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1,2-DIAMINATION OF ALKENES VIA REDUCTION OF 1,2,3-TRIAZOLINIUM IONS

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DISSERTATION

A dissertation submitted in partial fulfillment of the
requirements for the degree of Doctor of Philosophy in the
College of Art and Sciences
at the University of Kentucky

By

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2022

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ABSTRACT OF DISSERTATION

1,2-DIAMINATION OF ALKENES VIA REDUCTION OF 1,2,3-TRIAZOLINIUM IONS

1,2-Diamine substructures are prevalent functional motifs in natural products, pharmaceutical compounds, and ligands. The interesting functionalities of 1,2-diamines have inspired many synthetic chemists to design various methodologies for preparing these structures from simple precursors such as alkenes. In this work, we described two different but related methods using simple and easily accessible reagents for 1,2-diamination of alkenes. In the first method, an alkene undergoes 1,3-dipolar cycloaddition with an organic azide to form a 1,2,3-triazoline. Subsequent *N*-alkylation of the generated 1,2,3-triazoline gives the 1,2,3-triazolinium ion, which is then hydrogenated over Raney Ni with a balloon of H_2 to produce 1,2-diamine. Traditionally, it has been believed that a 1,2,3-triazoline is an unstable species in the presence of heat or light and will readily extrude N_2 to form an imine or an aziridine. However, most of the 1,2,3-triazolines prepared in this work were stable to the extrusion of N_2 at the temperature required for their formation.

In the second method, an alkene undergoes 1,3-dipolar cycloaddition with a 1,3-diaza-2-azoniaallene (*azidium* ion, our neologism) to afford a 1,2,3-triazolinium ion directly. The 1,2,3-triazolinium ions are reduced to the corresponding 1,2-diamines using the same conditions described above. As was expected, cyclic alkenes provide cis 1,2-diamines, and acyclic trans alkenes provide threo 1,2-diamines due to syn cycloaddition of the alkene to the azidium ion and preservation of the stereochemistry of the 1,2,3-triazolinium ion during the hydrogenation. Surprisingly, the reduction of acyclic cis alkenes proceeded with complete or partial *inversion* of relative stereochemistry instead of the complete formation of the expected erythro isomer. We hypothesized that this isomerization occurs during the hydrogenation step by Raney Ni. More surprisingly, the reduction of the 1,2,3-triazolinium derived from 5-hexen-2-one produced the diamine product with an additional C–C bond. The X-ray crystallographic analysis and 1D/2D NMR spectra confirmed the structure and the relative stereochemistry of the synthesized 1,2,3-triazolinium ions and 1,2-diamines.

Additionally, we had planned to apply the developed 1,2-diamination methodology toward the total synthesis of loline alkaloids. Lolines are a group of nitrogen-containing natural products produced in cool-season grasses and have shown insecticidal and antifeedant properties. In our designed retrosynthesis, disconnection between C(3) and N(4) in loline tricyclic ring, will lead us to the bicyclic intermediate consist of tetrahydrofuran and pyrrolidine ring. We hypothesized that this intermediate can be produced by hydrogenolysis of the corresponding 1,2,3-triazolinium ion synthesized from 2-deoxy-D-ribose (the ether linkage provider). In my attempt toward this total synthesis, the corresponding 1,2,3-triazoline was synthesized as a first key intermediate in seven steps from 2-deoxy-D-ribose. The *N*-alkylation of the 1,2,3-triazoline, reduction of the produced 1,2,3-triazolinium ion, and completion of the final stages of this total synthesis are still under investigation.

Keywords: 1,2-diamines, hydrogenolysis, 1,2,3-triazolinium ion, azide–alkene cycloaddition, azidium ion–alkene cycloaddition, loline alkaloids total synthesis.

Setareh Saryazdi

08/04/2022

1,2-DIAMINATION OF ALKENES VIA REDUCTION OF 1,2,3-TRIAZOLINIUM IONS

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Date

To my beloved family,

for their unconditional love and support

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LIST OF SCHEMES

LIST OF ABBREVIATION

1D	One Dimentional
2D	Two dimentional
AcAP	1-*exo*-Acetamidopyrrolizidine
BnOTf	Benzyl triflate
Boc	tert-Butyloxycarbonyl
$CF_3CO_2^-$	Triflouroacetate
^{13}C NMR	Carbon-13 Nuclear Magnetic Resonance
COSY	Correlation Spectroscopy
DBU	1,8-Diazabicyclo[5.4.0]undec-7-ene
DIAD	Diisopropyl azodicarboxylate
DMAP	4-Dimethylaminopyridine
DMSO	Dimethyl sulfoxide
DPPA	Diphenylphosphoryl azide
EtOAC	Ethyl acetate
GC-MS	Gas Chromatography-Mass Spectrometer
^1H NMR	Proton Nuclear Magnetic Resonance
HRMS	High Resolution Mass Spectrometry
HSQC	Heteronuclear Single Quantum Coherence
IR	Infrared
MgSO4	Magnesium sulfate
NEt_3	Triethylamine
NOESY	Nuclear Overhauser Effect Spectroscopy
PPh_3	Triphenylphosphine
RT	Room Temperature
TLC	Thin Layer Chromatography
TFA	Triflouroacetic acid
TfO^-	Triflate
TBAF	Tetra-n-butylammonium fluoride
TBSCl	tert-Butyldimethylsilyl chloride

TBDPSCl	tert-Butyl(chloro)diphenylsilane

Chapter 1 Introduction

The 1,2- diamine moiety is a prevalent structural motif across various disciplines. They are in biologically active natural products such as loline alkaloids, biotin, and agelastatin A. They are found in various drugs and medicinal agents, including but not limited to anti-infective, anticancer, and antagonist molecules.[1] They are also employed as ligands for organic transformations and can be served as precursors to *N*-heterocyclic carbenes and imidazolines, which themselves have numerous applications in catalysis and pharmaceuticals sciences.[2] To date, significant signs of progress have been achieved in developing a broad range of strategies for preparing 1,2-diamines.[3] The interesting utilities of 1,2-diamines have encouraged chemists to establish new methodologies for their synthesis. Among all the reported methods, 1,2-diamination of alkenes is one of the interesting approaches considering the availability and easy handling of the alkene substrates.[4] This chapter includes an overview of the importance of 1,2-diamines and explains some of the previously reported methodologies for 1,2-diamination of alkenes.

1.1 Importance of 1,2-diamines

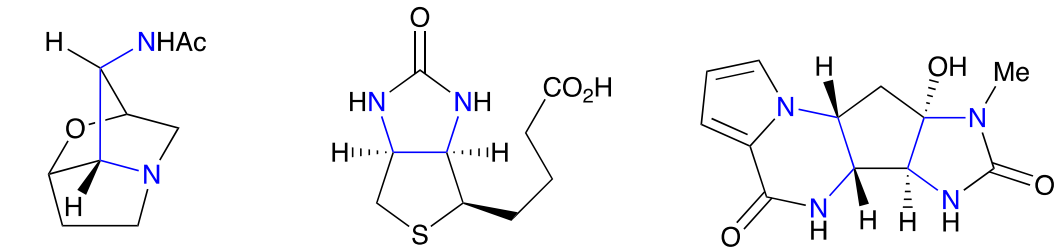
1.1.1 1,2-Diamines in natural products

Loline alkaloids are a group of tricyclic natural products containing the 1,2-diamine moiety in their skeleton. They are produced by fungal endophytes (*Epichloe* or *Neotyphodium* species) in cool-season grasses and provide a remarkable range of survival benefits to the host plants. Loline alkaloids protect their host against certain insects and aphids, enhance the host plant's resistance to numerous stress conditions such as drought and poor soil conditions, and improve root growth and seed production. Although most

loline alkaloids have anti-feedant and insecticidal properties, it has been reported that they are nontoxic to mammalian herbivores (Figure 1.1).[5]

Biotin is another example of a natural compound that has the 1,2-diamine moiety included in its imidazolidinone ring. Biotin is a bicyclic water-soluble vitamin and serves as a required coenzyme for five carboxylases in humans that are involved in the metabolism of carbohydrates and amino acids. Biotin is also covalently attached to the histones in the chromatin core to affect chromatin stability and mediate gene regulation (Figure 1.1).[6]

Agelastatin A is a marine natural product isolated from the axinellid marine sponge *Agelas dendromorpha* in 1993. It belongs to the pyrrole-aminoimidazole family and contains two 1,2-diamine moieties in its tetracyclic structure. Agelastatin A demonstrates cytotoxic activity against various human cancer cell lines and inhibits the glycogen synthase kinase-3 (GSK-3), an important kinase in the early stages of Alzheimer's disease (Figure 1.1).[7]



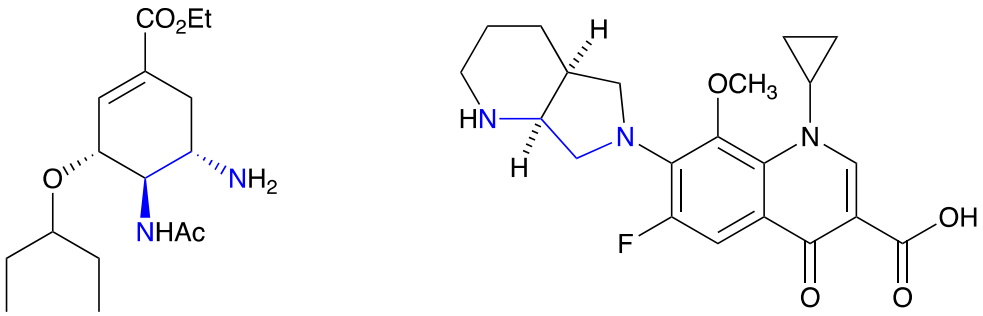
N-Acetylnorloline Biotin Agelastatin A

Figure 1.1 1,2-Diamine moieties in natural products

1.1.2 1,2-Diamines applications in medicinal chemistry

The 1,2-diamine functionality is found in various synthetic therapeutic agents and has been utilized as a remarkable template for synthesizing medicinal agents.[1] For instance, oseltamivir- the antiviral medication bearing a 1,2-diamine moiety- is used to treat

influenza A and B infections by inhibition of the influenza's neuraminidase enzymes which is an enzyme that helps the virus particles to escape the human cells and infect the others (Figure 1.2).[8] Another anti-infective example is moxifloxacin that contains a 1,2-diamine substituent at the 7-position of flouroquinolone ring.[9] This 1,2-diamine substituent appeared to be essential for moxifloxacin effectiveness (Figure 1.2).[10]



Oseltamivir Moxifloxacin

Figure 1.2 Examples of anti-infective therapeutic agents containing 1,2-diamine moieties

In addition to anti-infectives, 1,2-diamines are also found in anticancer agents such as 1,2-diaminocyclohexane platinum (II) complexes (Figure 1.3).[11] These complexes are designed after the discovery of anticancer properties of cis-diamminedichloroplatinum(II) (cisplatin) by Rosenberg et al. in late 1960s.[12] These 1,2-diaminocyclohexane platinum (II) complexes have shown higher antitumoral activity and less toxicity to humane cells compared to cisplatin. Modification of the ligands X (such as oxaliplatin)[11] as well as the diamine ligands (such as 1,2-dihydroxy-4,5-diaminocyclohexane platinum (II) complex)[13] have evolved various generations of the 1,2-diamine platinum (II) complexes that have been evaluated for antitumor activities over the decades (Figure 1.3).

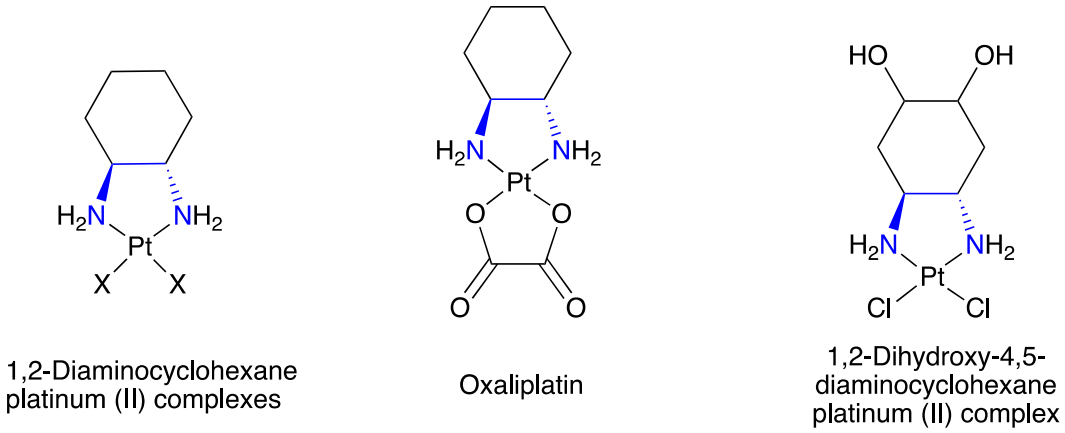


Figure 1.3 Examples of anticancer therapeutic agents containing 1,2-diamine moieties

In 2019, Awuah et al. reported synthesis of cyclometalated gold (III) complexes bearing the *trans*-1,2-diaminocyclohexane ligand (Figure 1.4).[14] These complexes display IC_{50} in the low micromolar range against various humane cancer cell lines. They also proposed that the presence of this ligand increases the stability of these complexes, which can potentially encourage synthetic chemists to employ similar 1,2-diamines in designing future anticancer complexes.[14] In collaboration with Dr. Awuah's group, one of the 1,2-diamines I synthesized was utilized as a chelating ligand to prepare similar cyclometalated gold (III) complexes with different scaffolds. The synthesis of this 1,2-diamine will be discussed in chapter 2.

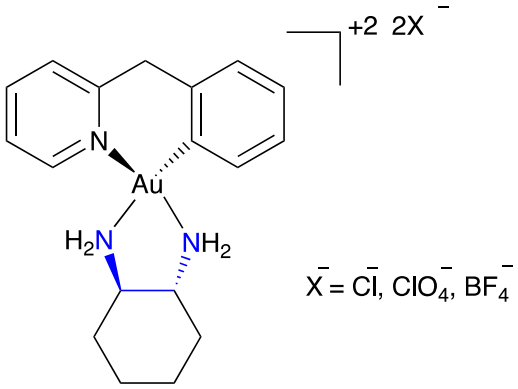
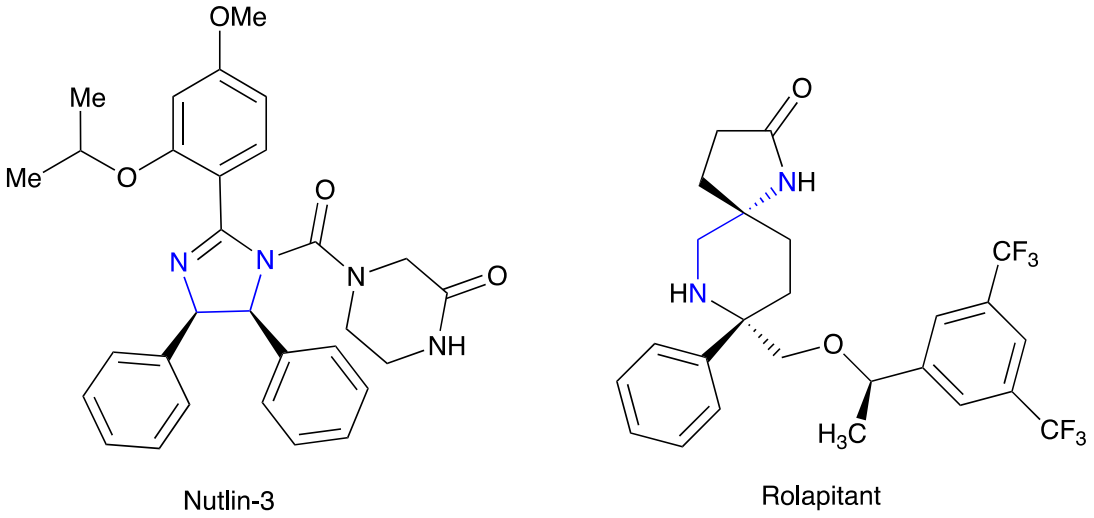


Figure 1.4 Cyclometalated gold (III) complexes bearing *trans*-1,2-diaminocyclohexane ligand

Figure 1.5 illustrates other significant examples of medicinal agents that incorporate 1,2-diamines in their structures. Nutlin-3 is a *cis*-imidazoline antagonist that inhibits the binding between MDM2 and the p53 protein. In many human tumors, the MDM2 is overexpressed, which can impair the tumor suppression ability of p35 protein. Nutlin-3 inhibits the MDM2–p53 interaction by displacing the p53 in the MDM2–p53 complex[15]. Rolapitant is another antagonist that prevents nausea in chemotherapy patients in combination with other antiemetic agents. It blocks the neurokinin NK1 receptors in the brain, which are responsible for the physiological responses of the stomach.[16]

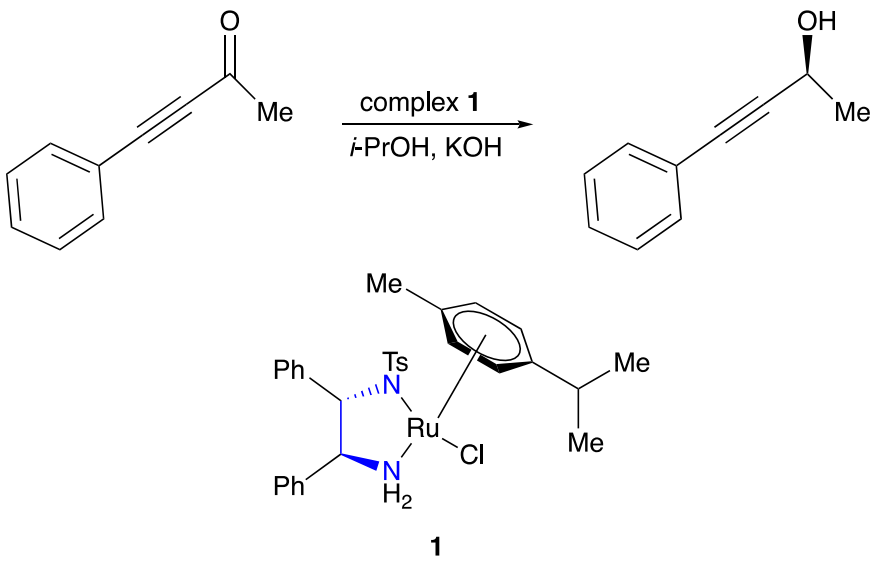


Nutlin-3 Rolapitant

Figure 1.5 Examples of antagonist agents bearing 1,2-diamine moieties

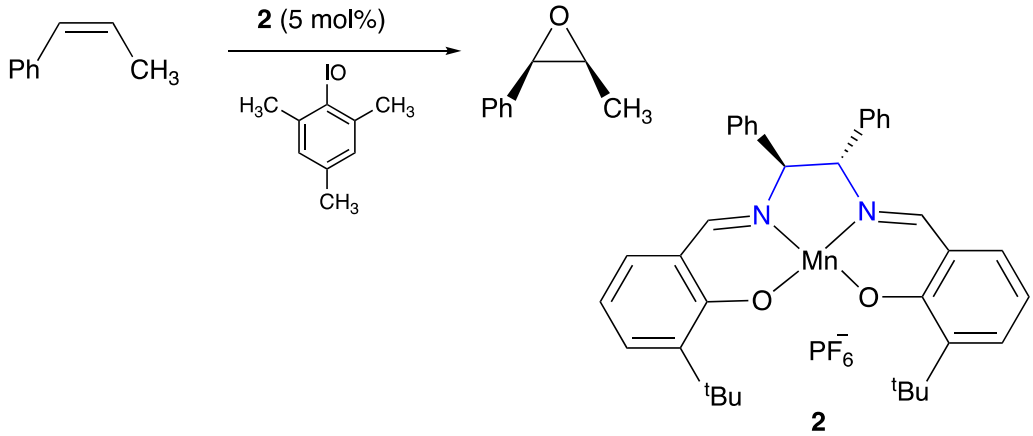
1.1.3 1,2-Diamines applications in catalysis

1,2-Diamines have been employed as chiral ligands in transition metal complexes to catalyze stereoselective organic transformations.[17, 18] Noyori et al. developed the asymmetric transfer hydrogenation of α,β-acetylenic ketones mediated by Ru (II) catalysts **1** to synthesize the propargylic alcohols (Scheme 1.1).[18] This chemo- and enantioselective method utilizes 2-propanol as a source of hydrogen, facilitating the hydrogen transfer to the carbonyl without affecting the alkyne functional group.



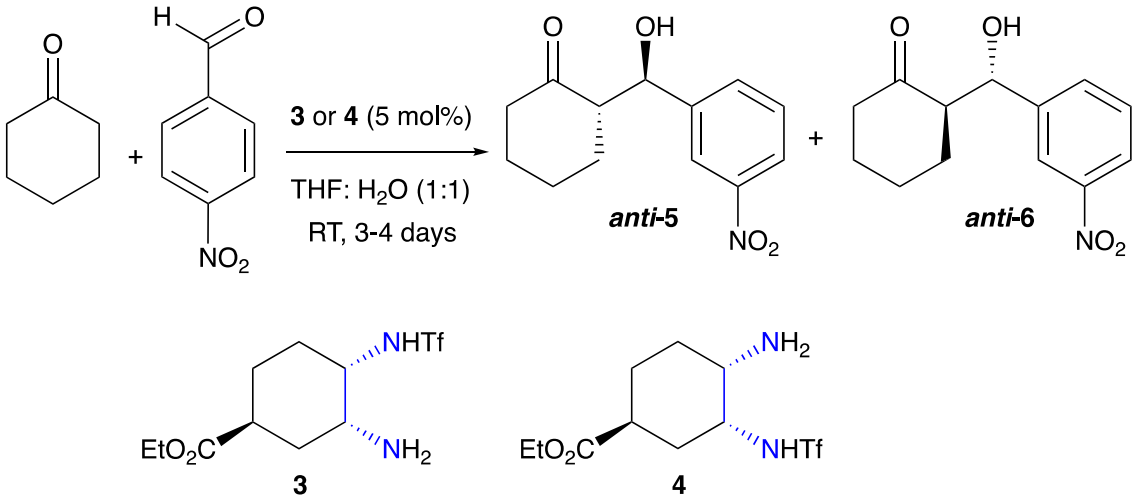
Scheme 1.1 Conversion of α,β-acetylenic ketones to propargylic alcohol by Ru(II) catalyst

Manganese salen complexes [Mn(salen)] can catalyze epoxidation of alkenes and their tetradentate salen ligands contain the 1,2-diamine moiety.[19, 20] Jacobson et al. reported the enantioselective epoxidation of alkyl- and aryl-substituted alkenes in the presence of the chiral manganese salen complex **2** and iodosylmesitylene as the oxygen source.[19] They reported alkenes with bulky terminal groups resulted in higher enantioselectivity due to unfavorable steric interaction of the hindered terminus in alkenes with tert-butyl groups on the salen complex (Scheme 1.2).[19]



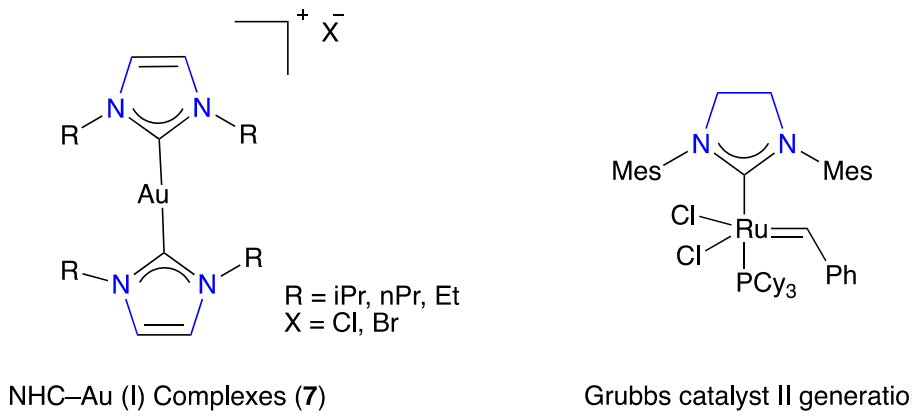
Scheme 1.2 Enantioselective alkene epoxidation catalyzed by [Mn(salen)] complex

1,2-Diamine moieties are found in organocatalysts. Maruoka et al. reported syntheses of two chiral organocatalysts **3** and **4** that can catalyze asymmetric aldol condensation of cyclic ketones and substituted benzaldehydes (Scheme 1.3).[21] Both catalysts **3** and **4** showed anti selectivity. Catalyst **3** afforded the enantiomeric aldol products of **5**, while the use of catalyst **4** yielded the product **6**.[21]



Scheme 1.3 Asymmetric aldol condensation catalyzed by 1,2-diamine organocatalyst

1,2-Diamines can also serve as precursors for the synthesis of imidazolines and *N*-heterocyclic carbenes (NHCs) which have the ability to coordinate to metals to make various complexes useful in medicines and catalysis (Figure 1.6).[2, 22, 23] The antimicrobial and anticancer properties of silver-NHC and gold-NHC complexes have been investigated over the years. For instance, gold (I) complexes of **7** can selectively inhibit the selenoenzyme thioredoxin reductase and induce apoptosis of cancer cells.[24] *N*-hetereocyclic carbenes coordinate to transition metals to catalyze various reactions such as C–H activation reactions (Pd, Ru, Ir complexes)[23] and alkene metathesis (Grubbs II generation and Hoveyda-Grubbs II generation)[2].



NHC–Au (I) Complexes (**7**) Grubbs catalyst II generation

Figure 1.6 Examples of NHC–metal complexes useful in medicine and catalysis

1.2 1,2-Diamination of alkenes

The presence of 1,2-diamine substructures in natural products, pharmaceutical compounds, and ligands has motivated chemists to design new methods for preparing these structures. A very simple and interesting approach to synthesize 1,2-diamines is by adding two nitrogen atoms across the π bond of an alkene. The syn or anti stereospecificity of the reaction is determined by the mechanism of addition of the N atoms (Figure 1.7).

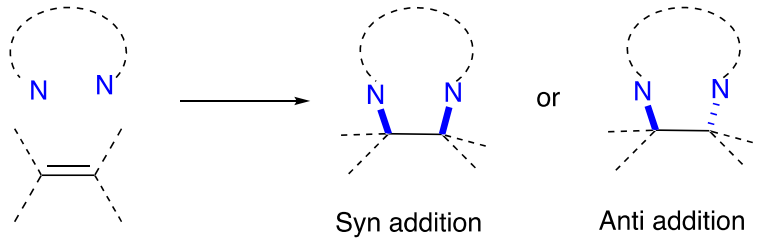


Figure 1.7 Stereospecific syn or anti addition of N atoms across the π bond of an alkene

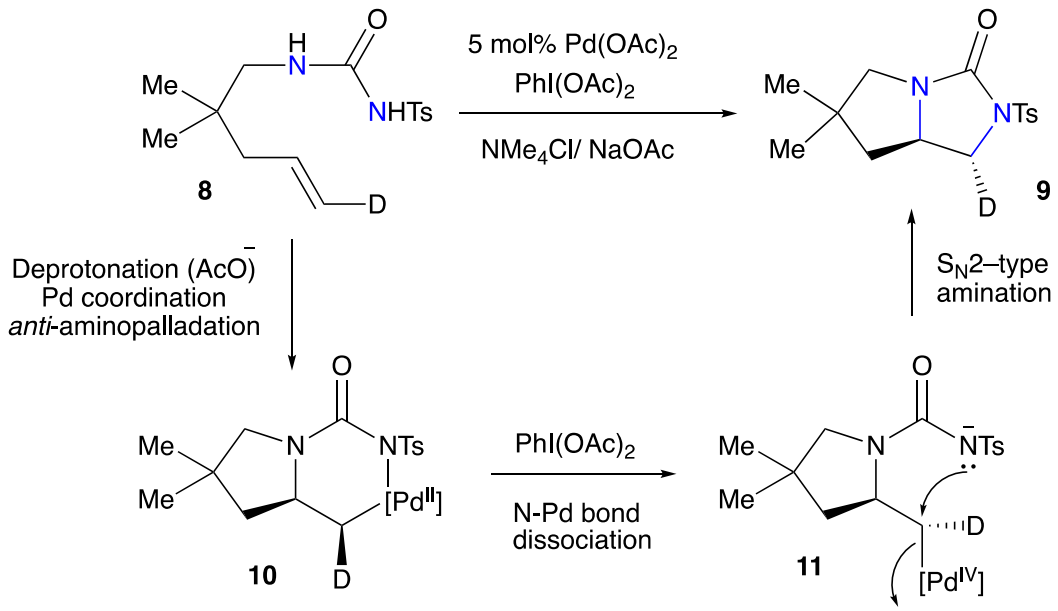
This approach is appealing because it converts readily accessible simple hydrocarbon (alkene) to a more complicated and advanced product (1,2-diamine) with various practical applications. The approach is interesting enough that it has encouraged many organic synthetic chemists to develop new methodologies for the 1,2-diamination of alkenes over the years. In this section, I will provide some of the significant examples of

these synthetic approaches, which are divided into three groups: Those in which a) both N atoms are tethered to an alkene; b) one N atom is tethered to the alkene, and the other is delivered externally, and c) both N atoms are delivered externally.

1.2.1 1,2-Diamination of alkenes: Both N atoms are tethered to an alkene

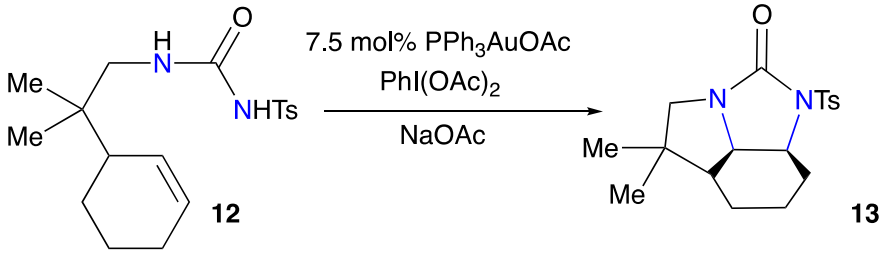
In this group, most of the reported alkene substrates are bearing a pendant N–X–N linkage (X = CO, SO_2), which can be activated in the presence of a transition metal (such as Pd(II), Au(III), Cu(II)) or a reagent such as IPy_2BF_4) to internally install both N atoms across the double bond of an alkene.

Muñiz et al. reported intramolecular 1,2-diamination of ω-alkenyl-substituted ureas **8** in the presence of palladium (II) catalyst, oxidant $PhI(OAc)_2$, and acetate base (Scheme 1.4).[25] They proposed a diamination mechanism using spectroscopic and labeling studies. First, a urea anion was produced using the acetate base. Palladium coordination and aminopalladation formed the complex **10**. Oxidation of Pd(II) complex **10** with iodobenzene diacetate forms the Pd(IV) complex. Dissociation of the urea from the palladium (IV) center forms complex **11** and further S_N2-type amination forms the cyclic product **9** and regenerates the Pd(II) catalyst.



Scheme 1.4 1,2-Diamination of alkenes catalyzed by $Pd(OAc)_2$

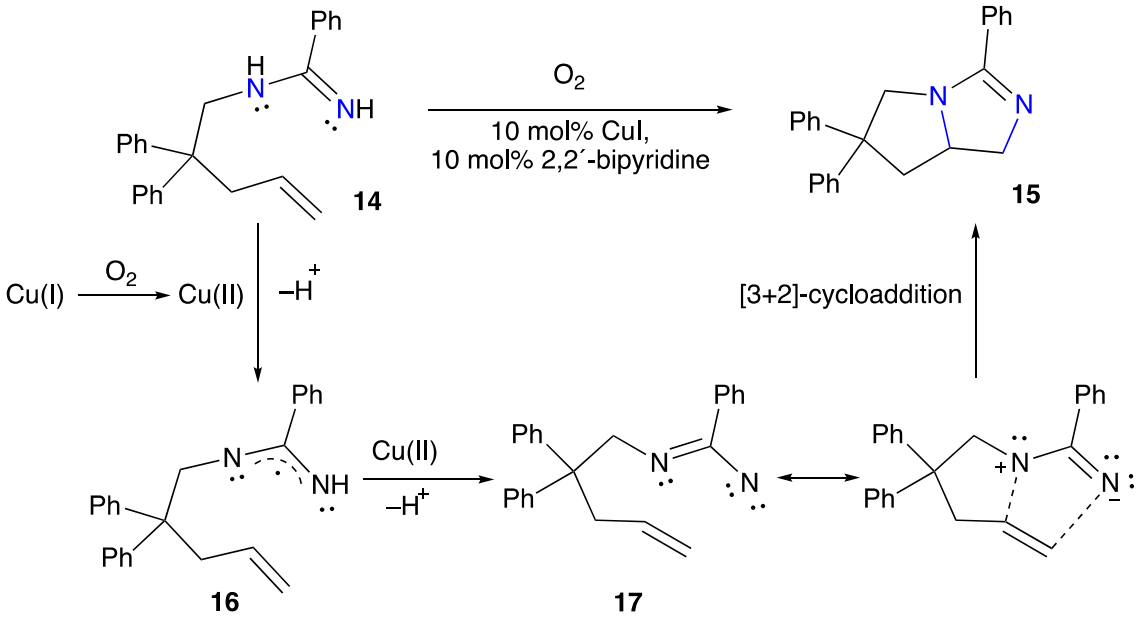
In 2009, Muñiz et al. developed a 1,2-diamination of cyclic alkene in the presence of Triphenylphosphine gold(I) acetate catalyst (synthesized from Ph_3AuCl and AgOAc), $PhI(OAc)_2$ as an oxidant and acetate base (Scheme 1.5).[26] The overall *syn*-1,2-diamination was confirmed by the formation of tricyclic product **13** and a deuterium-labeling study.



Scheme 1.5 1,2-Diamination of alkenes catalyzed by $PPh_3Au(OAc)$

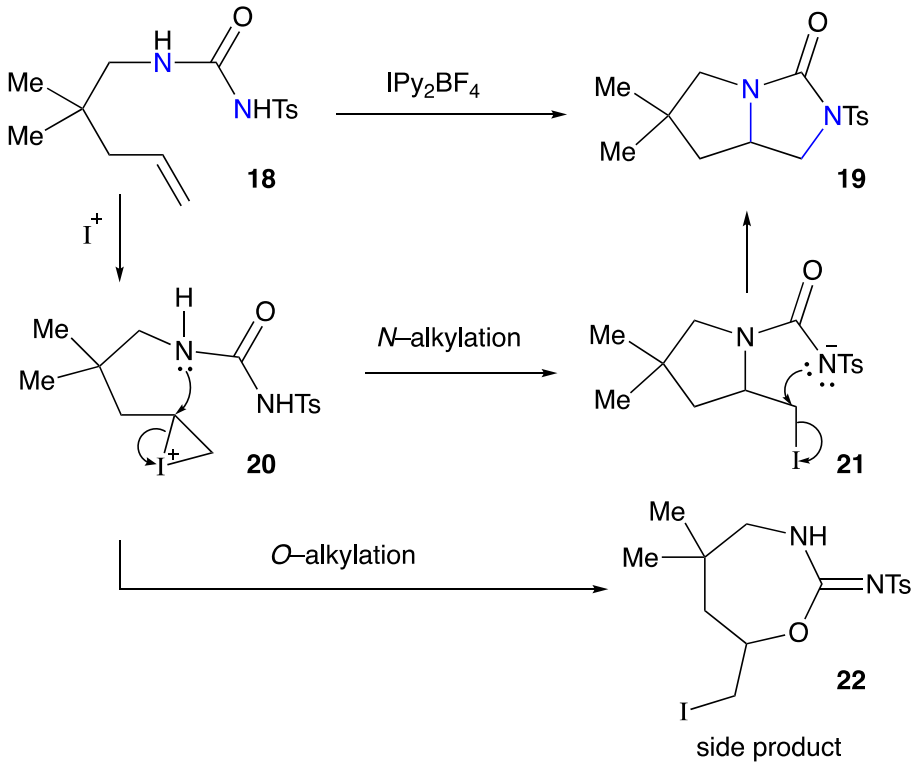
In 2012, Chiba et al. reported the intramolecular 1,2-diamination of alkenes bearing a pendant amidine functional group through Cu-mediated aerobic [3+2]-cycloaddition (Scheme 1.6).[27] The proposed mechanism begins with oxidation of Cu(I) catalyst with oxygen to generate Cu(II) superoxo or peroxo species. This catalyst species converts the *N*-alkenyl amidine **14** to the radical **16** through one-electron oxidation. Further oxidation

of **16** with another Cu(II) species produces nitrene intermediate **17** which potentially can undergo concerted [3+2] cycloaddition with the alkene to form the cyclic amidine **15**.



Scheme 1.6 1,2-Diamination of alkenes catalyzed by Cu(II) catalyst

Besides using transition metals, alkenes can be electrophilically activated using reagents such as IPy_2BF_4. Muñiz et al. reported the 1,2-diamination of ω-alkenyl ureas **18** in the presence of IPy_2BF_4, bis(pyridine)iodonium tetrafluoroborate, to form the iodonium intermediate **20** (Scheme 1.7).[28] Nucleophilic attack of the proximal N atom on the proximal C of the electrophilic alkene forms the iodoamine **21**, causing the iodine to migrate to the terminal C. Nucleophilic attack of the distal N on the terminal C of the electrophilic alkene affords the cyclic urea **19**. Despite the efficient formation of **19**, undesired product **22** also forms by nucleophilic attack of carbonyl oxygen and ring-opening of the iodonium cation in intermediate **20**. The nucleophilicity of the oxo group increases by a mesomeric effect of urea functionality which causes competition between desired *N*-alkylation and *O*-alkylation reactions.



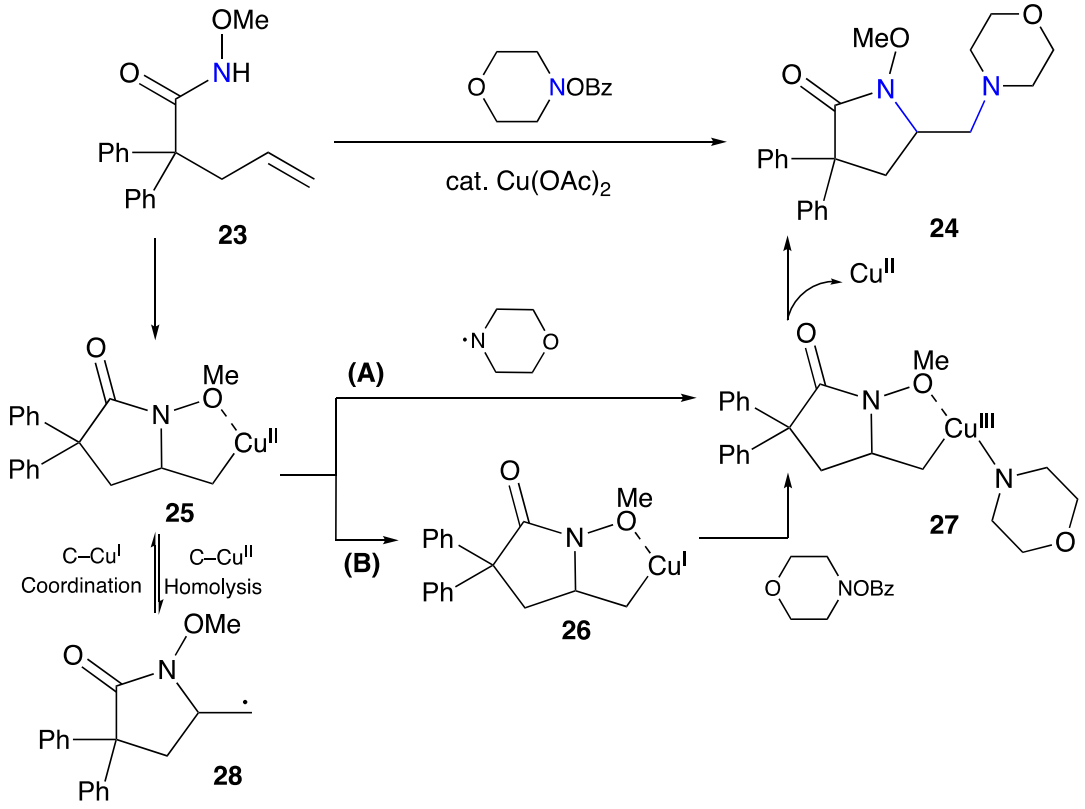
Scheme 1.7 1,2-Diamination of alkenes catalyzed by IPy_2BF_4

1.2.2 1,2-Diamination of alkenes: one N atom is tethered to the alkene, and the other is delivered externally

In this group, the introduction of N atoms to the double bond occurs via two different N sources. This process uses a substrate that already contains one of the two N atoms in a product, and an external N source delivers the second N atom.

Wang et al. developed 1,2-diamination of alkenes in *N*-alkoxypentamides using Cu(II) catalyst and *O*–acylatedhydroxylamine derivatives as both oxidants and the electrophilic external nitrogen source (Scheme 1.8).[29] They reported that this reagent offered a good N source for installation of various amino groups without poisoning the Cu(II) catalyst despite the free amines. The reaction proceeds through the formation of Cu(II) complex **25** via intramolecular aminocupration of the alkene substrate **23**. The complex **25** can proceed via two proposed pathways to form Cu(III) complex **27**: A)

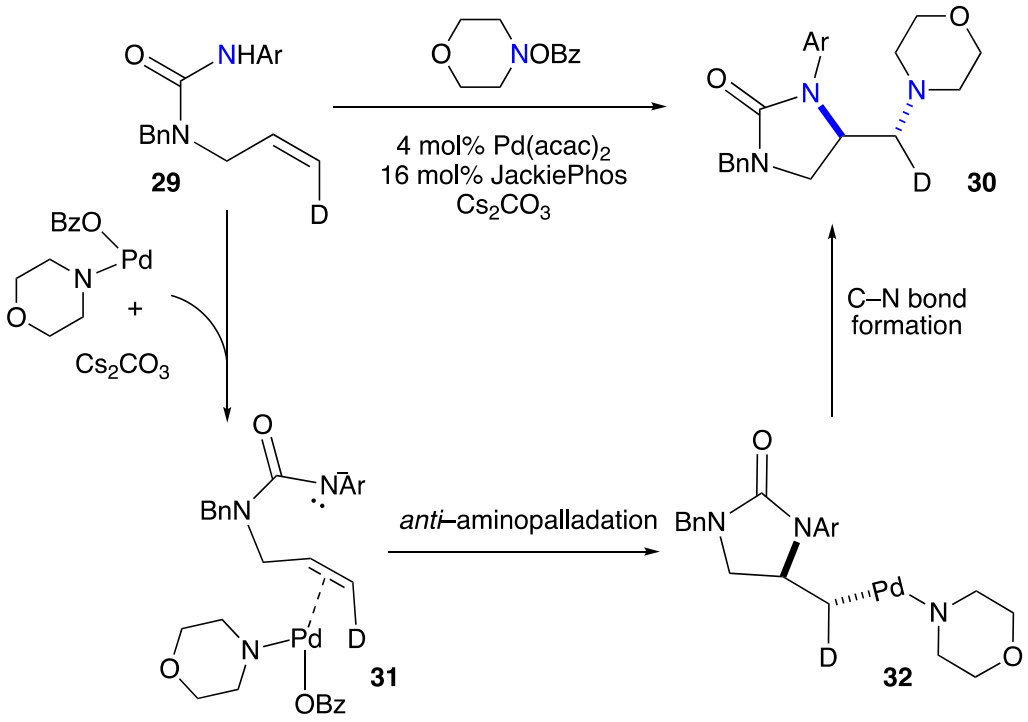
coordination to the amino radical (formed from *O*–benzoylhydroxylamine in the presence of copper catalyst), B) reduction to Cu(I) complex **26** followed by amination with *O*–benzoylhydroxylamine. Complex **27** underwent reductive elimination to form the 1,2-diamine product **24** and regenerate Cu(II) complex. They proposed that homolytic cleavage of C–Cu(II) in complex **25** can form the radical intermediate **28**, making this methodology nonstereospecific.



Scheme 1.8 1,2-Diamination of alkenes catalyzed by Cu(II) catalyst with *O*–benzoylhydroxylamine

In 2018, Wolfe et al. reported *anti*-1,2-diamination of alkenes in *N*–allylguanidines and *N*-allylureas in the presence *O*-benzoylhydroxylamine (similar to Wang's method) and Pd(II) catalyst (Scheme 1.9).[30] However, the reaction proceeded through a different mechanism (not forming radical intermediate) using the Pd(II) catalyst catalyst, which caused their methodology to be stereospecific. They proposed that the intermediate **31** can

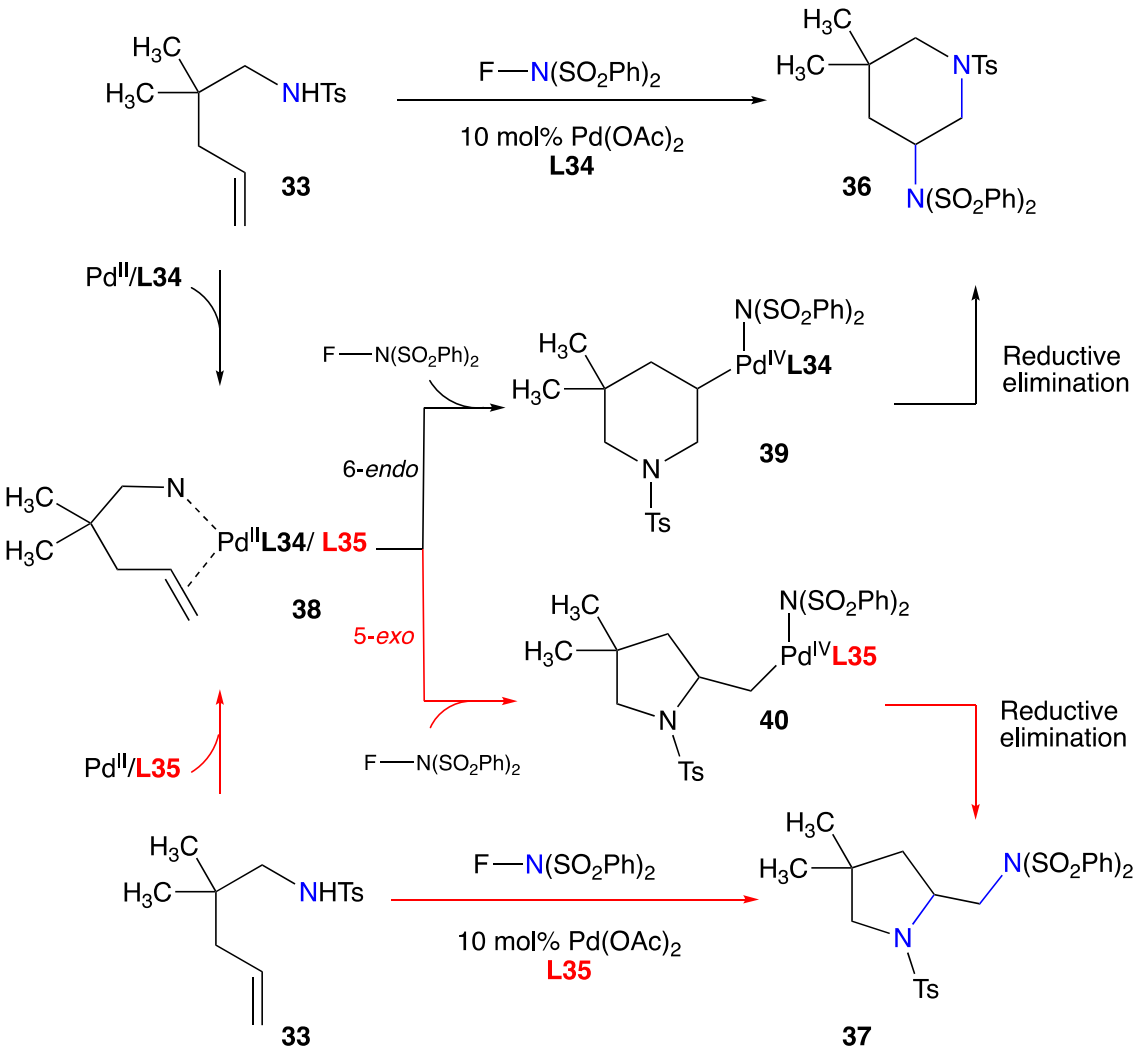
be formed after coordination of the alkene to the Pd(II) complex, which can undergo deprotonation and *anti*–aminopalladation to form complex **32**. Further reductive elimination and C–N bond formation regenerated the catalyst and produced the desired anti product **30**.

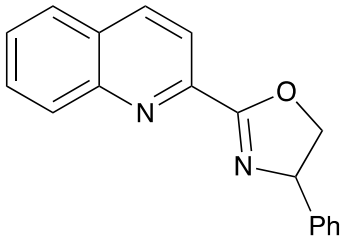


Scheme 1.9 *anti*-1,2-Diamination of alkenes catalyzed by Pd(II) catalyst with *O*-benzoylhydroxylamine

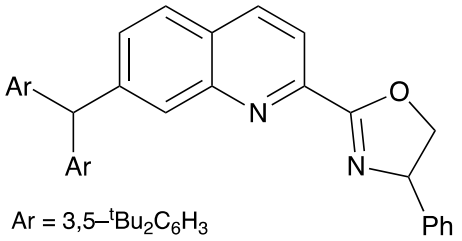
In 2020, Peng, Chen, and Liu reported regioselective palladium-catalyzed 1,2-diamination of alkenes with *N*-fluorobenzenesulfonimide [F–N(SO_2Ph)$_2$] as an oxidant and external aminating agent (Scheme 1.10)[31]. They controlled the regioselectivity of the reaction by employing pyridinyloxazoline ligands **L34** and **L35** to form various pyrrolidine and piperidine products. Coordination of Pd(II) to the alkene formed the π-complex **38**. Use of the less sterically hindered ligand **L34** promotes the 6-endo cyclization which followed by oxidative addition of F–N(SO_2Ph)$_2$ to form the Pd(IV)complex **39** (black route). On the other hand, the bulky ligand **L35** promotes the 5-exo cyclization and further

oxidative addition of F–N(SO$_2$Ph)$_2$ formed the Pd(IV)complex **40** (red route). In both cases, reductive elimination and second C–N bond formation regenerated the catalysts and produced the desired products **36** and **37**, respectively.





L34



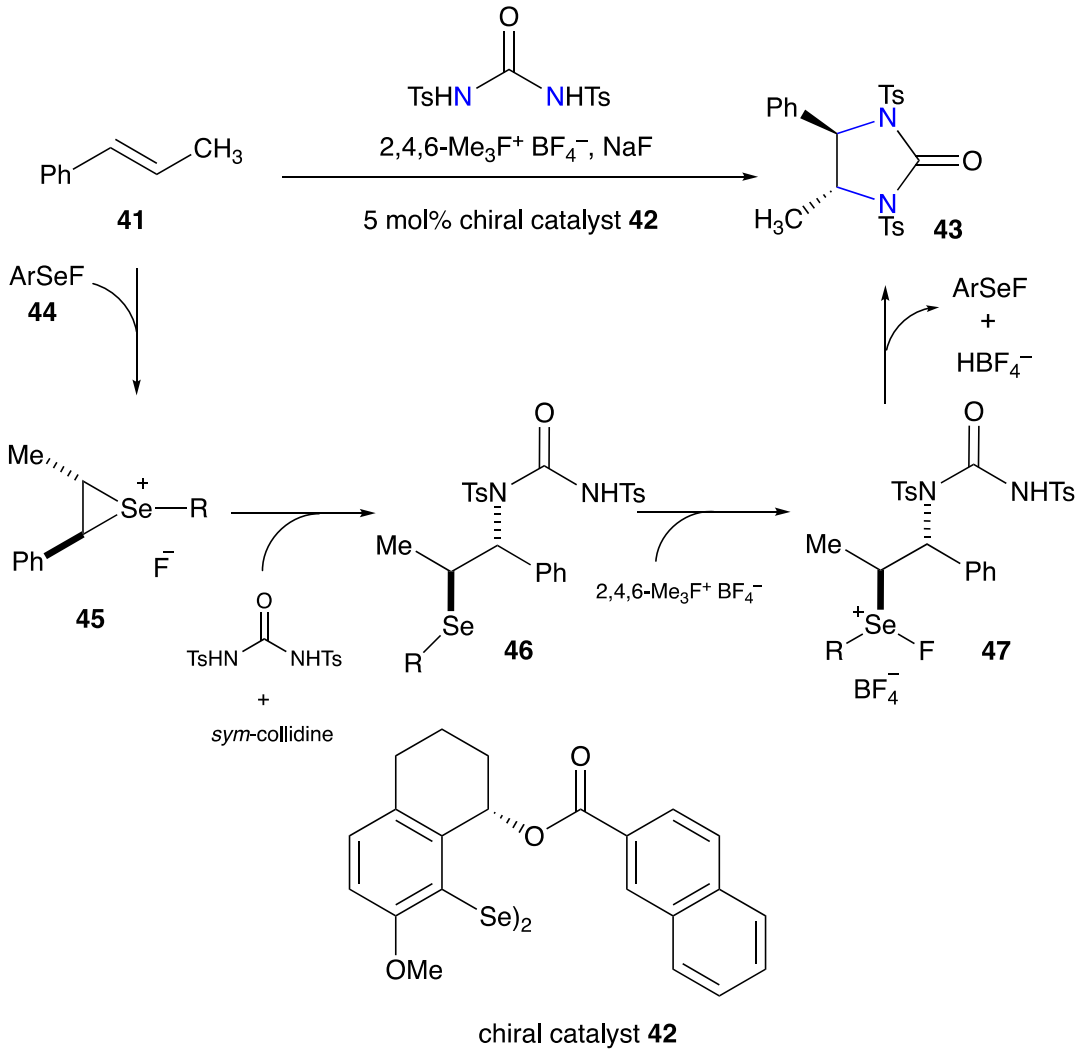
L35

Scheme 1.10 Regioselective 1,2-diamination of alkenes catalyzed by Pd(II) catalyst with $F–N(SO_2Ph)_2$

1.2.3 1,2-Diamination of alkenes: both N atoms are delivered externally

In this group, both N atoms are delivered externally to an electrophically activated alkene to form a 1,2-diamine product. These N atoms can be provided from a single or two different nitrogen sources.

