THESIS

THE DEVELOPMENT OF *N*-HETEROCYCLIC CARBENES FOR APPLICATION IN

THE INTERMOLECULAR STETTER REACTION

Submitted by

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ABSTRACT

THE DEVELOPMENT OF *N*-HETEROCYCLIC CARBENES FOR APPLICATION IN THE

INTERMOLECULAR STETTER REACTION

An *N*-heterocyclic carbene scaffold has been developed containing a protected oxygen moiety in the backbone. The oxygen provides a similar electronic effect known to fluorinated analogues, and also has the potential to be modulated via substitution. This substitution introduces steric differentiation distil to the reaction site and electronic manipulation of the calculated catalyst substrate interaction. A short synthesis has been designed with an intermediate that allows for divergent manipulation of the oxygen substituent. The resultant carbenes catalyze the intermolecular Stetter reaction with similar yields and enantioselectivities to those observed with previously designed catalysts with only fluorine substitution.

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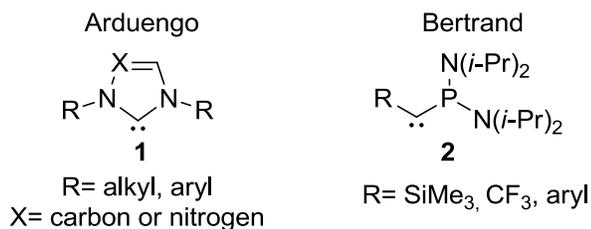The Development of *N*-Heterocyclic Carbenes for Application in the Intermolecular Stetter Reaction

THE DEVELOPMENT OF *N*-HETEROCYCLIC CARBENES FOR APPLICATION IN THE

INTERMOLECULAR STETTER REACTION

1.1 **Introduction**

Isolation of the first stable *N*-heterocyclic carbenes (NHCs) independently by Arduengo[1] and Bertrand[2] opened a new field of organic chemistry (scheme 1). Prior to their pioneering work, evidence for carbenes was largely theoretical. Wanzlick had established nucleophilic carbenes as a reactive species in the 1960s but was unable to isolate them due to their inherent reactivity.[3] Since their initial isolation, carbenes have been used in a variety of transformations. The ability of NHCs to act as ligands for transition metal species has impacted the field of organometallic chemistry.[4] Carbenes also show the ability to act independently as organocatalysts in a variety of transformations.[5]

Scheme 1.

Arduengo

1

R= alkyl, aryl
X= carbon or nitrogen

Bertrand

$N(i\text{-Pr})_2$

$R \quad P$

$N(i\text{-Pr})_2$

2

R= SiMe$_3$, CF$_3$, aryl

N-Heterocyclic carbenes are neutral molecules that feature a divalent carbon atom with only six valence electrons (scheme 2). Their unique reactivity is derived from a nonbonding pair of electrons and an empty orthogonal *p*-orbital. The nonbonding electron pair can be either spin paired in the singlet state (**4**) or unpaired in the triplet state (**5**). While both states are highly reactive, the triplet state is much higher in energy and not often invoked in organocatalytic reactions.

Scheme 2.

X Y
••
X= N
Y= N or S $\equiv$

Singlet   Triplet

3   **4**   **5**
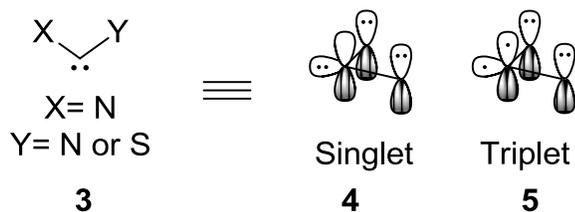
The reactivity of carbenes is influenced by the electronic nature of the lone pair. The stability of carbenes is attributed to both steric and electronic factors. The empty *p*-orbital is stabilized by donation of electron density from the heteroatom's lone pairs. Steric bulk, often from the substituent on the nitrogen atom near the carbene center provides kinetic stability. Both alkyl and aryl substitution has been used for stable carbenes; a mix of these factors is responsible for their overall stability.[6]
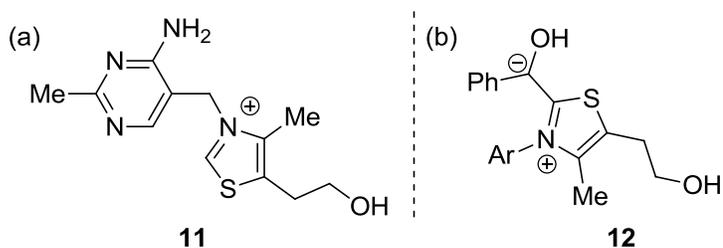
1.2 **The Benzoin Reaction**

N-Heterocyclic carbenes catalyze reactions through several different pathways. The most common is the conversion of normally electrophilic aldehydes into nucleophilic species. This inversion of reactivity, termed umpolung reactivity,[7] can stoichiometrically or catalytically generate new C-C or C-X bonds. The benzoin reaction is the conventional example of this reactivity. In 1832 Wöhler and Liebig reported the dimerization of benzaldehyde **6** to an α-hydroxy ketone **10** when exposed to cyanide.[8] Lapworth proposed a mechanism for this transformation in 1903, in which he invoked an acyl anion equivalent (**8**).[9]

Scheme 3.
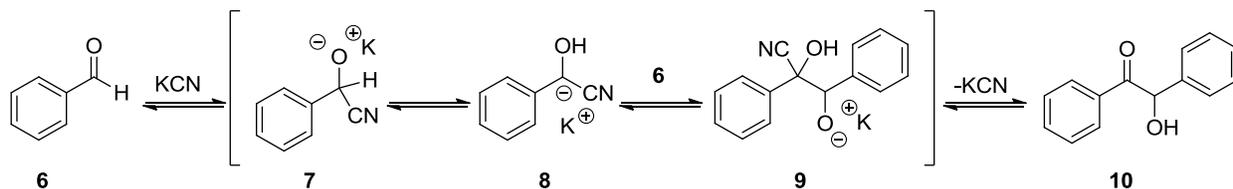
The acyl anion equivalent can also be generated by NHCs. A report by Ukai demonstrated that the thiazolium salt thiamine **11** in the presence of base catalyzes the benzoin reaction presumably through a similar acyl anion equivalent (**12**).[10] This discovery turned out to be pivotal because thiazolium salts could be made with stereocenters and act as enantioselective catalysts.
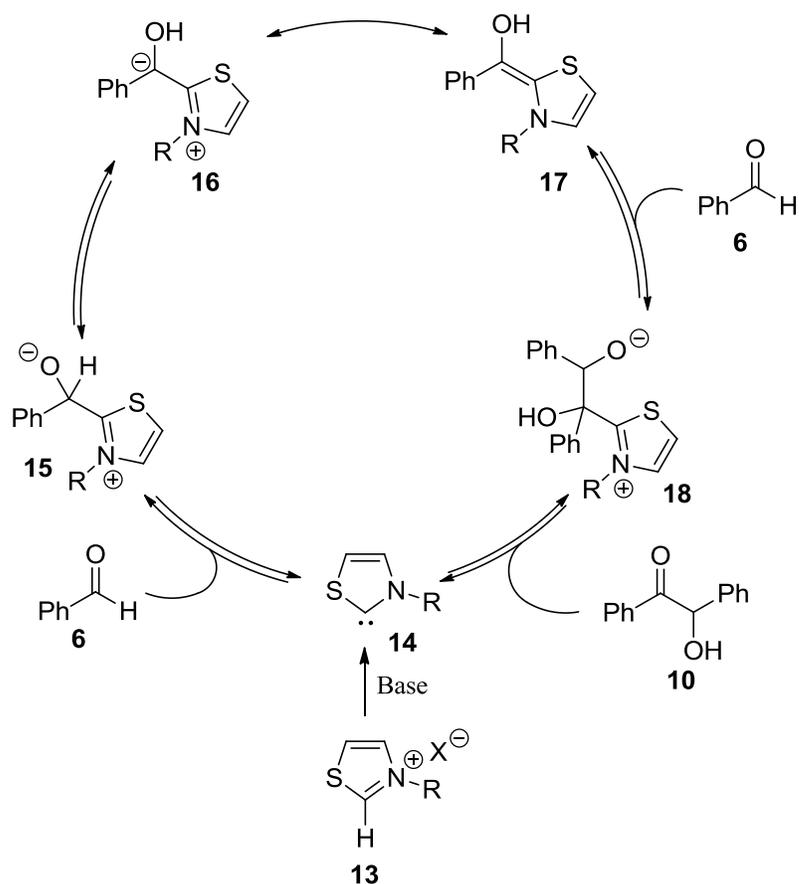
Scheme 4.

Building on Lapworth and Ukai's work, Breslow proposed a mechanism for the carbene catalyzed Benzoin reaction (Scheme 3).[11] Deprotonation of the thiazolium salt precursor **13** generates nucleophilic carbene **14**. Subsequent nucleophilic addition into an aldehyde (**6**) generates the initial tetrahedral intermediate **15**. Proton transfer generates acyl anion equivalent **16** which along with its resonance form **17**, is known as the Breslow intermediate. Nucleophilic attack by the Breslow intermediate into another equivalent of aldehyde generates a second tetrahedral intermediate (**18**) and is the key C-C bond forming event of the reaction. Proton transfer and collapse regenerates the carbene **14** and yields α-hydroxy ketone product **10**. The

mechanism has been shown to be completely reversible in many cases, which poses a significant challenge to enantioselective catalysis.
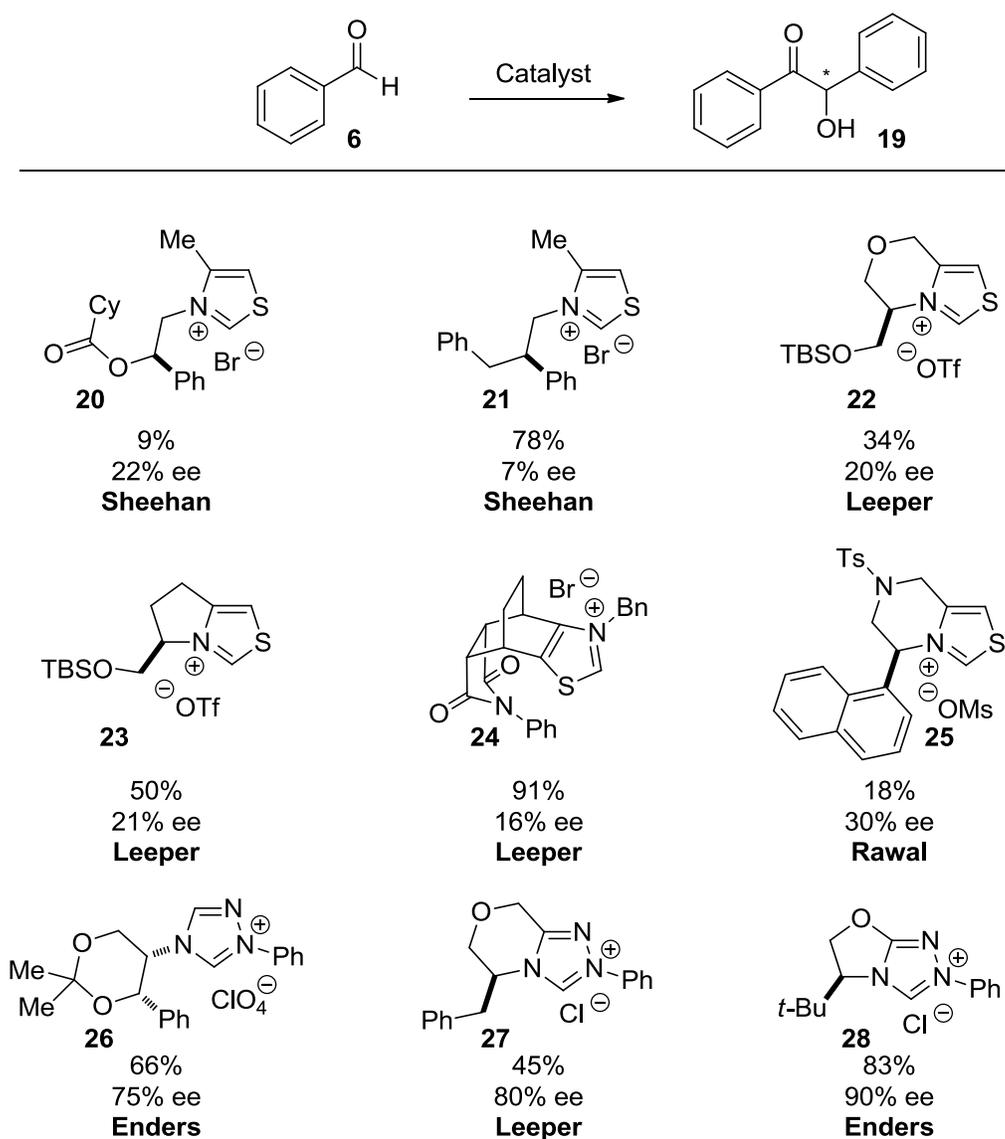
Scheme 5.

