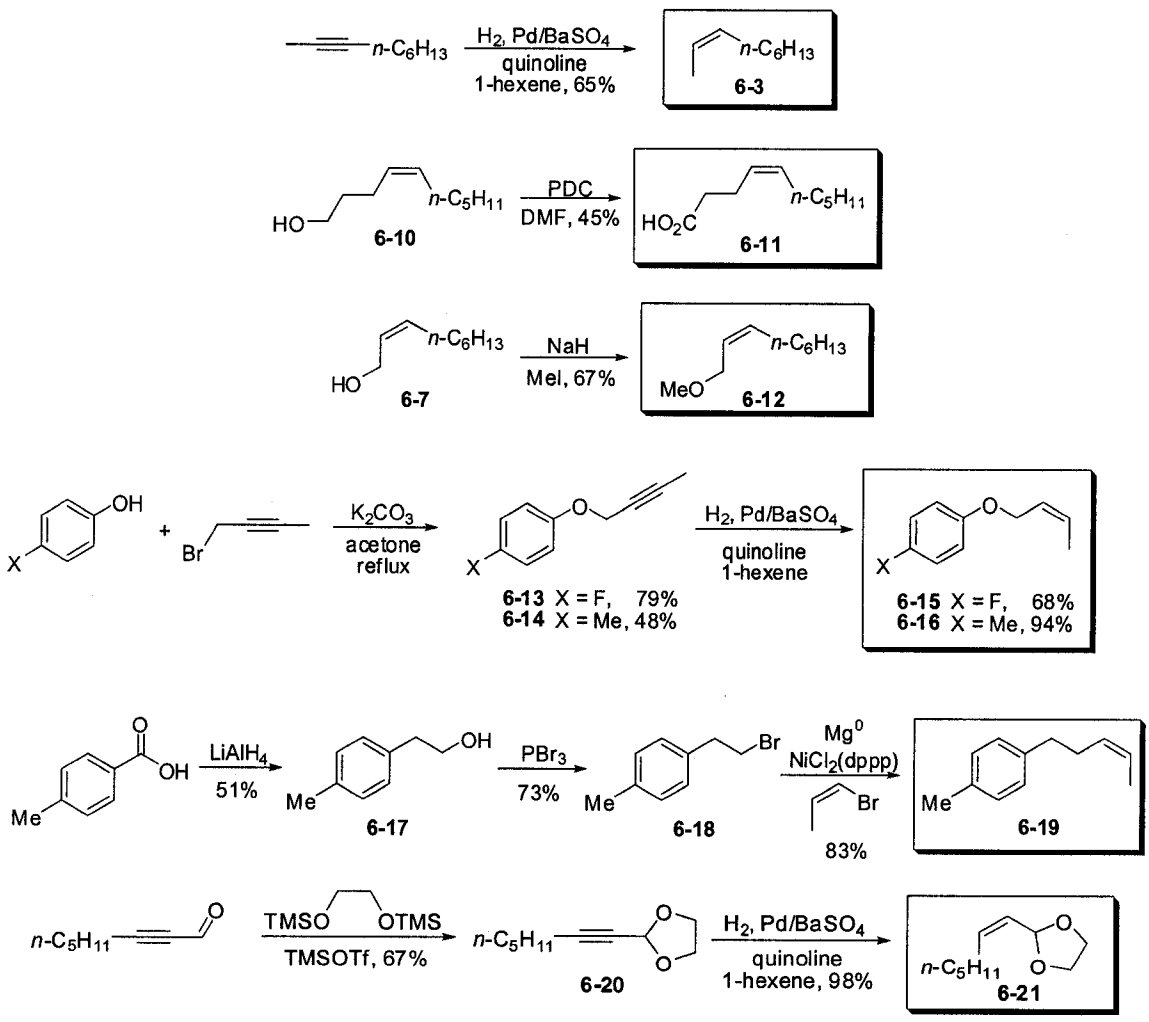
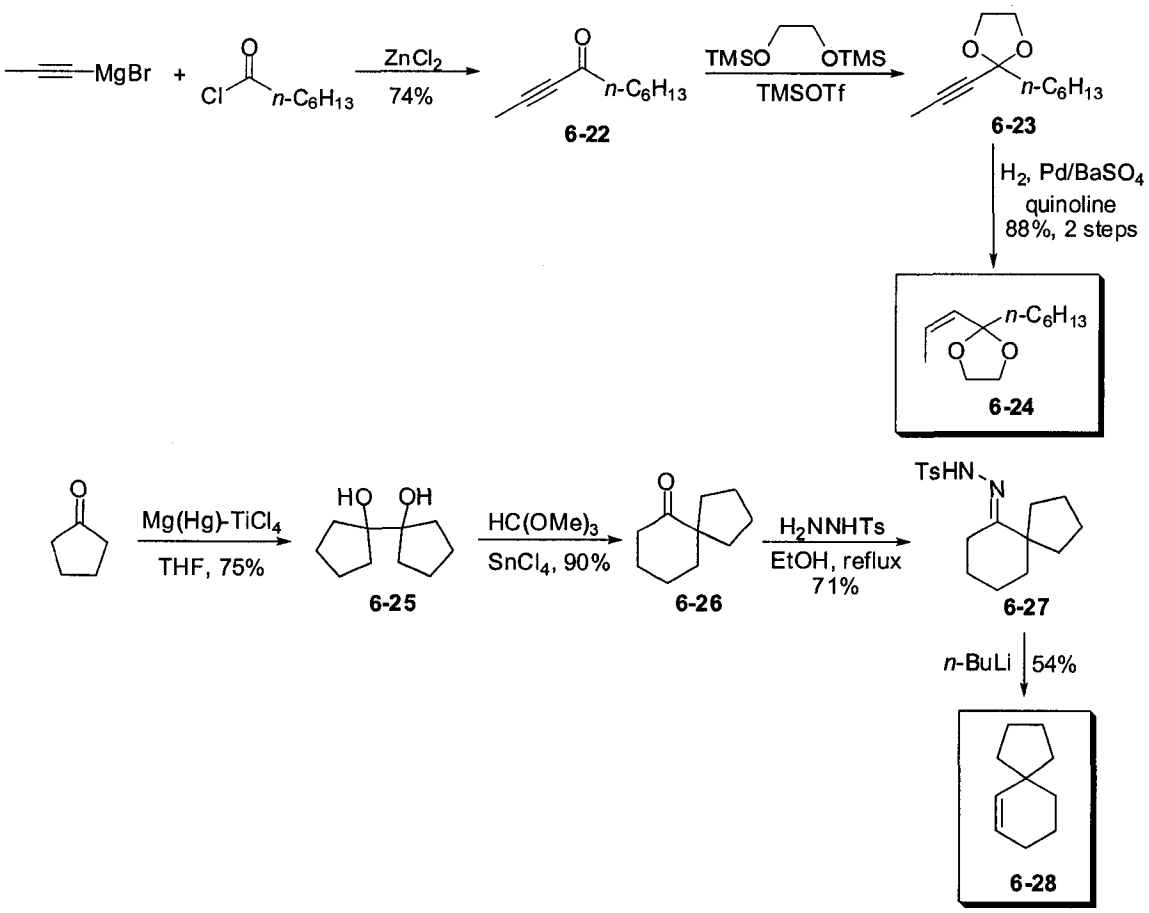



**Figure 6.1**

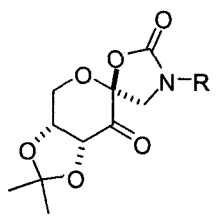



**Scheme 6.3**




**Scheme 6.3 (continued)**

## 6.B.ii. Asymmetric Epoxidation of Unconjugated *cis*-Olefins

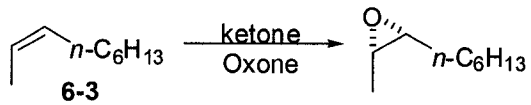



**2-8** R = Boc
**3-62** R = (4-Me)-Ph
**3-64** R = (4-*n*-Bu)-Ph
**3-66** R = (4-Et)-Ph
**6-29** R = (4-*n*-$C_7H_{15}$)-Ph
**6-30** R = (4-*n*-$C_{10}H_{21}$)-Ph

**Figure 6.2**

Epoxidation study was begun with **6-3**. Ketones **2-8**, **3-62**, **3-64**, **3-66**, **6-29**, and **6-30** with different groups on nitrogen (Figure 6.2) were screened for enantioselectivity (Table 6.1). Ketone **2-8** gave the lowest ee while the *N*-aryl ketones were more effective. As Table 6.1 shows, ee increased with increasing length of the *p*-alkyl chain on the aryl ring of the catalyst up to seven carbons. However, ketone **6-30** with an *n*-decyl chain on the phenyl ring gave lower ee (Table 6.1, entries 2-6). The absolute configuration of the epoxide is not known,[222a] but we believe the enantioselectivity in this reaction is derived solely from hydrophobic interactions—i.e. spiro transition state **A** is favored over spiro **B** (Figure 6.3) because the hydrophobic *n*-hexyl group is more likely to be aligned adjacent to the hydrophobic *N*-aryl group of the catalyst rather than out in the aqueous reaction medium, whereas the less hydrophobic methyl group is better tolerated in the aqueous medium.

**Table 6.1**[a]




**6-3**

| Entry | ketone [R] | conv. (%)[b] | ee (%)[c] |
|---|---|---|---|
| 1 | **2-8** [Boc] | 75 | 44 |
| 2 | **3-62** [(4-Me)-Ph] | 53 | 56 |
| 3 | **3-66** [(4-Et)-Ph] | 57 | 58 |
| 4 | **3-64** [(4-*n*-Bu)-Ph] | 63 | 65 |
| 5 | **6-29** [(4-*n*-$C_7H_{15}$)-Ph] | 89 | 65 |
| 6 | **6-30** [(4-*n*-$C_{10}H_{21}$)-Ph] | 94 | 54 |

[a] For ketone **2-8**: the reaction was carried out with olefin (1.0 eq.), catalyst (0.25 eq.), Oxone (1.6 eq.), and $K_2CO_3$ (3.8 eq.) in

[222] (a) Asami, M.; Kanemaki, N. *Tetrahedron Lett.* **1989**, *30*, 2125-2128. (b) Utaka, M.; Konishi, S.; Takeda, A. *Tetrahedron Lett.* **1986**, *27*, 4737-4740. (c) Zaks, A.; Dodds, D. R. *J. Am. Chem. Soc.* **1995**, *117*, 10419-10424.

DME/DMM (3:1, v/v) and buffer (0.1 M $K_2CO_3$-AcOH in 4 x $10^{-4}$ M aq. EDTA, pH 8.0) (1.5:1, v/v). For ketones **3-62** – **6-30**: reactions were carried out with olefin (1.0 eq.), catalyst (0.25 eq.), Oxone (1.6 eq.), and $K_2CO_3$ (6.7 eq.) in DME/DMM (3:1, v/v) and buffer (0.1 M $K_2CO_3$-AcOH in 4 x $10^{-4}$ M aq. EDTA, pH 9.3) (1.5:1, v/v). In all cases Oxone and $K_2CO_3$ were added separately and simultaneously over 4 h at 0 °C. [b] The conversion was determined by GC of the crude reaction mixture. [c] Enantioselectivity was determined by chiral GC (Chiraldex B-DM column) of the crude reaction mixture.

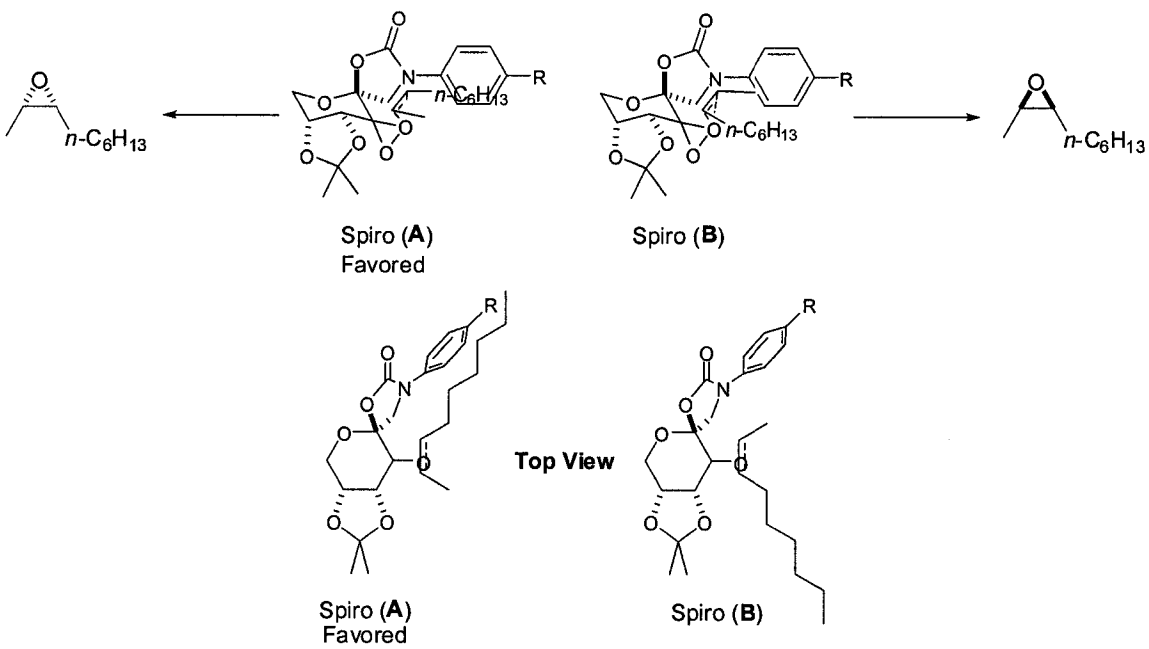


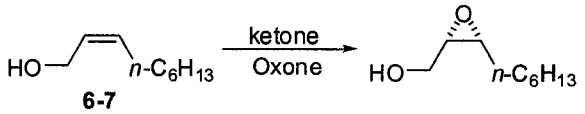

**Figure 6.3**

Ketones **2-8**, **3-62**, **3-64**, and **3-66** were also screened with **6-7**. We expected much higher ee's for this substrate than for **6-3** due to the addition of the polar hydroxyl group. However, the observed ee's were similar to those observed for **6-3** with ketones **3-62**, **3-64**, and **3-66** and almost no ee was observed with ketone **2-8** (Table 6.2). The

absolute configuration of the epoxide indicates that the hexyl chain prefers to be proximal to the oxazolidinone of the ketone during the transition state.

Screening of **6-12** with ketones **2-8**, **3-62**, and **3-66** gave very interesting results. Epoxidation with **2-8** gave 49% ee of the (2R, 3S) enantiomer (Table 6.3, entry 1) while **3-62** gave no ee (entry 2), and **3-66** gave 14% ee in favor of the (2S, 3R) enantiomer (Table 6.3, entry 3).

**Table 6.2**[a]

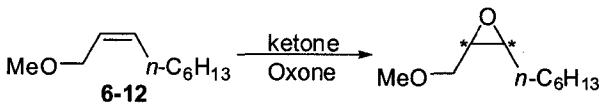



**6-7**

| Entry | ketone [R] | T (°C) | t (h) | conv. (%)[b] | ee (%)[c] |
|---|---|---|---|---|---|
| 1 | **2-8** [Boc] | 0 | 4 | 75 | 10 |
| 2 | **3-62** [(4-Me)-Ph] | 0 | 4 | 100 | 63 |
| 3 | **3-66** [(4-Et)-Ph] | 0 | 4 | 100 | 67 |
| 4 | **3-64** [(4-*n*-Bu)-Ph] | -10 | 8 | 100 | 79[d] |

[a] For ketone **2-8**: the reaction was carried out with olefin (1.0 eq.), catalyst (0.25 eq.), Oxone (1.6 eq.), and $K_2CO_3$ (3.8 eq.) in DME/DMM (3:1, v/v) and buffer (0.1 M $K_2CO_3$-AcOH in 4 x $10^{-4}$ M aq. EDTA, pH 8.0) (1.5:1, v/v). For ketones **3-62**, **3-66**, **3-64**: reactions were carried out with olefin (1.0 eq.), catalyst (0.25 eq.), Oxone (1.6 eq.), and $K_2CO_3$ (6.7 eq.) in DME/DMM (3:1, v/v) and buffer (0.1 M $K_2CO_3$-AcOH in 4 x $10^{-4}$ M aq. EDTA, pH 9.3) (1.5:1, v/v). In all cases Oxone and $K_2CO_3$ were added separately and simultaneously over the time at the temperature indicated. [b] The conversion was determined by $^1$H NMR of the crude reaction mixture. [c] Enantioselectivity was determined by chiral HPLC (Chiralcel OJ column) of the benzoate derivative. [d] Enantioselectivity was determined by chiral GC (Chiraldex B-DM column) of the methyl ether derivative.

**Table 6.3**[a]




| Entry | ketone [R] | conv. (%)[b] | ee (%)[c] | config. |
|---|---|---|---|---|
| 1 | **2-8** [Boc] | 52 | 49 | (2R, 3S) |
| 2 | **3-62** [(4-Me)-Ph] | 55 | 0 | |
| 3 | **3-66** [(4-Et)-Ph] | 56 | 14 | (2S, 3R) |

[a] For ketone **2-8**: the reaction was carried out with olefin (1.0 eq.), catalyst (0.25 eq.), Oxone (1.6 eq.), and $K_2CO_3$ (3.8 eq.) in DME/DMM (3:1, v/v) and buffer (0.1 M $K_2CO_3$-AcOH in 4 x $10^{-4}$ M aq. EDTA, pH 8.0) (1.5:1, v/v). For ketones **3-62**, **3-66**: reactions were carried out with olefin (1.0 eq.), catalyst (0.25 eq.), Oxone (1.6 eq.), and $K_2CO_3$ (6.7 eq.) in DME/DMM (3:1, v/v) and buffer (0.1 M $K_2CO_3$-AcOH in 4 x $10^{-4}$ M aq. EDTA, pH 9.3) (1.5:1, v/v). In both cases Oxone and $K_2CO_3$ were added separately and simultaneously over 4 h at -10 °C. [b] The conversion was determined by GC of the crude reaction mixture. [c] Enantioselectivity was determined by chiral GC (Chiraldex B-DM column) of the crude reaction mixture.

The results from Table 6.3 indicate that the methoxy ether of **6-12** has a preference to be proximal to the oxazolidinone of **2-8** during the transition state—i.e. spiro **F** is favored over spiro **E** (Figure 6.4). This is counter to what was observed in Tables 6.1 and 6.2 where the alkyl chains of the olefins preferred to be proximal to the oxazolidinone.

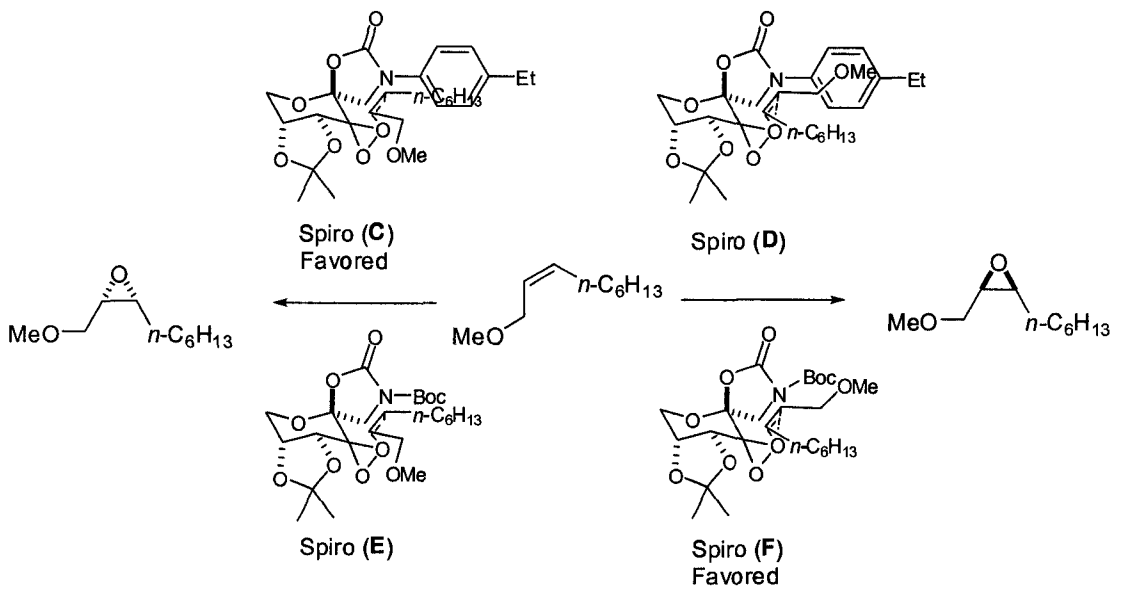
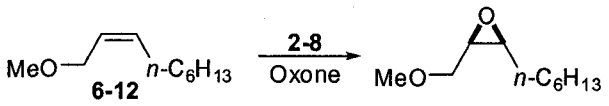



**Figure 6.4**

We then tried to optimize this reaction in hopes of further favoring the apparent attraction between the ether substituent of the olefin and the oxazolidinone of ketone **2-8**. First, several different solvents and solvent combinations were screened (Table 6.4, entries 1-12). Of these, combinations of DME, DMM, and several alcohols gave the best results. Different ratios of these promising solvent combinations were then tested (Table 6.4, entries 13-19). Finally, the solvent/buffer ratio was then varied for these solvents (Table 6.4, entries 20-25). Overall, [DME/DMM/*n*-BuOH (3:1:2, v/v/v)]/buffer (4:1, v/v) gave the best combination of conversion and ee (entry 22), and the ee for **6-12** was increased to 61% under these conditions.

**Table 6.4**[a]



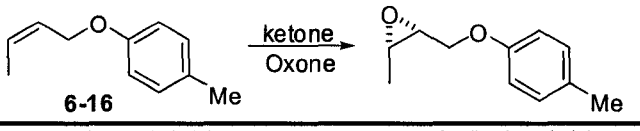

| Entry | solvent (v/v/v) | solvent/buffer (v/v) | conv. (%)[b] | ee (%)[c] |
|---|---|---|---|---|
| 1 | DME | 3:2 | 55 | 47 |
| 2 | DME/DMM (3:1) | 3:2 | 52 | 49 |
| 3 | DME/DMM/$CH_2Cl_2$ (3:1:1) | 3:2 | 0 | |
| 4 | DME/DMM/THF (3:1:1) | 3:2 | 49 | 52 |
| 5 | DME/DMM/dioxane (3:1:1) | 3:2 | 49 | 48 |
| 6 | DME/DMM/EtOH (3:1:1) | 3:2 | 63 | 47 |
| 7 | DME/DMM/*i*-PrOH (3:1:1) | 3:2 | 90 | 52 |
| 8 | DME/DMM/*n*-BuOH (3:1:1) | 3:2 | 100 | 58 |
| 9 | DME/DMM/*s*-BuOH (3:1:1) | 3:2 | 88 | 55 |
| 10 | DME/DMM/*t*-BuOH (3:1:1) | 3:2 | 75 | 49 |
| 11 | DME/DMM/amyl alcohol (3:1:1) | 3:2 | 13 | 60 |
| 12 | DME/DMM/cyclohexanol (3:1:1) | 3:2 | 67 | 58 |
| 13 | DME/DMM/*n*-BuOH (3:1:2) | 3:2 | 76 | 58 |
| 14 | DME/DMM/*n*-BuOH (3:1:4) | 3:2 | 43 | 60 |
| 15 | DME/DMM/*n*-BuOH (3:1:8) | 3:2 | 8 | 56 |
| 16 | DME/DMM/*n*-BuOH (3:1:0.67) | 3:2 | 77 | 55 |
| 17 | DME/DMM/cyclohexanol (3:1:0.67) | 3:2 | 65 | 52 |
| 18 | DME/DMM/cyclohexanol (3:1:2.5) | 3:2 | 7 | 54 |
| 19 | DME/DMM/cyclohexanol (3:1:8) | 3:2 | 10 | 46 |
| 20 | DME/DMM/*n*-BuOH (3:1:2) | 1:1 | 43 | 48 |
| 21 | DME/DMM/*n*-BuOH (3:1:2) | 2:1 | 62 | 59 |
| 22 | DME/DMM/*n*-BuOH (3:1:2) | 4:1 | 73 | 61 |
| 23 | DME/DMM/*n*-BuOH (3:1:2) | 7:1 | 62 | 62 |
| 24 | DME/DMM/*n*-BuOH (3:1:2) | 12:1 | 15 | 60 |
| 25 | DME/DMM/cyclohexanol (3:1:1) | 2:1 | 67 | 60 |

[a] All reactions were carried out with olefin (1.0 eq.), catalyst (0.25 eq.), Oxone (1.6 eq.), and $K_2CO_3$ (3.8 eq.) in solvent and buffer (0.1 M $K_2CO_3$-AcOH in 4 x $10^{-4}$ M aq. EDTA, pH 8.0). Oxone and $K_2CO_3$ were added separately and simultaneously over 4 h at -10 °C. [b] The conversion was determined by GC of the crude reaction mixture. [c] Enantioselectivity was determined by chiral GC (Chiraldex B-DM column) of the crude reaction mixture.

These new optimized conditions were then applied to the epoxidation of aromatic allylic ether **6-16** in hopes of increasing the apparent attraction between the ether and the oxazolidinone for this substrate as well. The ee dropped from 86% to 73%, however (Table 6.5). This suggests that the new conditions don't further favor an attraction

between ethers and the oxazolidinone, but rather that they disfavor the hydrophobic interaction between the substrate and catalyst. In other words, in the case of **6-12** above, the new conditions apparently disfavor spiro **E** rather than further favor spiro **F** leading to the observed increase in ee (Figure 6.4).

**Table 6.5**[a]

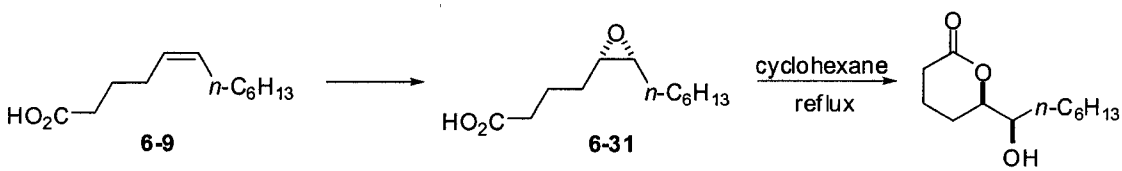



| Entry | ketone [R] | solvent (v/v/v) | solv./buffer (v/v) | conv. (%)[b] | ee (%)[c] |
|---|---|---|---|---|---|
| 1 | **3-62** [(4-Me)-Ph] | DME/DMM (3:1) | 3:2 | 69 | 76 |
| 2 | **3-66** [(4-Et)-Ph] | DME/DMM (3:1) | 3:2 | 76 | 79 |
| 3 | **2-8** [Boc] | DME/DMM (3:1) | 3:2 | 95 | 86 |
| 4 | **2-8** [Boc] | DME/DMM/*n*-BuOH (3:1:2) | 4:1 | 99 | 73 |

[a] For entries 1-2 the reactions were carried out with olefin (1.0 eq.), catalyst (0.25 eq.), Oxone (1.6 eq.), and $K_2CO_3$ (6.7 eq.) in DME/DMM (3:1, v/v) and buffer (0.1 M $K_2CO_3$-AcOH in 4 x $10^{-4}$ M aq. EDTA, pH 9.3) (1.5:1, v/v). Oxone and $K_2CO_3$ were added separately and simultaneously over 4 h at -10 °C. For entries 3-4 the reactions were carried out with olefin (1.0 eq.), catalyst (0.30 eq.), Oxone (2.9 eq.), and $K_2CO_3$ (6.9 eq.) in solvent and buffer (0.1 M $K_2CO_3$-AcOH in 4 x $10^{-4}$ M aq. EDTA, pH 8.0). Oxone and $K_2CO_3$ were added separately and simultaneously over 12 h at -10 °C. [b] The conversion was determined by GC of the crude reaction mixture. [c] Enantioselectivity was determined by chiral GC (Chiraldex B-DM column) of the crude reaction mixture.

A variety of *cis*-olefins were then epoxidized using the insights gained above, and the best results for each substrate are shown in Table 6.6. For entries 4 and 5 the products were obtained as the five and six-membered lactones respectively. The product in entry 4, 5-(1-hydroxyhexyl)-dihydro-furan-2-one (aka L-Factor), is the enantiomer of a natural product isolated from *Streptomyces griseus* and has been the subject of many

synthetic investigations.[223] For entry 5, the epoxide did not completely cyclize under the reaction conditions, so a mixture of epoxy acid **6-31** and the lactone were isolated from the crude reaction mixture. Refluxing this crude mixture overnight in cyclohexane cleanly gave the lactone product which was easier to isolate and purify (Scheme 6.4).[224] Allylic acetal **6-21** was a very effective substrate, but allylic ketal **6-24** was not (entries 9-10). **6-19** and **6-28**, the carbon analogs of **6-16** and **6-1** respectively, were also epoxidized and gave much lower enantioselectivity than their oxygen-containing counterparts (entries 11-12).

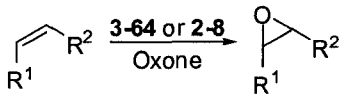


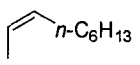
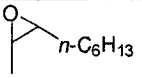
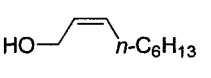
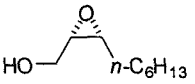
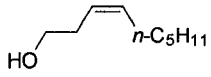
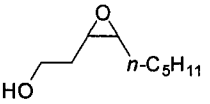
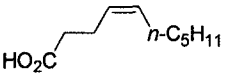
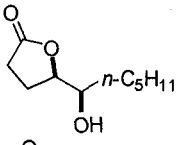
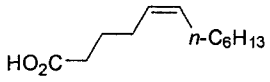
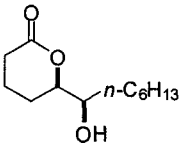
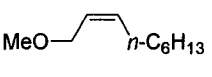
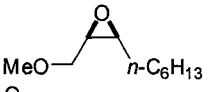
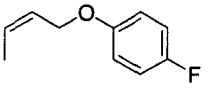
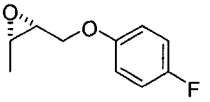
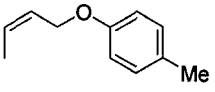
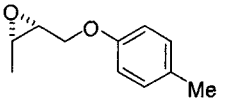
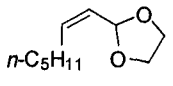
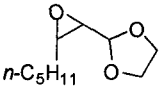

**Scheme 6.4**

[223] For leading references see: (a) Gräfe, U.; Reinhardt, G.; Schade, W.; Krebs, D.; Eritt, I.; Fleck, W. F.; Hienrich, E.; Radics, L. *J. Antibiotics* **1982**, *35*, 609-614. (b) Gräfe, U.; Eritt, I. *J. Antibiotics* **1983**, *36*, 1592-1593. (c) Cooper, R. D.; Jigajinni, V. B.; Wightman, R. H. *Tetrahedron Lett.* **1984**, *45*, 5215-5218. (d) Mori, K.; Otsuka, T. *Tetrahedron*, **1985**, *41*, 3253-3256. (e) Sato, F.; Kobayashi, Y.; Takahashi, O.; Chiba, T.; Takeda, Y.; Kusakabe, M. *J. Chem. Soc. Chem. Commun.* **1985**, 1636-1638. (f) Fujisawa, T.; Kojima, E.; Itoh, T.; Sato, T. *Chem. Lett.* **1985**, 1751-11754. (g) Kotsuki, H.; Kadota, I.; Ochi, M. *J. Org. Chem.* **1990**, *55*, 4417-4422. (h) Wang, Z.-M.; Zhang, X.-L.; Sharpless, K. B. *Tetrahedron Lett.* **1992**, *33*, 6407-6410. (i) Albrecht, W.; Tressl, R. *Tetrahedron: Asymmetry* **1993**, *4*, 1391-1396. (j) Clough, S.; Raggatt, M. E.; Simpson, T. J.; Willis, C. L.; Whiting, A.; Wrigley, S. K. *J. Chem. Soc., Perkin Trans. 1* **2000**, 2475-2481.