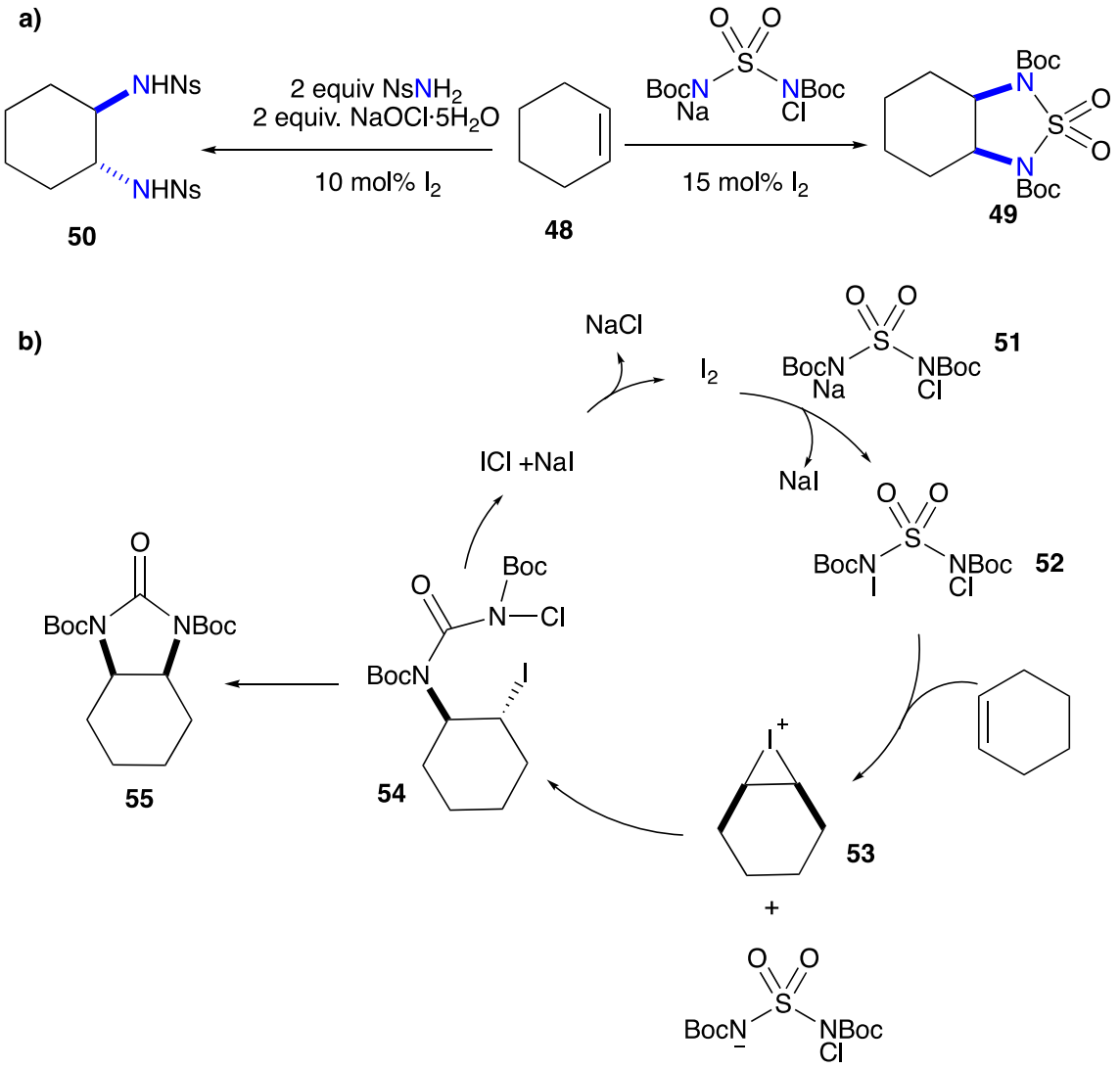
In 2019, Denmark et al. described the first catalytic asymmetric 1,2-diamination of alkenes (Scheme 1.11).[32] Their methodology employs a chiral organoselenium reagent together with *N*-fluorocollidinium tetrafluoroborate (2,4,6-Me_3-$F^+BF_4^-$) and sodium fluoride to catalyze the syn 1,2-diamination of alkenes. In their proposed mechanism, oxidation of the diselenide precatalyst **42** with 2,4,6-Me_3-$F^+BF_4^-$ produces the arylselenium (II) intermediate **44**. Reaction of the alkene with arylselenium (II) formed the seleniranium ion intermediate **45** in the concerted fashion. The nucleophilic ring opening reaction of the urea with intermediate **45** afforded the intermediate **46** which then oxidized to arylselenium (IV) **47**. The displacement of selenium with the urea distal N formed the product **43** and regenerate the selenium species.



Scheme 1.11 Asymmetric 1,2-diamination of alkenes by arylselenium (II) catalyst with urea and *N*-fluorocollidinium tetrafluoroborate

In 2021, Minakata et al. reported syn and anti 1,2-diamination of alkenes to form variety of racemic 1,2-diamines (Scheme 1.12).[33] The reaction was catalyzed in the presence of iodine and the stereospecificity of the reactions were controlled by the choice of nitrogen source. For instance, the syn-1,2-diamination was achieved by using chloramine-BBS **51** as a source of nitrogen. Transfer of the iodine to chloramine salt produced the *N*-iodonated reactive species **52** which transfers iodine to the alkene to form the iodonium intermediate **53**. Ring opening of the iodonium ion with nucleophilic nitrogen

generated the iodoaminated intermediate **54,** which can further produce the product of *syn*-1,2-diamination and regenerate the catalyst.



Scheme 1.12 a) Syn and anti 1,2-diamination of alkenes catalyzed by I_2 with use of different nitrogen sources, b) Mechanism of syn 1,2-diamination of alkenes catalyzed by I_2 with chloramine-BBS

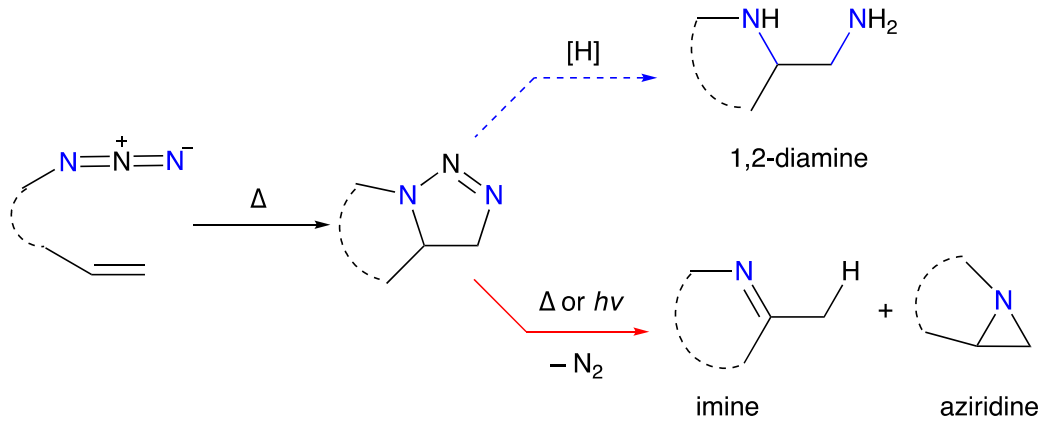
In chapter 1, an overview of the application of 1,2-diamines in natural products, medicinal agents, and catalysis was provided. All these uses of 1,2-diamines have convinced chemists to develop various methodologies for their synthesis from different substrates such as alkenes. Some of the significant approaches for 1,2-diamination of

alkenes were also discussed. Despite all the advances in this area, new methodologies that provide molecules with novel and interesting features, use simple and various substrates, and limit the use of expensive catalysts and reagents are worth exploring. In this dissertation, development of two methods for 1,2-diamination of alkenes is discussed in chapter 2 and 3. In these methods, 1,2,3-triazolinium ions are formed and then hydrogenated over Raney Ni with a balloon of H_2. The potential application of our 1,2-diamination methodology in the total synthesis of loline alkaloids is discussed in chapter 4.

Chapter 2 1,2-Diamination of alkenes via azide–alkene cycloaddition

2.1 Introduction

In the last few years, we turned our attention towards designing new methods for the synthesis of 1,2-diamines from alkenes. We were fascinated by the idea of using an azide as a source of nitrogen. We hypothesized that we could install two N atoms across a π bond of alkene through azide–alkene cycloaddition and make a 1,2,3-triazoline. Further reduction of N–N bonds in the 1,2,3-triazoline with an appropriate reducing agent would excise the middle N atom and form a 1,2-diamine (Scheme 2.1, blue route).



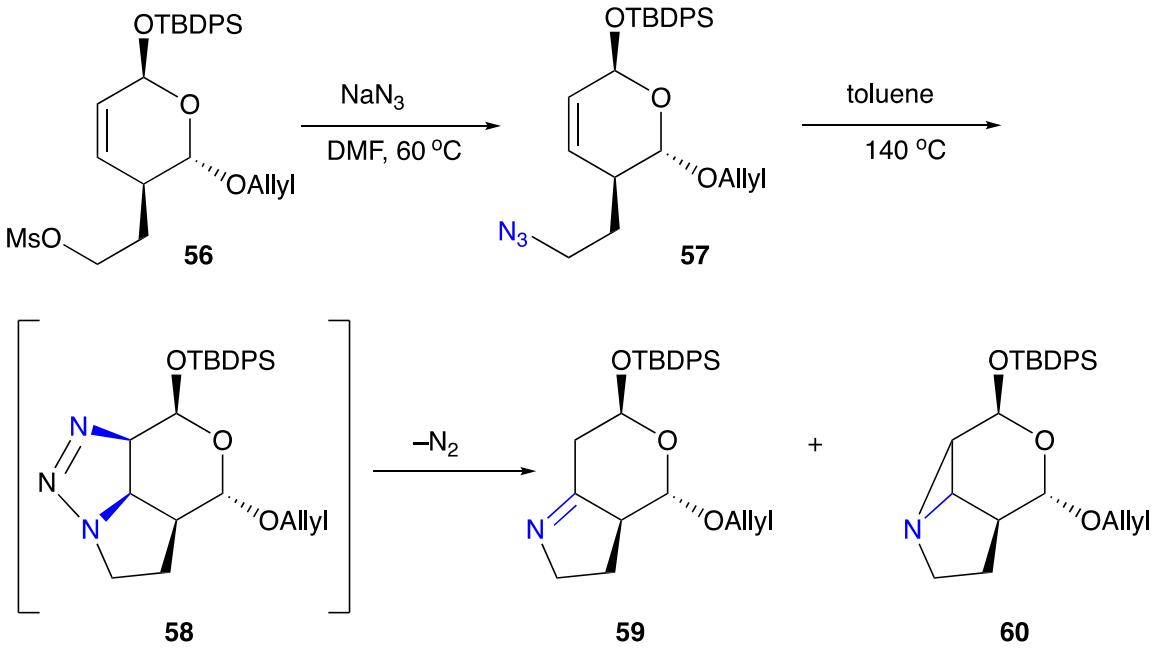
Scheme 2.1 Azide–alkene cycloaddition route to 1,2,3-triazoline and possible reduction of N–N bond to 1,2-diamine (blue route), or extrusion of N_2 to form imine or aziridine (red route)

This method is atom-economical as it utilizes an azide to make two new C–N bonds across a double bond of an alkene. It is appealing because an azide can easily react with alkenes in both inter- and intramolecular fashions, which can potentially allow us to achieve a wide variety of skeletal structures in the final 1,2-diamine products. However, this method can be challenging because 1,2,3-triazolines are generally reported to be unstable in the presence of heat or light. In fact, most organic chemists who have reported making 1,2,3-triazolines did not isolate them; instead, they deliberately heated them up or

photolyzed them to extrude the N_2 to obtain the desired imine or aziridine (Scheme 2.1, red route). Thus, two important questions to ask were, (1) can we synthesize stable 1,2,3-triazolines, and (2) under what conditions can we prevent extrusion of N_2?

2.1.1 Examples of stable 1,2,3-triazolines reported in the literature

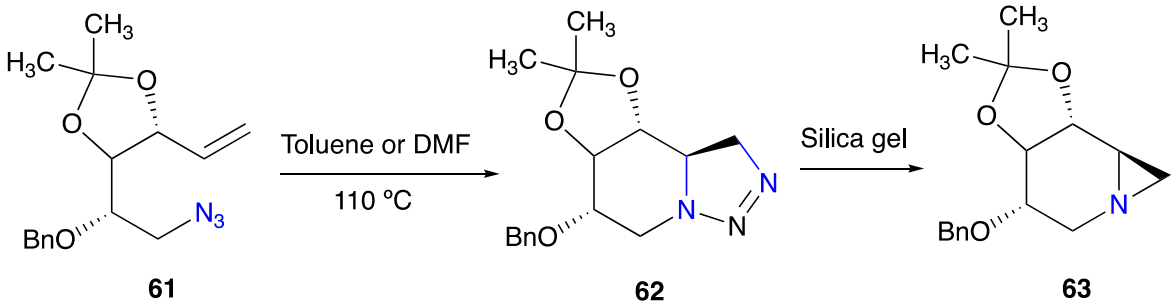
Mann et al. reported the first total synthesis of pyrrolizidine alkaloid amphorogynine C using azide–alkene cycloaddition to form desired imine **59** in their retrosynthesis.[34] They reported that they thermolyzed 1,2,3-triazoline intermediate **58** at 140 °C to extrude N_2 and form the desired product (Scheme 2.2), albeit a product that retained only one of the three N atoms of **58**.



Scheme 2.2 Thermolysis of 1,2,3-triazoline at 140 °C to extrude N_2

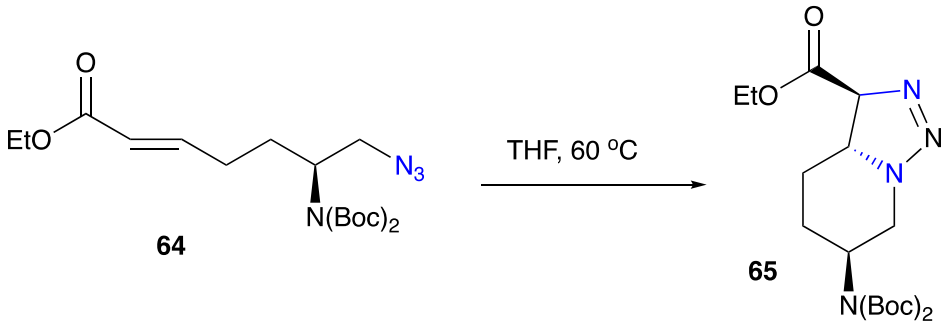
In 2008, Murphy et al. developed a synthetic route towards 1-deoxynojirimycine derivatives utilizing intramolecular azide-alkene cycloaddition.[35] In their synthesis, heating up the organic azide in toluene or DMF at 110 °C yielded a 1,2,3-triazoline **62** that was

stable at that high temperature. Further treatment of the 1,2,3-triazoline with silica gel was necessary to promote loss of N_2 to give the desired aziridine **63** (Scheme 2.3).



Scheme 2.3 Production of *stable* 1,2,3-triazoline at 110 °C and its treatment with silica gel to extrude N_2

In 2003, Kokotos et al. also reported formation of a stable 1,2,3-triazoline **65** from intramolecular azide–alkene cycloaddition of the aliphatic azide **64** at 60 °C in THF (Scheme 2.4).[36] In addition, they described that solvent, temperature, and substituents are important factors controlling the stability of produced 1,2,3-triazoline.



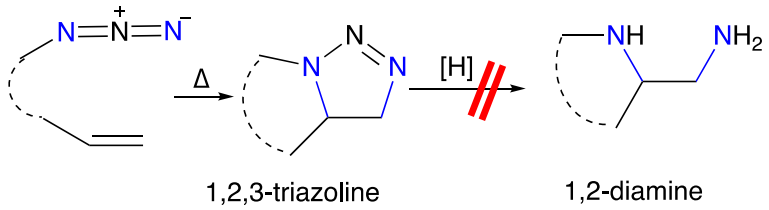
Scheme 2.4 Production of stable 1,2,3-triazoline from aliphatic azide at 60 °C

These observations helped us realize that the temperature required for the extrusion of N_2 (usually >100 °C) from 1,2,3-triazolines was usually much higher than the temperature required for the formation of 1,2,3-triazolines. This suggested that if we keep the temperature of cycloaddition fairly low, we should be able to prevent the extrusion of N_2 and isolate the 1,2,3-triazolines.

2.1.2 1,2-Diamination of alkenes via reduction of 1,2,3-triazolinium ions

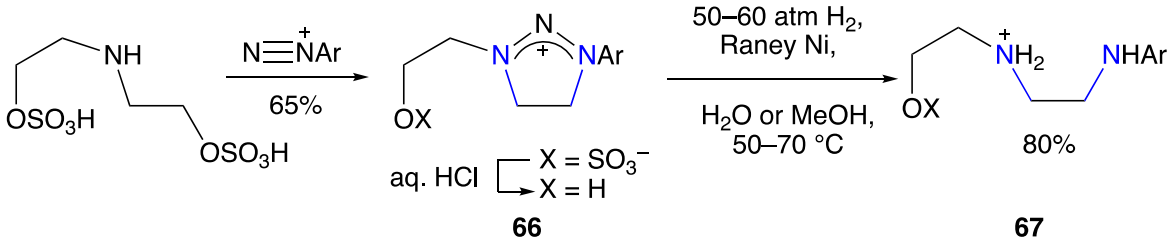
Now that we knew that formation of the stable 1,2,3-triazolines was possible, another key question to ask was: what reducing agent should we use to excise the middle N atom in 1,2,3-triazolines and synthesize the desired 1,2-diamines?

In an attempt to reduce 1,2,3-triazolines to their corresponding 1,2-diamines, I used a wide variety of reducing agents such as $LiAlH_4$, Ni_2B, Raney Ni, Pd/C, Pd(OH), PtO_2, etc. However, I was not able to find any conditions under which the 1,2,3-triazoline could be reduced to a 1,2-diamine (Scheme 2.5).



Scheme 2.5 Our initial approach to reduce 1,2-triazoline to 1,2-diamine

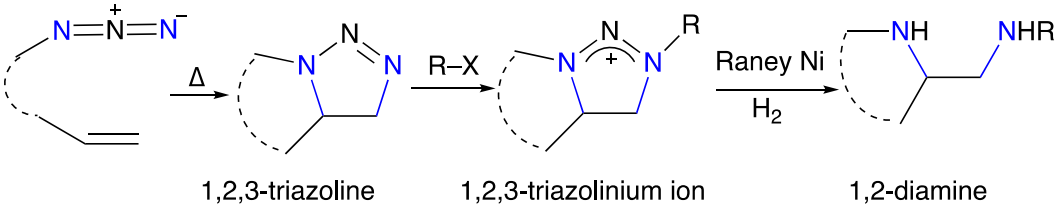
In 1963, Mohr and Hertel reported hydrogenation of the 1,2,3-triazolinium ions **66** (not the 1,2,3-triazoline) with 50-60 atm of H_2 over Raney Ni to give the corresponding 1,2-diamine **67** in high yields (Scheme 2.6).[37]



Scheme 2.6 Mohr and Hertel's reduction of 1,2,3-triazolinium ions to 1,2-diamine

The work of Mohr and Hertel suggested that we could modify our method by *N*-alkylation of the 1,2,3-triazolines to form 1,2,3-triazolinium ions and their subsequent reduction over Raney Ni with 50 atm H_2 (Scheme 2.7). In the following sections, I show

that a balloon of H_2 was sufficient to hydrogenate the 1,2,3-triazolinium ion, despite Mohr and Hertel's use of high pressure of H_2.



Scheme 2.7 Our modified approach for 1,2-diamination of alkenes via reduction of 1,2,3-triazolinium ion

Note: Figure 2.1 shows the structures of 1,2,3-triazoline and 1,2,3-triazolinium ions and their more- or less-hydrogenated structures. One should not confuse the 1,2,3-triazole, which contains N=N and C=C bonds, with the 1,2,3-triazoline, which contains an N=N bond but not a C=C bond, and the 1,2,3-triazolidine, which is a completely saturated molecule. The structures of their corresponding ions are also shown in Figure 2.1. The molecules of interest in this dissertation are 1,2,3-triazolines and 1,2,3-triazolinium ions (red box).

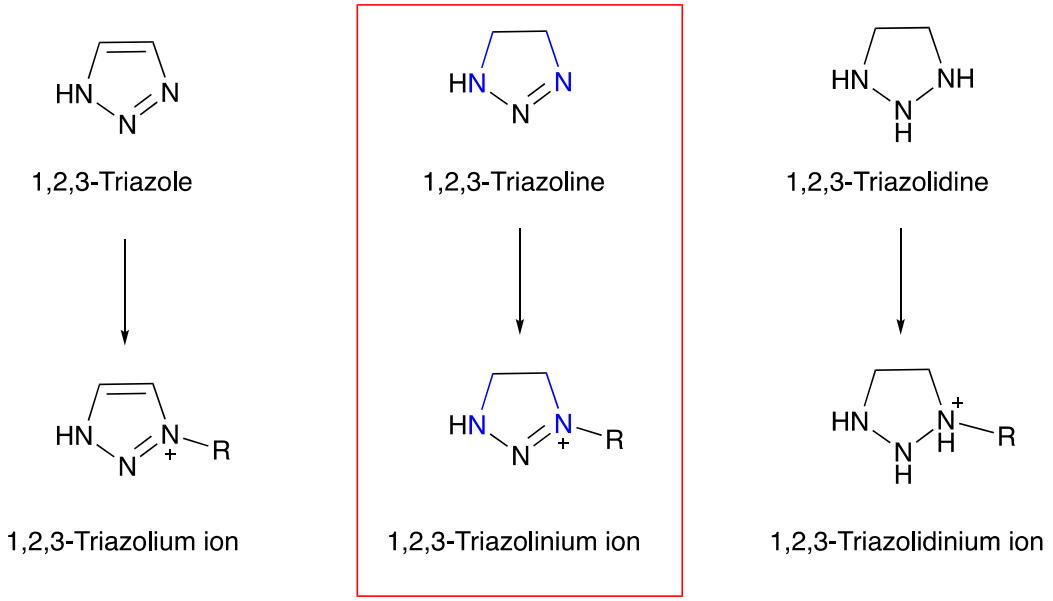
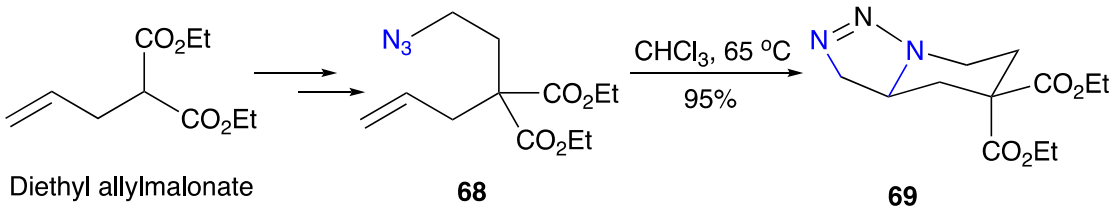


Figure 2.1 Structures of 1,2,3-triazoline and 1,2,3-triazolinium ion and their analogous structures

2.2 Results and Discussion

2.2.1 Exploring the scope of the 1,2-diamination of alkenes through intramolecular azide–alkene cycloaddition

We were interested to synthesize 1,2,3-triazolines by *intra*molecular cycloaddition, *N*-alkylate them to convert them into 1,2,3-triazolinium ions, and subject them to hydrogenation over Raney Ni. Therefore, I synthesized the alkenyl azide **68** from diethyl allylmalonate and converted it to the bicyclic 1,2,3-triazoline **69** at 65 °C in 95% yield (Scheme 2.8).



Scheme 2.8 Production of 1,2,3-triazoline **69** from diethyl allylmalonate

^{1}H NMR (Figure 2.2) and ^{13}C NMR (Figure 2.3) confirmed formation of the desired 1,2,3-triazoline, but not the corresponding imine or aziridine. The absence of C=C resonances in the ^{13}C NMR spectrum confirmed that the corresponding imine was not produced. In the ^{1}H NMR spectrum, I expected to see five downfield H atoms in both the 1,2,3-triazoline and aziridine. However, it was also expected that the H atoms in the 1,2,3-triazoline would be more deshielded than the corresponding H atoms in the aziridine due to the presence of an N=N–N group. In 2018, Diez-Gonzalez reported synthesis of various 1,2,3-triazolines and aziridines using choline chloride/urea (deep eutectic solvent) as a reaction medium.[38] Looking at their reported ^{1}H NMR chemical shifts, I realized the most downfield H atoms in aziridine usually show resonances below 3.5 ppm. In the ^{1}H NMR of the synthesized 1,2,3-triazoline **69**, I observed two H atoms at above 4.0 ppm which is more likely due to the deshielding effect of the N=N–N group in 1,2,3-triazolines.

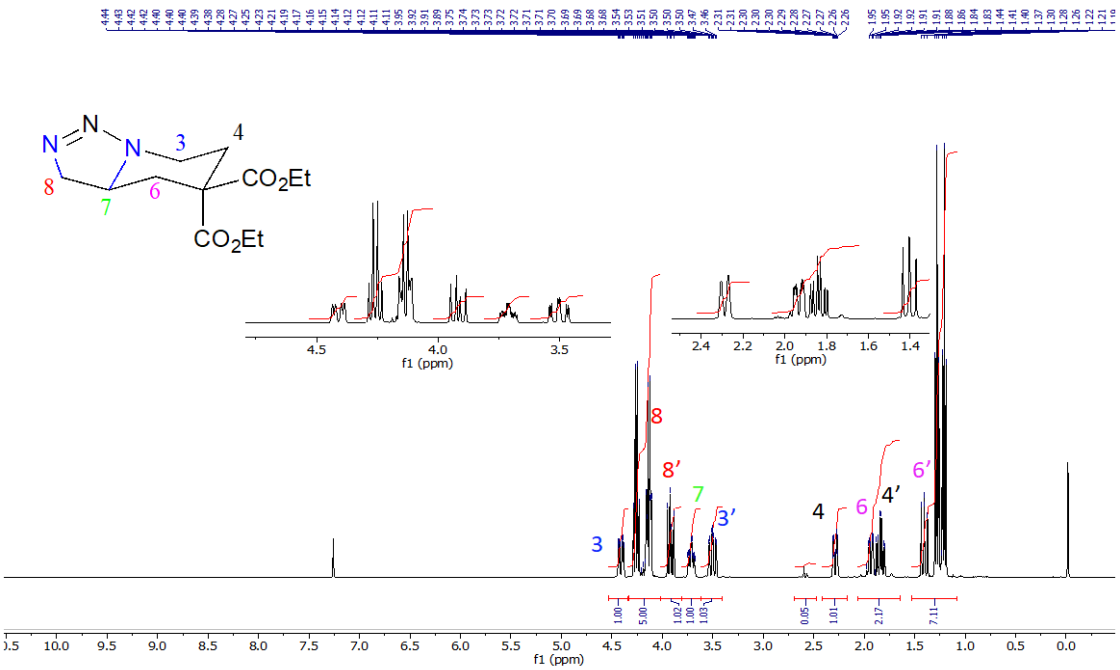


Figure 2.2 ^{1}H NMR 1,2,3-triazoline **69**

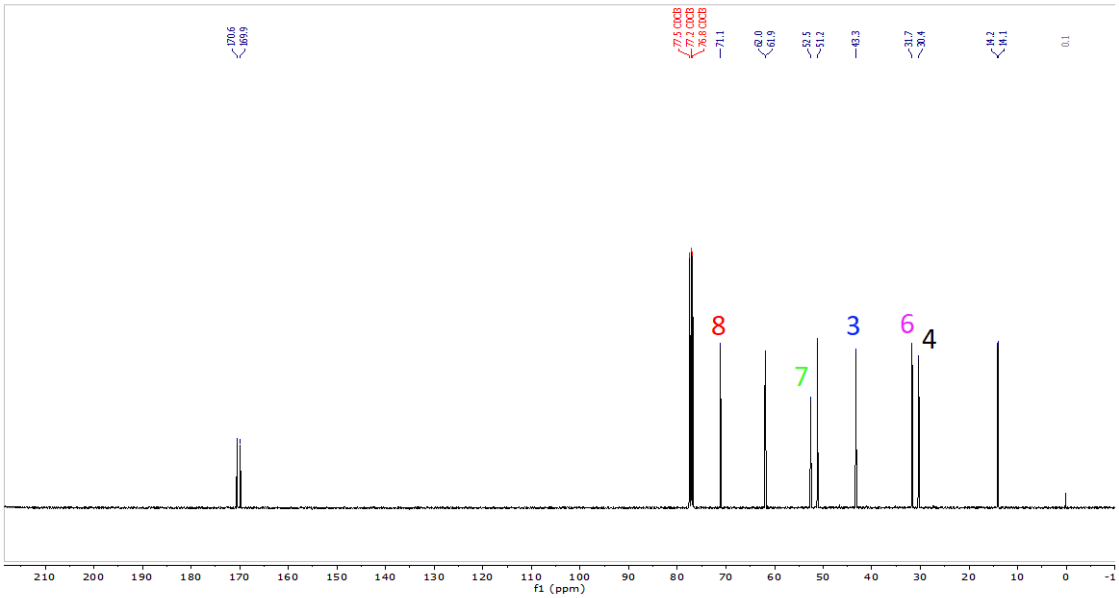
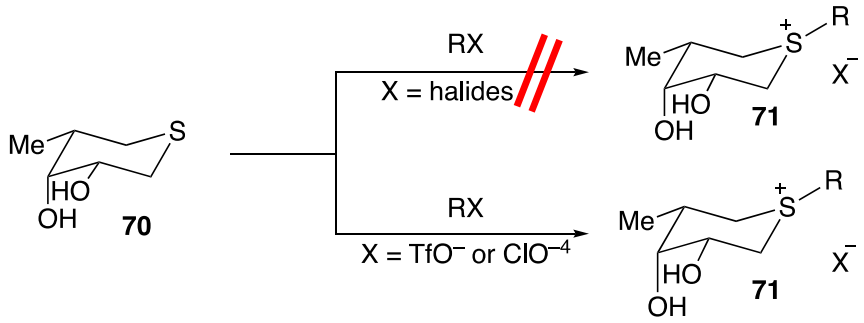


Figure 2.3 ^{13}C NMR 1,2,3-triazoline **69**

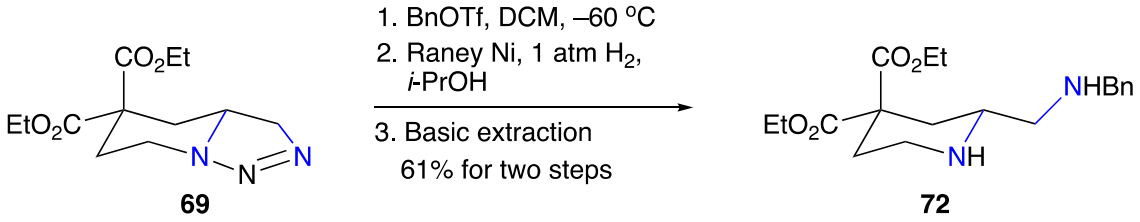
One option for *N*-alkylation of the 1,2,3-triazoline **69** was the use of alkyl halides. However, in 2002, Bols et al. reported decomposition of a sulfonium cation **71** while using

the alkylating agents with nucleophilic counterion (e.g. halides). They suggested using alkyl perchlorates or triflates to bypass this undesired reaction (Scheme 2.9).[39]



Scheme 2.9 Use of alkyl perchlorates or triflates to prevent decomposition of sulfonium cation

Therefore, I chose to use benzyl triflate as an alkylating agent instead of chloride or bromide. Benzyl triflate was prepared in situ from BnOH, Tf_2O, and *sym*-collidine at -60 °C. *N*-Alkylation of the 1,2,3-triazoline **69** produced the corresponding 1,2,3-triazolinium ion. I hydrogenated the crude 1,2,3-triazolinium ion over Raney Ni with a balloon of H_2. Further basic extraction and purification afforded the 1,2-diamine **72** as a free base in 61% yield (Scheme 2.10).



Scheme 2.10 Synthesis of 4,4-diethyl 2-[(benzylamino)methyl]piperidine-4,4-dicarboxylate **72**

The NMR spectroscopic data was consistent with the structure of 1,2-diamine **72**. The HSQC spectrum (Figure 2.4) showed the presence of one methine group, seven methylene groups and two methyl groups. The methine H atom at C(6) appeared at 2.80 ppm. I determined the geminal H atoms on methylene groups using the HSQC spectrum. The geminal pairs (excluding the ester groups) are: two H atoms resonating at 3.79 ppm;

H atoms resonating at 3.14 ppm and 2.74 ppm; two H atoms resonating at 2.75 ppm and 2.66 ppm; H atoms resonating at 2.33 ppm and 1.92 ppm; H atoms resonating at 2.29 ppm and at 1.61 ppm.

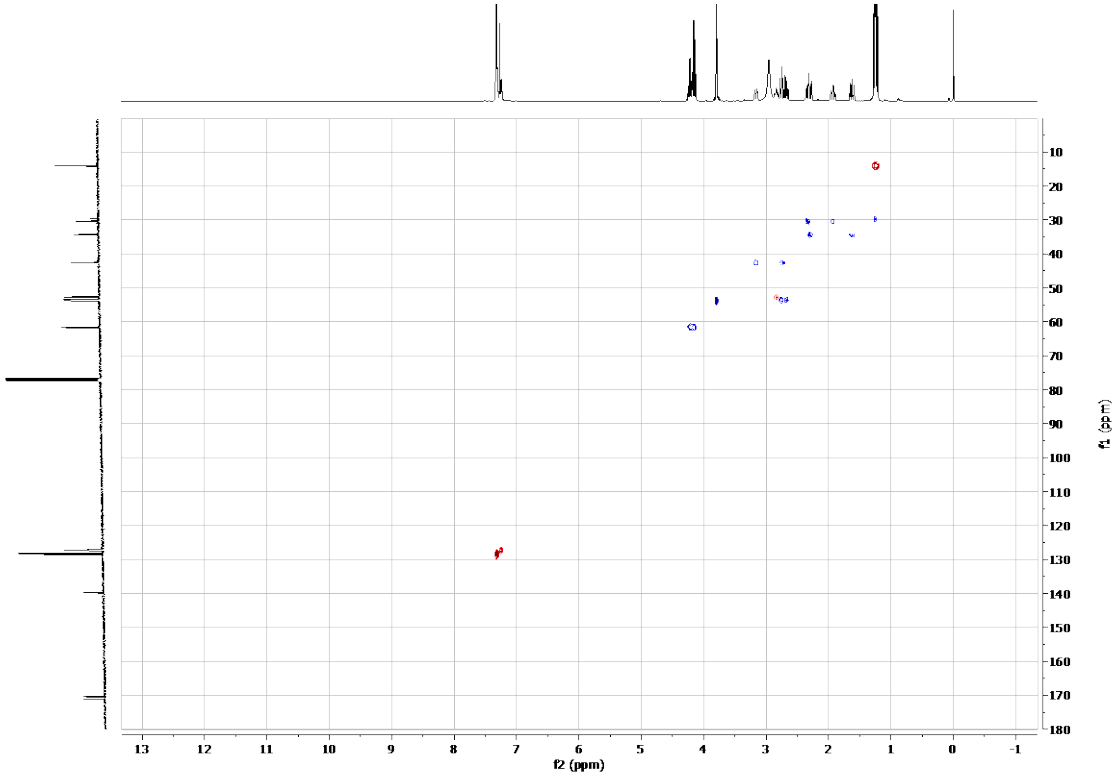


Figure 2.4 HSQC spectrum of 4,4-diethyl 2-[(benzylamino)methyl]piperidine-4,4-dicarboxylate **72**

I assigned these pairs of H atoms based on their chemical shifts and ^{1}H–^{1}H COSY correlations (Figure 2.6). I looked at the possible ^{1}H–^{1}H COSY correlation between the two upfield pairs of methylene H and the methine H atom at 2.80 ppm connected to C(6). The first pair of H atoms at 2.29 ppm and 1.61 showed strong correlation to the methine H atom at 2.80 ppm; however, the second pair of H atoms at 2.33 ppm and 1.92 ppm did not show any correlations to the methine H atom in COSY. This data suggested that the H atoms at 2.29 ppm and 1.61 are connected to C(5) and the H atoms at 2.33 ppm and 1.92 ppm are connected to C(3). Also, the methylene H atom connected to C(3) showed strong

correlation to the H atoms at 3.14 ppm and 2.74 ppm suggesting that these pair of geminal H atoms are connected to C(2) (Figure 2.5). The two H atoms resonating at 3.79 ppm did not correlate to any H atoms, suggesting that they are the benzylic H atoms connected to C(8). The only unassigned H atoms are the geminal H atoms resonating at 2.75 ppm and 2.66 ppm, which I assigned to C(7).

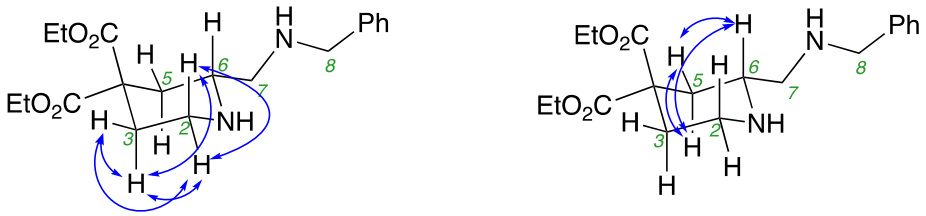


Figure 2.5 ^{1}H-^{1}H COSY correlation of H atoms at C(2) and C(3), and C(5) and C(6) in 1,2-diamine **72**

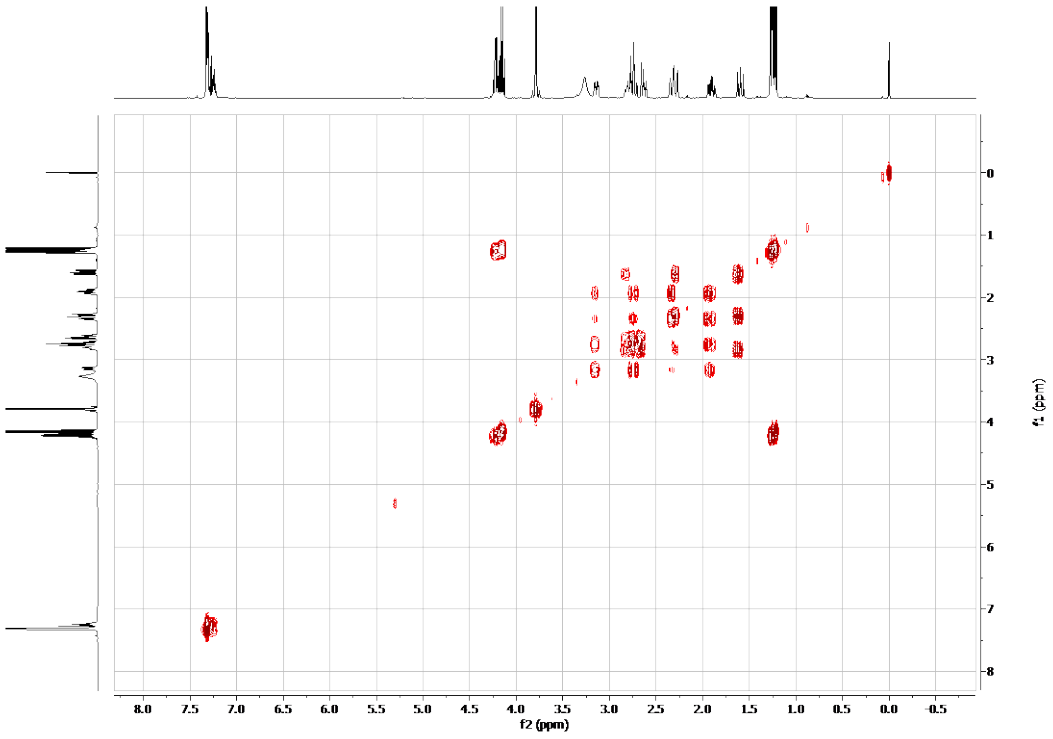
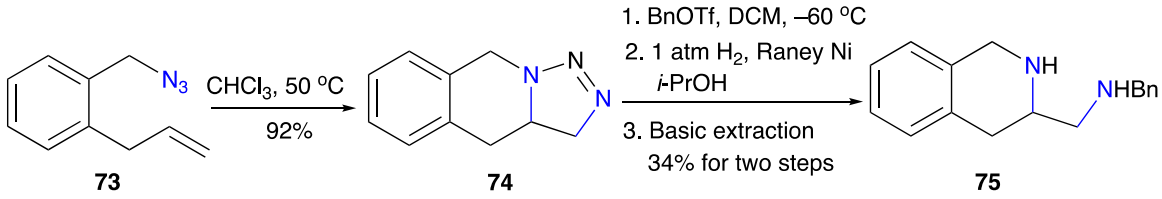


Figure 2.6 ^{1}H-^{1}H COSY spectrum of 4,4-diethyl 2-[(benzylamino)methyl]piperidine-4,4-dicarboxylate **72**

In addition to NMR evidence, HRMS revealed that the synthesized product had the molecular formula $C_{19}H_{28}N_2O_4$, which further confirmed formation of the desired 1,2-diamine **72**.

In another example, I synthesized the 1,2,3-triazoline **74** by intramolecular azide–alkene cycloaddition of allyl benzyl azide **73** at 55 °C. I then alkylated this 1,2,3-triazoline with BnOTf. I hydrogenated the 1,2,3-triazolinium ion over Raney Ni with a balloon of H_2 and basified and purified the crude product to yield the desired 1,2-diamine **75** (Scheme 2.11). The NMR spectroscopy confirmed formation of the product. HRMS revealed that the synthesized product had the molecular formula $C_{17}H_{20}N_2$, which further confirmed formation of the desired 1,2-diamine target product. This 1,2-diamine belongs to the family of tetrahydroisoquinolines which are found in a number of medicines and bioactive compounds.[40]

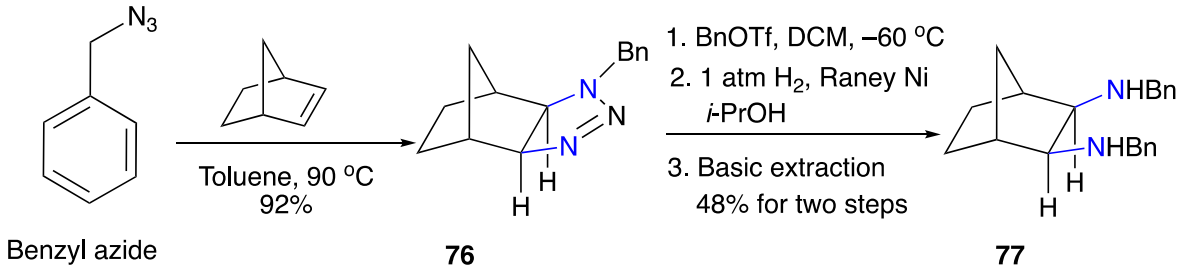


Scheme 2.11 Synthesis of benzyl[(1,2,3,4-tetrahydroisoquinolin-3-yl)methyl]amine **75**

2.2.2 Exploring the scope of the 1,2-diamination of alkenes through intramolecular azide–alkene cycloaddition

Besides making 1,2,3-triazolines through *intra*molecular cycloaddition, we were interested to synthesize 1,2,3-triazolines by *inter*molecular cycloaddition, *N*-alkylate them to convert them into 1,2,3-triazolinium ions, and subject them to hydrogenation over Raney Ni. Therefore, I combined the benzyl azide and norbornene to make the 1,2,3-triazoline **76**. *N*-Benzylation of this 1,2,3-triazoline formed the corresponding symmetrical 1,2,3-

triazolinium ion, which was hydrogenated over Raney Ni to afford the 1,2-diamine **77** after basic extraction and column chromatography. (Scheme 2.12).



Scheme 2.12 Synthesis of N^2,N^3-dibenzylbicyclo[2.2.1]heptane-2,3-diamine **77**

The X-ray crystallography analysis of the triflate salt of 1,2-diamine confirmed formation of the target product (Figure 2.7).

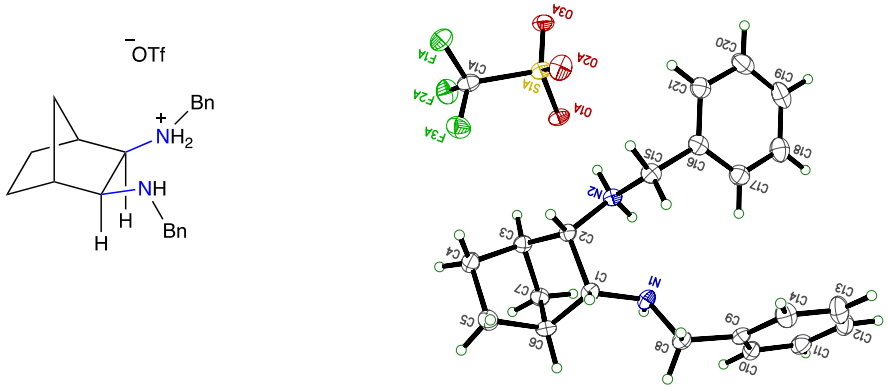


Figure 2.7 Thermal ellipsoid plot of **77** as a triflate salt

In collaboration with Dr. Samuel Awuah's medicinal inorganic group at University of Kentucky, the 1,2-diamine **77** (both as a free base and triflate salt) was employed as a chelating ligand for formation of cyclometalated Au(III) complexes **78** and **79** with various scaffolds (Figure 2.8). Previously, they have synthesized similar cyclometalated Au(III) complexes which have shown low micromolar cytotoxicity against human cancer cell

lines.[14] This opens the doors to investigate the potential application of the synthesized cyclometalated Au(III) complexes shown in Figure 2.8 in medicinal chemistry.

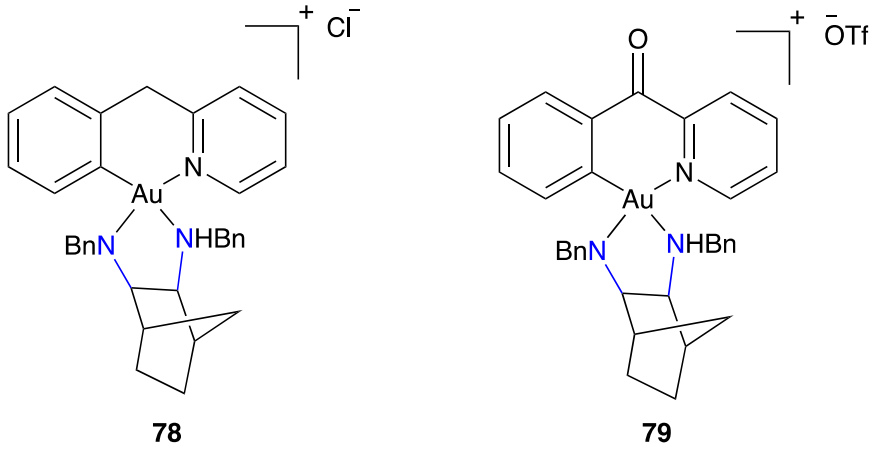
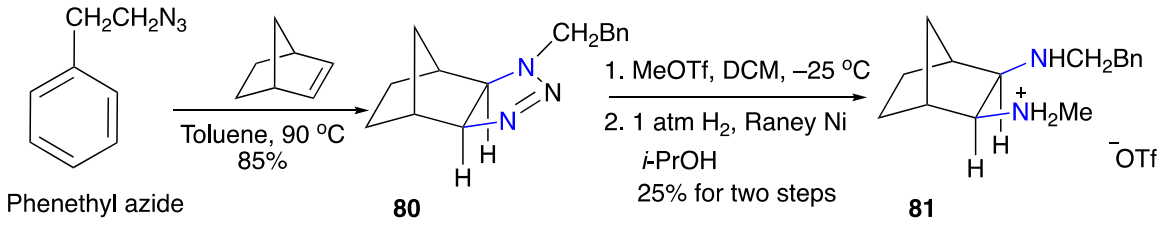


Figure 2.8 Potential anticancer Au(III) complexes bearing 1,2-diamine **77** as chelating ligands

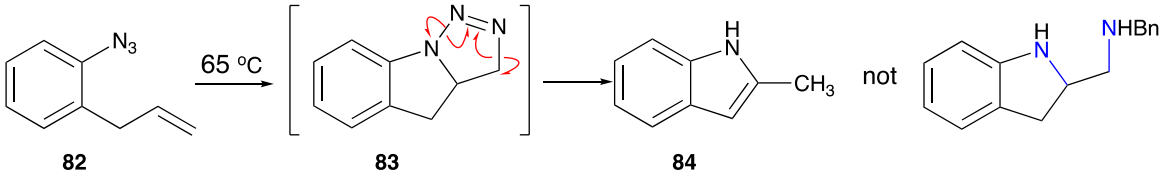
Shown in Scheme 2.13 is the preparation of a non-symmetrical 1,2-diamine **81** in 25% yield (Scheme 2.13). 1,3-Dipolar cycloaddition of phenethyl azide and norbornene formed the 1,2,3-triazoline **80**. I synthesized the corresponding 1,2,3-triazolinium ion after subjecting 1,2,3-triazoline **80** to MeOTf (or Me_2SO_4) and hydrogenated that over Raney Ni to form the 1-amino-2-ammonium product **81** after column chromatography.



Scheme 2.13 Synthesis of *N*-methyl-3-[(2-phenylethyl)amino]bicyclo[2.2.1]heptan-2-aminium trifluoromethanesulfonate **81**

Although this method of 1,2-diamination of alkene is very interesting, it can only work when the 1,2,3-triazolines are stable enough to be alkylated. For example, I attempted to prepare the 1,2,3-triazoline **83** from intramolecular azide–alkene cycloaddition of the 2-allyl phenyl azide **82**. This 1,2,3-triazoline was not as stable as the others, extruding N_2 as

fast as it forms to yield 2-methylindole **84** (Scheme 2.14). This can be explained by the tendency of the 1,2,3-triazoline **83** to undergo homolytic cleavage at the N–N bond to produce the benzylic N radical. This radical is stabilized by resonance with aromatic ring and is converted to the 2-methylindole after H atom shift.[41]



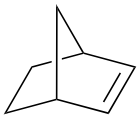
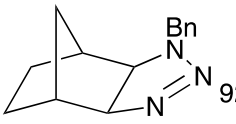
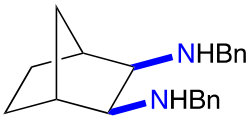
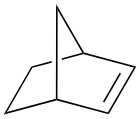
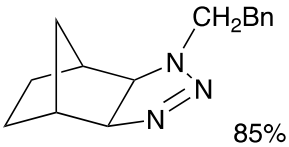
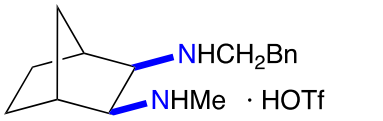
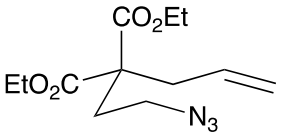
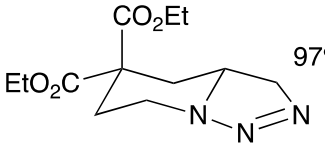
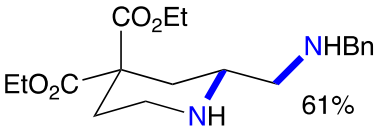
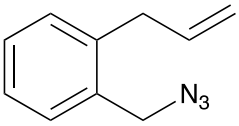
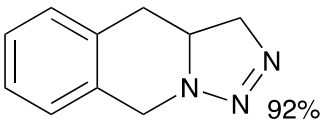
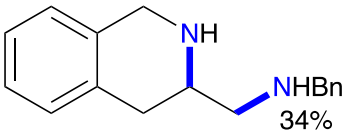
82 **83** **84**

Scheme 2.14 Extrusion of N_2 from 1,2,3-triazoline **83**

2.3 Conclusion

In this chapter, we showed that 1,2,3-triazolinium ions can be hydrogenated over Raney Ni with a balloon of H_2 to give 1,2-diamines. In our methodology, a balloon of H_2 was sufficient to complete the 1,2-diamination reactions which made our approach accessible and easy to apply. We also illustrated that stable 1,2,3-triazolines can be produced via inter- and intramolecular azide–alkene cycloaddition. The fact that 1,2,3-triazolines can potentially be isolated and manipulated, would open new doors for the possible application of these compounds in different transformations other than extrusion of N_2. A summary of the synthesized 1,2,3-triazolines and 1,2-diamines in this chapter is depicted in Table 2.1.

Table 2.1 List of 1,2-diamines synthesized through azide–alkene cycloaddition

entry	alkene	azide	triazoline	yield	1,2-diamine	yield[a]
1		BnN_3		92%		48%
2		$BnCH_2N_3$		85%		25%
3				97%		61%
4				92%		34%

[a]Yields are calculated for *N*–alkylation and hydrogenation steps.

2.4 Experimental Section

2.4.1 Safety for handling of azido compounds[42]

Sodium azide (NaN_3) is a toxic compound (LD50 oral = 27 mg/kg for rats), so appropriate personal protective equipment (gloves, safety glasses) is required for the safe handling of the chemical. Sodium azide is a health and safety hazard, and the excess amount of that must be quenched following the procedure described in *Prudent Practices* before disposal[43]. Chlorinated solvents such as CH_2Cl_2 and $CHCl_3$ can produce di- and tri-azidomethanes (explosive and unstable) in reaction with NaN_3, so these solvents should not be used as a reaction medium. Substitution reaction with NaN_3 can be performed in polar aprotic solvents such as DMSO; these solvents can carry the toxic azide ion through the skin, so extra caution must be taken while handling the reaction mixture.

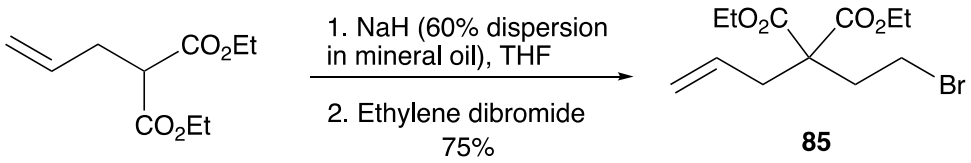
Organic azides are potentially explosive and can decompose with introduction of energy. All organic azides should be stored at –20 °C. When designing the synthesis for organic azides, the following equation must be taken to account.

$$\frac{N_C + N_O}{N_N} \geq 3$$

Organic azides with a $(C + O)/N > 3$ are not explosive and can be stored safely at –20 °C. We did not isolate the organic azides that contain the ratio of $(C + O)/N \leq 3$; instead, we carry them immediately to the next step after preparation.