In an effort to obtain enantioenriched benzoin products a number of carbene scaffolds have been designed and synthesized. The first asymmetric benzoin reaction was reported by Sheehan (**20**, scheme 4).[12] While modest, the first enantioselective reaction was a powerful proof of concept. Since then, many groups have designed new NHC catalysts in an effort to improve the yield and enantioselectivity of the transformation. Several of these catalysts show conceptual advances that are important steps towards the current state of carbene catalyst design. Sheehan discovered that a catalyst with increased steric bulk around the carbene center **21** could increase reactivity while

the enantioinduction remains low.[13] It was reasoned that the low enatioselectivities were due to the free rotation available to the group containing the stereogenic centers. Subsequently, Leeper and Rawal introduced several catalysts based on fused ring systems designed to reduce the rotation available (**22-25**, scheme 6).[14,15]

Scheme 6.

20	**21**	**22**
9%	78%	34%
22% ee	7% ee	20% ee
Sheehan	**Sheehan**	**Leeper**

23	**24**	**25**
50%	91%	18%
21% ee	16% ee	30% ee
Leeper	**Leeper**	**Rawal**

|		
26	**27**	**28**
66%	45%	83%
75% ee	80% ee	90% ee
Enders	**Leeper**	**Enders**

Enders dramatically increased reactivity and enantioselectivity of the transformation by switching the catalyst scaffold from a thiazolium to a triazolium based carbene **26**.[16] The best results were achieved when the fused bicyclic system was applied to a triazolium scaffold by Leeper (**27**) and Enders (**28**). [17,18]

Triazolium carbenes have the advantage of potential substitution on both sides of the carbene carbon. Additional substitution allows for the occupation of three quadrants about the catalytic center (**29**) whereas a divalent sulfur atom cannot (**30**). Moreover, the additional substituent allows for electronic modulation of the carbene by changing the electronics of the substituent.

Scheme 7.
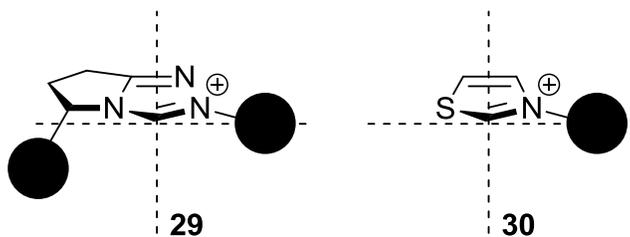
1.3 The Stetter Reaction

Since their initial application in the benzoin reaction, NHCs have also been applied to reactions beyond the benzoin reaction. In the 1970's, Stetter observed a conjugate addition of aldehydes onto Michael acceptors facilitated by cyanide, resulting in 1,4-dicarbonyl products.[19] Stetter also showed that carbenes could also catalyze the reaction, and proposed a mechanism for the transformation. The accepted mechanism is very close to that of the benzoin reaction (scheme 3). Deprotonation of the triazolium salt **31** generates free carbene **32**. Addition of **32** into an aldehyde (**6**) and proton transfer produces the Breslow intermediate **34**, **35** which

undergoes a 1,4-addition into a Michael acceptor **36** to generate tetrahedral intermediate **37**. Proton transfer and collapse results in a 1,4-dicarbonyl compound **38** and again regenerates the free carbene **32**. The 1,4-dicarbonyl product is formed irreversibly, which is a key difference between the two mechanisms.[20]

Scheme 8.
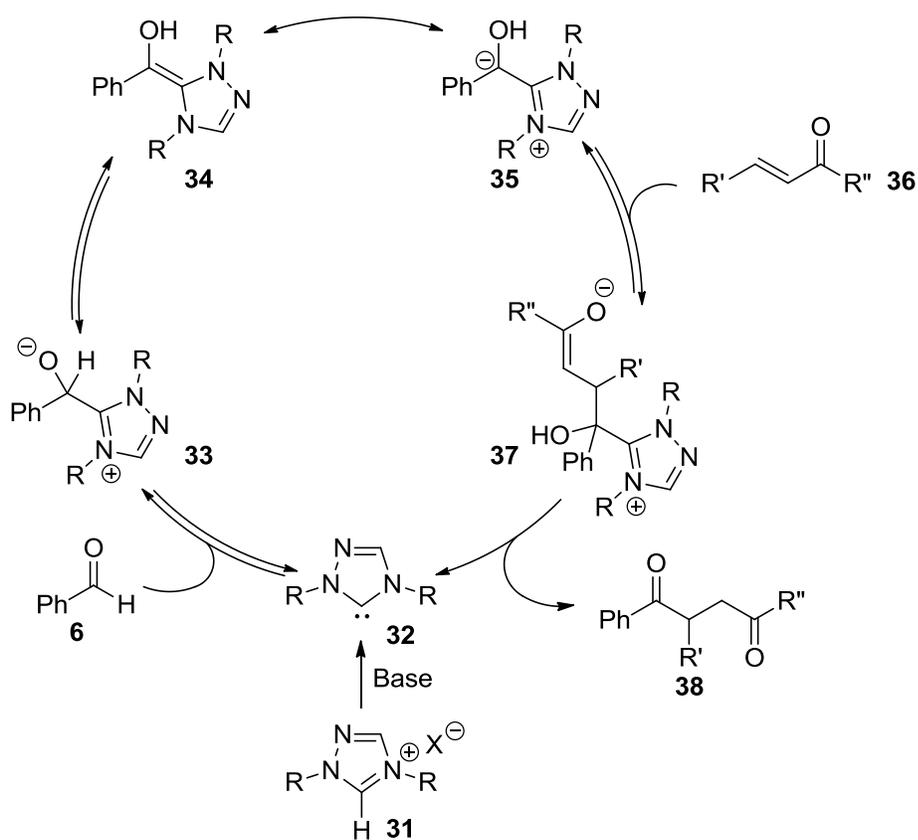
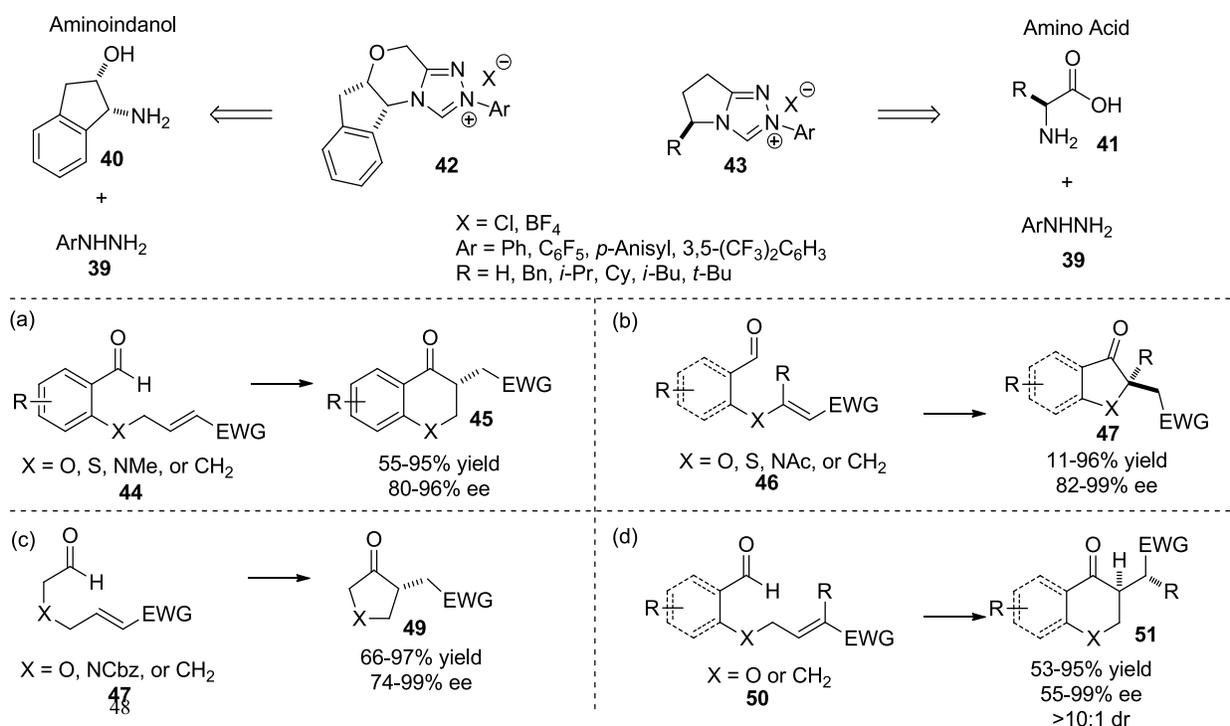## 1.4 Rovis Group Carbene Scaffolds

The Rovis group has developed two chiral triazolium scaffolds: aminoindanol derived (**42**), and amino acid derived (**43**). These two systems were concurrently developed with modularity in mind. The syntheses allow for variation of both the steric environment and the electronic nature of the carbene. The synthesis is simply the condensation of a lactam, hydrazine

and an orthoformate. Modification of the steric environment is achieved by choice of lactam precursor which arises from aminoindanol **40** or an amino acid **41**. The electronic nature of the carbene is largely influenced by the aryl substitution on the nitrogen atom. This substitution can be changed by choice of hydrazine precursor **39**. The aryl group also influences the steric environment near the reaction site.

Scheme 9.

Aminoindanol
40
+
ArNHNH$_2$
39

X = Cl, BF$_4$
Ar = Ph, C$_6$F$_5$, *p*-Anisyl, 3,5-(CF$_3$)$_2$C$_6$H$_3$
R = H, Bn, *i*-Pr, Cy, *i*-Bu, *t*-Bu

Amino Acid
41
+
ArNHNH$_2$
39

(a)
X = O, S, NMe, or CH$_2$
44
55-95% yield
80-96% ee
45

(b)
X = O, S, NAc, or CH$_2$
46
11-96% yield
82-99% ee
47

(c)
X = O, NCbz, or CH$_2$
47
48
66-97% yield
74-99% ee
49

(d)
X = O or CH$_2$
50
53-95% yield
55-99% ee
>10:1 dr
51

New carbene scaffolds were tested in the context of the intramolecular Stetter reaction. Both carbenes were able to give high yields and enantioselectivities across a range of transformations (scheme 9) starting with the synthesis of 4-chromanone products (eq a).[21] This process can also generate quaternary stereocenters (eq b).[22] Aliphatic backbones are tolerated and allowed for the construction of cyclopentanone products (eq c).[23] Subsitution at the α-

position of the Michael acceptor leads to the formation of two contiguous stereocenters in high enantio- and diastereoselectivities (eq d).[24]
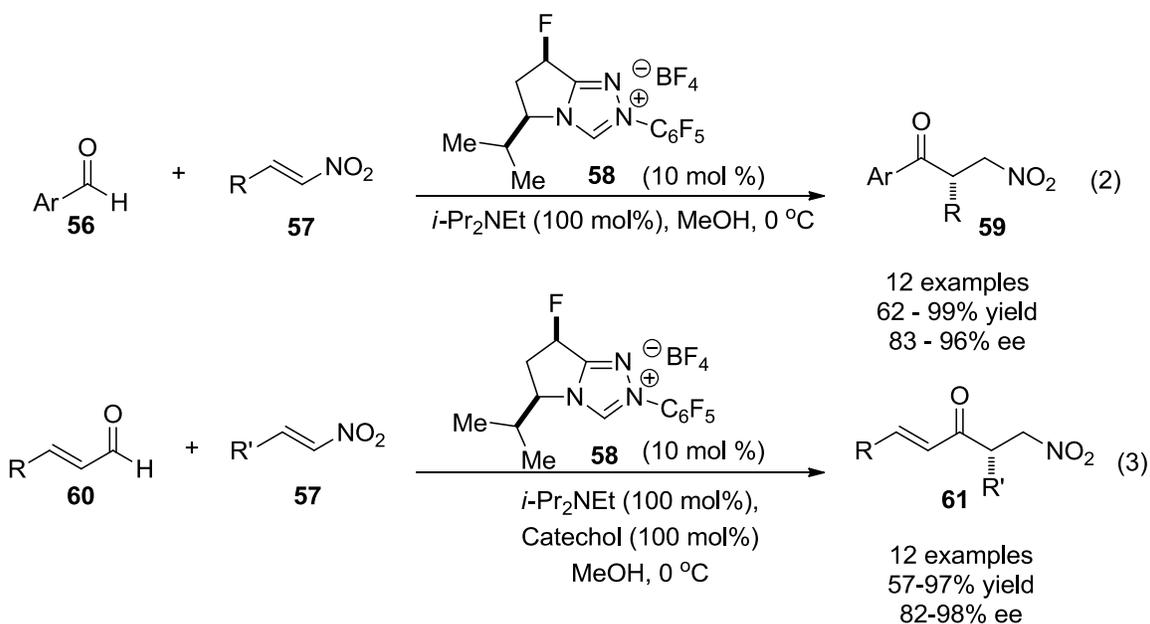
Scheme 9.
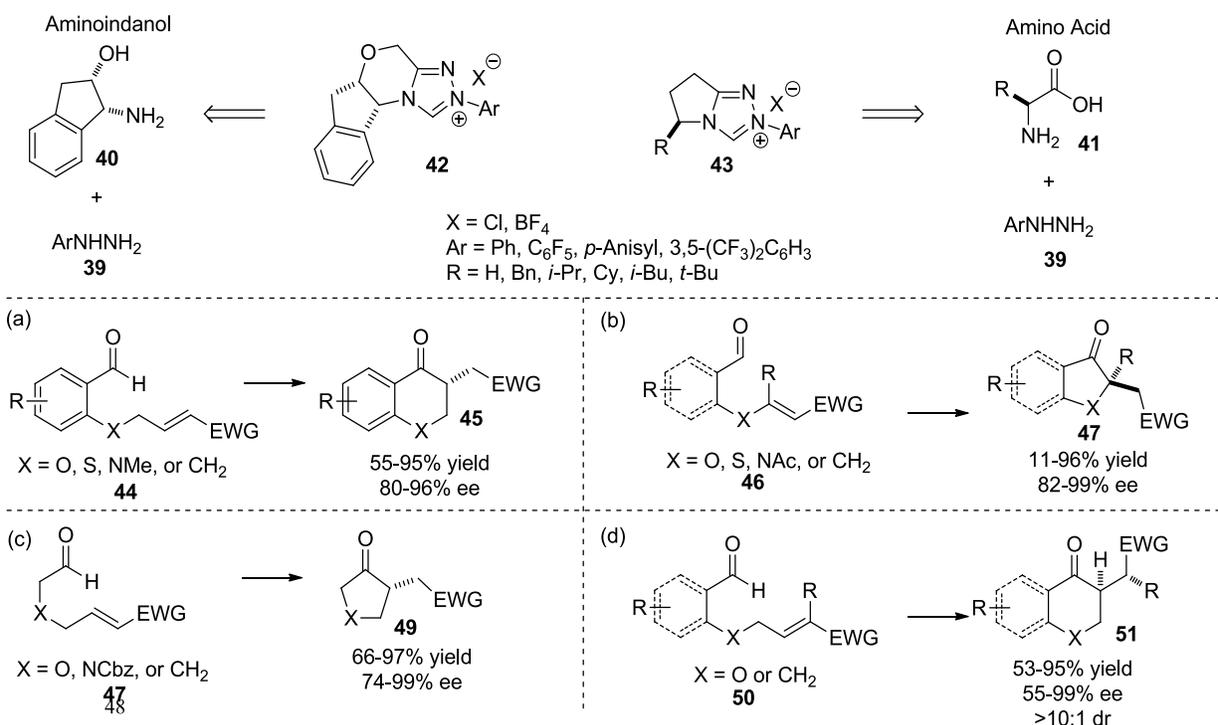
1.5 The Intermolecular Stetter Reaction