[224] Ochiai, M.; Ukita, T.; Iwaki, S.; Nagao, Y.; Fujita, E. *J. Org. Chem.* **1989**, *54*, 4832-4840.

**Table 6.6** Asymmetric Epoxidation of Unconjugated *cis*-Olefins[a]

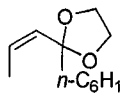
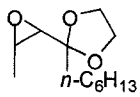
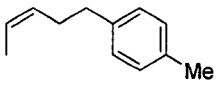
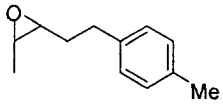
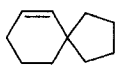
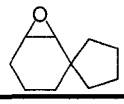



| Entry | Substrate | Product | Ketone [R] | T (°C) | t (h) | Yield (conv.) (%)[b] | ee (%) |
|---|---|---|---|---|---|---|---|
| 1 |  |  | **3-64** [(4-*n*-Bu)-Ph] | 0 | 8 | 52 (100)[c] | 65[d,209,222] |
| 2 |  |  | **3-64** [(4-*n*-Bu)-Ph] | -10 | 8 | 71 (100)[e] | 79[f,225] |
| 3 |  |  | **3-64** [(4-*n*-Bu)-Ph] | -10 | 4 | 89 (100)[e] | 82[f,226] |
| 4 |  |  | **3-64** [(4-*n*-Bu)-Ph] | -10 | 8 | 75 (nd) | 91[d,223] |
| 5 |  |  | **3-64** [(4-*n*-Bu)-Ph] | -10 | 8 | 88 (nd) | 86[g,227] |
| 6 |  |  | **2-8** [Boc] | -10 | 8 | 79 (98) | 61[d] |
| 7 |  |  | **2-8** [Boc] | -10 | 12 | 73 (98)[h,i,j] | 86[d] |
| 8 |  |  | **2-8** [Boc] | -10 | 12 | 71 (95)[h,i,j] | 85[d] |
| 9 |  |  | **2-8** [Boc] | -10 | 12 | 76 (94)[h,i] | 92[d] |

[225] (a) Kanerva, L. T.; Vänttinen, E. *Tetrahedron: Asymmetry* **1993**, *4*, 85-90. (b) Yu, L.; Wang, Z. *J. Chem. Soc., Chem. Commun.* **1993**, 232-234. (c) Zhang, W.; Basak, A.; Kosugi, Y.; Hoshino, Y.; Yamamoto, H. *Angew. Chem. Int. Ed.* **2005**, *44*, 4389-4391.

[226] (a) Zhang, W.; Yamamoto, H. *J. Am. Chem. Soc.* **2007**, *129*, 286-287. (b) Chiappe, C.; Cordoni, A.; Lo Moro, G.; Palese C. D. *Tetrahedron: Asymmetry* **1998**, *9*, 341-350. (c) Ikegami, S.; Katsuki, T.; Yamaguchi, M. *Chem. Lett.* **1987**, 83-84.

[227] Sala, L. F.; Cravero, R. M.; Signorella, S. R.; González-Sierra, M.; Rúveda, E. A. *Synth. Comm.* **1987**, *17*, 1287-1297.

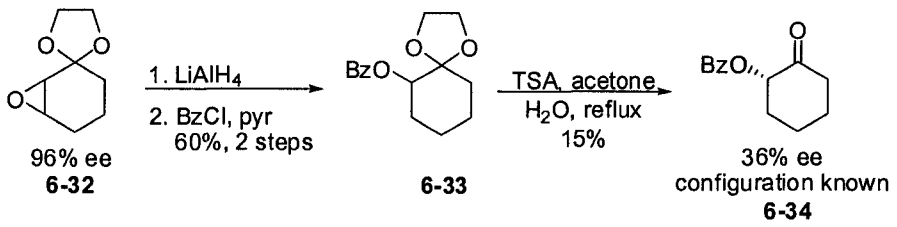
| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 10 |  |  | **2-8** [Boc] | 0 | 12 | 39 (75)[h,i] | 51[d] |
| 11 |  |  | **2-8** [Boc] | -10 | 12 | 80 (88)[e,h,i,j] | 32[k] |
| 12 |  |  | **2-8** [Boc] | 0 | 8 | 87 (89)[j] | 59[d,228] |

[a] For ketone **3-64**: unless otherwise stated, all reactions were carried out with olefin (1.0 eq.), catalyst (0.25 eq.), Oxone (1.6 eq.), and $K_2CO_3$ (6.7 eq.) in DME/DMM (3:1, v/v) and buffer (0.1 M $K_2CO_3$-AcOH in 4 x $10^{-4}$ M aq. EDTA, pH 9.3) (1.5:1, v/v). For ketone **2-8**: unless otherwise stated, all reactions were carried out with olefin (1.0 eq.), catalyst (0.25 eq.), Oxone (1.6 eq.), and $K_2CO_3$ (3.8 eq.) in DME/DMM/*n*-BuOH (3:1:2, v/v/v) and buffer (0.1 M $K_2CO_3$-AcOH in 4 x $10^{-4}$ M aq. EDTA, pH 8.0) (4:1, v/v). In both cases Oxone and $K_2CO_3$ were added separately and simultaneously over the time and temperature specified. [b] Unless stated otherwise the conversion was determined by GC of the crude reaction mixture. [c] DME was used as solvent. [d] Enantioselectivity was determined by chiral GC (Chiraldex B-DM column). [e] Conversion was determined by $^1$H NMR of the crude reaction mixture. [f] Enantioselectivity was determined by chiral GC (Chiraldex B-DM column) of the methyl ether derivative. [g] Enantioselectivity was determined by chiral HPLC (Chiralpak AD column) of the benzoate derivative. [h] 0.30 eq. catalyst used. [i] 2.9 eq. Oxone and 6.9 eq. $K_2CO_3$ were used. [j] DME/DMM (3:1, v/v) was used as solvent. [k] Enantioselectivity was determined by chiral HPLC (Chiralcel OD column).

Next, the absolute configuration of several of the epoxides was determined. The first epoxide examined was **6-32**. It was first opened with $LiAlH_4$ followed by benzoylation of the alcohol to give **6-33**. The ketone was then unmasked in a low-yielding process which resulted in some epimerization of the product (Scheme 6.5). Nevertheless, enough known compound **6-34** was obtained to determine its configuration by comparing its optical rotation with the reported value as well as by comparing the order of elution of the enantiomers by chiral HPLC.[229]

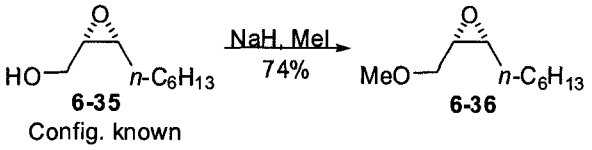
[228] (a) Gayet, A.; Bertilsson, S.; Andersson, P. G. *Org. Lett.* **2002**, *4*, 3777-3779. (b) Gayet, A.; Andersson, P. G. *Tetrahedron Lett.* **2005**, *46*, 4805-4807.

[229] Zhu, Y.; Shu, L.; Tu, Y.; Shi, Y. *J. Org. Chem.* **2001**, *66*, 1818-1826.




**Scheme 6.5**

Next, the absolute configuration of **6-36** was determined by simply methylating known compound **6-35** (Scheme 6.6).[225] Comparison of the optical rotation and the order of elution of enantiomers on chiral GC of **6-36** derived in this manner showed that it has the opposite configuration of **6-35** derived from direct epoxidation of **6-7** with **3-64**.

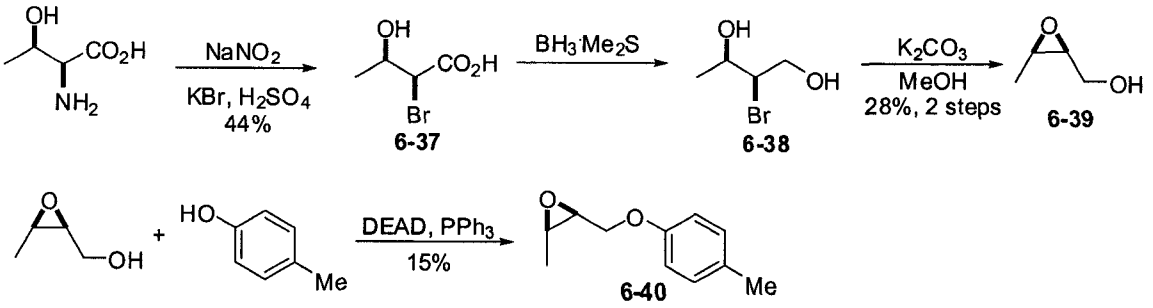



**Scheme 6.6**

The absolute configuration of **6-40** was determined beginning with diazotization of L-threonine in the presence of potassium bromide to give **6-37**.[230] The acid was then reduced to the diol which was then treated with methanolic $K_2CO_3$ to give **6-39**.[230] Mitsunobu reaction of this alcohol with *p*-cresol gave the desired epoxide in enantiopure

[230] Kang, J.; Park, M.; Shin, H. T.; Kim, J. K. *Bull. Korean Chem. Soc.* **1985**, 376-377.

form in low yield (Scheme 6.7).[231] The optical rotation and GC properties of this compound were then compared with **6-40** derived from epoxidation of **6-16** and the configurations were found to be opposite.




**Scheme 6.7**

The results of the epoxidations and the absolute configurations indicate that there are two mechanisms of stereodifferentiation at work for these olefins. The first is differentiation by hydrophobicity of the olefin substituents as discussed above (Figure 6.3). The second mechanism differentiates substituents that contain allylic oxygen functionality from those that do not (Figure 6.4). For olefins which rely primarily on hydrophobic properties for enantioselectivity, ketone **3-64** gave the best results. For substrates containing allylic oxygen functionality, ketone **2-8** was the most effective.

For entries 1-5 (Table 6.6) hydrophobicity of the olefin substituents is the dominant mechanism of sterodifferentiation. Entry 2 is an interesting case because both mechanisms are operating in competition with each other. For this substrate the free

[231] Manhas, M. S.; Hoffman, W. H.; Lal, B.; Bose, A. K. *J. Chem. Soc., Perkin Trans. 1* **1975**, 461-463.

hydroxyl group is just too polar and overrides the competing mechanism to give the observed epoxide.

Based purely on hydrophobic considerations, homoallylic alcohol **6-8** (Table 6.6, entry 3) would be expected to give lower ee than **6-7** (entry 2) since its alkyl substituent is one carbon shorter, and the alcohol substituent is one carbon longer. However it gives higher ee (82% vs 79% ee). This result indicates that the apparent attraction between oxygen-containing functionality and the oxazolidinone of the ketone is significantly weakened, if it is present at all, when the oxygen-containing functionality is not in the allylic position.

The high enantioselectivity observed for olefinic acids **6-11** (91% ee) and **6-9** (86% ee) is due only to the extreme difference in hydrophobicity of the two olefin substituents. The carboxylic acids are presumably deprotonated under the basic reaction conditions to give the corresponding carboxylates which are charged polar groups.

Entries 6-10 (Table 6.6) derive their enantioselectivity primarily from the apparent attraction of allylic oxygen functionality to the oxazolidinone of the ketone. Entry 6 is another case where both mechanisms of stereodifferentiation are operating in competition with each other. However, in this case the methyl ether substituent is not polar enough to override the attraction (at least with ketone **2-8**) and so the (2R, 3S) enantiomer predominates. With ketone **3-66** hydrophobic properties again dominate, but only slightly (Table 6.3).

For aromatic allylic ethers **6-15** and **6-16** (Table 6.6, entries 7, 8), both mechanisms of stereodifferentiation are again operating, but this time they are working in concert. For these cases application of the optimized conditions found for **6-12** resulted in lower ee because they disfavor the beneficial hydrophobic interactions that are present.

Allylic acetal **6-21** was a very effective substrate despite the competing hydrophobic interaction. This result along with the previous observations of high ee with spirocyclic ketals **6-1**, **6-4**, and **6-5** indicates that two allylic oxygens on the same side of the olefin create an even stronger attraction than one. Allylic ketal **6-24** was an ineffective substrate with this system. This could possibly be because the olefin is too hindered or because it cannot adopt a suitable conformation due to $A_{1,3}$ strain.

Finally, **6-9** and **6-28** were synthesized and epoxidized to see whether the high ee for their oxygen-containing counterparts is due the presence of oxygen or is more of a steric phenomenon (Table 6.6, entries 11, 12). Indeed, oxygen appears to be critical for stereodifferentiation based on the comparatively low ee's observed for the all-carbon analogs.

The origin of enantioselectivity for substrates which rely on differences in hydrophobicity of the olefin substituents is fairly straight-forward and was discussed above (Figure 6.3). However, the origin of the apparent attraction for allylic oxygen functionality to the oxazolidinone of the ketone is unclear, and there are several possible rationales that mirror those proposed for *cis*-olefins conjugated with $\pi$ systems. One possibility is that there is an attraction between the electron lone pairs on the oxygen-

containing functionality and a partial or transient positive charge on the oxazolidinone (Figure 6.5) which would favor spiro **G** (Figure 6.6). Another possibility is that a repulsion exists between the electron lone pairs of the oxygen functionality of the olefin and the fused ketal of the catalyst (Figure 6.5). Such a repulsion would disfavor spiro transition state **H** (Figure 6.6).

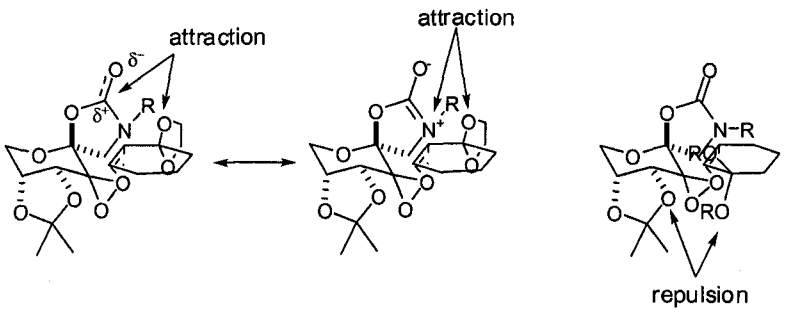



**Figure 6.5**

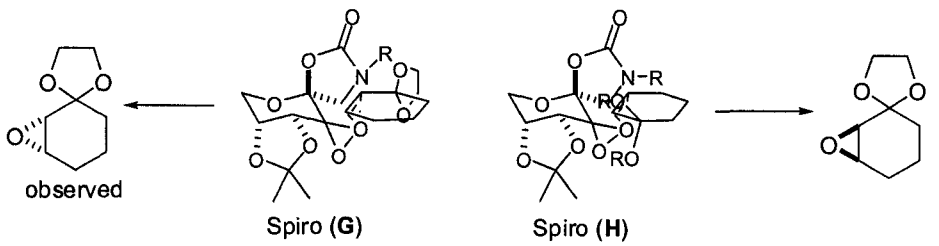



**Figure 6.6**

Another possibility is that the allylic oxygen functionality causes an asynchronous transition state due to spiroconjugation.[232] The theory of spiroconjugation according to

[232] For leading references see: (a) Simmons, H. E.; Fukunaga, T. *J. Am. Chem. Soc.* **1967**, *89*, 5208-5215. (b) Hoffmann, R.; Imamura, A.; Zeiss, G. D. *J. Am. Chem. Soc.* **1967**, *89*, 5215-5220.

Simmons states that "When two π systems are held in perpendicular planes by a common atom of tetrahedral geometry (*e.g.*, the spiro configuration), the overlap between p orbitals on atoms bound directly to the insulating atom is considerable, and consequently exchange interactions may become significant...Spiroconjugation is also expected to be important in molecules other than hydrocarbons whenever four orbitals of p character are on atoms separated by an insulating tetrahedral atom such that approximate spiro geometry is observed."[232a] Spiro ketals **6-1**, **6-4**, and **6-5** fit this description perfectly as do olefins **6-21**, **6-24** and to a lesser extent **6-12** and **6-15** and **6-16** (Figure 6.7). So if there is overlap between the olefin orbitals and the p orbitals on the allylic oxygens through spiroconjugation, these substrates may be behaving as conjugated systems and thus have asynchronous transition states and be subject to the steric interactions proposed by Singleton as discussed in Chapter 2.[233] Substrates with two allylic oxygens would have more overlap and consequently a more asynchronous transition state than substrates with only one possibly leading to the higher enantioselectivity observed with these substrates (Table 6.6, entry 6 vs 9).

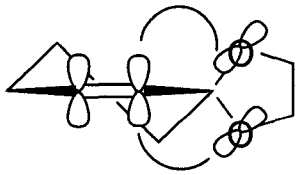


**Figure 6.7**

[233] Singleton, D. A.; Wang, Z. *J. Am. Chem. Soc.* **2005**, *127*, 6679-6685.

## 6.C. CONCLUSION

The scope of the ketone-catalyzed asymmetric epoxidation reaction has been expanded to include several types of unconjugated *cis*-olefins. With this system it is possible to use substituent polarity as an effective method of stereodifferentiation between two prochiral faces of an olefin. Allylic oxygen functionality also provides a mechanism for stereodifferentiation, although further experimentation is needed to define this mechanism clearly. This study opens up a whole new avenue of potential for this system that is yet unexplored and will be valuable for further studies and designing new ketone catalysts in the future.

## 6.D. EXPERIMENTAL

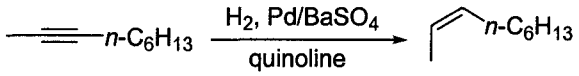
**General Methods.** All commercially available reagents were used without further purification. All glassware used for epoxidation was carefully washed with soap and water to be free of any trace metals which catalyze the decomposition of Oxone. Column chromatography was performed with silica gel (200-400 mesh) which was buffered with 1% $NEt_3$ (v/v). Melting points are uncorrected.

**Representative Asymmetric Epoxidation Procedure (Table 6.6, entry 4).** To a solution of olefin (**6-11**) (0.085 g, 0.5 mmol) and ketone **3-64** (0.047 g, 0.125 mmol) in DME (7.5 mL) were added buffer (0.1 M $K_2CO_3$-AcOH in 4 x $10^{-4}$ M aqueous EDTA, pH = 9.3) (5.0 mL) and $Bu_4NHSO_4$ (0.0075 g, 0.02 mmol) with stirring. After the mixture was cooled to -10 °C (bath temperature) via NaCl-ice bath, solutions of Oxone (0.20 M in 4 x $10^{-4}$ M aqueous EDTA, 4 mL) (0.49 g, 0.80 mmol) and $K_2CO_3$ (0.84 M in 4 x $10^{-4}$ M aqueous EDTA, 4 mL) (0.46 g, 3.36 mmol) were added dropwise separately and simultaneously over a period of 8 h via syringe pump. The reaction was then quenched with the addition $Et_2O$ and extracted with $Et_2O$. The combined organic layers were washed with water, brine, dried ($Na_2SO_4$), filtered, concentrated, and purified by flash chromatography [$Et_2O$ was used as eluent] to give the lactone as a colorless oil (0.070 g, 74% yield, 91% ee).

**Asymmetric Epoxidation Procedure (Table 6.6, entry 9).** To a solution of olefin (**6-21**) (0.085 g, 0.5 mmol) and ketone **2-8** (0.052 g, 0.150 mmol) in DME/DMM/*n*-BuOH (3:1:2) (10 mL) were added buffer (0.1 M $K_2CO_3$-AcOH in 4 x $10^{-4}$ M aqueous EDTA, pH = 8.0) (2.5 mL) and $Bu_4NHSO_4$ (0.0075 g, 0.02 mmol) with stirring. After the mixture was cooled to -10 °C (bath temperature) via NaCl-ice bath, solutions of Oxone (0.20 M in 4 x $10^{-4}$ M aqueous EDTA, 4 mL) (0.49 g, 0.80 mmol) and $K_2CO_3$ (0.48 M in 4 x $10^{-4}$ M aqueous EDTA, 4 mL) (0.26 g, 1.92 mmol) were added dropwise separately

and simultaneously over a period of 12 h via syringe pump. The reaction was then quenched with the addition hexanes and extracted with hexanes. The combined organic layers were washed with water, brine, dried ($Na_2SO_4$), filtered, concentrated, and purified by flash chromatography [95:5 hexanes:$Et_2O$ was used as eluent] to give the epoxide as a colorless oil (0.071 g, 76% yield, 91% ee).

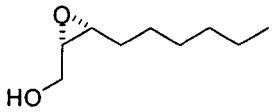
**(Table 6.6, entry 1)**




***cis*-2-Nonene (6-3) (CPB-3141).** To a solution of 2-nonyne (0.50 g, 4.0 mmol) in 1-hexene (103 mL) was added quinoline (4.7 mL, 40 mmol). The mixture was then degassed with Ar three times and then $Pd/BaSO_4$ was added. The Ar was then replaced with $H_2$ and the mixture was allowed to stir under $H_2$ atmosphere (balloon) while the reaction was closely followed by GC. After the starting material disappeared, the mixture was filtered through a pad of silica gel and the filtrate was concentrated. The residue was purified by column (hexanes) to yield 0.33 g (65%) of the title compound as a colorless oil: IR (NaCl): 3014, 1458 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 5.48-5.34 (m, 2H), 2.02 (q, $J$ = 6.8 Hz, 2H), 1.60 (d, $J$ = 6.0 Hz, 3H), 1.40-1.20 (m, 8H), 0.88 (t, $J$ = 6.8 Hz, 3H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 131.1, 123.8, 32.0, 29.8, 29.2, 27.1, 22.9, 14.3, 13.0.

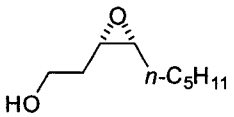
**Epoxide (CPB-3207).** Colorless oil; 65% ee $[\alpha]_D^{25}$ = -1.67 (*c* 0.36, $CHCl_3$); IR (NaCl): 1467, 1391 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 3.04 (qd, *J* = 5.6, 4.4 Hz, 1H), 2.92-2.87 (m, 1H), 1.60-1.24 (m, 10H), 1.27 (d, *J* = 5.6 Hz, 3H), 0.89 (t, *J* = 6.8 Hz, 3H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 57.4, 52.9, 32.0, 29.4, 27.7, 26.6, 22.8, 14.3, 13.4.

**(Table 6.6, entry 2)**




**Epoxide (CPB-3146).** White solid; 79% ee $[\alpha]_D^{25}$ = -2.58 (*c* 0.97, $CHCl_3$); mp: 29-31 °C; IR (NaCl): 3298, 1468, 1033 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 3.86 (ddd, *J* = 11.6, 7.2, 4.0 Hz, 1H), 3.68 (ddd, *J* = 11.6, 6.8, 4.4 Hz, 1H), 3.16 (dt, *J* = 7.2, 4.0 Hz, 1H), 3.06-3.01 (m, 1H), 1.87 (OH, dd, *J* = 7.2, 4.8 Hz, 1H), 1.62-1.24 (m, 10H), 0.89 (t, *J* = 6.8 Hz, 3H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 61.2, 57.6, 57.1, 31.9, 29.3, 28.2, 26.8, 22.8, 14.3. Anal. Calcd for $C_9H_{18}O_2$: C, 68.31; H, 11.47. Found: C, 68.06; H, 11.31.

**(Table 6.6, entry 3)**




**Epoxide (CPB-3217).** Colorless oil; 82% $[\alpha]_D^{25}$ = -19.5 (*c* 0.43, $CHCl_3$); IR (NaCl): 3428, 1467, 1054 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 3.94-3.76 (m, 2H), 3.13-3.07 (m,

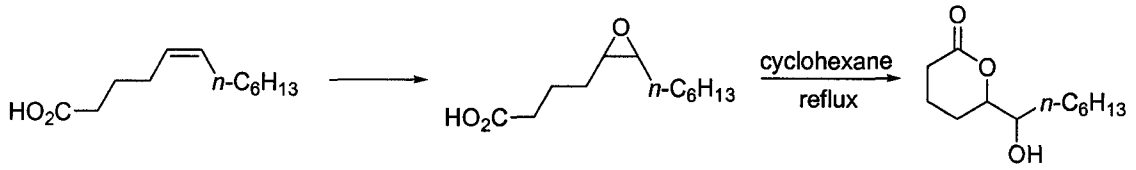
1H), 2.98-2.93 (m, 1H), 1.93-1.65 (m, 3H), 1.58-1.28 (m, 8H), 0.90 (t, $J$ = 7.2 Hz, 3H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 61.0, 57.0, 55.3, 31.9, 30.7, 28.1, 26.3, 22.8, 14.2. Anal. Calcd for $C_9H_{18}O_2$: C, 68.31; H, 11.47. Found: C, 68.13; H, 11.61.

**(Table 6.6, entry 4)**


***cis*-Dec-4-enoic acid (6-11) (CPB-2232).** The title compound was prepared from *cis*-dec-4-en-1-ol according to a literature procedure.[211] A mixture of *cis*-dec-4-en-1-ol (5.00 g, 32.0 mmol), PDC (42.1 g, 112 mmol), and DMF (90 mL) was stirred at rt overnight. The brown mixture was then poured in to 700 mL $H_2O$ and was extracted with $Et_2O$. The combined organic extracts were then filtered through a plug of silica gel and concentrated to give a pink oil. This was then purified by flash column chromatography (7:1 hexanes:$Et_2O$ to 100% $Et_2O$) to yield 2.23 g (45%) of the title compound as a colorless oil: IR (NaCl): 1712, 1413 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) δ 5.49-5.40 (m, 1H), 5.38-5.30 (m, 1H), 2.44-2.32 (m, 4H), 2.05 (q, $J$ = 6.4 Hz, 2H), 1.40-1.23 (m, 6H), 0.90 (t, $J$ = 6.8 Hz, 3H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 179.7, 132.2, 127.1, 34.3, 31.7, 29.5, 27.4, 22.8, 22.7, 14.3.

**5-(1-Hydroxyhexyl)-dihydro-furan-2-one (CPB-3309).** Colorless oil: 91% ee $[\alpha]_D^{25}$ = -20.4 (*c* 0.69, $CHCl_3$); IR (NaCl): 3433, 1769, 1190 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 4.42 (td, *J* = 7.2, 4.8 Hz, 1H), 3.60-3.52 (m, 1H), 2.66-2.47 (m, 2H), 2.30-2.19 (m, 2H), 2.17-2.06 (m, 1H), 1.58-1.22 (m, 8H), 0.88 (t, *J* = 6.8 Hz, 3H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 177.6, 83.2, 73.7, 33.1, 31.8, 28.9, 25.3, 24.2, 22.7, 14.2. Anal. Calcd for $C_{10}H_{18}O_3$: C, 64.49; H, 9.74. Found: C, 64.30; H, 9.60.

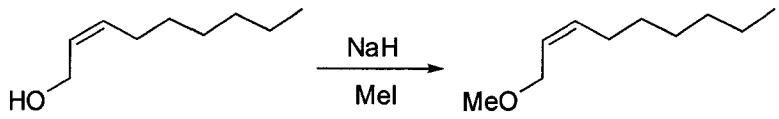
**(Table 6.6, entry 5)**




**6-(1-Hydroxy-heptyl)-tetrahydro-pyran-2-one (CPB-3314).** After epoxidation according to the general procedure, the reaction mixture was acidified to ~ pH 2 by addition of 10% aq. HCl. The mixture was then extracted with EtOAc, dried ($Na_2SO_4$), filtered and concentrated. The crude oil was then dissolved in cyclohexane (18 mL/mmol epoxide) and was gently refluxed overnight.[224] The solvent was then removed and the residue was purified by column ($Et_2O$) to yield the product as a white solid: mp 53-55 °C; 86% ee $[\alpha]_D^{25}$ = -6.88 (*c* 0.96, $CHCl_3$); IR (NaCl): 3420, 1743 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 4.19 (ddd, *J* = 11.6, 5.2, 3.2 Hz, 1H), 3.61-3.53 (m, 1H), 2.67-2.57 (m, 1H), 2.51-2.41 (m, 1H), 2.21-2.17 (m, 1H), 2.02-1.66 (m, 4H), 1.59-1.20 (m, 10H), 0.89 (t, *J* =

6.8 Hz, 3H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 171.6, 83.5, 73.6, 32.9, 31.9, 29.9, 29.4, 25.6, 24.4, 22.8, 18.6, 14.3. HRMS Calcd for $C_{12}H_{22}O_3$ (M+1): 215.1647 . Found: 215.1641.

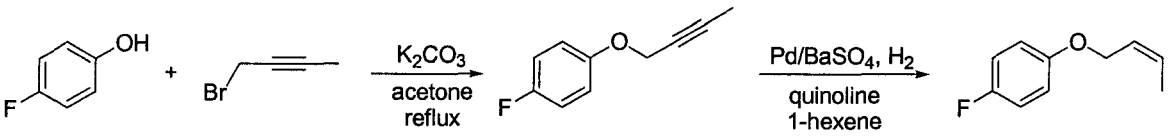
**(Table 6.6, entry 6)**




***cis*-1-Methoxy-2-nonene (6-12) (CPB-1817).** NaH (60% in mineral oil, 0.31 g, 7.73 mmol) was added to a flask and the oil was removed with pet. ether. THF (70 mL) was then added and the mixture was dropped to 0 °C. *cis*-2-Nonen-1-ol (**6-7**) (1.0 g, 7.0 mmol) was added and the mixture was stirred for 30 min. MeI (2.0 g, 14.1 mmol) was then added and the ice bath was removed. Them mixture was stirred at rt overnight and was then quenched by addition of $H_2O$. The mixture was extracted with $Et_2O$, washed with $H_2O$, brine, dried ($Na_2SO_4$), filtered and concentrated. The residue was purified by column (100% pet. ether to 97:3 pet. ether/$Et_2O$) to yield 0.74 g (67%) of the title compound as a colorless oil: IR (NaCl): 1465, 1113 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 5.64-5.49 (m, 2H), 3.98 (d, $J$ = 6.4 Hz, 2H), 3.34 (s, 3H), 2.07 (q, $J$ = 7.2 Hz, 2H), 1.39-1.23 (m, 8H), 0.89 (t, $J$ = 7.0 Hz, 3H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 134.1, 126.0, 68.3, 58.1, 31.9, 29.7, 29.1, 27.8, 22.8, 14.3.