2.4.2 Experimental procedures

1,3-Diethyl-2-(2-bromoethyl)-2-(prop-2-en-1-yl)propanedioate

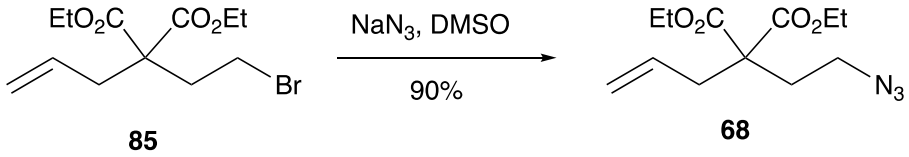


85

The procedure was adapted from Kuehne, M. E. et al.[44] A solution of diethyl allylmalonate (2.52 g, 12.6 mmol) in dry THF (3.5 mL) was added dropwise to the stirred suspension of NaH (60% dispersion in mineral oil, 0.76 g, 18.9 mmol) in dry THF (3.5 mL) at room temperature over a period of 15 minutes. The reaction mixture stirred at room temperature for 1 h. Then a solution of 1,2-dibromoethane (9.47 g, 50.4 mmol) in dry THF (3.5 mL) was added dropwise over a period of 15 minutes. The reaction mixture stirred at room temperature for 30 h. Then, H_2O was added, and the mixture was extracted with ether (3 × 10 mL). The combined organic layer was washed with brine, dried over anhydrous $MgSO_4$, and concentrated under reduced pressure. Further purification of the crude mixture with flash column chromatography (2% EtOAc in hexanes) yielded the pure bromoester

85 (2.92 g, 9.51 mmol, 75%) as a colorless viscous oil. The experimental data was in accordance with the previously reported data. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.71–5.60 (m, 1 H), 5.18–5.11 (m, 2 H), 4.21 (q, *J* = 7.2 Hz, 4 H), 3.39–3.33 (m, 2 H), 2.65 (d, *J* = 7.2 Hz, 2 H), 2.47–2.41 (m, 2 H), 1.27 (t, *J* = 7.2 Hz, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.3, 131.9, 119.8, 61.7, 57.6, 37.9, 36.3, 27.2, 14.2; IR (ATR) 3080, 2938, 1724 cm^{-1}; GC-MS (EI) 263 (4%), 234 (64%), 200 (82%), 199 (100%), 153 (61%), 125 (47%), 79 (52%).

1,3-Diethyl 2-(2-azidoethyl)-2-(prop-2-en-1-yl)propanedioate

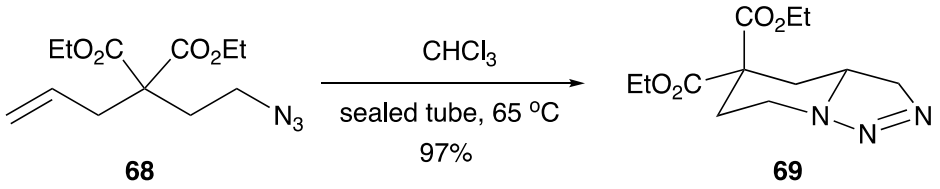


85 **68**

To the solution of bromoester **85** (2.26 g, 7.36 mmol) in dry DMSO (20 mL) was added NaN_3 (956 mg, 14.7 mmol) in one portion. The mixture stirred at room temperature for 7 h. After reaction completion, H_2O was added, and the mixture was extracted with ether (3 × 20 mL). The combined organic layer was washed with H_2O one more time to remove the remaining DMSO. (**Caution:** The unreacted sodium azide in the aqueous layer was quenched according to the previously reported protocol.)[43] The combined organic layer was dried over anhydrous $MgSO_4$ and concentrated under vacuum to yield the azide **68** (1.79 g, 6.65 mmol, 90%) as a colorless liquid. The crude product was carried to the next step without further purification and was kept at –20 °C to prevent formation of the corresponding 1,2,3-triazoline. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.70–5.57 (m, 1 H), 5.18–5.10 (m, 2H), 4.21 (q, *J* = 7.4 Hz, 4 H), 3.33 (t, *J* = 7.4 Hz, 2 H), 2.68 (d, *J* = 7.4 Hz, 2 H), 2.17 (t, *J* = 7.4 Hz, 2 H), 1.27 (t, *J* = 7.1 Hz, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.6,

132.0, 119.7, 61.7, 55.8, 47.3, 37.7, 31.7, 14.1; IR (ATR) 3081, 2982, 2938, 2094, 1727 cm^{-1}; GC-MS (EI) 241 (10%), 195 (10%), 168 (100%), 138 (18%), 127 (44%), 99 (40%).

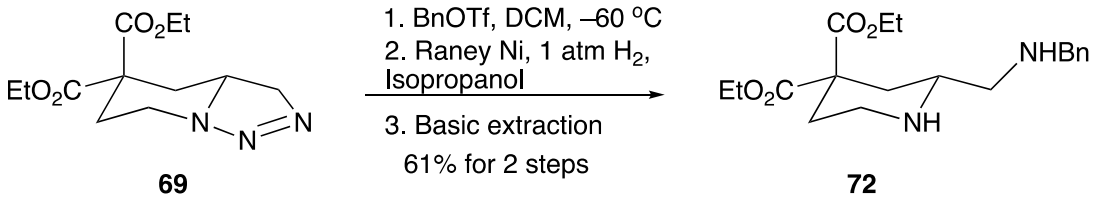
5,5-Diethyl 3H,3aH,4H,5H,6H,7H-[1,2,3]triazolo[1,5-a]pyridine-5,5-dicarboxylate



68 **69**

A solution of azide **68** (1.77 g, 6.57 mmol) in $CHCl_3$ (20 mL) was transferred to the sealed tube and heated at 65 °C for 17 h. (Attention: a NMR sample in $CDCl_3$ was also prepared and put into the same oil bath with the sealed tube. Progress of the reaction was monitored by NMR to prevent overheating of the sample and extrusion of N_2.) After completion of the cycloaddition, the solvent was evaporated to yield the 1,2,3-triazoline **69** as a colorless liquid (1.72 g, 6.39 mmol, 97%). The crude product was used in the next step without further purification. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.41 (dd, J = 14.4, 4.7 Hz, 1H), 4.26 (q, J = 7.1 Hz, 2H), 4.17–4.10 (m, 3H), 3.92 (dd, J = 15.6, 9.4 Hz, 1 H), 3.71 (dddd, J = 11.9, 9.4, 4.4, 2.6 Hz, 1 H), 3.50 (ddd, J = 14.7, 13.5, 3.3 Hz, 1 H), 2.32–2.25 (m, 1H), 1.93 (ddd, J = 13.4, 4.5, 2.3 Hz, 1H), 1.84 (dt, J_d = 5.1 Hz, J_t = 13.4 Hz, 1H), 1.40 (dd, J = 13.3, 11.9 Hz, 1H), 1.28 (t, J = 7.1 Hz, 3H), 1.21 (t, J = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.6, 169.9, 71.1, 62.0, 61.9, 52.5, 51.2, 43.3, 31.7, 30.4, 14.2, 14.1; IR (ATR) 2979, 2937, 2868, 1724 cm^{-1}; GC-MS (EI) 241 (20%), 195 (17%), 168 (100%), 138 (20%), 127 (47%), 99 (54%).

4,4-Diethyl 2-[(benzylamino)methyl]piperidine-4,4-dicarboxylate



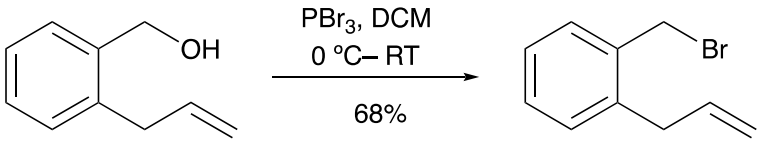
69 **72**

A solution of 2,4,6-trimethylpyridine (104 mg, 0.860 mmol) and benzyl alcohol (93.0 mg, 0.860 mmol) in 0.5 mL of dry CH_2Cl_2 was added dropwise to the solution trifluoromethanesulfonic anhydride (243 mg, 0.860 mmol) in 3 mL dry CH_2Cl_2 at –60 °C. The mixture stirred at the same temperature for 30 minutes. Then, a solution of 1,2,3-triazoline **69** (193 mg, 0.717 mmol) in 2 mL dry CH_2Cl_2 was added dropwise and the mixture stirred at –60 °C for 30 minutes. The crude mixture was transferred to another flask and CH_2Cl_2 was evaporated under reduced pressure at room temperature. The crude product was used in the next step without further purification.

One small spatula of Raney Ni 2400 slurry in water (0.7 g) was added to the mixture in isopropanol (6 mL), under N_2 atmosphere. Then a balloon of H_2 was placed on top of the flask while removing N_2. The reaction mixture was stirred for 4 h at room temperature. After reaction completion, the mixture was filtered through a short pad of Celite, washed with isopropanol and concentrated under vacuum. The crude mixture was dissolved in $CHCl_3$ and subjected to basic extraction using NaOH solution (pH = 9–10) and extracted with $CHCl_3$ (2 x 7 mL). The combined organic layer was dried over Na_2SO_4, and the solvent was evaporated under reduced pressure. Flash chromatography of the residue (5% MeOH in CH_2Cl_2) afforded the 1,2-diamine **72** as a colorless viscous liquid (152 mg, 0.436 mmol, 61% for 2 steps). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33–7.19 (m, 5H), 4.26–4.17 (m, 2H), 4.14 (q, J = 7.1 Hz, 2H), 3.79 (d, J = 1.1 Hz, 2H), 3.27 (broad s, 2NH), 3.14 (ddd, J = 12.7,

4.5, 2.4 Hz, 1 H), 2.88–2.68 (m, 2 H), 2.63 (dd, J = 12.1, 8.5 Hz, 1H), 2.31 (ddt, J_d = 15.9 Hz, J_d = 13.4 Hz, J_t = 2.4 Hz, 1H), 1.92 (dt, J_d = 4.5 Hz, J_t = 13.5 Hz, 1H), 1.60 (dd, J = 13.3, 11.7 Hz, 1H), 1.26 (t, J = 7.2 Hz, 3H), 1.23 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.3, 170.6, 140.0, 128.5, 128.3, 127.2, 61.7, 61.6, 54.0, 53.7, 52.8, 42.8, 34.6, 30.8, 29.8, 14.2, 14.1; IR (ATR) 3313, 2976, 2916, 2847, 1724 cm^{-1}; GC-MS (EI) 303 (3%), 228 (100%), 154 (58%), 91 (23%); HRMS (ESI) Calcd. For $C_{19}H_{29}N_2O_4$ $[M+H]^+$: 349.2122; Found: 349.2114.

1-(bromomethyl)-2-(prop-2-en-1-yl)benzene

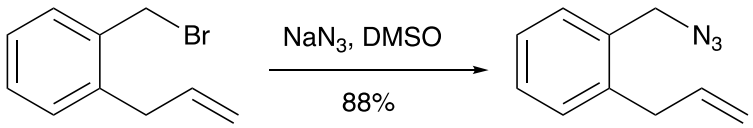


86

A solution of 2-allyl benzyl alcohol[45] (954 mg, 6.44 mmol) in dry CH_2Cl_2 (15 mL) was placed in the ice bath for 15 minutes. Then, PBr_3 (2.27 g, 8.38 mmol) was added dropwise to the cold solution. The resulting mixture was warmed up to room temperature and stirred for 15 minutes. Then the reaction cooled to 0 °C, quenched slowly with ice cooled water and extracted with CH_2Cl_2 (3 × 10mL). The combined organic layer was dried over anhydrous $MgSO_4$ and concentrated under vacuum. The crude mixture was purified with flash column chromatography (100% hexanes) to afford the bromide **86** as a colorless liquid (920 mg, 4.36 mmol, 68%). The experimental data was in accordance with the previously reported data[46]. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36–7.20 (m, 4H), 6.07–5.97 (m, 1H), 5.14–5.00 (m, 2H), 4.54 (d, J = 1.8 Hz, 2H), 3.55 (d, J = 6.3 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.0, 136.7, 135.9, 130.7, 130.4, 129.3, 127.1, 116.4, 36.8, 31.8; IR (ATR) 3075, 2980, 2889, 1638, 606 cm^{-1}; GC-MS (EI) 210 (8%), 131 (100%), 115 (34%),

91 (37%).

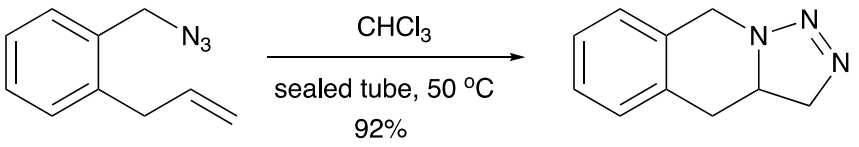
1-(azidomethyl)-2-(prop-2-en-1-yl)benzene



86 **73**

To the solution of 2-allyl benzyl bromide **86** (483 mg, 2.29 mmol) in dry DMSO (8 mL) was added NaN_3 (223 mg, 3.43 mmol) in one portion. The mixture stirred at room temperature for 45 minutes. After reaction completion, H_2O was added, and the mixture was extracted with ether (3 × 5 mL). The combined organic layer was washed with H_2O one more time to remove the rest of DMSO. (**Caution:** The unreacted sodium azide in the aqueous layer was quenched according to the previously reported protocol.)[43] Then the combined organic layer was dried over anhydrous $MgSO_4$ and concentrated under vacuum to yield the azide **73** as a pale yellow liquid (349 mg, 2.01 mmol, 88%). The crude product was kept at –20 °C to prevent formation of corresponding triazoline. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33–7.21 (m, 4H), 5.96 (ddt, J_d = 16.7 Hz, J_d = 9.8 Hz, J_t = 6.3 Hz, 1H), 5.09 (dd, J = 10.2, 1.6 Hz, 1H), 4.99 (dd, J = 17.1, 1.7 Hz, 1H), 4.36 (s, 2H), 3.45 (dd, J = 6.1, 1.7 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.5, 136.6, 133.5, 130.4, 129.8, 129.0, 126.9, 116.3, 52.6, 37.0; IR (ATR) 3074, 2972, 2859, 2089 cm^{-1}; GC-MS (EI) 143 (100%), 115 (52%), 104 (31%), 128 (4%), 89 (10%), 63 (10%).

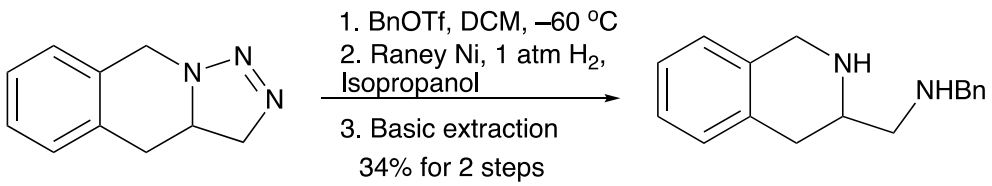
3H,3aH,4H,9H-[1,2,3]triazolo[1,5-b]isoquinoline



73 **74**

A solution of azide **73** (349 mg, 2.01 mmol) in $CHCl_3$ (5 mL) was transferred to the sealed tube and heated at 50 °C for 12 h. (Attention: a NMR sample in $CDCl_3$ was also prepared and put into the same oil bath with the sealed tube. Progress of the reaction was monitored by NMR to prevent overheating of the sample and extrusion of N_2.) After completion of the cycloaddition, the solvent was evaporated to yield a crude 1,2,3-triazoline **74** as a pale yellow solid (322 mg, 1.86 mmol, 92%). The crude product was kept at –20 °C to prevent loss of N_2. The crude product was used in the next step without further purification. m.p.: 42.5–44.6 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25–7.07 (m, 4H), 5.35 (d, J = 16.8 Hz, 1H), 4.85 (d, J = 16.8 Hz, 1H), 4.19 (dd, J = 15.6, 9.4 Hz, 1H), 4.11 (dd, J = 15.6, 9.4 Hz, 1H), 3.67 (ddt, J_d = 9.3 Hz, J_d = 4.6 Hz, J_t = 7.5 Hz, 1H), 2.55 (d, J = 7.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) 133.6, 133.2, 129.0, 126.9, 126.8, 126.4, 70.2, 52.5, 48.6, 32.0; IR (ATR) 3062, 2956, 2827, 2096 cm^{-1}; GC-MS (EI) 143 (100%), 115 (55%), 104 (36%), 89 (11%), 63 (10%).

Benzyl[(1,2,3,4-tetrahydroisoquinolin-3-yl)methyl]amine



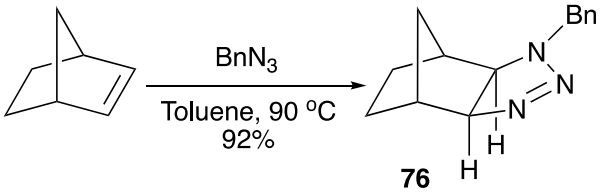
74 **75**

A solution of 2,4,6-trimethylpyridine (134 µL, 1.02 mmol) and benzyl alcohol (106 µL, 1.02 mmol) in 0.5 mL of dry CH_2Cl_2 was added dropwise to the solution trifluoromethanesulfonic anhydride (171 µL, 1.02 mmol) in 3 mL dry CH_2Cl_2 at –60 °C. The mixture stirred at the same temperature for 30 minutes. Then solution of 1,2,3-triazoline **74** (176 mg, 1.02 mmol) in 1 mL dry CH_2Cl_2 was added dropwise and the mixture stirred at –60 °C for 20 minutes. The crude mixture was transferred to another flask and CH_2Cl_2 was evaporated under reduced pressure at room temperature. The crude product was used in the next step without further purification.

One small spatula of Raney Ni 2400 slurry in water (0.7 g) was added to the mixture in isopropanol (6 mL), under N_2 atmosphere. Then a balloon of H_2 was placed on top of the flask while removing N_2. The reaction mixture was stirred for 1 h at room temperature. After reaction completion, the mixture was filtered through a short pad of Celite, washed with isopropanol and concentrated under vacuum. The crude mixture was dissolved in chloroform and subjected to basic extraction using NaOH solution (pH = 10) and extracted with $CHCl_3$ (3 x 5 mL). The combined organic layer was dried over Na_2SO_4, and the solvent was evaporated. Flash chromatography of the residue (5% MeOH in CH_2Cl_2) afforded the 1,2-diamine **75** as a white solid (87.0 mg, 0.345 mmol, 34%). m.p.: 154.4–157.3 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43–7.24 (m, 5H), 7.17–7.11 (m, 2H), 7.09–6.97 (m, 2H), 4.89 (s, 2NH), 4.15–4.03 (m, 2H), 3.96–3.87 (m, 2H), 3.26 (ddt, J_d = 10.2 Hz, J_d = 8.8, J_t = 4.3 Hz, 1H), 2.95 (dd, J = 12.6, 4.1 Hz, 1H), 2.89–2.80 (m, 2H), 2.72 (dd, J = 16.5, 10.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.3, 133.2, 133.1, 129.3, 128.8, 128.7, 127.7, 126.9, 126.4, 126.4, 53.5, 52.9, 52.1, 46.7, 32.1; IR (ATR) 3270, 3221, 3022, 2917, 2863 cm^{-1};

GC-MS (EI) 145 (2%), 132 (100%), 130 (37%), 117(5%), 105 (4%), 91 (32%); HRMS (ESI) Calcd. For $C_{17}H_{21}N_2$ $[M+H]^+$: 253.1699; Found: 253.1686.

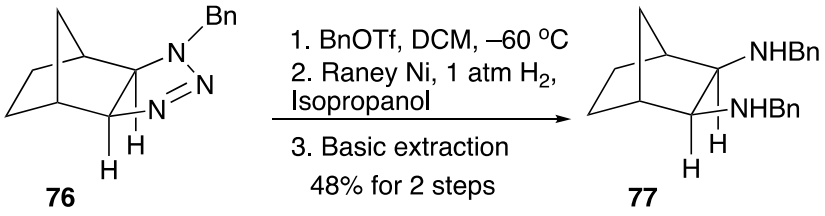
5-benzyl-3,4,5-triazatricyclo[5.2.1.0^{2,6}]dec-3-ene



76

To the solution of benzyl azide[47] (3.51 g, 26.4 mmol) in toluene (40 mL), norbornene (2.98 g, 31.7 mmol) was added and the reaction mixture was warmed up to 90 °C and stirred for 10 h. After the completion of the reaction, solvent was evaporated under reduced pressure. The product was dissolved in ether/ hexane (1:1) and solvents were evaporated under medium flow of N_2 to afford the solid product. Then, the solid was placed on a filter paper and washed with cold hexanes to obtain the 1,2,3-triazoline **76** as a white solid (5.52 g, 24.3 mmol, 92%).). m.p.: 72.5–73.7 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62–7.12 (m, 5H), 4.90 (d, J = 15.1 Hz, 1H), 4.66 (d, J = 15.2 Hz, 1H), 4.35 (d, J = 9.7 Hz, 1H), 3.09 (d, J = 9.7 Hz, 1H), 2.65 (d, J = 4.2 Hz, 1H), 2.13 (d, J = 4.4 Hz, 1H), 1.45 (m, 2H), 1.13 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.1, 128.8, 128.3, 127.9, 86.4, 62.0, 52.7, 41.6, 40.5, 32.6, 25.9, 24.8; IR (ATR) 3030, 2958, 2869 cm^{-1}; GC-MS (EI) 199 (8%), 170 (42%), 108 (9%), 91 (100%), 65 (20%).

N^2,N^3-dibenzylbicyclo[2.2.1]heptane-2,3-diamine

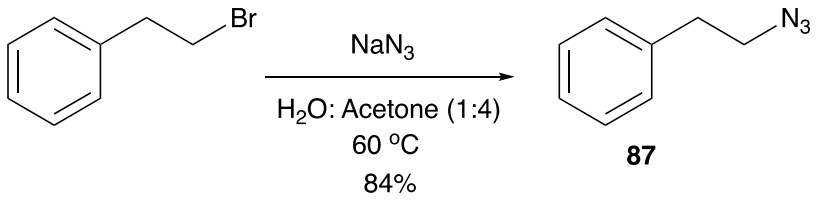


A solution of 2,4,6-trimethylpyridine (117 mg, 0.966 mmol) and benzyl alcohol (105 mg, 0.966 mmol) in 1.0 mL of dry CH_2Cl_2 was added dropwise to the solution of trifluoromethanesulfonic anhydride (273 mg, 0.966 mmol) in 6 mL dry CH_2Cl_2 at –60 °C. The mixture stirred at the same temperature for 30 minutes. Then solution of 1,2,3-triazoline **76** (183 mg, 0.805 mmol) in 1.5 mL of dry CH_2Cl_2 was added dropwise and the mixture stirred at –60 °C for 1 h. The crude mixture was transferred to another flask and CH_2Cl_2 was evaporated under reduced pressure at room temperature. The crude product was used in the next step without further purification.

To the solution of crude mixture in isopropanol (10 mL), I added one small spatula of Raney Ni 2400 slurry in water (0.81 g) under N_2 atmosphere. Then a balloon of H_2 was placed on top of the flask while removing N_2. The reaction mixture was stirred for 10 h at room temperature. After reaction completion, the mixture was filtered through a short pad of Celite and concentrated under vacuum. The crude mixture was dissolved in CH_2Cl_2 and subjected to basic extraction using NaOH solution (pH = 11) for 18 h. The crude mixture was extracted with CH_2Cl_2 two more times (2 x 7 mL). The combined organic layer was dried over Na_2SO_4, and the solvent was evaporated. Flash chromatography of the residue (3% MeOH in CH_2Cl_2) afforded the 1,2-diamine **77** as a white solid (119 mg, 0.388 mmol, 48% for 2 steps). Crystals of the triflate salt of **77** were grown by diffusion method from

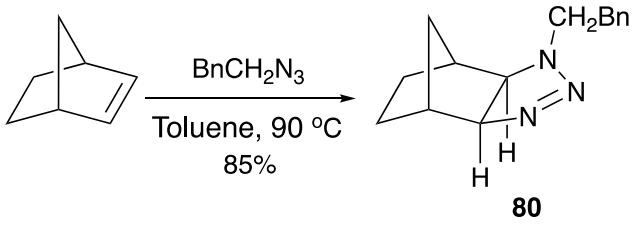
DCM/ hexanes for X-ray crystallographic analysis. m.p.: 126.1–128.0 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50–7.12 (m, 10H), 5.28 (broad s, 2NH), 4.00 (dd, J = 13.4, 4.1 Hz, 2H), 3.84 (dd, J = 13.3, 3.2 Hz, 2H), 2.66 (s, 2H), 2.48–2.26 (m, 2H), 2.01 (t, J = 10.9 Hz, 1H), 1.61–1.39 (m, 2H), 1.11 (ddt, J_d = 10.9 Hz, J_d = 3.4, J_t = 1.7 Hz, 1H), 0.99 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 129.3, 129.2, 128.7, 127.8, 62.9, 52.5, 40.2, 33.4, 26.7; IR (ATR) 3314, 3247, 3059, 2948, 2866, 2807 cm^{-1}; GC-MS (EI) 306 (5%), 215 (24%), 200 (49%), 146 (20 %), 91 (100%), 65 (10%); HRMS (ESI) Calcd. For $C_{21}H_{27}N_2$ $[M+H]^+$: 307.2169; Found: 307.2170.

(2-azidoethyl)benzene



Sodium azide (596 mg, 9.17 mmol) was added to the stirred solution of (2-bromoethyl)benzene (1.13 g, 6.11 mmol) in H_2O: Acetone mixture (1:4 v/v, 2 mL: 8 mL). The resulting suspension was stirred at 60 °C for overnight. Then acetone was evaporated, and the aqueous layer was extracted with diethyl ether (3 × 15 mL). The combined organic layers were dried over anhydrous $MgSO_4$, and the solvent was evaporated under reduced pressure to yield the azide **87** as a colorless liquid (760 mg, 5.16 mmol, 84%). The crude product was immediately used in the next step without further purification. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.78–6.20 (m, 5H), 2.75 (t, J = 7.3 Hz, 2H), 2.51–1.78 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.2, 128.9, 128.8, 126.9, 52.6, 35.5; IR (ATR) 3066, 3029, 2930, 2090 cm^{-1}.

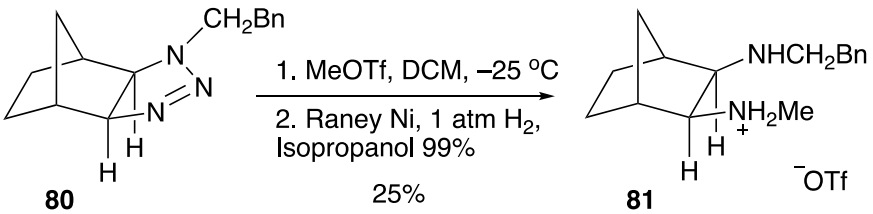
5-(2-phenethyl)-3,4,5-triazatricyclo[5.2.1.0^{2,6}]dec-3-ene



80

To the solution of phenethyl azide **87** (3.25 g, 22.1 mmol) in toluene (35 mL), norbornene (2.50 g, 26.5 mmol) was added and the reaction mixture was warmed up to 90 °C and stirred for 5 h. After the completion of the reaction, solvent was evaporated under reduced pressure. The product was dissolved in ether (2 mL) and solvent was evaporated under medium flow of N_2 afford the solid product. Then, the solid was placed on a filter paper and washed with cold hexanes to obtain the 1,2,3-triazoline **80** as a white solid (4.55 g, 18.8 mmol, 85%). m.p.: 55.8–56.8 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36–7.22 (m, 5H), 4.37 (d, *J* = 9.7 Hz, 1H), 3.86 (ddd, *J* = 14.0, 8.8, 6.7 Hz, 1H), 3.76 (ddd, *J* = 14.1, 8.7, 6.3 Hz, 1H), 3.19 (d, *J* = 9.7 Hz, 1H), 3.08–2.93 (m, 2H), 2.65 (d, *J* = 3.9 Hz, 1H), 2.28 (d, *J* = 3.9 Hz, 1H), 1.59–1.45 (m, 2H), 1.32 – 1.24 (m, 1H), 1.17–1.06 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.0, 128.9, 128.7, 126.6, 85.7, 63.1, 49.9, 41.4, 40.9, 35.6, 32.5, 25.9, 24.9; IR (ATR) 3060, 2961, 2867 cm^{-1}; GC-MS (EI) 213 (6%), 122 (100%), 105 (44%), 91 (41%), 77 (27%).

***N*-methyl-3-[(2-phenylethyl)amino]bicyclo[2.2.1]heptan-2-aminium trifluoromethanesulfonate**



80 **81**

A solution of 1,2,3-triazoline **80** (152 mg, 0.630 mmol) in 1.0 mL of dry CH_2Cl_2 was added dropwise to the solution of MeOTf (124 mg, 0.756 mmol) in 3 mL of dry CH_2Cl_2 at –25 °C . The resulting mixture stirred at the same temperature for 40 minutes. Then the crude mixture was transferred to another flask and CH_2Cl_2 was evaporated under reduced pressure at room temperature. The crude product was used in the next step without further purification.

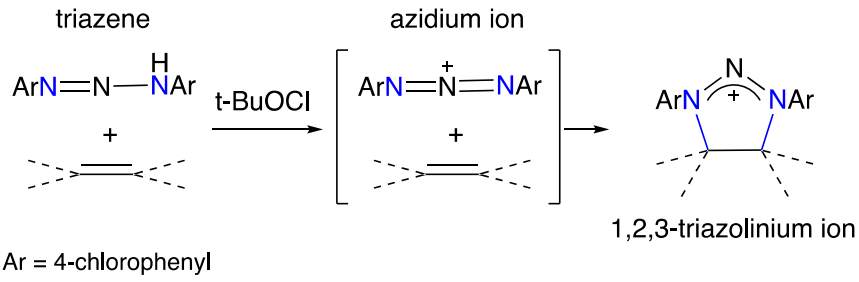
One small spatula of Raney Ni 2400 slurry in water (0.63 g) was added to the mixture in isopropanol (6 mL), under N_2 atmosphere. Then a balloon of H_2 was placed on top of the flask while removing N_2. The reaction mixture was stirred for 7 h at room temperature. After reaction completion, the mixture was filtered through a short pad of Celite washed with isopropanol and concentrated under vacuum. Flash chromatography of the residue (2% MeOH in CH_2Cl_2) afforded the 1,2-diamine **81** as a white triflate salt (61 mg, 0.155 mmol, 25% for 2 steps). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35–7.29 (m, 2H), 7.25–7.20 (m, 3H), 4.82 (s, 3NH), 3.26–3.18 (m, 1H), 2.90–2.78 (m, 3H), 2.76 (dd, J = 6.8, 1.5 Hz, 1H), 2.69 (dd, J = 7.0, 1.6 Hz, 1H), 2.50–2.46 (m, 1H), 2.40 (s, 3H), 2.29–2.26 (m, 1H), 1.57 (ddd, J = 9.2, 4.6, 2.6 Hz, 2H), 1.24 (dt, J_d = 11.6 Hz, J_t = 1.6 Hz, 2H), 1.19–1.10 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.9, 129.0, 128.9, 126.8, 122.1, 118.9, 65.8, 63.0, 51.4, 41.9, 39.7, 35.8, 34.5, 33.3, 26.5, 26.4; IR (ATR) 3311, 3086, 2965, 2880 cm^{-1}; HRMS (ESI) Calcd. For $C_{16}H_{25}N_2$ $[M+H]^+$: 245.2012; Found: 245.2005.

Chapter 3 1,2-Diamination of alkenes via azidium ion–alkene cycloaddition

3.1 Introduction

The idea that 1,2,3-triazolinium ions were reducible to 1,2-diamines was very captivating. We were eager to expand the scope of our 1,2-diamination methodology by synthesizing 1,2-diamines from 1,2,3-triazolinium ions with various skeletal structures and functional groups. Therefore, we looked for alternative routes for synthesizing 1,2,3-triazolinium ions.

In 1996, Jochims et al. reported numerous examples of the intermolecular cycloaddition of alkenes and 1,3-diaza-2-azoniaallene salts (azidium ions, $ArN{=}N^{+}{=}NAr$) to give various 1,2,3-triazolinium ions (Scheme 3.1).[48] The azidium ions were themselves synthesized by oxidation of a triazene with *t*-BuOCl. We hypothesized that 1,2,3-triazolinium ions prepared in this way could be hydrogenated over Raney Ni and a balloon of H_2 to prepare various 1,2-diamines.



Scheme 3.1 Jochims et al. approach to synthesize 1,2,3-triazolinium ions

3.2 Results and discussion

I have synthesized various 1,2,3-triazolinium ions using 1,3-bis(4-chlorophenyl)triazene, *t*-BuOCl, and cyclic, terminal, acyclic trans, and acyclic cis alkenes bearing various functional groups such as alcohol and ketone. The stereospecific syn

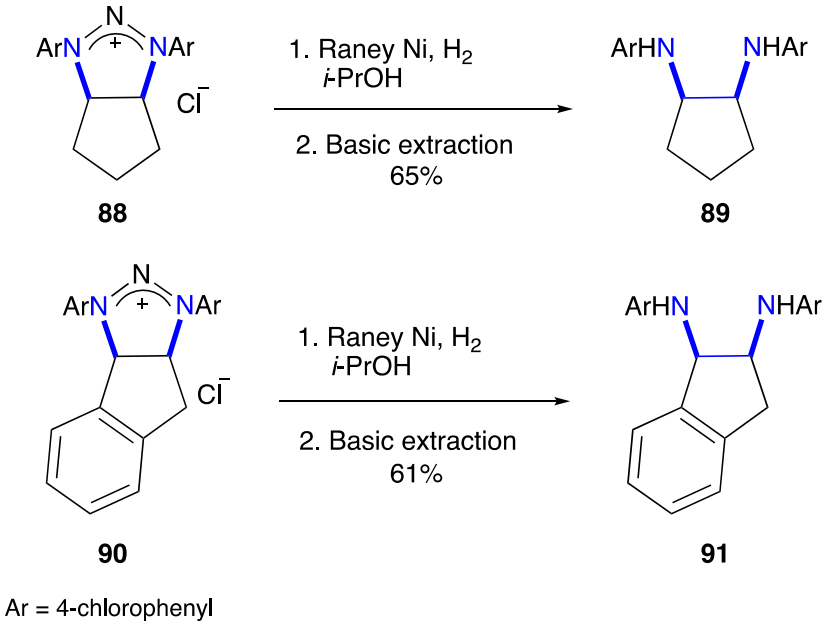
cycloaddition of the azidium ion to the alkenes was confirmed by obtaining the X-ray crystallographic analysis of eight out of ten synthesized 1,2,3-triazolinium ions.

The 1,2,3-triazolinium ions were hydrogenated over Raney Ni with a balloon of H_2, and I could successfully prepare a variety of 1,2-diamines in two steps from the triazene. All of the synthesized 1,2-diamines bore a 4-chlorophenyl group on each N atom. The C–Cl bonds of the aryl groups survived the reduction condition and were not cleaved during the time required to complete the reduction of the N–N bonds. We have also investigated the possibility of using 1,3-bis(4-methoxyphenyl)triazene, which could install 4-methoxyphenyl group on each N atom instead of the 4-chlorophenyl group. The 4-methoxyphenyl group can be oxidatively removed by treatment with aqueous ceric ammonium nitrate (CAN)[49] to afford a more useful 1,2-diamine product. Unfortunately, I have not yet been able to obtain a 1,2,3-triazolinium ion from 1,3-bis(4-methoxyphenyl)triazene. The difference may be that during the oxidation of triazene with *t*-BuOCl, a triazene bearing electron-rich 4-methoxyphenyl group may undergo side reactions more quickly than will the triazene bearing a 4-chlorophenyl group.

We were very careful to clearly establish the relative stereochemistry of the prepared 1,2-diamines and further examine the stereospecificity of this method with respect to the alkene stereochemistry.

3.2.1 Reduction of 1,2,3-triazolinium ions from cyclic alkenes

The X-ray crystallographic analysis of 1,2,3-triazolinium ions **88** and **90** confirmed the syn 1,3-dipolar cycloaddition of the azidium ion to their corresponding alkenes. (Appendix). Hydrogenolysis of these triazolinium ions resulted in the formation of the cis-1,2-diamines, as expected (Scheme 3.2).



Scheme 3.2 Synthesis of N^1,N^2-bis(4-chlorophenyl)cyclopentane-1,2-diamine **91**, and N^1,N^2-bis(4-chlorophenyl)-2,3-dihydro-1H-indene-1,2-diamine **93**

I used NMR spectroscopy to confirm the cis configurations of the 1,2-diamines **89** and **91**. For cyclopentane-1,2-diamine **89**, the HSQC spectrum (Figure 3.2) revealed the presence of two distinct geminal resonances at 1.67 ppm and 1.82 ppm connected to C(3), which is a result of the diastereotopic relationship between these H atoms. This evidence was consistent with the cis isomer depicted in Figure 3.1.

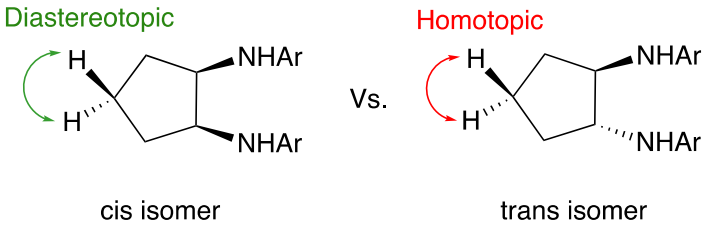


Figure 3.1 Cis and trans isomers of N^1,N^2-bis(4-chlorophenyl)cyclopentane-1,2-diamine **89**

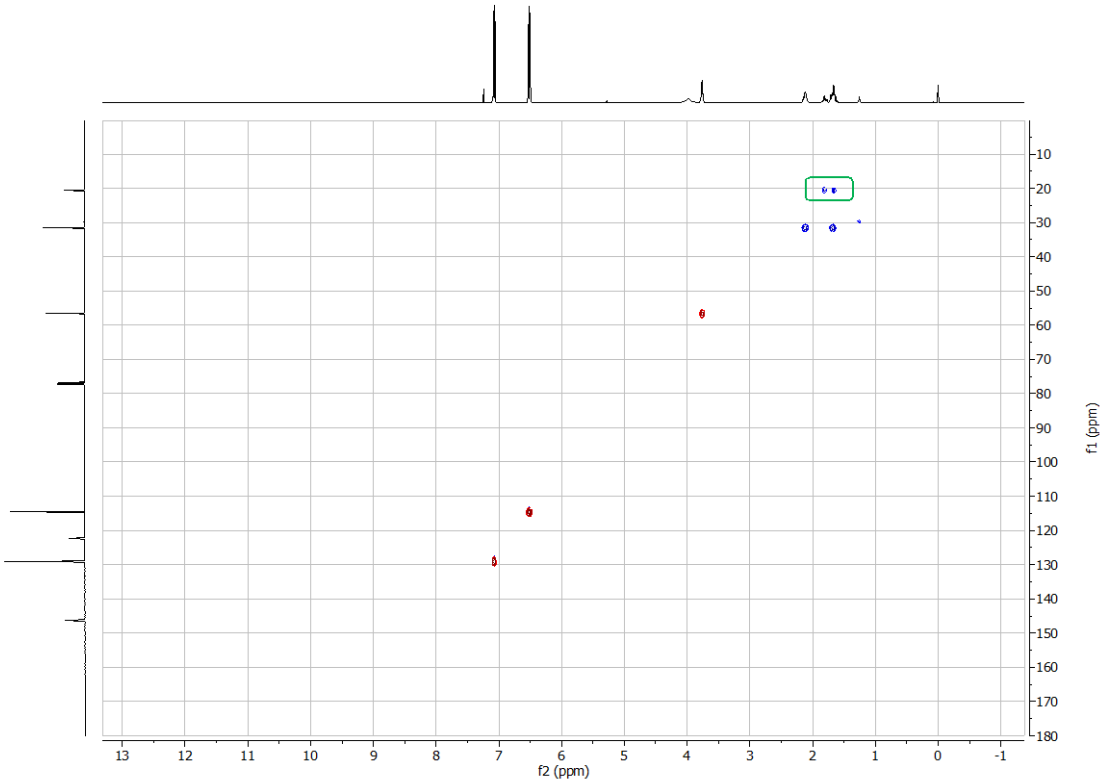


Figure 3.2 HSQC spectrum of N^1,N^2-bis(4-chlorophenyl)cyclopentane-1,2-diamine **89**

The cis configuration of the indane-1,2-diamine **91** was established using the NOESY spectrum (Figure 3.4). I observed a correlation between H atoms at C(1) and C(2). This correlation is possible if the two NH groups have the cis orientation, which is consistent with the cis isomer of indane-1,2-diamine **91** (Figure 3.3).

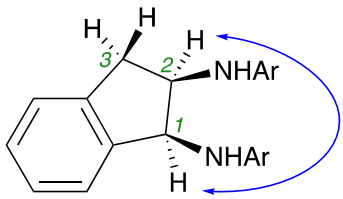


Figure 3.3 ^{1}H–^{1}H NOESY correlations between H atoms at C(1) and C(2) in N^1,N^2-bis(4-chlorophenyl)-2,3-dihydro-1H-indene-1,2-diamine **91**

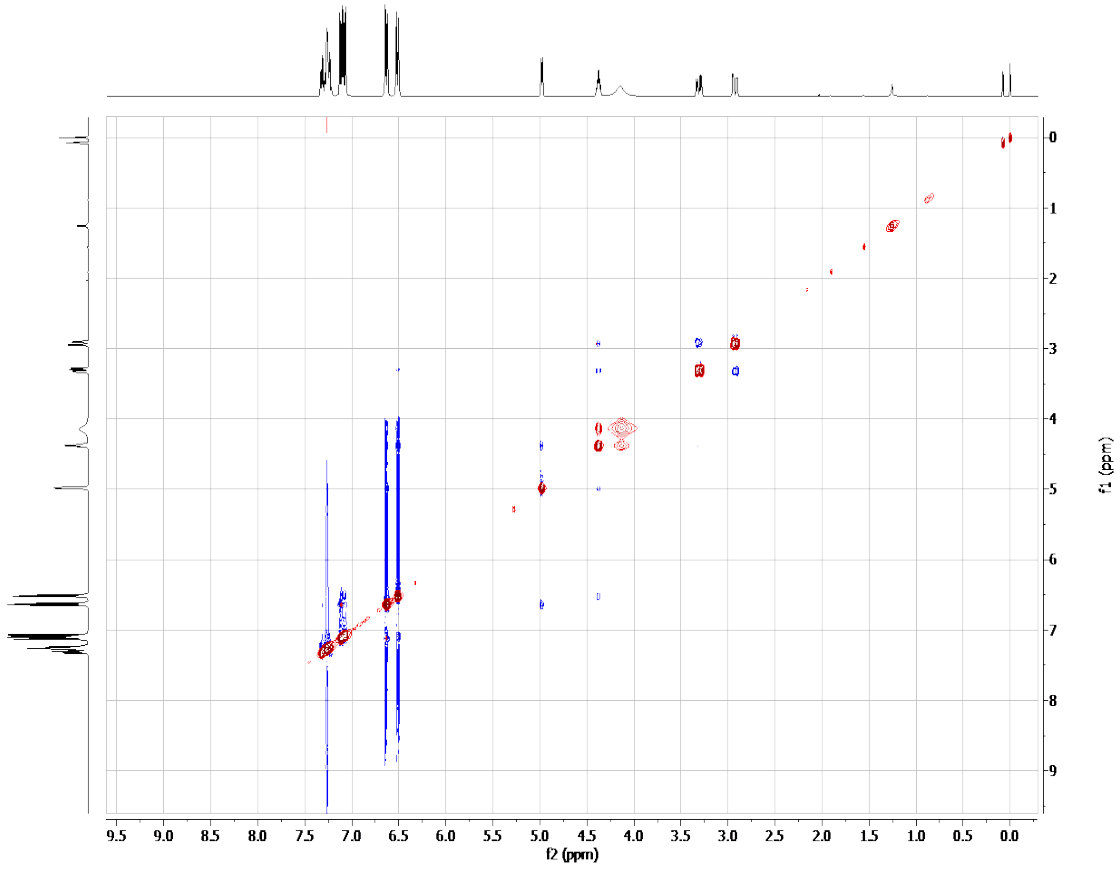
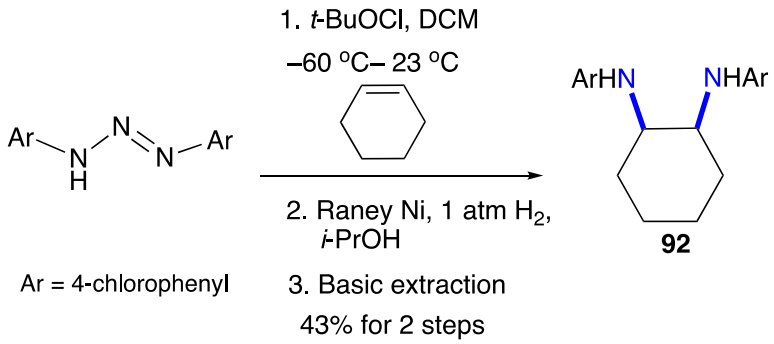


Figure 3.4 ^{1}H–^{1}H NOESY spectrum of N^{1},N^{2}-bis(4-chlorophenyl)-2,3-dihydro-1H-indene-1,2-diamine **91**

Similarly, the cyclohexane-1,2-diamine **92** was synthesized (Scheme 3.3), and the X-ray crystallographic analysis of its HCl salt confirmed the cis stereochemistry of the product (Figure 3.5). This result further confirmed the retention of the stereochemistry during the hydrogenolysis of the corresponding 1,2,3-triazolinium ion.



Scheme 3.3 Synthesis of N^{1},N^{2}-bis(4-chlorophenyl)cyclohexane-1,2-diamine **92**

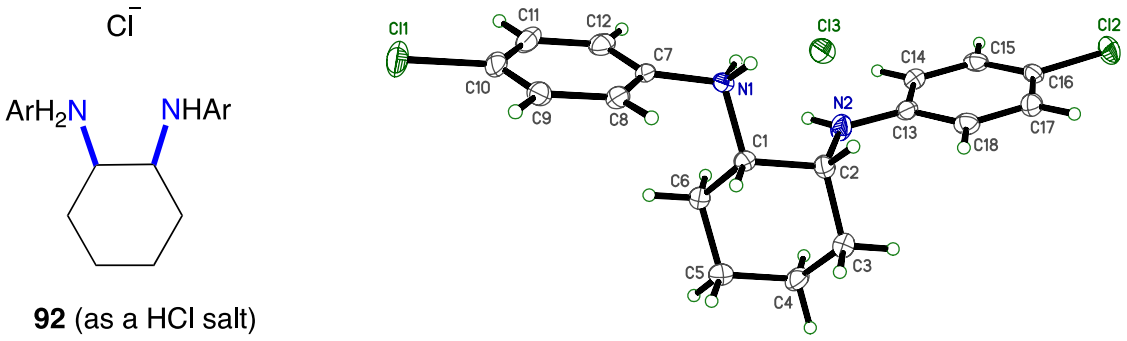
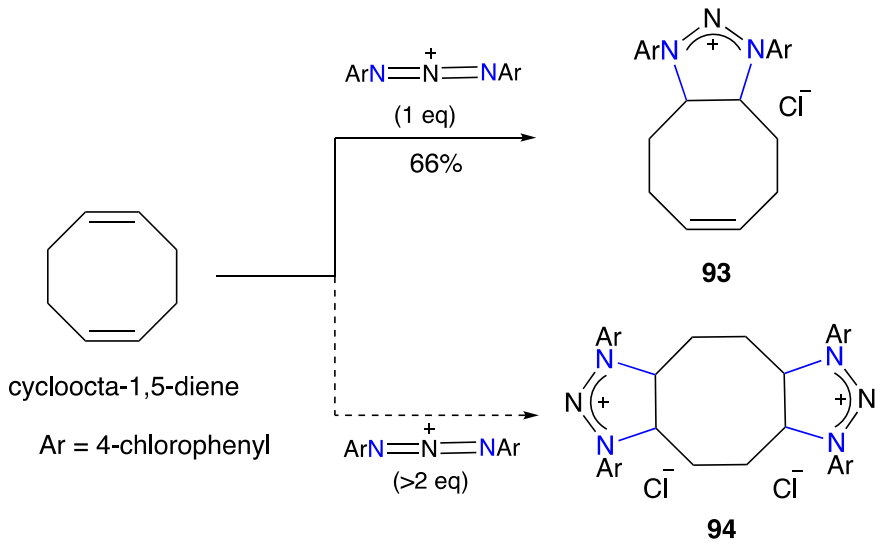


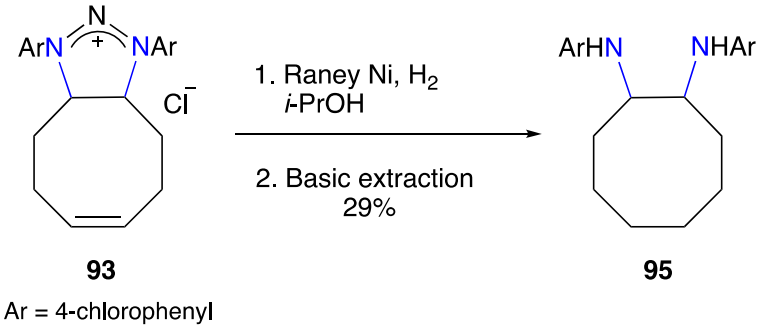
Figure 3.5 The thermal ellipsoid plot of N^1,N^2-bis(4-chlorophenyl)cyclohexane-1,2-diamine **92** as a HCl salt

We also investigated cycloocta-1,5-diene as a substrate that could potentially allow us to prepare the mono or double 1,2,3-triazolinium ions **93** and **94**, respectively (Scheme 3.4). Combination of one equivalent of azidium ion with cycloocta-1,5-diene formed the mono adduct 1,2,3-triazolinium ion **93** in 66% yield, as confirmed by NMR analysis. However, I was unable to find appropriate conditions to prepare or isolate the double adduct 1,2,3-triazolinium ion **94**.



Scheme 3.4 Formation of mono adduct 1,2,3-triazolinium ion **93** via cycloaddition of the azidium ion with cycloocta-1,5-diene

The reaction of this 1,2,3-triazolinium ion **93** with Raney Ni and a balloon of H_2 reduced both the 1,2,3-triazolinium ion and the alkene bond to give the cyclooctane-1,2-diamine **95** (Scheme 3.5). In this example, the reduction time was significantly longer comparing to the other examples, which possibly provided enough time for the C–Cl bonds to cleave, and I was able to recover the 1,2-diamine product **95** with only 29% yield.



93

Ar = 4-chlorophenyl

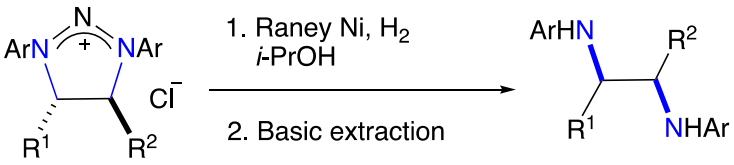
95

Scheme 3.5 Synthesis of N^1,N^2-bis(4-chlorophenyl)cyclooct-5-ene-1,2-diamine **95**

Based on the stereochemistry of other mentioned cycloalkane 1,2,3-triazolinium ions and 1,2-diamines being cis, it was reasonable to assume that the 1,2,3-triazolinium ion **93** and cyclooctane-1,2-diamine **95** would have the same cis stereochemistry. However, this assumption was not yet proven, and their stereochemistry had yet to be established rigorously.

3.2.2 Reduction of 1,2,3-triazolinium ion from the acyclic trans and terminal alkenes

The trans configuration of 1,2,3-triazolinium ions **96**, **98**, and **100** was established by X-ray crystallographic analysis (Appendix). Upon hydrogenation, the corresponding 1,2-diamines **97**, **99**, and **101** were prepared (Scheme 3.6). These results further confirmed the expected syn cycloaddition of the azidium ion to the trans alkenes and the preservation of the stereochemistry of the C–N bonds during hydrogenolysis.

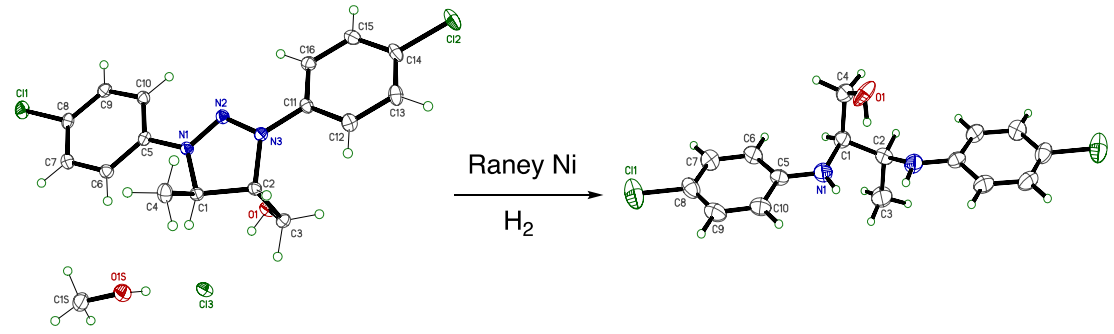


R^1	R^2	1,2,3-triazolinium ion	1,2-diamine[a]
Me	CH_2OH	**96**,88%	**97**,62%
Et	Et	**98**,73%	**99**,65%
Ph	Ph	**100**,82%	**101**,54%
Ph	H	**102**,83%	**103**,58%

Ar = 4-chlorophenyl; [a]Isolated yield of 1,2-diamine from 1,2,3-triazolinium ions.

Scheme 3.6 Synthesis of various 1,2-diamines from trans and terminal alkenes

Analysis of the X-ray crystallography of the 1,2-diamine **97** and **99** (as a HCl salt) confirmed the threo configuration of the products (Appendix). As we expected, the stereochemistry of their corresponding 1,2,3-triazolinium ions was preserved during their hydrogenation over Raney Ni. Figure 3.6 shows an example of the trans-1,2,3-triazolinium ion and its corresponding threo 1,2-diamine.



(trans 1,2,3-triazolinium ion **96**) (threo 1,2-diamine **97**)

Figure 3.6 Thermal ellipsoid plots of the 1,2,3-triazolinium **96**, and the 1,2-diamine **97**

Note: The terms erythro and threo designate the difference between diastereomers containing two adjacent stereocenters and bearing two different pairs of identical substituents. In the Fischer projection, the threo isomer contains the identical substituents

on the opposite side, whereas the erythro isomer has them on the same side (Figure 3.7). These terminologies are adapted from the saccharides D-erythrose and D-threose.