The intermolecular Stetter reaction has proven a more challenging reaction to render asymmetric. Enders and co-workers reported an intermolecular Stetter reaction of aryl aldehydes with chalcones albeit in 4% yield and 39% ee.[25] Concurrently the Rovis group reported the Stetter reaction of glyoxamides and alkylidenemalonates (eq 2).[26] Shortly thereafter Enders reported the addition of heteroaromatic aldehydes to arylidenemalonates.[27]

(1)

52   **53**   **54**   **55**

10 examples
68- 97% yield
80-90% ee
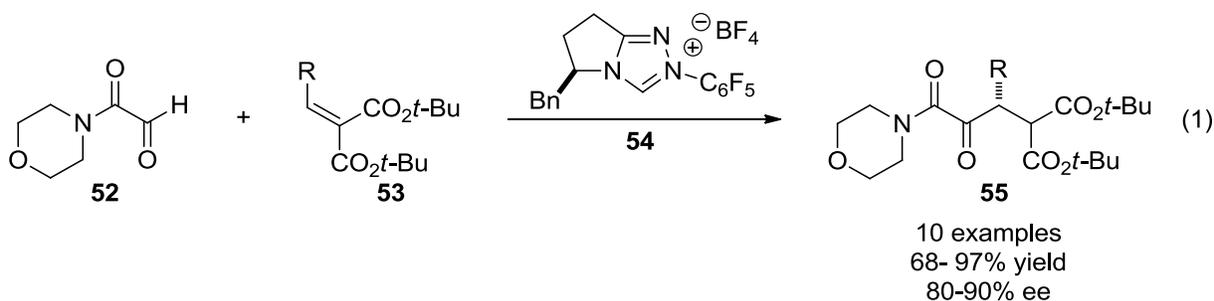
The Rovis group sought to broaden the scope of the reaction as well as improve the utility of the products, leading to the Stetter reaction of heteroaromatic aldehydes (**56**) with nitroalkenes (**57**, eq 3)[28] A subsequent report expanded the scope to include unsaturated aldehydes (**60**) as nucleophiles (eq 4).[29]

(2)

56   **57**   **58** (10 mol %)

i-Pr$_2$NEt (100 mol%), MeOH, 0 °C

59

12 examples
62 - 99% yield
83 - 96% ee

(3)

60   **57**   **58** (10 mol %)

i-Pr$_2$NEt (100 mol%), Catechol (100 mol%) MeOH, 0 °C

61

12 examples
57-97% yield
82-98% ee

After the initial screen an effort was made to increase the enantioselectivity seen with catalyst **65**, but using a more sterically demanding catalyst shut down the reaction (**66**). Without increasing the sterics at the reaction site, another potential method to improve enantioselectivity was a carbene catalyst containing a fluorine atom in the backbone (**58**). Inspired by the effect fluorine substitution has on the ring conformation of pyrrolidines, it was theorized the addition

10

could increase the enantioselectivity.[30] The incorporation of fluorine into the catalyst backbone proved to be quite successful increasing the enantioselectivity from 88 to 95% ee.

Scheme 10.

65	66	58	67
90%, 88% ee	trace, ee nd	95%, 95% ee	93%, 63% ee
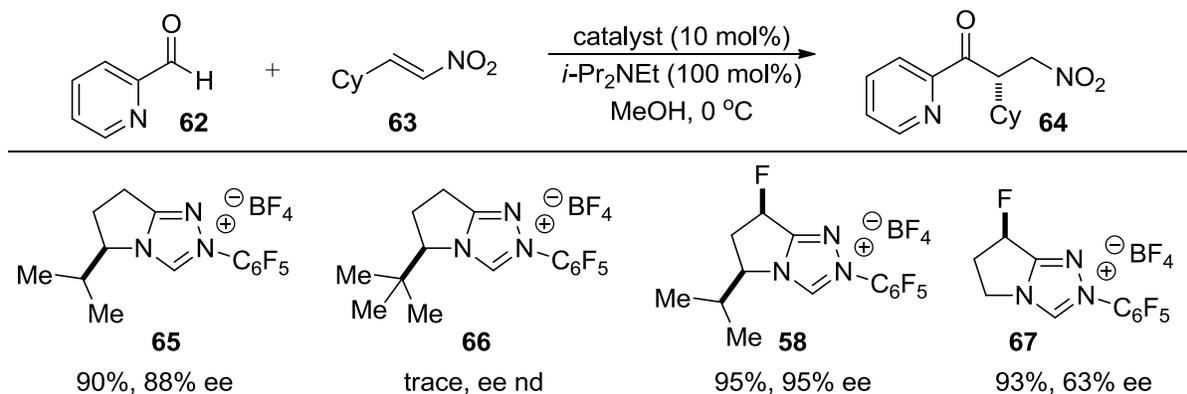
The initial theory for the observed improvement on enantioselectivity is an *exo*-ring conformation induced by the fluorine atom (**68**). An X-ray crystal of the carbene confirmed the presence of the ring pucker in the ground state of the catalyst. The cause of this effect was further explored in conjunction with the Houk group. Their calculations support the theory that fluorine in the backbone induces a strong preference for the *exo*-ring flip in the solid state. However, in the Breslow intermediate the same conformational preference is not present. The high selectivity of the fluorine carbenes was calculated to arise from stabilization of the forming negative charge on the nitro group of the Michael acceptor by the C-F bond σ*-orbital **69**.[31]
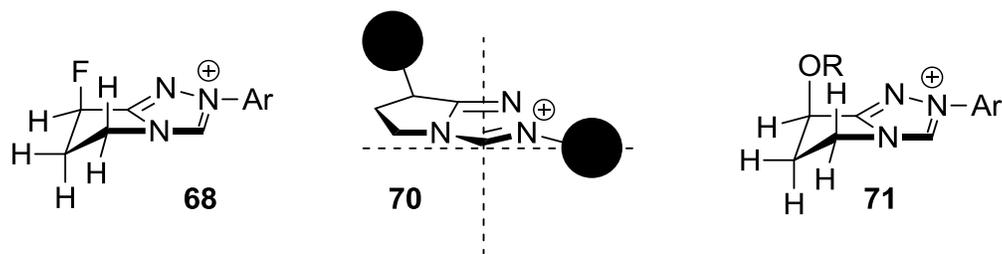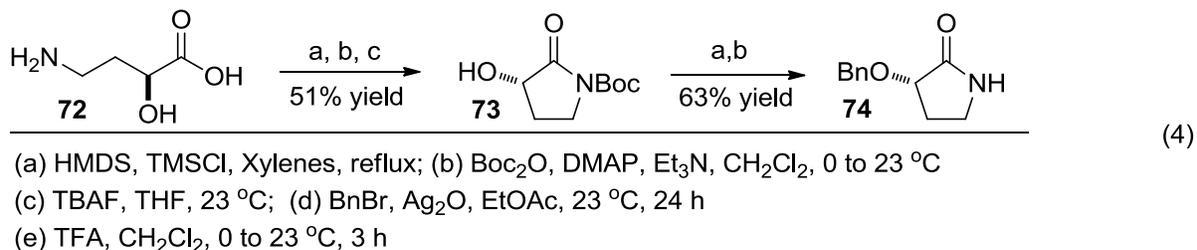
Scheme 11.
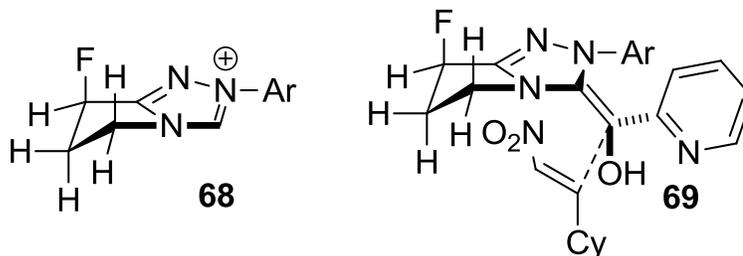
1.6 First Generation Oxygenated Catalyst

During the investigation of fluorinated carbenes it was observed that the catalyst bearing only a fluorine based stereocenter gave remarkable enantioselectivity (**67**, scheme 10). This inspired an investigation into a new series of triazolium catalysts. While electronically different, fluorine (1.47 Å) is similar in size to a hydrogen atom (1.20 Å) and can form only one bond.[32] However, if fluorine was replaced by a similarly electronegative atom which was also divalent it was theorized that a similar electronic stabilization would be maintained in the transition state. In addition there can be opportunity to modify the steric environment (**70**). Oxygen was the first choice to replace fluorine for several reasons. The electronic nature of the C-O σ-bond and subsequently the C-O σ* orbital is similar to a C-F σ-bond. Oxygen is also divalent allowing differential substitution **71**.

Scheme 12.

The synthesis of these new catalysts begins with commercially available (S)-(-)-4-amino-2-hydroxybutyric acid **72**, which can be cyclized and silylated in one step (scheme 13). The crude lactam is then taken through two protecting group modifications, which yield the Boc protected lactam with a free hydroxyl group **72**. This intermediate is bench stable white solid, and serves as a branch point from which multiple different protecting groups can be installed.

(a) HMDS, TMSCl, Xylenes, reflux; (b) Boc$_2$O, DMAP, Et$_3$N, CH$_2$Cl$_2$, 0 to 23 ^{o}C
(c) TBAF, THF, 23 ^{o}C; (d) BnBr, Ag$_2$O, EtOAc, 23 ^{o}C, 24 h
(e) TFA, CH$_2$Cl$_2$, 0 to 23 ^{o}C, 3 h

(4)

Protection of the alcohol by formation of the alkoxide and subsequent reaction with an electrophile such as benzyl bromide or iodomethane led to decomposition of the lactam starting material **73**. Installation of a benzyl group proceeds with silver (I) oxide and benzyl bromide.[33] Boc deprotection is rapid with trifluoroacetic acid and results in the lactam **74**. Conditions previously optimized by the Rovis group for triazolium salt formation from lactams were applied to lactam **74** in a one pot three step procedure and resulted in triazolium salt **77**.[34]

Scheme 13.