**Epoxide (CPB-2436).** Colorless oil; 61% ee $[\alpha]_D^{25}$ = -3.5 (*c* 0.68, $CHCl_3$); IR (NaCl): 1460, 1112 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 3.65 (dd, *J* = 11.1, 3.9 Hz, 1H), 3.46-3.39 (m, 1H), 3.43 (s, 3H), 3.17-3.11 (m, 1H), 3.02-2.96 (m, 1H), 1.62-1.24 (m, 10H, 0.91 (t, *J* = 6.9 Hz, 3H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 70.9, 59.3, 56.3, 55.3, 31.9, 29.3, 28.3, 26.8, 22.8, 14.3. Anal. Calcd for $C_{10}H_{20}O_2$: C, 69.72; H, 11.70. Found: C, 69.47; H, 11.49.

**(Table 6.6, entry 7)**

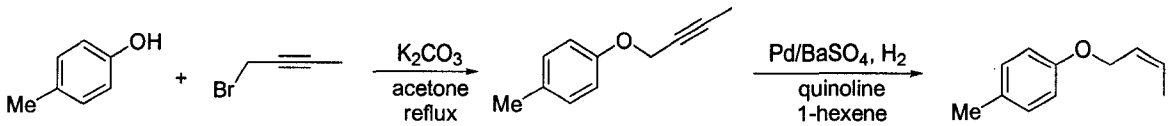



***p*-Fluorophenoxy-2-butyne (6-13) (CPB-2022).** The title compound was prepared according to a literature procedure.[212] To a solution of *p*-fluorophenol (2.24 g, 20 mmol) and 1-bromo-2-butyne (2.66 g, 20 mmol) in acetone (40 mL) was added $K_2CO_3$ (3.32 g, 24 mmol). The mixture was stirred at reflux for 18 h and then cooled to rt. The solvent was removed under vacuum and hexane was added to the residue. The organic phase was washed with water, brine, dried ($Na_2SO_4$) and concentrated. The residue was purified by column (hexanes) to yield 2.60 g (79%) of the title compound as a colorless oil: IR (NaCl): 2229, 1505, 1207, 1010 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 7.03-6.88 (m, 4H), 4.62 (q, *J* = 3.2 Hz, 2H), 1.87 (t, *J* = 3.2 Hz, 3H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 159.4, 156.2, 154.1, 116.23, 116.15, 115.8, 84.1, 74.1, 57.2, 3.9.

***cis-p*-Fluorophenoxy-2-butene (6-15) (CPB-2025).** A solution of *p*-fluorophenoxy-2-butyne (**6-13**) (CPB-2022) (2.60 g, 15.8 mmol) in 1-hexene/EtOAc (1:1, v/v, 200 mL) under Ar was added 5% Pd on $BaSO_4$ (1.67 g) and quinoline (20.4 g, 158 mmol). The mixture was dropped to 0 °C and the Ar was replaced with $H_2$. The reaction was followed closely by GC and was filtered through a pad of silica gel when the starting material had disappeared. The solvent was then evaporated and the residue purified by flash column chromatography (hexane) to yield 1.78 g (68%) of a colorless oil: IR (NaCl): 1505, 1210 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.02-6.94 (m, 2H), 6.89-6.83 (m, 2H), 5.82-5.65 (m, 2H), 4.58-4.54 (m, 2H), 1.76-1.72 (m, 3H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 158.6, 156.3, 155.0, 129.0, 125.7, 116.1, 115.9, 115.86, 115.80, 64.5, 13.6.

**Epoxide (CPB-2317a).** Colorless oil; 86% ee $[\alpha]_D^{25}$ = -3.0 (*c* 0.44, $CHCl_3$); IR (NaCl): 1506, 1209 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.03-6.96 (m, 2H), 6.93-6.86 (m, 2H), 4.13 (dd, *J* = 10.4, 4.4 Hz, 1H), 4.04 (dd, *J* = 10.4, 6.0 Hz, 1H), 3.32-3.30 (m, 1H), 3.25-3.19 (m, 1H), 1.37 (d, *J* = 5.6 Hz, 3H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 158.9, 156.5, 154.9, 116.2, 116.0, 115.9, 67.1, 54.6, 52.3, 13.7. Anal. Calcd for $C_{10}H_{11}O_2F$: C, 65.92; H, 6.09. Found: C, 65.90; H, 5.97.

**(Table 6.6, entry 8)**



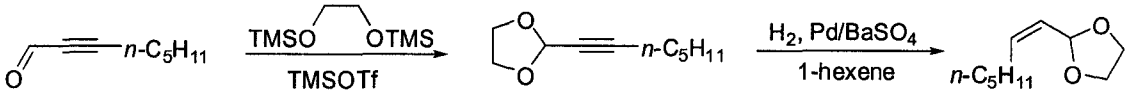

***p*-Tolyloxy-2-butyne (6-14) (CPB-1942).** The title compound was prepared from *p*-cresol and 1-bromo-2-butyne according to the same procedure used for *p*-fluorophenoxy-2-butyne (**6-13**) (CPB-2022) above. Yield (48%) Colorless oil; IR (NaCl): 2228, 1511, 1218, 1015 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.13-7.08 (m, 2H), 6.90-6.85 (m, 2H), 4.63 (q, $J$ = 2.4 Hz, 2H), 2.30 (s, 3H), 1.87 (t, $J$ = 2.4 Hz, 3H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 155.9, 130.7, 130.1, 114.9, 83.7, 74.4, 56.7, 20.7, 3.9.

***cis-p*-Tolyloxy-2-butene (6-15) (CPB-2034).** The title compound was prepared from *p*-tolyloxy-2-butyne (CPB-1942) (**6-14**) according to the same procedure used for *cis-p*-fluorophenoxy-2-butene (**6-15**) (CPB-2025). Yield (94%) Colorless oil; IR (NaCl): 1613, 1510, 1241 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.12-7.06 (m, 2H), 6,86-6.81 (m, 2H), 5.80-5.67 (m, 2H), 4.60-4.56 (m, 2H), 2.30 (s, 3H), 1.76-1.72 (m, 3H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 156.8, 130.14, 130.08, 128.68, 126.1, 114.7, 64.0, 20.7, 13.6.

**Epoxide (CPB-2317b).** Colorless oil; 85% ee $[\alpha]_D^{25}$ = -4.2 (*c* 0.48, $CHCl_3$); IR (NaCl): 1512, 1243, 1037, 817 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.12-7.09 (m, 2H), 6.87-6.83 (m, 2H), 4.11(dd, $J$ = 10.8, 4.8 Hz, 1H), 4.07 (dd, $J$ = 10.8, 6.0 Hz, 1H), 3.35-3.30 (m, 1H), 3.21 (qd, $J$ = 5.6, 4.4 Hz, 1H), 2.30 (s, 3H), 1.37 (d, $J$ = 5.6 Hz, 3H); $^{13}C$ NMR (101

MHz, $CDCl_3$) δ 156.7, 130.7, 130.2, 114.7, 66.4, 54.7, 52.4, 20.7, 13.7. Anal. Calcd for $C_{11}H_{14}O_2$: C, 74.13; H, 7.92. Found: C, 73.86; H, 7.70.

**(Table 6.6, entry 9)**

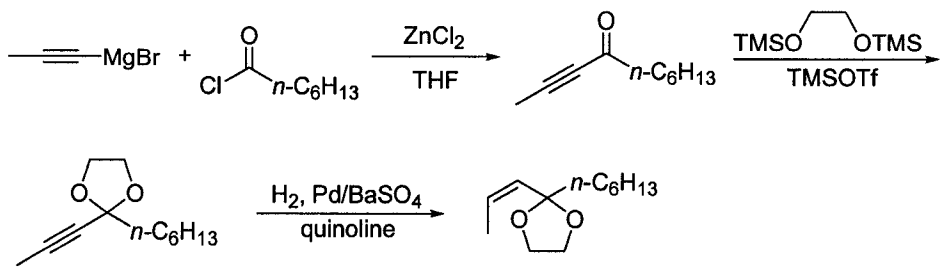



**2-Hept-1-ynyl-[1,3]dioxolane (6-20) (CPB-2430).** The title compound was prepared based on a literature method.[215] To a solution of trimethylsilyltrifluoromethanesulfonate (0.080 g, 0.35 mmol) in 3.4 mL $CH_2Cl_2$ at -78 °C was added 1,2-bistrimethylsilylethane (7.25 g, 35.1 mmol) and 2-octynal (4.36 g, 35.1 mmol). After about 5 min. the reaction was complete as judged by TLC. The reaction mixture was poured into sat. aq. $NaHCO_3$ solution and the phases were separated. The aq. phase was extracted with $CH_2Cl_2$ and the combined organic phases were washed with brine, dried ($Na_2SO_4$), and concentrated. The residue was distilled (bp 100 °C @ 4 mmHg) to give 3.94 g (67%) of the title compound as a colorless oil: IR (NaCl): 2254, 1083 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 5.63 (t, $J$ = 1.6 Hz, 1H), 2.23 (td, $J$ = 7.2, 1.6 Hz, 2H), 1.56-1.49 (m, 2H), 1.38-1.27 (m, 4H), 0.90 (t, $J$ = 6.8 Hz, 3H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 93.4, 87.2, 76.0, 64.7, 31.2, 28.1, 22.4, 18.8, 14.2.

***cis*-2-Hept-1-enyl-[1,3]dioxolane (6-21) (CPB-2431).** The olefin substrate was prepared from 2-hept-1-ynyl-[1,3]dioxolane (**6-20**) (CPB-2430) according to the same method used to prepare *cis*-2-nonene (**6-3**) (CPB-3141) with 1-hexene/EtOAc (1:1, v/v) used as solvent. The product was purified by column (9:1 hexanes:$Et_2O$). Yield (98%) Colorless oil; IR (NaCl): 1115 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 5.78 (dtd, $J$ = 11.2, 6.8, 0.8 Hz, 1H), 5.55 (dd, $J$ = 7.2, 0.8 Hz, 1H), 5.46-5.41 (m, 1H), 4.07-3.85 (m, 4H), 2.18 (qd, $J$ = 7.2, 1.2 Hz, 2H), 1.46-1.24 (m, 6H), 0.89 (t, $J$ = 7.2 Hz, 3H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 138.1, 125.9, 99.4, 65.2, 31.6, 29.4, 27.0, 22.7, 14.2.

**Epoxide (CPB-2437).** Colorless oil; 91% ee $[\alpha]_D^{25}$ = -17.2 (*c* 0.54, $CHCl_3$); IR (NaCl): 1468, 1120, 1104 $cm^{-1}$; $^1H$ NMR (400 MHz, $CD_3OD$) δ 4.67 (d, $J$ = 6.8 Hz, 1H), 4.06-3.97 (m, 2H), 3.94-3.83 (m, 2H), 3.02-2.97 (m, 1H), 2.87 (dd, $J$ = 6.8, 4.4 Hz, 1H), 1.67-1.45 (m, 4H), 1.42-1.28 (m, 4H), 0.92 (t, $J$ = 7.2 Hz, 3H); $^{13}C$ NMR (101 MHz, $CD_3OD$) δ 104.0, 66.5, 66.3, 57.2, 32.9, 29.3, 27.4, 23.7, 14.5. HRMS Calcd for $C_{10}H_{18}O_3$ (M+1): 187.1334. Found: 187.1340.

**(Table 6.6, entry 10)**



**Dec-2-yn-4-one (6-22) (CPB-2206).** The title compound was prepared according to a literature procedure.[216] To a slurry of $ZnCl_2$ (6.88 g, 50.5 mmol) in THF (100 mL) was added propynyl magnesium bromide (0.5 M in THF, 101 mL, 50.5 mmol) at 0 °C with stirring. After stirring at 0 °C for 15 min, heptanoyl chloride (5.0 g, 33.6 mmol) was added. The ice bath was then removed and the mixture was stirred at rt for 1 h. The mixture was dropped to -10 °C and sat. aq. $NH_4Cl$ was added. The layers were separated and the aq. layer was extracted with $Et_2O$. The combined organic layers were then washed with sat. aq. $NH_4Cl$, $H_2O$, brine, dried ($Na_2SO_4$), and concentrated. The residue was then distilled to yield 3.80 g (74%) of the title compound as a colorless oil (bp 89-91 °C @ 4 mmHg): IR (NaCl): 2221, 1675, 1169 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 2.52 (t, $J$ = 7.2 Hz, 2H), 2.02 (s, 3H), 1.69-1.62 (m, 2H), 1.35-1.24 (m, 6H), 0.89 (t, $J$ = 7.2 Hz, 3H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 188.8, 90.0, 80.5, 45.7, 31.7, 28.9, 24.2, 22.7, 14.2, 4.3.

**2-Hexyl-2-prop-1-ynyl-[1,3]dioxolane (6-23) (CPB-2213).** The title compound was prepared based on a literature method.[217] To a solution of trimethylsilyl-trifluoromethanesulfonate (0.037g, 0.16 mmol) in 2.7 mL $CH_2Cl_2$ at -78 °C was added 1,2-bistrimethylsilylethane (2.83 g, 13.7 mmol) and dec-2-yn-4-one (**6-22**) (1.00 g, 6.57 mmol). The mixture was then stirred at -30 °C for 12 h and -20 °C for 3h. The reaction mixture was then poured into sat. aq. $NaHCO_3$ and the phases were separated. The aq.

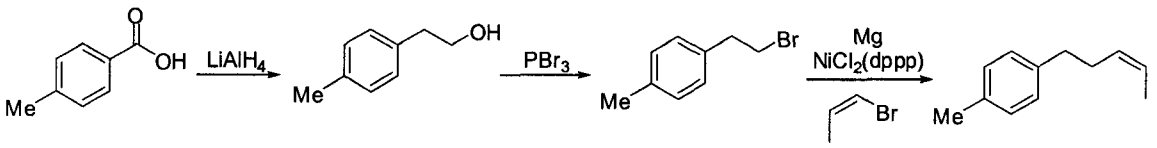
phase was extracted with $CH_2Cl_2$ and the combined organic phases were washed with brine, dried ($Na_2SO_4$), and concentrated. The residue was purified by column (9:1 hexanes:$Et_2O$) to yield 1.67 g (quant) of a colorless oil that contained a silane impurity. This mixture was carried on to the next step without further purification: IR (NaCl): 2237, 1468, 1034 $cm^{-1}$; $^1H$ NMR (400 MHz, $CD_3OD$) δ 4.02-3.89 (m, 4H), 1.82 (s, 3H), 1.79-1.74 (m, 2H), 1.52-1.45 (m, 2H), 1.36-1.26 (m, 8H), 0.91 (t, $J$ = 7.2 Hz, 3H); $^{13}C$ NMR (101 MHz, $CD_3OD$) δ 104.7, 81.2, 78.5, 65.5, 40.7, 33.1, 30.4, 25.1, 23.8, 14.6, 3.0.

***cis*-2-Hexyl-2-prop-1-enyl-[1,3]dioxolane (6-24) (CPB-2219).** The olefin substrate was prepared from 2-hexyl-2-prop-1-ynyl-[1,3]dioxolane (**6-23**) (CPB-2213) according to the same method used to prepare *cis*-2-hept-1-enyl-[1,3]dioxolane (**6-21**) (CPB-2123). Yield (88%) Colorless oil; IR (NaCl): 1658, 1467, 1192, 1039 $cm^{-1}$; $^1H$ NMR (400 MHz, $CD_3OD$) δ 5.41 (dq, $J$ = 12.0, 7.2 Hz, 1H), 5.12 (dq, $J$ = 12.0, 2.0 Hz, 1H), 3.76-3.65 (m, 4H), 1.63 (dd, $J$ = 7.2, 2.0 Hz, 3H), 1.56-1.52 (m, 2H), 1.26-1.08 (m, 8H), 0.74 (t, $J$ = 7.2 Hz, 3H); $^{13}C$ NMR (101 MHz, $CD_3OD$) δ 132.5, 128.8, 111.4, 65.3, 39.9, 33.2, 30.8, 24.7, 23.8, 14.6, 13.9.

**Epoxide (CPB-3931).** Colorless oil; 51% ee $[\alpha]_D^{25}$ = +2.61 (*c* 1.4, $CHCl_3$); IR (NaCl): 1467, 1216, 1041, 950 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 4.10-4.03 (m, 2H), 3.99-3.88 (m, 2H), 3.01 (qd, $J$ = 5.6, 4.4 Hz, 1H), 2.96 (d, $J$ = 4.4 Hz, 1H), 1.79-1.61 (m, 2H), 1.47-1.24 (m, 8H), 1.46 (d, $J$ = 5.6 Hz, 3H), 0.89 (t, $J$ = 7.2 Hz, 3H); $^{13}C$ NMR (101 MHz,

$CDCl_3$) δ 108.2, 66.5, 65.0, 60.3, 52.4, 36.5, 32.0, 29.7, 22.8, 14.3, 13.0. Anal. Calcd for $C_{12}H_{23}O_3$: C, 67.26; H, 10.35. Found: C, 67.40; H, 10.43.

**(Table 6.6, entry 11)**




**2-(*p*-Tolyl)-ethanol (6-17) (CPB-2413).** The title compound was prepared according to a literature procedure.[213] A solution of *p*-tolylacetic acid (10.0 g, 66.6 mmol) in 54 mL $Et_2O$ was added slowly to a mixture of $LiAlH_4$ (2.66 g, 70 mmol) in 210 ml $Et_2O$ with stirring at 0 °C. The mixture was allowed to warm to rt and was stirred overnight. It was then quenched at 0 °C by addition of 0.24 ml $H_2O$, then 0.24 mL 15% aq. NaOH, and then an additional 7.2 mL $H_2O$. The mixture was then filtered through Celite and the filtrate was washed with sat. aq. $NaHCO_3$, brine, dried ($Na_2SO_4$), and concentrated to yield 4.66 g (51%) of a colorless oil. The product was taken on without further purification: IR (NaCl): 3340, 1515, 1047 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.16-7.12 (m, 4H), 3.85 (t, $J$ = 6.6 Hz, 2H), 2.85 (t, $J$ = 6.6 Hz, 2H), 2.34 (s, 3H), 1.44 (brs, 1H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 136.3, 135.5, 129.5, 129.1, 64.0, 39.0, 21.2.

**1-Bromo-2-(*p*-tolyl)-ethane (6-18) (CPB-2415).** The title compound was prepared according to a literature procedure.[213] 2-(*p*-Tolyl)-ethanol (**6-17**) (CPB-2413) (4.66 g,

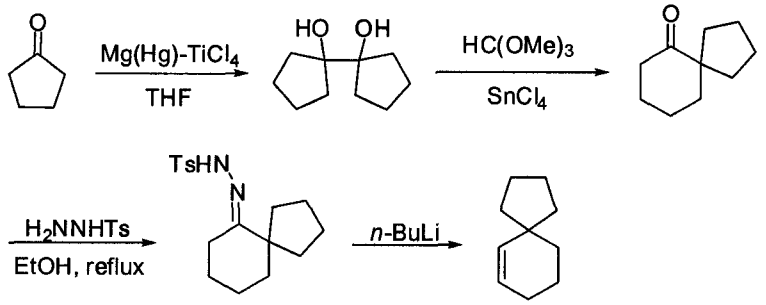
34.2 mmol) was placed in a flask with reflux condenser and was cooled to 0° C. $PBr_3$ (3.40 g, 12.6 mmol) was then added dropwise with stirring. After the addition was complete the mixture was stirred at 0 °C for 3 h and then it was heated to 100 °C for 14 h. The mixture was then cooled to rt and 1.2 mL $H_2O$ was added. The organic layer was separated and the aqueous layer was extracted with $CH_2Cl_2$. The combined organic fractions were washed with sat. aq. $NaHCO_3$, dried ($Na_2SO_4$), and the solvent was distilled off. The residue was then distilled to give 4.98 g (73%) of a colorless oil (bp 80 °C at 3 mmHg): IR (NaCl): 1515, 1208, 807, 634 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.16-7.10 (m, 4H), 3.56 (t, $J$ = 7.6 Hz, 2H), 3.14 (t, $J$ = 7.6 Hz, 2H), 2.34 (s, 3H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 136.7, 136.0, 129.5, 128.7, 39.2, 33.4, 21.3.

***cis*-5-(*p*-Tolyl)-2-pentene (6-19) (CPB-2419).** The olefin was prepared by an adapted literature procedure.[214] To a mixture of $Cl_2Ni$(dppp) (0.016 g, 0.03 mmol) and *cis*-1-bromopropene (1.09 g, 9.0 mmol) at -78 °C was added 2-(*p*-tolyl)-ethyl magnesium bromide [prepared by mixing Mg powder (0.072 g, 3.0 mmol) and 1-bromo-2-(*p*-tolyl)-ethane (**6-18**) (CPB-2415) (0.60 g, 3.0 mmol) in 3 mL $Et_2O$ at rt for 1 h with stirring]. The mixture was then stirred at 0 °C for 4 h and was gradually allowed to warm to rt and was stirred overnight at rt. The reaction was then quenched by addition of 10% aq. HCl, extracted with hexanes, washed with sat. aq. $NaHCO_3$, $H_2O$, brine, dried ($Na_2SO_4$), and concentrated. The residue was purified by column (hexanes) to give 0.80 g (83%) of a colorless oil: IR (NaCl): 1515 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.16-7.07 (m, 4H),

5.52-5.40 (m, 2H), 2.66-2.61 (m, 2H), 2.39-2.34 (m, 2H), 2.33 (s, 3H), 1.58 (d, $J$ = 5.2 Hz, 3H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 139.3, 135.4, 130.0, 129.2, 128.5, 124.6, 35.6, 29.1, 21.2, 13.0.

**Epoxide (CPB-2445).** Colorless oil; 32% ee $[\alpha]_D^{25}$ = -2.8 (*c* 0.54, $CHCl_3$); IR (NaCl): 1515 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.14-7.10 (m, 4H), 3.05 (qd, $J$ = 5.6, 4.4 Hz, 1H), 2.98-2.94 (m, 1H), 2.82 (ddd, $J$ = 13.6, 9.2, 6.0 Hz, 1H), 2.72 (ddd, $J$ = 13.6, 9.2, 7.2 Hz, 1H), 2.34 (s, 3H), 1.88-1.74 (m, 2H), 1.20 (d, $J$ = 5.6 Hz, 3H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 138.5, 135.7, 129.3, 128.5, 56.8, 53.1, 2.5, 29.8, 21.2, 13.4. Anal. Calcd for $C_{12}H_{16}O_3$: C, 81.77; H, 9.15. Found: C, 81.59; H, 9.25.

**(Table 6.6, entry 12)**




**Bicyclopentyl-1,1'-diol (6-25) (CPB-2147).** The title compound was prepared by a method based on literature procedure.[218] To a solution of $HgCl_2$ (2.2 g, 8.0 mmol) in 150 mL THF was added 50 mesh Mg powder (7.2 g, 300 mmol). The mixture was stirred at rt for 15 min and then the cloudy gray supernatant liquid was removed via cannula. The

remaining amalgam was then washed with THF (3 x 50 mL) removing the supernatant each time. 250 mL THF was then added to the amalgam and the mixture was dropped to -10 °C. $TiCl_4$ (28.5 g, 150 mmol) was then added slowly via syringe (the mixture turned green with a cloudy yellow vapor above it). Cyclopentanone (8.4 g, 100 mmol) in 150 mL THF was then added and the purple mixture was stirred at 0 °C for 1 h. The reaction was then quenched at 0 °C with 50 mL sat. aq. $K_2CO_3$ and stirred at the same temperature for 15 min. The mixture was then filtered through Celite to remove the solids. The filter was washed with $Et_2O$ and the liquid was concentrated to about ¼ its original volume and diluted with $Et_2O$. It was then washed with $H_2O$, brine, dried ($Na_2SO_4$), and filtered through Celite a second time, again washing with $Et_2O$. The filtrate was then concentrated to yield a yellow syrup. This was purified by column (1:1 hexanes:$Et_2O$ to 100% $Et_2O$) to yield 6.4 g (75%) of a white crystalline solid: mp 108-109 °C; IR (NaCl): 3407, 997 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 1.88-1.59 (m, 18H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 87.4, 36.6, 25.1.

**Spiro[4.5]decan-6-one (6-26) (CPB-2116).** The title compound was prepared according to a literature procedure.[219] To a solution of bicyclopentyl-1,1'-diol (**6-25**) (CPB-2147) (4.0 g, 23.5 mmol) in 235 mL $CH_2Cl_2$ was added $HC(OMe)_3$ (2.49 g, 23.5 mmol), and $SnCl_4$ (1.22 g, 4.70 mmol) at -20 °C. The mixture was stirred at rt for 10 min. It was then quenched by addition of sat. aq. $NaHCO_3$. The layers were separated, and the aq. layer was extracted with $CH_2Cl_2$. The combined organic extracts were then washed with

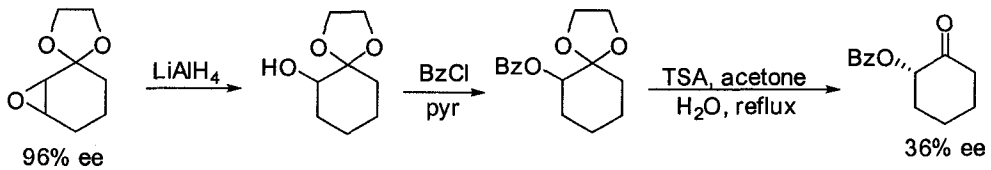
$H_2O$, brine, dried ($Na_2SO_4$), and concentrated. The residue was purified by column (95:5 hexanes:$Et_2O$) to yield 3.2 g (90%) of the title compound as a colorless oil: IR (NaCl): 1706, 1449, 1127 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 2.41 (t, $J$ = 6.4 Hz, 2H), 2.10-2.03 (m, 2H), 1.88-1.78 (m, 2H), 1.74-1.68 (m, 2H), 1.64-1.54 (m, 4H), 1.44-1.35 (m, 2H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 215.0, 57.1, 40.2, 39.7, 35.7, 27.6, 25.5, 23.1.

**Spiro[4.5]dec-6-one *p*-toluenesulfonylhydrazone (6-27) (CPB-2150).** The title compound was prepared according to a literature procedure.[220] Spiro[4.5]decan-6-one (**6-26**) (CPB-2116) (3.71 g, 24.4 mmol) and *p*-toluenesulfonylhydrazine (4.54 g, 24.4 mmol) were refluxed in EtOH (15 mL) for 2 h. The mixture was then cooled to rt and then placed in a freezer overnight. The white crystals that formed were collected by vacuum filtration and recrystallized from absolute EtOH to yield 5.55 g (71%) of the title compound: IR (NaCl): 3202, 1329, 1161 $cm^{-1}$; $^1H$ NMR (400 MHz, $CD_3OD$) δ 7.81 (d, $J$ = 8.4 Hz, 2H), 7.35 (d, $J$ = 8.4 Hz, 2H), 2.42 (s, 3H), 2.30 (t, $J$ = 6.4 Hz, 2H), 2.02-1.94 (m, 2H), 1.62-1.22 (m, 12H); $^{13}C$ NMR (101 MHz, $CD_3OD$) δ 166.0, 143.7, 136.2, 129.0, 128.1, 51.3, 39.9, 36.0, 26.1, 24.6, 23.9, 22.8, 20.3.

**Spiro[4.5]dec-6-ene (6-28) (CPB-2204).** The title compound was prepared based on a literature method.[221] To a solution of spiro[4.5]dec-6-one *p*-toluenesulfonylhydrazone (**6-27**) (CPB-2150) (4.87 g, 15.2 mmol) in THF (150 mL) at -78 °C was added *n*-BuLi (1.6 M in hexanes, 38.0 mL, 60.8 mmol) slowly with stirring. The mixture was allowed

to warm to 0 °C and was stirred for 2 h and then was stirred at rt for 2h. It was then quenched by addition of $H_2O$ and the mixture was extracted with hexanes. The combined organic extracts were washed with $H_2O$, brine, dried ($Na_2SO_4$) and concentrated. The residue was then purified by column (hexanes) to yield 1.12 g (54%) of the title compound as a colorless oil: IR (NaCl): 1445 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 5.58 (dt, $J$ = 10.0, 3.6 Hz, 1H), 5.48 (dt, $J$ = 10.0, 2.0 Hz, 1H), 1.99-1.93 (m, 2H), 1.67-1.57 (m, 6H), 1.50-1.42 (m, 6H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 137.5, 124.9, 43.4, 40.4, 35.2, 25.5, 24.5, 20.8.

**Epoxide (CPB-2215).** Colorless oil; 60% ee $[\alpha]_D^{25}$ = +9.7 (*c* 0.68, $CHCl_3$); IR (NaCl): 2938, 1440 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 3.20 (td, $J$ = 4.0, 0.8 Hz, 1H), 2.82 (d, $J$ = 4.0 Hz, 1H), 1.94-1.08 (m, 14H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 60.4, 54.1, 42.1, 37.8, 36.6, 33.0, 25.2, 24.8, 24.2, 18.0. Anal. Calcd for $C_{10}H_{16}O$: C, 78.90; H, 10.59. Found: C, 78.73; H, 10.41.



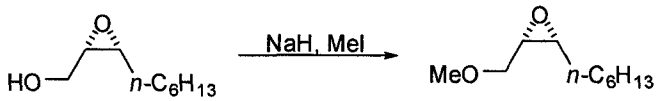

**1,4-Dioxaspiro[4.5]decan-6-ol (CPB-3112a).** To a suspension of $LiAlH_4$ (0.029 g, 0.76 mmol) in 0.8 mL THF at rt under Ar was added 7-oxaspiro[bicyclo[4.1.0]heptane-2,2'-

[1,3]dioxolane] (**6-32**) (0.079 g, 0.51 mmol, 96% ee) in 2.6 mL THF with stirring. After about 4 h TLC indicated the reaction was complete. $H_2O$ (1 mL) was added and the mixture was extracted with $Et_2O$. The combined organic phases were then dried ($Na_2SO_4$) and concentrated to give 0.065 g (80% crude) of the title compound as a colorless oil which was taken on without further characterization.

**1,4-Dioxaspiro[4.5]decan-6-yl benzoate (6-33) (CPB-3112b).** To a solution of 1,4-dioxaspiro[4.5]decan-6-ol (CPB-3112a) from above in 4 mL $CH_2Cl_2$ was added pyridine (0.07 mL, 0.8 mmol) and benzoyl chloride (0.05 mL, 0.4 mmol) with stirring at rt. The mixture was stirred overnight and then the solvent was removed. The residue was then directly chromatographed (3:1 hexanes:$Et_2O$) to give 0.064 g (60% over 2 steps) of the title compound contaminated with a small amount of benzoyl chloride as a colorless oil: IR (NaCl): 1720 1451, 1271 $cm^{-1}$; $^1H$ NMR (400 MHz, acetone-$d_6$) δ 8.08-8.02 (m, 2H), 7.67-7.61 (m, 1H), 7.56-7.50 (m, 2H), 5.07 (dd, $J$ = 7.6, 3.6 Hz, 1H), 4.11-4.03 (m, 1H), 4.01-3.87 (m, 3H), 1.93-1.43 (m, 8H) ; $^{13}C$ NMR (101 MHz, acetone-$d_6$) δ 166.0, 133.9, 131.7, 130.3, 129.5, 108.4, 74.0, 66.1, 65.9, 34.4, 29.8, 23.9, 22.4.