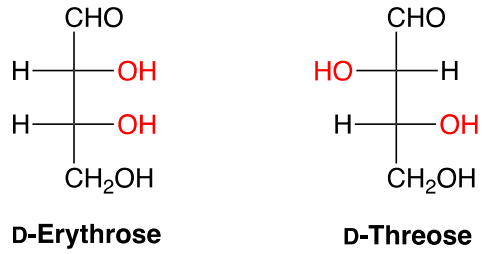
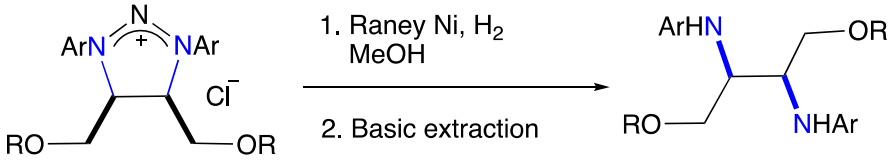


Figure 3.7 Fischer projection of D-erythrose and D-threose

3.2.3 Reduction of the 1,2,3-triazolinium ion from acyclic cis alkenes

I prepared the 1,2,3-triazolinium ions **104** and **106** from their acyclic cis alkenes, and their cis configuration were confirmed by X-ray crystallographic analysis (Appendix).



R	1,2,3-triazolinium ion	1,2-diamine[a]
H	**104**,85%	**105**,58%
Bn	**106**,56%	**107**,58%

Ar = 4-chlorophenyl; [a]Isolated yield of 1,2-diamine from 1,2,3-triazolinium ions.

Scheme 3.7 Synthesis of 2,3-bis[(4-chlorophenyl)amino]butane-1,4-diol **105**, and 1,4-bis(benzyloxy)-N^2,N^3-bis(4-chlorophenyl)butane-2,3-diamine **107**

Surprisingly, X-ray crystallographic analysis showed that the reduction of these 1,2,3-triazolinium ions with Raney Ni formed the 1,2-diamines **105** and **107**, which had the threo configuration instead of the expected erythro configuration (Scheme 3.7). Figure 3.8 illustrates the reduction of the cis 1,2,3-triazolinium ion to the threo 1,2-diamine.

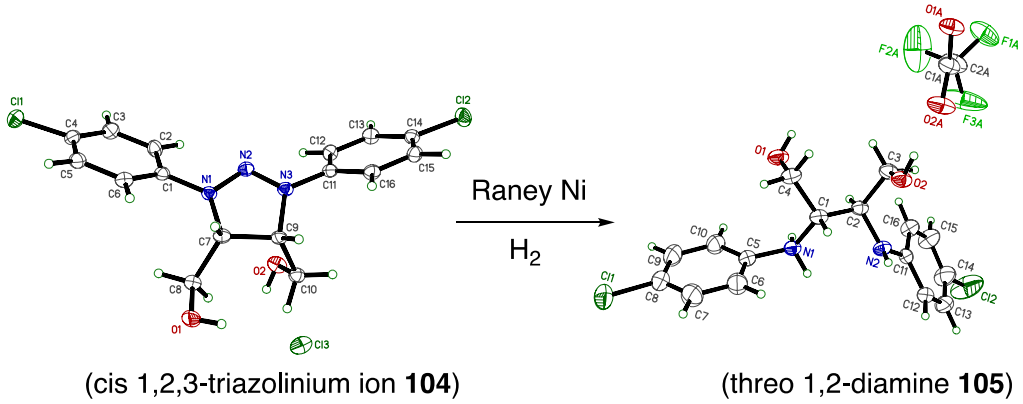
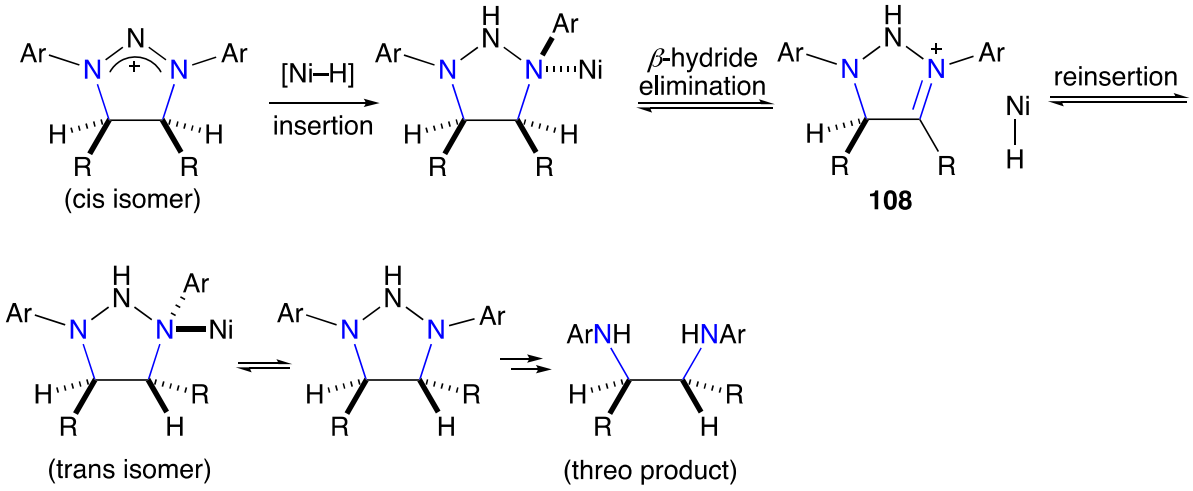


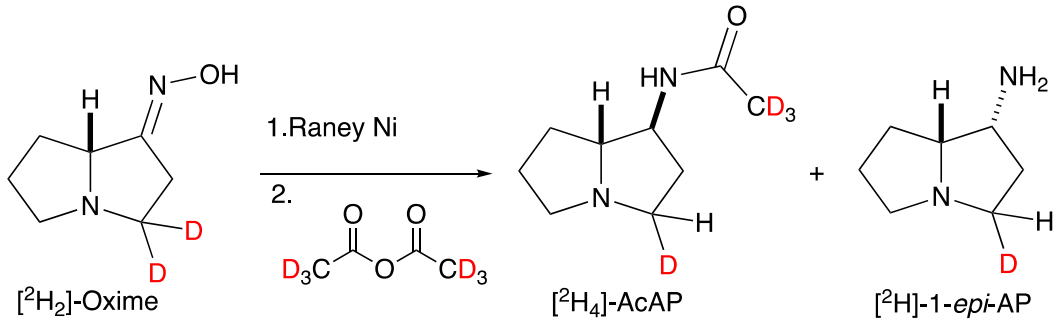
Figure 3.8 Thermal ellipsoid plots of the 1,2,3-triazolinium **104**, and the 1,2-diamine **105** (as a trifluoroacetate salt)

The 1,2,3-triazolinium ions **104** and **106** had inherited the cis configuration from the cis alkene, implying that the cycloaddition occurred via syn fashion, as expected. Therefore, we concluded that the isomerization must have happened during the hydrogenation step (Scheme 3.8). We hypothesized that the isomerization had occurred before the ring-opening in the triazolinium ion. The threo and erythro isomers of the 1,2-diamines were not likely to be far apart in energy; therefore, the conversion of cis 4,5-disubstituted ring to trans 4,5-disubstituted ring was possibly the driving force for the isomerization to occur. We proposed that Raney Ni coordinated to N(1) or N(3) of cis 4,5-disubstituted ring and underwent *β*-hydride elimination to form the intermediate **108**. This intermediate can undergo reinsertion to afford the more stable trans 4,5-disubstituted ring. The mechanism of hydrogenolysis by Raney Ni is not completely known, but Raney Ni can possibly cleave the N–N bonds and form the 1,2-diamine product.[50, 51]



Scheme 3.8 Possible mechanism by which Raney Ni converts the cis-1,2,3-triazolinium ions to the threo 1,2-diamines

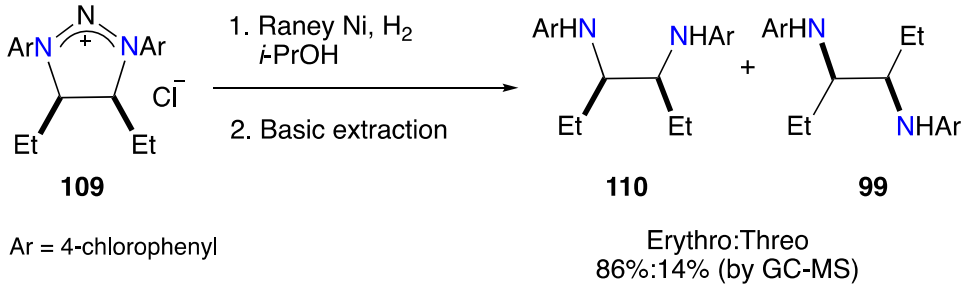
This is not the first time that we have been shocked by Raney Ni. Previous work in our lab has reported replacing H with D (or vice versa) in the synthesis of pentadeuterated AcAP (Scheme 3.9).[52] We observed that the products contained 85% monodeuterated, 13% undeuterated, and only a trace amount of dideuterated pyrrolizidine ring. This result suggested that Raney Ni may have catalyzed substitution of the D with H through β-hydride elimination and reinsertion to form a monodeuterated pyrrolizidine ring.



Scheme 3.9 Replacement of D with H by Raney Ni

In another example (Scheme 3.10), the 1,2,3-triazolinium ion **109** was subjected to Raney Ni, and the corresponding 1,2-diamine was purified as a mixture of erythro **110** and

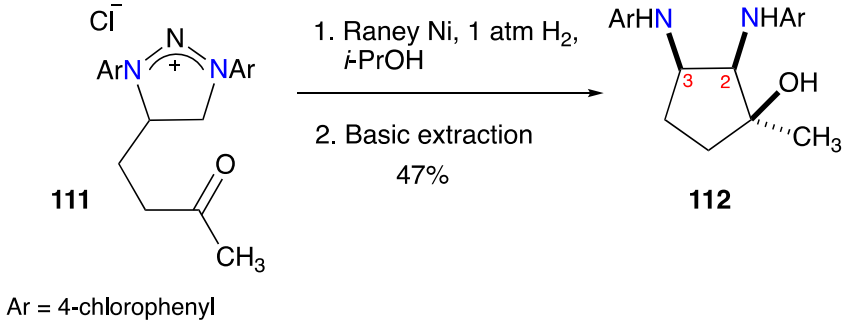
threo **99** isomers (86%:14% by GC-MS in favor of the expected erythro isomer). Unlike previous examples, the major product was the erythro isomer. In this case, it is likely that the low yield of the undesired threo isomer is because of the slower isomerization.



Scheme 3.10 Reduction of the 1,2,3-triazolinium **109** formed the 1,2-diamine product with partial inversion of the stereochemistry

3.2.4 Reduction of the 1,2,3-triazolinium ion derived from 5-hexen-2-one

The triazolinium ion **111** was prepared from addition of the azidium ion to 5-hexen-2-one. X-ray crystallographic (Figure 3.9) and NMR analysis confirmed formation of the product with the carbonyl group remaining intact. Surprisingly, hydrogenolysis of 1,2,3-triazolinium ion over Raney Ni formed the 1,2-diamine **112** in 47% yield (Scheme 3.11).



Scheme 3.11 Synthesis of 2,3-bis[(4-chlorophenyl)amino]-1-methylcyclopentan-1-ol **112**

NMR analysis confirmed formation of the 1,2 diamine **112** (Appendix). The ^{1}H NMR presented two downfield H atoms resonating at 3.44 ppm (doublet) and at 3.92 ppm (doublet of triplet), which were consistent with the H atoms connected to C(2) and C(3),

respectively. Also, disappearance of the carbonyl carbon was noticeable in ^{13}C NMR. The HSQC and ^{1}H-^{1}H COSY correlations matched the structure of the 1,2-diamine **112** (Appendix). Additionally, the X-ray crystallographic analysis of 1,2-diamine **112** (as a HCl salt) validated the proposed structure (Figure 3.9).

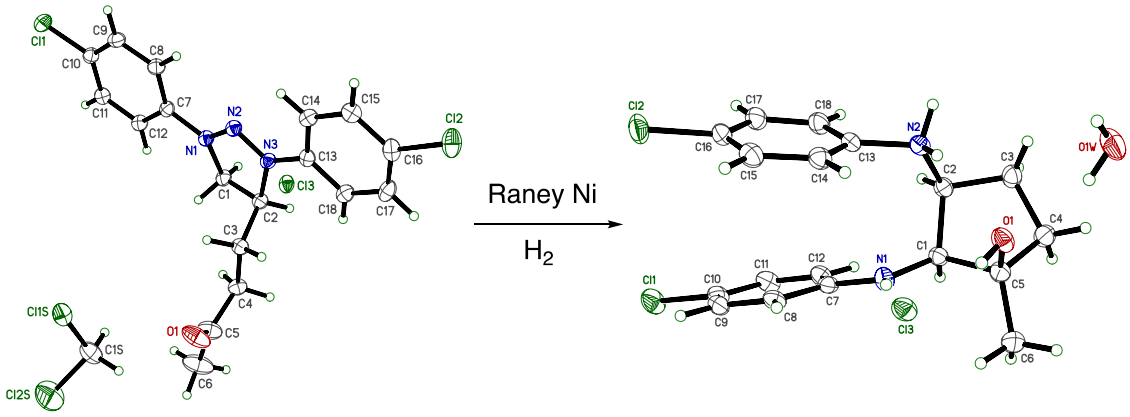
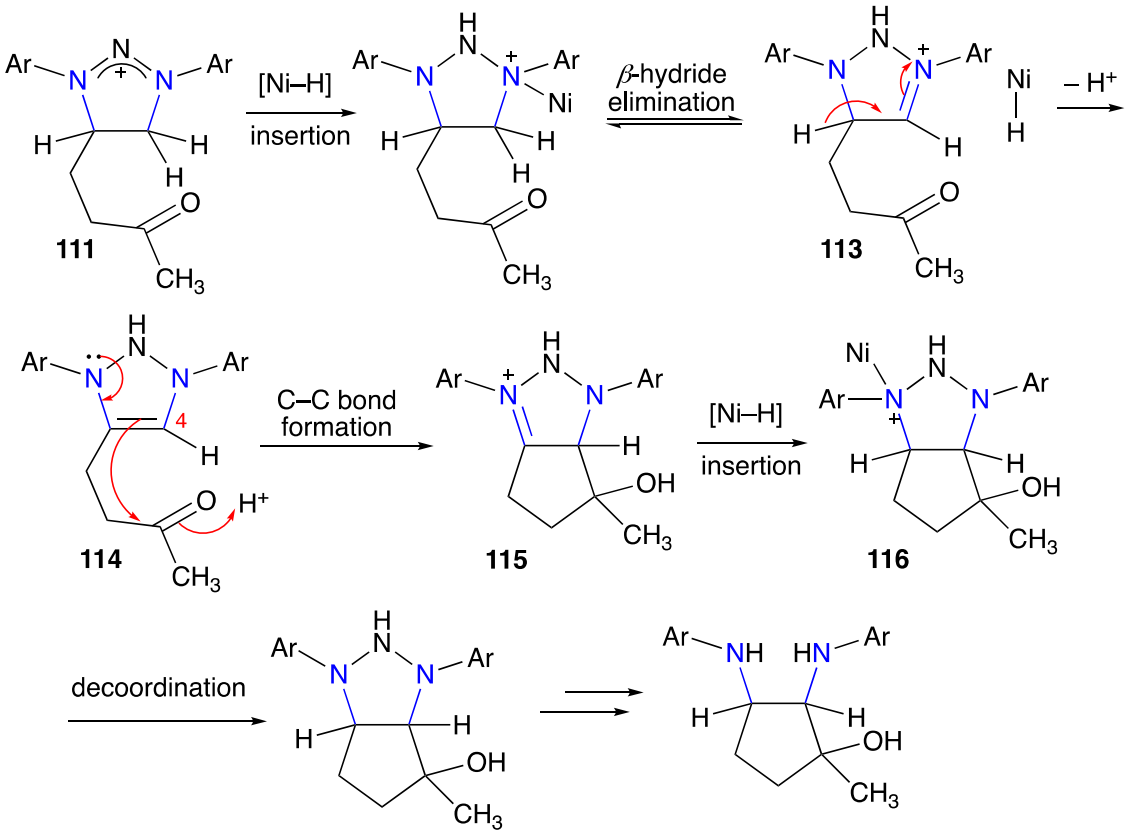


Figure 3.9 Thermal ellipsoid plot of 1,2,3-triazolinium **111**, and 1,2-diamine **112**

To explain the C–C bond formation in this reaction, we hypothesized that similar to the above mechanism, Raney Ni coordinates to an N(1) or N(3) and catalyzes the β-hydride elimination to form the hydrazone intermediate **113** (Scheme 3.12). We proposed that deprotonation of the iminium ion at the alpha position formed the enamine intermediate **114**. Further nucleophilic attack of the C(4) to the carbonyl group could possibly form the cyclic intermediate **115**. Reinsertion of the Ni–H to the iminium ion bond in intermediate **115** formed the intermediate **116**, which would likely undergo N–N bonds cleavage by Raney Ni to form the 1,2-diamine **112**.



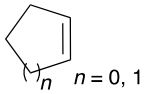
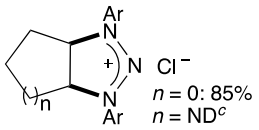
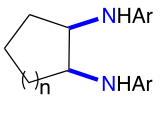
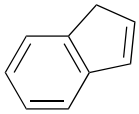
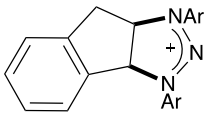
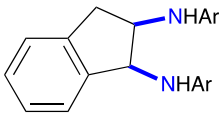
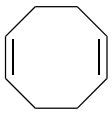
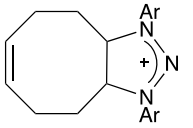
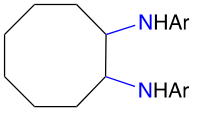
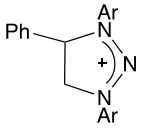
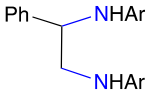
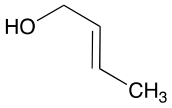
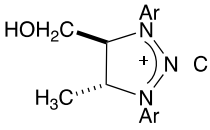
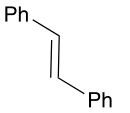
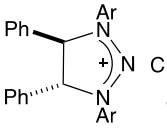
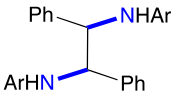
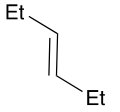
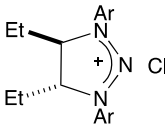
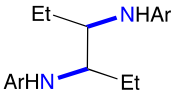
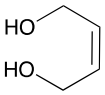
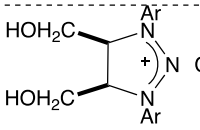
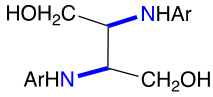
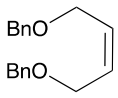
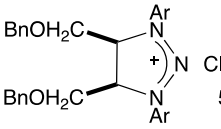
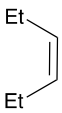
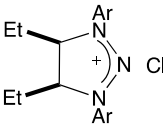
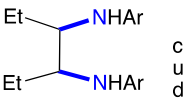
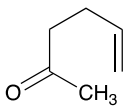
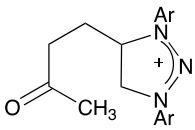
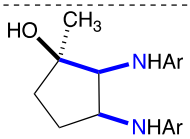
Scheme 3.12 Possible mechanism by which Raney Ni converts 1,2,3-triazolinium **111** to 1,2-diamine **112**

3.3 Summary

In chapter 3, I have shown that 1,2,3-triazolinium ions can also be prepared by azidium ion–alkene cycloaddition. I also reduced these 1,2,3-triazolinium ions over Raney Ni with a balloon of H_2. Reduction of the 1,2,3-triazolinium ions derived from the cyclic alkenes formed the cis-1,2-diamine, as expected. The stereochemistry of these 1,2-diamines was confirmed by NMR or X-ray crystallographic except for cyclooctane-1,2-diamine **95**. Hydrogenation of the 1,2,3-triazolinium ions from acyclic trans alkenes also proceeded with retention of the stereochemistry. Unexpectedly, the reduction of 1,2,3-triazolinium ions derived from the acyclic cis alkenes proceeded with partial or complete inversion of the stereochemistry. The evidence suggested that this isomerization occurred

during the hydrogenation step. Shockingly, the reduction of the 1,2,3-triazolinium ion derived from the 5-hexen-2-one proceeded by making an additional C–C bond. Additionally, I was able to crystalize most of the 1,2,3-triazolinium ions and 1,2-diamines to confirm their structure and stereochemistry with X-ray crystallographic analysis. A summary of the synthesized 1,2,3-triazolinium ions and 1,2-diamines in this chapter is depicted in Table 2.1.

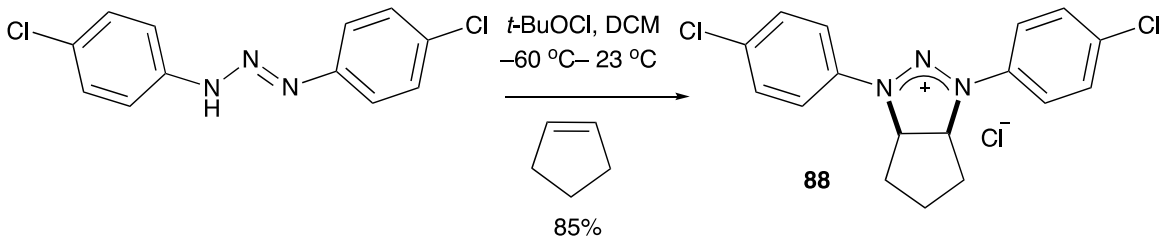
Table 3.1 List of 1,2-diamines synthesized through azidium ion–alkene cycloaddition

entry	*alkene*	*1,2,3-triazolinium ion*[a]	*1,2-diamine*	*yield*
1				*n* = 0: 65% *n* = 1: 43%[b]
2				61%
3				29%[d]
4				58%
5				62%
6				54%
7				65%
8				58%
9				58%
10				33% ca. 14% unexpected diastereomer
11				47%

Ar = 4-chlorophenyl; [b]Isolated yield of 1,2-diamine from triazene; [c]ND = not determined; [d]The relative stereochemistry has not yet been proven to be cis.

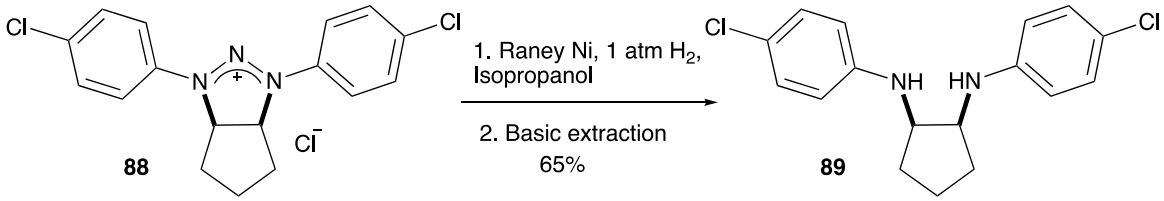
3.4 Experimental Section

1,3-bis(4-chlorophenyl)-3H,3aH,4H,5H,6H,6aH-cyclopenta[d][1,2,3]triazol-1-ylium chloride



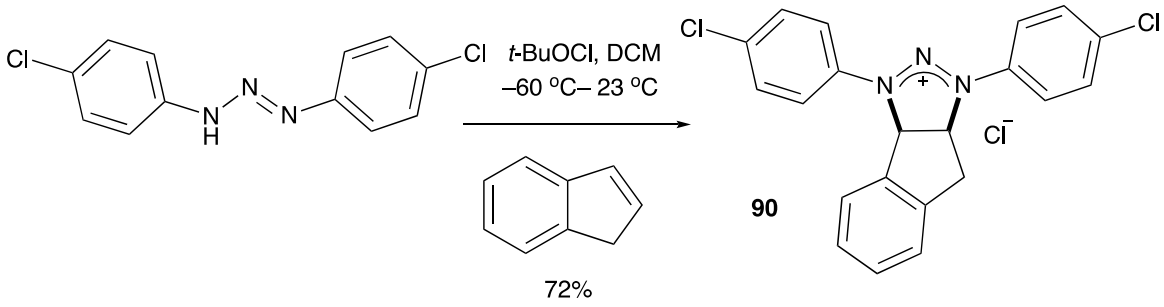
To the suspension of 1,3-bis(4-chlorophenyl)triazene[53, 54] (503 mg, 1.89 mmol) and cyclopentene (155 mg, 2.27 mmol) in dry CH_2Cl_2 (10 mL), *t*-BuOCl (246 mg, 2.27 mmol) was added dropwise at –60 °C with exclusion of light. The resulting light red solution was stirred at –45 °C for 1h, then at 0 °C for 30 minutes, and at room temperature for 20 minutes. Then, the solvent was evaporated under reduced pressure. The resulting yellow solid was precipitated from chloroform (9 mL) and ether (20 mL). The solvent was decanted and the yellow solid was washed with ether one more time. To evaporate the residue of ether the yellow solid was redissolved in CH_2Cl_2 and the mixture of solvents was evaporated under reduced pressure to result the yellow 1,2,3-triazolinium ion **88** as a yellow chloride salt (594 mg, 1.61 mmol, 85%). Crystals of **88** were grown by dissolving the substrate in $CHCl_3$ and the slow evaporation of solvent for X-ray crystallographic analysis. m.p.: 235.0–237.6 °C; ^{1}H NMR (400 MHz, $CDCl_3$) 7.94–7.66 (m, 4H), 7.54–7.39 (m, 4H), 6.95–6.71 (m, 2H), 2.53 (m, 2H), 2.21 (ddd, J=14.8, 6.7, 3.0 Hz, 2H), 1.96 (dtt, J_d= 12.8 Hz, J_t = 6.3 Hz, J_t = 3.0 Hz, 1H), 1.46 (ddt, J_d = 13.3, J_d = 3.3 Hz, J_t = 6.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.3, 133.3, 130.7, 121.1, 72.7, 34.7, 24.0; IR (ATR) 3085, 2977, 2858 cm^{-1}; HRMS (ESI) Calcd. For $C_{17}H_{16}Cl_2N_3$ $[M]^+$: 332.0716; Found: 332.0679.

N^1,N^2-bis(4-chlorophenyl)cyclopentane-1,2-diamine



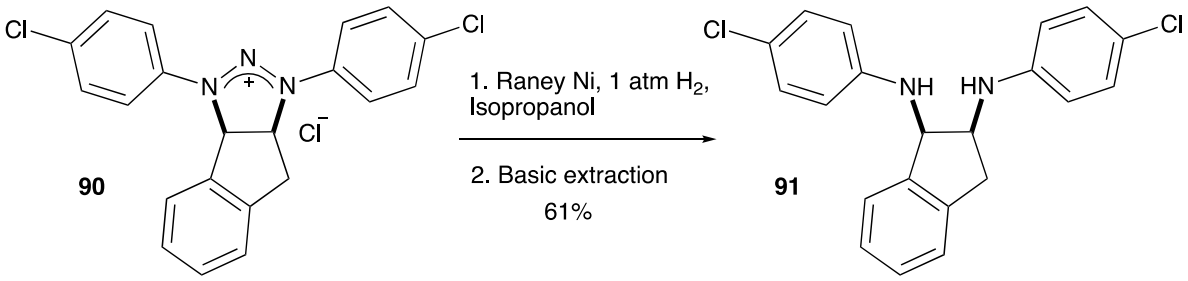
One small spatula of Raney Ni 2400 slurry in water (0.43 g) was added to the solution of 1,2,3-triazolinium **88** (159 mg, 0.430 mmol) in isopropanol (3 mL), under N_2 atmosphere. Then a balloon of H_2 was placed on top of the flask while removing N_2. The reaction mixture was stirred at room temperature for 2 h and 30 min (Reaction completion was accompanied by the reaction mixture color change from yellow to colorless and monitored by running TLC in 5% MeOH in CH_2Cl_2). After reaction completion, the mixture was filtered through a short pad of Celite, washed with isopropanol and concentrated under vacuum. The crude mixture was redissolved in CH_2Cl_2 and subjected to basic extraction using NaOH solution (pH = 10). The combined organic layer was dried over Na_2SO_4, filtered and concentrated under vacuum. Flash chromatography of the residue (5% EtOAc in Hexanes) afforded the 1,2-diamine **89** as a light orange viscous liquid (89.8 mg, 0.279 mmol, 65%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.20–6.99 (m, 4H), 6.67–6.39 (m, 4H), 4.01 (broad s, 2NH), 3.78 (t, J = 4.8Hz, 2H), 2.20–2.06 (m, 2H), 1.96–1.76 (m, 1H), 1.75–1.58 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.4, 129.2, 122.4, 114.7, 56.7, 31.7, 20.8; IR (ATR) 3387, 3052, 2953, 2862 cm^{-1}; GC-MS (EI) 320 (4%), 196 (35%), 194 (100%), 166 (8%), 140 (8%), 127 (23%); HRMS (ESI) Calcd. For $C_{17}H_{19}Cl_2N_2$ $[M+H]^+$: 321.0920; Found: 321.0931.

1,3-bis(4-chlorophenyl)-3H,3aH,8H,8aH-indeno[1,2-d][1,2,3]triazol-1-ylium chloride



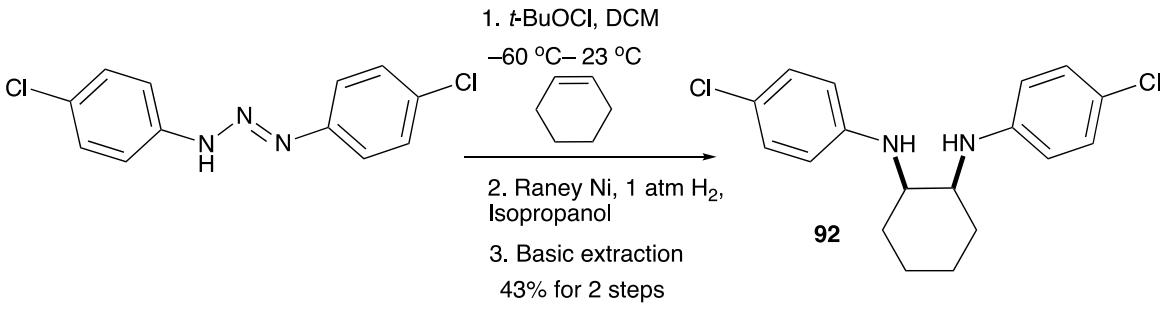
To the suspension of 1,3-bis(4-chlorophenyl)triazene (178 mg, 0.669 mmol) and indene (93.3 mg, 0.803 mmol) in dry CH_2Cl_2 (5 mL), *t*-BuOCl (87.0 mg, 0.803 mmol) was added dropwise at –60 °C with exclusion of light. The resulting light red solution was stirred at –45 °C for 1 h, then at 0 °C for 30 minutes, and at room temperature for 20 minutes. Then, the solvent was evaporated under reduced pressure. The resulting yellow solid was precipitated from chloroform (9 mL) and ether (60 mL). The solvent was decanted and the yellow solid was washed with ether one more time. To evaporate the residue of ether the yellow solid was re-dissolved in CH_2Cl_2 and the mixture of solvents was evaporated under reduced pressure to result the orangish-yellow 1,2,3-triazolinium ion **90** as a chloride salt (200 mg, 0.480 mmol, 72%). Crystals of **90** were grown by diffusion method from CH_2Cl_2/ THF for X-ray crystallographic analysis. m.p.: 178.5–182.2 °C; ^{1}H NMR (400 MHz, CD_3OD) δ 8.05 (d, J = 8.6 Hz, 2H), 7.89 (d, J = 8.7 Hz, 2H), 7.85–7.64 (m, 4H), 7.44 (d, J = 4.1 Hz, 2H), 7.38–7.21 (m, 3H), 6.44 (ddd, J = 11.2, 8.1, 2.3 Hz, 1H), 3.98 (dd, J = 17.9, 8.0 Hz, 1H), 3.66 (dd, J = 18.0, 2.2 Hz, 1H); ^{13}C NMR (100 MHz, CD_3OD) δ 141.7, 137.8, 137.1, 135.6, 135.3, 135.1, 132.2, 131.7, 131.7, 129.4, 126.9, 126.8, 124.1, 122.3, 76.7, 71.0, 39.4; IR (ATR) 3016, 2980, 2922, 2866 cm^{-1}; HRMS (ESI) Calcd. For $C_{21}H_{16}Cl_2N_3$ $[M]^+$: 380.0716; Found: 380.0693.

N^1,N^2-bis(4-chlorophenyl)-2,3-dihydro-1H-indene-1,2-diamine



One small spatula of Raney Ni 2400 slurry in water (0.22 g) was added to the solution of 1,2,3-triazolinium ion **90** (89.1 mg, 0.214 mmol) in isopropanol (5 mL), under N_2 atmosphere. Then a balloon of H_2 was placed on top of the flask while removing N_2. The reaction mixture was stirred at room temperature for 7 h (Reaction completion was accompanied by the reaction mixture color change from yellow to colorless and monitored by running TLC in 5% MeOH in CH_2Cl_2). After reaction completion, the mixture was filtered through a short pad of Celite, washed with isopropanol and concentrated under vacuum. The crude mixture was redissolved in CH_2Cl_2 and subjected to basic extraction using NaOH solution (pH = 10). The combined organic layer was dried over Na_2SO_4, filtered and concentrated under vacuum. Flash chromatography of the residue (6% EtOAc in Hexanes) afforded the 1,2-diamine **91** as a viscous liquid (48.2 mg, 0.130 mmol, 61%). ^{1}H NMR (400 MHz, $CDCl_3$) 7.36–7.22 (m, 4H), 7.16–7.06 (m, 4H), 6.65 (d, J = 8.5, 2H), 6.53 (d, J = 8.5 Hz, 2H), 4.99 (d, J = 5.8 Hz, 1H), 4.39 (dt, J_t = 6.0 Hz, J_d = 3.9 Hz, 1H), 4.15 (broad s, 2NH), 3.32 (dd, J = 16.1, 6.1 Hz, 1H), 2.93 (dd, J = 16.1, 3.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.5, 146.1, 142.3, 140.6, 129.4, 129.2, 128.7, 127.5, 125.7, 124.6, 123.0, 122.5, 114.9, 114.8, 61.6, 57.2, 38.0. IR (ATR) 3410, 3356, 3044, 2980, 2896 cm^{-1}; GC-MS (EI) 368 (1.37%), 242 (100%), 207 (4.47%), 127 (8.0%), 115 (7.0%), 103 (3.2%); HRMS (ESI) Calcd. For $C_{21}H_{19}Cl_2N_2$ $[M+H]^+$: 369.0920; Found: 369.0931.

N^1,N^2-bis(4-chlorophenyl)cyclohexane-1,2-diamine

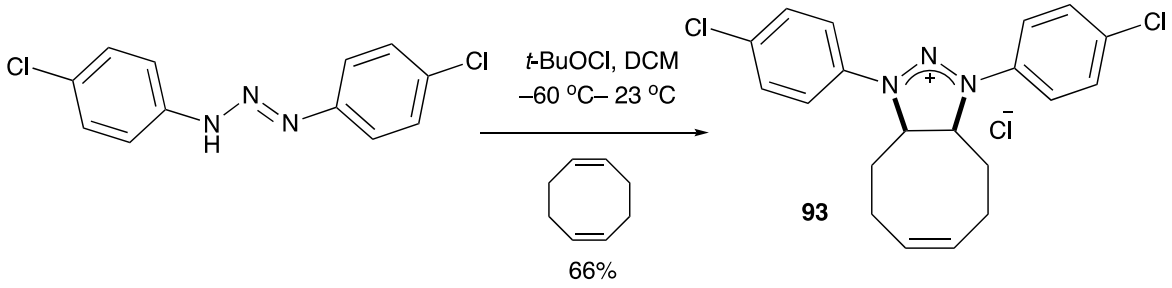


To a suspension of 1,3-bis(4-chlorophenyl)triazene (529 mg, 1.99 mmol) and cyclohexene (196 mg, 2.38 mmol) in dry CH_2Cl_2 (15 mL), *t*-BuOCl (259 mg, 2.38 mmol) was added dropwise at –60 °C with exclusion of light. The resulting light red solution was stirred at –45 °C for 1 h, then at 0 °C for 30 minutes, and at room temperature for 20 minutes. Then, the solvent was evaporated under reduced pressure. The resulting yellow solid was precipitated from chloroform (6 mL) and ether (50 mL). The solvent was decanted and the yellow solid was washed with ether one more time. To evaporate the residue of ether, the yellow solid was redissolved in CH_2Cl_2, and the mixture of solvents was evaporated under reduced pressure to give the yellow 1,2,3-triazolinium ion as a chloride salt (crude mass: 443 mg).

One small spatula of Raney Ni 2400 slurry in water (1.3 g) was added to the solution of crude 1,2,3-triazolinium ion (443 mg, 1.16 mmol) in isopropanol (7 mL), under N_2 atmosphere. Then a balloon of H_2 was placed on top of the flask while removing N_2. The reaction mixture was stirred at room temperature for 2 h and 30 min. (Reaction completion was accompanied by the reaction mixture color change from yellow to colorless and monitored by running TLC in 5% MeOH in CH_2Cl_2.) After reaction completion, the mixture was filtered through a short pad of Celite, washed with isopropanol and concentrated under vacuum. The crude mixture was redissolved in CH_2Cl_2 and subjected

to basic extraction using NaOH solution (pH = 10). The combined organic layer was dried over Na_2SO_4, filtered and concentrated under vacuum. Flash chromatography of the residue (5% EtOAc in Petroleum ether) afforded the 1,2-diamine **92** as a yellow viscous liquid (265 mg, 0.791 mmol, 43% from the triazene). Crystals of HCl salt of **92** were grown by diffusion method from MeOH/ ether for X-ray crystallographic analysis. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26–6.81 (m, 4H), 6.72–6.35 (m, 4H), 3.90 (broad s, 2NH), 3.64 (dt, J_d = 6.3, J_t = 3.1 Hz, 2H), 1.76 (ddt, J_d = 12.1, J_t = 7.8, J_d = 4.1 Hz, 2H), 1.69–1.42 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.1, 129.3, 122.2, 115.0, 53.0, 28.4, 22.2; IR (ATR) 3397, 3024, 2924, 2853 cm^{-1}; GC-MS (EI) 334 (12 %), 210 (31%), 208 (100%), 166 (17%), 153 (45%), 152 (35%), 130 (28%), 117 (22%), 91 (22%); HRMS (ESI) Calcd. For $C_{18}H_{21}Cl_2N_2$ $[M+H]^+$: 335.1076; Found: 335.1071.

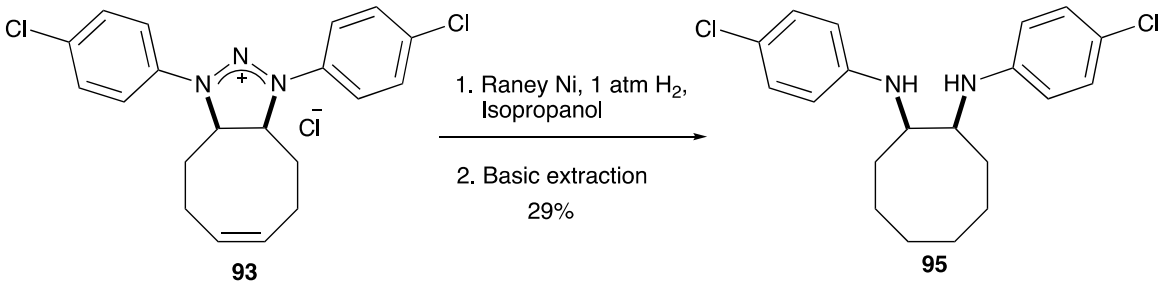
1,3-bis(4-chlorophenyl)-3H,3aH,4H,5H,8H,9H,9aH-cycloocta[d][1,2,3]triazol-1-ylium chloride



To the suspension of 1,3-bis(4-chlorophenyl)triazene (338 mg, 1.27 mmol) and cyclooctadiene (138 mg, 1.27 mmol) in dry CH_2Cl_2 (8 mL), *t*-BuOCl (166 mg, 1.53 mmol) was added dropwise at –60 °C with exclusion of light. The resulting solution was stirred at –45 °C for 1 h and 30 min, at 0 °C for 40 minutes, and at room temperature for 20 minutes. Then, the solvent was evaporated under reduced pressure. The resulting yellow solid was precipitated from chloroform (6 mL) and ether (40 mL). The solvent was decanted and the

yellow solid was washed with ether (8 mL) one more time. The yellow solid was redissolved in CH_2Cl_2 and the mixture of solvents was evaporated under reduced pressure to result the orange-yellow 1,2,3-triazolinium ion **93** as a chloride salt (344 mg, 0.842 mmol, 66%). m.p.: 112.2–114.6 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, *J* = 8.4 Hz, 4H), 7.48 (d, *J* = 8.4 Hz, 4H), 6.53 (t, *J* = 3.2 Hz, 2H), 5.69 (t, *J* = 4.6 Hz, 2H), 2.50–2.30 (m, 6H), 2.11 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.8, 133.5, 130.7, 130.6, 123.2, 68.6, 27.6, 22.5; IR (ATR) 3085, 3021, 2923, 2866 cm^{-1}; HRMS (ESI) Calcd. For $C_{20}H_{20}Cl_2N_3$ $[M]^+$: 372.1029; Found: 372.0991.

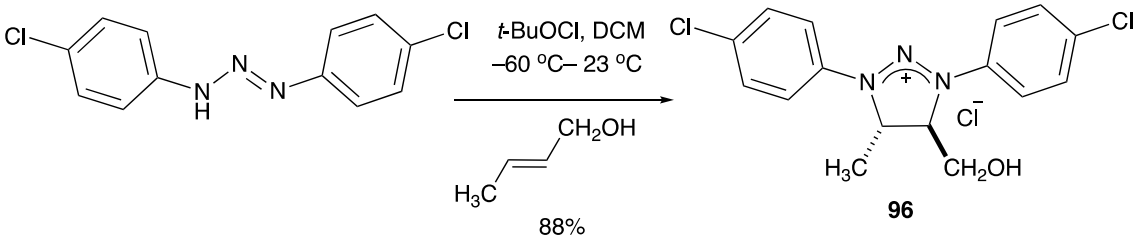
N^1,N^2-bis(4-chlorophenyl)cyclooct-5-ene-1,2-diamine



One small spatula of Raney Ni 2400 slurry in water (0.64 g) was added to the solution of 1,2,3-triazolinium ion **93** (262 mg, 0.641 mmol) in isopropanol (7 mL), under N_2 atmosphere. Then a balloon of H_2 was placed on top of the flask while removing N_2. The reaction mixture was stirred at room temperature for 12 h. (Reaction completion was accompanied by the reaction mixture color change from yellow to colorless and monitored by running TLC in 5% MeOH in CH_2Cl_2.) After reaction completion, the mixture was filtered through a short pad of Celite, washed with isopropanol and concentrated under vacuum. The crude mixture was redissolved in CH_2Cl_2 and subjected to basic extraction using NaOH solution (pH = 10). The combined organic layer was dried over Na_2SO_4,

filtered and concentrated under vacuum. Flash chromatography of the residue (5% EtOAc in PE) afforded the 1,2-diamine **95** as a yellow viscous liquid (67.0 mg, 0.184 mmol, 29%).^{1}H NMR (400 MHz, $CDCl_3$) δ 7.14–7.04 (m, 4H), 6.56–6.48 (m, 4H), 3.86 (s, 2NH), 3.77 (dd, *J* = 8.1, 3.4 Hz, 2H), 1.91–1.79 (m, 2H), 1.79–1.52 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.2, 129.3, 122.2, 115.1, 54.7, 29.7, 27.1, 25.0; IR (ATR) 3385, 3050, 2915, 2850 cm^{-1} ; GC-MS (EI) 362 (16%), 236 (100%), 166 (91%), 153 (51%), 140 (70%), 130 (56%), 111 (24%), 91 (19%), 75 (11%); HRMS (ESI) Calcd. For $C_{20}H_{25}Cl_2N_2$ $[M+H]^+$: 363.1389; Found: 363.1384.

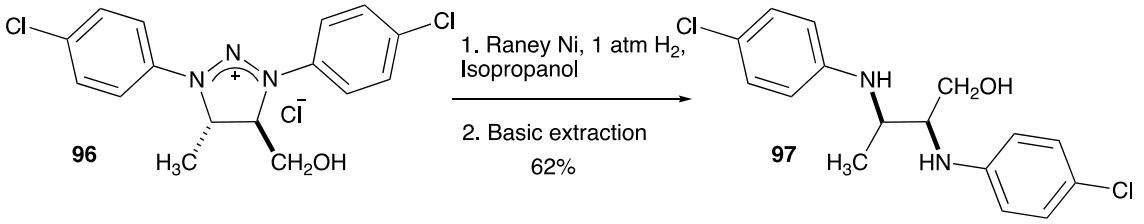
1,3-bis(4-chlorophenyl)-5-(hydroxymethyl)-4-methyl-4,5-dihydro-3H-1,2,3-triazol-1-ylium chloride



To the suspension of 1,3-bis(4-chlorophenyl)triazene (388 mg, 1.46 mmol) and *trans*-Crotyl alcohol (126 mg, 1.75 mmol) in dry CH_2Cl_2 (7 mL), *t*-BuOCl (190 mg, 1.75 mmol) was added dropwise at –60 °C with exclusion of light. The resulting solution was stirred at –45 °C for 1 h, then at 0 °C for 45 minutes, and at room temperature for 30 minutes. After the reaction completion the product was precipitated in CH_2Cl_2. Then 5 mL ether was added to the mixture, filtered and the yellow precipitate was washed with ether two more times. The yellow solid was kept under vacuum to evaporate the residue of solvents and yield a yellow 1,2,3-triazolinium ion **96** as a chloride salt (475 mg, 1.27 mmol, 88%). Crystals of **96** were grown by diffusion method from CH_2Cl_2 + 1 drop of MeOH/ hexanes for X-ray crystallographic analysis. m.p.: 220.0–220.9 °C; ^{1}H NMR (400 MHz,

D_2O) δ 7.87–7.73 (m, 4H), 7.73–7.61 (m, 4H), 5.82–5.63 (m, 1H), 5.56 (dt, J_d = *5*.4 Hz, J_t = 2.5 Hz, 1H), 4.14 (dd, *J* = 13.2, 2.7 Hz, 1H), 3.97 (dd, *J* = 13.2, 2.2 Hz, 1H), 1.72 (d, *J* = 6.8 Hz, 3H).; ^{13}C NMR (100 MHz, D_2O) δ 135.7, 135.5, 133.4, 132.9, 130.4, 130.3, 121.1, 120.9, 73.0, 64.4, 59.7, 17.8; IR (ATR) 3294, 3072, 2954, 2924 cm^{-1}; HRMS (ESI) Calcd. For $C_{16}H_{16}Cl_2N_3O$ $[M]^+$: 336.0665; Found: 336.0620.

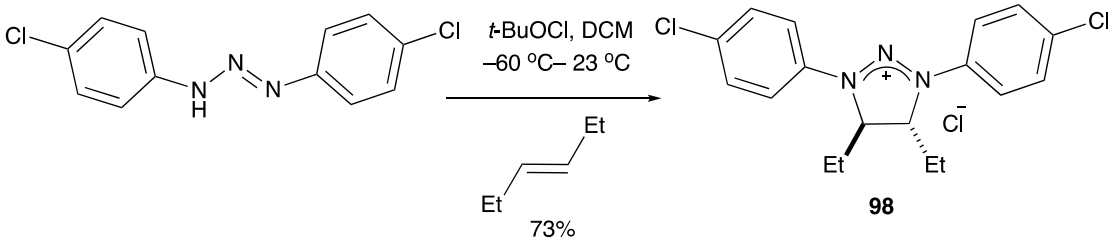
2,3-bis[(4-chlorophenyl)amino]butan-1-ol



One small spatula of Raney Ni 2400 slurry in water (1.0 g) was added to the solution of 1,2,3-triazolinium ion **96** (387 mg, 1.04 mmol) in methanol (15 mL), under N_2 atmosphere. Then a balloon of H_2 was placed on top of the flask while removing N_2. The reaction mixture was stirred at room temperature for 1 h and 30 min. (Reaction completion was accompanied by the reaction mixture color change from yellow to colorless and monitored by running TLC in 5% MeOH in CH_2Cl_2.) After reaction completion, the mixture was filtered through a short pad of Celite, washed with methanol and concentrated under vacuum. The crude mixture was redissolved in CH_2Cl_2 and subjected to basic extraction using NaOH solution (pH = 10). The combined organic layer was dried over Na_2SO_4, filtered and concentrated under vacuum. Flash chromatography of the residue (25% EtOAc in PE) and trituration in hexanes afforded the 1,2-diamine **97** as a white solid (209 mg, 0.643 mmol, 62%). Crystals of **97** were grown by diffusion method from CH_2Cl_2/ hexanes for X-ray crystallographic analysis m.p.: 125.4–127.0 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.21–7.06 (m, 4H), 6.73–6.48 (m, 4H), 3.91–3.67 (m, 3H), 3.44 (q, *J* = 4.5 Hz,

1H), 1.55 (s, 1H), 1.25 (d, J = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.6, 145.8, 129.4, 123.3, 123.1, 115.6, 115.2, 63.2, 59.3, 51.7, 18.5; IR (ATR) 3369, 3277, 2964, 2925, 2847 cm^{-1}; GC-MS (EI) 207 (2%), 170 (11%), 154 (100%), 138 (14%), 127 (4%), 118 (9%), 111 (15%), 91 (2%), 75 (6%); HRMS (ESI) Calcd. For $C_{16}H_{19}Cl_2N_2O$ $[M+H]^+$: 325.0869; Found: 325.0868.

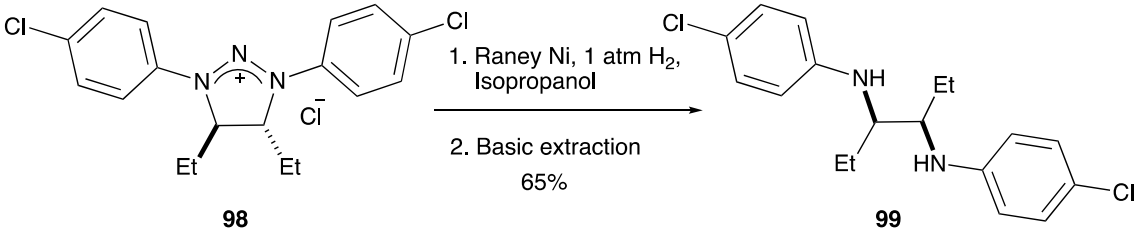
1,3-bis(4-chlorophenyl)-4,5-diethyl-4,5-dihydro-3H-1,2,3-triazol-1-ylium chloride



To the suspension of 1,3-bis(4-chlorophenyl)triazene (304 mg, 1.14 mmol) and *trans*-3-hexene (115 mg, 1.37 mmol) in dry CH_2Cl_2 (7 mL), *t*-BuOCl (149 mg, 1.37 mmol) was added dropwise at –60 ºC with exclusion of light. The resulting solution was stirred at –45 ºC for 1 h and 30 min, at 0 ºC for 40 minutes, and at room temperature for 20 minutes. Then, the solvent was evaporated under reduced pressure. The resulting yellow solid was precipitated from chloroform (6 mL) and ether (40 mL). The solvent was decanted and the yellow solid was washed with ether (5 mL) one more time. To evaporate the residue of ether the yellow solid was redissolved in CH_2Cl_2 and the mixture of solvents was evaporated under reduced pressure to result the yellow 1,2,3-triazolinium ion **98** as a chloride salt (319 mg, 0.830 mmol, 73%). Crystals of **98** were grown by diffusion method from CH_2Cl_2/ petroleum ether for X-ray crystallographic analysis. m.p.: 141.9–143.5 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13–7.93 (m, 4H), 7.62–7.51 (m, 4H), 6.44–6.39 (m, 2H), 2.23–1.94 (m, 4H), 1.05 (t, J = 7.1 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.7, 133.3,

130.9, 121.8, 71.0, 25.5, 8.2; IR (ATR) 3032, 2958, 2911 cm^{-1}; HRMS (ESI) Calcd. For $C_{18}H_{20}Cl_2N_3$ $[M]^+$: 348.1029; Found: 348.0996.

N^3,N^4-bis(4-chlorophenyl)hexane-3,4-diamine

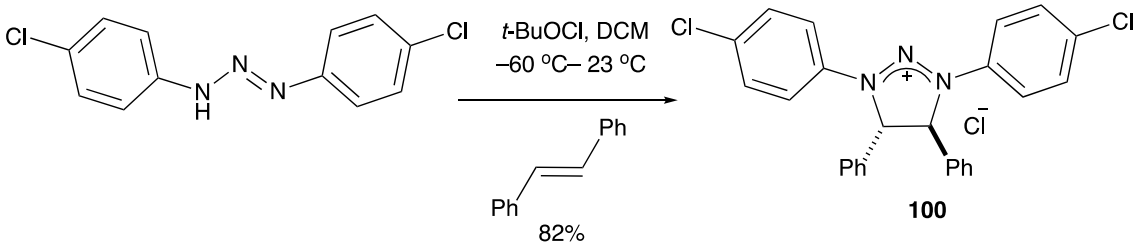


98 **99**

One small spatula of Raney Ni 2400 slurry in water (1.2 g) was added to the solution of 1,2,3-triazolinium ion **98** (406 mg, 1.05 mmol) in isopropanol (5 mL), under N_2 atmosphere. Then a balloon of H_2 was placed on top of the flask while removing N_2. The reaction mixture was stirred at room temperature for 8 h. (Reaction completion was accompanied by the reaction mixture color change from yellow to colorless and monitored by running TLC in 5% MeOH in CH_2Cl_2.) After reaction completion, the mixture was filtered through a short pad of Celite, washed with isopropanol and concentrated under vacuum. The crude mixture was redissolved in CH_2Cl_2 and subjected to basic extraction using NaOH solution (pH = 10). The combined organic layer was dried over Na_2SO_4, filtered and concentrated under vacuum. Flash chromatography of the residue (5% EtOAc in Petroleum ether) afforded the 1,2-diamine **99** as a yellow viscous liquid (229 mg, 0.680 mmol, 65%). Crystals of HCl salt of **99** were grown from hot ethanol for X-ray crystallographic analysis. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21–7.02 (m, 4H), 6.69–6.31 (m, 4H), 3.49 (broad s, 2NH), 3.35 (m, 4H), 1.68 (ddq, J_d = 14.7, J_d = 4.2 Hz, J_q = 7.4 Hz, 2H), 1.47 (m, 2H), 0.95 (t, J = 7.4 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.3, 129.3, 121.8, 114.3, 58.4, 26.0, 11.2; IR (ATR) 3409, 3028, 2963, 2931, 2874 cm^{-1}; GC-MS (EI) 336

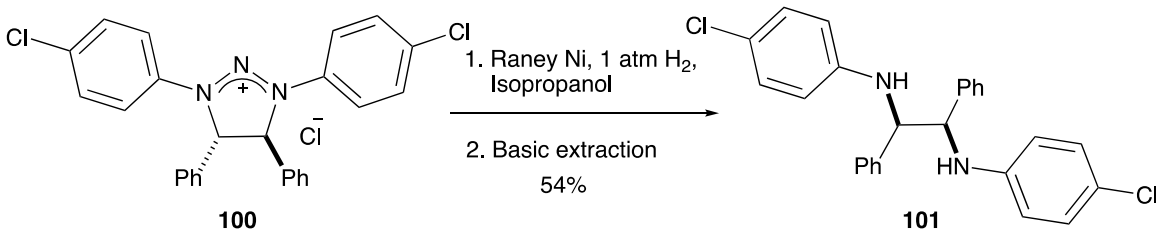
(0.6 %), 170 (35%), 168 (100%), 152 (4%), 138 (11%), 111 (10%) 91 (3%); HRMS (ESI) Calcd. For $C_{18}H_{23}Cl_2N_2$ $[M+H]^+$: 337.1233; Found: 349.1237.