(a) Me₃O⁺BF₄⁻, CH₂Cl₂, 23 °C; (b) C₆F₅NHNH₂, CH₂Cl₂, reflux; (c) CH(OMe)₃, PhCl, reflux
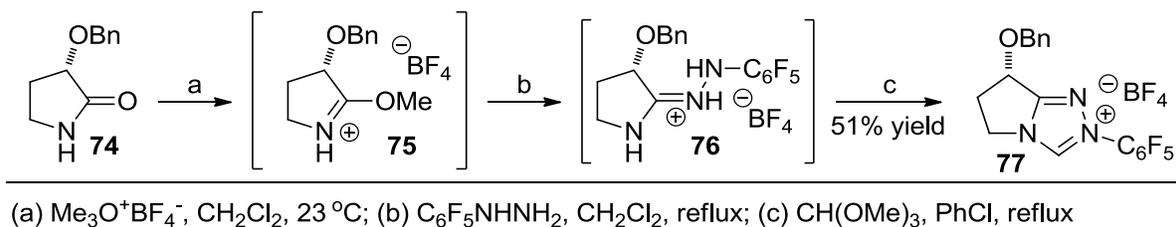
An X-ray crystal structure of the triazolium salt **77** was obtained. As in many of our other catalysts the aryl subtituent on the nitrogen is rotated out of the plane defined by the bicyclic system. Similar to the backbone fluorinated series a distinct ring pucker is observed in the pyrrolidine ring, but in the opposite direction. The reversal could stem from the lower sigma withdrawing nature of the oxygen atom, or the preference of the benzyl group to be in a pseudo equatorial position. The extended crystal structure shows strong pi-stacking between the benzyl groups which could cause the observed preference for pseudo-equatorial. However, this is an observation of the ground state and may not have any effect on the Breslow intermediate as was the case for the fluorinated catalysts.
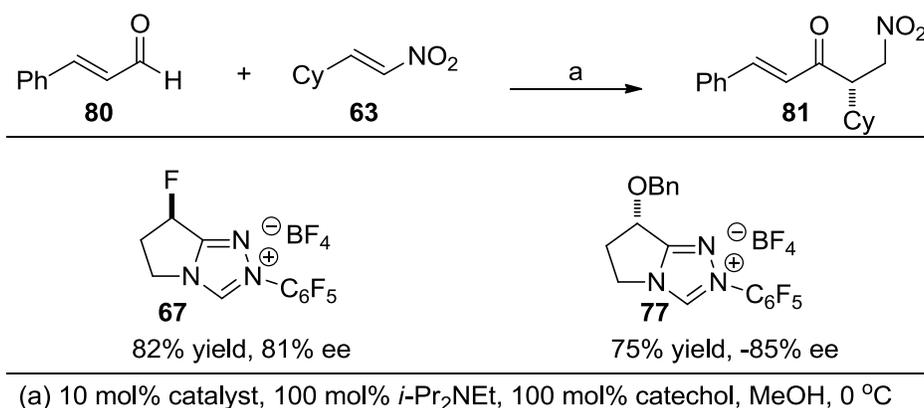
Scheme 14.
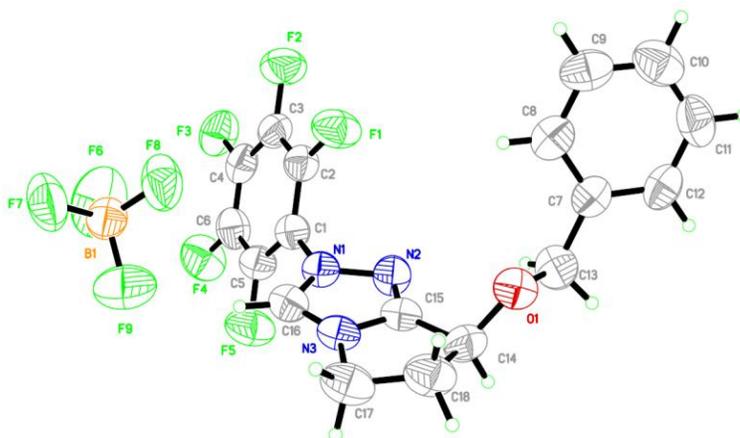
To test its performance as a catalyst in the Stetter reaction, triazolium salt **77** was subjected to the chromanone reaction. The carbene gave a moderate yield of the desired product but in markedly low enantioselectivity, which is not surprising as this reaction was shown to be very sensitive to the steric environment of the catalyst. Changing the base to sodium acetate decreased the yield to less than 5% but increased the enantioselectivity to 20%.

^{a}catalyst(10 mol %), NEt$_3$ (10 mol %), PhMe, 23 ^{o}C
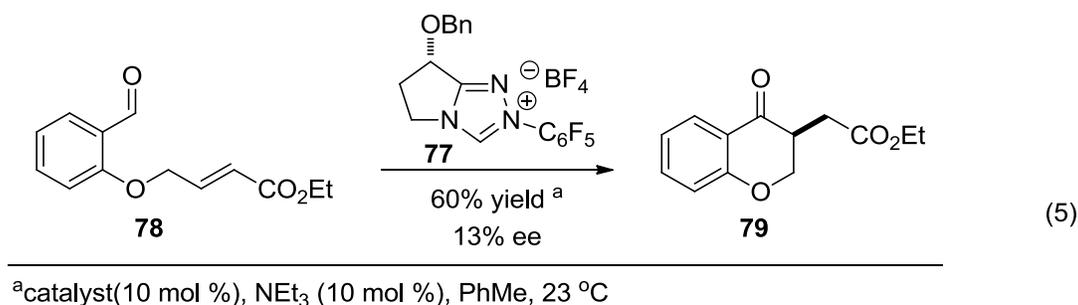
When used to catalyze the Stetter reaction between cinnamaldehyde and cyclohexyl nitroalkene, catalyst **77** gave similar yields but outperformed the fluorine analogue **67** in enantioselectivity by a small margin. The observed reversal of enantioselectivity is due to the opposite absolute stereochemistry at the chiral center.

Scheme 15.

(a) 10 mol% catalyst, 100 mol% i-Pr$_2$NEt, 100 mol% catechol, MeOH, 0 ^{o}C
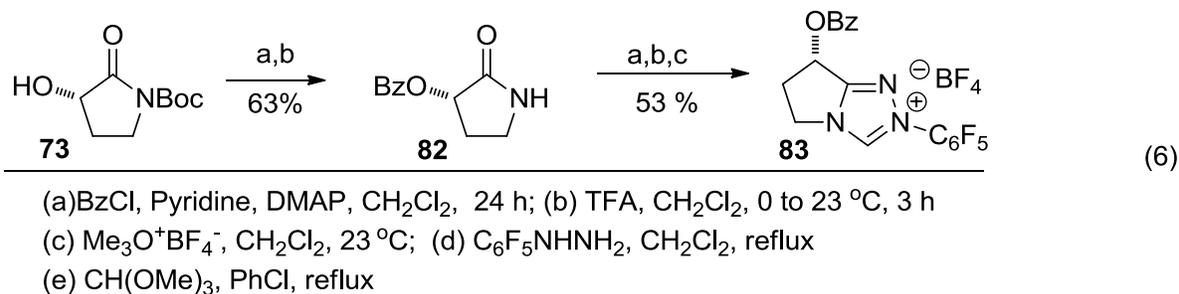
For the Stetter reaction of heteroaromatic aldehydes and nitroalkenes, the result was similar in that the enantioselectivity of the reaction remained almost exactly the same (scheme 18). These results seem to confirm the theory that a substituted oxygen-containing catalyst would behave similarly to the fluorinated catalysts. Unfortunately, the impact of the additional steric bulk is not observed in these systems.

Scheme 16.

(a) 10 mol% catalyst, 100 mol% i-Pr$_2$NEt, MeOH, 0 °C
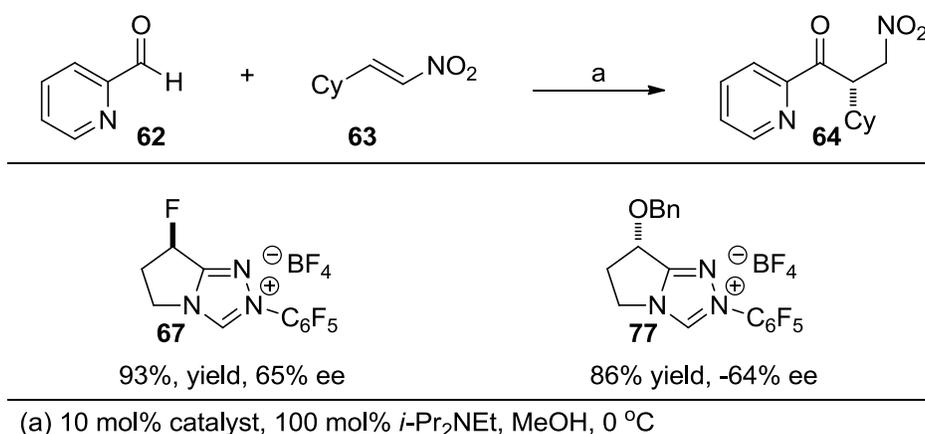
1.7 Second Generation Catalyst

With the success of the first catalyst, a second tiazolium catalyst was designed in an effort to maintain a similar steric environment but increase the electron withdrawing nature of the oxygen stereocenter. To this end a benzoyl group was installed in place of the benzyl group. Treatment of lactam **73** with benzoyl chloride and subsequent removal of the Boc group resulted in lactam **80**. Standard conditions were successful at converting lactam **82** into triazolium salt **83**.

(a)BzCl, Pyridine, DMAP, CH$_2$Cl$_2$, 24 h; (b) TFA, CH$_2$Cl$_2$, 0 to 23 °C, 3 h
(c) Me$_3$O$^+$BF$_4^-$, CH$_2$Cl$_2$, 23 °C; (d) C$_6$F$_5$NHNH$_2$, CH$_2$Cl$_2$, reflux
(e) CH(OMe)$_3$, PhCl, reflux

An X-ray crystal structure of triazolium salt **83** shows a few subtle differences. The ring pucker observed for the other catalysts is not well defined, but appears to adopt a conformation analogous to the fluorinated catalyst. This places the benzoyl in a pseudo-axial position.

Scheme 18.
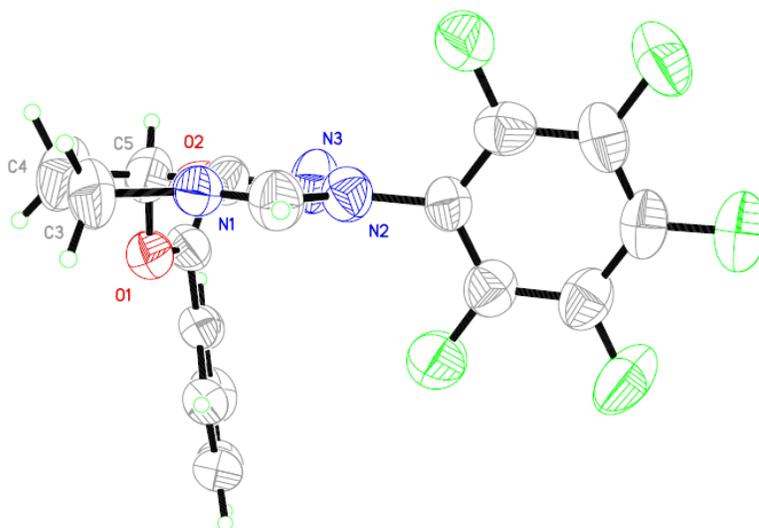
When applied to the intramolecular Stetter reaction, the 4-chromanone product was formed quantitatively albeit in less than 10% ee. For the intermolecular reactions it also showed a decreased ability to impart enantioselectivity in the transformation. A theory for the decreased enantioselectivity is the loss of the benzoyl group under the reaction conditions. A ^{1}H NMR experiment showed that in methanol, upon the addition of either sodium acetate or N-N-

diisopropylethylamine several new species were formed. One of them appears to be without the benzoyl group, but the evidence is *in situ* only; no carbene bearing a free hydroxyl group was isolated from the mixture.

(7)

(8)
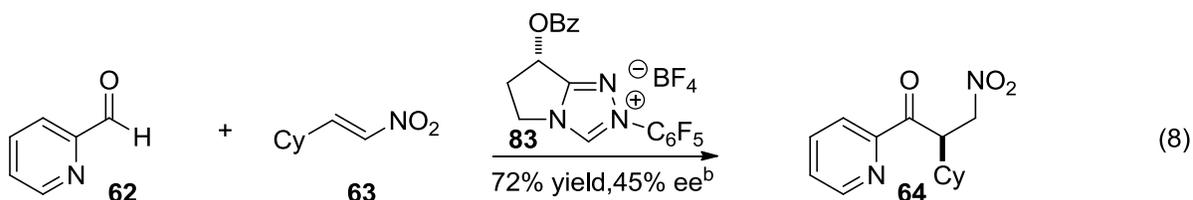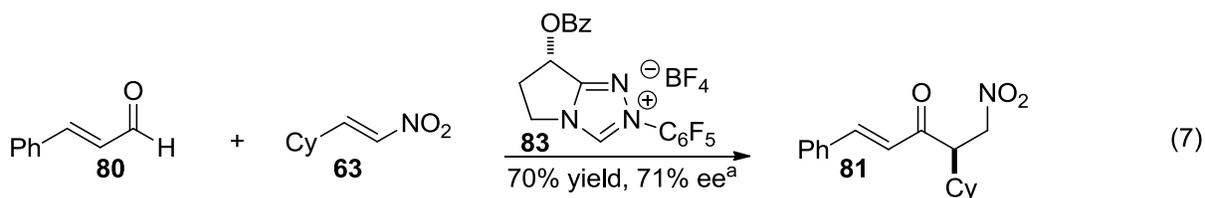
(a) 10 mol% catalyst, 100 mol% *i*-Pr$_2$NEt, 100 mol% catechol, MeOH, 0 ^{o}C
(b) 10 mol% catalyst, 100 mol% *i*-Pr$_2$NEt, MeOH, 0 ^{o}C

1.7 Conclusion

In conclusion, we have developed a new *N*-heterocyclic carbene scaffold to provide an orthogonal method for tuning the electronic and steric environment relative to the carbene scaffolds currently in use by the Rovis group. Starting from commercially available materials, a short synthesis is able to produce the carbenes in high purity. The synthetic route proceeds through a common intermediate which allows for expedited synthesis of multiple derivatives. These carbenes show promising levels of enantioselectivity for intermolecular Stetter reactions despite the steric bulk being distal to the reaction site. With that in mind the oxygenated backbone could be applied to the current carbene scaffolds to increase the potential tuning options and result in a series of improved catalysts.

References:

[1] Arduengo, A. J.; Dias, R. L.; Harlow, R.; Kline, M. J. *J. Am. Chem. Soc.* **1991**, *113*, 361-363.