**(S)-2-Benzoyloxycyclohexanone (6-34) (CPB-3124).** 1,4-Dioxaspiro[4.5]decan-6-yl benzoate (**6-33**) (CPB-3112b) (0.32 g, 0.12 mmol) was dissolved in 1 mL acetone and 0.10 mL $H_2O$ was added followed by *p*-toluenesulfonic acid (0.022 g, 0.12 mmol). The mixture was refluxed for 120 h after which time it was dissolved in $Et_2O$ and washed

with sat. aq. $NaHCO_3$, $H_2O$, and dried ($Na_2SO_4$), filtered and concentrated. The residue was purified by column (4:1 hexanes:$Et_2O$) to yield 0.004 g (15%) of the title compound as a white waxy solid: 36% ee $[\alpha]_D^{25}$ = -6.11 (*c* 0.18, $CHCl_3$) [lit. 99% ee $[\alpha]_D^{25}$ = +19.9 (*c* 0.87, $CHCl_3$) for (R) isomer[234]]; IR (NaCl): 1717, 1271 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 8.13-8.08 (m, 2H), 7.61-7.55 (m, 1H), 7.48-7.43 (m, 2H), 5.42 (dd, *J* = 11.6, 6.0 Hz, 1H), 2.62-2.40 (m, 3H), 2.20-1.64 (m, 5H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 204.6, 165.8, 133.4, 130.1, 129.9, 128.6, 41.0, 33.4, 27.4, 24.0.



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***cis*-(2S, 3R)-1-Methoxy-2,3-epoxynonane (6-36) (CPB-3207).** To a suspension of NaH (0.22 mmol) in 1mL THF was added solution of (2S, 3R)-*cis*-1-hydroxy-2,3-epoxynonane (**6-35**) (CPB-2321) (0.032 g, 0.20 mmol) in 1 mL THF with stirring at 0 °C under Ar. After stirring for 20 min. MeI (0.06 g, 0.42 mmol) was added and the mixture was stirred overnight while warming to rt. $H_2O$ was then added and the mixture was extracted with $Et_2O$. The combined organic phases were dried ($Na_2SO_4$), concentrated, and the residue was purified by column (95:5 hexanes:$Et_2O$) to give 0.025 g (74%) of the title compound as a colorless oil: 74% ee $[\alpha]_D^{25}$ = +2.85 (*c* 1.23, $CHCl_3$).

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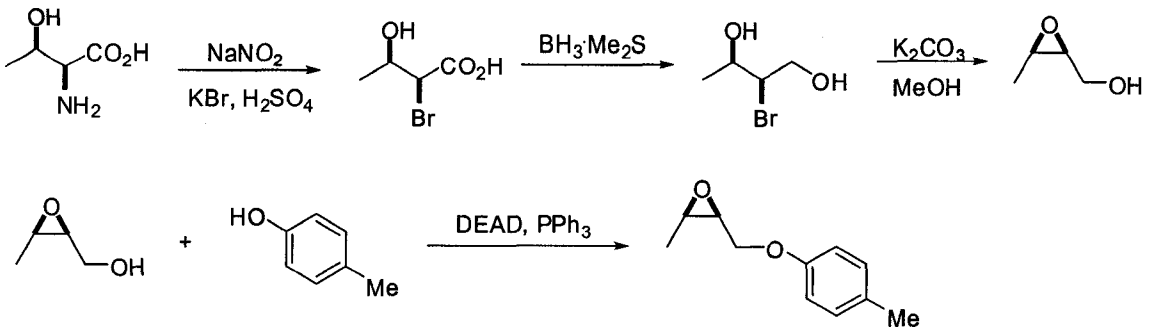
[234] Zhu, Y.; Shu, L.; Tu, Y.; Shi, Y. *J. Org. Chem.* **2001**, *66*, 1818-1826.




**(2S,3R)-2-Bromo-3-hydroxybutanoic acid (6-37) (CPB-3235).** The title compound was prepared according to a literature method:[230] L-threonine (5.95 g, 50 mmol), and KBr (20.9 g, 175 mmol) were dissolved in 105 mL conc. $H_2SO_4$ and the mixture was cooled to 0 °C. $NaNO_2$ (5.58 g, 80 mmol) was then added in solid portions over 1 h. the mixture was then stirred at rt for 2 h. The reaction mixture was then extracted with EtOAc and the combined organic phases were washed with $H_2O$, brine, dried ($Na_2SO_4$), and concentrated to give 4.06 g (44% crude) of a volatile yellow oil which was taken on without further purification: IR (NaCl): 3398, 1724 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 4.31 (d, $J$ = 4.2 Hz, 1H), 4.25-4.15 (m, 1H), 1.36 (d, $J$ = 6.0 Hz, 3H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 173.3, 67.5, 20.4.

***cis*-(2S,3R)-Epoxybutanol (6-39) (CPB-3236).** The title compound was prepared by a method based on a literature procedure.[230] To a solution of (2S,3R)-2-bromo-3-hydroxybutanoic acid (**6-37**) (CPB-3235) from above (4.06 g, 22.2 mmol) in 74 mL THF at 0 °C was added $BH_3{\cdot}SMe_2$ (5.55 ml of a 10.0 M soln., 55.5 mmol) with stirring under Ar. The reaction was allowed to warm to rt and was stirred for 24 h. It was then cooled

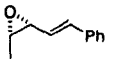
to 0 °C and 5 mL $H_2O$ was slowly added. The layers were then separated and the aq. phase was extracted with $Et_2O$. The combined organic phases were then washed with brine, dried, and concentrated. The residue was used in the next step without further purification or characterization. To a solution of crude diol (**6-38**) in 30 mL MeOH was added $K_2CO_3$ (5.0 g, 37 mmol) at 0 °C. The reaction was stirred for 1 h at 0 °C and overnight at rt. The mixture was then recooled to 0 °C and the precipitated solid was removed by filtration while washing with $Et_2O$. The filtrate was evaporated to about 1/3 its original volume and then 10 mL $H_2O$ was added. The aq. layer was extracted with $Et_2O$ and the combined organic phases were dried ($Na_2SO_4$), filtered, and concentrated. The crude material was passed through a short column with $Et_2O$, but still contained significant impurities. 0.55 g (28%) of impure product was obtained.

***cis*-(2S,3R)-*p*-Tolyloxyepoxybutane (6-40) (CPB-3243):** The title compound was prepared based on a literature procedure.[231] Epoxybutanol (**6-39**) (CPB-3236) (0.044 g, 0.50 mmol), *p*-cresol (0.054 g, 0.50 mmol), triphenylphosphine (0.13 g, 0.50 mmol), and diethylazodicarboxylate (0.087 g, 0.50 mmol) were dissolved in 12.5 mL THF and stirred at rt under Ar for 24 h. The solvent was then removed and the residue was purified by column twice (98:2 hexanes:$Et_2O$) to yield 0.014 g (15%) of the title compound as a colorless oil: $[\alpha]_D^{25} = +2.79$ (*c* 0.65, $CHCl_3$).

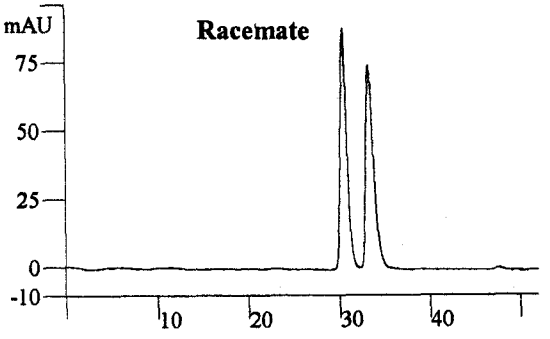
# SUPPLEMENTARY MATERIAL

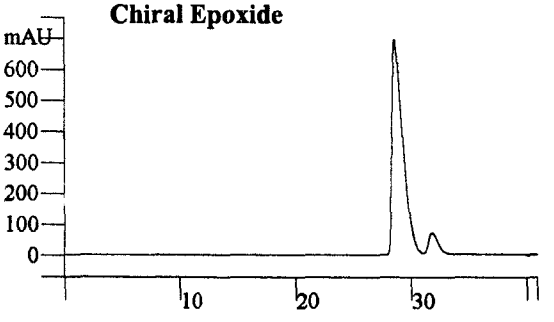
GC and HPLC and NMR Data for Determination of Enantiomeric Excess of Epoxides

**Table 3.3, Entry 1**



**HPLC Cond.:** **Column:** Chiralcel OJ (Column No. OJ00CE-DE008), Chiral Technologies, Inc.
**Eluent:** Hexanes/IPA (97/3); **Flow Rate:** 1.0mL/min; **Detection:** UV 270 nm

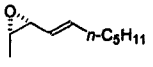


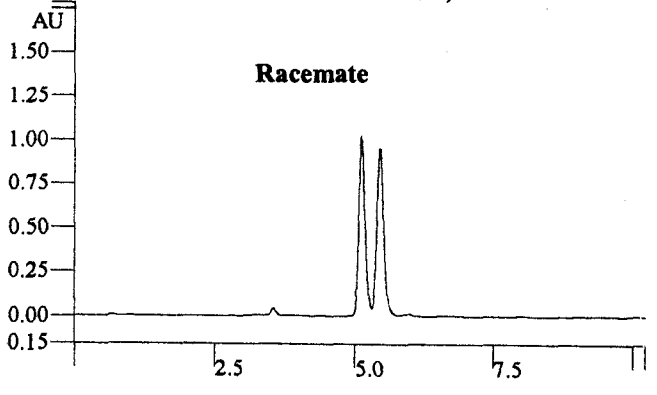

| Peak No | Peak Name | Ret. Time (min) | Result () | Area (counts) |
|---|---|---|---|---|
| 1 | | 30.361 | 50.1537 | 390624 |
| 2 | | 33.228 | 49.8463 | 375975 |
| | **Totals** | | **100.0000** | **766599** |

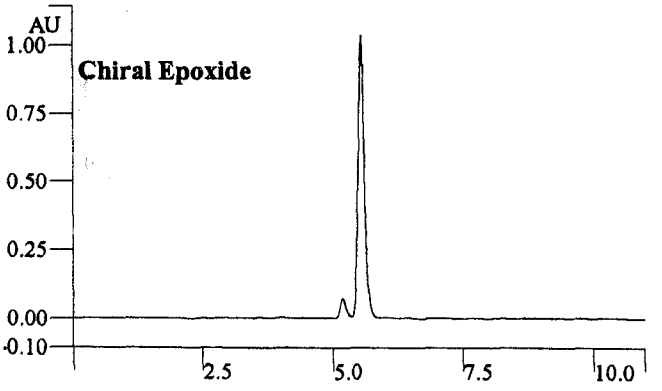
| Peak No | Peak Name | Ret. Time (min) | Result () | Area (counts) |
|---|---|---|---|---|
| 1 | | 28.546 | 92.4609 | 606524 |
| 2 | | 31.737 | 7.5391 | 924825 |
| | **Totals** | | **100.0000** | **531348** |

**Table 3.3, Entry 2**



**HPLC Cond.:** **Column:** Chiralcel OJ (Column No. OJ00CE-DE008), Chiral Technologies, Inc.
**Eluent:** Hexanes; **Flow Rate:** 1.0mL/min; **Detection:** UV 200 nm



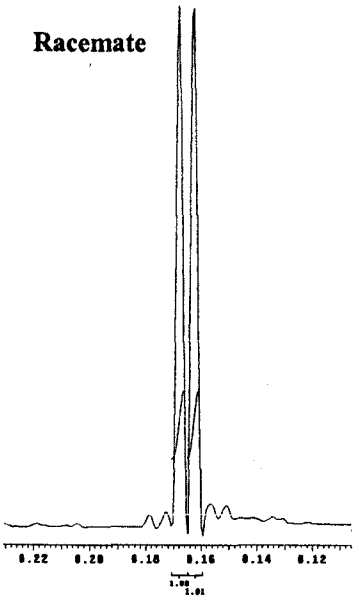

| Peak No | Peak Name | Ret. Time (min) | Result () | Area (counts) |
|---|---|---|---|---|
| 1 | | 5.102 | 49.9759 | 3890139 |
| 2 | | 5.429 | 50.0241 | 3893885 |
| | **Totals** | | **100.0000** | **7784024** |

| Peak No | Peak Name | Ret. Time (min) | Result () | Area (counts) |
|---|---|---|---|---|
| 1 | | 5.179 | 5.4355 | 264758 |
| 2 | | 5.519 | 94.5645 | 4606156 |
| | **Totals** | | **100.0000** | **4870914** |

**Table 3.3, Entry 3**


Enantioselectivity was determined by $^1$HNMR shift analysis with $Eu(hfc)_3$ in $CDCl_3$ (400 MHZ).

**Racemate**




**Chiral Epoxide**

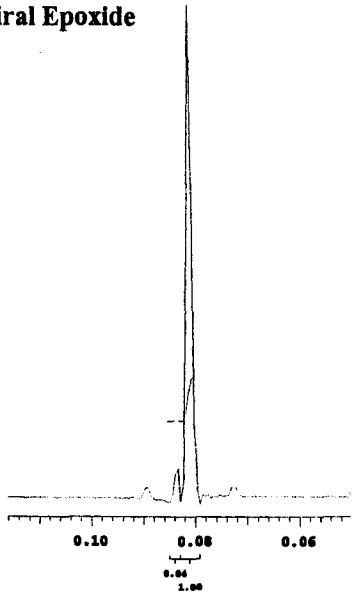
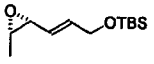
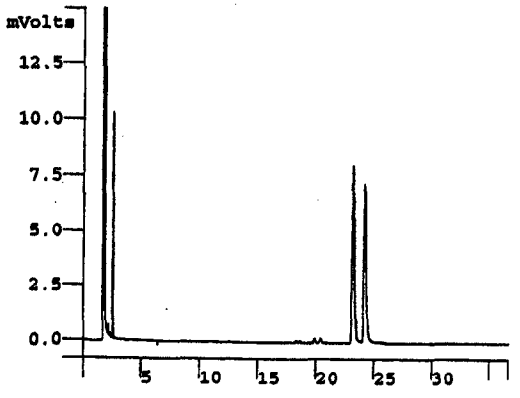



**Table 3.3, Entry 4**



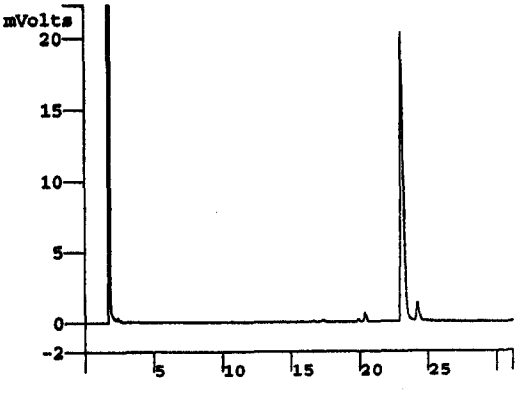

**GC Cond.:** **Column:** Chiraldex B-DM (Cat. No. 77023), Adv. Separation Technologies, Inc.
**Oven:** 110 °C; **Carrier:** Helium, head pressure 20 psi; **Detection:** FID 250 °C

**Racemate**



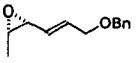

| Peak No | Peak Name | Result 0 | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 49.6889 | 23.171 | 107910 |
| 2 | | 50.3111 | 24.138 | 109261 |
| | Totals | 100.0000 | | 217171 |

**Chiral Epoxide**



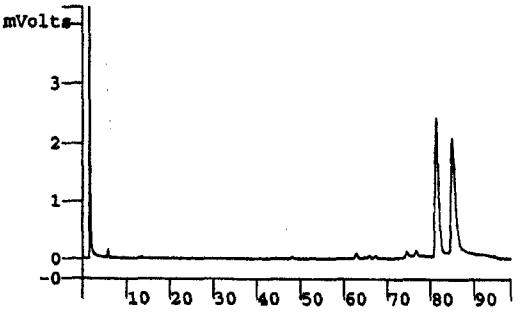

| Peak No | Peak Name | Result 0 | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 94.8818 | 23.051 | 327594 |
| 2 | | 5.1182 | 24.236 | 17672 |
| | Totals | 100.0000 | | 345266 |

**Table 3.3, Entry 5**



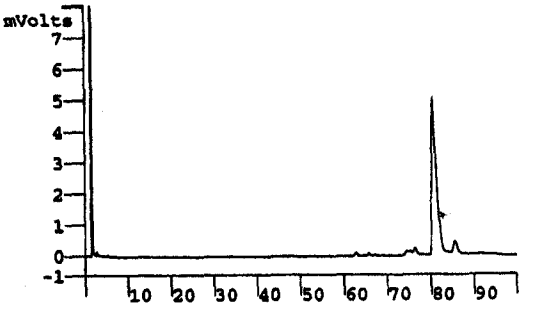
**GC Cond.:** **Column:** Chiraldex B-DM (Cat. No. 77023), Adv. Separation Technologies, Inc.
**Oven:** 120 °C; **Carrier:** Helium, head pressure 25 psi; **Detection:** FID 250 °C

**Racemate**



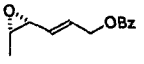

| Peak No | Peak Name | Result () | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 50.1800 | 81.079 | 132818 |
| 2 | | 49.8200 | 84.826 | 131865 |
| | Totals | 100.0000 | | 264683 |

**Chiral Epoxide**



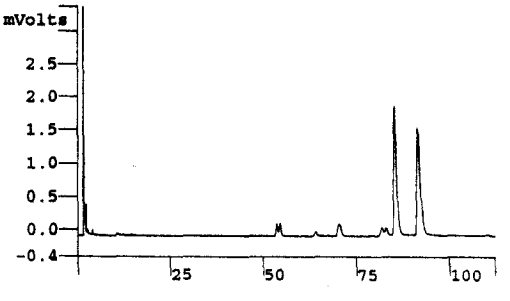

| Peak No | Peak Name | Result () | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 94.7537 | 80.284 | 393284 |
| 2 | | 5.2463 | 85.481 | 21775 |
| | Totals | 100.0000 | | 415059 |

**Table 3.3, Entry 6**



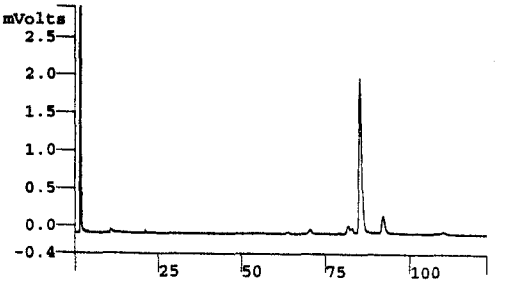
**GC Cond.:** **Column:** Chiraldex B-DM (Cat. No. 77023), Adv. Separation Technologies, Inc.
**Oven:** 130 °C; **Carrier:** Helium, head pressure 25 psi; **Detection:** FID 250 °C

**Racemate**



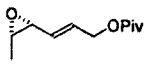

| Peak No | Peak Name | Result () | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 50.1045 | 85.154 | 106503 |
| 2 | | 49.8955 | 91.359 | 106059 |
| | Totals | 100.0000 | | 212562 |

**Chiral Epoxide**




| Peak No | Peak Name | Result () | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 89.8390 | 85.181 | 115302 |
| 2 | | 10.1610 | 92.131 | 13041 |
| | Totals | 100.0000 | | 128343 |

**Table 3.3, Entry 7**

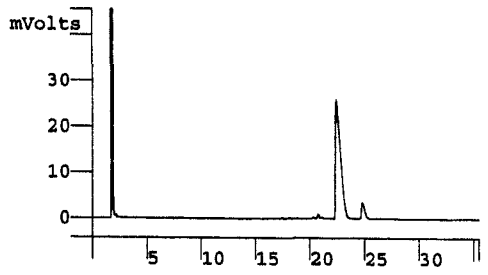



**GC Cond.:** **Column:** Chiraldex B-DM (Cat. No. 77023), Adv. Separation Technologies, Inc.
**Oven:** 110 °C; **Carrier:** Helium, head pressure 20 psi; **Detection:** FID 250 °C

**Racemate**

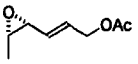

| Peak No | Peak Name | Result () | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 49.9220 | 22.862 | 149704 |
| 2 | | 50.0781 | 24.667 | 150172 |
| | **Totals** | **100.0001** | | **299876** |

**Chiral Epoxide**



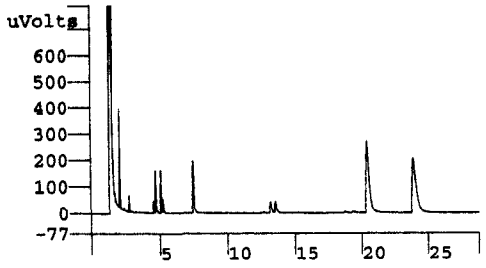

| Peak No | Peak Name | Result () | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 92.1212 | 22.339 | 810355 |
| 2 | | 7.8788 | 24.772 | 69307 |
| | **Totals** | **100.0000** | | **879662** |

**Table 3.3, Entry 8**



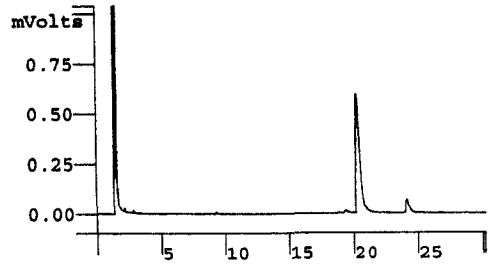

**GC Cond.:** **Column:** Chiraldex B-DM (Cat. No. 77023), Adv. Separation Technologies, Inc.
**Oven:** 90 °C; **Carrier:** Helium, head pressure 25 psi; **Detection:** FID 250 °C

**Racemate**



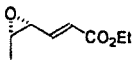

| Peak No | Peak Name | Result () | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 50.2811 | 20.424 | 4445 |
| 2 | | 49.7189 | 23.897 | 4395 |
| | **Totals** | **100.0000** | | **8840** |

**Chiral Epoxide**

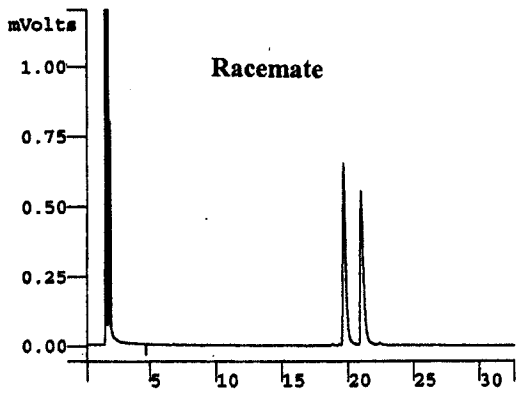



| Peak No | Peak Name | Result () | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 92.0512 | 20.257 | 12608 |
| 2 | | 7.9488 | 24.103 | 1089 |
| | **Totals** | **100.0000** | | **13697** |

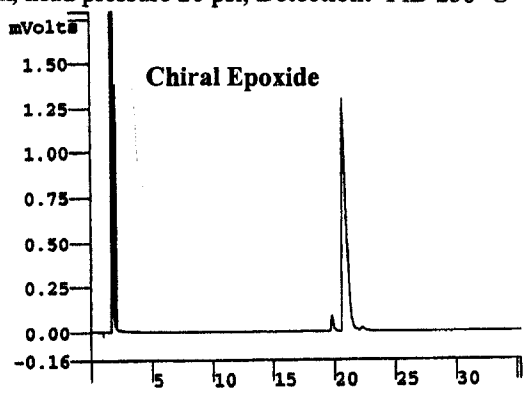
**Table 3.3, Entry 9**



**GC Cond.:** **Column:** Chiraldex B-DM (Cat. No. 77023), Adv. Separation Technologies, Inc.
**Oven:** 90 °C; **Carrier:** Helium, head pressure 20 psi; **Detection:** FID 250 °C




Racemate

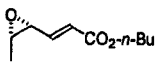



Chiral Epoxide

| Peak No | Peak Name | Result () | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 50.1996 | 19.686 | 9444 |
| 2 | | 49.8004 | 20.991 | 9369 |
| | Totals | 100.0000 | | 18813 |

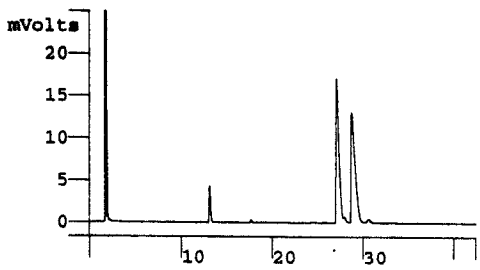
| Peak No | Peak Name | Result () | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 3.1683 | 19.804 | 1006 |
| 2 | | 96.8317 | 20.702 | 30731 |
| | Totals | 100.0000 | | 31737 |

**Table 3.3, Entry 10**

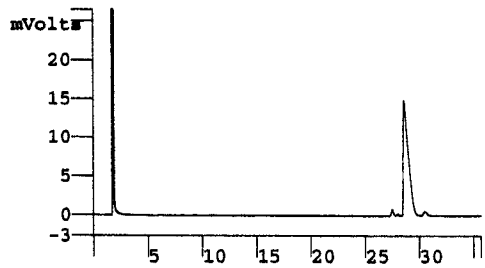


**GC Cond.:** **Column:** Chiraldex B-DM (Cat. No. 77023), Adv. Separation Technologies, Inc.
**Oven:** 110 °C; **Carrier:** Helium, head pressure 20 psi; **Detection:** FID 250 °C

Racemate



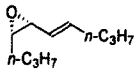

Chiral Epoxide



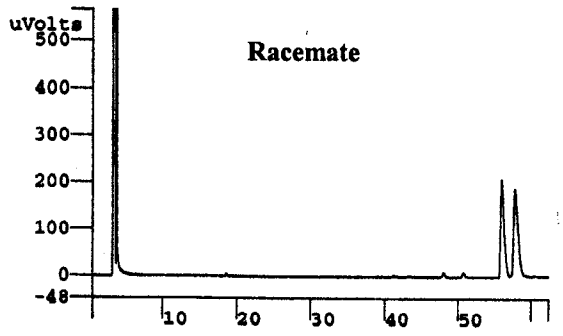

| Peak No | Peak Name | Result () | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 48.9097 | 27.038 | 387630 |
| 2 | | 51.0903 | 28.698 | 404913 |
| | Totals | 100.0000 | | 792543 |

| Peak No | Peak Name | Result () | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 2.1613 | 27.468 | 10719 |
| 2 | | 97.8387 | 28.566 | 485213 |
| | Totals | 100.0000 | | 495932 |

**Table 3.3, Entry 11**

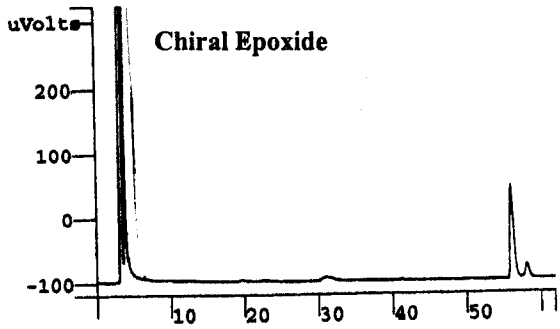


**GC Cond.:** **Column:** Chiraldex B-DM (Cat. No. 77023), Adv. Separation Technologies, Inc.
**Oven:** 75 °C; **Carrier:** Helium, head pressure 10 psi; **Detection:** FID 250 °C




Racemate

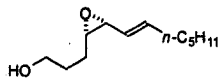
| Peak No | Peak Name | Result 0 | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 49.3961 | 55.952 | 6906 |
| 2 | | 50.6039 | 57.763 | 7075 |
| | Totals | 100.0000 | | 13981 |




Chiral Epoxide

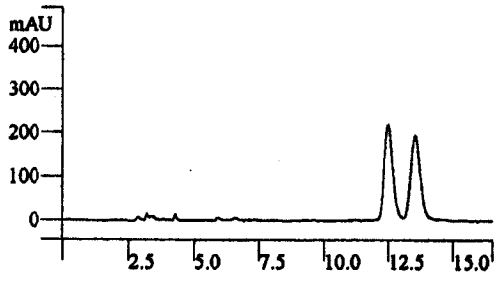
| Peak No | Peak Name | Result 0 | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 88.2370 | 56.016 | 4709 |
| 2 | | 11.7631 | 58.084 | 628 |
| | Totals | 100.0001 | | 5337 |

**Table 3.3, Entry 12**



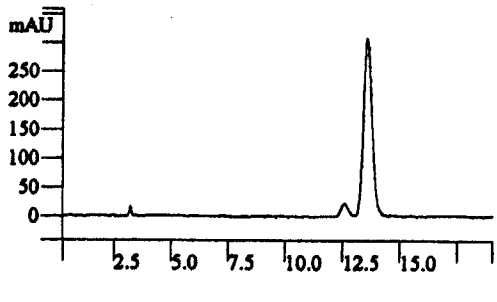
**HPLC Cond.:** **Column:** Chiralcel OJ (Column No. OJ00CE-DE008), Chiral Technologies, Inc.
**Eluent:** Hexanes/IPA (94/6); **Flow Rate:** 1.0mL/min; **Detection:** UV 210 nm

Racemate



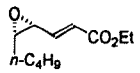

| Peak No | Peak Name | Ret. Time (min) | Result 0 | Area counts |
|---|---|---|---|---|
| 1 | | 12.454 | 49.9697 | 552557 |
| 2 | | 13.516 | 50.0303 | 555654 |
| | Totals | | 100.0000 | 108211 |

Chiral Epoxide



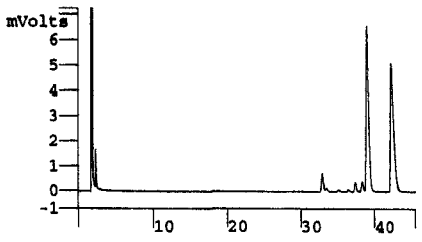

| Peak No | Peak Name | Ret. Time (min) | Result 0 | Area counts |
|---|---|---|---|---|
| 1 | | 12.546 | 5.3147 | 233279 |
| 2 | | 13.501 | 94.6853 | 156026 |
| | Totals | | 100.0000 | 389305 |

**Table 3.3, Entry 13**



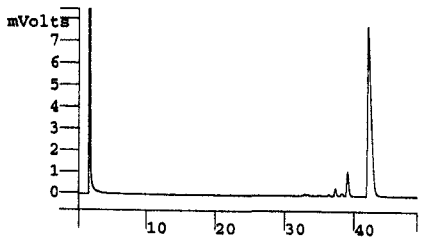

**GC Cond.:** **Column:** Chiraldex B-DM (Cat. No. 77023), Adv. Separation Technologies, Inc.
**Oven:** 110 °C; **Carrier:** Helium, head pressure 20 psi; **Detection:** FID 250 °C

**Racemate**



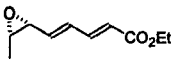

| Peak No | Peak Name | Result 0 | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 49.7124 | 38.897 | 156105 |
| 2 | | 50.2876 | 42.294 | 157911 |
| | **Totals** | **100.0000** | | **314016** |