1,3-bis(4-chlorophenyl)-4,5-diphenyl-4,5-dihydro-3H-1,2,3-triazol-1-ylium chloride



To the suspension of 1,3-bis(4-chlorophenyl)triazene (340 mg, 1.28 mmol) and *trans*-Stilbene (276 mg, 1.53 mmol) in dry CH_2Cl_2 (8 mL), *t*-BuOCl (166 mg, 1.53 mmol) was added dropwise at –60 °C with exclusion of light. The resulting solution was stirred at –45 °C for 1 h and 30 min, at 0 °C for 40 minutes, and at room temperature for 20 minutes. Then, the solvent was evaporated under reduced pressure. The resulting yellow solid was precipitated from chloroform (6 mL) and ether (30 mL). The solvent was decanted and the yellow solid was washed with ether (5 mL) one more time. The yellow solid was redissolved in CH_2Cl_2 and the mixture of solvents was evaporated under reduced pressure to result the orange-yellow 1,2,3-triazolinium ion **100** as a chloride salt (506 mg, 1.05 mmol, 82%). Crystals of **100** were grown by diffusion method from CH_2Cl_2/ THF for X-ray crystallographic analysis. m.p.: 137.0–138.2 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81–7.71 (m, 4H), 7.71–7.61 (m, 4H), 7.37–7.29 (m, 6H), 7.29–7.23 (m, 4H), 7.20 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.4, 133.8, 131.9, 130.8, 130.1, 130.1, 128.8, 123.1, 78.3; IR (ATR) 3027, 2933, 2881 cm^{-1}.

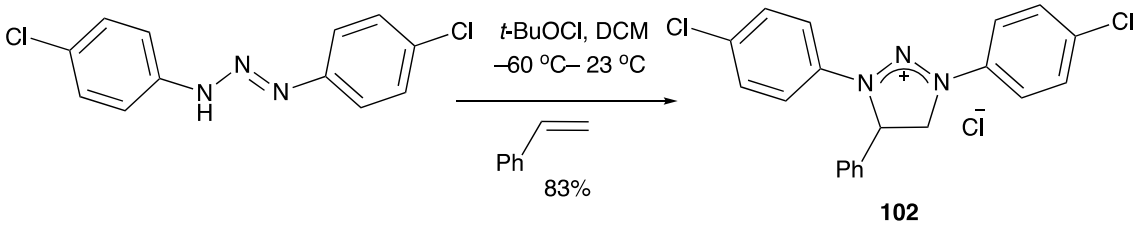
N^1,N^2-bis(4-chlorophenyl)-1,2-diphenylethane-1,2-diamine



100 **101**

One small spatula of Raney Ni 2400 slurry in water (1.6 g) was added to the solution of 1,2,3-triazolinium ion **100** (766 mg, 1.59 mmol) in isopropanol (20 mL), under N_2 atmosphere. Then a balloon of H_2 was placed on top of the flask while removing N_2. The reaction mixture was stirred at room temperature for 3h. (Reaction completion was accompanied by the reaction mixture color change from yellow to colorless and monitored by running TLC in 5% MeOH in CH_2Cl_2.) After reaction completion, the mixture was filtered through a short pad of Celite, washed with isopropanol and concentrated under vacuum. The crude mixture was redissolved in CH_2Cl_2 and subjected to basic extraction using NaOH solution (pH = 10). The combined organic layer was dried over Na_2SO_4, filtered and concentrated under vacuum. Flash chromatography of the residue (5% EtOAc in PE) and trituration in hexanes afforded the 1,2-diamine **101** as a white solid (371 mg, 0.856 mmol, 54%). m.p.: 110.8–111.8 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30–7.20 (m, 6H), 7.16–7.09 (m, 4H), 7.06–6.99 (m, 4H), 6.48–6.40 (m, 4H), 4.55 (broad s, 2NH), 4.53 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.6, 139.3, 129.1, 128.7, 128.0, 127.4, 123.1, 115.4, 64.1; IR (ATR) 3382, 3026, 2925, 2856 cm^{-1}; GC-MS (EI) 305 (2%), 216 (100%), 180 (7%), 138 (12%), 111 (19%), 75 (11%). HRMS (ESI) Calcd. For $C_{26}H_{23}Cl_2N_2$ $[M+H]^+$: 433.1233; Found: 433.1233.

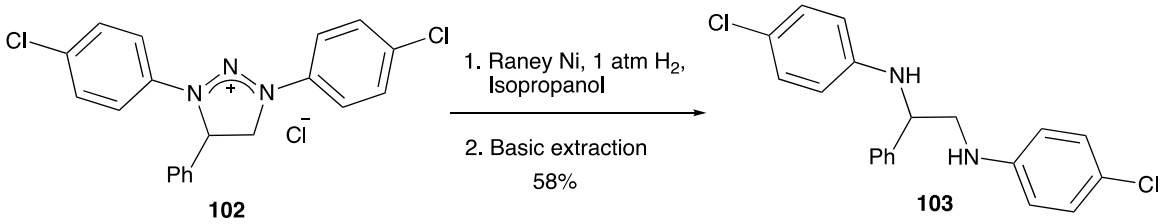
1,3-bis(4-chlorophenyl)-4-phenyl-4,5-dihydro-3H-1,2,3-triazol-1-ylium chloride



102

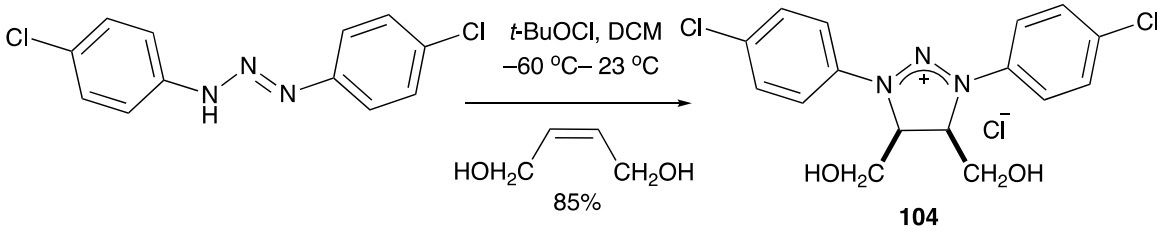
To the suspension of 1,3-bis(4-chlorophenyl)triazene (186 mg, 0.699 mmol) and styrene (87.4 mg, 0.839 mmol) in dry CH_2Cl_2 (8 mL), *t*-BuOCl (91.1 mg, 0.839 mmol) was added dropwise at –60 °C with exclusion of light. The resulting solution was stirred at –45 °C for 1 h and 30 min, at 0 °C for 40 minutes, and at room temperature for 20 minutes. Then, the solvent was evaporated under reduced pressure. The resulting yellow solid was precipitated from chloroform (4 mL) and ether (20 mL). The solvent was decanted and the yellow solid was washed with ether (5 mL) one more time. The yellow solid was redissolved in CH_2Cl_2 and the mixture of solvents was evaporated under reduced pressure to result the orange-yellow 1,2,3-triazolinium **102** as a chloride salt (235 mg, 0.580 mmol, 83%). m.p.: 147.2–148.3 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (dd, J = 14.6, 8.4 Hz, 1H), 7.80 (d, J = 8.6 Hz, 2H), 7.67 (d, J = 8.6 Hz, 2H), 7.50–7.39 (m, 4H), 7.31 (m, 5H), 6.33 (t, J = 14.0 Hz, 1H), 4.83 (dd, J = 13.5, 8.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.5, 136.3, 134.5, 134.4, 133.6, 130.6, 130.5, 130.3, 130.1, 127.4, 122.1, 120.5, 69.9, 61.9; IR (ATR) 3094, 2986, 2907 cm^{-1}; HRMS (ESI) Calcd. For $C_{20}H_{16}Cl_2N_3$ $[M]^+$: 368.0716; Found: 368.0666.

N^1,N^2-bis(4-chlorophenyl)-1-phenylethane-1,2-diamine



One small spatula of Raney Ni 2400 slurry in water (0.6 g) was added to the solution of 1,2,3-triazolinium ion **102** (257 mg, 0.635 mmol) in isopropanol (8 mL), under N_2 atmosphere. Then a balloon of H_2 was placed on top of the flask while removing N_2. The reaction mixture was stirred at room temperature for 2 h. (Reaction completion was accompanied by the reaction mixture color change from yellow to colorless and monitored by running TLC in 5% MeOH in CH_2Cl_2.) After reaction completion, the mixture was filtered through a short pad of Celite, washed with isopropanol and concentrated under vacuum. The crude mixture was redissolved in CH_2Cl_2 and subjected to basic extraction using NaOH solution (pH = 10). The combined organic layer was dried over Na_2SO_4, filtered and concentrated under vacuum. Flash chromatography of the residue (5% EtOAc in PE) and trituration in hexanes afforded the 1,2-diamine **103** as a white solid (131 mg, 0.367 mmol, 58%). m.p.: 122.3–123.4 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41–7.34 (m, 4H), 7.28–7.34 (m, 1H), 7.14 (d, J = 8.6, 2H), 7.04 (d, J = 8.6 Hz, 2H), 6.57 (d, J = 8.6 Hz, 2H), 6.47 (d, J = 8.6 Hz, 2H), 4.59 (dd, J = 7.8, 4.8 Hz, 1H), 4.15 (broad s, 2NH), 3.49 (dd, J = 12.6, 4.7 Hz, 1H), 3.37 (dd, J = 12.5, 7.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.4, 145.6, 140.7, 129.4, 129.2, 128.0, 126.5, 123.0, 122.7, 115.0, 114.5, 57.5, 51.0; IR (ATR) 3380, 3035, 2917, 2847 cm^{-1}; GC-MS (EI) 356 (0.03%), 216(100%), 180 (5%), 138 (22%), 111 (31%), 75(30%); HRMS (ESI) Calcd. For $C_{20}H_{19}Cl_2N_2$ $[M+H]^+$: 357.0920; Found: 357.0910.

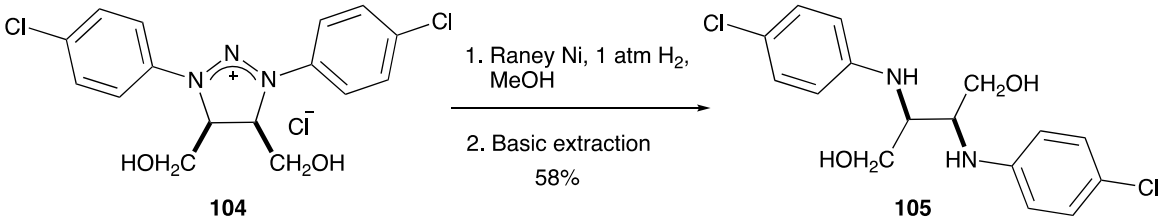
1,3-bis(4-chlorophenyl)-4,5-bis(hydroxymethyl)-4,5-dihydro-3H-1,2,3-triazol-1-ylium chloride



104

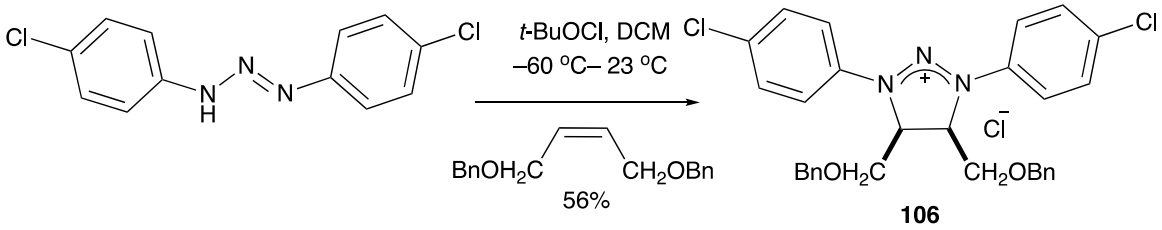
To the suspension of 1,3-bis(4-chlorophenyl)triazene (610 mg, 2.29 mmol) and *cis*-2-Butene-1,4-diol (242 mg, 2.75 mmol) in dry CH_2Cl_2 (15 mL), *t*-BuOCl (299 mg, 2.75 mmol) was added dropwise at –60 ºC with exclusion of light. The resulting solution was stirred at –45 ºC for 1 h, then at 0 ºC for 30 minutes, and at room temperature for 20 minutes. After the reaction completion the product was precipitated in CH_2Cl_2. Then 10 mL ether was added to the mixture and the solvents were decanted. The yellow precipitate was washed with ether two more times and it was kept under vacuum to evaporate the residue of solvent and yield a yellow 1,2,3-triazolinium ion **104** as a chloride salt (756 mg, 1.95 mmol, 85%). Crystals of **104** were grown by diffusion method from CH_2Cl_2 + 1 drop of MeOH/ THF for X-ray crystallographic analysis. m.p.: 186.0–187.5 °C; ^{1}H NMR (400 MHz, CD_3OD) δ 7.97–7.78 (m, 4H), 7.77–7.51 (m, 4H), 5.87 (dd, J = 3.0, 1.5 Hz, 2H), 4.17 (t, J = 1.5 Hz, 4H); ^{13}C NMR (100 MHz, CD_3OD) δ 137.6, 135.3, 131.4, 124.2, 70.9, 57.3; IR (ATR) 3716, 3061, 2961, 2889 cm^{-1}; HRMS (ESI) Calcd. For $C_{16}H_{16}Cl_2N_3O_2$ $[M]^+$: 352.0614.2122; Found: 352.0552.

2,3-bis[(4-chlorophenyl)amino]butane-1,4-diol



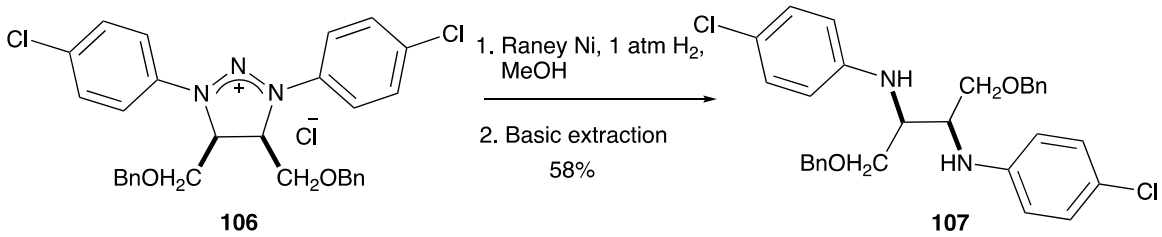
One small spatula of Raney Ni 2400 slurry in water (0.23 g) was added to the solution of 1,2,3-triazolinium ion **104** (91.5 g, 0.235 mmol) in methanol (3 mL), under N_2 atmosphere. Then a balloon of H_2 was placed on top of the flask while removing N_2. The reaction mixture was stirred at room temperature for 1 h. (Reaction completion was accompanied by the reaction mixture color change from yellow to colorless and monitored by running TLC in 5% MeOH in CH_2Cl_2.) After reaction completion, the mixture was filtered through a short pad of Celite, washed with methanol and concentrated under vacuum. The crude mixture was redissolved in CH_2Cl_2 and subjected to basic extraction using NaOH solution (pH = 10). The combined organic layer was dried over Na_2SO_4, filtered and concentrated under vacuum. Flash chromatography of the residue (60% EtOAc in PE) and trituration in hexanes afforded the 1,2-diamine **105** as a white solid (46.8 mg, 0.137 mmol, 58%). Crystals of triflouroacetate salt of **105** were grown from hot EtOAc for X-ray crystallographic analysis. m.p.: 132.7–134.8 °C; ^{1}H NMR (400 MHz, CD_3OD) δ 7.09–7.01 (m, 4H), 6.73–6.66 (m, 4H), 3.85–3.78 (broad s, 2H), 3.66–3.54 (m, 4H); ^{13}C NMR (100 MHz, CD_3OD) δ 148.8, 129.8, 122.1, 115.3, 62.3, 56.1; IR (ATR) 3407,3387, 3319, 3024, 2927, 2875 cm^{-1}; GC-MS (EI) after treatment with BSTFA: 251 (5%), 220 (27%), 205 (100%), 175(11%), 161 (31%), 105 (8%), 91 (10%); HRMS (ESI) Calcd. For $C_{16}H_{19}Cl_2N_2O_2$ $[M+H]^+$: 341.0818; Found: 341.0811.

4,5-bis[(benzyloxy)methyl]-1,3-bis(4-chlorophenyl)-4,5-dihydro-3H-1,2,3-triazol-1-ylium chloride



To the suspension of 1,3-bis(4-chlorophenyl)triazene (407 mg, 1.53 mmol) and *cis*-1,4-Bis(benzyloxy)but-2-ene[55] (494 mg, 1.84 mmol) in dry CH_2Cl_2 (10 mL), *t*-BuOCl (199 mg, 1.84 mmol) was added dropwise at –60 ºC with exclusion of light. The resulting solution was stirred at –45 ºC for 1 h and 30 min, at 0 ºC for 40 minutes, and at room temperature for 20 minutes. Then, the solvent was evaporated under reduced pressure. The resulting yellow solid was precipitated from CH_2Cl_2 (6 mL) and ether (40 mL). The solvent was decanted and the yellow solid was washed with ether (10 mL) one more time. The yellow solid was re-dissolved in CH_2Cl_2 and the mixture of solvents was evaporated under reduced pressure to result the light yellow 1,2,3-triazolinium ion **106** as a chloride salt (484 mg, 0.850 mmol, 56%). Crystals of **106** were grown by diffusion method from CH_2Cl_2 / Petroleum ether for X-ray crystallographic analysis. m.p.: 121.9–123.5 °C; ^{1}H NMR (400 MHz, CD_3OD) δ 7.75–7.69 (m, 4H), 7.64–7.54 (m, 4H), 7.33–7.22 (m, 6H), 7.12–7.05 (m, 4H), 6.01 (m, 2H), 4.37 (d, J = 11.7 Hz, 2H), 4.32 (d, J = 11.7 Hz, 2H), 3.98–3.92 (m, 4H); ^{13}C NMR (100 MHz, CD_3OD) δ 137.9, 137.7, 135.0, 131.3, 129.6, 129.4, 129.3, 124.6, 74.3, 69.4, 65.1; IR (ATR) 3087, 2948, 2895 cm^{-1}; HRMS (ESI) Calcd. For $C_{30}H_{28}Cl_2N_3O_2$ $[M]^+$: 532.1553; Found: 532.1475.

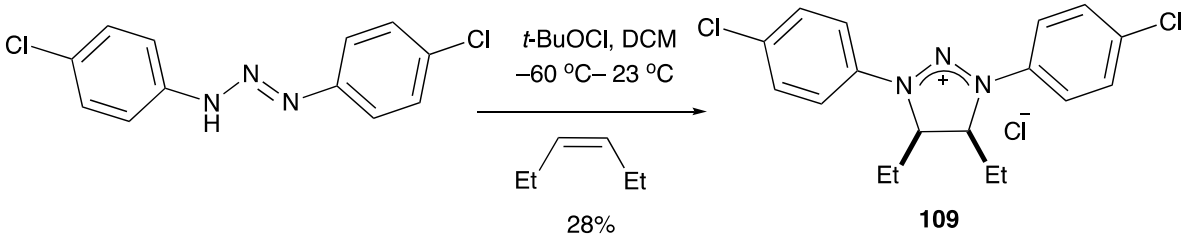
1,4-bis(benzyloxy)-*N*^{2},*N*^{3}-bis(4-chlorophenyl)butane-2,3-diamine



106 **107**

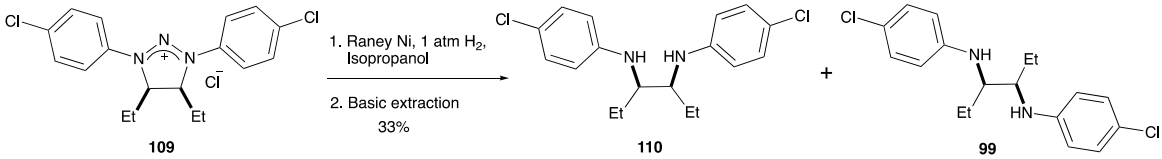
One small spatula of Raney Ni 2400 slurry in water (0.23 g) was added to the solution of 1,2,3-triazolinium ion **106** (136 mg, 0.239 mmol) in methanol (3 mL) it was added under N_2 atmosphere. Then a balloon of H_2 was placed on top of the flask while removing N_2. The reaction mixture was stirred at room temperature for 1 h. The product was precipitated as a white solid as it is not soluble in MeOH. (Reaction completion was accompanied by the reaction mixture color change from yellow to colorless and monitored by running TLC in 5% MeOH in CH_2Cl_2.) After reaction completion, CH_2Cl_2 (15 mL) was added to the mixture to dissolve the product. The mixture was filtered through a short pad of Celite, washed with CH_2Cl_2 and concentrated under vacuum. The crude mixture was subjected to basic extraction using NaOH solution (pH = 10). The combined organic layer was dried over Na_2SO_4, filtered and concentrated under vacuum. Flash chromatography of the residue (6% EtOAc in PE) and trituration in hexanes afforded the 1,2-diamine **107** as a white solid (72.3 mg, 0.139 mmol, 58%). Crystals of **107** were grown by diffusion method from CH_2Cl_2/ petroleum ether for X-ray crystallographic analysis. m.p.: 149.3–151.2 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41–7.24 (m, 10H), 7.12–7.05 (m, 4H), 6.59–6.49 (m, 4H), 4.47 (s, 4H), 4.05 (broad s, 2NH), 3.91 (m, 2H), 3.58 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.3, 137.8, 129.3, 128.6, 128.1, 128.0, 122.5, 114.7, 73.6, 69.8, 54.1; IR (ATR) 3318, 3018, 2915, 2952, 2891 cm^{-1}; HRMS (ESI) Calcd. For $C_{30}H_{31}Cl_2N_2O_2$ $[M+H]^+$: 521.1757; Found: 521.1746.

1,3-bis(4-chlorophenyl)-4,5-diethyl-4,5-dihydro-3H-1,2,3-triazol-1-ylium



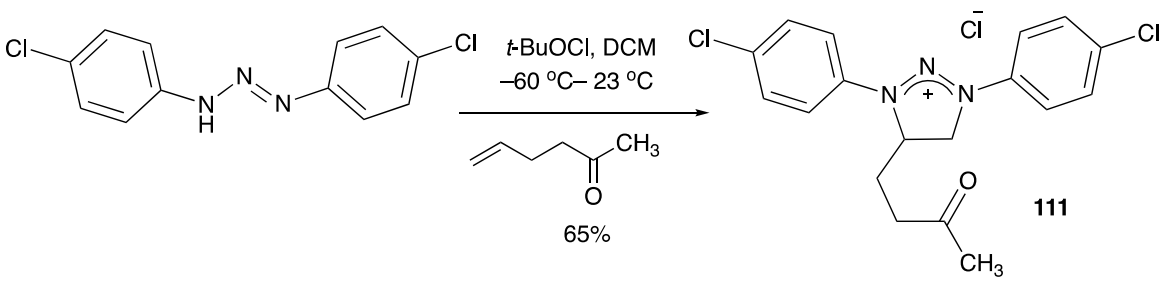
To the suspension of 1,3-bis(4-chlorophenyl)triazene (275 mg, 1.03 mmol) and *cis*-3-hexene (104 mg, 1.24 mmol) in dry CH_2Cl_2 (7 mL), *t*-BuOCl (135 mg, 1.24 mmol) was added dropwise at –60 ºC with exclusion of light. –45 ºC for 1 h and 15 min, at 0 ºC for 30 minutes, and at room temperature for 20 minutes. Then, the solvent was evaporated under reduced pressure. The resulting yellow solid was precipitated from CH_2Cl_2 (1 mL) and ether (35 mL). The solvent was decanted and the yellow solid was washed with ether (5 mL) one more time. The yellow solid was redissolved in CH_2Cl_2 and the mixture of solvents was evaporated under reduced pressure to result the orange-yellow 1,2,3-triazolinium ion **109** as a chloride salt (112 mg, 0.291 mmol, 28%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, J = 8.6 Hz, 4H), 7.53 (d, J = 8.7 Hz, 4H), 6.69 (m, 2H), 1.99 (m, 4H), 1.04 (t, J = 7.4 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.3, 133.7, 130.8, 123.7, 70.7, 19.7, 10.5; IR (ATR) 3093, 2972, 2878 cm^{-1}; HRMS (ESI) Calcd. For $C_{18}H_{20}Cl_2N_3$ $[M]^+$: 348.1029; Found: 348.1037.

N^3,N^4-bis(4-chlorophenyl)hexane-3,4-diamine (Mix of erythro and threo isomers)



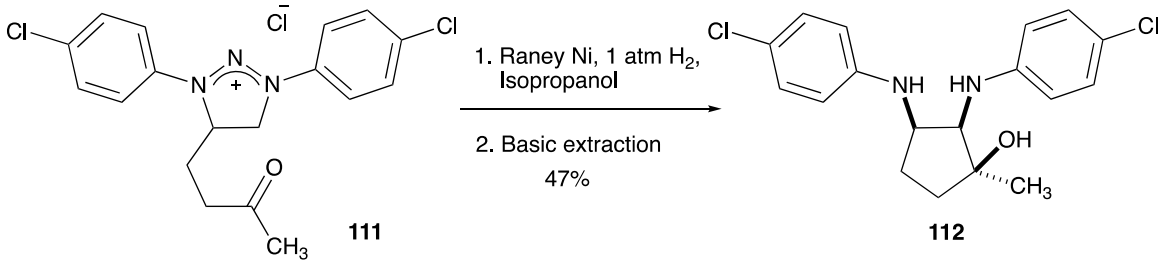
One small spatula of Raney Ni 2400 slurry in water (0.3 g) was added to the solution of 1,2,3-triazolinium ion **109** (114 mg, 0.297 mmol) in isopropanol (3 mL), under N_2 atmosphere. Then a balloon of H_2 was placed on top of the flask while removing N_2. The reaction mixture was stirred at room temperature for 4 h. (Reaction completion was accompanied by the reaction mixture color change from yellow to colorless and monitored by running TLC in 5% MeOH in CH_2Cl_2.) After reaction completion, the mixture was filtered through a short pad of Celite, washed with methanol and concentrated under vacuum. The crude mixture was redissolved in CH_2Cl_2 and subjected to basic extraction using NaOH solution (pH = 10). The combined organic layer was dried over Na_2SO_4, filtered and concentrated under vacuum. Flash chromatography of the residue (5% EtOAc in PE) afforded the mixture of 1,2-diamines **110** and **99** as a yellow viscous liquid (33.0 mg, 0.097 mmol, 33% for the mixture of isomers (**110** to **99**: 86% to 14% by GC-MS)).^{1}H NMR of mixture of isomers (400 MHz, $CDCl_3$) δ 7.13–7.09 (m, 4H minor), 7.09–7.04 (m, 4H major), 6.56–6.51 (m, 4H minor), 6.47–6.40 (m, 4H major), 3.48 (s, 2NH), 3.43–3.30 (m, 2H major and minor), 1.77–1.56 (m, 2H major and minor), 1.52–1.34 (m, 2H major and minor), 1.06–0.86 (m, 2H major and minor); ^{13}C NMR (100 MHz, $CDCl_3$) δ major: 147.2, 129.3, 121.8, 114.4, 58.3, 24.7, 11.5; minor: 147.3, 129.3, 121.8, 114.3, 58.4, 26.0, 11.2; GC-MS (EI) major: 336 (0.7%), 170 (35%), 168(100%), 138 (15%), 111 (13%) 91 (4%); minor: 336 (0.9%), 170 (36%), 168(100%), 138 (17%), 111 (14%) 91 (4%).

1,3-bis(4-chlorophenyl)-5-(3-oxobutyl)-4,5-dihydro-3H-1,2,3-triazol-1-ylium chloride



To the suspension of 1,3-bis(4-chlorophenyl)triazene (417 mg, 1.57 mmol) and 5-hexen-2-one (185 mg, 1.88 mmol) in dry CH_2Cl_2 (8 mL), *t*-BuOCl (204 mg, 1.88 mmol) was added dropwise at –60 ºC with exclusion of light. The resulting solution was stirred at –45 ºC for 1 h and 15 min, at 0 ºC for 30 minutes, and at room temperature for 20 minutes. After the reaction completion the product was precipitated in CH_2Cl_2. Then 30 mL ether was added to the mixture and the solvents were decanted. The yellow precipitate was washed with ether one more times (5 mL) and it was kept under vacuum to evaporate the residue of solvent and yield a yellow 1,2,3-triazolinium ion **111** as a chloride salt (404 mg, 1.01 mmol, 65%). Crystals of **111** were grown by diffusion method from CH_2Cl_2 / hexanes for X-ray crystallographic analysis. m.p.: 171.6–173.8 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (dd, J = 21.5, 8.6 Hz, 4H), 7.49 (dd, J = 19.5, 8.6 Hz, 4H), 6.45–6.30 (m, 1H), 5.60 (d, J = 9.7 Hz, 2H), 3.13 (ddd, J = 19.0, 8.3, 6.0 Hz, 1H), 2.83 (dt, J_d = 19.0, J_t = 6.1 Hz, 2H), 2.35–2.25 (m, 1H), 2.16 (s, 3H), 2.09–1.98 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 208.0, 136.6, 136.5, 134.6, 133.2, 130.8, 130.6, 121.7, 120.6, 65.9, 58.8, 38.1, 30.2, 26.0; IR (ATR) 3004, 2927, 2846, 1713 cm^{-1}; HRMS (ESI) Calcd. For $C_{18}H_{18}Cl_2N_3O$ $[M]^+$: 362.0821; Found: 362.0754.

2,3-bis[(4-chlorophenyl)amino]-1-methylcyclopentan-1-ol



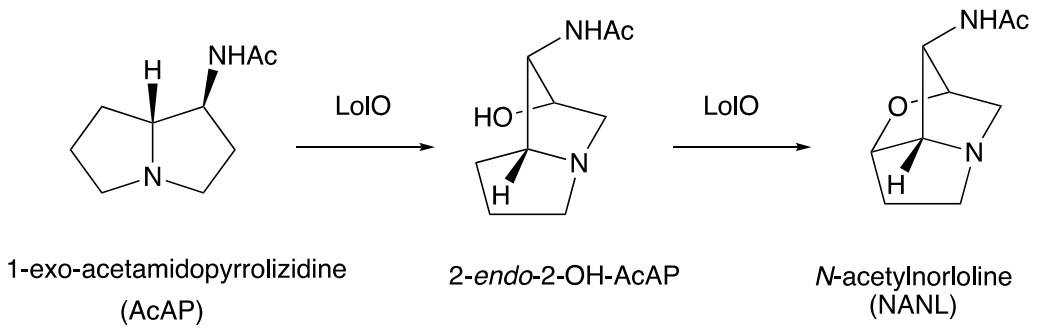
111 **112**

One small spatula of Raney Ni 2400 slurry in water (0.28 g) was added to the solution of 1,2,3-triazolinium ion **111** (113 mg, 0.284 mmol) in isopropanol (3 mL), under N_2 atmosphere. Then a balloon of H_2 was placed on top of the flask while removing N_2. The reaction mixture was stirred at room temperature for 4 h and 30 minutes. (Reaction completion was accompanied by the reaction mixture color change from yellow to colorless and monitored by running TLC in 5% MeOH in CH_2Cl_2.) After reaction completion, the mixture was filtered through a short pad of Celite, washed with isopropanol and concentrated under vacuum. The crude mixture was redissolved in CH_2Cl_2 and subjected to basic extraction using NaOH solution (pH = 10). The combined organic layer was dried over Na_2SO_4, filtered and concentrated under vacuum. Flash chromatography of the residue (10% EtOAc in PE) afforded the 1,2-diamine **112** as a yellow viscous liquid (47.3 mg, 0.135 mmol, 47%).^{1}H NMR (400 MHz, $CDCl_3$) δ 7.10 (m, 4H), 6.54 (m, 4H), 3.92 (dt, J_t = 6.8, J_d = 3.0 Hz, 1H), 3.43 (d, J = 6.7 Hz, 1H), 2.27–2.08 (m, 1H), 2.07–1.94 (m, 1H), 1.91–1.73 (m, 2H), 1.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.7, 146.1, 129.3, 129.2, 123.4, 122.9, 115.8, 115.0, 79.5, 64.7, 55.3, 36.6, 29.5, 26.2; IR (ATR) 3523, 3343, 2958, 2926 cm^{-1}; GC-MS (EI) 350 (16%), 224 (100%), 206 (95%), 166 (25%), 153 (16%), 130 (27%), 111 (17%), 91 (6%), 75 (10%); HRMS (ESI) Calcd. For $C_{18}H_{21}Cl_2N_2O$ $[M+H]^+$: 351.1031; Found: 351.1033.

Chapter 4 Attempt towards total synthesis of loline alkaloids

4.1 Introduction

Loline alkaloids are a group of nitrogen-containing natural products with distinct chemical and biological features. They are produced by *Epichloë* species–groups of grass fungal endophytes– in cool-season grasses. These endophytic fungi grow in the intercellular spaces of their host while providing many survival benefits to the host plant. The relationship between these groups of fungi and their host grass is mutualistic.[56] In this symbiotic relationship, the plant provides food and shelter to the fungus. These grass-associated endophytes can also provide chemoprotection to their host against certain insects and aphids such as the bird cherry-oat aphid, large milkweed bug, and American cockroach. Although most loline alkaloids are toxic to these animals, it has been reported that they are nontoxic to mammalian herbivores. Besides insecticidal properties, lolines enhance host plant resistance against numerous stress conditions such as drought, poor soil conditions and spatial competition. They can also improve the root growth, seed production and fitness of endophyte-infected plants.[57] Due to loline alkaloids' remarkable biological roles, their biosynthesis has been investigated over the past decades. In collaboration with other groups, our group has been involved in some of the discoveries in this area. For instance, in collaboration with Prof. Bollinger's lab at the Pennsylvania State University, our group has shown that the mononuclear non-heme iron oxygenase enzyme encoded by *lolO* gene catalyzes the conversion of AcAP to NANL (Scheme 4.1).[58] LolO abstracts the "endo H" atom from C(2) of AcAP to give a radical intermediate. Hydroxylation at this position produced 2-*endo*-OH-AcAP. LolO can also catalyze the next step to form an ether bridge of NANL (*N*-acetylnorloline) as a first loline alkaloid in the biosynthetic pathway.[58]



1-exo-acetamidopyrrolizidine (AcAP) | 2-*endo*-2-OH-AcAP | *N*-acetylnorloline (NANL)

Scheme 4.1 Conversion of AcAP to NANL catalyzed by LolO

Loline alkaloids consist of a saturated pyrrolizidine ring which contains a 1-exo amino group and an ether bridge between C(2) and C(7). Various substituents on the 1-amino group define different lolines, and the oxygen bridge causes the tricyclic ring to be strained. The various naturally occurring lolines are shown in Figure 4.1.

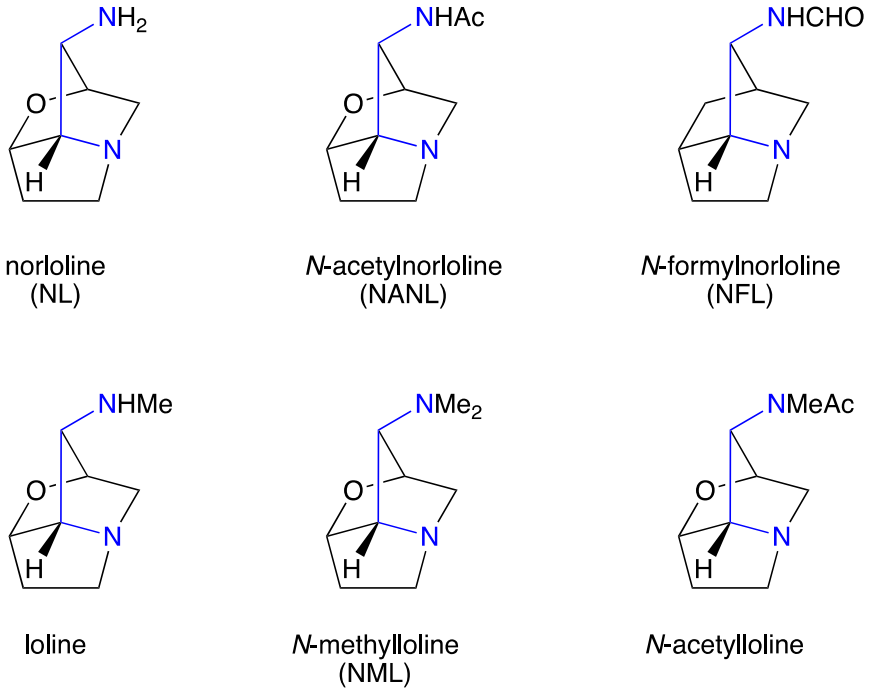


Figure 4.1 Various naturally occurring loline alkaloids

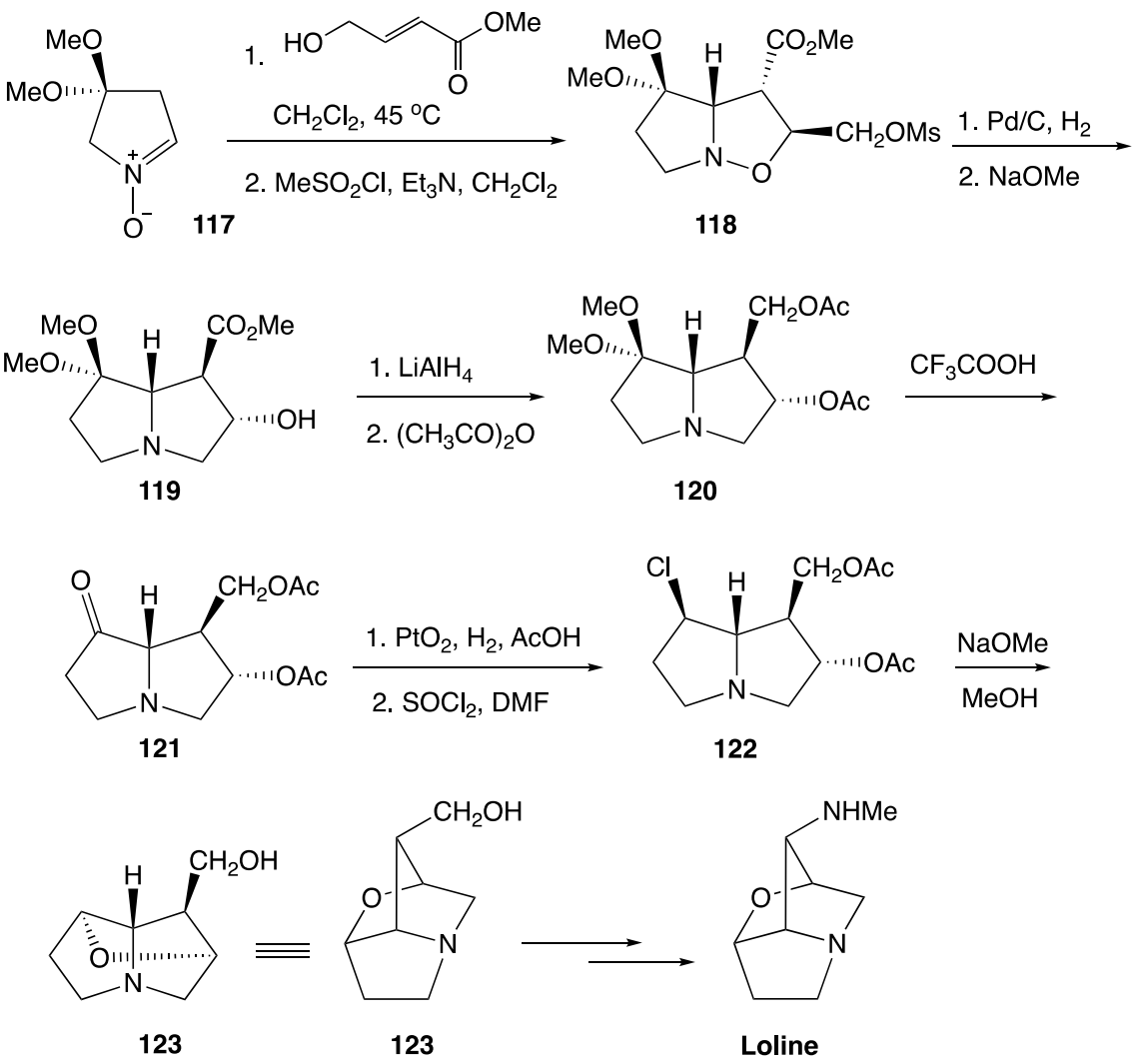
Despite their small structures, the total synthesis of lolines can be challenging due to their strained structure and the presence of four contiguous stereogenic centers in their heterotricyclic skeleton. Different groups have reported racemic and asymmetric total

synthesis of loline alkaloids through various approaches. We have also been interested to pursue a total synthesis of loline as a potential application for our developed 1,2-diamination methodology. In this chapter, I will describe some of the reported total synthesis of lolines and explain our retrosynthetic plan toward loline alkaloid.

4.2 Previously reported total synthesis of lolines

4.2.1 Tufariello et al. approach

In 1986, Tufariello et al. reported the racemic synthesis of loline alkaloids using nitrone cycloaddition (Scheme 4.2). In their total synthesis, 1,3-dipolar cycloaddition of nitrone **117** and methyl 4-hydroxybut-2-enoate was followed by mesylation of the hydroxyl group to form pyrrolizidine **118**. After hydrogenolysis of N–O bond, the C(1) epimerization was obtained using the NaOMe to achieve the desired stereochemistry required in lolines. Reduction of the C(1) ester group in pyrrolizidine **119** and acetylation of hydroxyl groups formed the acetal **120**. Hydrolysis of the C(7) acetal group with TFA afforded ketone **121**. Treatment of the carbonyl group with Adam's catalyst followed by Vilsmeier reagent, installed the chloride leaving group at C(7) with inverted stereochemistry in pyrrolizidine **122**. The next task was to construct the ether bridge, and therefore, deprotection of the hydroxyl group at C(2) position formed an intermediate that can undergo intramolecular ring closure to form the tricyclic **123**. Further manipulation of C(1) hydroxymethyl functional group led to racemic loline in 83% yield.[59]

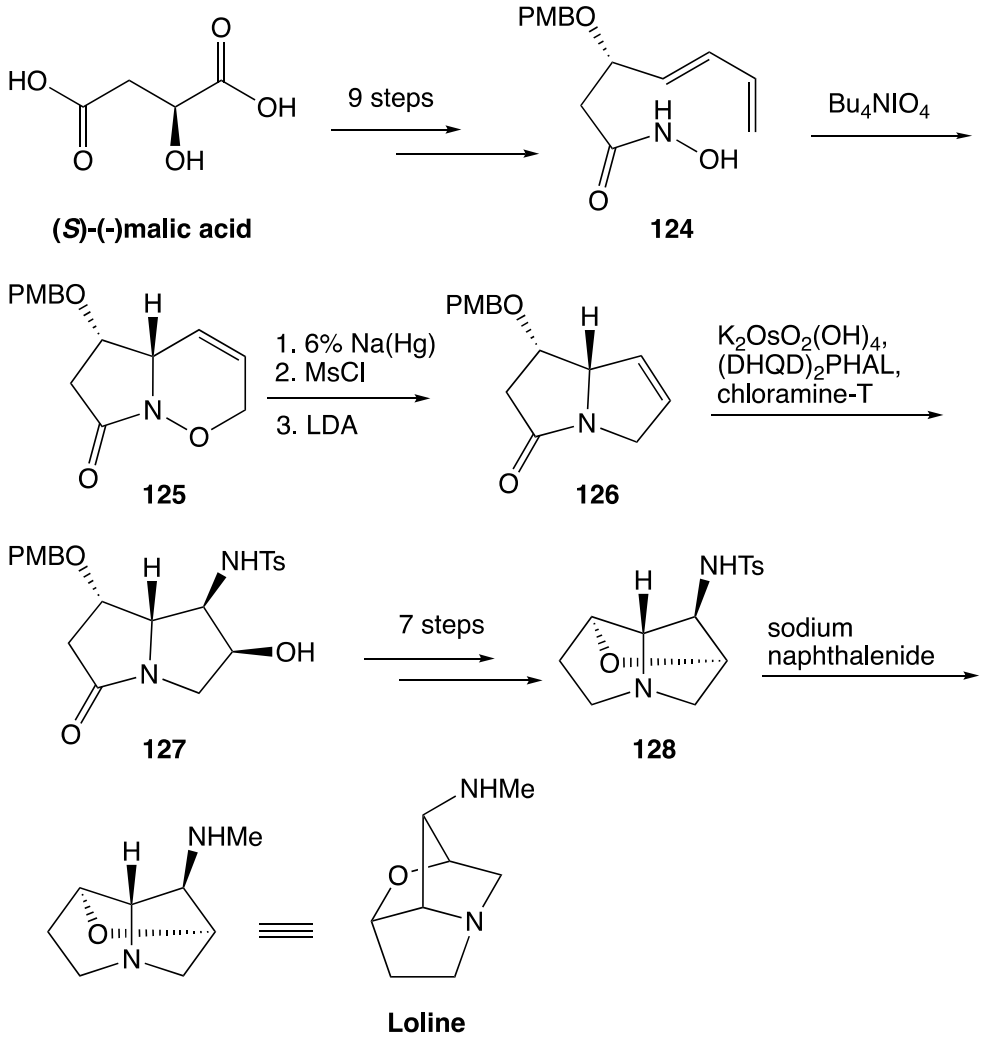


Scheme 4.2 Tufariello et al. total synthesis of loline

4.2.2 White et al. approach

In 2000, White et al. described the asymmetric synthesis of (+)-loline isolated as dihydrochloride salt (Scheme 4.3).[60] Their synthesis started with the conversion of (*S*)-(2) malic acid to the hydroxamic acid **124** in nine steps. Oxidation of **124** with periodate salt produces an acylnitroso intermediate that can afford **125** as a mixture of cis and trans isomers via intramolecular cycloaddition. The core pyrrolizidine structure **126** constructed via reductive scission of N-O bond in **125**, mesylation of the resulting alcohol and further

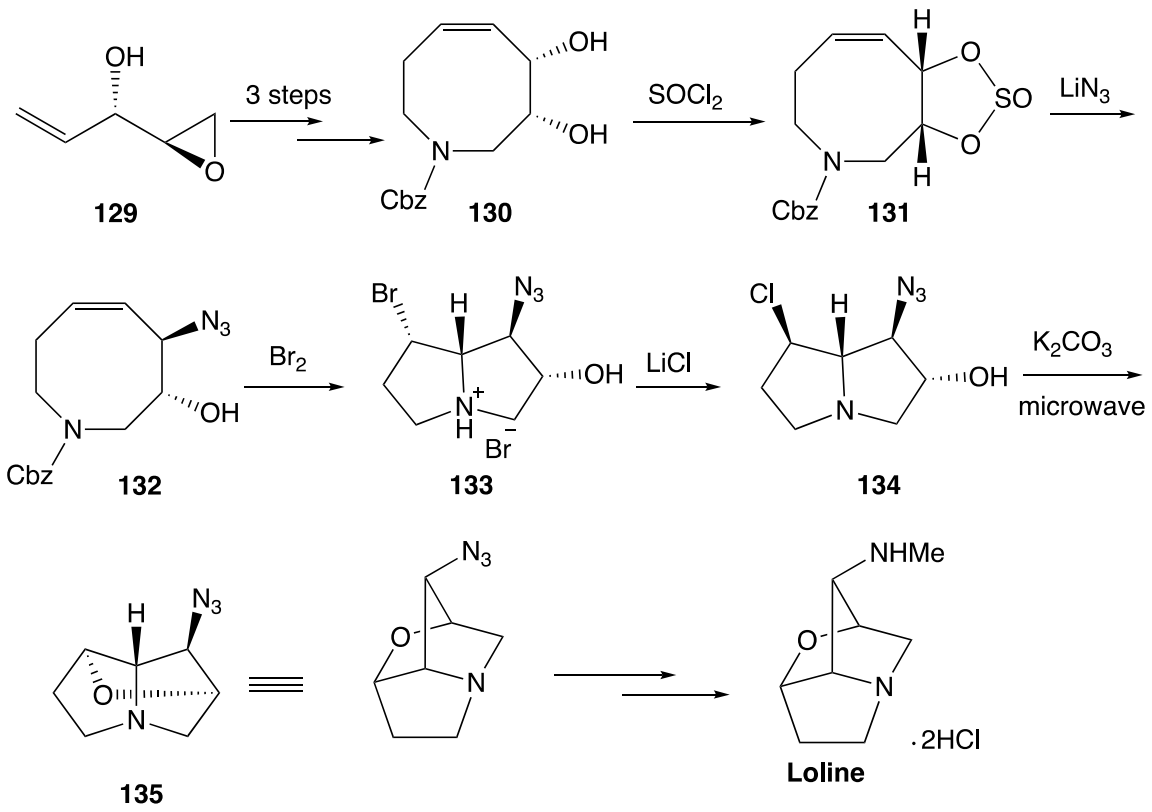
nucleophilic attack of lactam nitrogen. Then asymmetric aminohydroxylation of **126** installed the desired OH group at C(2) position to form pyrrolizidine **127**. This approach required seven more steps to install the ether bridge between the C(2) and C(7) position and form the tricyclic *N*-tosylloline **128**. Further removal of tosyl group afforded (+)-loline as dihydrochloride salt.



Scheme 4.3 White et al. total synthesis of loline

4.2.3 Trauner et al. approach

In 2011, Trauner et al. reported an asymmetric total synthesis of loline, norloline, and *N*-formylloline (Scheme 4.4).[61] Their approach started with the conversion of epoxy alcohol **129** to the diol **130** in three steps. This diol was activated by converting to the cyclic sulfite **131**. Nucleophilic attack of LiN_3 on **131** yielded azido alcohol **132**. The core pyrrolizidine ring was produced after treatment of azido alcohol **132** in methanol with one equivalent of bromine. This step proceeds via transannular attack of carbamate nitrogen to the target C atom activated by the formation of bromonium ion to yield bromopyrrolizidine hydrobromide **133**. Exchange of bromide with chloride via Finkelstein reaction using LiCl produced chloropyrrolizidine **134**. The ether bridge between C(2) and C(7) was constructed after treatment of **134** with potassium carbonate in a microwave. Further hydrogenation of azide **135** yielded norloline (NL). In their approach, they also synthesized loline and *N*-formylloline by further manipulation of the 1-amino group.

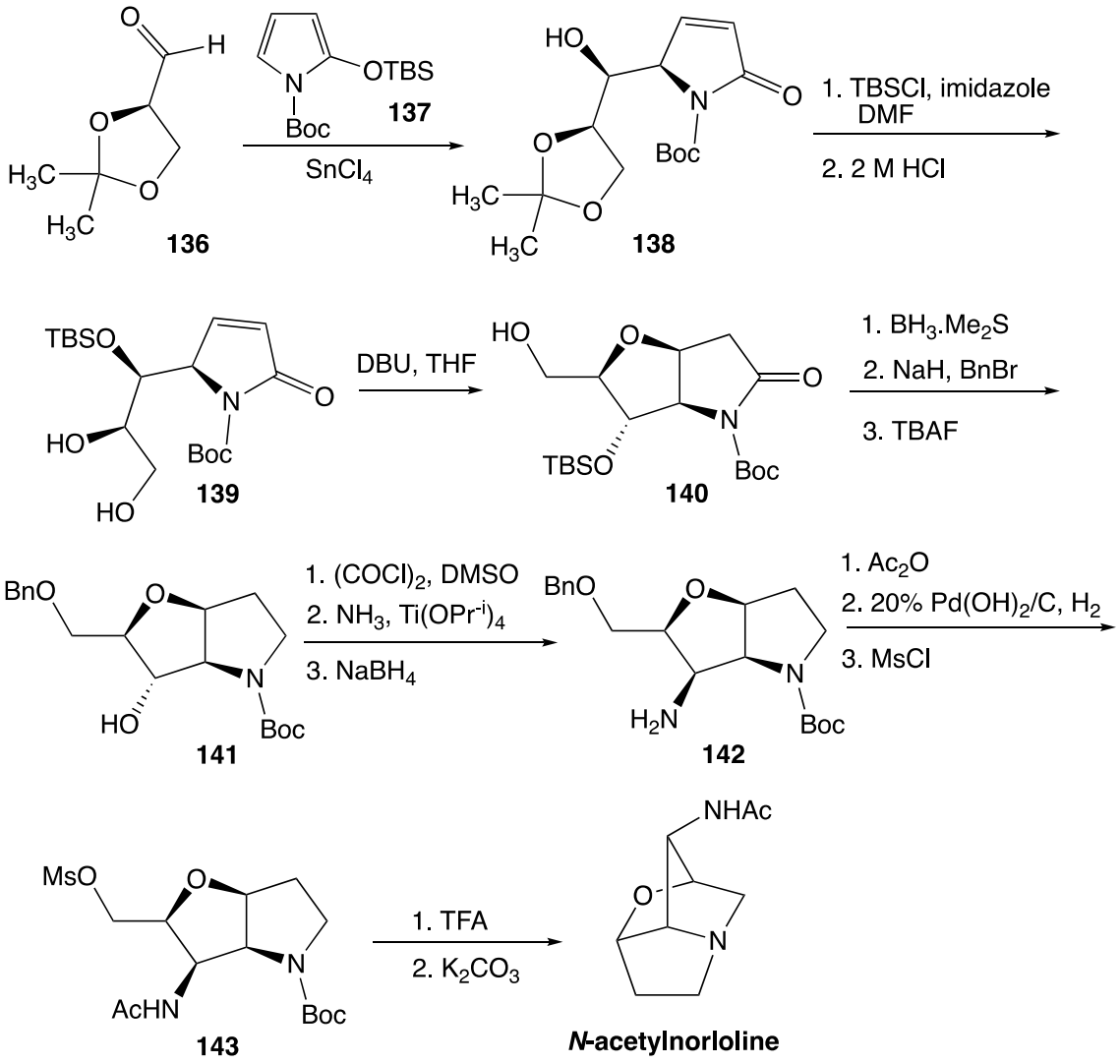


Scheme 4.4 Trauner et al. total synthesis of loline

4.2.4 Huang et al. approach

In 2013, Huang et al. reported asymmetric total synthesis of *N*-acetylnorloline (Scheme 4.5).[62] Their synthesis began by making intermediate **138** via *syn*-selective aldol condensation between aldehyde **136** and pyrrole **137** mediated by $SnCl_4$. Protection of hydroxyl group of **138** with TBSCl and hydrolysis of the acetonide produced diol **139**. Treatment of the diol **139** with DBU afforded the bicyclic imide **140** as a single desired diastereomer. This fused tetrahydrofuran ring contains the final ether bridge in the loline structure. Reduction of the carbonyl group in imide **140**, benzylation of the primary alcohol and desilylation with TBAF gave alcohol **141**. Swern oxidation of the alcohol **141** was followed by reaction of the resulting ketone with NH_3. The produced imine was reduced to the corresponding amine **142** with $NaBH_4$. Acetylation of the amine, catalytic

hydrogenation to remove the benzyl group, and mesylation of the resulting alcohol formed intermediate **143**. To form the tricyclic loline, the Boc group was cleaved with TFA, and the resulting amine was subjected to the cyclization condition to form *N*-acetylnorloline.