[2] (a) Baceiredo, A.; Bertrand, G.; Sicard, G. J. *J. Am. Chem. Soc.* **1985**, *107*, 4781-4783. (b) Igau, A.; Grutzmacher, H.; Baceiredo, A.; Bertrand, G. J. *J. Am. Chem. Soc.***1988**, *110*, 6463-6466.

[3] (a) Wanzlick, H. W.; Kleiner, H. J. *Angew. Chem.***1961**, *73*, 493. (b) Wanzlick, H. W. *Angew. Chem.* **1962**, *74*, 129. (c) Wanzlick, H. W.; Esser, T.; Kleiner, H. J. *Chem. Ber.* **1963***, 96*. 1208.

[4] For a review see; (a) Herrman, W. A. *Angew. Chem. Int. Ed.* **2002**, *41*, 1290. (b) Perry, C. M.; Burgess, K. *Tetrahedron: Asymmetry* **2003**, *14*, 951.

[5] For a review see; (a) Enders, D.; Balensiefer, T. *Acc. Chem. Res.* **2004**, *37*, 534-541. (b) Johnson, J. S. *Angew. Chem. Int. Ed.* **2004**, *43*, 1326-1328.

[6] (a) Bourissou, D.; Guerret, O.; Gabbaie, F. P.; Bertrand, G. *Chem. Rev.* **2000**, *100*, 39-91. (b) Nemirowski, A.; Schreiner, P. R. *J. Org. Chem.* **2007**, *72*, 9533-9540.

[7] Seebach, D. *Angew. Chem.* **1979**, *91*, 259; *Angew. Chem. Int. Ed.* **1979**, *18*, 239-258.

[8] Wöhler, F.; Liebig, J. *Ann. Pharm.* **1832**, *3*, 249-282.

[9] Lapworth, A. *J. Am. Chem. Soc.* **1903**, *83*, 995-1005.

[10] Ukai, T.; Tanaka, S.; Dokawa, S. *J. Pharm. Soc. Jpn*. **1943**, *63*, 296-300.

[11] (a) Breslow, R. *J. Am. Chem. Soc.* **1958**, *80*, 3719-3726. (b) Breslow, R.; Kim, R. *Tetrahedron Lett.* **1994**, *35*, 699-702.

[12] Sheehan, J. C.; Hunnemann, D. H. *J. Am. Chem. Soc.* **1966**, *88*, 3666-3667.

[13] Sheehan, J. C.; Hara, T. *J.Org. Chem.* **1974**, *39*, 1196-1199.

[14] (a) Knight, R. L.; Leeper, F. J. *Tetrahedron Lett.* **1997**, *38*, 3611-3614. (b) Gerhard, A. U.; Leeper, F. J. *Tetrahedron Lett.* **1997**, *38*, 3615-3618.

[15] Dvorak, C. A.; Rawal, V. H. *Tetrahedron Lett.* **1998***, 39*, 2925-2928.

[16] Enders, D.; Breuer, K.; Teles, J. H. *Helv. Chim. Acta.* **1996**, *79*, 1217-1221.

[17] Knight, R. L.; Leeper, F. J. *J. Chem. Soc. Perkin Trans I* **1998***, 1891-1894.

[18] Enders, D.; Kallfass, U. *Angew. Chem. Int. Ed.* **2002**, *41*, 1743-1745.

[19] Stetter, H.; Schreckenberg, M. *Angew. Chem. Int. Ed. Engl.* **1973**, *12*, 81-81.

[20] Stetter, H.; Khulmann, H. *Org. React.* **1991**, *40*, 407-496.

[21] Kerr, M. S.; Read de Alaniz, J.; Rovis, T. *J. Am. Chem. Soc.* **2002**, *124*, 10298-10299.

[22] Kerr, M. S.; Rovis, T. *J. Am. Chem. Soc.* **2004,** *126***,** 8876-8877.

[23] (a) Kerr, M. S.; Rovis, T. *Synlett.***2003,** *12,* 1934-1936. (b) Reynolds, N. T.; Rovis, T. *Tetrahedron Lett.* **2005**, *65*, 6368-6378.

[24] Read de Alaniz, J.; Rovis, T. *J. Am. Chem. Soc.* **2004**, *127*, 6284-6289.

[25] Enders, D.; Han, J.; Hensler, A. *Chem. Comm.* **2008***,* 3989-3991.

[26] Liu, Q.; Perreault, S.; Rovis, T. *J. Am.Chem. Soc.* **2008**, *130,* 14066-14067.

[27] Enders, D.; Han, J. *Synthesis*, **2008**, 3864-3868.

[28] DiRocco, D. A.; Oberg, K. M.; Dalton, D. M.; Rovis, T. *J. Am. Chem. Soc.* **2009***, 131*, 10872-10874.

[29] DiRocco, D. A.; Rovis, T. *J. Am. Chem. Soc.* **2011**, *133*, 10402-10405.

[30] Hodges, J. A.; Raines, R. T. *J. Am. Chem. Soc.* **2005**, *127*, 15923-15932.

[31] Um, J. M.; DiRocco, D. A.; Noey, E. L.; Rovis, T.; Houk, K. N. *J. Am. Chem. Soc.* **2011***, 133*, 11249-11254.

[32] Bondi, A. *J. Phys . Chem.***1964**, *68*, 441-451.

[33] Yoda, H.; Uemura, T.; Takabe, K. *Tetrahedron Lett.* **2003**, *44*, 977-979.

[34] Vora, H. U.; Lathrop, S. P.; Reynolds, N. T.; Kerr, M. S.; Read de Alaniz, J.; Rovis, T. *Org. Synth.* **2010**, *87*, 350.

Experimental:

All reactions were carried out under an atmosphere of argon in flame-dried glassware with magnetic stirring. Dichloromethane and tetrahydrofuran were degassed with argon and passed through two columns of neutral alumina. Methanol was purchased from Aldrich and dried with activated 3Å mol sieves prior to use. N,N'-diisopropylethylamine and triethylamine were purchased from Aldrich and distilled from calcium hydride prior to use. All other reagent were purchased from Aldrich and used without further purification. Column chromatography was performed on SiliCycle®Silica*Flash*® P60, 43-60 μm 60A. Thin layer chromatography was performed on SiliCycle® 250 μm 60A plates. Visualization was accomplished by UV light or $KMnO_4$ stain followed by heating.

H^1 NMR spectra were recorded on a Varian 300 MHz spectrometer at ambient temperature. Data is reported as follows: chemical shift in parts per million from either $CDCl_3$ (7.26 ppm) or acetone-D_6 (2.03 ppm), multiplicity (s = singlet, bs = broad singlet, d = doublet, t = triplet, q = quartet, and m = multiplet), coupling constants (Hz). ^{13}C NMR spectra were recorded on either a Varian 300 or 400 MHz spectrometer (at 75 or 100 MHz) at ambient temperature. Chemical shifts are reported from either $CDCl_3$ (77.36) or acetone-D_6 (205.87, 30.6 ppm).

Stetter reactions were carried out following the appropriate literature precedent.[1,2]

**General procedure for the synthesis of triazolium salts**

A flame–dried round bottom flask is charged with CH_2Cl_2 and the appropriate lactam (1 equiv. 0.2M). Trimethyloxonium tetrafluoroborate (1 equiv.) is added at ambient temperature and the reaction is stirred until the trimethyloxonium tetrafluoroborate is completely dissolved, usually

less than 3 hours at 23 °C. To the solution is added the appropriate hydrazine (1 equiv.) and the solution is heated to reflux and held there for 3 hours. The solvent is removed *in vacuo* and chlorobenzene is added (0.2 M solution) along with 2.5 equiv. of triethyl orthoformate. The solution is heated to reflux for 12 hour or until judged to be complete by H[1] NMR. The solvent is removed *in vacuo* and the product is purified by precipitation.
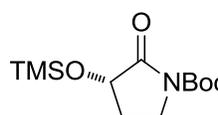
(S)-*tert*-butyl 2-oxo-3-(trimethylsiloxy)pyrollidine-1-carboxylate: A 100-mL round bottom flask fitted with a reflux condenser was charged (S)-(-)-4-amino-2-hydroxybutyric acid (5.0 g, 42 mmol) and 100 mL of xylenes (0.4 M). To the stirred solution was added 60 mL (0.29 mol, 7 equiv.) of 1,1,1,3,3,3-hexamethyldisilazane and 1 mL of trimethylsilyl chloride. The solution was heated to reflux and stirred for 12 hours. The solution was cooled to 23 °C and poured over reagent alcohol (100 mL) and the solvent was removed *in vacuo*. The resulting yellow oil was taken up in 100 mL of CH_2Cl_2 and 513 mg (4.2 mmol, 0.1 equiv) of DMAP was added. The flask was put under an argon atmosphere and cooled to 0 °C and 5.85 mL (42 mmol, 1 equiv.) of triethylamine was added portion wise. To the stirred solution was added 13.74 g (63 mmol, 1.5 equiv.) of di-*tert*-butyl dicarbonate as a solution in 10 mL CH_2Cl_2. The solution was allowed to warm to 23 °C and stir for 12 hours. The resulting solution was washed with 1 M HCl (3 x 30 mL), water (1 x 50 mL), and brine (1 x 30 mL). The organic phase was dried over $MgSO_4$ filtered and the solvent was removed *in vacuo*. The resulting oil was purified by flash column chromatography 10:1 hexanes:EtOAc to yield 8.2 g (30 mmol, 71%) of a colorless oil. Spectra are consistent with previously reported.[1] R_f (10:1 hexanes:EtOAc) = 0.3; ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.29 (dd, *J* = 7.8, 9.6 Hz, 1H), 3.79 (ddd = 11.1, 8.7, 2.4 Hz, 1H), 3.48 (m, 1H), 2.29 (m, 1H), 1.92 (m, 1H), 1.52 (s, 9H), 0.19 (s, 9H).
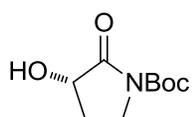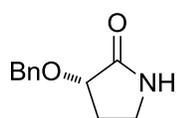
(S)-tert-butyl 3-hydroxy-2-oxopyrrolidine-1-carboxylate (73)[2]: A flame-dried round bottom flask was charged with (S)-*tert*-butyl 2-oxo-3-(trimethylsiloxy)pyrollidine-1-carboxylate (1.5 g, 5.48 mmol) and 65 mL of THF. The solution was cooled to 0 °C and tetrabutylammonium fluoride was added dropwise as a 1 M solution in THF (11 mL, 11 mmol.) After stirring 10 minutes at 0 °C the solution was poured over saturated ammonium chloride (50 mL). The Aqueous layer was extracted with ethyl acetate (3 x 30 mL). The collected organic fractions were washed with brine (1 x 50 mL) and dried over MgSO$_4$. The solvent was removed *in vacuo* and the crude solid was purified by flash column chromatography to yield a white solid (680 mg, 61 %). R$_f$ = 0.20, (1:1 hexane:EtOAc); [α]$_D^{21}$ = -87.7 (c = 0.01 g/ml, CHCl$_3$) **m.p.** (°C): 91-92; **^{1}H NMR** (300 MHz, CDCl$_3$) δ 4.33 (dd, *J* = 10.5, 8.1 Hz, 1H), 3.84 (ddd, *J* = 10.8, 9, 1.5 Hz, 1H), 3.51 (m, 1H), 2.89 (bs, 1H), 2.45 (m, 1H), 1.94 (m, 1H), 1.54 (s, 9H). **^{13}C NMR** (100 Hz, CDCl$_3$) δ 174.8, 149.1, 83.4, 70.5, 42.1, 27.9, 26.9. **IR** (NaCl, neat) 3451, 2980, 2935, 1781, 1718, 1369, 1314, 1155. **HRMS** (ESI+) calcd for C$_9$H$_{15}$NO$_4$, 201.100. Found 201.1001
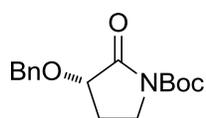
(S)-*tert*-butyl 3-(benzyloxy)-2-oxopyrrolidine-1-carboxylate: A round bottom flask was charged with **73** (1.0 g, 5 mmol) and 50 mL of ethyl acetate. To the stirred solution silver (I) oxide (1.73 g, 7.5 mmol) and benzyl bromide (0.645 mL, 5.5 mmol) were added. The solution was vigorously stirred at 23 °C for 12 hours. The solids were removed by filtration through a short pad of silica and washing with ethyl acetate. The solvent was removed *in vacuo* and the solid was purified by flash column chromatography to yield a

white solid (1.30 g, 90%). R_f = 0.4 (2:1 hexanes:EtOAc); **^{1}H NMR** (300 MHz, CDCl$_3$) δ 7.35 (m, 5H), 4.87 (m, 2H), 4.10 (m, 1H), 3.81 (m, 1H), 3.52 (m, 1H), 2.24 (m, 1H), 2.00 (m, 1H), 1.53 (s, 9H).