**Chiral Epoxide**



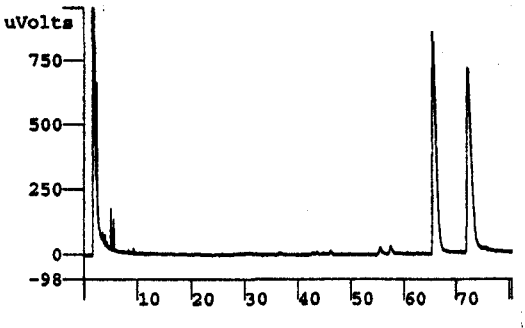

| Peak No | Peak Name | Result 0 | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 7.7408 | 39.033 | 24473 |
| 2 | | 92.2592 | 41.926 | 291684 |
| | **Totals** | **100.0000** | | **316157** |

**Table 3.3, Entry 14**



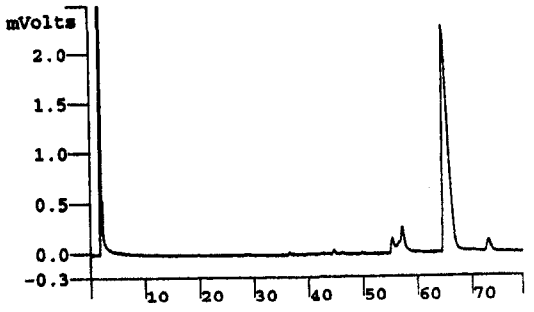

**GC Cond.:** **Column:** Chiraldex B-DM (Cat. No. 77023), Adv. Separation Technologies, Inc.
**Oven:** 110 °C; **Carrier:** Helium, head pressure 20 psi; **Detection:** FID 250 °C

**Racemate**



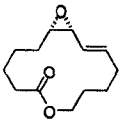

| Peak No | Peak Name | Result 0 | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 50.3119 | 65.729 | 39100 |
| 2 | | 49.6881 | 72.376 | 38616 |
| | **Totals** | **100.0000** | | **77716** |

**Chiral Epoxide**



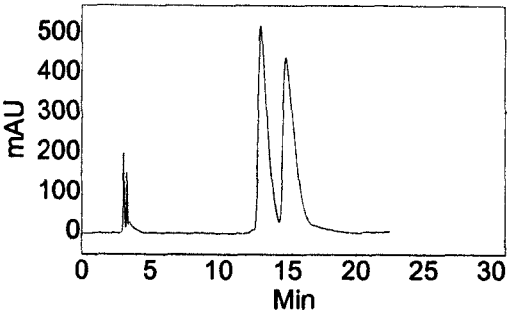

| Peak No | Peak Name | Result 0 | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 96.8301 | 64.827 | 163334 |
| 2 | | 3.1699 | 73.012 | 5347 |
| | **Totals** | **100.0000** | | **168681** |

**Table 3.3, Entry 15**



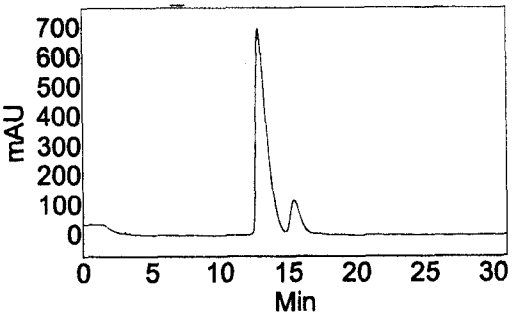
**HPLC Cond.:** **Column:** Chiralcel OJ (Column No. OJ00CE-DE008), Chiral Technologies, Inc.
**Eluent:** Hexanes/IPA (97/3); **Flow Rate:** 1.0mL/min; **Detection:** UV 210 nm

**Racemate**



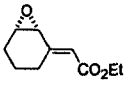

| Index | Time [Min] | Area % [%] |
|---|---|---|
| 1 | 13.01 | 48.878 |
| 2 | 14.85 | 51.122 |
| | | |
| Total | | 100.000 |

**Chiral Epoxide**



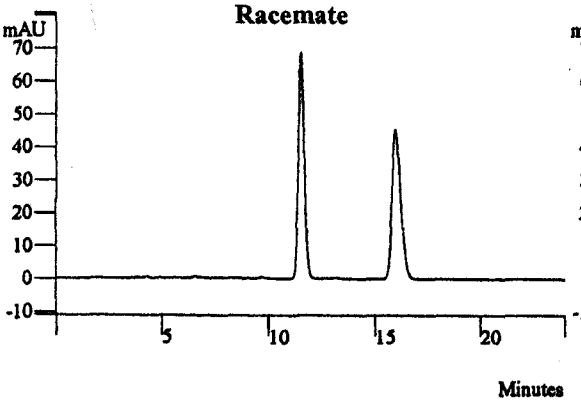

| Index | Time [Min] | Area % [%] |
|---|---|---|
| 1 | 12.84 | 87.590 |
| 2 | 15.43 | 12.410 |
| | | |
| Total | | 100.000 |

**Table 3.3, Entry 16**



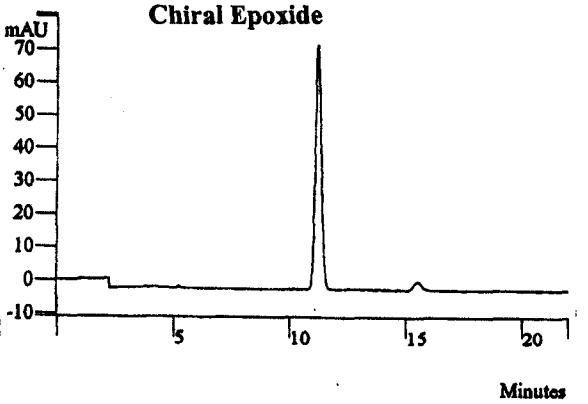

**HPLC Cond.:** **Column:** Chiralcel OD (Column No. OD00CE-DL010), Chiral Technologies, Inc.
**Eluent:** Hexanes/IPA (94/6); **Flow Rate:** 1.0mL/min; **Detection:** UV 254 nm

**Racemate**



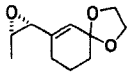

| Peak No | Peak Name | Ret. Time (min) | Result () | Area (counts) |
|---|---|---|---|---|
| 1 | | 11.481 | 50.1167 | 682304 |
| 2 | | 15.936 | 49.8833 | 679126 |
| | Totals | | 100.0000 | 1361430 |

**Chiral Epoxide**



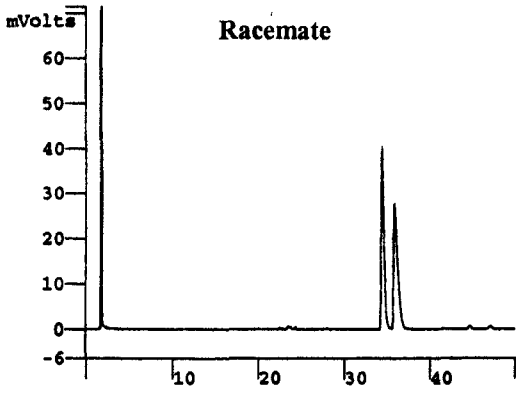

| Peak No | Peak Name | Ret. Time (min) | Result () | Area (counts) |
|---|---|---|---|---|
| 1 | | 11.172 | 95.4187 | 711094 |
| 2 | | 15.471 | 4.5813 | 34141 |
| | Totals | | 100.0000 | 745235 |

**Table 3.3, Entry 17**



**GC Cond.:** **Column:** Chiraldex B-DM (Cat. No. 77023), Adv. Separation Technologies, Inc.
**Oven:** 120 °C; **Carrier:** Helium, head pressure 20 psi; **Detection:** FID 250 °C

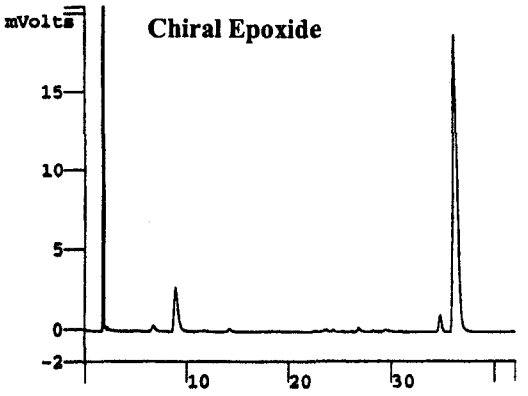
**Racemate**




| Peak No | Peak Name | Result () | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 50.0783 | 34.393 | 890474 |
| 2 | | 49.9217 | 35.831 | 887689 |
| | **Totals** | **100.0000** | | **1778163** |

Minutes

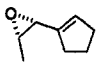
**Chiral Epoxide**




| Peak No | Peak Name | Result () | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 3.3287 | 34.776 | 18557 |
| 2 | | 96.6713 | 35.994 | 538915 |
| | **Totals** | **100.0000** | | **557472** |

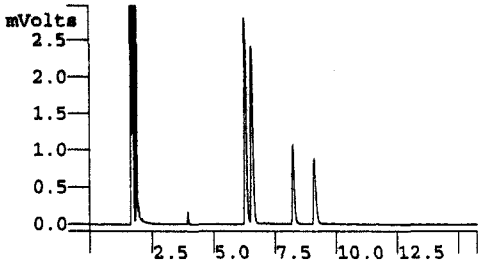
Minutes

**Table 3.3, Entry 18**



**GC Cond.:** **Column:** Chiraldex B-DM (Cat. No. 77023), Adv. Separation Technologies, Inc.
**Oven:** 85 °C; **Carrier:** Helium, head pressure 20 psi; **Detection:** FID 250 °C

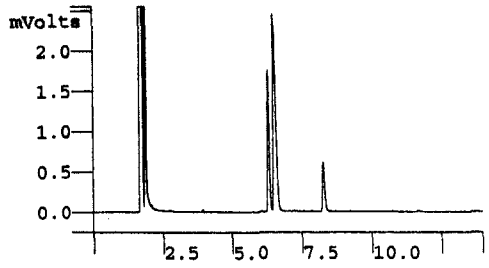
**Racemate**




| Peak No | Peak Name | Result () | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 49.9088 | 8.224 | 6136 |
| 2 | | 50.0912 | 9.086 | 6158 |
| | **Totals** | **100.0000** | | **12294** |

Minutes

**Chiral Epoxide**



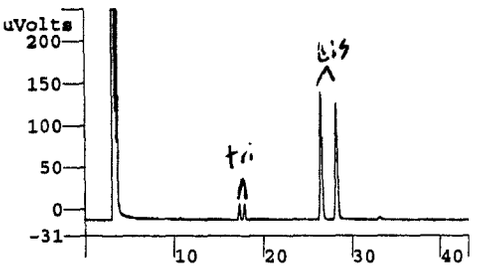

| Peak No | Peak Name | Result () | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 100.0000 | 8.250 | 3385 |
| | **Totals** | **100.0000** | | **3385** |

Minutes

**Table 3.3, Entry 19**

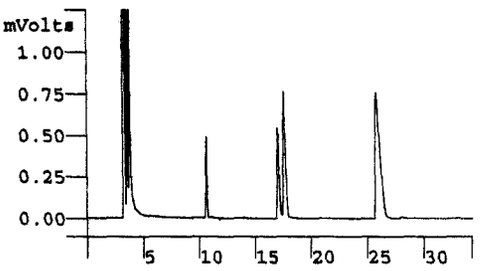
**GC Cond.:** **Column:** Chiraldex B-DM (Cat. No. 77023), Adv. Separation Technologies, Inc.
**Oven:** 90 °C; **Carrier:** Helium, head pressure 10 psi; **Detection:** FID 250 °C

**Racemate**



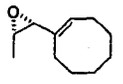

| Peak No | Peak Name | Result () | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 50.0826 | 26.434 | 2456 |
| 2 | | 49.9174 | 28.183 | 2448 |
| | **Totals** | **100.0000** | | **4904** |

**Chiral Epoxide**



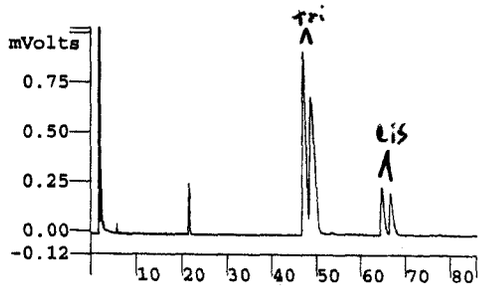

| Peak No | Peak Name | Result () | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 98.9664 | 25.804 | 21994 |
| 2 | | 1.0336 | 28.061 | 230 |
| | **Totals** | **100.0000** | | **22224** |

**Table 3.3, Entry 20**



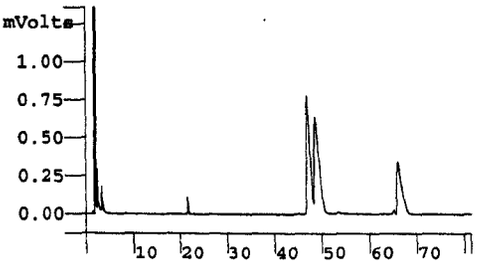
**GC Cond.:** **Column:** Chiraldex B-DM (Cat. No. 77023), Adv. Separation Technologies, Inc.
**Oven:** 85 °C; **Carrier:** Helium, head pressure 20 psi; **Detection:** FID 250 °C

**Racemate**



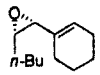

| Peak No | Peak Name | Result () | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 50.0390 | 64.589 | 11093 |
| 2 | | 49.9610 | 66.576 | 11075 |
| | **Totals** | **100.0000** | | **22168** |

**Chiral Epoxide**



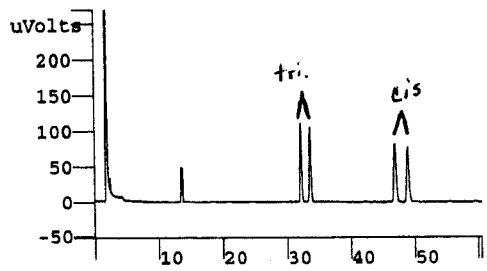

| Peak No | Peak Name | Result () | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 2.4436 | 64.931 | 609 |
| 2 | | 97.5564 | 65.834 | 24306 |
| | **Totals** | **100.0000** | | **24915** |

**Table 3.3, Entry 21**



**GC Cond.:** **Column:** Chiraldex B-DM (Cat. No. 77023), Adv. Separation Technologies, Inc.
**Oven:** 95 °C; **Carrier:** Helium, head pressure 20 psi; **Detection:** FID 250 °C

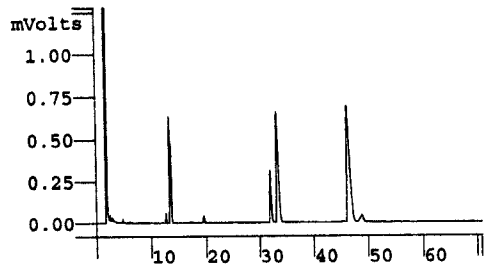
**Racemate**




Minutes

| Peak No | Peak Name | Result () | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 49.5367 | 46.889 | 2010 |
| 2 | | 50.4633 | 48.914 | 2048 |
| | **Totals** | **100.0000** | | **4058** |

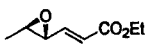
**Chiral Epoxide**




Minutes

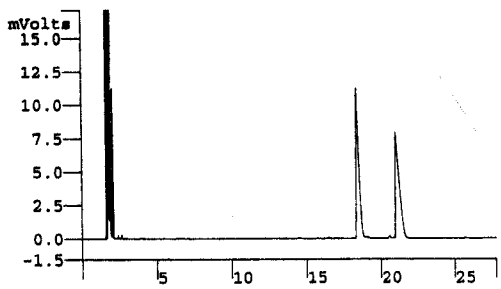
| Peak No | Peak Name | Result () | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 93.5415 | 46.214 | 25552 |
| 2 | | 6.4585 | 48.769 | 1764 |
| | **Totals** | **100.0000** | | **27316** |

**Table 3.4, Entry 1**



**GC Cond.:** **Column:** Chiraldex B-DM (Cat. No. 77023), Adv. Separation Technologies, Inc.
**Oven:** 90 °C; **Carrier:** Helium, head pressure 20 psi; **Detection:** FID 250 °C

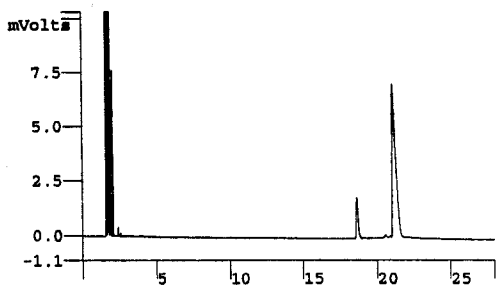
**Racemate**




Minutes

| Peak No | Peak Name | Result () | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 50.2343 | 18.380 | 141450 |
| 2 | | 49.7657 | 21.034 | 140130 |
| | **Totals** | **100.0000** | | **281580** |

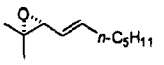
**Chiral Epoxide**




Minutes

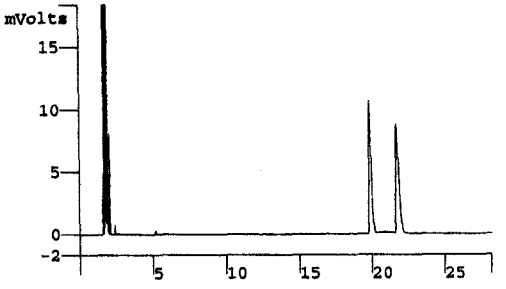
| Peak No | Peak Name | Result () | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 12.6324 | 18.624 | 16721 |
| 2 | | 87.3676 | 21.071 | 115648 |
| | **Totals** | **100.0000** | | **132369** |

**Table 3.4, Entry 2**



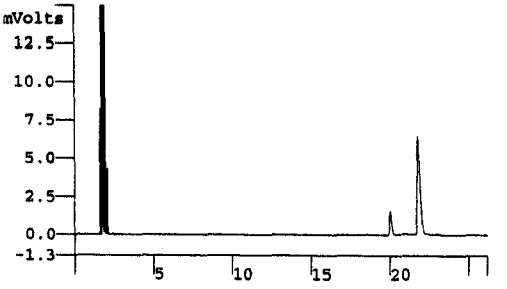
**GC Cond.:** **Column:** Chiraldex B-DM (Cat. No. 77023), Adv. Separation Technologies, Inc.
**Oven:** 90 °C; **Carrier:** Helium, head pressure 20 psi; **Detection:** FID 250 °C

**Racemate**



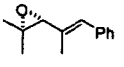

| Peak No | Peak Name | Result 0 | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 49.8706 | 19.821 | 121964 |
| 2 | | 50.1294 | 21.676 | 122597 |
| | **Totals** | **100.0000** | | **244561** |

**Chiral Epoxide**



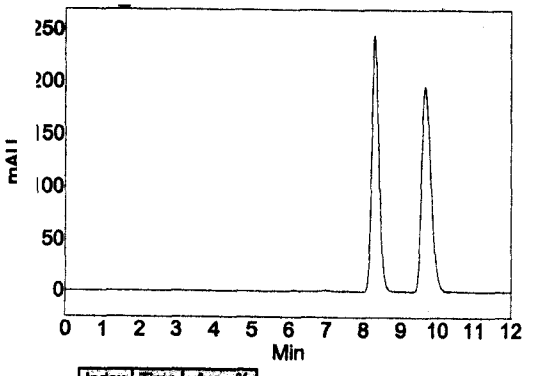

| Peak No | Peak Name | Result 0 | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 14.6861 | 20.028 | 14126 |
| 2 | | 85.3139 | 21.756 | 82063 |
| | **Totals** | **100.0000** | | **96189** |

**Table 3.4, Entry 3**



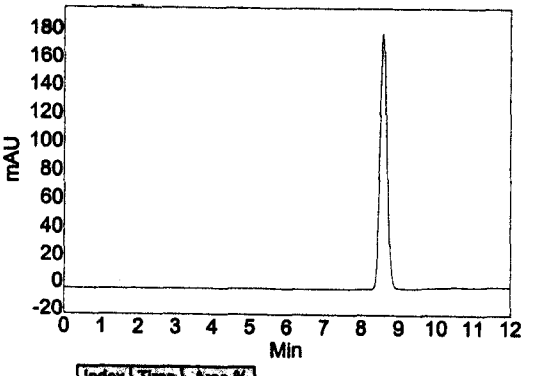
**HPLC Cond.:** **Column:** Chiralcel OD (Column No. OD00CE-DL010), Chiral Technologies, Inc.
**Eluent:** Hexanes/IPA (99/1); **Flow Rate:** 1.0mL/min; **Detection:** UV 270 nm

**Racemate**



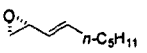

| Index | Time [Min] | Area % [%] |
|---|---|---|
| 1 | 8.30 | 49.850 |
| 2 | 9.67 | 50.150 |
| | | |
| Total | | 100.000 |

**Chiral Epoxide**



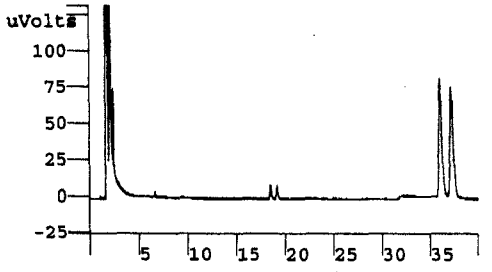

| Index | Time [Min] | Area % [%] |
|---|---|---|
| 1 | 8.57 | 100.000 |
| | | |
| Total | | 100.000 |

**Table 3.4, Entry 4**



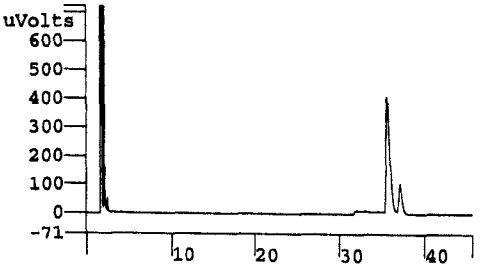
**GC Cond.:** **Column:** Chiraldex B-DM (Cat. No. 77023), Adv. Separation Technologies, Inc.
**Oven:** 65 °C; **Carrier:** Helium, head pressure 20 psi; **Detection:** FID 250 °C

**Racemate**



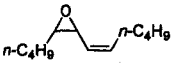

| Peak No | Peak Name | Result () | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 50.3499 | 36.037 | 1734 |
| 2 | | 49.6501 | 37.211 | 1710 |
| | **Totals** | **100.0000** | | **3444** |

**Chiral Epoxide**



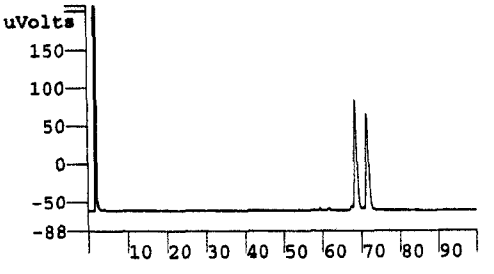

| Peak No | Peak Name | Result () | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 82.1578 | 35.579 | 12065 |
| 2 | | 17.8422 | 37.086 | 2620 |
| | **Totals** | **100.0000** | | **14685** |

**Table 3.4, Entry 5**



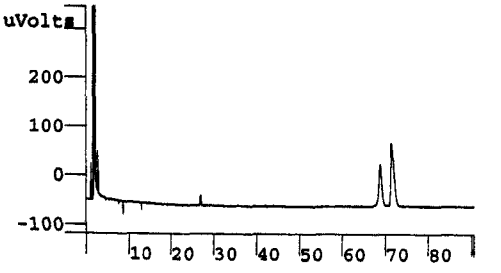
**GC Cond.:** **Column:** Chiraldex B-DM (Cat. No. 77023), Adv. Separation Technologies, Inc.
**Oven:** 85 °C; **Carrier:** Helium, head pressure 20 psi; **Detection:** FID 250 °C

**Racemate**



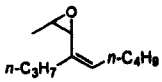

| Peak No | Peak Name | Result () | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 49.6281 | 68.457 | 6419 |
| 2 | | 50.3719 | 71.311 | 6515 |
| | **Totals** | **100.0000** | | **12934** |

**Chiral Epoxide**



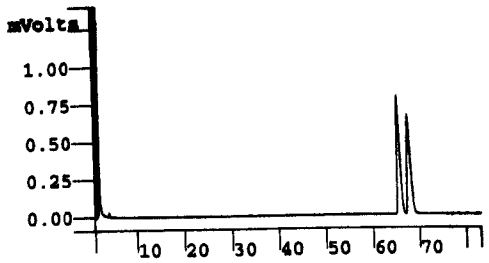

| Peak No | Peak Name | Result () | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 36.0543 | 68.749 | 3700 |
| 2 | | 63.9457 | 71.381 | 6562 |
| | **Totals** | **100.0000** | | **10262** |

**Table 3.4, Entry 6**



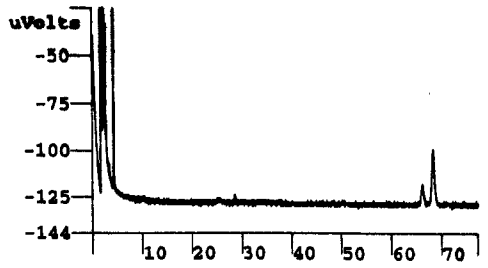

**GC Cond.:** **Column:** Chiraldex B-DM (Cat. No. 77023), Adv. Separation Technologies, Inc.
**Oven:** 65 °C; **Carrier:** Helium, head pressure 20 psi; **Detection:** FID 250 °C

**Racemate**



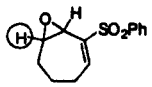

| Peak No | Peak Name | Result 0 | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 50.0729 | 65.564 | 31824 |
| 2 | | 49.9271 | 67.706 | 31731 |
| | Totals | 100.0000 | | 63555 |

**Chiral Epoxide**



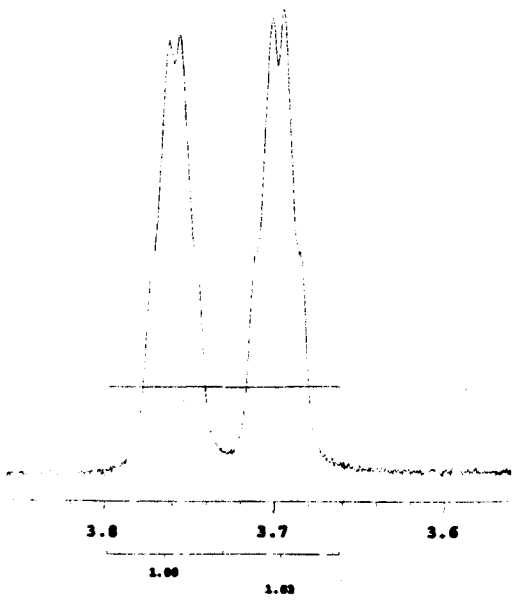

| Peak No | Peak Name | Result 0 | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 20.8260 | 66.089 | 310 |
| 2 | | 79.1740 | 68.283 | 1177 |
| | Totals | 100.0000 | | 1487 |

**Table 3.4, Entry 7**




Enantioselectivity was determined by $^1$HNMR shift analysis with Eu(hfc)$_3$ in $CDCl_3$ (400 MHZ).

**Racemate**




**Chiral Epoxide**

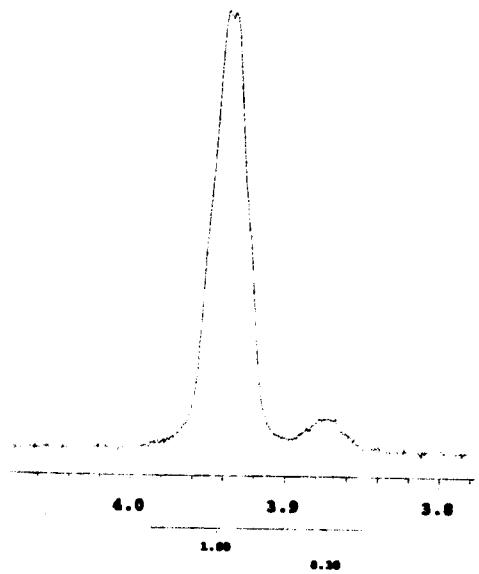
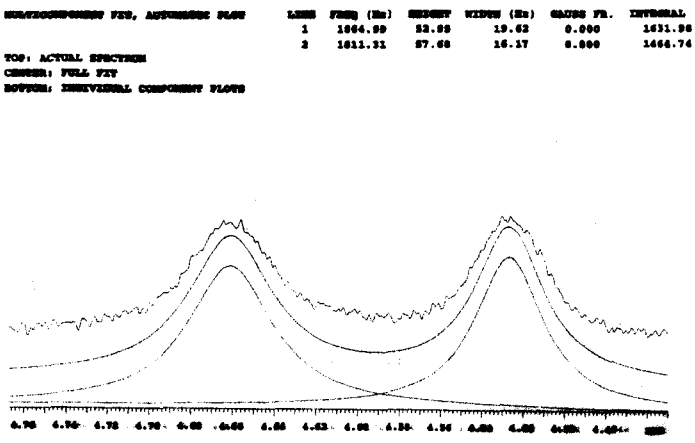


**Table 3.4, Entry 8**

Enantioselectivity was determined by $^1$HNMR shift analysis with $Eu(hfc)_3$ in $CDCl_3$ (400 MHZ).