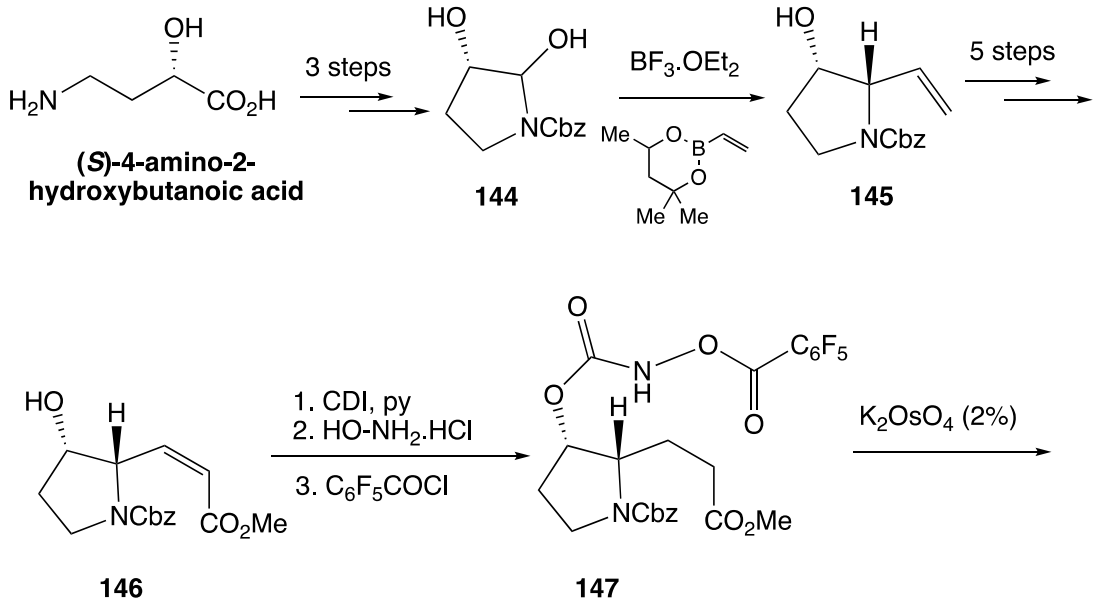


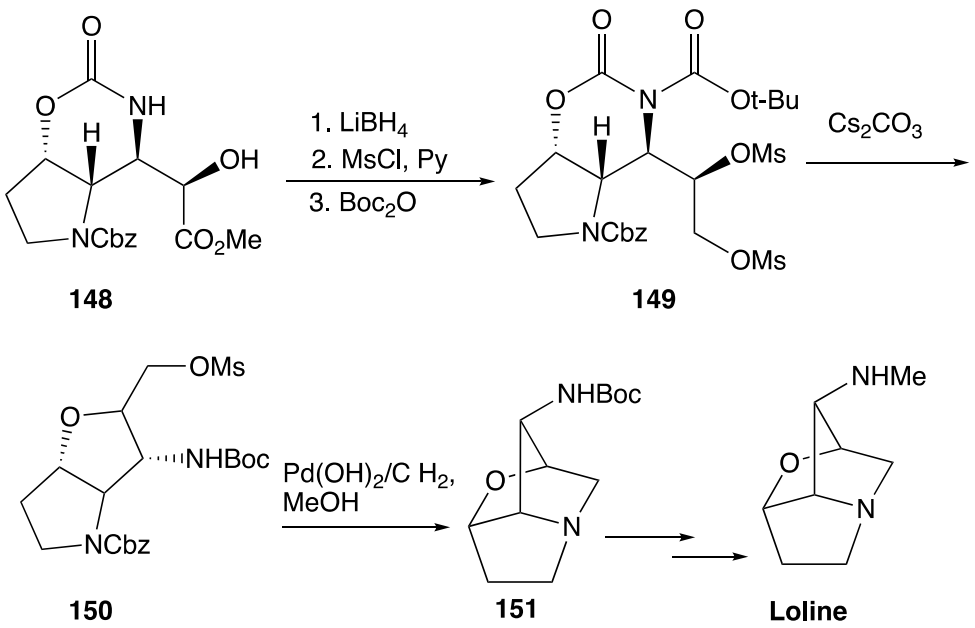
Scheme 4.5 Huang et al. total synthesis of *N*-acetylnorloline

4.2.5 Scheerer et al. approach

In 2015, Scheerer et al. published their asymmetric total synthesis of (+)-loline alkaloids (Scheme 4.6).[63] They started the total synthesis with a chiral substrate, (*S*)-4-amino-2-hydroxybutanoic acid, which was converted to intermediate **144** in three steps. A

vinyl group was added to the intermediate **144** via diastereoselective Petasis borono-Mannich reaction to form intermediate **145**, which was converted to intermediate **146** in five steps. Conversion of hydroxyl group to a carbamate functional group and then functionalization with a *N*-pentafluorobenzyloxy substituent afforded intermediate **147**. Tethered aminohydroxylation of **147** afforded the desired ester **148**. Reduction of the ester, mesylation of produced diol and protection of amino group led to formation of imide **149**. Selective cleavage of carbamate group and intramolecular etherification afforded bicyclic core **150**. Further hydrogenolysis with Perlman's catalyst removed a Cbz-group. Nucleophilic attack of produced secondary amine on mesylate built the pyrrolizidine core and afforded *N*-Boc norloline **151**, which was further manipulated to form the loline product.





Scheme 4.6 Scheerer et al. total synthesis of loline

Depicted in Figure 4.2 is a comparison of all mentioned approaches for the total synthesis of loline alkaloids, where two main retrosynthesis strategies are used. In the first strategy, the Tufariello, White, and Trauner groups initially disconnected the ether bridge to form the pyrrolizidine ring, and they developed different approaches to construct the pyrrolizidine ring in their synthesis plans. In the second strategy, the Scheerer and Huang groups initially disconnected the bond between N(3)–C(4) to form a bicyclic pyrrolizidine. Then, they disconnected the ether bridge to construct different intermediate, which can be synthesized from pyrrole derivatives.

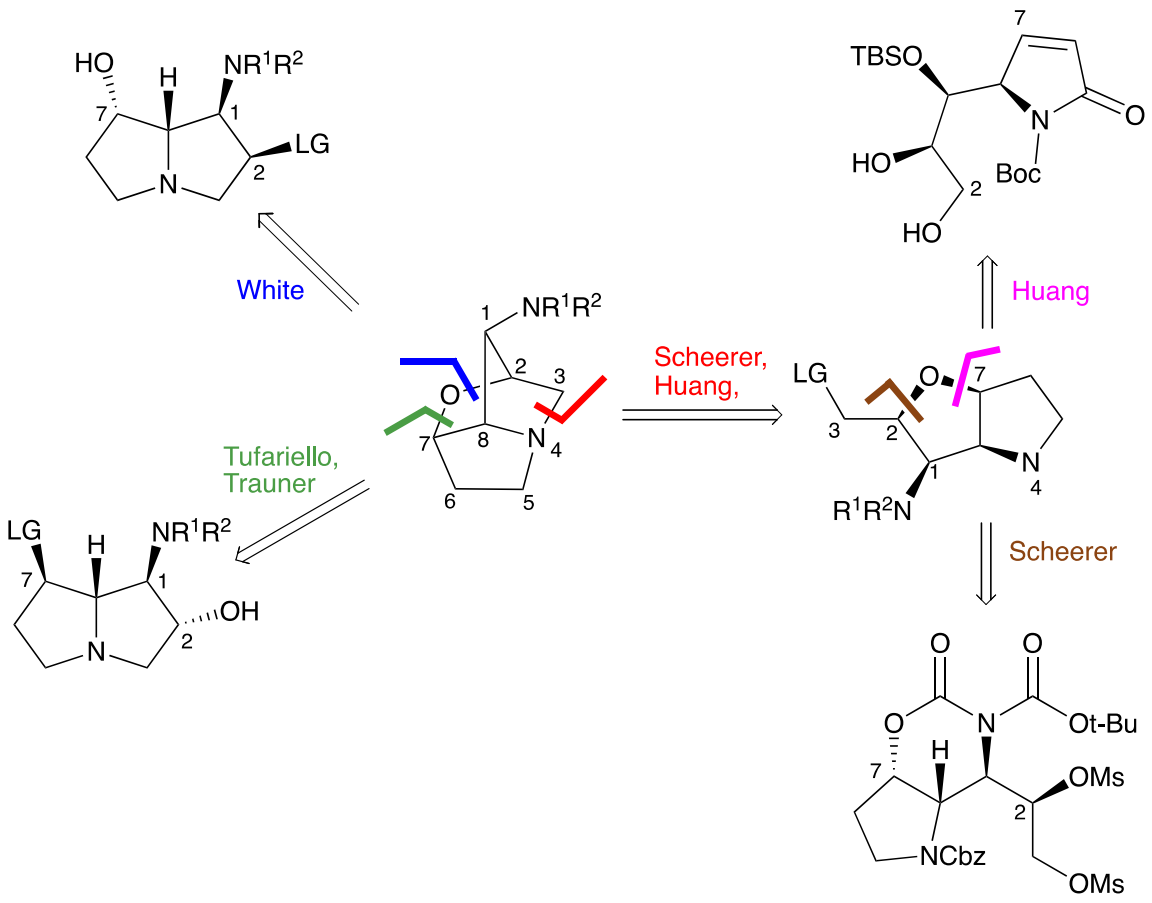
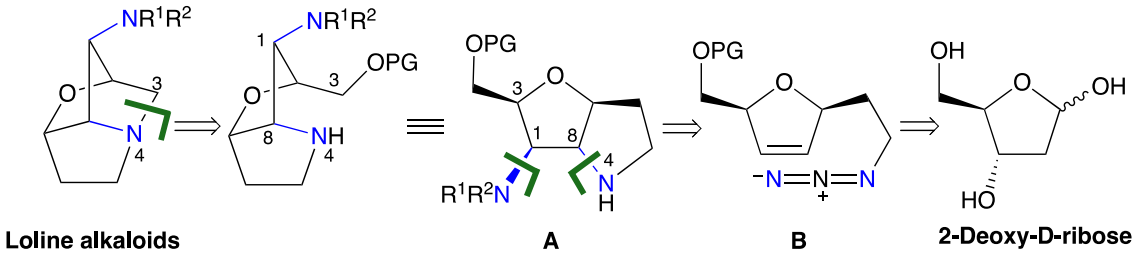


Figure 4.2 Comparison of previously reported total synthesis of loline alkaloids

4.3 Grossman's proposed total synthesis of loline alkaloids

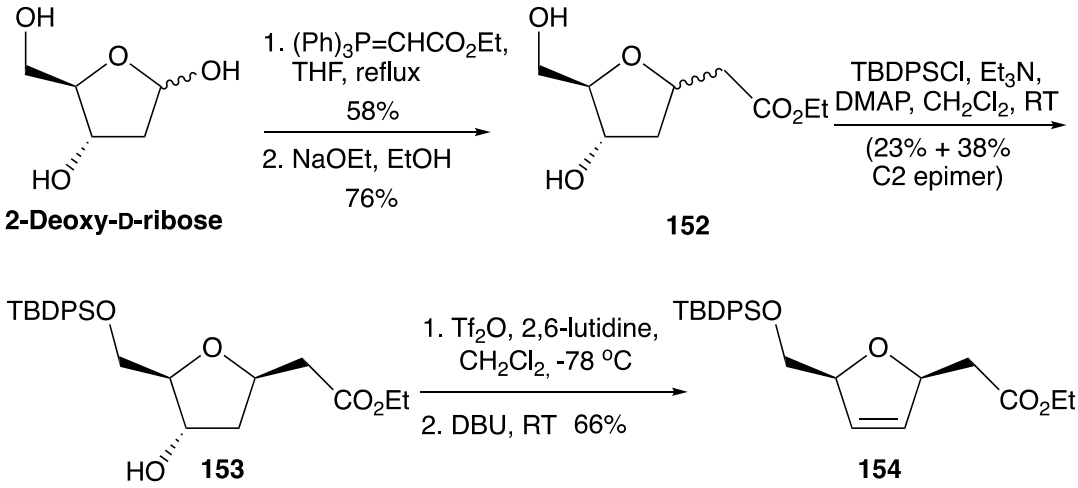
Our designed asymmetric retrosynthesis is similar to Scheerer and Huang's approach in the way that we first disconnect the bond between N(3)–C(4) to form a bicyclic substructure **A** (Scheme 4.7). Unlike Scheerer and Huang's approach, our retrosynthesis does not proceed with the ether bridge disconnection, instead; we disconnect the two C–N bonds on tetrahydrofuran ring **A**. These two C–N bonds can be synthesized by our 1,2-diamination methodology. The 2,5-dihydrofuran **B** can be made from inexpensive and readily available 2-deoxy-D-ribose (source of the ether linkage) in a few steps.



Scheme 4.7 Grossman's proposed total synthesis of loline alkaloids

4.3.1 Synthesis of 2,5-dihydrofuran ring

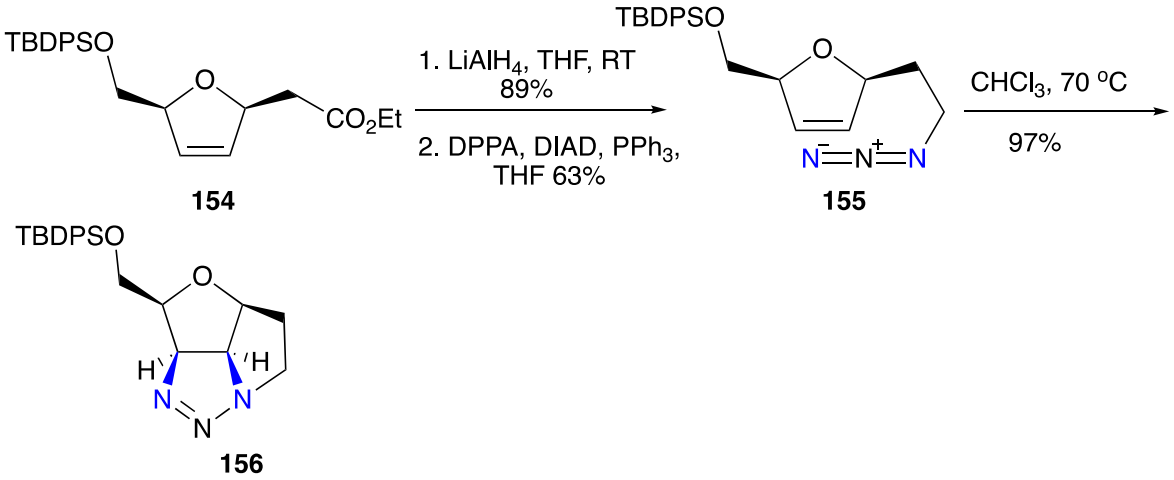
The 2,5-dihydrofuran ring was prepared from commercially available 2-deoxy-D-ribose in four steps (Scheme 4.8).[64, 65] Wittig reaction of 2-deoxy-D-ribose with ethyl(triphenylphosphoranylidene)acetate was followed by oxa-Michael cycloaddition to yield an inseparable C(2) epimeric mixture of **152**. The selective protection of the primary alcohol by *tert*-butyl(chloro)diphenylsilane afforded a mixture of epimers in **153**, which could now be separated by column chromatography. The endocyclic alkene **154** was obtained by forming the triflate ester using trifluoromethanesulfonic anhydride, followed by treatment with DBU in the same reaction mixture. This 2,5-dihydrofuran ring **154** will soon participate in intramolecular azide-alkene cycloaddition.



Scheme 4.8 Synthesis of 2,5-dihydrofuran ring **154**

4.3.2 Synthesis of 1,2,3-triazoline

The ester group on the 2,5-dihydrofuran ring was reduced with $LiAlH_4$ to the primary alcohol (Scheme 4.9). Treatment of the alcohol with diphenylphosphoryl azide (DPPA) in the presence of diisopropyl azodicarboxylate (DIAD) and triphenylphosphine (Bose-Mitsunobu method) produced the desired cyclic azide **155**. Mild thermolysis (70 °C) of **155** triggered intramolecular azide–alkene cycloaddition to provide the tricyclic 1,2,3-triazoline **156**.



Scheme 4.9. Synthesis of 1,2,3-triazoline **156** as a first key intermediate in the total synthesis of loline alkaloids

To validate the that we had made 1,2,3-triazoline **156**, it was very critical for us to establish the structure of the product before moving forward to the next step.

The HSQC spectrum (Figure 4.3) revealed the presence of four methine groups and three methylene groups (excluding the TBDPS signals). The HSQC spectrum also showed that the two upfield H atoms resonating at 1.81 ppm and 2.07 ppm were geminal and connected to C(8).

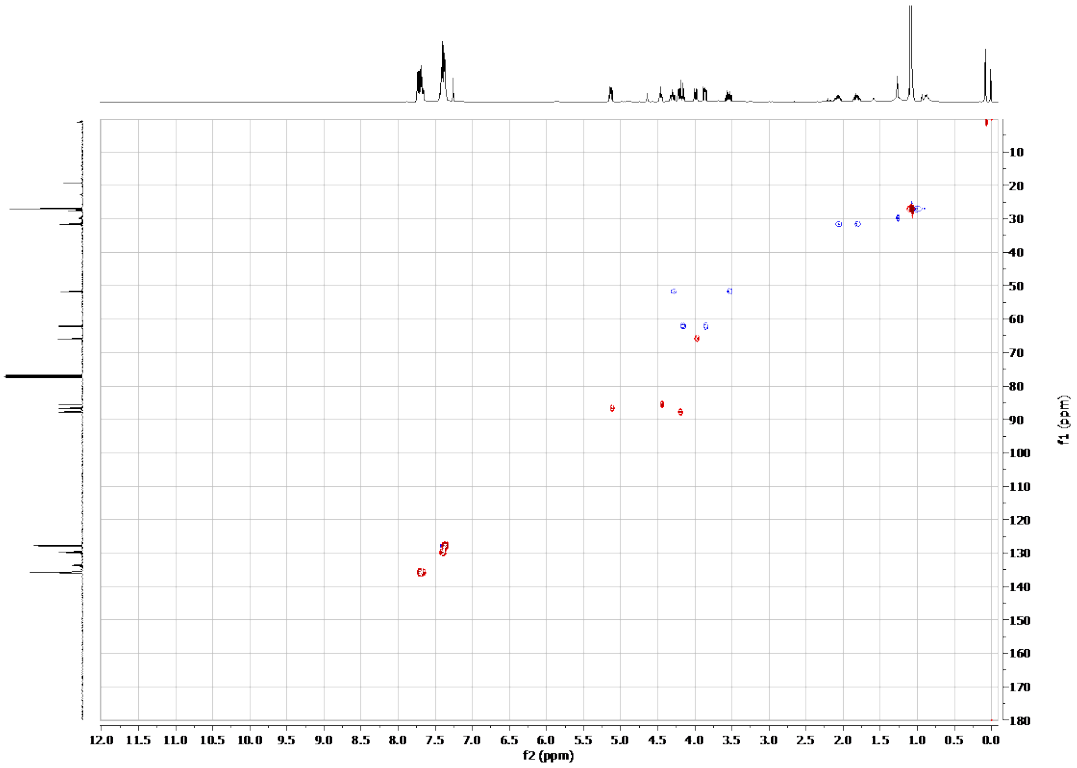


Figure 4.3 HSQC spectrum of 1,2,3-triazoline **156**

I assigned the remaining H atoms (excluding the H atoms at TBDPS group) with the help of ^{1}H–^{1}H COSY correlations (Figure 4.5). The H atoms at C(8) showed a correlation in COSY spectrum with geminal H atoms resonating at 3.53 ppm and 4.29 ppm and a methine H atom resonating at 4.45 ppm. These suggested that these geminal H atoms are connected to C(9), and the methine H atom is connected to C(7).

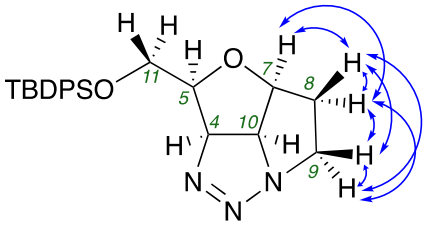


Figure 4.4 ^{1}H-^{1}H COSY correlation of H atoms at C(7) and C(8), and C(8) and C(9) in 1,2,3-triazoline **156**

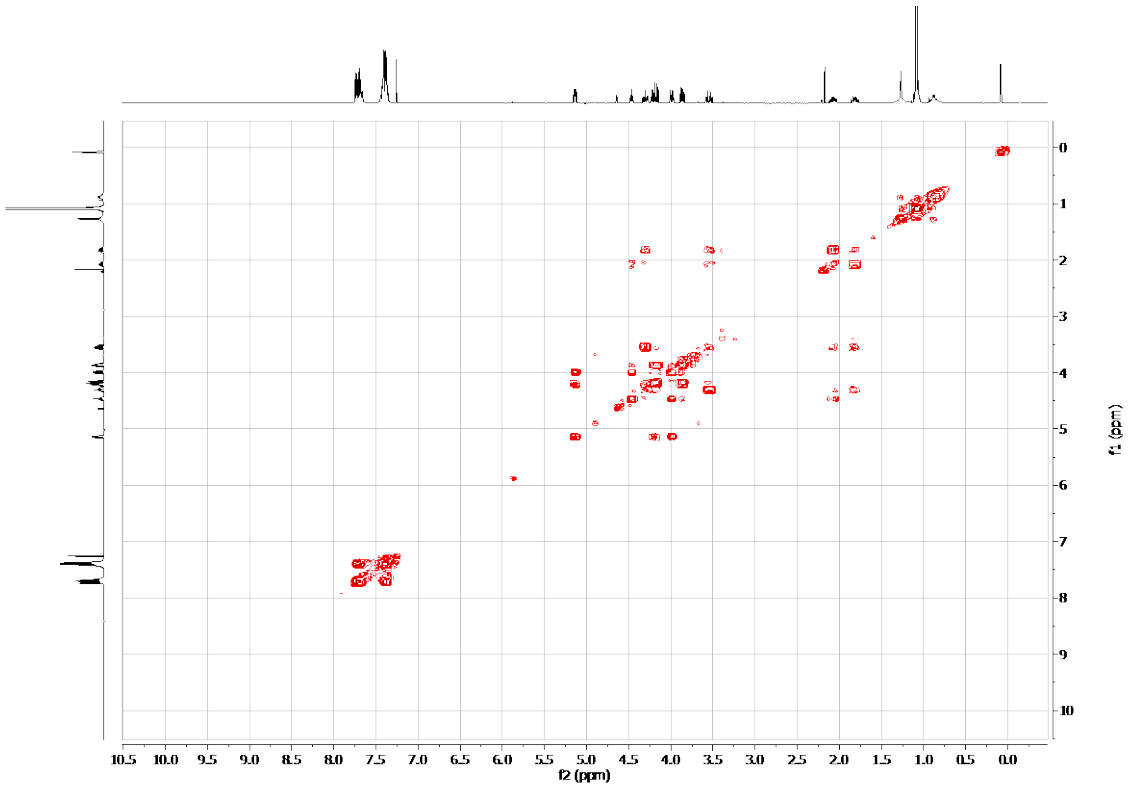


Figure 4.5 ^{1}H–^{1}H COSY spectrum of 1,2,3-triazoline **156**

The H atom at C(7) strongly correlated with the H atom resonating at 3.98 ppm which I assigned to C(10). The strong correlation between the H atom at C(10) and the downfield H atom resonating at 5.12 ppm was consistent with the H atom at C(4). The only unassigned methine H resonating at 4.20 ppm showed a strong correlation with the H atom at C(4) and the unassigned geminal H atoms resonating at 4.17 ppm and 3.86 ppm. I assigned the methine H and the germinal H atoms to C(5) and C(11), respectively.

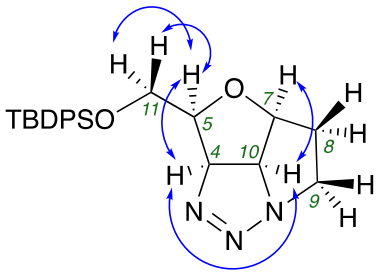
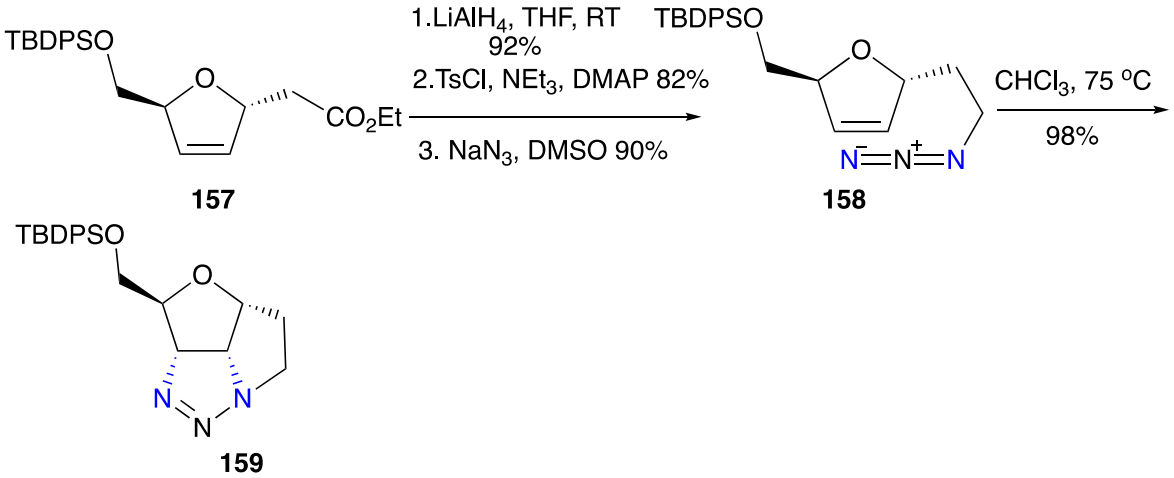


Figure 4.6 ^{1}H-^{1}H COSY correlation of H atoms at C(7) and C(10); at C(4) and C(10); at C(4) and C(5); and at C(5) and C(11) in 1,2,3-triazoline **156**

Similarly, I was able to synthesize the *epi*-1,2,3-triazoline **159** from the *trans*-2,5-dihydrofurane **157** (Scheme 4.10). I was also able to grow crystals of *epi*-1,2,3-triazoline **159** from ether and their analysis by X-ray crystallography confirmed formation of the product (Figure 4.7).



Scheme 4.10 Synthesis of *epi*-1,2,3-triazoline **159**

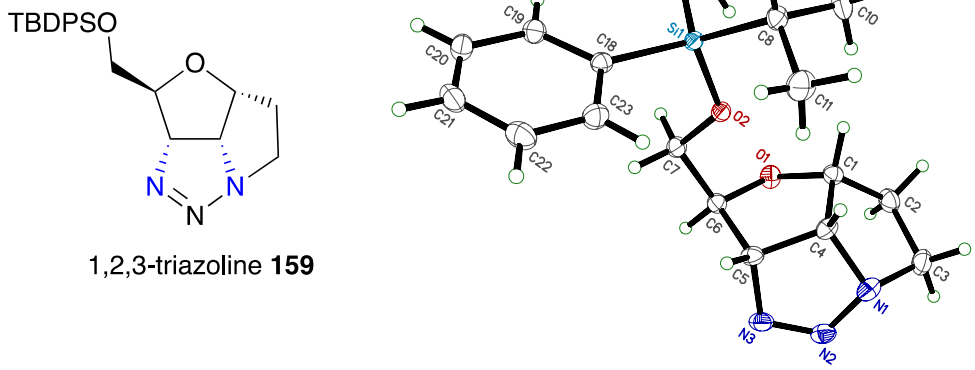
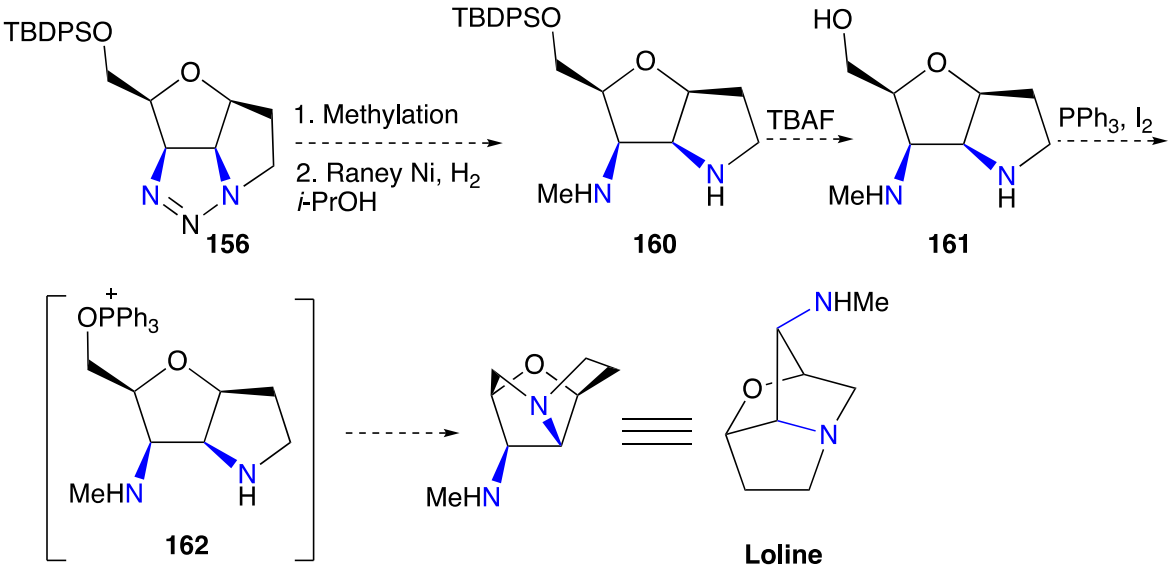


Figure 4.7 Thermal ellipsoid plot of *epi*-1,2,3-triazoline **159**

4.3.3 Future plan for completion of the loline total synthesis

We plan to methylate the N(3) of 1,2,3-triazoline **156** (to form loline) and then reduce the resulting 1,2,3-triazolinium ion over Raney Ni with H_2 to form the 1,2-diamine **160** (Scheme 4.11). Desilylation of **160** with tetrabutylammonium fluoride (TBAF) can afford alcohol **161**, which will be treated with PPh_3 and I_2 to cause the pyrrolidine N to undergo transannular nucleophilic substitution and make the tricyclic (+)-loline in 11 steps from 2-deoxy-D-ribose.



Scheme 4.11 Our plan to complete the total synthesis of loline from 1,2,3-triazoline **156**

I have already tried *N*-methylation of 1,2,3-triazoline **159** with Me_2SO_4 and MeOTf. However, the reactions did not proceed cleanly, making the results difficult to interpret. To overcome the challenges, we could manipulate the reaction conditions (temperature, solvent, etc.) or use other strong methylating agents such as $Me_3O^+BF_4^-$ (Meerwein salt). Additionally, it is possible that the N(3) atom in *cis*-1,2,3-triazoline **156** experience some steric hindrance by the adjacent cis $CH_2OTBDPS$ group which can obstruct the *N*-

methylation. Therefore, removal of the bulky silyl group before alkylation could potentially solve the problem.

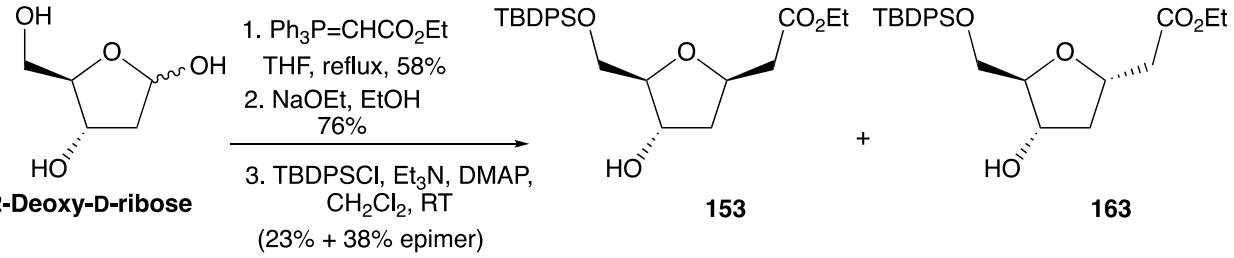
Although, I have not succeeded in finishing the total synthesis, the formation of a *stable* 1,2,3-triazoline **156**–as a first synthesized example– has inspired us to make various 1,2,3-triazolines and initiate the 1,2-diamination project in which I was able to develop two related methodologies for 1,2-diamination of alkenes.

4.4 Experimental Section

Ethyl 2-[(2*R*,4*S*,5*R*)-5-{[(tert-butyldiphenylsilyl)oxy]methyl}-4-hydroxyoxolan-2-yl]acetate

and

Ethyl 2-[(2*S*,4*S*,5*R*)-5-{[(tert-butyldiphenylsilyl)oxy]methyl}-4-hydroxyoxolan-2-yl]acetate



The procedure was adapted from Álvarez et al.[65] To the solution of 2-deoxy-D-ribose (1.01 g, 7.50 mmol) in dry THF (20 mL), Ethyl (triphenylphosphoranylidene) acetate (2.88 g, 8.25 mmol) was added. The mixture was stirred at the reflux temperature for 7 h. Then, the solvent was evaporated and the crude product with was purified with flash column chromatography (5-10% MeOH in CH_2Cl_2) to yield the triol **I** as a colorless oil (885 mg, 4.33 mmol, 58%). The experimental data was in accordance with the previously reported data.^{1}H NMR (400 MHz, $CDCl_3$) δ 7.04–6.86 (m, 1H), 5.91 (dt, J_d = 15.8 Hz, J_t = 2.4 Hz, 1H), 4.50–4.05 (m, 3H, OH), 4.15 (q, J = 7.5 Hz, 2H), 3.83–3.63 (m, 3H), 3.63–3.52 (m, 1H), 2.53–2.31 (m, 2H), 1.26 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.1, 145.9, 123.7, 74.3, 71.6, 63.3, 60.7, 35.9, 14.3.

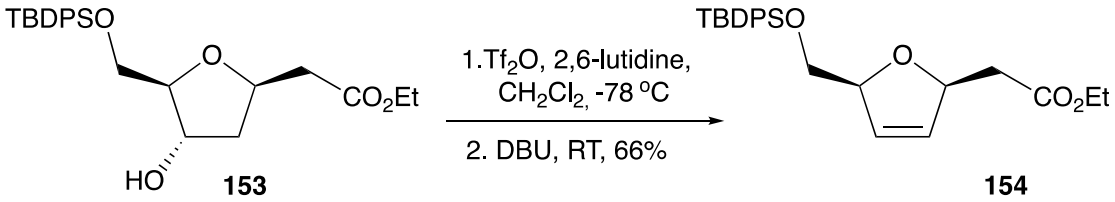
The procedure was adapted from Álvarez et al.[65] NaOEt (67.3 mg, 0.989 mmol) was added to a solution of **I** (2.02 g, 9.89 mmol) in anhydrous EtOH. The reaction mixture was stirred at room temperature for 20 h. Then, the solvent was removed under reduced pressure. Purification with flash column chromatography (10 % MeOH in CH_2Cl_2) afforded the pure product **II** as a mixture of diastromers (1.53 g, 7.50 mmol, 76%).The

experimental data was in accordance with the previously reported data.[1]H NMR (400 MHz, $CDCl_3$) δ 4.58–4.42 (m, $1H_{A+B}$), 4.37–4.28 (m, $1H_{A+B}$), 4.14 (q, J = 7.2 Hz, $2H_{A+B}$), 3.95–3.81 (m, $1H_{A+B}$), 3.79–3.49 (m, $2H_{A+B}$), 2.65–2.54 (m, $2H_{A+B}$), 2.41 and 2.04 (dt, J_d = 12.9 Hz, J_t = 7.0 Hz and ddd, J = 13.1, 5.8, 2.6 Hz, $1H_{A+B}$), 2.12 (broad s, 2H), 1.88 and 1.77 (ddd, J = 13.2, 9.4, 6.4 Hz and ddd, J = 12.7, 6.9, 5.7 Hz, $1H_{A+B}$), 1.26 (t, J = 7.1 Hz, $3H_{A+B}$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.6, 171.3, 87.3, 85.6, 74.8, 74.7, 73.5, 73.1, 72.9, 63.1, 62.6, 60.9, 60.8, 60.8, 41.0, 40.4, 40.0, 14.3.

The procedure was adapted from Álvarez et al.[65] To the solution of **II** (2.69 g, 13.2 mmol) in 80 mL of anhydrous CH_2Cl_2, Et_3N (2.66 g, 26.34 mmol) and DMAP (161 mg, 1.31 mmol) was added. The mixture was stirred for 15 minutes and TBDPSCl (3.44 g, 12.5 mmol) was added to the mixture. The reaction was stirred at room temperature for 48 h. Then, the reaction mixture was washed with 1 M aqueous HCl and was extracted with CH_2Cl_2 three times. The combined organic layer was dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purification with flash chromatography with hexane-CH_2Cl_2–Et_2O (5:3:2) yielded **153** (1.34 g, 3.03 mmol, 23%) and **163** (2.22 g, 5.02 mmol, 38%) as colorless oils. The experimental data was in accordance with the previously reported data. Data for **153**:[1]H NMR (400 MHz, $CDCl_3$) δ 7.70–7.63 (m,4H), 7.46–7.35 (m, 6H), 4.55 (ddt, J_d = 9.6 Hz, J_d = 7.1 Hz, J_t = 5.8 Hz, 1H), 4.48–4.42 (m, 1H), 4.14 (q, J = 7.1 Hz, 2H), 3.88 (ddd, J = 6.3, 3.8, 2.7 Hz, 1H), 3.76 (dd, J = 10.6, 3.8 Hz, 1H), 3.58 (dd, J = 10.6, 6.0 Hz, 1H), 2.64 (dd, J = 15.4, 7.1 Hz, 1H), 2.48 (dd, J = 15.4, 6.0 Hz, 1H), 2.07 (ddd, J = 13.1, 5.7, 2.3 Hz, 1H), 1.84 (ddd, J = 13.1, 9.6, 6.2 Hz, 1H), 1.73 (broad s, 1H), 1.25 (t, J = 7.2 Hz, 3H), 1.05 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171 .2, 135.7, 135.7, 133.3, 133.3, 130.0, 129.9, 127.9, 127.9, 87.1, 74.8, 74.5, 64.8, 60.7, 40.8, 40.7,

27.0, 19.4, 14.3. Data for **163**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63–7.69 (m,4H), 7.47–7.35 (m, 6H), 4.53–4.41 (m, 2H), 4.15 (q, J = 7.1 Hz, 2H), 3.97 (dt, J_d = 6.2 Hz, J_t = 3.8 Hz, 1H), 3.75 (dd, J = 10.6, 4.0 Hz, 1H), 3.61 (dd, J = 10.6, 3.8 Hz, 1H), 2.71 (dd, J = 10.6, 6.0 Hz, 1H), 2.63 (dd, J = 15.4, 7.1 Hz, 1H), 2.48 (dt, J_d = 13.2, J_t = 7.2 Hz, 1H), 2.39 (d, J = 5.0 Hz, 1H), 1.80 (ddd, J = 13.2, 6.4, 4.7 Hz, 1H), 1.25 (t, J = 7.1 Hz, 3H), 1.05 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.6, 135.7, 135.7, 133.3, 133.2, 130.0, 129.9, 127.9, 127.9, 85.9, 75.1, 74.8, 65.0, 60.7, 41.0, 40.0, 27.0, 19.3, 14.3.

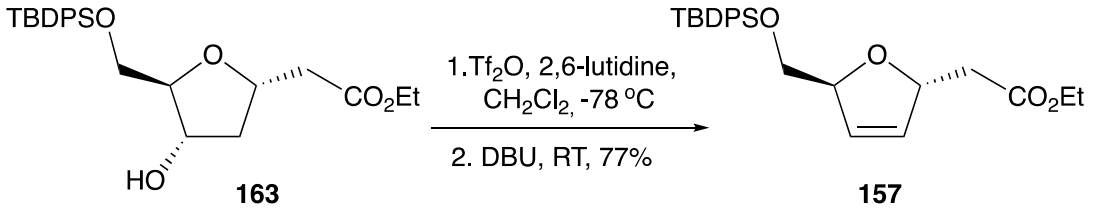
Ethyl 2-[(2*S*,5*S*)-5-{[(tert-butyldiphenylsilyl)oxy]methyl}-2,5-dihydrofuran-2-yl]acetate



To a solution of **153** (851 mg, 1.92 mmol) in CH_2Cl_2 (16 mL) were added 2,6-lutidine (618 mg, 5.76 mmol) and Tf_2O (813 mg, 2.88 mmol) at –78 °C. The mixture was stirred for 30 min at –78 °C, followed by the addition of DBU (2.92 g, 19.2 mmol). The resulting mixture was warmed to room temperature and stirred for 2 h. The reaction mixture was quenched by the addition of saturated $NaHCO_3$ solution. After removal of CH_2Cl_2 by evaporation, the residue was extracted with hexanes/ EtOAc (5/1) (3 × 20 mL). The combined organic layer was washed with 1 M aqueous HCl (let it stir for 30 minutes) and brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography (10% EtOAc in hexanes) to yield the alkene **154** (538 mg, 1.27 mmol, 66%) as a colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76–7.65 (m, 4H), 7.47–7.34 (m, 6H), 5.97–5.88 (m, 2H), 5.27–5.19 (m, 1H),

4.93–4.87 (m, 1H), 4.15 (q, J = 7.0 Hz, 2H), 3.76–3.61 (m, 2H), 2.68 (dd, J = 15.6, 7.5 Hz, 1H), 2.52 (dd, J = 15.6, 6.1 Hz, 1H), 1.24 (t, J = 7.1 Hz, 3H), 1.08 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.1, 135.8, 135.7, 134.9, 133.6, 133.5, 130.3, 129.8, 129.7, 128.8, 127.8, 87.2, 82.6, 66.9, 60.6, 42.1, 27.0, 19.4, 14.3; IR (ATR) 3070, 3048, 2930, 2856, 1731 cm^{-1}; GC-MS (EI) 367 (100%), 269 (17%), 227 (19%), 211 (16%), 199 (86%), 181 (42%), 155 (20%), 135 (53%), 105 (20%), 81 (32%).

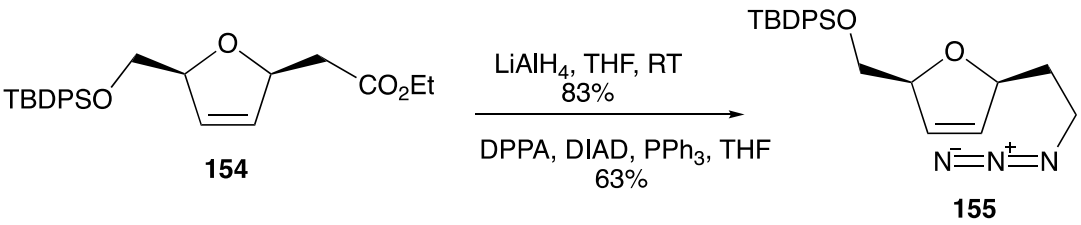
Ethyl 2-[(2*R*,5*S*)-5-{[(tert-butyldiphenylsilyl)oxy]methyl}-2,5-dihydrofuran-2-yl]acetate



To a solution of **163** (672 mg, 1.52 mmol) in CH_2Cl_2 (13 mL) were added 2,6-lutidine (488 mg, 4.56 mmol) and Tf_2O (643 mg,2.28 mmol) at –78 °C. The mixture was stirred for 30 min at –78 °C, followed by the addition of DBU (2.31 g, 1.52 mmol). The resulting mixture was warmed to room temperature and stirred for 2 h. The reaction mixture was quenched by the addition of saturated $NaHCO_3$ solution. After removal of CH_2Cl_2 by evaporation, the residue was extracted with hexanes/ EtOAc (5/1) (3 × 20 mL). The combined organic layer was washed with 1 M aqueous HCl (let it stir for 30 minutes) and brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography (10% EtOAc in hexanes) to yield the alkene **157** (496 mg, 1.17 mmol, 77%) as a colorless liquid. ^{1}H NMR (400 MHz, CDCl3) δ 7.76–7.65 (m, 4H), 7.46–7.34 (m, 6H), 5.97–5.90 (m, 2H), 5.28–5.20 (m, 1H), 4.95 (ddt, J_d = 7.1 Hz, J_d = 5.7 Hz, J_t = 3.0 Hz, 1H), 4.17 (q, J = 7.1 Hz, 2H), 3.73 (dd, J =

10.3, 4.4 Hz, 1H), 3.67 (dd, *J* = 10.3, 5.4 Hz, 1H), 2.62 (dd, *J* = 15.2, 7.0 Hz, 1H), 2.52 (dd, *J* = 15.2, 6.1 Hz, 1H), 1.27 (t, *J* = 7.1 Hz, 3H), 1.05 (s, 9H); ^{13}C NMR (100 MHz, CDCl3) δ 171.1, 135.8, 135.7, 134.9, 133.8, 133.7, 130.4, 129.8, 129.7, 129.0, 127.8, 86.6, 82.6, 66.5, 60.6, 41.5, 26.9, 19.4, 14.3; IR (ATR) 3071, 3050, 2929, 2856, 1732 cm^{-1}; GC-MS (EI) 367 (100%), 269 (15%), 227 (17%), 211 (14%), 199 (71%), 181 (35%), 155 (16%), 135 (40%), 105 (15%), 81 (22%).

{[(2*S*,5*S*)-5-(2-azidoethyl)-2,5-dihydrofuran-2-yl]methoxy}(tert-butyl)diphenylsilane

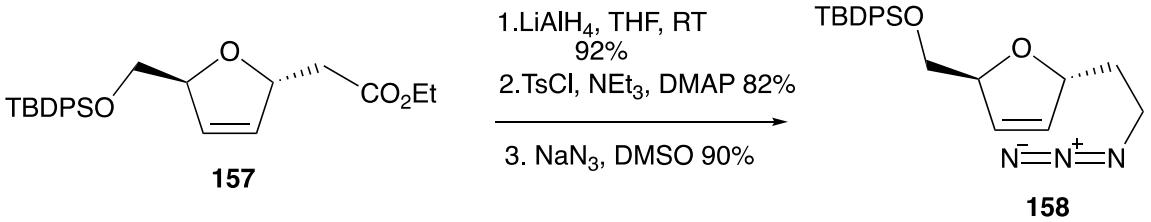


A solution of ester **154** (600 mg, 1.40 mmol) in dry THF (2.0 mL) was added dropwise to the suspension of $LiAlH_4$ (160 mg, 4.20 mmol) in dry THF (9.5 mL) at –78 °C. The resulting mixture stirred at –78 °C for 1.5 h and at room temperature for 30 minutes. After reaction completion, the mixture was diluted by adding ether (10 mL) and cooled down to 0 °C. Then 160 μL of H_2O, 160 μL of 15% NaOH, 480 μL of H_2O was added, respectively. The mixture warmed up to room temperature and anhydrous $MgSO_4$ was added to the mixture. After stirring for 2-3 minutes the mixture filtered and washed with ether. Organic solvents were evaporated under reduced pressure to yield the crude alcohol **154a** as a colorless viscous liquid (443 mg, 1.16 mmol, 83%). The crude product was used in the next step without further purification. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70–7.64 (m, 4H), 7.47–7.32 (m, 6H), 5.91– 5.79 (m, 2H), 5.06–4.99 (m, 1H), 4.98–4.91 (m, 1H), 3.85–3.71 (m, 2H), 3.68 (d, *J* = 4.8 Hz, 2H), 1.86 (ddt, J_d = 14.0 Hz, J_t = 6.1 Hz, J_d =

3.9 Hz, 1H), 1.73 (ddt, J_d = 14.5 Hz, J_t = 7.6 Hz, J_d = 4.6 Hz, 1H), 1.04 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.8, 135.8, 133.7, 133.5, 131.3, 129.9, 129.8, 128.0, 128.0, 127.8, 87.2, 86.1, 67.2, 61.1, 38.7, 27.0, 19.4; IR (ATR) 3375, 3070, 3048, 2928, 2855 cm^{-1}; GC-MS (EI) 325 (37%), 247 (10%), 217 (13%), 199 (100%), 181 (32%), 135(36%), 105 (9%), 95 (19%).

To the ice cold solution of PPh_3 (450 mg, 1.71 mmol) in THF (3 mL), DIAD (354 mg, 1.75 mmol) was added dropwise and the mixture stirred for 15 minutes at the same tempreture. Then, a solution of alcohol **154a** (328 mg, 0.857 mmol) in THF (1 mL) was added dropwise and the mixture stirred for 15 minutes at the same temperature. Then DPPA (498 mg,1.81 mmol) was added dropwise and the resulting mixture stirred at room temperature for 30 h. Then water was added and the mixture was extracted with EtOAc (3 × 10 ml). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography (5% EtOAc in hexanes) to yield the azide **155** (221 mg, 0.542 mmol, 63%) as a light yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$) 7.74–7.62 (m, 4H), 7.49–7.32 (m, 6H), 5.87 (ddt, J_d = 7.1 Hz, J_d = 0.9 Hz, J_t = 6.1 Hz, 2H), 4.94–4.84 (m, 2H), 3.77–3.60 (m, 2H), 3.38 (ddd, J = 7.6, 6.4, 1.1 Hz, 2H), 1.86 (ddt, J_d = 13.9, J_d = 3.9, J_t = 7.7, 1H), 1.76 (dddd, J = 13.8, 7.7, 6.7, 6.0 Hz, 1H), 1.07 (s, 9H). IR (ATR) 3070, 3049, 2928, 2858, 2092 cm^{-1}; GC-MS (EI) 322 (100%), 253 (9%), 223 (9%), 199 (23%), 181 (19%), 163 (20%), 135 (10%), 105 (10%), 80 (28%).

{[(2*S*,5*R*)-5-(2-azidoethyl)-2,5-dihydrofuran-2-yl]methoxy}(tert-butyl)diphenylsilane



157 **158**

A a solution of ester **157** (451 mg, 1.06 mmol) in dry THF (2 mL) was added dropwise to the suspension of $LiAlH_4$ (121 mg, 3.19 mmol) in dry THF (9 mL) at –78 °C. The resulting mixture stirred at –78 °C for 1.5 h and at room temperature for 30 minutes. After reaction completion, the mixture was diluted by adding ether (10 mL) and cooled down to 0 °C. Then 120 μL of H_2O, 120 μL of 15% NaOH, 360 μL of H_2O was added, respectively. The mixture warmed up to room temperature and anhydrous $MgSO_4$ was added to the mixture. After stirring for 2-3 minutes the mixture filtered and washed with ether. Organic solvents were evaporated under reduced pressure to yield the crude alcohol **157a** as a colorless viscous liquid (375 mg, 0.980 mmol, 92%). The crude product was used in the next step without further purification. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77–7.66 (m, 4H), 7.47–7.33 (m, 6H), 5.86 (d, *J* = 1.6 Hz, 2H), 5.07–5.00 (m, 1H), 4.99–4.91 (m, 1H), 3.85–3.73 (m, 2H), 3.70 (d, *J* = 4.8 Hz, 2H), 2.60 (s, 1H), 1.92–1.82 (m, 1H), 1.79–1.69 (m, 1H), 1.06 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.8, 135.7, 134.9, 133.7, 133.6, 131.3, 129.8, 129.7, 128.0, 127.8, 86.7, 86.3, 66.5, 61.1, 37.6, 26.9, 19.4; IR (ATR) 3375, 3070, 3048, 2928, 2855 cm^{-1}; GC-MS (EI) 325 (23%), 247 (8%), 217 (9%), 199 (100%), 181 (30%), 135(27%), 105 (13%), 95 (15%).