(S)-3-(benzyloxy)pyrrolidin-2-one (74): A solution of (S)-*tert*-butyl 3-(benzyloxy)-2-oxopyrrolidine-1-carboxylate (1.30 g, 4.46 mmol) in 50 mL of CH$_2$Cl$_2$ was stirred at 0 °C. Trifluoroacetic acid (1.7 mL, 22.31 mmol) was added drop wise to the solution. The solution was allowed to gradually warm to 23 °C. Upon consumption of starting material as judged by TLC the reaction was quenched by the addition of saturated sodium bicarbonate. The aqueous layer was extracted with CH$_2$Cl$_2$ (2 x 50 mL). The combined organic fractions were washed with saturated sodium bicarbonate (1 x30 mL), water (2 x 30 mL), and brine (1 x 30 mL). The solvent was removed *in vacuo* and the resulting solid was purified by flash column chromatography to yield a white solid (400 mg, 41%, 71% BRSM). R_f = 0.2 (1:9 hexanes:EtOAc); **^{1}H NMR** (300 MHz, CDCl$_3$) δ 7.25-7.41 (m, 5H), 7.20 (bs, 1H), 4.92 (d, *J* = 11.7 Hz, 1H), 4.72 (m, 1H), 4.07 (t, *J* = 7.2 Hz, 1H), 3.41 (td, *J* = 9.9, 3.9 Hz), 3.24 (m, 1H), 2.33 (m, 1H), 2.07 (m, 1H).
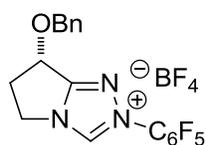
Triazolium Salt (77): To a flame dried round bottom flask equipped with a reflux condenser was added lactam **74** (400 mg, 2.09 mmol) and 10 mL CH$_2$Cl$_2$. Trimethyloxonium tetrafluoroborate (310 mg, 2.09 mmol) was added and the reaction was stirred for 3 hours. Pentafluorophenylhydrazine (414 mg, 2.09 mmol) was added and the reaction was heated to reflux and held there for 12 hours. The solvent was

removed *in vacuo* and the crude solid was taken up in 10 mL of chlorobenzene. To the stirred

suspention was added triethylorthoformate and the solution was heated to reflux. After stirring

at reflux for 3 hours the reaction was cooled to 23 °C and the solvent was removed to yield a

dark brown solid. The crude solid was purified by precipitation out of CH_2Cl_2 by the slow

addition of pentanes. The precipitate was filtered and washed with ice cold CH_2Cl_2 to yield a

fluffy white solid (500 mg, 51%). **m.p.** (°C): 186; $[\alpha]_D^{21}$ = -19.6 (c = 0.0099, MeOH); **¹H NMR**

(300 MHz, acetone-D_6) δ 10.40 (s, 1H), 7.39 (m, 5H) 5.55 (dd, *J* = 7.2, 4.2 Hz, 1H), 4.87 (m,

3H), 3.37 (m, 1H) 2.96 (m, 1H), 2.82 (d, *J* = 9.6). **¹³C NMR** (100 MHz, Acetone-D_6) δ 162.7,

145.0 (m), 144.5 (m), 144.2, 142.5 (m), 142.0 (m), 137.1 (m), 136.9, 71.8, 71.2, 47.4, 35.0. **IR**

(NaCl, neat) 3146, 1595, 1528, 1467, 1426, 1069. **HRMS** (ESI+) calcd for $C_{18}H_{13}F_5N_3O$,

382.0979. Found 382.0973.
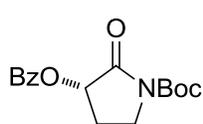
(S)-tert-butyl 3-(benzoyloxy)-2-oxopyrrolidine-1-carboxylate: A solution of

73 (750 mg, 3.70 mmol), pyridine (0.42 mL, 3.70 mmol) and 4-

Dimethylaminopyridine (45.2 mg, 0.37 mmol) was stirred in CH_2Cl_2 at 0 °C. To the solution

benzoyl chloride (0.30 mL, 3.70 mmol) was added dropwise. The solution was allowed to warm

to 23 °C as it stirred for 12 hours. The reaction mixture was quenched by the addition of water.

The organic layer was subsequently washed with water (2 x 30 mL) and brine (1 x 30 mL). The

organic phase was dried over $MgSO_4$ and the solvent was removed. The product was purified by

flash column chromatography (4:1 hexanes:EtOAc). Solvent removed to yield a brown solid

(600 mg, 51% yield, 70% BRSM). R_f = 0.35 (4:1 hexanes:EtOAc). **¹H NMR** (300 MHz, CDCl₃)

δ 8.06 (m, 2H), 7.56 (m, 1H), 7.43 (m, 2H), 5.60 (dd, *J* = 9.9, 8.4 Hz, 1H), 3.92 (ddd, *J* = 11.1,

9.0, 2.1 Hz, 1H), 3.64 (m, 1H), 2.62 (m, 1H), 2.12 (m, 1H), 1.54 (s, 9H). ^{13}C NMR (100 MHz, CDCl$_3$) δ 168.9, 165.5, 133.5, 129.9, 128.4, 83.6, 71.5, 42.1, 27.9, 25.0.
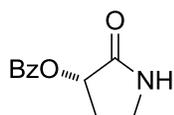
(S)-3-(benzyloxy)pyrrolidin-2-one (82): A round bottom flask was charged with (S)-tert-butyl 3-(benzoyloxy)-2-oxopyrrolidine-1-carboxylate (550mg, 1.08 mmol) 18 mL of CH$_2$Cl$_2$ and cooled to 0 °C. Trifluoroacetic acid (0.551 mL, 7.02 mmol) was added drop wise to the solution. The solution was allowed to warm to 23 °C and stirred until starting material was no longer visible by TLC. The reaction was quenched by the addition of saturated sodium bicarbonate solution. The organic layer was washed with saturated sodium bicarbonate (1 x 30 mL), water (2 x 30 mL), and brine (1 x 3o mL) . The organic phase was dried over MgSO$_4$ and condensed to yield a brown solid (190 mg, 0.92 mmol, 85%). ^{1}H NMR (300 MHz, CDCl$_3$) δ 8.09 (d, J = 7.2 Hz, 2H), 7.57 (t, J = 7.2 Hz, 1H) 7.44 (t, J = 8.1 Hz, 2H), 6.80 (bs, 1H), 5.32 (t, J = 8.1, 1H) 3.47 (m, 2H), 2.74 (m, 1H), 2.22 (m, 1H).
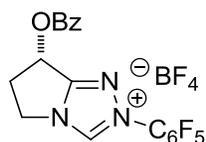
Triazolium Salt (83): A flame dried round bottom flask equipped with a reflux condenser was charged with lactam **82** (560 mg, 2.73 mmol) and CH$_2$Cl$_2$. Trimethyloxonium tetrafluoroborate (403 mg, 2.73 mmol) was added and the reaction was stirred at 23 °C for 3 hours. Pentafluorophenylhydrazine (540 mg, 2.73 mmol) was added and the solution was stirred at reflux for 2 hours. The solvent was removed *in vacuo* and the crude solid was taken up in 14 mL of chlorobenzene and triethyl orthoformate (1.36 mL, 8.18 mmol) was added . The resulting solution was heated to reflux and stirred for 12 hours. After returning to 23 °C the solvent was removed to yield a brown solid. The solid was

purified by precipitation by vigorous stirring in a mixture of ether and ethyl acetate. After filtration the solid was washed with ice cold ethyl acetate and dried to yield a white solid (700 mg, 53%). **m.p.** (°C): 178-179; $[\alpha]_D^{21}$ = + 38.1 (c = 0.0099 g/mL, MeOH) **^{1}H NMR** (300 MHz, acetone-D$_6$) δ 10.43 (s, 1H), 8.05 (m, 2H) 7.72 (t, J = 7.5 Hz, 1H), 7.57 (t, J = 7.8 Hz, 2H), 6.79 (dd, J = 7.8, 4.2 Hz, 1H), 5.08 (m, 1H), 4.96 (m, 1H), 3.65 (m, 1H), 3.23 (m, 1H). **^{13}C NMR** (100 MHz, Acetone-D$_6$) 164.9, 161.7, 145.1 (m), 144.6 (m), 144.4, 142.5 (m), 142.0 (m), 139.5 (m), 136.9 (m), 134.0, 129.7, 128.8, 128.6, 66.4, 47.6, 34.3. **IR** (NaCl, neat) 3136, 1729, 1600, 1528, 1497, 1266, 1069, 712. **HRMS** (ESI+) calcd for $C_{18}H_{11}F_5N_3O_2$, 396.0771. Found 396.0766.

^{1}H and ^{13}C data for **73**
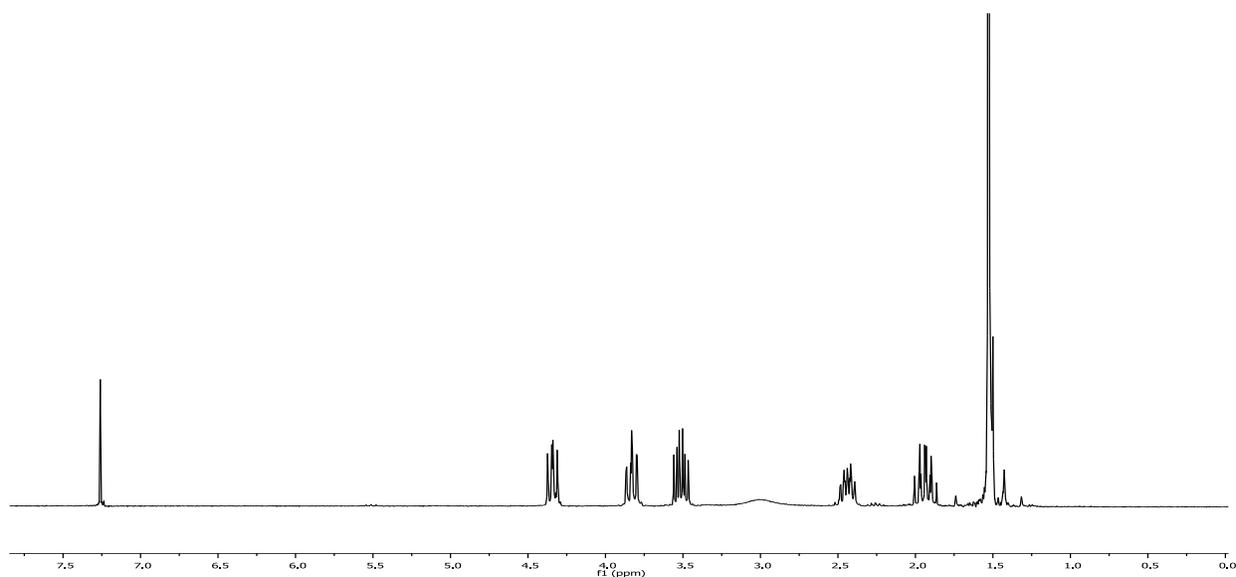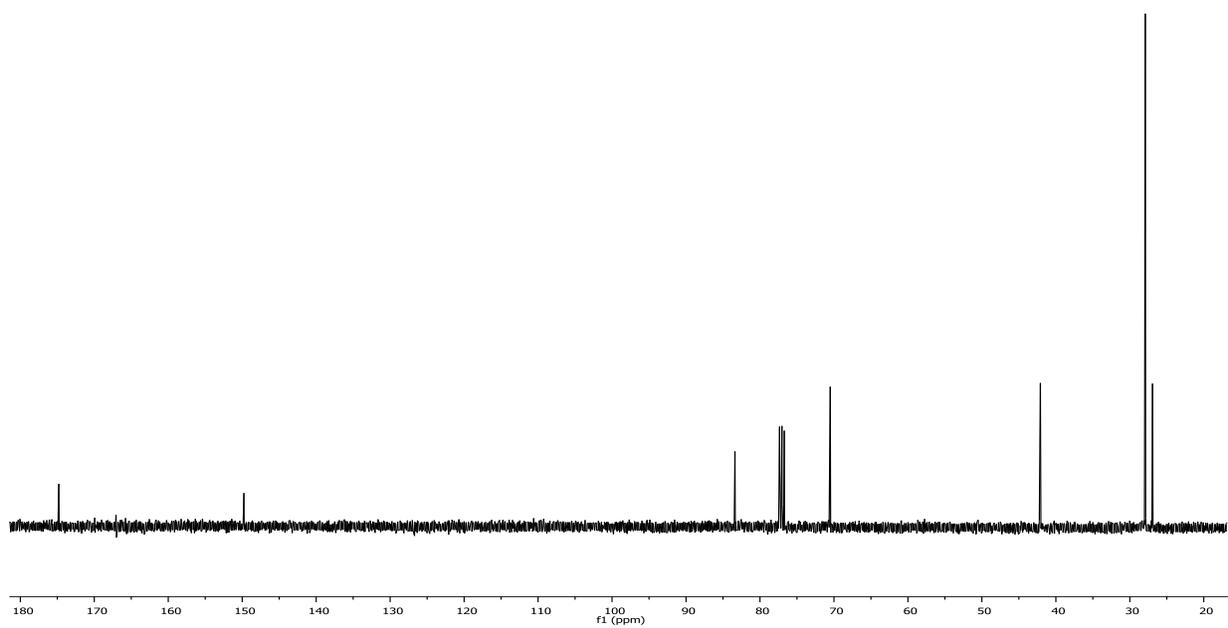
^{1}H and ^{13}C NMR data for tirazolium salt **77**