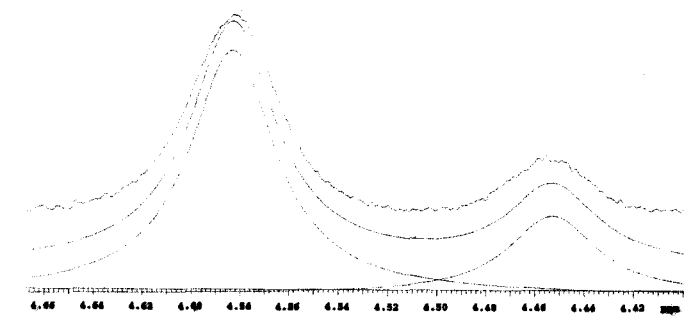
**Racemate**



| LINE | FREQ (Hz) | HEIGHT | WIDTH (Hz) | GAUSS FR. | INTEGRAL |
|---|---|---|---|---|---|
| 1 | 1864.89 | 52.89 | 19.62 | 0.000 | 1631.96 |
| 2 | 1811.31 | 57.68 | 16.17 | 0.000 | 1464.74 |

TOP: ACTUAL SPECTRUM
CENTER: FULL FIT
BOTTOM: INDIVIDUAL COMPONENT PLOTS

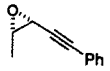
**Chiral Epoxide**



| LINE | FREQ (Hz) | HEIGHT | WIDTH (Hz) | GAUSS FR. | INTEGRAL |
|---|---|---|---|---|---|
| 1 | 1833.93 | 91.89 | 16.99 | 0.000 | 2653.60 |
| 2 | 1781.76 | 39.44 | 17.68 | 0.000 | 817.89 |

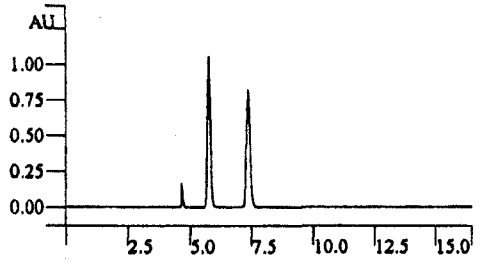
TOP: ACTUAL SPECTRUM
CENTER: FULL FIT
BOTTOM: INDIVIDUAL COMPONENT PLOTS

**Table 4.3, Entry 1**



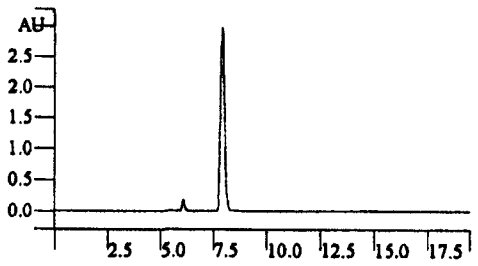
**HPLC Cond.:** **Column:** Chiralcel OD (Column No. OD00CE-DL010), Chiral Technologies, Inc.
**Eluent:** Hexanes/IPA (96/4); **Flow Rate:** 1.0mL/min; **Detection:** UV 254 nm

**Racemate**



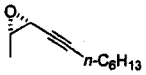

| Peak No | Ret. Time (min) | Result () | Area (counts) |
|---|---|---|---|
| 1 | 5.754 | 49.7155 | 4514572 |
| 2 | 7.341 | 50.2845 | 4566234 |
| | | **100.0000** | **9080806** |

**Chiral Epoxide**



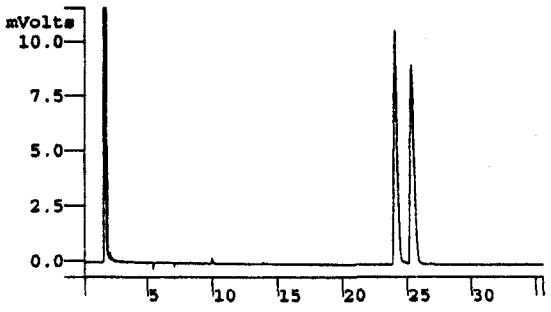

| Peak No | Ret. Time (min) | Result () | Area (counts) |
|---|---|---|---|
| 1 | 6.029 | 3.6275 | 806710 |
| 2 | 7.887 | 96.3725 | 21431754 |
| | | **100.0000** | **22238464** |

**Table 4.3, Entry 2**



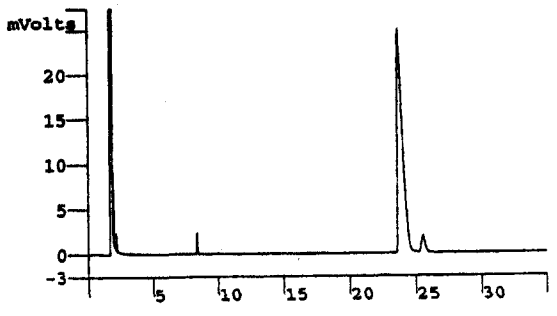
**GC Cond.:** **Column:** Chiraldex B-DM (Cat. No. 77023), Adv. Separation Technologies, Inc.
**Oven:** 100 °C; **Carrier:** Helium, head pressure 20 psi; **Detection:** FID 250 °C

**Racemate**



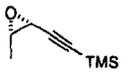

| Peak No | Peak Name | Result 0 | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 49.9541 | 24.009 | 184553 |
| 2 | | 50.0459 | 25.284 | 184892 |
| | **Totals** | **100.0000** | | **369445** |

**Chiral Epoxide**



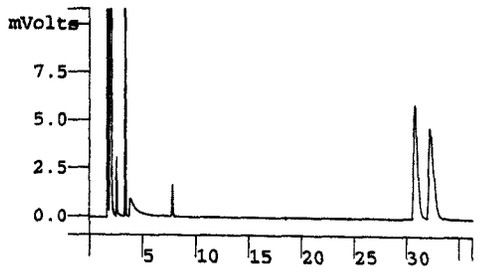

| Peak No | Peak Name | Result 0 | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 95.0000 | 23.691 | 682403 |
| 2 | | 5.0000 | 25.507 | 35916 |
| | **Totals** | **100.0000** | | **718319** |

**Table 4.3, Entry 3**



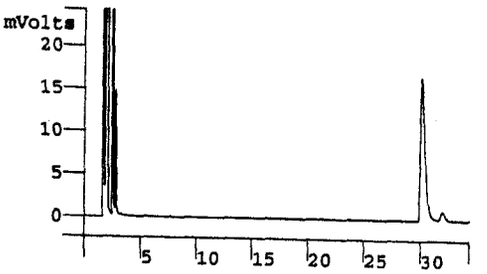

**GC Cond.:** **Column:** Chiraldex B-DM (Cat. No. 77023), Adv. Separation Technologies, Inc.
**Oven:** 45 °C; **Carrier:** Helium, head pressure 20 psi; **Detection:** FID 250 °C

**Racemate**



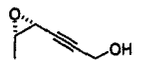

| Peak No | Peak Name | Result () | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 50.1831 | 30.736 | 149945 |
| 2 | | 49.8169 | 32.199 | 148851 |
| | **Totals** | **100.0000** | | **298796** |

**Chiral Epoxide**



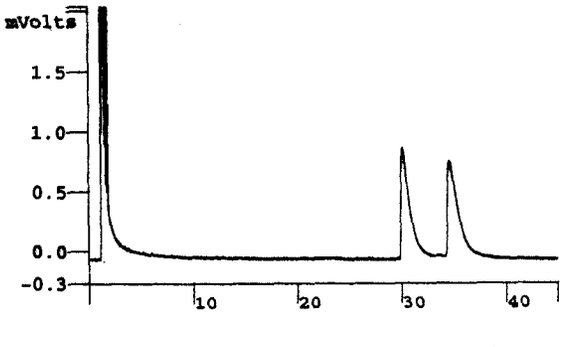

| Peak No | Peak Name | Result () | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 94.9561 | 30.044 | 462404 |
| 2 | | 5.0439 | 31.949 | 24562 |
| | **Totals** | **100.0000** | | **486966** |

**Table 4.3, Entry 4**



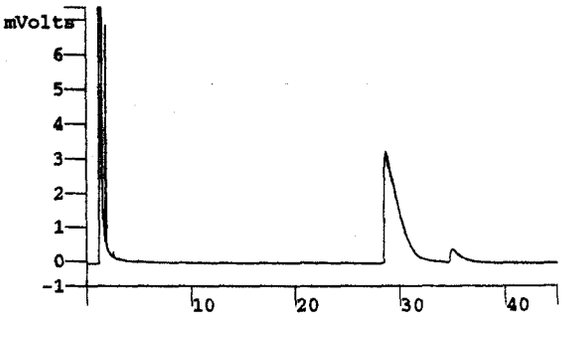

**GC Cond.:** **Column:** Chiraldex B-DM (Cat. No. 77023), Adv. Separation Technologies, Inc.
**Oven:** 90 °C; **Carrier:** Helium, head pressure 30 psi; **Detection:** FID 250 °C

**Racemate**



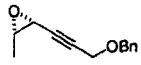

| Peak No | Peak Name | Result () | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 49.4756 | 30.076 | 54117 |
| 2 | | 50.5244 | 34.581 | 55265 |
| | **Totals** | **100.0000** | | **109382** |

**Chiral Epoxide**



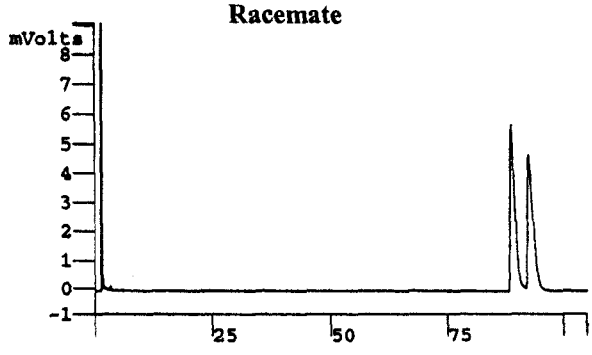

| Peak No | Peak Name | Result () | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 92.4677 | 28.669 | 302653 |
| 2 | | 7.5323 | 35.006 | 24654 |
| | **Totals** | **100.0000** | | **327307** |

**Table 4.3, Entry 5**



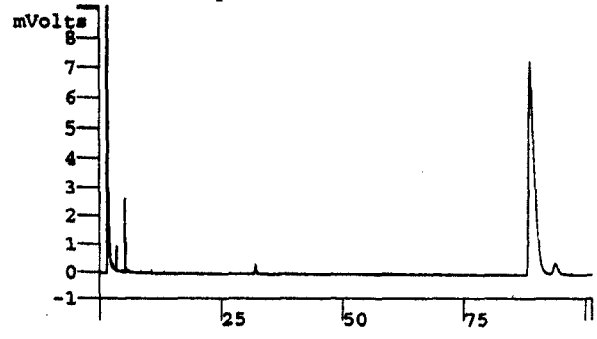

**GC Cond.:** **Column:** Chiraldex B-DM (Cat. No. 77023), Adv. Separation Technologies, Inc.
**Oven:** 120 °C; **Carrier:** Helium, head pressure 25 psi; **Detection:** FID 250 °C

**Racemate**




| Peak No | Peak Name | Result 0 | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 50.4584 | 88.622 | 386967 |
| 2 | | 49.5416 | 92.418 | 379935 |
| | **Totals** | **100.0000** | | **766902** |

**Chiral Epoxide**

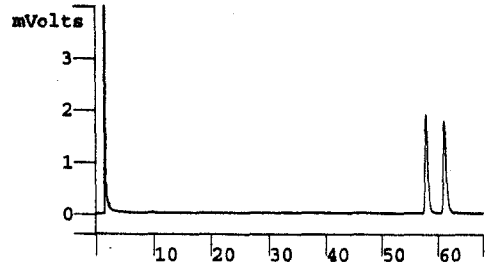



| Peak No | Peak Name | Result 0 | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 96.0029 | 88.408 | 586139 |
| 2 | | 3.9971 | 93.761 | 24404 |
| | **Totals** | **100.0000** | | **610543** |

**Table 4.3, Entry 6**

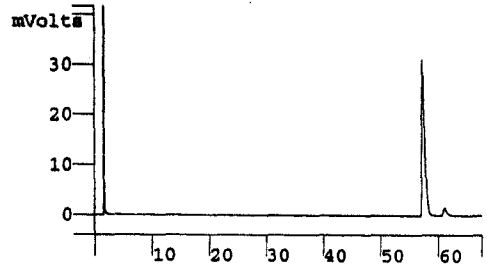

**GC Cond.:** **Column:** Chiraldex B-DM (Cat. No. 77023), Adv. Separation Technologies, Inc.
**Oven:** 140 °C; **Carrier:** Helium, head pressure 25 psi; **Detection:** FID 250 °C

**Racemate**



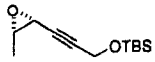

| Peak No | Peak Name | Result 0 | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 49.7052 | 57.919 | 64862 |
| 2 | | 50.2948 | 61.151 | 65631 |
| | **Totals** | **100.0000** | | **130493** |

**Chiral Epoxide**



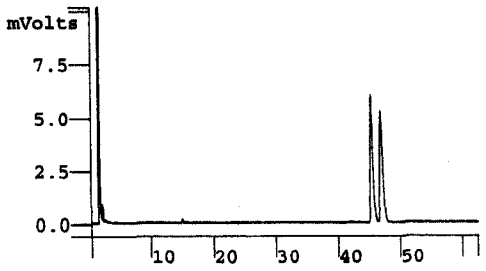

| Peak No | Peak Name | Result 0 | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 94.4657 | 57.316 | 1072159 |
| 2 | | 5.5343 | 61.084 | 62813 |
| | **Totals** | **100.0000** | | **1134972** |

**Table 4.3, Entry 7**



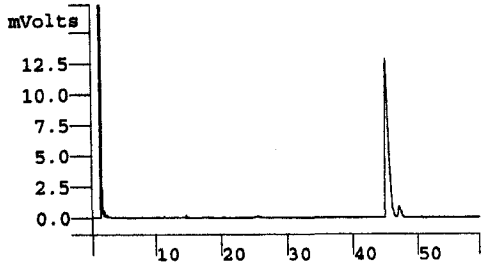

**GC Cond.:** **Column:** Chiraldex B-DM (Cat. No. 77023), Adv. Separation Technologies, Inc.
**Oven:** 100 °C; **Carrier:** Helium, head pressure 20 psi; **Detection:** FID 250 °C

**Racemate**



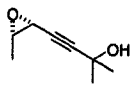

| Peak No | Peak Name | Result () | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 50.0398 | 45.423 | 165928 |
| 2 | | 49.9602 | 46.904 | 165664 |
| | **Totals** | **100.0000** | | **331592** |

**Chiral Epoxide**



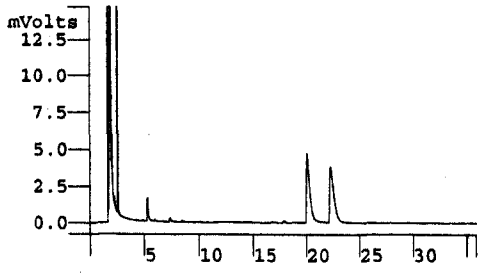

| Peak No | Peak Name | Result () | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 94.6315 | 45.201 | 441463 |
| 2 | | 5.3685 | 47.221 | 25045 |
| | **Totals** | **100.0000** | | **466508** |

**Table 4.3, Entry 8**



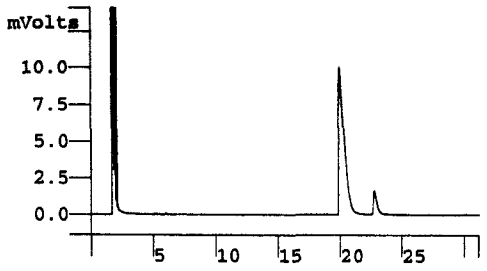

**GC Cond.:** **Column:** Chiraldex B-DM (Cat. No. 77023), Adv. Separation Technologies, Inc.
**Oven:** 90 °C; **Carrier:** Helium, head pressure 20 psi; **Detection:** FID 250 °C

**Racemate**



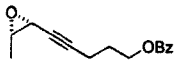

| Peak No | Peak Name | Result () | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 50.1782 | 20.052 | 102466 |
| 2 | | 49.8218 | 22.257 | 101738 |
| | **Totals** | **100.0000** | | **204204** |

**Chiral Epoxide**



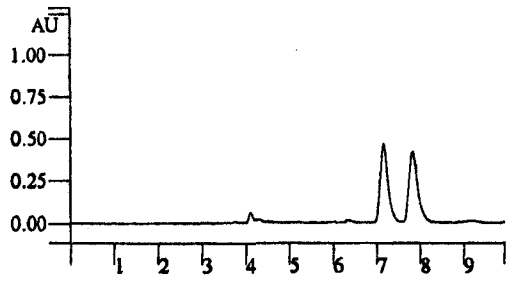

| Peak No | Peak Name | Result () | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 90.4725 | 19.927 | 324804 |
| 2 | | 9.5275 | 22.759 | 34205 |
| | **Totals** | **100.0000** | | **359009** |

**Table 4.3, Entry 9**




**HPLC Cond.:** **Column:** Chirapak AD (Column No. AD00CE-EA001), Chiral Technologies, Inc.
**Eluent:** Hexanes/IPA (92/8); **Flow Rate:** 1.0mL/min; **Detection:** UV 270 nm

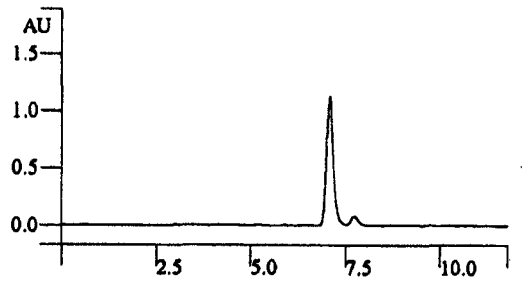
**Racemate**




| Peak No | Ret. Time (min) | Result () | Area (counts) |
|---|---|---|---|
| 1 | 7.146 | 50.0215 | 3027775 |
| 2 | 7.819 | 49.9785 | 3025178 |
| | | **100.0000** | **6052953** |

Minutes

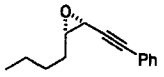
**Chiral Epoxide**




| Peak No | Ret. Time (min) | Result () | Area (counts) |
|---|---|---|---|
| 1 | 7.044 | 93.9168 | 7234500 |
| 2 | 7.714 | 6.0832 | 468598 |
| | | **100.0000** | **7703098** |

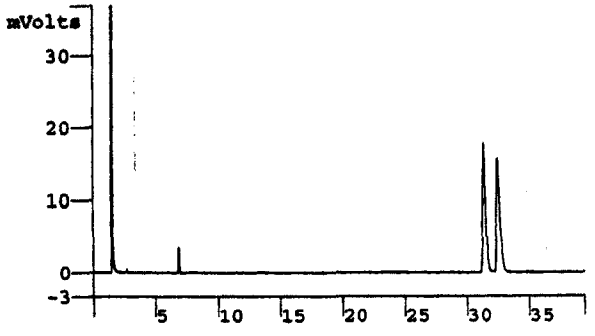
Minutes

**Table 4.3, Entry 10**




**GC Cond.:** **Column:** Chiraldex B-DM (Cat. No. 77023), Adv. Separation Technologies, Inc.
**Oven:** 135 °C; **Carrier:** Helium, head pressure 25 psi; **Detection:** FID 250 °C

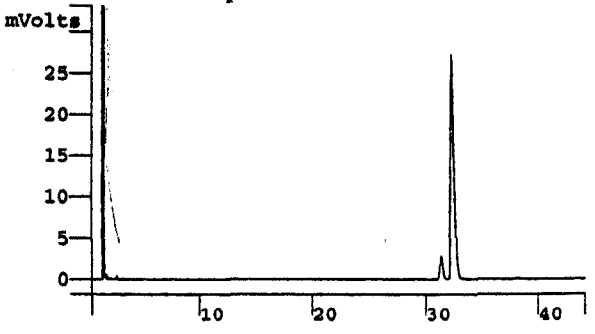
**Racemate**




| Peak No | Peak Name | Result () | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 49.8305 | 31.358 | 315240 |
| 2 | | 50.1695 | 32.466 | 317384 |
| | **Totals** | **100.0000** | | **632624** |

Minutes

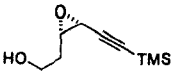
**Chiral Epoxide**




| Peak No | Peak Name | Result () | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 7.7968 | 31.361 | 48673 |
| 2 | | 92.2031 | 32.263 | 575590 |
| | **Totals** | **99.9999** | | **624263** |

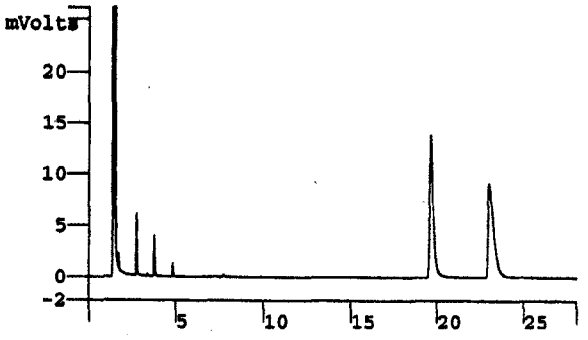
Minutes

**Table 4.3, Entry 14**



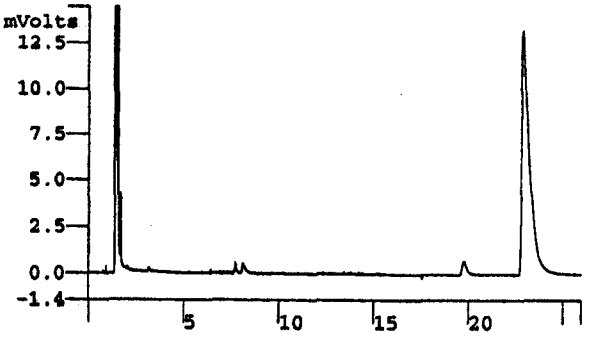

**GC Cond.:** **Column:** Chiraldex B-DM (Cat. No. 77023), Adv. Separation Technologies, Inc.
**Oven:** 110 °C; **Carrier:** Helium, head pressure 25 psi; **Detection:** FID 250 °C

**Racemate**



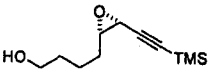

| Peak No | Peak Name | Result 0 | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 50.0373 | 19.636 | 209856 |
| 2 | | 49.9627 | 23.036 | 209543 |
| | **Totals** | **100.0000** | | **419399** |

**Chiral Epoxide**



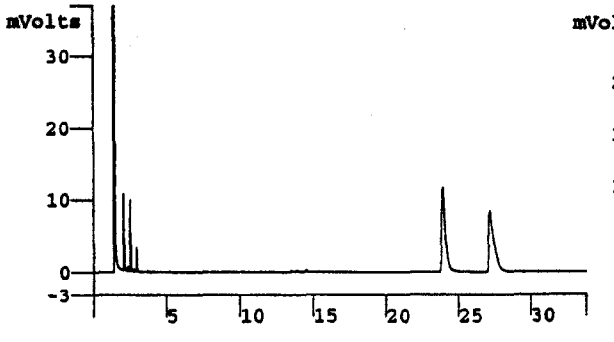

| Peak No | Peak Name | Result 0 | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 3.0681 | 19.759 | 11889 |
| 2 | | 96.9319 | 22.864 | 375619 |
| | **Totals** | **100.0000** | | **387508** |

**Table 4.3, Entry 15**



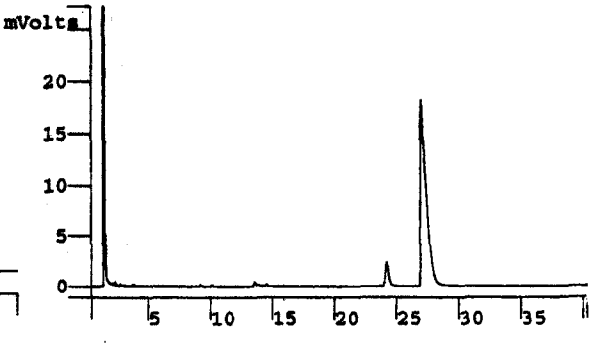

**GC Cond.:** **Column:** Chiraldex B-DM (Cat. No. 77023), Adv. Separation Technologies, Inc.
**Oven:** 130 °C; **Carrier:** Helium, head pressure 25 psi; **Detection:** FID 250 °C

**Racemate**



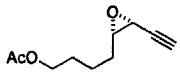

| Peak No | Peak Name | Result 0 | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 49.6323 | 23.931 | 213597 |
| 2 | | 50.3677 | 27.214 | 216762 |
| | **Totals** | **100.0000** | | **430359** |

**Chiral Epoxide**



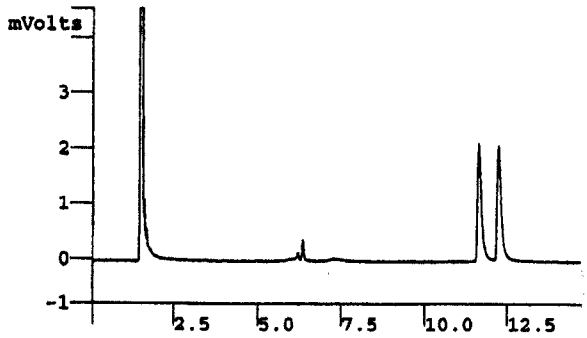

| Peak No | Peak Name | Result 0 | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 6.7327 | 24.167 | 42739 |
| 2 | | 93.2673 | 27.029 | 592055 |
| | **Totals** | **100.0000** | | **634794** |

**Table 4.3, Entry 16**



**GC Cond.:** **Column:** Chiraldex B-DM (Cat. No. 77023), Adv. Separation Technologies, Inc.
**Oven:** 125 °C; **Carrier:** Helium, head pressure 25 psi; **Detection:** FID 250 °C

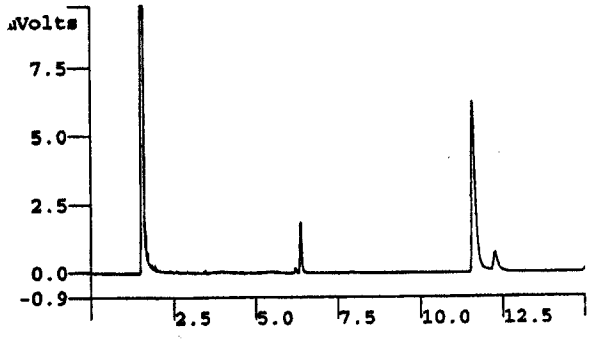
**Racemate**




| Peak No | Peak Name | Result 0 | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 49.5730 | 11.626 | 17749 |
| 2 | | 50.4270 | 12.217 | 18055 |
| | **Totals** | **100.0000** | | **35804** |

Minutes

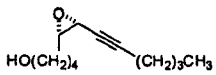
**Chiral Epoxide**




| Peak No | Peak Name | Result 0 | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 90.2378 | 11.579 | 51732 |
| 2 | | 9.7622 | 12.257 | 5597 |
| | **Totals** | **100.0000** | | **57329** |

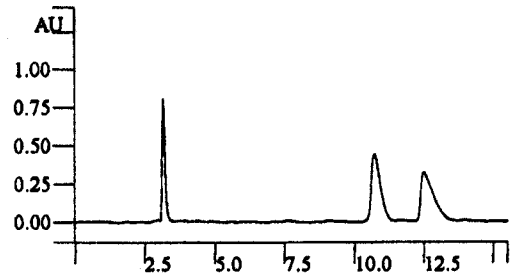
Minutes

**Table 4.3, Entry 17**



**HPLC Cond.:** **Column:** Chiralcel OJ (Column No. OJ00CE-DE008), Chiral Technologies, Inc.
**Eluent:** Hexanes/IPA (92/8); **Flow Rate:** 1.0mL/min; **Detection:** UV 210 nm

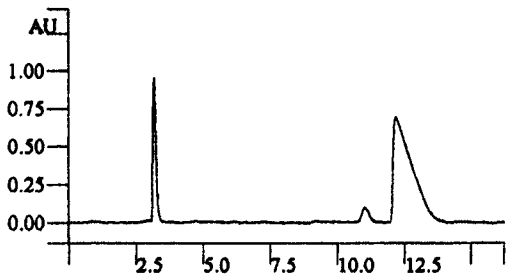
**Racemate**




| Peak No | Ret. Time (min) | Result 0 | Area (counts) |
|---|---|---|---|
| 1 | 10.704 | 49.5158 | 5191821 |
| 2 | 12.493 | 50.4842 | 5293368 |
| | | **100.0000** | **10485189** |

Minutes

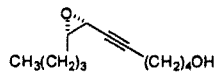
**Chiral Epoxide**




| Peak No | Ret. Time (min) | Result 0 | Area (counts) |
|---|---|---|---|
| 1 | 11.014 | 4.8570 | 873081 |
| 2 | 12.161 | 95.1430 | 17102756 |
| | | **100.0000** | **17975836** |

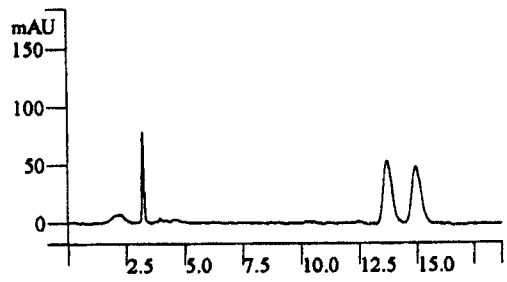
Minutes

**Table 4.3, Entry 18**




**HPLC Cond.:** **Column:** Chiralcel OD (Column No. OD00CE-DL010), Chiral Technologies, Inc.
**Eluent:** Hexanes/IPA (92/8); **Flow Rate:** 1.0mL/min; **Detection:** UV 210 nm

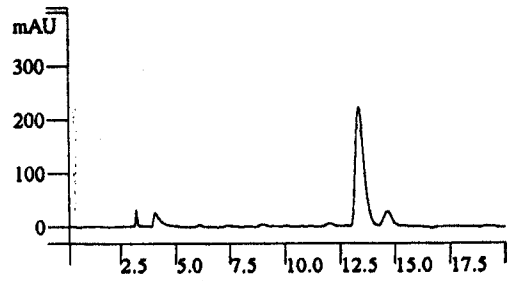
**Racemate**




| Peak No | Ret. Time (min) | Result () | Area (counts) |
|---|---|---|---|
| 1 | 13.686 | 50.2666 | 721994 |
| 2 | 14.934 | 49.7334 | 714334 |
| | | **100.0000** | **1436328** |

Minutes

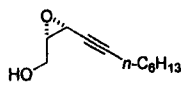
**Chiral Epoxide**




| Peak No | Ret. Time (min) | Result () | Area (counts) |
|---|---|---|---|
| 1 | 13.339 | 90.0670 | 3212628 |
| 2 | 14.659 | 9.9330 | 354304 |
| | | **100.0000** | **3566932** |

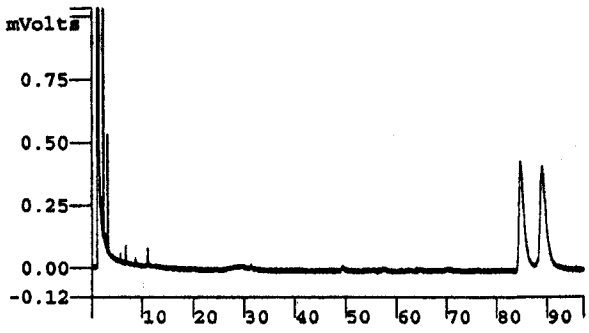
Minutes

**Table 4.3, Entry 19**




**GC Cond.:** **Column:** Chiraldex B-DM (Cat. No. 77023), Adv. Separation Technologies, Inc.
**Oven:** 110 °C; **Carrier:** Helium, head pressure 30 psi; **Detection:** FID 250 °C

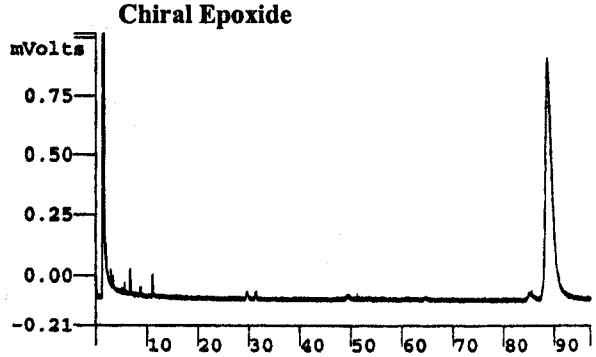
**Racemate**




| Peak No | Peak Name | Result () | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 49.6269 | 84.719 | 29469 |
| 2 | | 50.3731 | 89.128 | 29912 |
| | **Totals** | **100.0000** | | **59381** |

Minutes

**Chiral Epoxide**



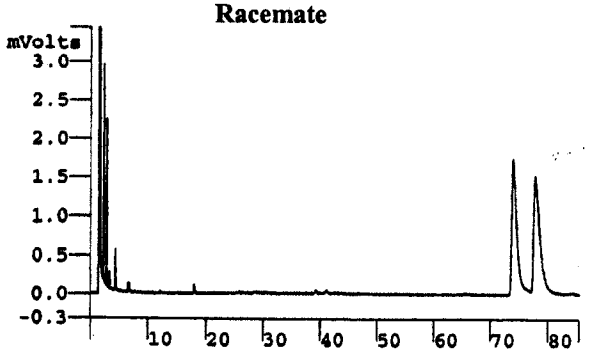

| Peak No | Peak Name | Result () | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 1.7002 | 85.567 | 1540 |
| 2 | | 98.2998 | 88.494 | 89032 |
| | **Totals** | **100.0000** | | **90572** |