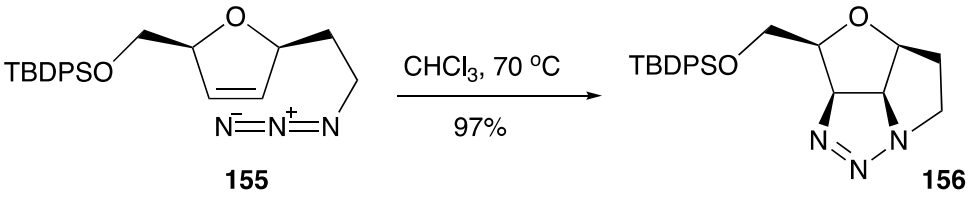
Et_3N (300 mg, 2.94 mmol) and DMAP (9.00 mg, 0.073 mmol) was added to the solution of crude alcohol **157a** (562 mg, 1.47 mmol) in anhydrous CH_2Cl_2 (14 mL). The mixture was stirred for 10 minutes and then cooled down to 0 °C . A solution of TsCl (344

mg, 1.81 mmol) in anhydrous CH_2Cl_2 (2 mL) was added to the mixture dropwise. The reaction was stirred at 0 °C for 1 h and then warmed up to room temperature and continue stirring for 30 h. Then, the reaction mixture was washed with 1 M aqueous HCl and was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layer was dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purification with flash chromatography (5-10% EtOAc in hexanes) yielded the pure tosylate **157b** as a colorless liquid (649 mg, 1.21 mmol, 82%). This tosylated product is prone to decomposition and should be used immediately in the next step. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (dd, J = 8.3, 1.8 Hz, 2H), 7.68–7.61 (m, 4H), 7.49–7.28 (m, 8H), 5.83–5.77 (m, 2H), 4.88 (dd, J = 7.0, 4.6 Hz, 1H), 4.84–4.74 (m, 1H), 4.20–4.09 (m, 2H), 3.68–3.55 (m, 2H), 2.42 (s, 3H), 2.04–1.91 (m, 1H), 1.88–1.78 (m, 1H), 1.03 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.8, 135.8, 135.7, 133.7, 133.6, 133.2, 130.4, 129.9, 129.8, 129.8, 128.6, 128.1, 127.8, 86.6, 82.6, 67.7, 66.5, 35.2, 26.9, 21.8, 19.4; IR (ATR) 3069, 2928, 2855 cm^{-1}.

To the solution of **157b** (496 mg, 0.923 mmol) in dry DMSO (15 mL), it was added NaN_3 (180 mg, 2.77 mmol) in one portion. The mixture stirred at room temperature for 10 h. After reaction completion, H_2O was added and the mixture was extracted with ether (3 × 7 mL). The combined organic layer was washed with H_2O one more time to remove the rest of DMSO. (**Caution:** The unreacted sodium azide in the aqueous layer was quenched according to the previously reported protocol)[43]. The combined organic layer was dried over anhydrous $MgSO_4$ and concentrated under vacuum to yield the azide **158** (340 mg, 0.835 mmol, 90%) as a colorless liquid. The crude product was carried to the next step without further purification and was kept at –20 °C to prevent formation of the corresponding triazoline. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72–7.64 (m, 4H), 7.46–7.35 (m,

6H), 5.91–5.84 (m, 2H), 4.99–4.88 (m, 2H), 3.74–3.64 (m, 2H), 3.40 (t, J = 7.0 Hz, 2H), 1.90 (ddt, J_d = 14.7 Hz, J_d = 4.0 Hz, J_t = 7.4 Hz, 1H), 1.77 (m, 1H), 1.05 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.8, 135.8, 133.8, 133.7, 130.6, 129.8, 129.8, 128.6, 127.8, 86.7, 83.5, 66.6, 48.0, 35.1, 26.9, 19.4; IR (ATR) 3071, 3049, 2929, 2857, 2093 cm^{-1}; GC-MS (EI) 322 (100%), 244 (13%), 223 (17%), 199 (33%), 181 (21%), 163 (42%), 135 (12%), 105 (13%), 80 (22%), 77 (8%).

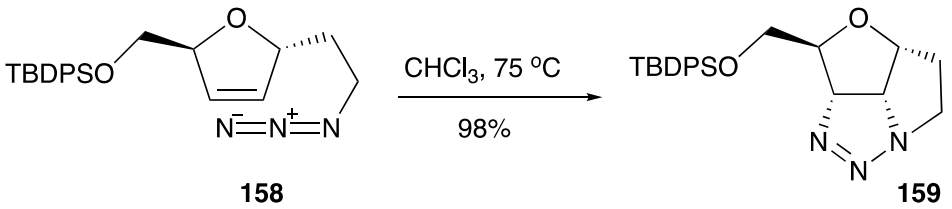
(4*R*,5*R*,7*S*,10*S*)-5-[(tert-butyldiphenylsilyl)oxy]-6-oxa-1,2,3-triaztricyclo[5.2.1.0^{4,10}]dec-2-ene



155 **156**

A solution of azide **155** (35.0 mg, 0.086 mmol) in $CHCl_3$ (0.6 mL) was transferred to the NMR tube and heated at 70 °C for 64 h. After completion of the cycloaddition, the solvent was evaporated to yield the 1,2,3-triazoline **156** as a light yellow solid (34.1 mg, 0.083 mmol, 97%). The crude product was kept at –20 °C to prevent loss of N_2. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76–7.64 (m, 4H), 7.46–7.33 (m, 6H), 5.12 (dd, J = 8.1 Hz, 1H), 4.45 (ddd, J= 6.9, 5.0, 2.0 Hz, 1H), 4.30 (ddd, J = 12.9, 9.1, 4.0 Hz, 1 H), 4.25–4.13 (m, 2H), 3.98 (dd, J = 8.1, 5.1 Hz, 1H), 3.86 (dd, J = 10.3, 6.0 Hz, 1H), 3.53 (dt, J_d = 12.8 Hz, J_t = 8.6 Hz, 1H), 2.13–2.01 (m, 1H), 1.87–1.76 (m, 1H), 1.09 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.8, 135.8, 133.7, 133.6, 129.8, 127.8, 127.8, 87.9, 86.7, 85.6, 66.0, 62.1, 51.8, 31.6, 27.0, 19.4; IR (ATR) 3069, 3047, 2928, 2855 cm^{-1}; GC-MS (EI) 322 (100%), 253 (12%), 223 (9%), 199 (25%), 181 (20%), 163 (23%), 135 (12%), 105 (10%), 82 (37%).

(4*S*,5*R*,7*R*,10*R*)-5-[(tert-butyldiphenylsilyl)oxy]-6-oxa-1,2,3-triaztricyclo[5.2.1.0^{4,10}]dec-2-ene



158 **159**

A solution of azide **158** (423 mg, 1.18 mmol) in $CHCl_3$ (6 mL) was transferred to the sealed tube and heated at 75 °C for 17 h. (Attention: a NMR sample in $CDCl_3$ was also prepared and put into the same oil bath with the sealed tube. Progress of the reaction was monitored by NMR to prevent overheating of the sample and extrusion of N_2). After completion of the cycloaddition, the solvent was evaporated and the product was re-dissolved in ether and kept under medium flow of N_2 to yield the 1,2,3-triazoline **159** (473 mg, 1.16 mmol) as a pale yellow solid The crude product was kept at –20 °C to prevent loss of N_2. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72–7.64 (m, 4H), 7.49–7.37 (m, 6H), 5.16 (d, J = 8.3 Hz, 1H), 4.89 (dt, J_d = 3.0 Hz, J_t = 4.89 Hz, 1H), 4.58 (t, J = 3.4 Hz, 1 H), 4.37 (ddd, J = 12.4, 8.9, 2.8 Hz, 1H), 4.16 (dd, J = 8.3, 5.8 Hz, 1H), 3.81 (dd, J = 11.1, 3.6 Hz, 1H), 3.74 (dd, J = 11.1, 3.1 Hz, 1H), 3.49 (ddd, J = 12.8, 9.6, 8.3 Hz, 1H), 2.11 (dddd, J = 13.9, 8.1, 7.0, 2.8, Hz, 1H), 1.62 (ddt, J_d = 13.9 Hz, J_d = 3.1 Hz, J_t = 9.3 Hz, 1H), 1.09 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.7, 135.6, 132.8, 132.7, 130.2, 130.1, 128.1, 128.0, 88.6, 88.4, 87.5, 66.9, 66.4, 52.4, 32.7, 27.0, 19.2; IR (ATR) 3070, 3047, 2931, 2855 cm^{-1}; GC-MS (EI) 322 (100%), 244 (13%), 223 (15%), 199 (41%), 181 (26%), 163 (40%), 135 (12%), 105 (13%), 82 (19%).

Chapter 5 Conclusions and Future Directions

1,2-Diamine moieties are ubiquitous substructures found in pharmaceutical agents and natural products. They can also serve as ligands in transition metal complexes useful in catalysis and medicine. In this report, we have developed two different methods for 1,2-diamination of alkenes via reduction of 1,2,3-triazolinium ions over Raney Ni with only a balloon of H_2.

In the first method, azide–alkene cycloaddition formed a 1,2,3-triazoline which was then *N*-alkylated to form a 1,2,3-triazolinium ion. A summary of all the synthesized 1,2-diamines in this method is depicted in Table 2.1. Through this approach, I have also shown that the synthesis of a stable 1,2,3-triazoline is not only possible, but they can also be isolated and manipulated without extrusion of N_2. This finding provides opportunities for researchers to utilize stable 1,2,3-triazolines in various reactions other than the formation of an imine or an aziridine.

In the second method, the 1,2,3-triazolinium ions were directly synthesized through the cycloaddition of an azidium ion and alkenes. I prepared 1,2-diamines from cyclic, trans acyclic, cis acyclic, and terminal alkenes (Table 3.1). The cyclic alkenes afforded cis 1,2,3-triazolinium ions and their hydrogenation over Raney Ni produced 1,2-diamines with cis stereochemistry. The retention of the stereochemistry was confirmed by NMR and X-ray crystallographic analysis.

The acyclic trans alkenes gave threo 1,2-diamines and the X-ray crystallographic analysis of 1,2-diamines and confirmed preservation of the corresponding 1,2,3-triazolinium ion stereochemistry during the hydrogenolysis.

Shockingly, hydrogenolysis of the 1,2,3-triazolinium ion derived from the acyclic cis alkene formed products with complete or partial inversion of stereochemistry. We hypothesized that the isomerization has possibly occurred during the hydrogenation step when the triazolinium ring was still intact. Coordination of Ni to the cis 4,5-disubstituted ring possibly catalyzed a series of *β*-hydride eliminations and reinsertions to form the more stable trans 4,5-disubstituted ring leading to the threo product.

The hydrogenolysis of the 1,2,3-triazolinium ion **111** derived from 5-hexen-2-one gave more surprising results. The 1,2-diamine product formed with an additional C–C bond. We hypothesized it is probably due to the formation of the hydrazone intermediate during the reduction. This intermediate can possibly act as a C nucleophile and form a new C–C bond by attacking the carbonyl group.

We were also interested to apply our 1,2-diamination methodology in total synthesis of loline alkaloids. Our proposed reterosynthesis involves formation of the 1,2,3-triazoline as a first key intermediate. I successfully synthesized this 1,2,3-triazoline from 2-deoxy-D-ribose in seven steps. The *N*-alkylation of the 1,2,3-triazoline, reduction of the produced 1,2,3-triazolinium ion, and completion of the final stages of this total synthesis are still under investigation.

The undesired isomerization outcomes and the low yields in some examples are the important limitations of this methodology. Raney Ni was among the first few catalysts that I utilized to hydrogenate the 1,2,3-triazolinium ions. In future, one could use catalysts other than Raney Ni, such as $Pd(OH)_2$, PtO_2, etc. to possibly bypass these limitations or might explore the use of higher pressure of H_2 to improve the yields and the scope of the methodology.

In our 1,2-diamination methodology, we prepared 1,2-diamines with benzyl (method A) or aryl (method B) substituents on the N atoms. One could possibly develop methods to remove these substituents and form more useful 1,2-diamines. Debenzylation of 1,2-diamines synthesized in method A, can probably be done by hydrogenolysis of the substrate over $Pd(OH)_2$ with H_2. However, the removal of *N*-chlorophenyl group may imply more challenges as there are not many methods known for removing the aryl groups. One could possibly replace the Cl with methoxy group in chlorophenyl substituents using the pd-catalyst-ligand system developed by Buchwald group.[66] The 4-methoxyphenyl group can oxidatively be removed by treatment with aqueous ceric ammonium nitrate (CAN).[49]

Appendix

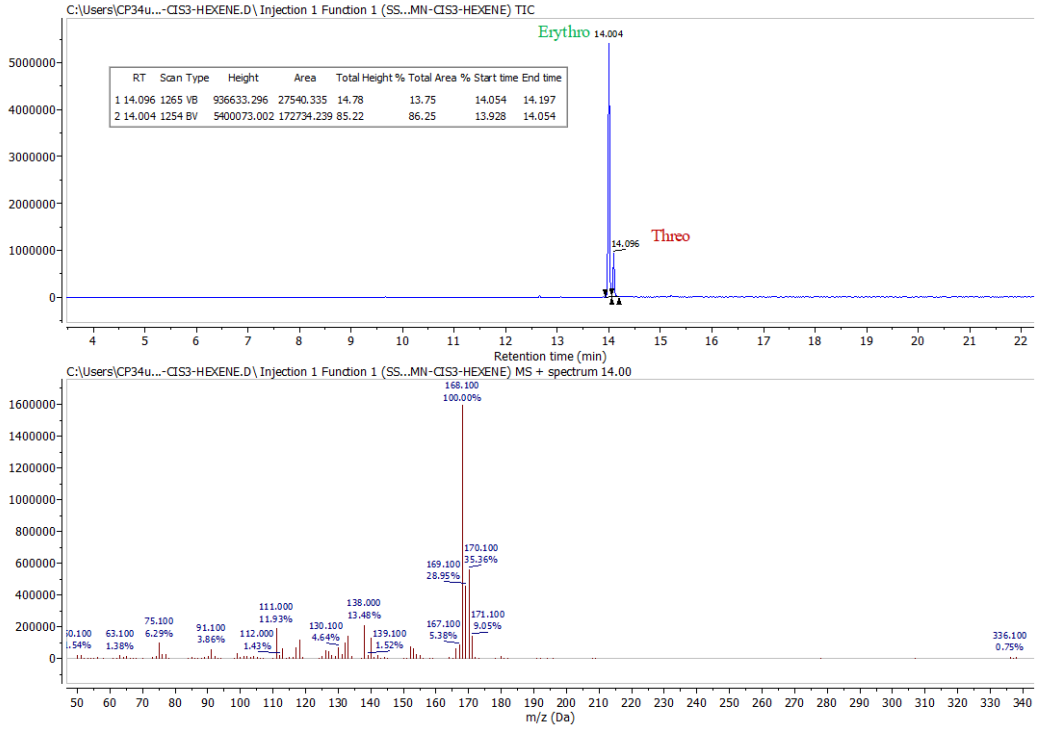


Figure A.1 GC-MS analysis of the 1,2-diamines derived from *cis*-3-hexene

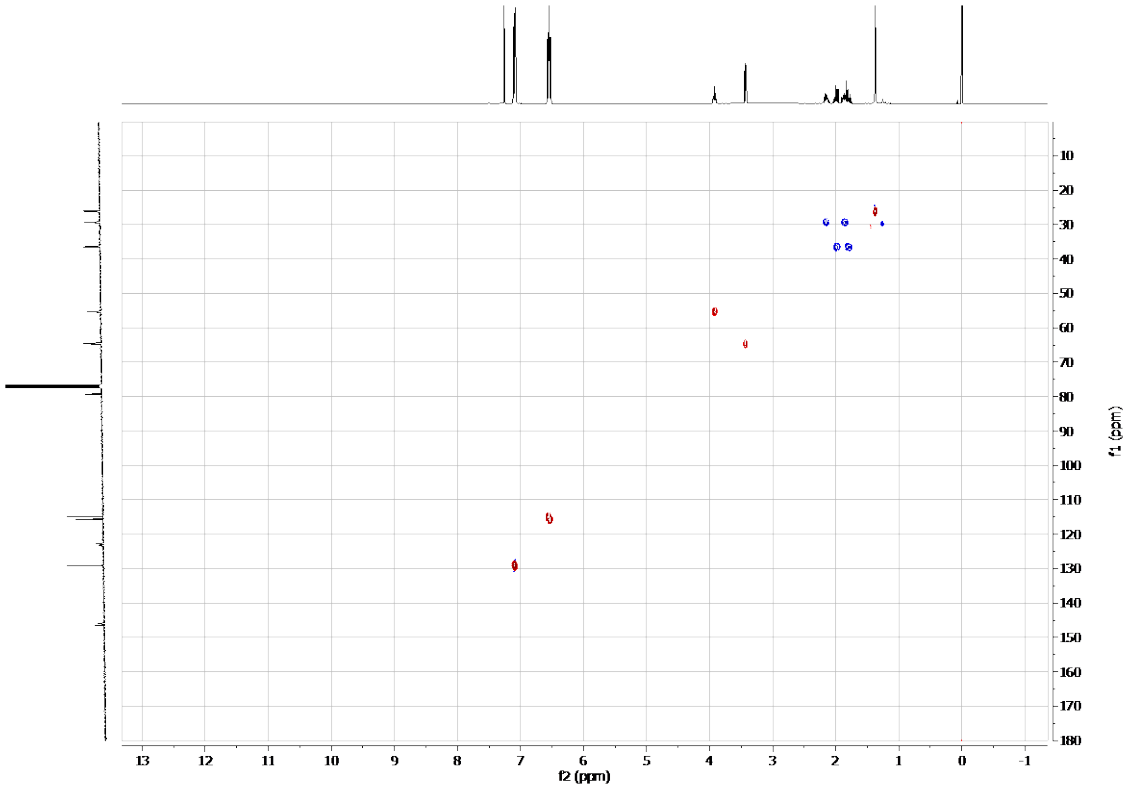


Figure A.2 HSQC spectrum of 2,3-bis[(4-chlorophenyl)amino]-1-methylcyclopentan-1-ol **112**

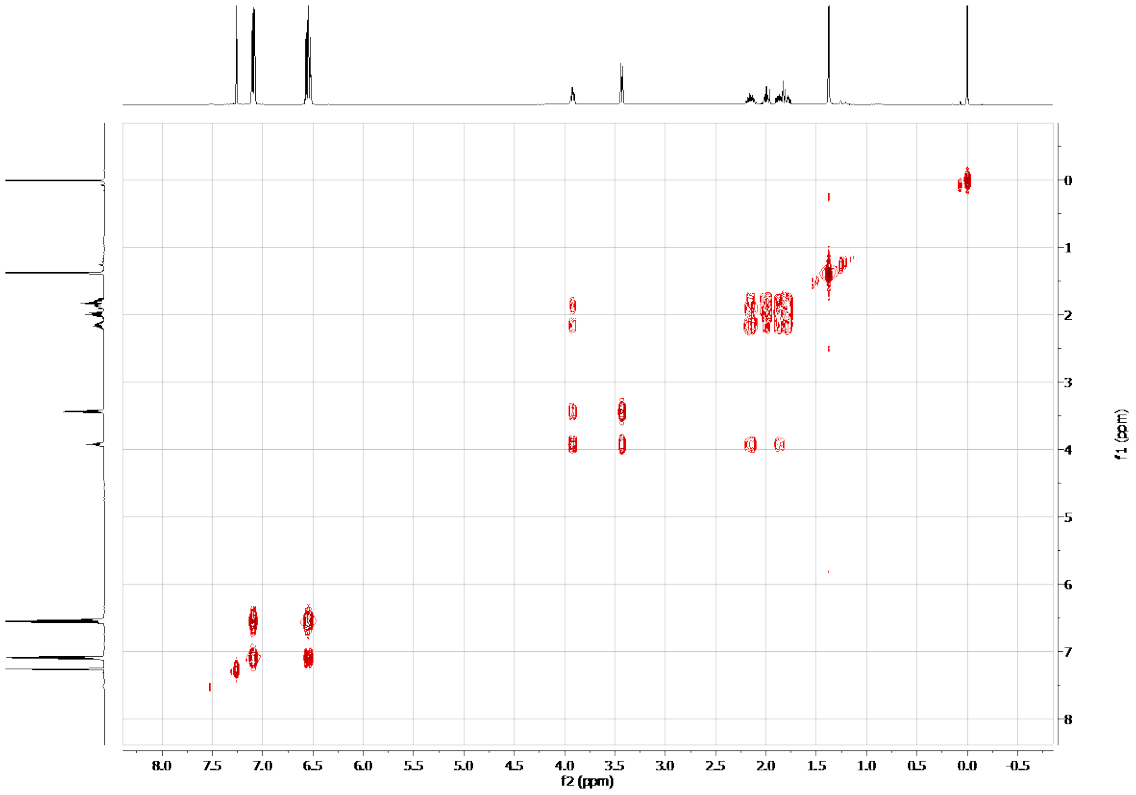
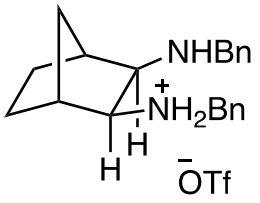


Figure A.3 $^{1}H–^{1}H$ COSY spectrum of spectrum of 2,3-bis[(4-chlorophenyl)amino]-1-methylcyclopentan-1-ol **112**

Crystal data for N^2,N^3-dibenzylbicyclo[2.2.1]heptane-2,3-diamine as a triflate salt

CCDC reference number: 2179887

UK Chem reference number: m21092



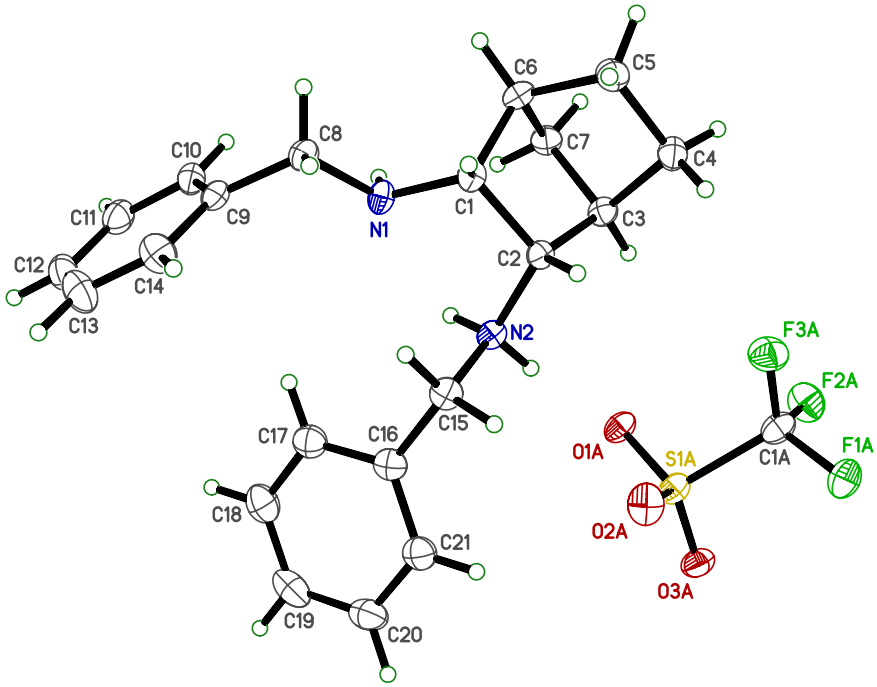


Table A.1 Crystal data and structure refinement for N^2,N^3-dibenzylbicyclo[2.2.1]heptane-2,3-diamine as a triflate salt.

Empirical formula	C_{22} H_{27} F_3 N_2 O_3 S
Formula weight	456.51
Temperature	90.0(2) K
Wavelength	0.71073 Å
Crystal system, space group	Triclinic, P-1
Unit cell dimensions	a = 8.9559(4) Å alpha = 113.448(1) deg. b = 10.8064(5) Å beta = 97.634(1) deg. c = 12.6474(6) Å gamma = 95.970(1) deg.
Volume	1096.31(9) Å^3
Z, Calculated density	2, 1.383 Mg/m^3
Absorption coefficient	0.199 mm^-1
F(000)	480
Crystal size	0.290 x 0.100 x 0.020 mm
Theta range for data collection	2.085 to 27.537 deg.
Limiting indices	-11<=h<=11, -14<=k<=14, -16<=l<=16
Reflections collected / unique	25410 / 4973 [R(int) = 0.0634]
Completeness to theta = 25.242	99.9 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.971 and 0.893
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4973 / 0 / 284
Goodness-of-fit on F^2	1.029
Final R indices [I>2sigma(I)]	R1 = 0.0444, wR2 = 0.0724
R indices (all data)	R1 = 0.0917, wR2 = 0.0852
Extinction coefficient	0.0056(7)
Largest diff. peak and hole	0.325 and -0.338 e. Å^-3

Table A.2 Mol Representation of N^2,N^3-dibenzylbicyclo[2.2.1]heptane-2,3-diamine as a triflate salt.

```
Mrv2211 05162214383D

 58 60  0  0  0  0            999 V2000
    0.2937    3.3994    8.0773 S   0  0  1  0  0  0  0  0  0  0  0  0
    0.4366    4.9759    5.9916 F   0  0  0  0  0  0  0  0  0  0  0  0
   -1.5514    4.7705    6.7898 F   0  0  0  0  0  0  0  0  0  0  0  0
   -0.0979    5.9747    7.8185 F   0  0  0  0  0  0  0  0  0  0  0  0
   -0.6312    3.3816    9.2061 O   0  0  0  0  0  0  0  0  0  0  0  0
    1.6345    3.7619    8.4465 O   0  5  0  0  0  0  0  0  0  0  0  0
    0.1505    2.2924    7.1800 O   0  0  0  0  0  0  0  0  0  0  0  0
   -0.2667    4.8445    7.1204 C   0  0  1  0  0  0  0  0  0  0  0  0
    6.2626    5.7731    6.3537 N   0  0  1  0  0  0  0  0  0  0  0  0
    6.5123    6.0758    7.1430 H   0  0  0  0  0  0  0  0  0  0  0  0
    3.9978    4.5097    6.9382 N   0  3  2  0  0  0  0  0  0  0  0  0
    3.2779    4.2659    7.4386 H   0  0  0  0  0  0  0  0  0  0  0  0
    4.7212    4.5450    7.4893 H   0  0  0  0  0  0  0  0  0  0  0  0
    5.0976    6.5350    5.8899 C   0  0  1  0  0  0  0  0  0  0  0  0
    5.1108    6.5953    4.8915 H   0  0  0  0  0  0  0  0  0  0  0  0
    3.7551    5.8701    6.3612 C   0  0  2  0  0  0  0  0  0  0  0  0
    3.1376    5.7883    5.5786 H   0  0  0  0  0  0  0  0  0  0  0  0
    3.1686    6.8787    7.3618 C   0  0  2  0  0  0  0  0  0  0  0  0
    2.5759    6.4865    8.0650 H   0  0  0  0  0  0  0  0  0  0  0  0
    2.5274    7.9884    6.5057 C   0  0  2  0  0  0  0  0  0  0  0  0
    2.0470    8.6443    7.0708 H   0  0  0  0  0  0  0  0  0  0  0  0
    1.8993    7.6107    5.8406 H   0  0  0  0  0  0  0  0  0  0  0  0
    3.7585    8.6366    5.8137 C   0  0  1  0  0  0  0  0  0  0  0  0
    3.7505    8.4643    4.8389 H   0  0  0  0  0  0  0  0  0  0  0  0
    3.7806    9.6141    5.9690 H   0  0  0  0  0  0  0  0  0  0  0  0
    4.9563    7.9405    6.4901 C   0  0  1  0  0  0  0  0  0  0  0  0
    5.8001    8.4769    6.4925 H   0  0  0  0  0  0  0  0  0  0  0  0
```

Table A.2 Mol Representation of N^2,N^3-dibenzylbicyclo[2.2.1]heptane-2,3-diamine as a triflate salt, continued

4.4059	7.6146	7.8852	C	0	0	2	0	0	0	0	0	0	0	0	0
5.0082	7.0287	8.4078	H	0	0	0	0	0	0	0	0	0	0	0	0
4.1782	8.4250	8.4062	H	0	0	0	0	0	0	0	0	0	0	0	0
7.4260	5.8769	5.4557	C	0	0	2	0	0	0	0	0	0	0	0	0
7.8111	6.7870	5.5162	H	0	0	0	0	0	0	0	0	0	0	0	0
7.1380	5.7260	4.5209	H	0	0	0	0	0	0	0	0	0	0	0	0
8.4733	4.8598	5.8315	C	0	0	0	0	0	0	0	0	0	0	0	0
9.1498	4.9718	7.0379	C	0	0	0	0	0	0	0	0	0	0	0	0
8.9837	5.7174	7.6029	H	0	0	0	0	0	0	0	0	0	0	0	0
10.0673	4.0054	7.4279	C	0	0	0	0	0	0	0	0	0	0	0	0
10.5115	4.0846	8.2637	H	0	0	0	0	0	0	0	0	0	0	0	0
10.3359	2.9308	6.6064	C	0	0	0	0	0	0	0	0	0	0	0	0
10.9620	2.2689	6.8751	H	0	0	0	0	0	0	0	0	0	0	0	0
9.6909	2.8221	5.3927	C	0	0	0	0	0	0	0	0	0	0	0	0
9.8853	2.0936	4.8144	H	0	0	0	0	0	0	0	0	0	0	0	0
8.7570	3.7763	5.0154	C	0	0	0	0	0	0	0	0	0	0	0	0
8.3045	3.6856	4.1847	H	0	0	0	0	0	0	0	0	0	0	0	0
4.2370	3.4675	5.8790	C	0	0	1	0	0	0	0	0	0	0	0	0
3.4098	3.3437	5.3486	H	0	0	0	0	0	0	0	0	0	0	0	0
4.9484	3.7803	5.2660	H	0	0	0	0	0	0	0	0	0	0	0	0
4.6411	2.1546	6.4797	C	0	0	0	0	0	0	0	0	0	0	0	0
5.9324	1.9731	6.9604	C	0	0	0	0	0	0	0	0	0	0	0	0
6.5614	2.6829	6.9042	H	0	0	0	0	0	0	0	0	0	0	0	0
6.3062	0.7630	7.5186	C	0	0	0	0	0	0	0	0	0	0	0	0
7.1871	0.6492	7.8569	H	0	0	0	0	0	0	0	0	0	0	0	0
5.4023	-0.2788	7.5861	C	0	0	0	0	0	0	0	0	0	0	0	0
5.6605	-1.1071	7.9731	H	0	0	0	0	0	0	0	0	0	0	0	0
4.1257	-0.1196	7.0923	C	0	0	0	0	0	0	0	0	0	0	0	0
3.5104	-0.8428	7.1256	H	0	0	0	0	0	0	0	0	0	0	0	0

Table A.2 Mol Representation of N^2,N^3-dibenzylbicyclo[2.2.1]heptane-2,3-diamine as a triflate salt, continued

```
  3.7379    1.0989    6.5462 C   0  0  0  0  0  0  0  0  0  0  0  0
  2.8532    1.2103    6.2178 H   0  0  0  0  0  0  0  0  0  0  0  0
 1  5  2  0  0  0  0
 1  6  1  0  0  0  0
 1  7  2  0  0  0  0
 1  8  1  0  0  0  0
 2  8  1  0  0  0  0
 3  8  1  0  0  0  0
 4  8  1  0  0  0  0
 9 10  1  0  0  0  0
 9 14  1  0  0  0  0
 9 31  1  0  0  0  0
11 12  1  0  0  0  0
11 13  1  0  0  0  0
11 16  1  0  0  0  0
11 45  1  0  0  0  0
14 15  1  0  0  0  0
14 16  1  0  0  0  0
14 26  1  0  0  0  0
16 17  1  0  0  0  0
16 18  1  0  0  0  0
18 19  1  0  0  0  0
18 20  1  0  0  0  0
18 28  1  0  0  0  0
20 21  1  0  0  0  0
20 22  1  0  0  0  0
20 23  1  0  0  0  0
23 24  1  0  0  0  0
```

Table A.2 Mol Representation of N^2,N^3-dibenzylbicyclo[2.2.1]heptane-2,3-diamine as a triflate salt, continued

```
 23 25  1  0  0  0  0
 23 26  1  0  0  0  0
 26 27  1  0  0  0  0
 26 28  1  0  0  0  0
 28 29  1  0  0  0  0
 28 30  1  0  0  0  0
 31 32  1  0  0  0  0
 31 33  1  0  0  0  0
 31 34  1  0  0  0  0
 34 35  2  0  0  0  0
 34 43  1  0  0  0  0
 35 36  1  0  0  0  0
 35 37  1  0  0  0  0
 37 38  1  0  0  0  0
 37 39  2  0  0  0  0
 39 40  1  0  0  0  0
 39 41  1  0  0  0  0
 41 42  1  0  0  0  0
 41 43  2  0  0  0  0
 43 44  1  0  0  0  0
 45 46  1  0  0  0  0
 45 47  1  0  0  0  0
 45 48  1  0  0  0  0
 48 49  2  0  0  0  0
 48 57  1  0  0  0  0
 49 50  1  0  0  0  0
 49 51  1  0  0  0  0
 51 52  1  0  0  0  0
```

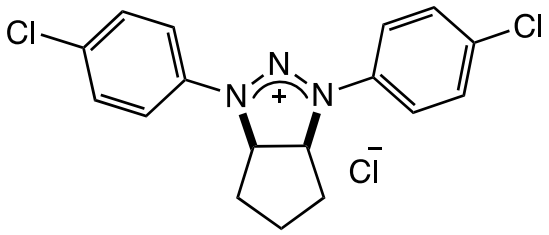
Table A.2 Mol Representation of N^2,N^3-dibenzylbicyclo[2.2.1]heptane-2,3-diamine as a triflate salt, continued

```
 51 53  2  0  0  0  0
 53 54  1  0  0  0  0
 53 55  1  0  0  0  0
 55 56  1  0  0  0  0
 55 57  2  0  0  0  0
57 58  1  0  0  0  0
M  CHG  2   6  -1  11   1
M  END
```

Crystal data for 1,3-bis(4-chlorophenyl)-3H,3aH,4H,5H,6H,6aH-cyclopenta[d][1,2,3]triazol-1-ylium

CCDC reference number: 2179891

UK Chem reference number: m22040



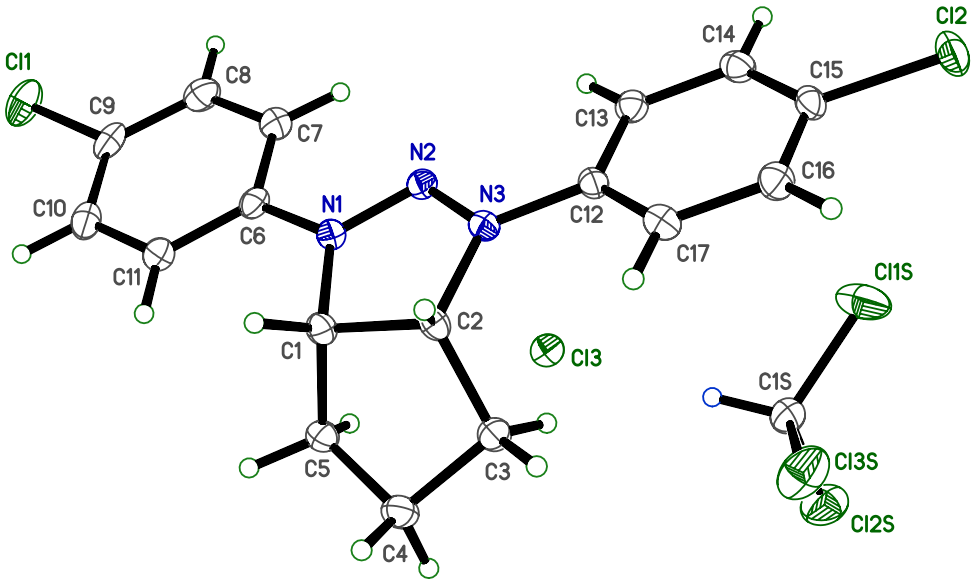


Table B.1 Crystal data and structure refinement for 1,3-bis(4-chlorophenyl)-3H,3aH,4H,5H,6H,6aH-cyclopenta[d][1,2,3]triazol-1-ylium chloride.

Empirical formula	C_{18} H_{16} C_{16} D N_3
Formula weight	489.05
Temperature	90.0(2) K
Wavelength	0.71073 Å
Crystal system, space group	Monoclinic, P2(1)/n
Unit cell dimensions	a = 16.4136(3) Å alpha = 90 deg. b = 7.4744(2) Å beta = 90.481(1) deg. c = 17.1540(4) Å gamma = 90 deg.
Volume	2104.41(8) Å^3
Z, Calculated density	4, 1.544 Mg/m^3
Absorption coefficient	0.826 mm^-1
F(000)	992
Crystal size	0.200 x 0.160 x 0.100 mm
Theta range for data collection	2.375 to 27.510 deg.
Limiting indices	-21<=h<=21, -9<=k<=9, -22<=l<=22
Reflections collected / unique	33843 / 4839 [R(int) = 0.0403]
Completeness to theta = 25.242	99.7 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.971 and 0.860
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4839 / 6 / 257
Goodness-of-fit on F^2	1.037
Final R indices [I>2sigma(I)]	R1 = 0.0289, wR2 = 0.0709
R indices (all data)	R1 = 0.0330, wR2 = 0.0739
Extinction coefficient	n/a
Largest diff. peak and hole	0.379 and -0.352 e.Å^-3

Table B.2 Mol representation of 1,3-bis(4-chlorophenyl)-3H,3aH,4H,5H,6H,6aH-cyclopenta[d][1,2,3]triazol-1-ylium chloride.

```
Mrv2211 05162211133D

 44 45  0  0  0  0            999 V2000
   12.9065    1.0903   10.3931 Cl  0  0  0  0  0  0  0  0  0  0  0  0
    3.9516    5.1320    2.0312 Cl  0  0  0  0  0  0  0  0  0  0  0  0
    8.6240    0.5235    6.3803 N   0  3  0  0  0  0  0  0  0  0  0  0
    8.0473    1.5636    5.8674 N   0  0  0  0  0  0  0  0  0  0  0  0
    7.2272    1.1857    4.9427 N   0  0  0  0  0  0  0  0  0  0  0  0
    8.1422   -0.7611    5.8339 C   0  0  2  0  0  0  0  0  0  0  0  0
    8.8872   -1.2995    5.4399 H   0  0  0  0  0  0  0  0  0  0  0  0
    7.1484   -0.2824    4.7546 C   0  0  1  0  0  0  0  0  0  0  0  0
    7.4417   -0.5528    3.8376 H   0  0  0  0  0  0  0  0  0  0  0  0
    5.7833   -0.8912    5.1151 C   0  0  1  0  0  0  0  0  0  0  0  0
    5.2147   -0.2315    5.5860 H   0  0  0  0  0  0  0  0  0  0  0  0
    5.3094   -1.2033    4.3038 H   0  0  0  0  0  0  0  0  0  0  0  0
    6.1320   -2.0698    6.0337 C   0  0  1  0  0  0  0  0  0  0  0  0
    5.3694   -2.2942    6.6241 H   0  0  0  0  0  0  0  0  0  0  0  0
    6.3742   -2.8701    5.5042 H   0  0  0  0  0  0  0  0  0  0  0  0
    7.3255   -1.5754    6.8507 C   0  0  1  0  0  0  0  0  0  0  0  0
    7.8533   -2.3345    7.2049 H   0  0  0  0  0  0  0  0  0  0  0  0
    7.0296   -1.0076    7.6058 H   0  0  0  0  0  0  0  0  0  0  0  0
    9.6005    0.6734    7.4011 C   0  0  0  0  0  0  0  0  0  0  0  0
    9.9235    1.9382    7.8829 C   0  0  0  0  0  0  0  0  0  0  0  0
    9.4552    2.7056    7.5759 H   0  0  0  0  0  0  0  0  0  0  0  0
   10.9397    2.0612    8.8185 C   0  0  0  0  0  0  0  0  0  0  0  0
   11.1759    2.9160    9.1587 H   0  0  0  0  0  0  0  0  0  0  0  0
   11.6088    0.9276    9.2529 C   0  0  0  0  0  0  0  0  0  0  0  0
   11.2563   -0.3338    8.8088 C   0  0  0  0  0  0  0  0  0  0  0  0
   11.7065   -1.1024    9.1391 H   0  0  0  0  0  0  0  0  0  0  0  0
   10.2385   -0.4650    7.8740 C   0  0  0  0  0  0  0  0  0  0  0  0
```

Table B.2 Mol representation of 1,3-bis(4-chlorophenyl)-3H,3aH,4H,5H,6H,6aH-cyclopenta[d][1,2,3]triazol-1-ylium chloride, continued

9.9813	-1.3244	7.5616	H	0	0	0	0	0	0	0	0	0	0	0	0		
6.4615	2.1540	4.2421	C	0	0	0	0	0	0	0	0	0	0	0	0		
6.4824	3.4904	4.6356	C	0	0	0	0	0	0	0	0	0	0	0	0		
7.0125	3.7665	5.3739	H	0	0	0	0	0	0	0	0	0	0	0	0		
5.7203	4.4109	3.9356	C	0	0	0	0	0	0	0	0	0	0	0	0		
5.7250	5.3277	4.1849	H	0	0	0	0	0	0	0	0	0	0	0	0		
4.9486	3.9779	2.8648	C	0	0	0	0	0	0	0	0	0	0	0	0		
4.9332	2.6576	2.4608	C	0	0	0	0	0	0	0	0	0	0	0	0		
4.4044	2.3845	1.7204	H	0	0	0	0	0	0	0	0	0	0	0	0		
5.7057	1.7351	3.1575	C	0	0	0	0	0	0	0	0	0	0	0	0		
5.7157	0.8231	2.8920	H	0	0	0	0	0	0	0	0	0	0	0	0		
2.4884	3.4757	5.3720	Cl	0	0	0	0	0	0	0	0	0	0	0	0		
1.1563	1.5226	7.0316	Cl	0	0	0	0	0	0	0	0	0	0	0	0		
2.3837	0.7132	4.5420	Cl	0	0	0	0	0	0	0	0	0	0	0	0		
2.4954	1.8018	5.9164	C	0	0	1	0	0	0	0	0	0	0	0	0		
3.3547	1.6243	6.3963	D	0	0	0	0	0	0	0	0	0	0	0	0		
8.5417	3.7917	0.0000	Cl	0	5	0	0	0	0	0	0	0	0	0	0		
1 24	1	0	0	0	0												
2 34	1	0	0	0	0												
3 4	2	0	0	0	0												
3 6	1	0	0	0	0												
3 19	1	0	0	0	0												
4 5	1	0	0	0	0												
5 8	1	0	0	0	0												
5 29	1	0	0	0	0												
6 7	1	0	0	0	0												
6 8	1	0	0	0	0												
6 16	1	0	0	0	0												
8 9	1	0	0	0	0												

Table B.2 Mol representation of 1,3-bis(4-chlorophenyl)-3H,3aH,4H,5H,6H,6aH-cyclopenta[d][1,2,3]triazol-1-ylium chloride, continued

```
  8 10  1  0  0  0  0
 10 11  1  0  0  0  0
 10 12  1  0  0  0  0
 10 13  1  0  0  0  0
 13 14  1  0  0  0  0
 13 15  1  0  0  0  0
 13 16  1  0  0  0  0
 16 17  1  0  0  0  0
 16 18  1  0  0  0  0
 19 20  1  0  0  0  0
 19 27  2  0  0  0  0
 20 21  1  0  0  0  0
 22 23  1  0  0  0  0
 22 24  1  0  0  0  0
 24 25  2  0  0  0  0
 25 26  1  0  0  0  0
 25 27  1  0  0  0  0
 27 28  1  0  0  0  0
 29 30  2  0  0  0  0
 29 37  1  0  0  0  0
 30 31  1  0  0  0  0
 30 32  1  0  0  0  0
 32 33  1  0  0  0  0
 32 34  2  0  0  0  0
 34 35  1  0  0  0  0
 35 36  1  0  0  0  0
 35 37  2  0  0  0  0
 37 38  1  0  0  0  0
```

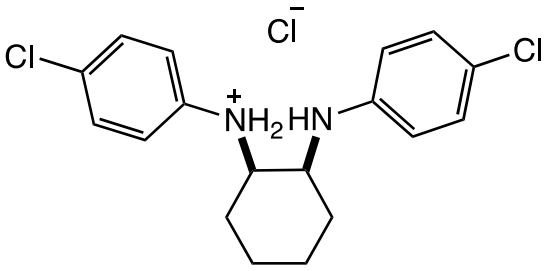
Table B.2 Mol representation of 1,3-bis(4-chlorophenyl)-3H,3aH,4H,5H,6H,6aH-cyclopenta[d][1,2,3]triazol-1-ylium chloride, continued

```
 39 42  1  0  0  0  0
 40 42  1  0  0  0  0
 41 42  1  0  0  0  0
 42 43  1  0  0  0  0
 20 22  2  0  0  0  0
M  CHG  2   3   1  44  -1
M  END
```

Crystal data for N^1,N^2-bis(4-chlorophenyl)cyclopentane-1,2-diamine as a HCl salt

CCDC reference number: 2179894

UK Chem reference number: m21371



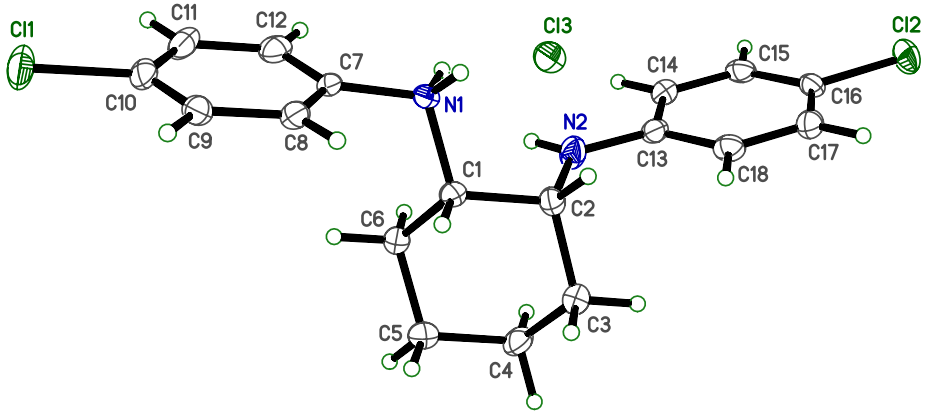


Table C.1 Crystal data and structure refinement for N^1,N^2-bis(4-chlorophenyl)cyclopentane-1,2-diamine as a HCl salt.

Empirical formula	C_{18} H_{21} C_{13} N_2
Formula weight	371.72
Temperature	90.0(2) K
Wavelength	0.71073 Å
Crystal system, space group	Orthorhombic, Pna2(1)
Unit cell dimensions	a = 13.8660(4) Å alpha = 90 deg. b = 21.1936(7) Å beta = 90 deg. c = 6.0462(2) Å gamma = 90 deg.
Volume	1776.8(1) Å^3
Z, Calculated density	4, 1.390 Mg/m^3
Absorption coefficient	0.516 mm^-1
F(000)	776
Crystal size	0.330 x 0.020 x 0.010 mm
Theta range for data collection	1.922 to 27.542 deg.
Limiting indices	-17<=h<=18, -27<=k<=27, -7<=l<=7
Reflections collected / unique	31407 / 4068 [R(int) = 0.0569]
Completeness to theta = 25.242	99.9 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.971 and 0.846
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4068 / 1 / 221
Goodness-of-fit on F^2	1.055
Final R indices [I>2sigma(I)]	R1 = 0.0343, wR2 = 0.0709
R indices (all data)	R1 = 0.0444, wR2 = 0.0757
Absolute structure parameter	0.01(3)
Extinction coefficient	n/a
Largest diff. peak and hole	0.389 and -0.309 e.Å^-3

Table C.2 Mol representation of N^1,N^2-bis(4-chlorophenyl)cyclopentane-1,2-diamine as a Hcl salt.

```
Mrv2211 05162213413D

 44 45  0  0  0  0            999 V2000
   10.2035   12.0637    0.3237 Cl  0  0  0  0  0  0  0  0  0  0  0  0
   -3.0807   11.5212    5.5030 Cl  0  0  0  0  0  0  0  0  0  0  0  0
    4.7530   11.1473    2.5004 N   0  3  1  0  0  0  0  0  0  0  0  0
    4.2135   10.8398    1.9007 H   0  0  0  0  0  0  0  0  0  0  0  0
    4.3521   11.8866    2.8433 H   0  0  0  0  0  0  0  0  0  0  0  0
    2.7397   10.9782    4.5793 N   0  0  0  0  0  0  0  0  0  0  0  0
    3.2462   11.6205    4.7565 H   0  0  0  0  0  0  0  0  0  0  0  0
    4.8076   10.0890    3.5887 C   0  0  2  0  0  0  0  0  0  0  0  0
    5.1484    9.2510    3.1626 H   0  0  0  0  0  0  0  0  0  0  0  0
    3.3983    9.7854    4.1033 C   0  0  1  0  0  0  0  0  0  0  0  0
    2.8624    9.4163    3.3436 H   0  0  0  0  0  0  0  0  0  0  0  0
    3.4959    8.7001    5.1938 C   0  0  1  0  0  0  0  0  0  0  0  0
    2.5986    8.5459    5.5823 H   0  0  0  0  0  0  0  0  0  0  0  0
    3.8005    7.8519    4.7840 H   0  0  0  0  0  0  0  0  0  0  0  0
    4.4562    9.0955    6.2961 C   0  0  2  0  0  0  0  0  0  0  0  0
    4.5017    8.3718    6.9706 H   0  0  0  0  0  0  0  0  0  0  0  0
    4.1265    9.9136    6.7450 H   0  0  0  0  0  0  0  0  0  0  0  0
    5.8463    9.3503    5.7289 C   0  0  2  0  0  0  0  0  0  0  0  0
    6.1949    8.5198    5.3178 H   0  0  0  0  0  0  0  0  0  0  0  0
    6.4602    9.6131    6.4600 H   0  0  0  0  0  0  0  0  0  0  0  0
    5.7943   10.4630    4.6758 C   0  0  2  0  0  0  0  0  0  0  0  0
    5.5170   11.3131    5.1013 H   0  0  0  0  0  0  0  0  0  0  0  0
    6.6930   10.5930    4.2820 H   0  0  0  0  0  0  0  0  0  0  0  0
    6.0778   11.4099    1.8989 C   0  0  0  0  0  0  0  0  0  0  0  0
    6.7041   10.3907    1.2107 C   0  0  0  0  0  0  0  0  0  0  0  0
    6.2626    9.5607    1.0712 H   0  0  0  0  0  0  0  0  0  0  0  0
```

Table C.2 Mol representation of N^1,N^2-bis(4-chlorophenyl)cyclopentane-1,2-diamine as a Hcl salt, continued

```
  7.9868   10.5949    0.7265 C   0  0  0  0  0  0  0  0  0  0  0  0
  8.4406    9.9058    0.2555 H   0  0  0  0  0  0  0  0  0  0  0  0
  8.5942   11.8158    0.9414 C   0  0  0  0  0  0  0  0  0  0  0  0
  7.9477   12.8434    1.6023 C   0  0  0  0  0  0  0  0  0  0  0  0
  8.3767   13.6834    1.7182 H   0  0  0  0  0  0  0  0  0  0  0  0
  6.6702   12.6377    2.0932 C   0  0  0  0  0  0  0  0  0  0  0  0
  6.2111   13.3302    2.5544 H   0  0  0  0  0  0  0  0  0  0  0  0
  1.3750   11.0511    4.7766 C   0  0  0  0  0  0  0  0  0  0  0  0
  0.8429   12.2271    5.3248 C   0  0  0  0  0  0  0  0  0  0  0  0
  1.4236   12.9460    5.5450 H   0  0  0  0  0  0  0  0  0  0  0  0
 -0.5168   12.3549    5.5498 C   0  0  0  0  0  0  0  0  0  0  0  0
 -0.8633   13.1545    5.9282 H   0  0  0  0  0  0  0  0  0  0  0  0
 -1.3671   11.3226    5.2224 C   0  0  0  0  0  0  0  0  0  0  0  0
 -0.8817   10.1449    4.6920 C   0  0  0  0  0  0  0  0  0  0  0  0
 -1.4737    9.4340    4.4761 H   0  0  0  0  0  0  0  0  0  0  0  0
  0.4897   10.0135    4.4771 C   0  0  0  0  0  0  0  0  0  0  0  0
  0.8288    9.2012    4.1196 H   0  0  0  0  0  0  0  0  0  0  0  0
  3.9457   12.8470   -0.3326 Cl  0  5  0  0  0  0  0  0  0  0  0  0
 1 29  1  0  0  0  0
 2 39  1  0  0  0  0
 3  4  1  0  0  0  0
 3  5  1  0  0  0  0
 3  8  1  0  0  0  0
 3 24  1  0  0  0  0
 6  7  1  0  0  0  0
 6 10  1  0  0  0  0
 6 34  1  0  0  0  0
 8  9  1  0  0  0  0
```

Table C.2 Mol representation of N^1,N^2-bis(4-chlorophenyl)cyclopentane-1,2-diamine as a Hcl salt, continued

```
  8 10  1  0  0  0  0
  8 21  1  0  0  0  0
 10 11  1  0  0  0  0
 10 12  1  0  0  0  0
 12 13  1  0  0  0  0
 12 14  1  0  0  0  0
 12 15  1  0  0  0  0
 15 16  1  0  0  0  0
 15 17  1  0  0  0  0
 15 18  1  0  0  0  0
 18 19  1  0  0  0  0
 18 20  1  0  0  0  0
 18 21  1  0  0  0  0
 21 22  1  0  0  0  0
 21 23  1  0  0  0  0
 24 25  2  0  0  0  0
 24 32  1  0  0  0  0
 25 26  1  0  0  0  0
 25 27  1  0  0  0  0
 27 28  1  0  0  0  0
 27 29  2  0  0  0  0
 29 30  1  0  0  0  0
 30 31  1  0  0  0  0
 30 32  2  0  0  0  0
 32 33  1  0  0  0  0
 34 35  1  0  0  0  0
 34 42  2  0  0  0  0
 35 36  1  0  0  0  0
```

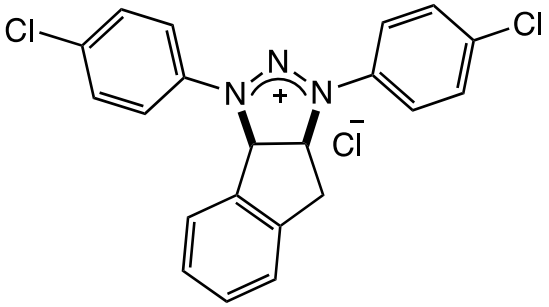
Table C.2 Mol representation of N^1,N^2-bis(4-chlorophenyl)cyclopentane-1,2-diamine as a Hcl salt, continued

```
 35 37  2  0  0  0  0
 37 38  1  0  0  0  0
 37 39  1  0  0  0  0
 39 40  2  0  0  0  0
 40 41  1  0  0  0  0
 40 42  1  0  0  0  0
 42 43  1  0  0  0  0
M  CHG  2   3   1  44  -1
M  END
```

1,3-bis(4-chlorophenyl)-3H,3aH,8H,8aH-indeno[1,2-d][1,2,3]triazol-1-ylium chloride

CCDC reference number: 2179892

UK Chem reference number: m21081



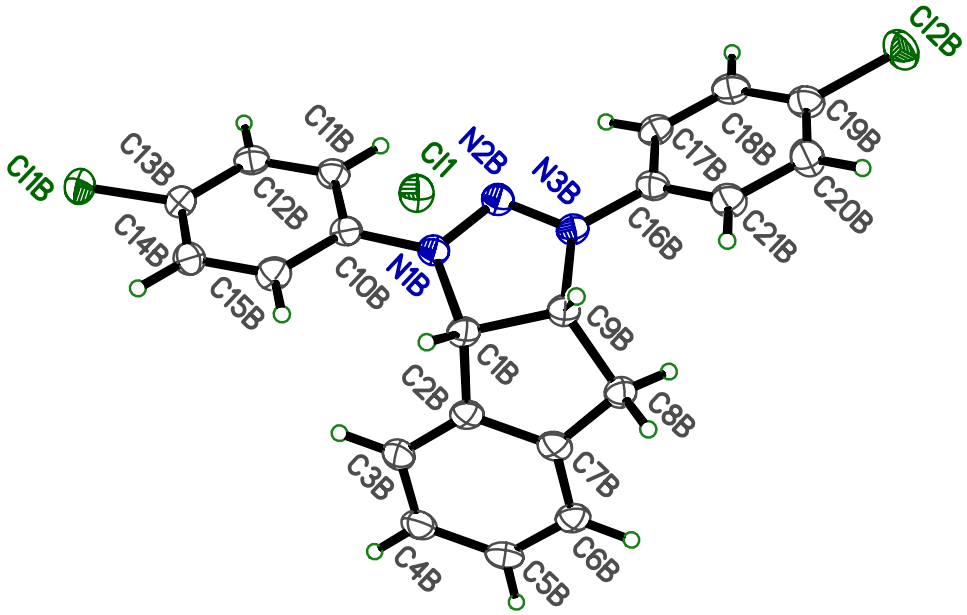


Table D.1 Crystal data and structure refinement for 1,3-bis(4-chlorophenyl)-3H,3aH,8H,8aH-indeno[1,2-d][1,2,3]triazol-1-ylium chloride.