28
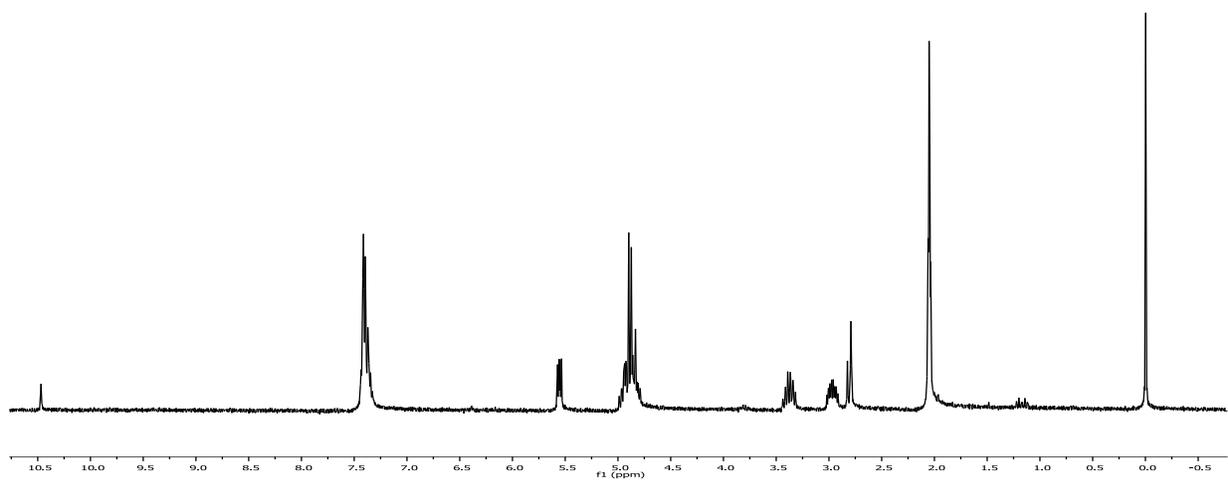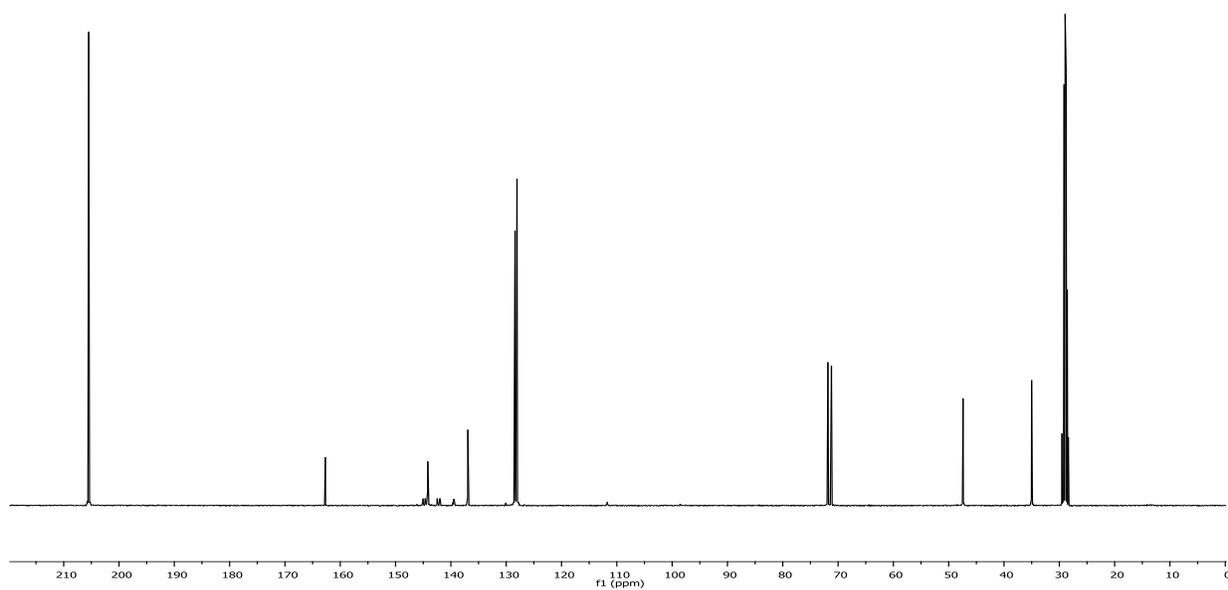
1H and 13C NMR data for triazolium salt 83
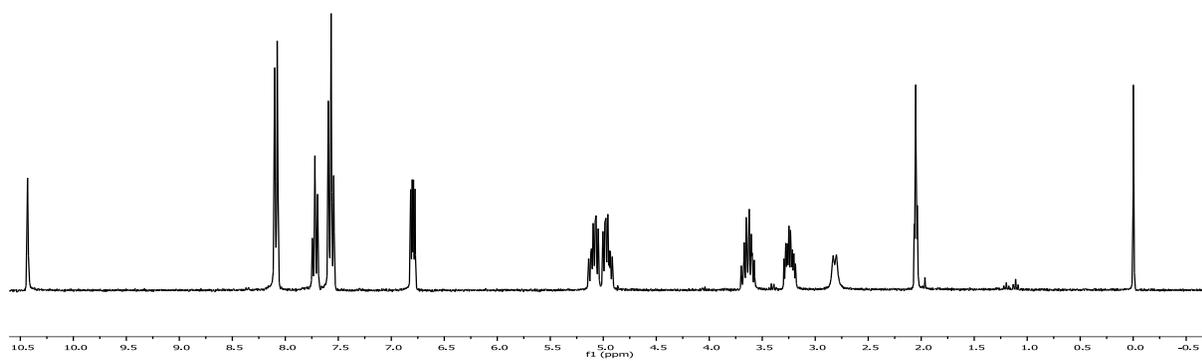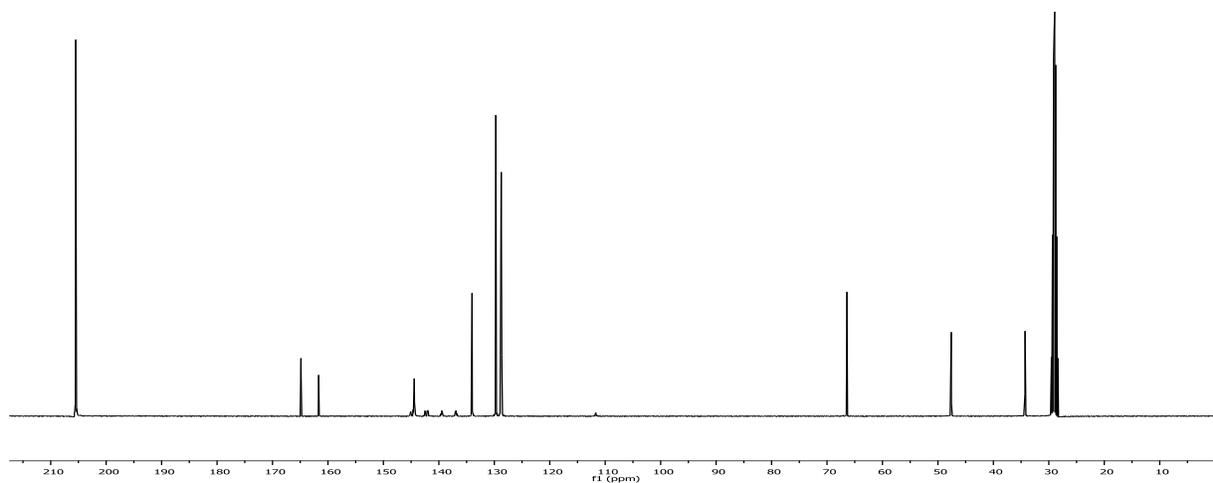
Crystallographic Data for Triazolium Salt **77**.
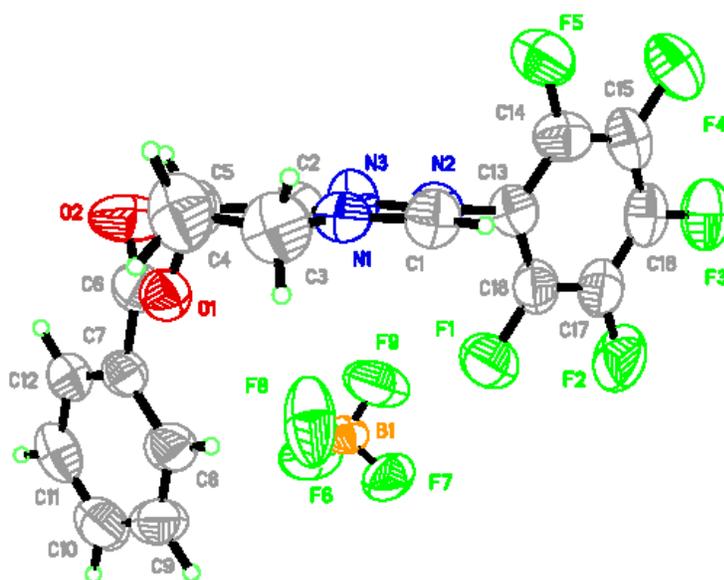
Table 1. Crystal data and structure refinement for triazolium salt **77**.

Identification code	rovis154_0m
Empirical formula	$C_{18}H_{11}BF_9N_3O_2$
Formula weight	483.11
Temperature	120(2) K
Wavelength	0.71073 Å
Crystal system	Orthorhombic
Space group	$P2_12_12_1$
Unit cell dimensions	$a = 7.843(2)$ Å $\quad\quad \square = 90°.$
	$b = 11.716(3)$ Å $\quad\quad \square = 90°.$
	$c = 21.554(6)$ Å $\quad\quad \square = 90°.$
Volume	1980.5(9) Å^3
Z	4
Density (calculated)	1.620 Mg/m^3
Absorption coefficient	0.163 mm^{-1}
F(000)	968
Crystal size	0.24 x 0.18 x 0.17 mm^3
Theta range for data collection	1.89 to 27.11°.
Index ranges	-9<=h<=10, -15<=k<=15, -27<=l<=27
Reflections collected	28747
Independent reflections	4358 [R(int) = 0.0753]
Completeness to theta = 27.11°	100.0 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9725 and 0.9619
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4358 / 0 / 298
Goodness-of-fit on F^2	0.954
Final R indices [I>2sigma(I)]	R1 = 0.0554, wR2 = 0.1337
R indices (all data)	R1 = 0.1674, wR2 = 0.1766
Absolute structure parameter	0.0(12)
Largest diff. peak and hole	0.255 and -0.256 e.Å^{-3}

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^2x 10^3)

for triazolium salt **77**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
N(3)	6257(6)	5415(3)	1139(2)	68(1)
N(2)	6175(5)	6467(3)	873(2)	59(1)
C(2)	6069(6)	4748(4)	666(2)	54(1)
C(1)	5964(6)	6408(5)	266(2)	65(1)
N(1)	5901(5)	5320(3)	133(2)	57(1)
C(5)	5928(7)	3489(4)	566(2)	68(1)
C(3)	5619(8)	4571(5)	-406(2)	84(2)
C(4)	5813(9)	3408(5)	-146(2)	95(2)
C(12)	2540(6)	1723(4)	2156(2)	63(1)
C(7)	2724(5)	2530(4)	1695(2)	53(1)
C(6)	4418(6)	2687(4)	1420(2)	60(1)
C(9)	-168(7)	3058(5)	1813(3)	76(2)
C(8)	1357(6)	3209(4)	1517(2)	64(1)
C(11)	974(8)	1568(5)	2428(2)	78(2)
C(10)	-378(7)	2232(5)	2257(3)	79(2)
C(13)	6254(6)	7467(4)	1258(2)	54(1)
C(16)	6362(8)	9288(4)	2055(2)	66(1)
C(18)	4826(7)	7828(4)	1568(2)	62(1)
C(14)	7721(7)	8050(5)	1346(2)	65(1)
C(15)	7796(8)	8955(4)	1734(2)	68(1)
C(17)	4869(7)	8725(4)	1963(2)	69(1)
O(1)	4321(4)	3135(2)	837(1)	60(1)
O(2)	5746(5)	2470(4)	1666(2)	96(1)
F(5)	9141(4)	7718(3)	1042(1)	82(1)
F(3)	6460(5)	10160(2)	2452(1)	93(1)
F(2)	3481(5)	9072(3)	2264(2)	103(1)
F(4)	9269(4)	9512(3)	1816(1)	94(1)
F(1)	3352(4)	7268(3)	1484(2)	89(1)

B(1)	464(9)	5284(7)	9918(3)	84(2)
F(6)	-262(5)	4646(4)	10357(2)	148(2)
F(7)	-597(5)	6123(3)	9741(2)	139(2)
F(8)	848(11)	4644(4)	9435(3)	230(4)
F(9)	1909(6)	5817(5)	10081(3)	179(2)

Crystallographic Data for Triazolium Salt **83**.

Table 3. Crystal data and structure refinement Triazolium **83**.

Identification code	Rovis142
Empirical formula	$C_{18} H_{13} B F_9 N_3 O$
Formula weight	469.12
Temperature	120(2) K
Wavelength	0.71073 Å
Crystal system	Orthorhombic
Space group	$P\ 2_1 2_1 2_1$

Unit cell dimensions	$a = 7.422(4)$ Å	$\alpha = 90°$.
	$b = 11.802(5)$ Å	$\beta = 90°$.
	$c = 22.358(10)$ Å	$\gamma = 90°$.