Minutes

**Table 4.3, Entry 20**

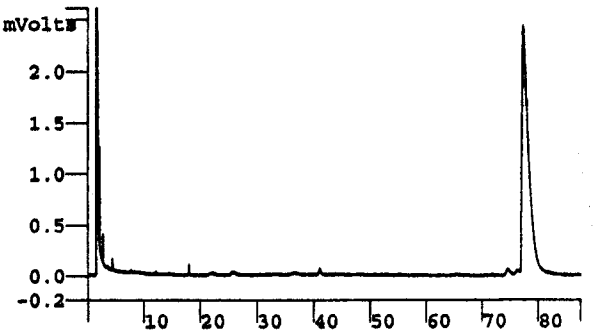
**GC Cond.:** **Column:** Chiraldex B-DM (Cat. No. 77023), Adv. Separation Technologies, Inc.
**Oven:** 125 °C; **Carrier:** Helium, head pressure 25 psi; **Detection:** FID 250 °C

**Racemate**



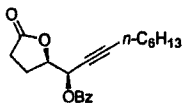

| Peak No | Peak Name | Result 0 | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 50.1102 | 73.851 | 107289 |
| 2 | | 49.8898 | 77.746 | 106817 |
| | Totals | 100.0000 | | 214106 |

**Chiral Epoxide**



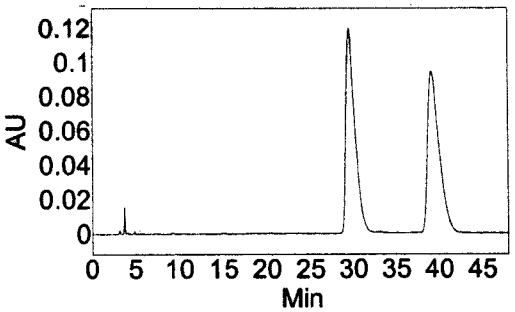

| Peak No | Peak Name | Result 0 | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 1.4356 | 74.537 | 2848 |
| 2 | | 98.5644 | 77.316 | 195542 |
| | Totals | 100.0000 | | 198390 |

**Table 4.3, Entry 21**



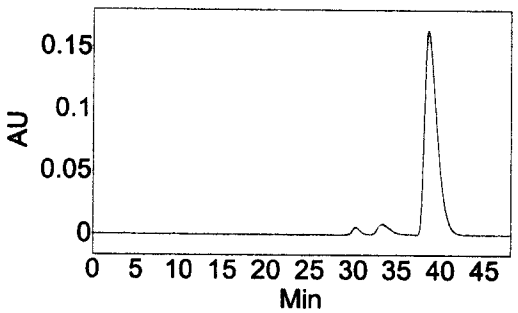
**HPLC Cond.:** **Column:** Chiralcel OD (Column No. OD00CE-DL010), Chiral Technologies, Inc.
**Eluent:** Hexanes/IPA (85/15); **Flow Rate:** 1.0mL/min; **Detection:** UV 240 nm

**Racemate**



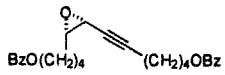

| Index | Time [Min] | Area % [%] |
|---|---|---|
| 1 | 29.525 | 49.716 |
| 2 | 39.108 | 50.284 |
| | | |
| Total | | 100.000 |

**Chiral Epoxide**



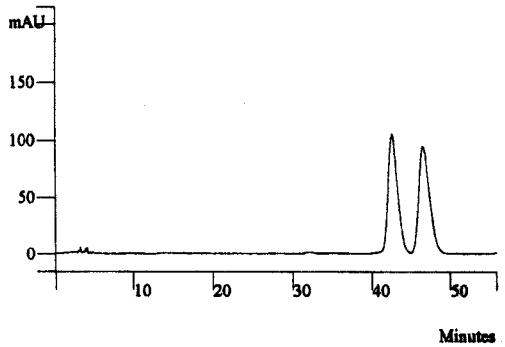

| Index | Time [Min] | Area % [%] |
|---|---|---|
| 2 | 30.248 | 2.121 |
| 1 | 38.553 | 97.879 |
| | | |
| Total | | 100.000 |

**Table 4.3, Entry 22**



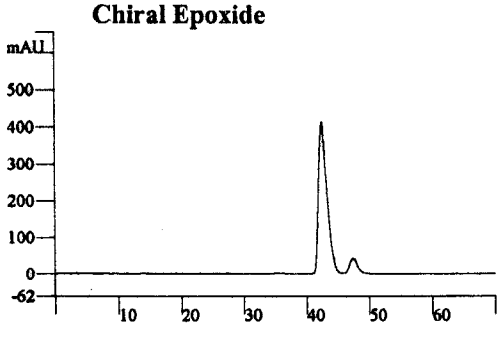

**HPLC Cond.:** **Column:** Chiralcel OD (Column No. OD00CE-DL010), Chiral Technologies, Inc.
**Eluent:** Hexanes/IPA (94/6); **Flow Rate:** 1.0mL/min; **Detection:** UV 226 nm

**Racemate**



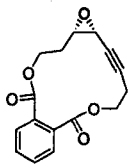

| Peak No | Peak Name | Ret. Time (min) | Result () | Area (counts) |
|---|---|---|---|---|
| 1 | | 42.609 | 50.1060 | 4652853 |
| 2 | | 46.499 | 49.8940 | 4633173 |
| | Totals | | 100.0000 | 9286026 |

**Chiral Epoxide**



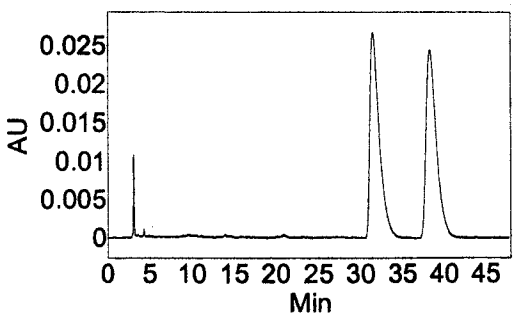

| Peak No | Peak Name | Ret. Time (min) | Result () | Area (counts) | r f u |
|---|---|---|---|---|---|
| 1 | | 42.444 | 90.9048 | 20299866 | ) |
| 2 | | 47.314 | 9.0952 | 2031038 | ) |
| | Totals | | 100.0000 | 22330904 | 0 |

**Table 4.3, Entry 23**



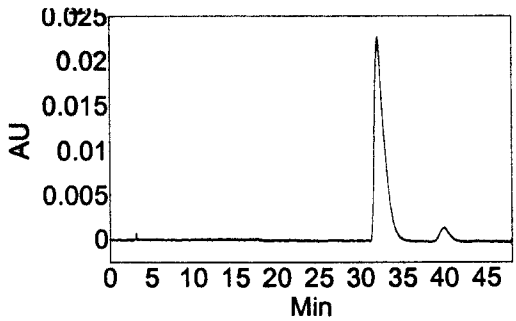
**HPLC Cond.:** **Column:** Chiralcel OD (Column No. OD00CE-DL010), Chiral Technologies, Inc.
**Eluent:** Hexanes/IPA (90/10); **Flow Rate:** 1.0mL/min; **Detection:** UV 270 nm

**Racemate**



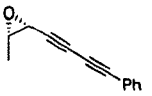

| Index | Time [Min] | Area % [%] |
|---|---|---|
| 1 | 31.460 | 50.165 |
| 2 | 38.278 | 49.835 |
| | | |
| Total | | 100.000 |

**Chiral Epoxide**



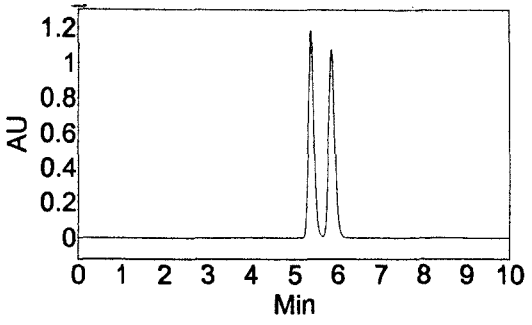

| Index | Time [Min] | Area % [%] |
|---|---|---|
| 1 | 32.080 | 93.378 |
| 2 | 39.902 | 6.622 |
| | | |
| Total | | 100.000 |

**Table 4.3, Entry 24**



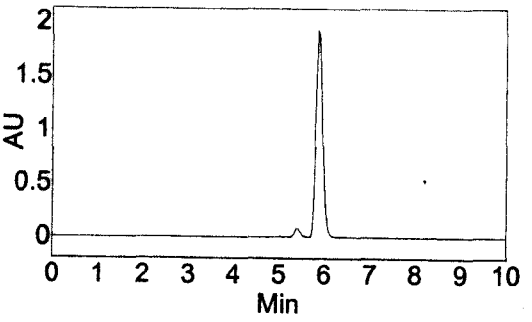

**HPLC Cond.:** **Column:** Chiralcel OD (Column No. OD00CE-DL010), Chiral Technologies, Inc.
**Eluent:** Hexanes/IPA (97/03); **Flow Rate:** 1.0mL/min; **Detection:** UV 254 nm

**Racemate**



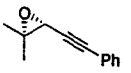

| Index | Time [Min] | Area % [%] |
|---|---|---|
| 1 | 5.383 | 50.001 |
| 2 | 5.847 | 49.999 |
| | | |
| Total | | 100.000 |

**Chiral Epoxide**



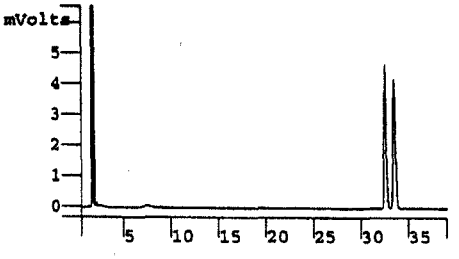

| Index | Time [Min] | Area % [%] |
|---|---|---|
| 1 | 5.408 | 3.575 |
| 2 | 5.870 | 96.425 |
| | | |
| Total | | 100.000 |

**Table 4.3, Entry 25**



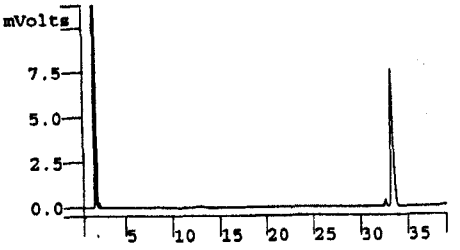

**GC Cond.:** **Column:** Chiraldex B-DM (Cat. No. 77023), Adv. Separation Technologies, Inc.
**Oven:** 110 °C; **Carrier:** Helium, head pressure 20 psi; **Detection:** FID 250 °C

**Racemate**



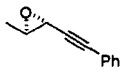

| Peak No | Peak Name | Result () | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 49.8989 | 32.466 | 71182 |
| 2 | | 50.1011 | 33.426 | 71470 |
| | **Totals** | **100.0000** | | **142652** |

**Chiral Epoxide**



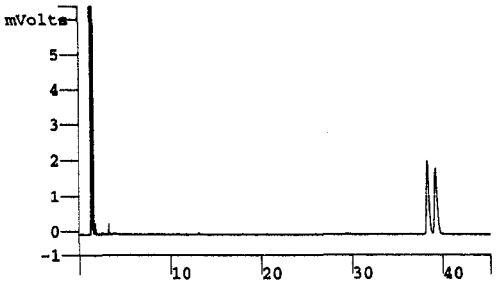

| Peak No | Peak Name | Result () | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 3.0543 | 32.607 | 4579 |
| 2 | | 96.9457 | 33.274 | 145330 |
| | **Totals** | **100.0000** | | **149909** |

**Table 4.3, Entry 26**



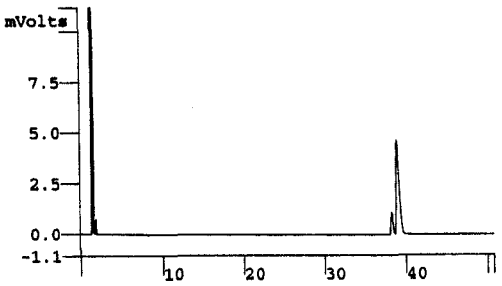

**GC Cond.:** **Column:** Chiraldex B-DM (Cat. No. 77023), Adv. Separation Technologies, Inc.
**Oven:** 100 °C; **Carrier:** Helium, head pressure 25 psi; **Detection:** FID 250 °C

**Racemate**



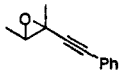

| Peak No | Peak Name | Result () | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 49.8699 | 38.338 | 38194 |
| 2 | | 50.1301 | 39.232 | 38394 |
| | **Totals** | **100.0000** | | **76588** |

**Chiral Epoxide**



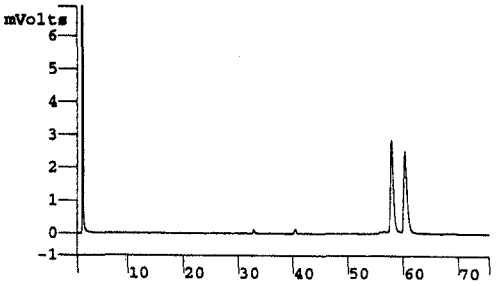

| Peak No | Peak Name | Result () | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 12.7865 | 38.338 | 16829 |
| 2 | | 87.2135 | 38.932 | 114788 |
| | **Totals** | **100.0000** | | **131617** |

**Table 4.3, Entry 27**



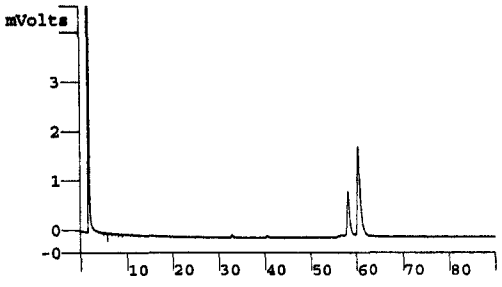

**GC Cond.:** **Column:** Chiraldex B-DM (Cat. No. 77023), Adv. Separation Technologies, Inc.
**Oven:** 100 °C; **Carrier:** Helium, head pressure 20 psi; **Detection:** FID 250 °C

**Racemate**




| Peak No | Peak Name | Result () | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 49.8087 | 57.799 | 101026 |
| 2 | | 50.1913 | 60.221 | 101802 |
| | **Totals** | **100.0000** | | **202828** |

**Chiral Epoxide**

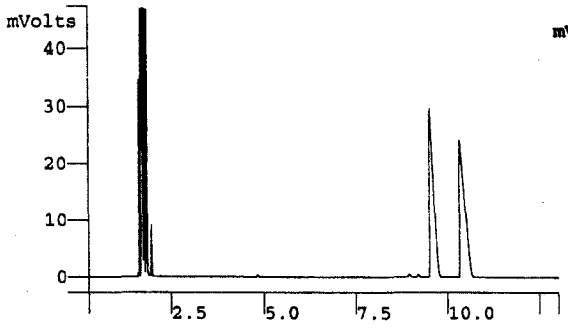



| Peak No | Peak Name | Result () | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 29.7450 | 58.141 | 32429 |
| 2 | | 70.2550 | 60.496 | 76595 |
| | **Totals** | **100.0000** | | **109024** |

**Table 5.6, Entry 1**

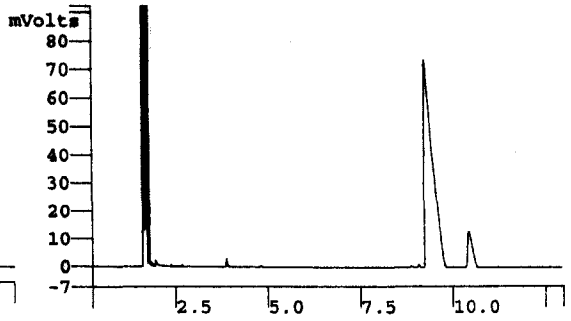
**GC Cond.:** **Column:** Chiraldex B-DM (Cat. No. 77023), Adv. Separation Technologies, Inc.
**Oven:** 100 °C; **Carrier:** Helium, head pressure 20 psi; **Detection:** FID 250 °C

**Racemate**




| Peak No | Peak Name | Result () | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 50.0758 | 9.528 | 231507 |
| 2 | | 49.9242 | 10.351 | 230806 |
| | **Totals** | **100.0000** | | **462313** |

**Chiral Epoxide**

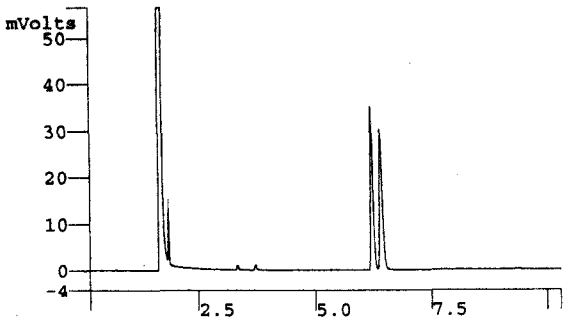



| Peak No | Peak Name | Result () | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 91.1285 | 9.243 | 1148947 |
| 2 | | 8.8715 | 10.424 | 111851 |
| | **Totals** | **100.0000** | | **1260798** |

**Table 5.6, Entry 2**

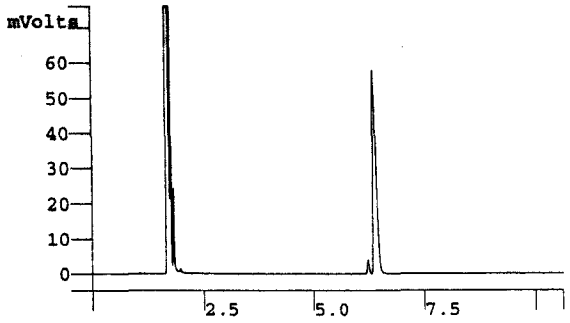
**GC Cond.:** **Column:** Chiraldex B-DM (Cat. No. 77023), Adv. Separation Technologies, Inc.
**Oven:** 110 °C; **Carrier:** Helium, head pressure 20 psi; **Detection:** FID 250 °C

**Racemate**




| Peak No | Peak Name | Result () | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 50.2361 | 6.204 | 129911 |
| 2 | | 49.7639 | 6.403 | 128689 |
| | **Totals** | **100.0000** | | **258600** |

**Chiral Epoxide**

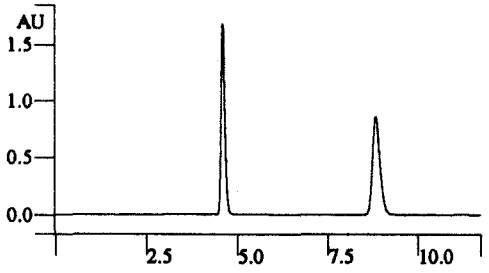



| Peak No | Peak Name | Result () | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 3.8117 | 6.226 | 11569 |
| 2 | | 96.1883 | 6.358 | 291935 |
| | **Totals** | **100.0000** | | **303504** |

**Table 5.6, Entry 3**

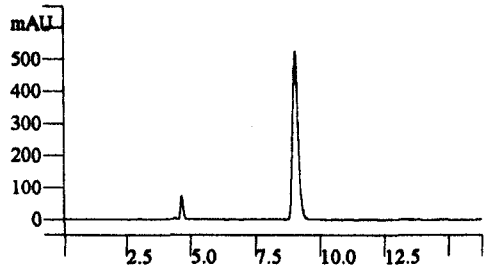
**HPLC Cond.:** **Column:** Chiralcel OD (Column No. OD00CE-DL010), Chiral Technologies, Inc.
**Eluent:** Hexanes/IPA (90/10); **Flow Rate:** 1.0mL/min; **Detection:** UV 220 nm

**Racemate**



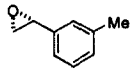

| Peak No | Ret. Time (min) | Result () | Minutes Area (counts) |
|---|---|---|---|
| 1 | 4.604 | 49.5471 | 6552150 |
| 2 | 8.824 | 50.4529 | 6671940 |
| | | **100.0000** | **13224090** |

**Chiral Epoxide**



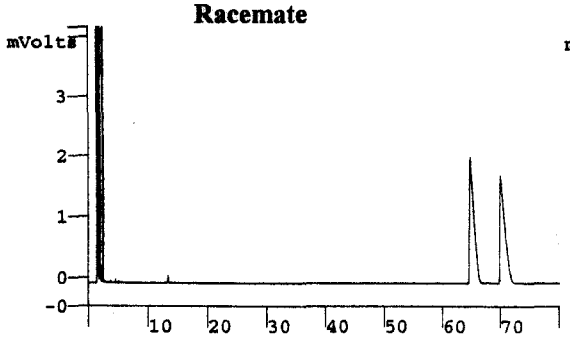

| Peak No | Ret. Time (min) | Result () | Minutes Area (counts) |
|---|---|---|---|
| 1 | 4.648 | 6.1437 | 276157 |
| 2 | 9.049 | 93.8563 | 4218784 |
| | | **100.0000** | **4494941** |

**Table 5.6, Entry 4**



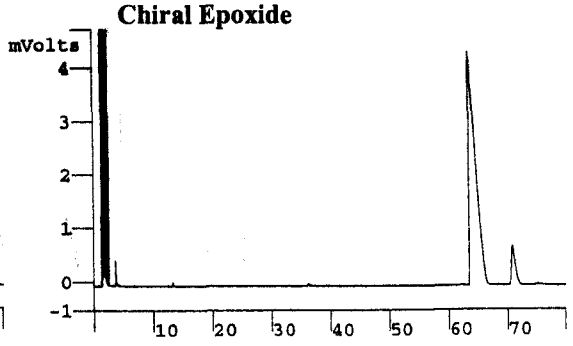
**GC Cond.:** **Column:** Chiraldex B-DM (Cat. No. 77023), Adv. Separation Technologies, Inc.
**Oven:** 60 °C; **Carrier:** Helium, head pressure 25 psi; **Detection:** FID 250 °C

**Racemate**



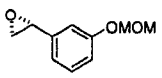

| Peak No | Peak Name | Result () | Ret. Time (min) | Minutes Area (counts) |
|---|---|---|---|---|
| 1 | | 49.9753 | 64.793 | 106964 |
| 2 | | 50.0247 | 69.984 | 107069 |
| | **Totals** | **100.0000** | | **214033** |

**Chiral Epoxide**



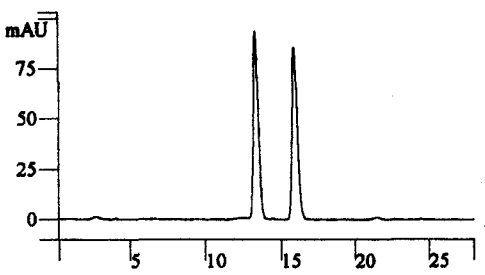

| Peak No | Peak Name | Result () | Ret. Time (min) | Minutes Area (counts) |
|---|---|---|---|---|
| 1 | | 91.5201 | 63.609 | 355116 |
| 2 | | 8.4799 | 70.793 | 32904 |
| | **Totals** | **100.0000** | | **388020** |

**Table 5.6, Entry 5**



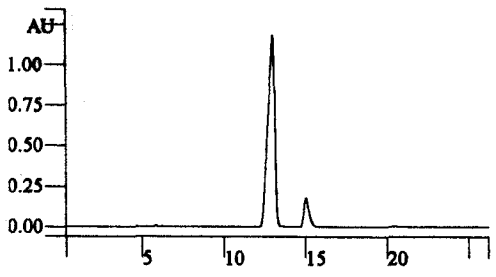

**HPLC Cond.:** **Column:** Chiralcel OD (Column No. OD00CE-DL010), Chiral Technologies, Inc.
**Eluent:** Hexanes/IPA (95/5); **Flow Rate:** 1.0mL/min; **Detection:** UV 270 nm

**Racemate**



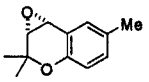

| Peak No | Ret. Time (min) | Result () | Area (counts) |
|---|---|---|---|
| 1 | 13.314 | 49.8727 | 1111818 |
| 2 | 15.894 | 50.1273 | 1117493 |
| | | **100.0000** | **2229311** |

**Chiral Epoxide**



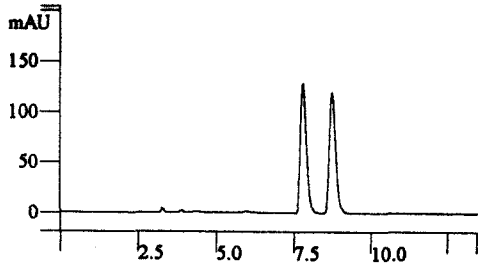

| Peak No | Ret. Time (min) | Result () | Area (counts) |
|---|---|---|---|
| 1 | 13.009 | 89.8571 | 18704434 |
| 2 | 15.012 | 10.1429 | 2111319 |
| | | **100.0000** | **20815752** |

**Table 5.6, Entry 6**



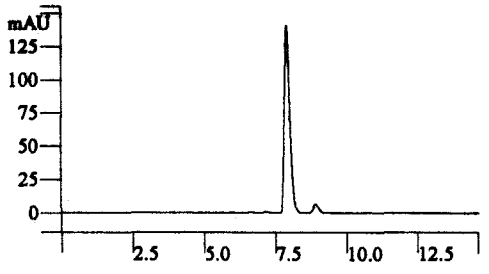

**HPLC Cond.:** **Column:** Chiralcel OD (Column No. OD00CE-DL010), Chiral Technologies, Inc.
**Eluent:** Hexanes/IPA (94/6); **Flow Rate:** 1.0mL/min; **Detection:** UV 270 nm

**Racemate**



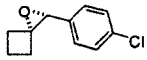

| Peak No | Ret. Time (min) | Result () | Area (counts) |
|---|---|---|---|
| 1 | 7.786 | 50.0249 | 924890 |
| 2 | 8.719 | 49.9751 | 923971 |
| | | **100.0000** | **1848861** |

**Chiral Epoxide**



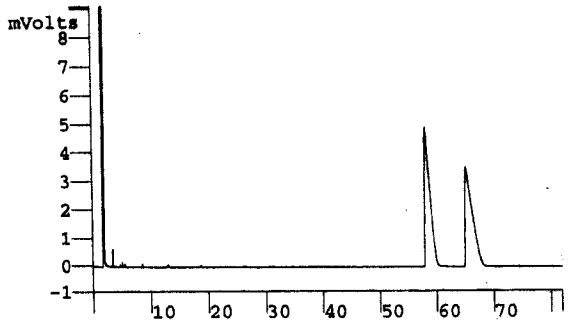

| Peak No | Ret. Time (min) | Result () | Area (counts) |
|---|---|---|---|
| 1 | 7.901 | 95.6605 | 1013522 |
| 2 | 8.901 | 4.3395 | 45977 |
| | | **100.0000** | **1059499** |

**Table 5.6, Entry 7**



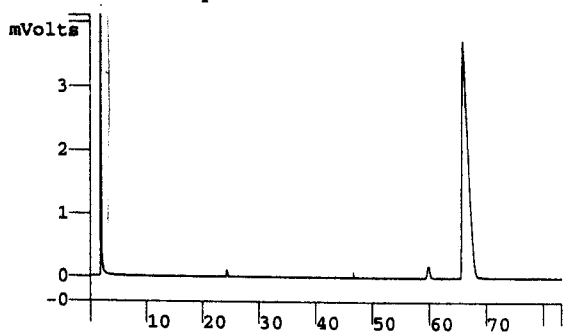
**GC Cond.:** **Column:** Chiraldex B-DM (Cat. No. 77023), Adv. Separation Technologies, Inc.
**Oven:** 110 °C; **Carrier:** Helium, head pressure 20 psi; **Detection:** FID 250 °C

**Racemate**



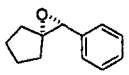

| Peak No | Peak Name | Result () | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 50.5482 | 58.069 | 319385 |
| 2 | | 49.4518 | 65.256 | 312458 |
| | **Totals** | **100.0000** | | **631843** |

**Chiral Epoxide**



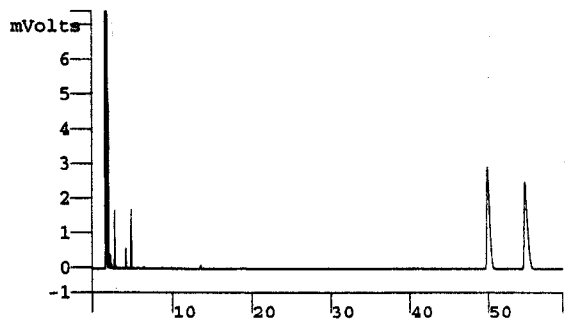

| Peak No | Peak Name | Result () | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 1.9166 | 59.787 | 5181 |
| 2 | | 98.0834 | 65.827 | 265155 |
| | **Totals** | **100.0000** | | **270336** |

**Table 5.6, Entry 8**



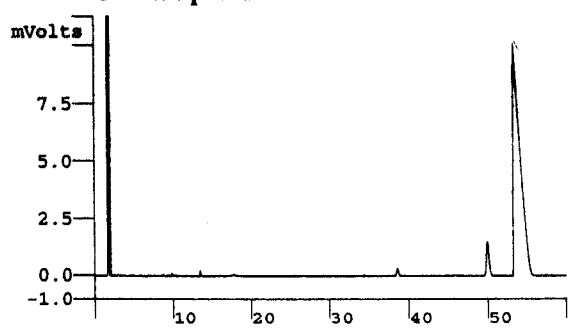
**GC Cond.:** **Column:** Chiraldex B-DM (Cat. No. 77023), Adv. Separation Technologies, Inc.
**Oven:** 100 °C; **Carrier:** Helium, head pressure 20 psi; **Detection:** FID 250 °C

**Racemate**



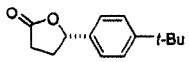

| Peak No | Peak Name | Result () | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 49.6437 | 49.916 | 73367 |
| 2 | | 50.3563 | 54.688 | 74420 |
| | **Totals** | **100.0000** | | **147787** |

**Chiral Epoxide**



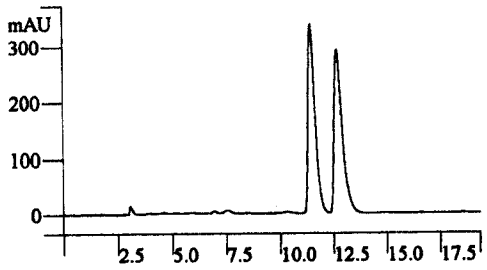

| Peak No | Peak Name | Result () | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 4.9804 | 49.951 | 32480 |
| 2 | | 95.0196 | 53.323 | 619691 |
| | **Totals** | **100.0000** | | **652171** |

**Table 5.6, Entry 9**



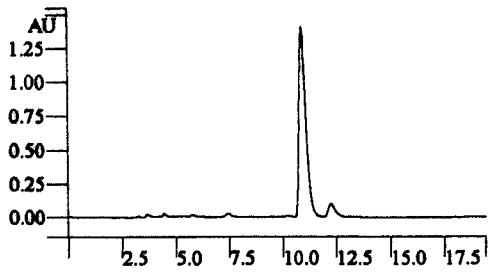

**HPLC Cond.:** **Column:** Chiralcel OD (Column No. OD00CE-DL010), Chiral Technologies, Inc.
**Eluent:** Hexanes/IPA (90/10); **Flow Rate:** 1.0mL/min; **Detection:** UV 220 nm

**Racemate**



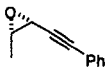

| Peak No | Ret. Time (min) | Result () | Area (counts) |
|---|---|---|---|
| 1 | 11.471 | 49.8700 | 4048501 |
| 2 | 12.704 | 50.1300 | 4069601 |
| | | **100.0000** | **8118102** |

**Chiral Epoxide**



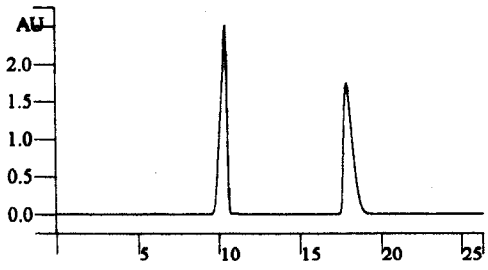

| Peak No | Ret. Time (min) | Result () | Area (counts) |
|---|---|---|---|
| 1 | 10.879 | 93.1628 | 16322941 |
| 2 | 12.238 | 6.8372 | 1197942 |
| | | **100.0000** | **17520884** |

**Table 5.6, Entry 10**



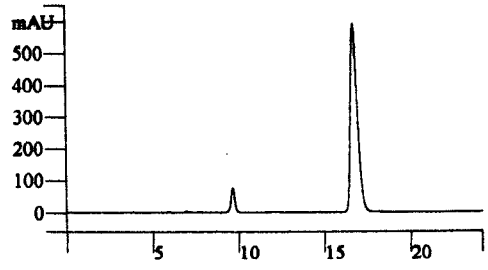

**HPLC Cond.:** **Column:** Chiralcel OD (Column No. OD00CE-DL010), Chiral Technologies, Inc.
**Eluent:** Hexanes/IPA (96/4); **Flow Rate:** 1.0mL/min; **Detection:** UV 254 nm

**Racemate**



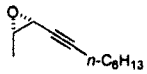

| Peak No | Ret. Time (min) | Result () | Area (counts) |
|---|---|---|---|
| 1 | 10.399 | 49.3402 | 34150416 |
| 2 | 17.862 | 50.6598 | 35063752 |
| | | **100.0000** | **69214168** |

**Chiral Epoxide**



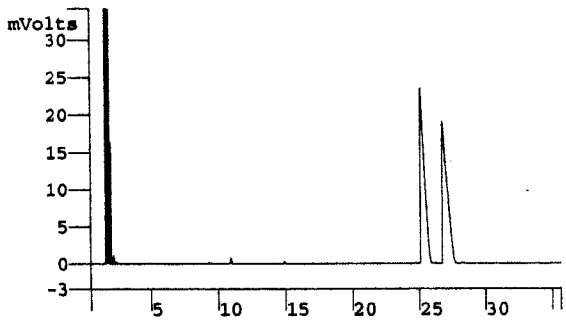

| Peak No | Ret. Time (min) | Result () | Area (counts) |
|---|---|---|---|
| 1 | 9.649 | 5.8764 | 567739 |
| 2 | 16.698 | 94.1236 | 9093566 |
| | | **100.0000** | **9661305** |

**Table 5.6, Entry 11**



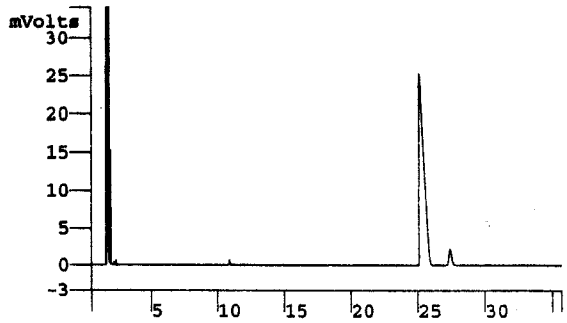

**GC Cond.:** **Column:** Chiraldex B-DM (Cat. No. 77023), Adv. Separation Technologies, Inc.
**Oven:** 10 0 °C; **Carrier:** Helium, head pressure 20 psi; **Detection:** FID 250 °C

**Racemate**



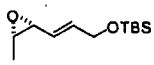

| Peak No | Peak Name | Result () | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 50.1930 | 25.129 | 495145 |
| 2 | | 49.8070 | 26.796 | 491338 |
| | **Totals** | **100.0000** | | **986483** |

**Chiral Epoxide**



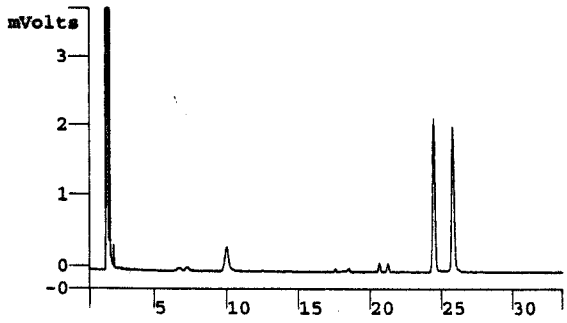

| Peak No | Peak Name | Result () | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 94.9904 | 25.139 | 596376 |
| 2 | | 5.0096 | 27.409 | 31452 |
| | **Totals** | **100.0000** | | **627828** |

**Table 5.6, Entry 12**



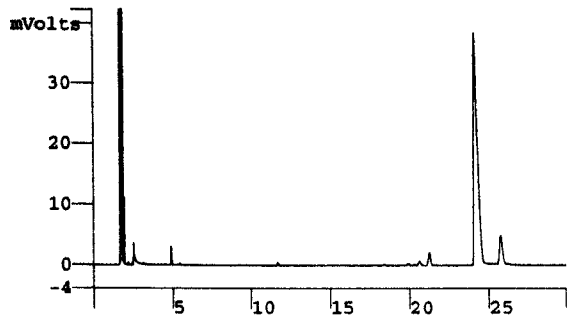

**GC Cond.:** **Column:** Chiraldex B-DM (Cat. No. 77023), Adv. Separation Technologies, Inc.
**Oven:** 110 °C; **Carrier:** Helium, head pressure 20 psi; **Detection:** FID 250 °C

**Racemate**



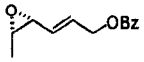

| Peak No | Peak Name | Result () | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 49.8737 | 24.469 | 24316 |
| 2 | | 50.1263 | 25.791 | 24439 |
| | **Totals** | **100.0000** | | **48755** |

**Chiral Epoxide**



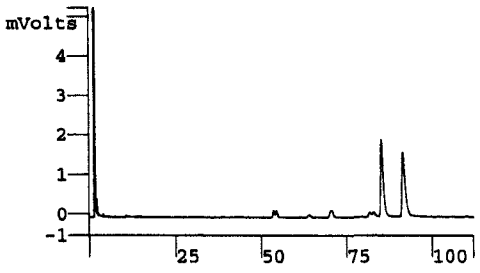

| Peak No | Peak Name | Result () | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 91.1583 | 24.099 | 623515 |
| 2 | | 8.8417 | 25.726 | 60476 |
| | **Totals** | **100.0000** | | **683991** |

**Table 5.6, Entry 13**



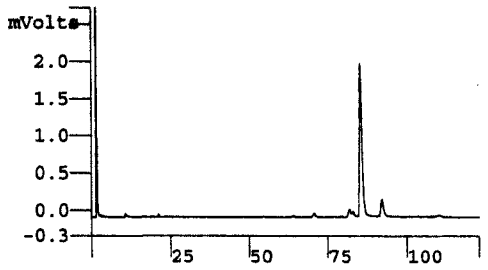

**GC Cond.:** **Column:** Chiraldex B-DM (Cat. No. 77023), Adv. Separation Technologies, Inc.
**Oven:** 130 °C; **Carrier:** Helium, head pressure 25 psi; **Detection:** FID 250 °C

**Racemate**



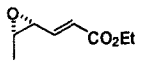

| Peak No | Peak Name | Result () | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 50.1045 | 85.154 | 106503 |
| 2 | | 49.8955 | 91.359 | 106059 |
| | **Totals** | **100.0000** | | **212562** |

**Chiral Epoxide**



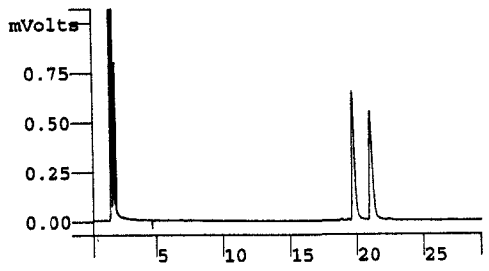

| Peak No | Peak Name | Result () | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 89.7930 | 85.181 | 116179 |
| 2 | | 10.2070 | 92.131 | 13206 |
| | **Totals** | **100.0000** | | **129385** |

**Table 5.6, Entry 14**



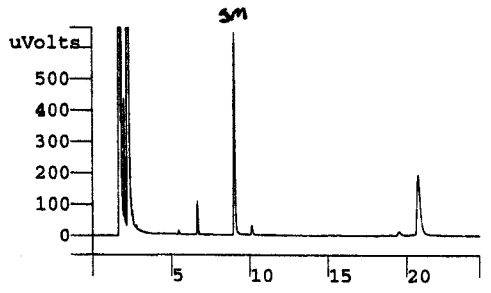

**GC Cond.:** **Column:** Chiraldex B-DM (Cat. No. 77023), Adv. Separation Technologies, Inc.
**Oven:** 90 °C; **Carrier:** Helium, head pressure 20 psi; **Detection:** FID 250 °C

**Racemate**



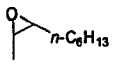

| Peak No | Peak Name | Result () | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 50.1996 | 19.686 | 9444 |
| 2 | | 49.8004 | 20.991 | 9369 |
| | **Totals** | **100.0000** | | **18813** |

**Chiral Epoxide**



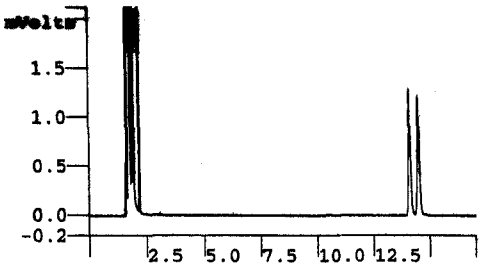

| Peak No | Peak Name | Result () | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 6.3239 | 19.501 | 191 |
| 2 | | 93.6761 | 20.714 | 2834 |
| | **Totals** | **100.0000** | | **3025** |

**Table 6.6, Entry 1**



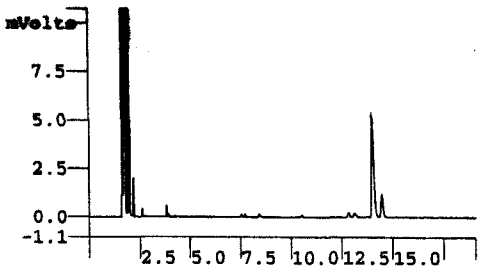
**GC Cond.:** **Column:** Chiraldex B-DM (Cat. No. 77023), Adv. Separation Technologies, Inc.
**Oven:** 80 °C; **Carrier:** Helium, head pressure 20 psi; **Detection:** FID 250 °C

**Racemate**



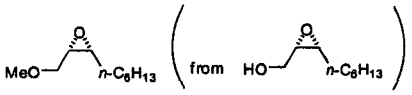

| Peak No | Peak Name | Result () | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 50.0425 | 14.084 | 8486 |
| 2 | | 49.9575 | 14.474 | 8471 |
| | **Totals** | **100.0000** | | **16957** |

**Chiral Epoxide**



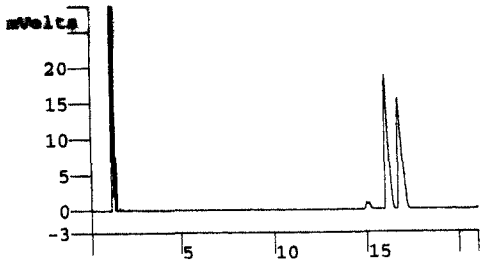

| Peak No | Peak Name | Result () | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 82.2115 | 13.974 | 42358 |
| 2 | | 17.7885 | 14.454 | 9165 |
| | **Totals** | **100.0000** | | **51523** |

**Table 6.6, Entry 2**



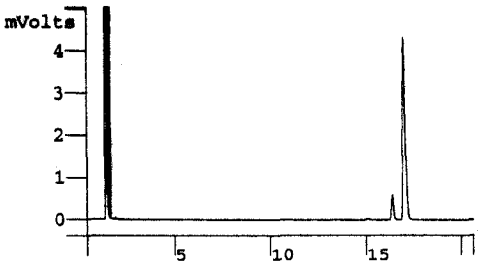

**GC Cond.:** **Column:** Chiraldex B-DM (Cat. No. 77023), Adv. Separation Technologies, Inc.
**Oven:** 100 °C; **Carrier:** Helium, head pressure 25 psi; **Detection:** FID 250 °C

**Racemate**



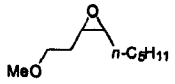

| Peak No | Peak Name | Result () | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 50.1029 | 15.993 | 241063 |
| 2 | | 49.8971 | 16.704 | 240073 |
| | **Totals** | **100.0000** | | **481136** |

**Chiral Epoxide**



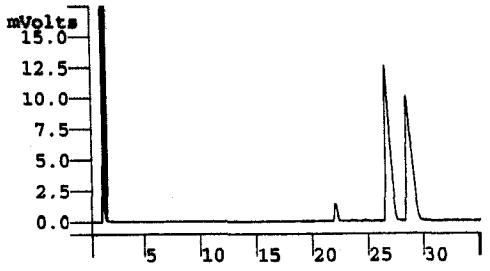

| Peak No | Peak Name | Result () | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 10.6625 | 16.399 | 4829 |
| 2 | | 89.3375 | 16.993 | 40460 |
| | **Totals** | **100.0000** | | **45289** |

**Table 6.6, Entry 3**



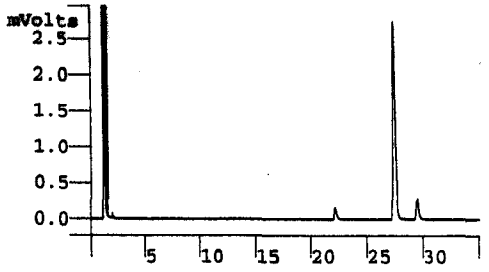

**GC Cond.:** **Column:** Chiraldex B-DM (Cat. No. 77023), Adv. Separation Technologies, Inc.
**Oven:** 90 °C; **Carrier:** Helium, head pressure 25 psi; **Detection:** FID 250 °C

**Racemate**



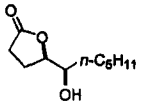

| Peak No | Peak Name | Result () | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 49.9996 | 26.561 | 361435 |
| 2 | | 50.0004 | 28.426 | 361441 |
| | **Totals** | **100.0000** | | **722876** |

**Chiral Epoxide**



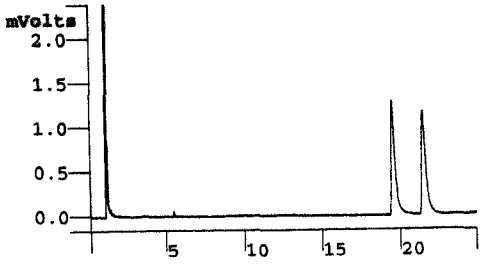

| Peak No | Peak Name | Result () | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 91.0449 | 27.356 | 45555 |
| 2 | | 8.9551 | 29.496 | 4481 |
| | **Totals** | **100.0000** | | **50036** |

**Table 6.6, Entry 4**



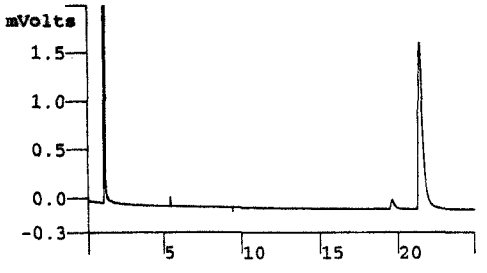

**GC Cond.:** **Column:** Chiraldex B-DM (Cat. No. 77023), Adv. Separation Technologies, Inc.
**Oven:** 150 °C; **Carrier:** Helium, head pressure 30 psi; **Detection:** FID 250 °C

**Racemate**



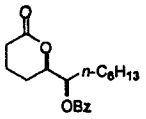

| Peak No | Peak Name | Result () | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 50.2131 | 19.481 | 21935 |
| 2 | | 49.7869 | 21.461 | 21749 |
| | **Totals** | **100.0000** | | **43684** |

**Chiral Epoxide**



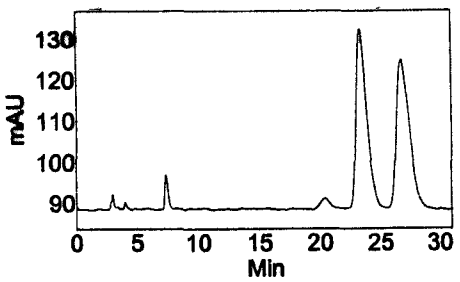

| Peak No | Peak Name | Result () | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 4.5135 | 19.601 | 1661 |
| 2 | | 95.4865 | 21.381 | 35146 |
| | **Totals** | **100.0000** | | **36807** |

**Table 6.6, Entry 5**



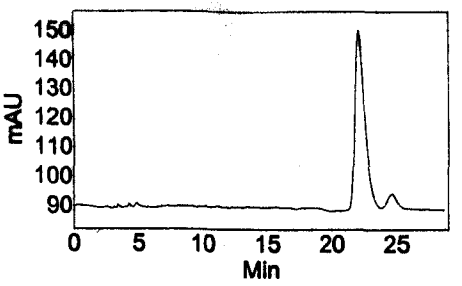

**HPLC Cond.:** **Column:** Chiralpak AD (Column No. AD00CE-EA001), Chiral Technologies, Inc.
**Eluent:** Hexanes/IPA (95/5); **Flow Rate:** 1.0mL/min; **Detection:** UV 254 nm

**Racemate**



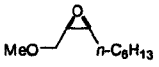

| Index | Time [Min] | Area % [%] |
|---|---|---|
| 1 | 23.38 | 49.599 |
| 2 | 26.79 | 50.401 |
| | | |
| Total | | 100.000 |

**Chiral Epoxide**



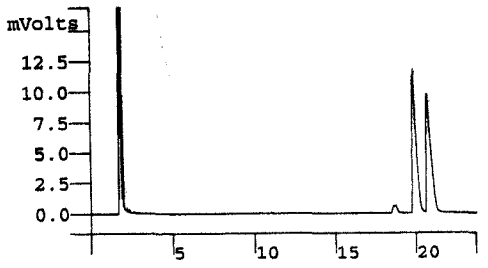

| Index | Time [Min] | Area % [%] |
|---|---|---|
| 1 | 22.08 | 92.965 |
| 2 | 24.66 | 7.035 |
| | | |
| Total | | 100.000 |

**Table 6.6, Entry 6**



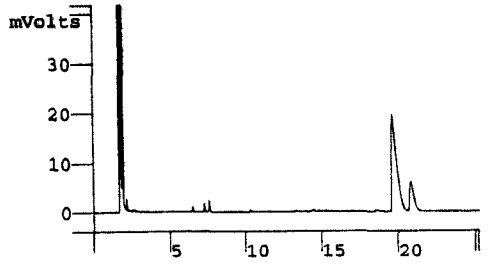

**GC Cond.:** **Column:** Chiraldex B-DM (Cat. No. 77023), Adv. Separation Technologies, Inc.
**Oven:** 100 °C; **Carrier:** Helium, head pressure 20 psi; **Detection:** FID 250 °C

**Racemate**



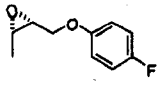

| Peak No | Peak Name | Result () | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 50.2079 | 19.811 | 195741 |
| 2 | | 49.7921 | 20.691 | 194119 |
| | **Totals** | **100.0000** | | **389860** |

**Chiral Epoxide**



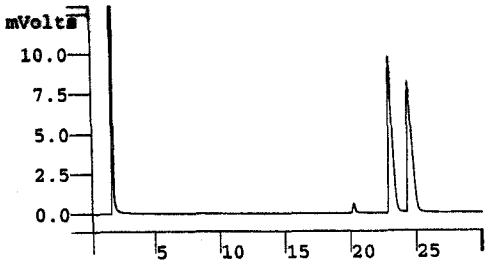

| Peak No | Peak Name | Result () | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 80.3602 | 19.608 | 453703 |
| 2 | | 19.6398 | 20.788 | 110883 |
| | **Totals** | **100.0000** | | **564586** |

**Table 6.6, Entry 7**



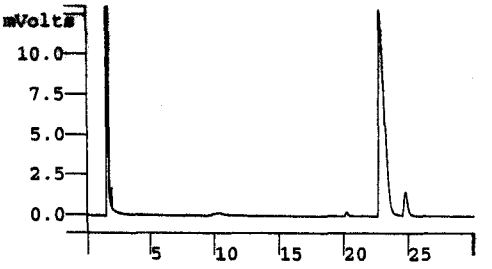
**GC Cond.:** **Column:** Chiraldex B-DM (Cat. No. 77023), Adv. Separation Technologies, Inc.
**Oven:** 115 °C; **Carrier:** Helium, head pressure 20 psi; **Detection:** FID 250 °C

**Racemate**



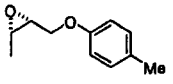

| Peak No | Peak Name | Result () | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 50.1167 | 22.964 | 210856 |
| 2 | | 49.8833 | 24.419 | 209874 |
| | **Totals** | **100.0000** | | **420730** |

**Chiral Epoxide**



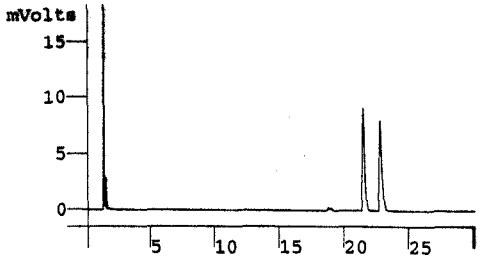

| Peak No | Peak Name | Result () | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 92.8040 | 22.819 | 370004 |
| 2 | | 7.1960 | 24.788 | 28690 |
| | **Totals** | **100.0000** | | **398694** |

**Table 6.6, Entry 8**



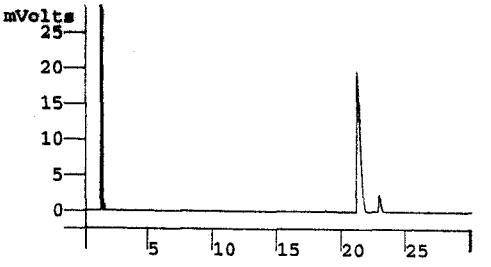
**GC Cond.:** **Column:** Chiraldex B-DM (Cat. No. 77023), Adv. Separation Technologies, Inc.
**Oven:** 120 °C; **Carrier:** Helium, head pressure 25 psi; **Detection:** FID 250 °C

**Racemate**



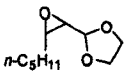

| Peak No | Peak Name | Result () | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 49.8455 | 21.450 | 117363 |
| 2 | | 50.1545 | 22.767 | 118090 |
| | **Totals** | **100.0000** | | **235453** |

**Chiral Epoxide**



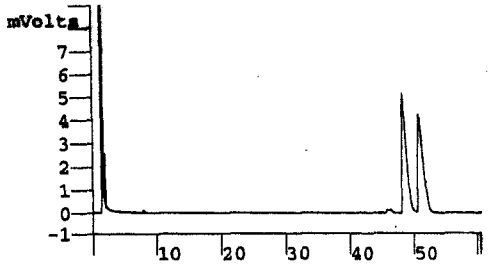

| Peak No | Peak Name | Result () | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 92.3549 | 21.208 | 365935 |
| 2 | | 7.6451 | 22.952 | 30292 |
| | **Totals** | **100.0000** | | **396227** |

**Table 6.6, Entry 9**



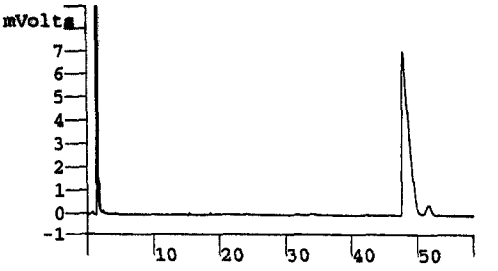
**GC Cond.:** **Column:** Chiraldex B-DM (Cat. No. 77023), Adv. Separation Technologies, Inc.
**Oven:** 100 °C; **Carrier:** Helium, head pressure 25 psi; **Detection:** FID 250 °C

**Racemate**



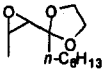

| Peak No | Peak Name | Result () | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| | | | | Minutes |
| 1 | | 50.0789 | 48.309 | 239218 |
| 2 | | 49.9211 | 50.779 | 238464 |
| | **Totals** | **100.0000** | | **477682** |

**Chiral Epoxide**



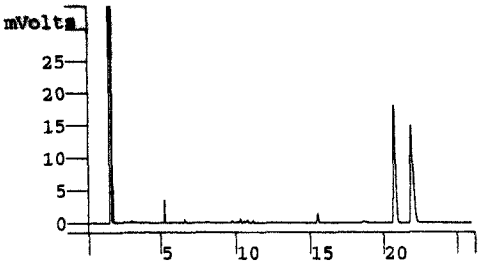

| Peak No | Peak Name | Result () | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| | | | | Minutes |
| 1 | | 95.9749 | 47.816 | 475675 |
| 2 | | 4.0251 | 51.604 | 19949 |
| | **Totals** | **100.0000** | | **495624** |

**Table 6.6, Entry 10**



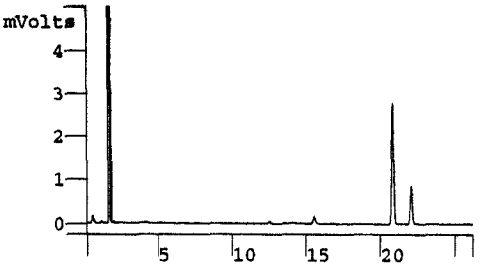
**GC Cond.:** **Column:** Chiraldex B-DM (Cat. No. 77023), Adv. Separation Technologies, Inc.
**Oven:** 120 °C; **Carrier:** Helium, head pressure 20 psi; **Detection:** FID 250 °C

**Racemate**



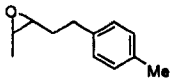

| Peak No | Peak Name | Result () | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| | | | | Minutes |
| 1 | | 50.1088 | 20.711 | 187738 |
| 2 | | 49.8912 | 21.872 | 186923 |
| | **Totals** | **100.0000** | | **374661** |

**Chiral Epoxide**



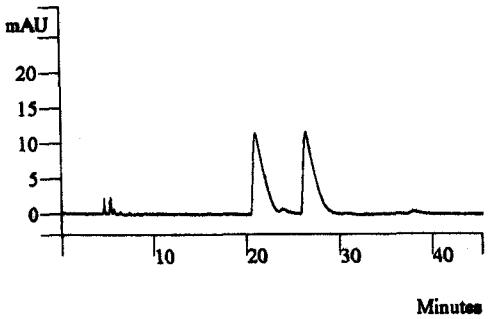

| Peak No | Peak Name | Result () | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| | | | | Minutes |
| 1 | | 75.4483 | 20.841 | 26254 |
| 2 | | 24.5516 | 22.094 | 8543 |
| | **Totals** | **99.9999** | | **34797** |

**Table 6.6, Entry 11**



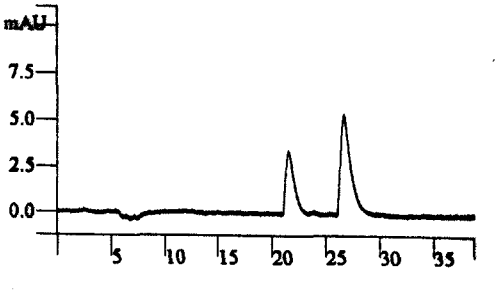

**HPLC Cond.:** **Column:** Chiralcel OD (Column No. OD00CE-DL010), Chiral Technologies, Inc.
**Eluent:** Hexanes/IPA (99/1); **Flow Rate:** 1.0mL/min; **Detection:** UV 270 nm

**Racemate**




| Peak No | Ret. Time (min) | Result () | Area (counts) |
|---|---|---|---|
| 1 | 20.948 | 50.1751 | 460432 |
| 2 | 26.406 | 49.8249 | 457218 |
| | | **100.0000** | **917650** |

**Chiral Epoxide**

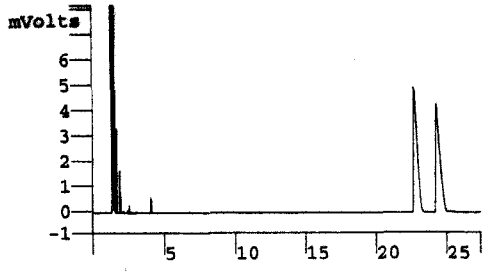



| Peak No | Ret. Time (min) | Result () | Area (counts) |
|---|---|---|---|
| 1 | 21.484 | 33.8965 | 93424 |
| 2 | 26.584 | 66.1035 | 182192 |
| | | **100.0000** | **275616** |

**Table 6.6, Entry 12**

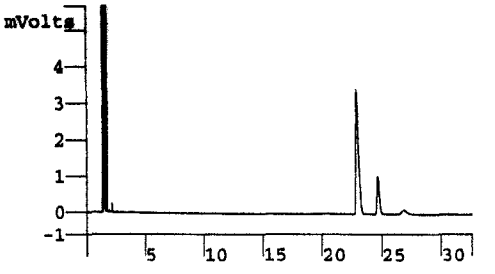
**GC Cond.:** **Column:** Chiraldex B-DM (Cat. No. 77023), Adv. Separation Technologies, Inc.
**Oven:** 90 °C; **Carrier:** Helium, head pressure 25 psi; **Detection:** FID 250 °C

**Racemate**




| Peak No | Peak Name | Result () | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 50.1116 | 22.677 | 91814 |
| 2 | | 49.8884 | 24.259 | 91405 |
| | **Totals** | **100.0000** | | **183219** |

**Chiral Epoxide**




| Peak No | Peak Name | Result () | Ret. Time (min) | Area (counts) |
|---|---|---|---|---|
| 1 | | 79.3262 | 22.869 | 53352 |
| 2 | | 20.6738 | 24.654 | 13905 |
| | **Totals** | **100.0000** | | **67257** |

# BIOSKETCH

Christopher Patrick Burke was born on September 7, 1978, in Sioux Falls, South Dakota. He received his B.A. from Augustana College in Sioux Falls, South Dakota in 2001 while working on the synthesis of novel biodegradable surfactants under the direction of Professor Gary W. Earl. He then joined the research group of Professor Yian Shi at Colorado State University where he studied chiral ketone-catalyzed asymmetric epoxidation of *cis*-olefins. After completing his graduate work in the spring of 2007 he joined Professor Dale L. Boger's research group as a post-doctoral researcher at the Scripps Research Institute in La Jolla, California.