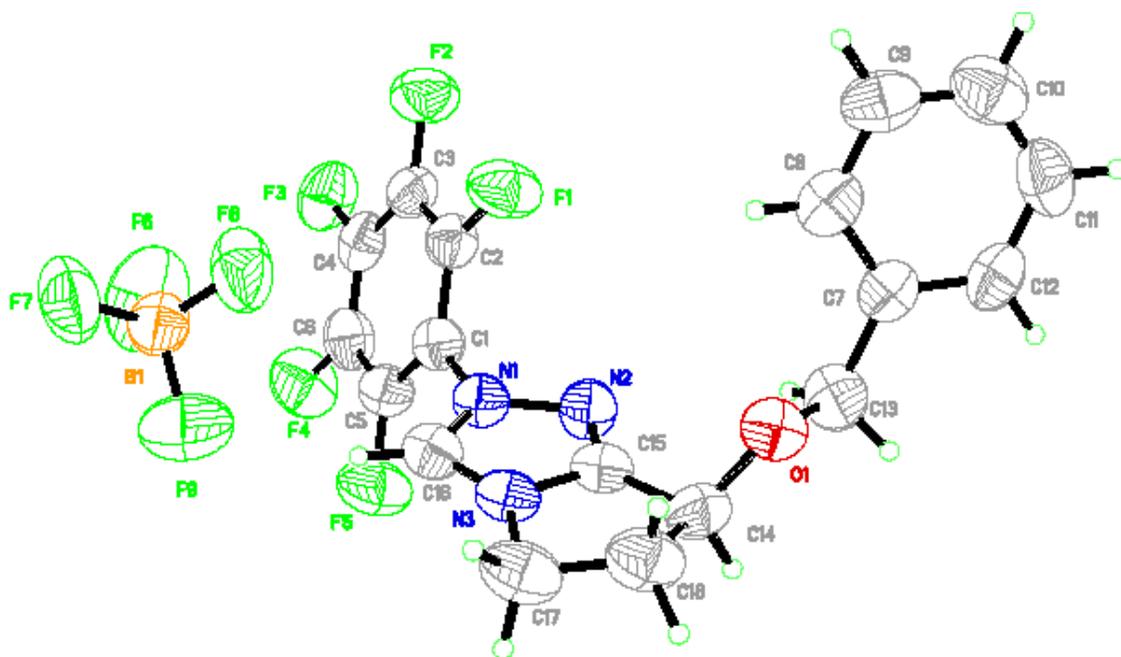|	
Volume	1958.4(16) Å^3
Z	4
Density (calculated)	1.591 Mg/m^3
Absorption coefficient	0.159 mm^{-1}
F_{000}	944
Crystal size	0.72 x 0.13 x 0.10 mm^3
Theta range for data collection	1.95 to 24.72°.
Index ranges	$-8 \leq h \leq 8$, $-13 \leq k \leq 13$, $-26 \leq l \leq 26$
Reflections collected	27677
Independent reflections	3346 [$R_{int} = 0.0283$]
Completeness to theta = 24.72°	99.9 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9838 and 0.8938
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3346 / 0 / 289
Goodness-of-fit on F^2	1.045
Final R indices [I>2sigma(I)]	$R1 = 0.0348$, $wR2 = 0.0915$
R indices (all data)	$R1 = 0.0440$, $wR2 = 0.0983$
Absolute structure parameter	0.6(8)

Largest diff. peak and hole   0.204 and -0.183 e.Å^{-3}

Table 4. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^{2}x 10^3) for triazolium salt **83**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
B(1)	1422(4)	5420(3)	102(2)	68(1)
C(1)	8050(4)	2462(2)	1706(1)	54(1)
C(2)	7676(4)	3352(2)	2088(1)	65(1)
C(3)	6017(5)	3451(3)	2358(1)	77(1)
C(4)	4723(5)	2677(3)	2244(1)	80(1)
C(5)	5051(4)	1791(3)	1870(1)	75(1)
C(6)	6721(4)	1673(2)	1599(1)	64(1)
C(7)	9883(4)	2337(3)	1435(1)	67(1)
C(8)	11240(4)	1718(2)	536(1)	60(1)
C(9)	10996(4)	1746(3)	-146(1)	72(1)
C(10)	11692(4)	647(3)	-400(1)	72(1)
C(11)	11491(3)	477(2)	646(1)	50(1)
C(12)	11792(3)	-1179(2)	262(1)	56(1)
C(13)	11777(3)	-2224(2)	1215(1)	49(1)
C(14)	13332(3)	-2849(2)	1262(1)	56(1)
C(15)	13398(4)	-3798(2)	1614(1)	62(1)
C(16)	11881(4)	-4122(2)	1922(1)	59(1)

C(17)	10335(4)	-3512(2)	1884(1)	57(1)
C(18)	10272(3)	-2562(2)	1529(1)	53(1)
F(1)	8747(2)	-1975(2)	1491(1)	79(1)
F(2)	8874(2)	-3837(2)	2192(1)	86(1)
F(3)	11936(3)	-5050(1)	2268(1)	83(1)
F(4)	14911(3)	-4385(2)	1657(1)	90(1)
F(5)	14807(2)	-2526(2)	969(1)	82(1)
F(6)	161(2)	6119(2)	344(1)	104(1)
F(7)	2814(3)	6109(2)	-70(1)	136(1)
F(8)	653(3)	4854(2)	-364(1)	109(1)
F(9)	2017(4)	4697(2)	523(1)	143(1)
N(1)	11654(3)	-102(2)	128(1)	51(1)
N(2)	11714(3)	-1248(2)	851(1)	51(1)
N(3)	11520(3)	-185(2)	1110(1)	57(1)
O(1)	9683(2)	2146(2)	807(1)	60(1)

Table 5.   Bond lengths [Å] and angles [°] for triazolium salt **83**.

B(1)-F(9)	1.344(4)
B(1)-F(6)	1.359(4)
B(1)-F(8)	1.364(4)
B(1)-F(7)	1.370(4)
C(1)-C(6)	1.377(4)
C(1)-C(2)	1.381(4)
C(1)-C(7)	1.497(4)
C(2)-C(3)	1.376(4)
C(3)-C(4)	1.349(5)
C(4)-C(5)	1.361(5)
C(5)-C(6)	1.387(4)

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C(7)-O(1)	1.430(3)	F(9)-B(1)-F(6)	109.4(3)
C(8)-O(1)	1.399(3)	F(9)-B(1)-F(8)	111.2(3)
C(8)-C(11)	1.497(4)	F(6)-B(1)-F(8)	108.2(2)
C(8)-C(9)	1.535(4)	F(9)-B(1)-F(7)	109.0(3)
C(9)-C(10)	1.507(4)	F(6)-B(1)-F(7)	105.8(3)
C(10)-N(1)	1.475(3)	F(8)-B(1)-F(7)	113.0(3)
C(11)-N(3)	1.299(3)	C(6)-C(1)-C(2)	118.5(3)
C(11)-N(1)	1.350(3)	C(6)-C(1)-C(7)	120.9(2)
C(12)-N(1)	1.309(3)	C(2)-C(1)-C(7)	120.5(2)
C(12)-N(2)	1.321(3)	C(3)-C(2)-C(1)	121.0(3)
C(13)-C(14)	1.373(4)	C(4)-C(3)-C(2)	119.8(3)
C(13)-C(18)	1.378(4)	C(3)-C(4)-C(5)	120.6(3)
C(13)-N(2)	1.411(3)	C(4)-C(5)-C(6)	120.4(3)
C(14)-F(5)	1.332(3)	C(1)-C(6)-C(5)	119.8(3)
C(14)-C(15)	1.370(4)	O(1)-C(7)-C(1)	108.6(2)
C(15)-F(4)	1.323(3)	O(1)-C(8)-C(11)	112.6(2)
C(15)-C(16)	1.374(4)	O(1)-C(8)-C(9)	108.9(2)
C(16)-F(3)	1.341(3)	C(11)-C(8)-C(9)	101.5(2)
C(16)-C(17)	1.357(4)	C(10)-C(9)-C(8)	108.3(2)
C(17)-F(2)	1.341(3)	N(1)-C(10)-C(9)	102.0(2)
C(17)-C(18)	1.374(4)	N(3)-C(11)-N(1)	112.3(2)
C(18)-F(1)	1.329(3)	N(3)-C(11)-C(8)	136.2(2)
N(2)-N(3)	1.390(3)	N(1)-C(11)-C(8)	111.4(2)

N(1)-C(12)-N(2)	106.5(2)	C(12)-N(2)-C(13)	128.6(2)
C(14)-C(13)-C(18)	119.1(2)	N(3)-N(2)-C(13)	119.97(18)
C(14)-C(13)-N(2)	120.7(2)	C(11)-N(3)-N(2)	102.21(19)
C(18)-C(13)-N(2)	120.2(2)	C(8)-O(1)-C(7)	113.3(2)
F(5)-C(14)-C(15)	119.1(2)		
F(5)-C(14)-C(13)	120.0(2)		
C(15)-C(14)-C(13)	120.9(2)		
F(4)-C(15)-C(14)	120.0(3)		
F(4)-C(15)-C(16)	120.9(2)		
C(14)-C(15)-C(16)	119.0(2)		
F(3)-C(16)-C(17)	119.7(3)		
F(3)-C(16)-C(15)	119.4(3)		
C(17)-C(16)-C(15)	120.9(2)		
F(2)-C(17)-C(16)	120.0(2)		
F(2)-C(17)-C(18)	120.1(2)		
C(16)-C(17)-C(18)	119.9(2)		
F(1)-C(18)-C(17)	119.4(2)		
F(1)-C(18)-C(13)	120.5(2)		
C(17)-C(18)-C(13)	120.1(2)		
C(12)-N(1)-C(11)	107.6(2)		
C(12)-N(1)-C(10)	139.7(2)		
C(11)-N(1)-C(10)	112.6(2)		
C(12)-N(2)-N(3)	111.4(2)		

Symmetry transformations used to generate equivalent atoms:

Table 6.   Anisotropic displacement parameters ($\mathring{A}^2$x 10^3) triazolium salt **83**. The anisotropic displacement factor exponent takes the form: $-2p^2[\ h^2a*^2U^{11} + ... + 2\ h\ k\ a*\ b*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
B(1)	45(2)	71(2)	86(2)	-10(2)	-10(2)	5(2)
C(1)	60(1)	51(1)	51(1)	8(1)	-10(1)	-2(1)
C(2)	77(2)	44(1)	74(2)	7(1)	-10(2)	-1(1)
C(3)	90(2)	64(2)	75(2)	2(2)	5(2)	27(2)
C(4)	68(2)	95(2)	77(2)	17(2)	6(2)	17(2)
C(5)	62(2)	87(2)	75(2)	20(2)	-10(2)	-13(2)
C(6)	72(2)	62(2)	57(2)	4(1)	-11(1)	-7(1)
C(7)	61(2)	75(2)	65(2)	-6(1)	-10(1)	-1(2)
C(8)	59(2)	56(1)	65(2)	12(1)	2(1)	-7(1)
C(9)	75(2)	81(2)	62(2)	24(2)	9(1)	3(2)
C(10)	67(2)	95(2)	52(1)	23(2)	3(1)	7(2)
C(11)	41(1)	64(1)	45(1)	6(1)	1(1)	-3(1)
C(12)	50(1)	65(2)	51(1)	1(1)	1(1)	1(1)
C(13)	51(1)	53(1)	45(1)	0(1)	-4(1)	-1(1)
C(14)	50(1)	61(2)	57(1)	2(1)	1(1)	-1(1)
C(15)	64(2)	58(2)	64(2)	-4(1)	-8(1)	17(1)
C(16)	79(2)	43(1)	54(1)	-1(1)	-7(1)	-2(1)

C(17)	66(2)	50(1)	57(1)	-1(1)	6(1)	-10(1)
C(18)	53(1)	53(1)	54(1)	-2(1)	-1(1)	2(1)
F(1)	56(1)	81(1)	101(1)	24(1)	12(1)	13(1)
F(2)	83(1)	76(1)	98(1)	19(1)	26(1)	-7(1)
F(3)	112(1)	50(1)	89(1)	15(1)	-7(1)	0(1)
F(4)	80(1)	87(1)	103(1)	14(1)	-3(1)	34(1)
F(5)	54(1)	98(1)	95(1)	21(1)	12(1)	11(1)
F(6)	71(1)	118(2)	125(2)	-59(1)	-21(1)	15(1)
F(7)	78(1)	157(2)	173(2)	-6(2)	16(1)	-32(2)
F(8)	93(1)	133(2)	102(1)	-60(1)	-4(1)	9(1)
F(9)	178(3)	100(2)	152(2)	16(2)	-54(2)	27(2)
N(1)	41(1)	65(1)	47(1)	8(1)	1(1)	0(1)
N(2)	50(1)	55(1)	47(1)	3(1)	-1(1)	-1(1)
N(3)	68(1)	54(1)	50(1)	4(1)	-2(1)	1(1)
O(1)	55(1)	67(1)	59(1)	7(1)	-2(1)	4(1)

Table 7. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (Å^2x 10^3) for triazolium salt **83**.

	x	y	z	U(eq)
H(2)	8559	3892	2163	78
H(3)	5788	4049	2618	92
H(4)	3598	2750	2423	96
H(5)	4150	1262	1795	89
H(6)	6943	1063	1346	76
H(7A)	10584	3018	1503	80
H(7B)	10510	1704	1617	80
H(8)	12307	2148	658	72
H(9A)	9732	1839	-245	87
H(9B)	11659	2379	-314	87
H(10A)	10913	366	-715	86
H(10B)	12906	732	-554	86
H(12)	11919	-1777	-5	67

References:

[1] DiRocco, D. A.; Oberg, K. M.; Dalton, D. M.; Rovis, T. *J. Am. Chem. Soc.* **2009**, *131*, 10872-10874.

[2] DiRocco, D. A.; Rovis, T. *J. Am. Chem. Soc.* **2011**, *133*, 10402-10405.

[3] Yoda, H.; Uemura, T.; Takabe, K. *Tetrahedron Lett.* **2003**, *44*, 977-979.