Empirical formula	C_{43} H_{34} C_{18} N_6
Formula weight	918.36
Temperature	90.0(2) K
Wavelength	0.71073 Å
Crystal system, space group	Triclinic, P-1
Unit cell dimensions	a = 8.3639(9) Å alpha = 84.642(3) deg. b = 13.0400(18) Å beta = 88.148(4) deg. c = 18.756(3) Å gamma = 86.631(5) deg.
Volume	2032.5(5) Å^3
Z, Calculated density	2, 1.501 Mg/m^3
Absorption coefficient	0.596 mm^-1
F(000)	940
Crystal size	0.240 x 0.080 x 0.060 mm
Theta range for data collection	1.993 to 27.517 deg.
Limiting indices	-10<=h<=9, -16<=k<=16, -24<=l<=24
Reflections collected / unique	67981 / 9338 [R(int) = 0.0452]
Completeness to theta = 25.242	99.9 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.971 and 0.893
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	9338 / 0 / 514
Goodness-of-fit on F^2	1.019
Final R indices [I>2sigma(I)]	R1 = 0.0448, wR2 = 0.1015
R indices (all data)	R1 = 0.0610, wR2 = 0.1115
Extinction coefficient	n/a
Largest diff. peak and hole	0.948 and -0.854 e.Å^-3

Table D.2 Mol representation of 1,3-bis(4-chlorophenyl)-3H,3aH,8H,8aH-indeno[1,2-d][1,2,3]triazol-1-ylium chloride.

```
Mrv2211 05162211313D

 91 96  0  0  0  0            999 V2000
    4.8880    7.7600   11.0065 Cl  0  5  0  0  0  0  0  0  0  0  0  0
    4.9207   10.5156   17.8481 Cl  0  5  0  0  0  0  0  0  0  0  0  0
    1.4218   17.3669   14.2687 Cl  0  0  0  0  0  0  0  0  0  0  0  0
    1.8675   14.9013   12.7932 Cl  0  0  0  0  0  0  0  0  0  0  0  0
    1.1160   15.6283   14.2041 C   0  0  1  0  0  0  0  0  0  0  0  0
    1.4733   15.2011   15.0229 H   0  0  0  0  0  0  0  0  0  0  0  0
    0.1398   15.4670   14.1760 H   0  0  0  0  0  0  0  0  0  0  0  0
   11.5158    6.1299   12.6542 Cl  0  0  0  0  0  0  0  0  0  0  0  0
    0.1129   10.4731    9.3615 Cl  0  0  0  0  0  0  0  0  0  0  0  0
    7.2149   10.1638   12.6923 N   0  3  0  0  0  0  0  0  0  0  0  0
    6.1459    9.9098   12.0209 N   0  0  0  0  0  0  0  0  0  0  0  0
    5.2981   10.8760   12.1608 N   0  0  0  0  0  0  0  0  0  0  0  0
    7.1385   11.4383   13.4820 C   0  0  2  0  0  0  0  0  0  0  0  0
    7.9093   12.0486   13.2976 H   0  0  0  0  0  0  0  0  0  0  0  0
    6.9269   11.2024   14.9674 C   0  0  0  0  0  0  0  0  0  0  0  0
    7.8205   10.6671   15.8877 C   0  0  0  0  0  0  0  0  0  0  0  0
    8.6754   10.3569   15.6127 H   0  0  0  0  0  0  0  0  0  0  0  0
    7.4312   10.5977   17.2220 C   0  0  0  0  0  0  0  0  0  0  0  0
    8.0137   10.2074   17.8631 H   0  0  0  0  0  0  0  0  0  0  0  0
    6.1943   11.0965   17.6242 C   0  0  0  0  0  0  0  0  0  0  0  0
    5.9530   11.0624   18.5425 H   0  0  0  0  0  0  0  0  0  0  0  0
    5.3115   11.6403   16.7066 C   0  0  0  0  0  0  0  0  0  0  0  0
    4.4700   11.9815   16.9863 H   0  0  0  0  0  0  0  0  0  0  0  0
    5.6849   11.6770   15.3586 C   0  0  0  0  0  0  0  0  0  0  0  0
    4.9119   12.2831   14.2240 C   0  0  2  0  0  0  0  0  0  0  0  0
    4.7821   13.2547   14.3633 H   0  0  0  0  0  0  0  0  0  0  0  0
```

Table D.2 Mol representation of 1,3-bis(4-chlorophenyl)-3H,3aH,8H,8aH-indeno[1,2-d][1,2,3]triazol-1-ylium chloride, continued

4.0264	11.8508	14.1282	H	0	0	0	0	0	0	0	0	0	0	0	0
5.7969	12.0149	12.9814	C	0	0	2	0	0	0	0	0	0	0	0	0
5.9277	12.8403	12.4321	H	0	0	0	0	0	0	0	0	0	0	0	0
8.2585	9.1980	12.6823	C	0	0	0	0	0	0	0	0	0	0	0	0
7.9930	7.9134	12.1813	C	0	0	0	0	0	0	0	0	0	0	0	0
7.1286	7.6890	11.8567	H	0	0	0	0	0	0	0	0	0	0	0	0
9.0090	6.9867	12.1712	C	0	0	0	0	0	0	0	0	0	0	0	0
8.8546	6.1126	11.8327	H	0	0	0	0	0	0	0	0	0	0	0	0
10.2620	7.3348	12.6574	C	0	0	0	0	0	0	0	0	0	0	0	0
10.5192	8.6006	13.1527	C	0	0	0	0	0	0	0	0	0	0	0	0
11.3816	8.8161	13.4879	H	0	0	0	0	0	0	0	0	0	0	0	0
9.5088	9.5539	13.1579	C	0	0	0	0	0	0	0	0	0	0	0	0
9.6724	10.4321	13.4811	H	0	0	0	0	0	0	0	0	0	0	0	0
4.0450	10.7769	11.5009	C	0	0	0	0	0	0	0	0	0	0	0	0
3.6808	9.5705	10.9171	C	0	0	0	0	0	0	0	0	0	0	0	0
4.2542	8.8146	10.9680	H	0	0	0	0	0	0	0	0	0	0	0	0
2.4719	9.4930	10.2633	C	0	0	0	0	0	0	0	0	0	0	0	0
2.2089	8.6784	9.8510	H	0	0	0	0	0	0	0	0	0	0	0	0
1.6357	10.6004	10.2040	C	0	0	0	0	0	0	0	0	0	0	0	0
1.9852	11.7861	10.8045	C	0	0	0	0	0	0	0	0	0	0	0	0
1.3979	12.5320	10.7709	H	0	0	0	0	0	0	0	0	0	0	0	0
3.1999	11.8832	11.4591	C	0	0	0	0	0	0	0	0	0	0	0	0
3.4556	12.6973	11.8768	H	0	0	0	0	0	0	0	0	0	0	0	0
10.2816	5.8357	16.0021	Cl	0	0	0	0	0	0	0	0	0	0	0	0
-0.8286	12.1619	14.0046	Cl	0	0	0	0	0	0	0	0	0	0	0	0
4.6560	6.5146	14.3332	N	0	0	0	0	0	0	0	0	0	0	0	0
4.0581	7.6538	14.4042	N	0	0	0	0	0	0	0	0	0	0	0	0
2.8253	7.5304	14.0271	N	0	3	0	0	0	0	0	0	0	0	0	0
3.7516	5.3979	13.9281	C	0	0	1	0	0	0	0	0	0	0	0	0

Table D.2 Mol representation of 1,3-bis(4-chlorophenyl)-3H,3aH,8H,8aH-indeno[1,2-d][1,2,3]triazol-1-ylium chloride, continued

4.1275	4.8600	13.1734	H	0	0	0	0	0	0	0	0	0	0	0
3.3375	4.5326	15.1009	C	0	0	0	0	0	0	0	0	0	0	0
4.1291	3.7569	15.9371	C	0	0	0	0	0	0	0	0	0	0	0
5.0668	3.6939	15.7964	H	0	0	0	0	0	0	0	0	0	0	0
3.5230	3.0760	16.9813	C	0	0	0	0	0	0	0	0	0	0	0
4.0489	2.5398	17.5631	H	0	0	0	0	0	0	0	0	0	0	0
2.1471	3.1726	17.1846	C	0	0	0	0	0	0	0	0	0	0	0
1.7477	2.7044	17.9084	H	0	0	0	0	0	0	0	0	0	0	0
1.3527	3.9395	16.3482	C	0	0	0	0	0	0	0	0	0	0	0
0.4143	3.9940	16.4862	H	0	0	0	0	0	0	0	0	0	0	0
1.9613	4.6319	15.2967	C	0	0	0	0	0	0	0	0	0	0	0
1.3049	5.5240	14.2879	C	0	0	2	0	0	0	0	0	0	0	0
0.7559	6.2172	14.7337	H	0	0	0	0	0	0	0	0	0	0	0
0.7277	5.0013	13.6767	H	0	0	0	0	0	0	0	0	0	0	0
2.4790	6.1607	13.5241	C	0	0	1	0	0	0	0	0	0	0	0
2.3329	6.1501	12.5350	H	0	0	0	0	0	0	0	0	0	0	0
6.0202	6.3899	14.6892	C	0	0	0	0	0	0	0	0	0	0	0
6.6478	7.3795	15.4463	C	0	0	0	0	0	0	0	0	0	0	0
6.1720	8.1639	15.6930	H	0	0	0	0	0	0	0	0	0	0	0
7.9581	7.2162	15.8343	C	0	0	0	0	0	0	0	0	0	0	0
8.3906	7.8870	16.3499	H	0	0	0	0	0	0	0	0	0	0	0
8.6462	6.0623	15.4673	C	0	0	0	0	0	0	0	0	0	0	0
8.0356	5.0854	14.6991	C	0	0	0	0	0	0	0	0	0	0	0
8.5167	4.3062	14.4468	H	0	0	0	0	0	0	0	0	0	0	0
6.7199	5.2505	14.3006	C	0	0	0	0	0	0	0	0	0	0	0
6.2964	4.5899	13.7653	H	0	0	0	0	0	0	0	0	0	0	0
1.9494	8.6457	14.0361	C	0	0	0	0	0	0	0	0	0	0	0
2.2488	9.7632	14.8163	C	0	0	0	0	0	0	0	0	0	0	0

Table D.2 Mol representation of 1,3-bis(4-chlorophenyl)-3H,3aH,8H,8aH-indeno[1,2-d][1,2,3]triazol-1-ylium chloride, continued

```
    3.0343    9.7763   15.3506 H   0  0  0  0  0  0  0  0  0  0  0  0
    1.3987   10.8475   14.8073 C   0  0  0  0  0  0  0  0  0  0  0  0
    1.5973   11.6185   15.3256 H   0  0  0  0  0  0  0  0  0  0  0  0
    0.2459   10.8007   14.0282 C   0  0  0  0  0  0  0  0  0  0  0  0
   -0.0634    9.6841   13.2645 C   0  0  0  0  0  0  0  0  0  0  0  0
   -0.8614    9.6632   12.7492 H   0  0  0  0  0  0  0  0  0  0  0  0
    0.7996    8.6020   13.2581 C   0  0  0  0  0  0  0  0  0  0  0  0
    0.6077    7.8378   12.7272 H   0  0  0  0  0  0  0  0  0  0  0  0
  3  5  1  0  0  0  0
  4  5  1  0  0  0  0
  5  6  1  0  0  0  0
  5  7  1  0  0  0  0
  8 35  1  0  0  0  0
  9 45  1  0  0  0  0
 10 11  2  0  0  0  0
 10 13  1  0  0  0  0
 10 30  1  0  0  0  0
 11 12  1  0  0  0  0
 12 28  1  0  0  0  0
 12 40  1  0  0  0  0
 13 14  1  0  0  0  0
 13 15  1  0  0  0  0
 13 28  1  0  0  0  0
 15 16  1  0  0  0  0
 15 24  2  0  0  0  0
 16 17  1  0  0  0  0
 16 18  2  0  0  0  0
 18 19  1  0  0  0  0
```

Table D.2 Mol representation of 1,3-bis(4-chlorophenyl)-3H,3aH,8H,8aH-indeno[1,2-d][1,2,3]triazol-1-ylium chloride, continued

```
 18 20  1  0  0  0  0
 20 21  1  0  0  0  0
 20 22  2  0  0  0  0
 22 23  1  0  0  0  0
 22 24  1  0  0  0  0
 24 25  1  0  0  0  0
 25 26  1  0  0  0  0
 25 27  1  0  0  0  0
 25 28  1  0  0  0  0
 28 29  1  0  0  0  0
 30 31  2  0  0  0  0
 30 38  1  0  0  0  0
 31 32  1  0  0  0  0
 31 33  1  0  0  0  0
 33 34  1  0  0  0  0
 33 35  2  0  0  0  0
 35 36  1  0  0  0  0
 36 37  1  0  0  0  0
 36 38  2  0  0  0  0
 38 39  1  0  0  0  0
 40 41  2  0  0  0  0
 40 48  1  0  0  0  0
 41 42  1  0  0  0  0
 41 43  1  0  0  0  0
 43 44  1  0  0  0  0
 43 45  2  0  0  0  0
 45 46  1  0  0  0  0
 46 47  1  0  0  0  0
```

Table D.2 Mol representation of 1,3-bis(4-chlorophenyl)-3H,3aH,8H,8aH-indeno[1,2-d][1,2,3]triazol-1-ylium chloride, continued

```
 46 48  2  0  0  0  0
 48 49  1  0  0  0  0
 50 77  1  0  0  0  0
 51 87  1  0  0  0  0
 52 53  1  0  0  0  0
 52 55  1  0  0  0  0
 52 72  1  0  0  0  0
 53 54  2  0  0  0  0
 54 70  1  0  0  0  0
 54 82  1  0  0  0  0
 55 56  1  0  0  0  0
 55 57  1  0  0  0  0
 55 70  1  0  0  0  0
 57 58  1  0  0  0  0
 57 66  2  0  0  0  0
 58 59  1  0  0  0  0
 58 60  2  0  0  0  0
 60 61  1  0  0  0  0
 60 62  1  0  0  0  0
 62 63  1  0  0  0  0
 62 64  2  0  0  0  0
 64 65  1  0  0  0  0
 64 66  1  0  0  0  0
 66 67  1  0  0  0  0
 67 68  1  0  0  0  0
 67 69  1  0  0  0  0
 67 70  1  0  0  0  0
 70 71  1  0  0  0  0
```

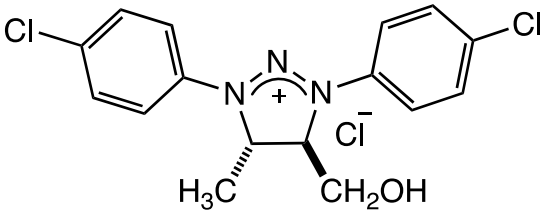
Table D.2 Mol representation of 1,3-bis(4-chlorophenyl)-3H,3aH,8H,8aH-indeno[1,2-d][1,2,3]triazol-1-ylium chloride, continued

```
 72 73  1  0  0  0  0
 72 80  2  0  0  0  0
 73 74  1  0  0  0  0
 73 75  2  0  0  0  0
 75 76  1  0  0  0  0
 75 77  1  0  0  0  0
 77 78  2  0  0  0  0
 78 79  1  0  0  0  0
 78 80  1  0  0  0  0
 80 81  1  0  0  0  0
 82 83  2  0  0  0  0
 82 90  1  0  0  0  0
 83 84  1  0  0  0  0
 83 85  1  0  0  0  0
 85 86  1  0  0  0  0
 85 87  2  0  0  0  0
 87 88  1  0  0  0  0
 88 89  1  0  0  0  0
 88 90  2  0  0  0  0
 90 91  1  0  0  0  0
M  CHG  4   1  -1   2  -1  10   1  54   1
M  END
```

Crystal data for 1,3-bis(4-chlorophenyl)-5-(hydroxymethyl)-4-methyl-4,5-dihydro-3H-1,2,3-triazol-1-ylium chloride

CCDC reference number: 2179895

UK Chem reference number: m21299



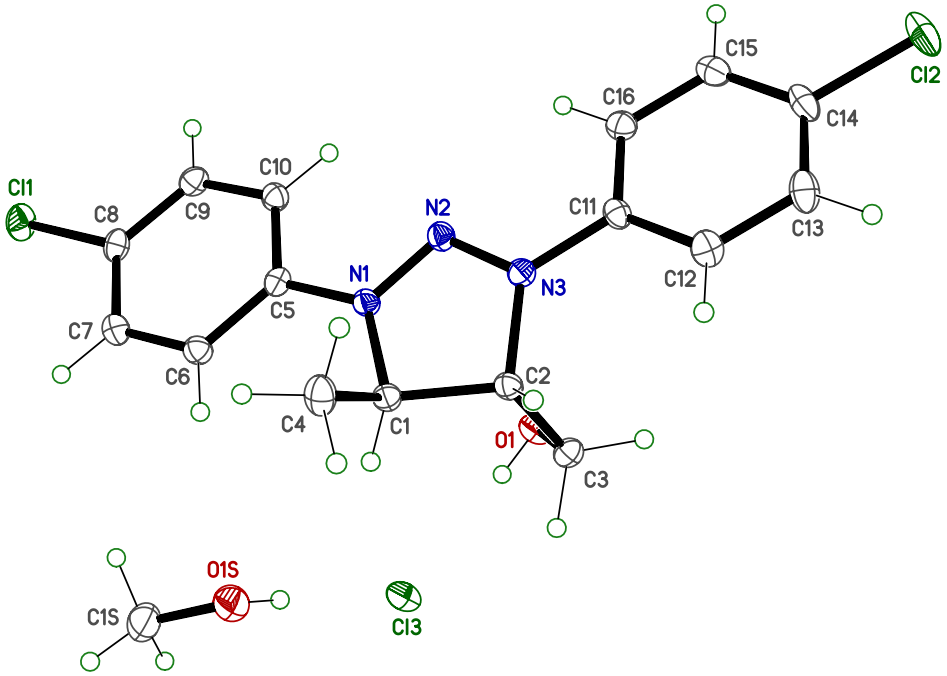


Table E.1 Crystal data and structure refinement for 1,3-bis(4-chlorophenyl)-5-(hydroxymethyl)-4-methyl-4,5-dihydro-3H-1,2,3-triazol-1-ylium chloride.

Empirical formula	C_{17} H_{20} C_{13} N_3 O_2
Formula weight	404.71
Temperature	90.0(2) K
Wavelength	0.71073 Å
Crystal system, space group	Monoclinic, P2(1)/n
Unit cell dimensions	a = 11.7659(3) Å alpha = 90 deg. b = 7.9907(2) Å beta = 103.232(1) deg. c = 20.5734(5) Å gamma = 90 deg.
Volume	1882.91(8) Å^3
Z, Calculated density	4, 1.428 Mg/m^3
Absorption coefficient	0.503 mm^-1
F(000)	840
Crystal size	0.310 x 0.250 x 0.090 mm
Theta range for data collection	2.034 to 27.529 deg.
Limiting indices	-15<=h<=15, -10<=k<=10, -26<=l<=26
Reflections collected / unique	30635 / 4339 [R(int) = 0.0347]
Completeness to theta = 25.242	99.8 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.971 and 0.867
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4339 / 0 / 235
Goodness-of-fit on F^2	1.040
Final R indices [I>2sigma(I)]	R1 = 0.0266, wR2 = 0.0663
R indices (all data)	R1 = 0.0298, wR2 = 0.0688
Extinction coefficient	0.0039(9)
Largest diff. peak and hole	0.383 and -0.228 e.Å^-3

Table E.2 Mol representation of (1,3-bis(4-chlorophenyl)-5-(hydroxymethyl)-4-methyl-4,5-dihydro-3H-1,2,3-triazol-1-ylium chloride.

```
Mrv2211 05162212093D

 45 45  0  0  0  0            999 V2000
    8.3200    6.0499   16.2048 Cl  0  0  0  0  0  0  0  0  0  0  0  0
   -1.4458    9.0522    8.5281 Cl  0  0  0  0  0  0  0  0  0  0  0  0
    0.9567    4.4589   13.6278 O   0  0  0  0  0  0  0  0  0  0  0  0
    1.1229    3.9269   14.2151 H   0  0  0  0  0  0  0  0  0  0  0  0
    3.8382    4.8461   12.5526 N   0  0  0  0  0  0  0  0  0  0  0  0
    3.2227    5.8159   11.9551 N   0  0  0  0  0  0  0  0  0  0  0  0
    2.2335    5.3411   11.2731 N   0  3  0  0  0  0  0  0  0  0  0  0
    3.3244    3.4966   12.1795 C   0  0  1  0  0  0  0  0  0  0  0  0
    3.1594    2.9441   12.9965 H   0  0  0  0  0  0  0  0  0  0  0  0
    1.9943    3.8894   11.5126 C   0  0  1  0  0  0  0  0  0  0  0  0
    1.8643    3.3985   10.6511 H   0  0  0  0  0  0  0  0  0  0  0  0
    0.7824    3.7257   12.4279 C   0  0  2  0  0  0  0  0  0  0  0  0
   -0.0299    4.0448   11.9606 H   0  0  0  0  0  0  0  0  0  0  0  0
    0.6572    2.7672   12.6417 H   0  0  0  0  0  0  0  0  0  0  0  0
    4.2954    2.7927   11.2435 C   0  0  0  0  0  0  0  0  0  0  0  0
    4.4244    3.3357   10.4379 H   0  0  0  0  0  0  0  0  0  0  0  0
    3.9316    1.9179   10.9930 H   0  0  0  0  0  0  0  0  0  0  0  0
    5.1559    2.6710   11.6966 H   0  0  0  0  0  0  0  0  0  0  0  0
    4.9128    5.1406   13.4329 C   0  0  0  0  0  0  0  0  0  0  0  0
    5.5946    4.0902   14.0340 C   0  0  0  0  0  0  0  0  0  0  0  0
    5.3430    3.1910   13.8595 H   0  0  0  0  0  0  0  0  0  0  0  0
    6.6512    4.3716   14.8952 C   0  0  0  0  0  0  0  0  0  0  0  0
    7.1337    3.6655   15.3090 H   0  0  0  0  0  0  0  0  0  0  0  0
    6.9918    5.6888   15.1430 C   0  0  0  0  0  0  0  0  0  0  0  0
    6.2890    6.7380   14.5644 C   0  0  0  0  0  0  0  0  0  0  0  0
    6.5256    7.6366   14.7623 H   0  0  0  0  0  0  0  0  0  0  0  0
```

Table E.2 Mol representation of (1,3-bis(4-chlorophenyl)-5-(hydroxymethyl)-4-methyl-4,5-dihydro-3H-1,2,3-triazol-1-ylium chloride, continued

```
    5.2429    6.4698   13.6983 C   0  0  0  0  0  0  0  0  0  0  0  0
    4.7583    7.1785   13.2919 H   0  0  0  0  0  0  0  0  0  0  0  0
    1.3725    6.2340   10.5759 C   0  0  0  0  0  0  0  0  0  0  0  0
    0.3876    5.7134    9.7459 C   0  0  0  0  0  0  0  0  0  0  0  0
    0.3116    4.7757    9.6139 H   0  0  0  0  0  0  0  0  0  0  0  0
   -0.4847    6.5911    9.1122 C   0  0  0  0  0  0  0  0  0  0  0  0
   -1.1776    6.2577    8.5543 H   0  0  0  0  0  0  0  0  0  0  0  0
   -0.3355    7.9536    9.3005 C   0  0  0  0  0  0  0  0  0  0  0  0
    0.6655    8.4742   10.1025 C   0  0  0  0  0  0  0  0  0  0  0  0
    0.7596    9.4139   10.2050 H   0  0  0  0  0  0  0  0  0  0  0  0
    1.5271    7.6092   10.7529 C   0  0  0  0  0  0  0  0  0  0  0  0
    2.2156    7.9475   11.3133 H   0  0  0  0  0  0  0  0  0  0  0  0
    1.7132    2.3495   15.6870 Cl  0  5  0  0  0  0  0  0  0  0  0  0
    4.7247    0.6471   13.8640 O   0  0  0  0  0  0  0  0  0  0  0  0
    3.9819    0.6748   14.2252 H   0  0  0  0  0  0  0  0  0  0  0  0
    5.4628   -0.3321   14.5696 C   0  0  0  0  0  0  0  0  0  0  0  0
    5.9220    0.0878   15.3266 H   0  0  0  0  0  0  0  0  0  0  0  0
    5.9589   -1.0329   14.5696 H   0  0  0  0  0  0  0  0  0  0  0  0
    4.8537   -1.0248   14.9004 H   0  0  0  0  0  0  0  0  0  0  0  0
  1 24  1  0  0  0  0
  2 34  1  0  0  0  0
  3  4  1  0  0  0  0
  3 12  1  0  0  0  0
  5  6  1  0  0  0  0
  5  8  1  0  0  0  0
  5 19  1  0  0  0  0
  6  7  2  0  0  0  0
  7 10  1  0  0  0  0
```

Table E.2 Mol representation of (1,3-bis(4-chlorophenyl)-5-(hydroxymethyl)-4-methyl-4,5-dihydro-3H-1,2,3-triazol-1-ylium chloride, continued

```
  7 29  1  0  0  0  0
  8  9  1  0  0  0  0
  8 10  1  0  0  0  0
  8 15  1  0  0  0  0
 10 11  1  0  0  0  0
 10 12  1  0  0  0  0
 12 13  1  0  0  0  0
 12 14  1  0  0  0  0
 15 16  1  0  0  0  0
 15 17  1  0  0  0  0
 15 18  1  0  0  0  0
 19 20  2  0  0  0  0
 19 27  1  0  0  0  0
 20 21  1  0  0  0  0
 20 22  1  0  0  0  0
 22 23  1  0  0  0  0
 22 24  2  0  0  0  0
 24 25  1  0  0  0  0
 25 26  1  0  0  0  0
 25 27  2  0  0  0  0
 27 28  1  0  0  0  0
 29 30  2  0  0  0  0
 29 37  1  0  0  0  0
 30 31  1  0  0  0  0
 30 32  1  0  0  0  0
 32 33  1  0  0  0  0
 32 34  2  0  0  0  0
 34 35  1  0  0  0  0
```

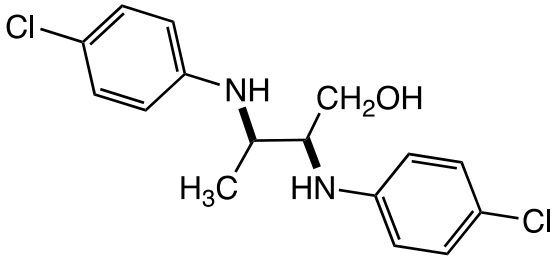
Table E.2 Mol representation of (1,3-bis(4-chlorophenyl)-5-(hydroxymethyl)-4-methyl-4,5-dihydro-3H-1,2,3-triazol-1-ylium chloride, continued

```
 35 36  1  0  0  0  0
 35 37  2  0  0  0  0
 37 38  1  0  0  0  0
 40 41  1  0  0  0  0
 40 42  1  0  0  0  0
 42 43  1  0  0  0  0
 42 44  1  0  0  0  0
 42 45  1  0  0  0  0
M  CHG  2   7   1  39  -1
M  END
```

Crystal data for 2,3-bis[(4 chlorophenyl)amino]butan-1-ol

CCDC reference number: 2179883

UK Chem reference number: m21079



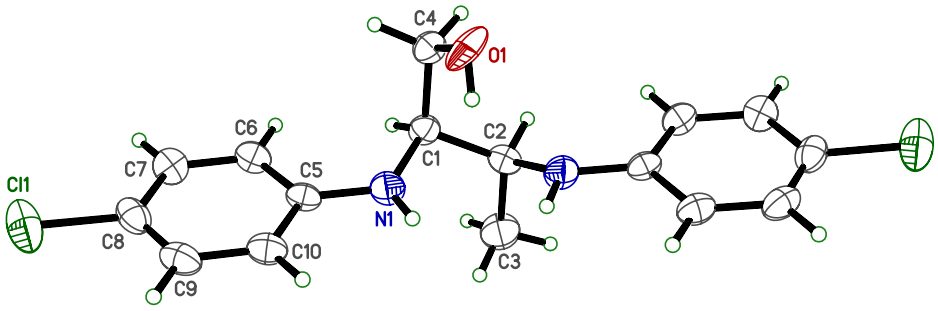


Table F.1 Crystal data and structure refinement for 2,3-bis[(4 chlorophenyl)amino]butan-1-ol.

Empirical formula	C_{16} H_{18} C_{12} N_2 O
Formula weight	325.22
Temperature	90.0(2) K
Wavelength	0.71073 Å
Crystal system, space group	Orthorhombic, Cmc2(1)
Unit cell dimensions	a = 19.5373(7) Å alpha = 90 deg. b = 10.5565(4) Å beta = 90 deg. c = 7.7748(3) Å gamma = 90 deg.
Volume	1603.52(10) Å^3
Z, Calculated density	4, 1.347 Mg/m^3
Absorption coefficient	0.405 mm^-1
F(000)	680
Crystal size	0.400 x 0.160 x 0.140 mm
Theta range for data collection	2.085 to 27.507 deg.
Limiting indices	-25<=h<=25, -13<=k<=13, -8<=l<=10
Reflections collected / unique	25035 / 1809 [R(int) = 0.0294]
Completeness to theta = 25.242	99.8 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.971 and 0.852
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	1809 / 2 / 124
Goodness-of-fit on F^2	1.093
Final R indices [I>2sigma(I)]	R1 = 0.0314, wR2 = 0.0765
R indices (all data)	R1 = 0.0327, wR2 = 0.0778
Absolute structure parameter	0.014(15)
Extinction coefficient	n/a
Largest diff. peak and hole	0.298 and -0.269 e.Å^-3

Table F.2 Mol representation for 2,3-bis[(4 chlorophenyl)amino]butan-1-ol.

```
  Mrv2211 06202218503D

 49 63  0  0  0  0            999 V2000
   11.2378    6.8476    4.1901 N   0  0  2  0  0  0  0  0  0  0  0  0
   10.9145    6.1566    3.8481 H   0  0  0  0  0  0  0  0  0  0  0  0
   12.6294    6.8526    4.1813 C   0  0  0  0  0  0  0  0  0  0  0  0
   13.3975    7.8670    4.7582 C   0  0  0  0  0  0  0  0  0  0  0  0
   12.9675    8.5866    5.2055 H   0  0  0  0  0  0  0  0  0  0  0  0
   14.7818    7.8324    4.6856 C   0  0  0  0  0  0  0  0  0  0  0  0
   15.2977    8.5240    5.0829 H   0  0  0  0  0  0  0  0  0  0  0  0
   15.4076    6.7892    4.0315 C   0  0  0  0  0  0  0  0  0  0  0  0
   14.6778    5.7762    3.4579 C   0  0  0  0  0  0  0  0  0  0  0  0
   15.1182    5.0609    3.0149 H   0  0  0  0  0  0  0  0  0  0  0  0
   13.3033    5.8066    3.5306 C   0  0  0  0  0  0  0  0  0  0  0  0
   12.8006    5.1057    3.1321 H   0  0  0  0  0  0  0  0  0  0  0  0
   17.1471    6.7643    3.8952 Cl  0  0  0  0  0  0  0  0  0  0  0  0
   10.4675    7.9824    4.6220 C   0  0  0  0  0  0  0  0  0  0  0  0
   10.9528    8.4312    5.3734 H   0  0  0  0  0  0  0  0  0  0  0  0
    9.1182    7.4801    5.1392 C   0  0  0  0  0  0  0  0  0  0  0  0
    8.5907    8.2888    5.3980 H   0  0  0  0  0  0  0  0  0  0  0  0
    9.2434    6.6150    6.3952 C   0  0  0  0  0  0  0  0  0  0  0  0
    8.3491    6.3893    6.7270 H   0  0  0  0  0  0  0  0  0  0  0  0
    9.7322    7.1099    7.0860 H   0  0  0  0  0  0  0  0  0  0  0  0
    9.7286    5.7916    6.1787 H   0  0  0  0  0  0  0  0  0  0  0  0
   10.2871    8.9883    3.4838 C   0  0  0  0  0  0  0  0  0  0  0  0
    9.6544    9.6927    3.7720 H   0  0  0  0  0  0  0  0  0  0  0  0
   11.1574    9.4222    3.2945 H   0  0  0  0  0  0  0  0  0  0  0  0
    9.7985    8.3828    2.2892 O   0  0  0  0  0  0  0  0  0  0  0  0
    9.7990    7.6333    2.6148 H   0  0  0  0  0  0  0  0  0  0  0  0
```

Table F.2 Mol representation for 2,3-bis[(4 chlorophenyl)amino]butan-1-ol, continued

8.3337	6.7710	4.1241	N	0	0	1	0	0	0	0	0	0	0	0
8.7081	6.0984	3.7979	H	0	0	0	0	0	0	0	0	0	0	0
6.9456	6.7028	4.0520	C	0	0	0	0	0	0	0	0	0	0	0
6.0997	7.6747	4.5922	C	0	0	0	0	0	0	0	0	0	0	0
6.4705	8.4153	5.0577	H	0	0	0	0	0	0	0	0	0	0	0
4.7238	7.5674	4.4568	C	0	0	0	0	0	0	0	0	0	0	0
4.1548	8.2303	4.8294	H	0	0	0	0	0	0	0	0	0	0	0
4.1843	6.4935	3.7763	C	0	0	0	0	0	0	0	0	0	0	0
4.9916	5.5209	3.2376	C	0	0	0	0	0	0	0	0	0	0	0
4.6101	4.7839	2.7759	H	0	0	0	0	0	0	0	0	0	0	0
6.3580	5.6236	3.3726	C	0	0	0	0	0	0	0	0	0	0	0
6.9144	4.9506	2.9982	H	0	0	0	0	0	0	0	0	0	0	0
2.4565	6.3772	3.5610	Cl	0	0	0	0	0	0	0	0	0	0	0
9.0227	7.9444	4.5892	C	0	0	0	0	0	0	0	0	0	0	0
8.4808	8.3661	5.3171	H	0	0	0	0	0	0	0	0	0	0	0
10.3717	7.5132	5.1677	C	0	0	0	0	0	0	0	0	0	0	0
10.8436	8.3482	5.4493	H	0	0	0	0	0	0	0	0	0	0	0
10.2353	6.6411	6.4178	C	0	0	0	0	0	0	0	0	0	0	0
11.1243	6.4624	6.7901	H	0	0	0	0	0	0	0	0	0	0	0
9.8044	5.7936	6.1804	H	0	0	0	0	0	0	0	0	0	0	0
9.2015	8.9597	3.4591	C	0	0	0	0	0	0	0	0	0	0	0
9.7824	9.6961	3.7749	H	0	0	0	0	0	0	0	0	0	0	0
8.3190	9.3474	3.2299	H	0	0	0	0	0	0	0	0	0	0	0

1	2	1	0	0	0
1	3	1	0	0	0
1	14	1	0	0	0
1	42	1	0	0	0
3	4	2	0	0	0
3	11	1	0	0	0

Table F.2 Mol representation for 2,3-bis[(4 chlorophenyl)amino]butan-1-ol, continued

```
  4  5  1  0  0  0  0
  4  6  1  0  0  0  0
  6  7  1  0  0  0  0
  6  8  2  0  0  0  0
  8  9  1  0  0  0  0
  8 13  1  0  0  0  0
  9 10  1  0  0  0  0
  9 11  2  0  0  0  0
 11 12  1  0  0  0  0
 14 15  1  0  0  0  0
 14 22  1  0  0  0  0
 14 40  1  0  0  0  0
 14 43  1  0  0  0  0
 15 42  1  0  0  0  0
 16 17  1  0  0  0  0
 16 18  1  0  0  0  0
 16 27  1  0  0  0  0
 16 41  1  0  0  0  0
 16 42  1  0  0  0  0
 17 40  1  0  0  0  0
 18 19  1  0  0  0  0
 18 20  1  0  0  0  0
 18 21  1  0  0  0  0
 18 44  1  0  0  0  0
 18 46  1  0  0  0  0
 20 44  1  0  0  0  0
 21 44  1  0  0  0  0
 22 23  1  0  0  0  0
```

Table F.2 Mol representation for 2,3-bis[(4 chlorophenyl)amino]butan-1-ol, continued

```
 22 24  1  0  0  0  0
 22 25  1  0  0  0  0
 22 47  1  0  0  0  0
 22 48  1  0  0  0  0
 23 47  1  0  0  0  0
 25 26  1  0  0  0  0
 25 47  1  0  0  0  0
 27 28  1  0  0  0  0
 27 29  1  0  0  0  0
 27 40  1  0  0  0  0
 29 30  2  0  0  0  0
 29 37  1  0  0  0  0
 30 31  1  0  0  0  0
 30 32  1  0  0  0  0
 32 33  1  0  0  0  0
 32 34  2  0  0  0  0
 34 35  1  0  0  0  0
 34 39  1  0  0  0  0
 35 36  1  0  0  0  0
 35 37  2  0  0  0  0
 37 38  1  0  0  0  0
 40 41  1  0  0  0  0
 40 47  1  0  0  0  0
 42 43  1  0  0  0  0
 42 44  1  0  0  0  0
 44 45  1  0  0  0  0
 44 46  1  0  0  0  0
 47 48  1  0  0  0  0
```

Table F.2 Mol representation for 2,3-bis[(4 chlorophenyl)amino]butan-1-ol, continued

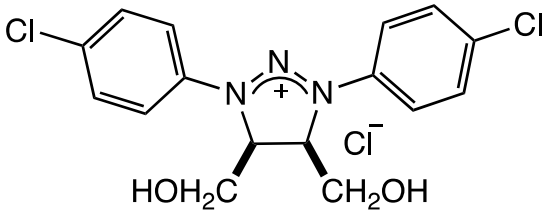
```
 47 49  1  0  0  0  0

M  END
```

Crystal data for 1,3-bis(4-chlorophenyl)-4,5-bis(hydroxymethyl)-4,5-dihydro-3H-1,2,3-triazol-1-ylium chloride

CCDC reference number: 2179889

UK Chem reference number: m21167



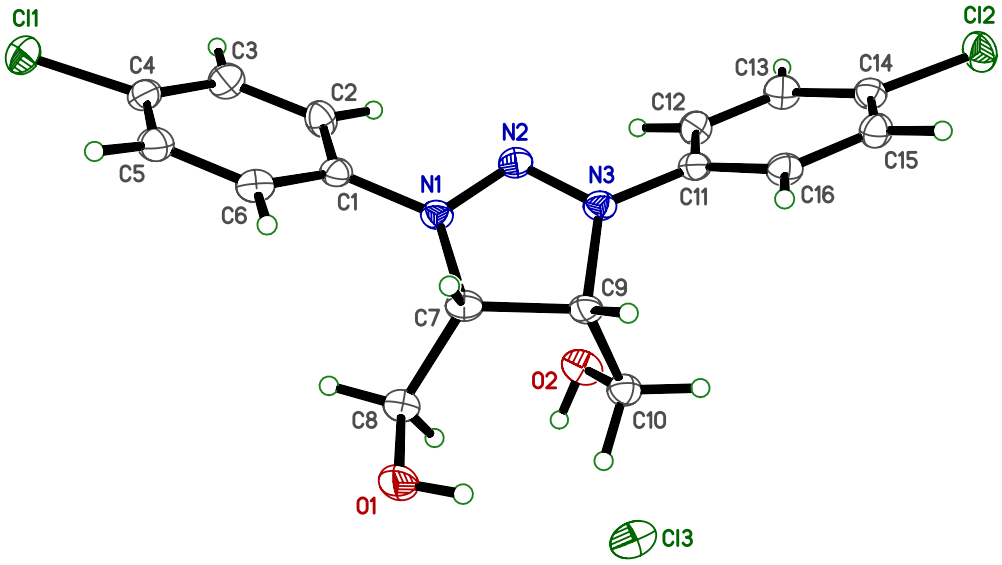


Table G.1 Crystal data and structure refinement for 1,3-bis(4-chlorophenyl)-4,5-bis(hydroxymethyl)-4,5-dihydro-3H-1,2,3-triazol-1-ylium chloride.

Empirical formula	C_{16} H_{16} C_{13} N_3 O_2
Formula weight	388.67
Temperature	90.0(2) K
Wavelength	0.71073 Å
Crystal system, space group	Orthorhombic, P2(1)2(1)2(1)
Unit cell dimensions	a = 7.9430(2) Å alpha = 90 deg. b = 9.8809(2) Å beta = 90 deg. c = 21.9643(5) Å gamma = 90 deg.
Volume	1723.85(7) Å^3
Z, Calculated density	4, 1.498 Mg/m^3
Absorption coefficient	0.546 mm^-1
F(000)	800
Crystal size	0.240 x 0.070 x 0.020 mm
Theta range for data collection	2.260 to 27.485 deg.
Limiting indices	-10<=h<=10, -12<=k<=12, -28<=l<=28
Reflections collected / unique	26690 / 3961 [R(int) = 0.0429]
Completeness to theta = 25.242	99.8 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.959 and 0.861
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3961 / 0 / 224
Goodness-of-fit on F^2	1.097
Final R indices [I>2sigma(I)]	R1 = 0.0283, wR2 = 0.0679
R indices (all data)	R1 = 0.0310, wR2 = 0.0695
Absolute structure parameter	0.49(6)
Extinction coefficient	n/a
Largest diff. peak and hole	0.335 and -0.214 e.Å^-3

Table G.2 Mol representation of (1,3-bis(4-chlorophenyl)-4,5-bis(hydroxymethyl)-4,5-dihydro-3H-1,2,3-triazol-1-ylium chloride.

```
Mrv2211 05162213473D

 40 41  0  0  0  0            999 V2000
    2.9814   -0.3864   10.1060 Cl  0  5  0  0  0  0  0  0  0  0  0  0
    6.3353    7.7719   15.7851 Cl  0  0  0  0  0  0  0  0  0  0  0  0
   -2.3746    6.0528    6.5185 Cl  0  0  0  0  0  0  0  0  0  0  0  0
    3.9539    1.0561   12.6486 O   0  0  0  0  0  0  0  0  0  0  0  0
    3.6422    0.7161   11.9446 H   0  0  0  0  0  0  0  0  0  0  0  0
    0.2477    3.0552   12.1494 O   0  0  0  0  0  0  0  0  0  0  0  0
    0.1301    2.5351   12.7646 H   0  0  0  0  0  0  0  0  0  0  0  0
    3.0664    4.6200   12.0084 N   0  3  0  0  0  0  0  0  0  0  0  0
    2.2628    5.2214   11.1970 N   0  0  0  0  0  0  0  0  0  0  0  0
    1.7564    4.3738   10.3818 N   0  0  0  0  0  0  0  0  0  0  0  0
    3.8680    5.4121   12.8857 C   0  0  0  0  0  0  0  0  0  0  0  0
    3.3407    6.5764   13.4196 C   0  0  0  0  0  0  0  0  0  0  0  0
    2.4605    6.8558   13.1980 H   0  0  0  0  0  0  0  0  0  0  0  0
    4.1272    7.3291   14.2867 C   0  0  0  0  0  0  0  0  0  0  0  0
    3.7902    8.1343   14.6606 H   0  0  0  0  0  0  0  0  0  0  0  0
    5.4010    6.8975   14.6005 C   0  0  0  0  0  0  0  0  0  0  0  0
    5.9433    5.7676   14.0139 C   0  0  0  0  0  0  0  0  0  0  0  0
    6.8404    5.5146   14.1977 H   0  0  0  0  0  0  0  0  0  0  0  0
    5.1635    5.0079   13.1569 C   0  0  0  0  0  0  0  0  0  0  0  0
    5.5141    4.2199   12.7598 H   0  0  0  0  0  0  0  0  0  0  0  0
    3.2644    3.1745   11.6953 C   0  0  1  0  0  0  0  0  0  0  0  0
    4.1385    3.0727   11.2202 H   0  0  0  0  0  0  0  0  0  0  0  0
    3.2812    2.2789   12.9337 C   0  0  2  0  0  0  0  0  0  0  0  0
    3.7417    2.7460   13.6752 H   0  0  0  0  0  0  0  0  0  0  0  0
    2.3527    2.0883   13.2185 H   0  0  0  0  0  0  0  0  0  0  0  0
    2.1227    2.9542   10.6698 C   0  0  1  0  0  0  0  0  0  0  0  0
```

Table G.2 Mol representation of (1,3-bis(4-chlorophenyl)-4,5-bis(hydroxymethyl)-4,5-dihydro-3H-1,2,3-triazol-1-ylium chloride, continued

```
    2.4733    2.5084    9.8458 H   0  0  0  0  0  0  0  0  0  0  0  0
    0.8661    2.2533   11.1613 C   0  0  2  0  0  0  0  0  0  0  0  0
    0.2432    2.1108   10.4053 H   0  0  0  0  0  0  0  0  0  0  0  0
    1.1003    1.3705   11.5423 H   0  0  0  0  0  0  0  0  0  0  0  0
    0.7517    4.7957    9.4583 C   0  0  0  0  0  0  0  0  0  0  0  0
   -0.1576    5.7775    9.8355 C   0  0  0  0  0  0  0  0  0  0  0  0
   -0.1203    6.1615   10.7035 H   0  0  0  0  0  0  0  0  0  0  0  0
   -1.1193    6.1862    8.9267 C   0  0  0  0  0  0  0  0  0  0  0  0
   -1.7452    6.8619    9.1571 H   0  0  0  0  0  0  0  0  0  0  0  0
   -1.1522    5.5917    7.6722 C   0  0  0  0  0  0  0  0  0  0  0  0
   -0.2396    4.6183    7.2987 C   0  0  0  0  0  0  0  0  0  0  0  0
   -0.2755    4.2358    6.4297 H   0  0  0  0  0  0  0  0  0  0  0  0
    0.7283    4.2073    8.2059 C   0  0  0  0  0  0  0  0  0  0  0  0
    1.3601    3.5378    7.9718 H   0  0  0  0  0  0  0  0  0  0  0  0
  2 16  1  0  0  0  0
  3 36  1  0  0  0  0
  4  5  1  0  0  0  0
  4 23  1  0  0  0  0
  6  7  1  0  0  0  0
  6 28  1  0  0  0  0
  8  9  2  0  0  0  0
  8 11  1  0  0  0  0
  8 21  1  0  0  0  0
  9 10  1  0  0  0  0
 10 26  1  0  0  0  0
 10 31  1  0  0  0  0
 11 12  1  0  0  0  0
 11 19  2  0  0  0  0
```

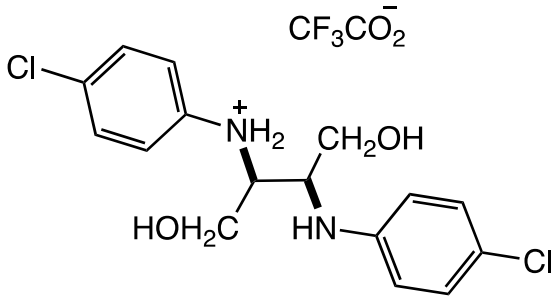
Table G.2 Mol representation of (1,3-bis(4-chlorophenyl)-4,5-bis(hydroxymethyl)-4,5-dihydro-3H-1,2,3-triazol-1-ylium chloride, continued

```
 12 13  1  0  0  0  0
 12 14  2  0  0  0  0
 14 15  1  0  0  0  0
 14 16  1  0  0  0  0
 16 17  2  0  0  0  0
 17 18  1  0  0  0  0
 17 19  1  0  0  0  0
 19 20  1  0  0  0  0
 21 22  1  0  0  0  0
 21 23  1  0  0  0  0
 21 26  1  0  0  0  0
 23 24  1  0  0  0  0
 23 25  1  0  0  0  0
 26 27  1  0  0  0  0
 26 28  1  0  0  0  0
 28 29  1  0  0  0  0
 28 30  1  0  0  0  0
 31 32  2  0  0  0  0
 31 39  1  0  0  0  0
 32 33  1  0  0  0  0
 32 34  1  0  0  0  0
 34 35  1  0  0  0  0
 34 36  2  0  0  0  0
 36 37  1  0  0  0  0
 37 38  1  0  0  0  0
 37 39  2  0  0  0  0
 39 40  1  0  0  0  0
M  CHG  2   1  -1   8   1
M  END
```

Crystal data for 2,3-bis[(4-chlorophenyl)amino]butane-1,4-diol as a triflouroacetate salt

CCDC reference number: 2179885

UK Chem reference number: m21241



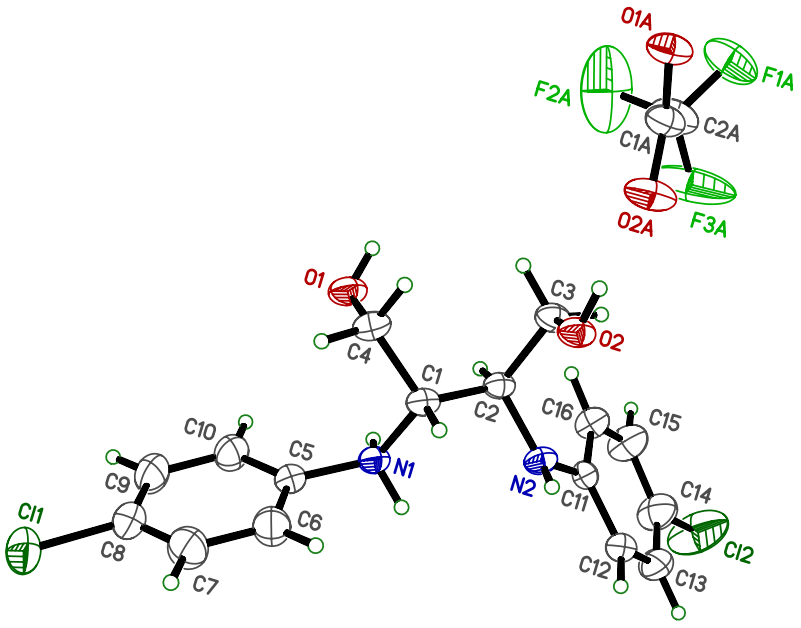


Table H.1 Crystal data and structure refinement for 2,3-bis[(4-chlorophenyl)amino]butane-1,4-diol as a triflouroacetate salt.

Empirical formula	C_{18} H_{19} C_{12} F_3 N_2 O_4
Formula weight	455.25
Temperature	180(2) K
Wavelength	0.71073 Å
Crystal system, space group	Monoclinic, P2(1)/n
Unit cell dimensions	a = 12.9188(4) Å alpha = 90 deg. b = 9.4899(3) Å beta = 107.351(1) deg. c = 17.4781(6) Å gamma = 90 deg.
Volume	2045.28(12) Å^3
Z, Calculated density	4, 1.478 Mg/m^3
Absorption coefficient	0.371 mm^-1
F(000)	936
Crystal size	0.300 x 0.220 x 0.160 mm
Theta range for data collection	2.328 to 27.528 deg.
Limiting indices	-16<=h<=16, -12<=k<=12, -22<=l<=22
Reflections collected / unique	42546 / 4703 [R(int) = 0.0399]
Completeness to theta = 25.242	99.9 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.942 and 0.871
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4703 / 525 / 405
Goodness-of-fit on F^2	1.041
Final R indices [I>2sigma(I)]	R1 = 0.0454, wR2 = 0.1183
R indices (all data)	R1 = 0.0576, wR2 = 0.1283
Extinction coefficient	n/a
Largest diff. peak and hole	0.342 and -0.587 e.Å^-3

Table H.2 Mol representation of 2,3-bis[(4-chlorophenyl)amino]butane-1,4-diol as a triflouroacetate salt.

```
Mrv2211 05162214033D

 48 48  0  0  0  0            999 V2000
   -0.0929    1.9530    5.2424 O   0  0  0  0  0  0  0  0  0  0  0  0
    0.2224    1.2146    4.9959 H   0  0  0  0  0  0  0  0  0  0  0  0
    3.5632    3.1077    3.3650 O   0  0  0  0  0  0  0  0  0  0  0  0
    3.7911    2.6113    2.7269 H   0  0  0  0  0  0  0  0  0  0  0  0
    1.3538    3.8729    5.0708 C   0  0  1  0  0  0  0  0  0  0  0  0
    1.6202    4.6102    4.4501 H   0  0  0  0  0  0  0  0  0  0  0  0
    2.6151    3.1605    5.5738 C   0  0  1  0  0  0  0  0  0  0  0  0
    2.3301    2.5432    6.3070 H   0  0  0  0  0  0  0  0  0  0  0  0
    3.2968    2.3098    4.5162 C   0  0  2  0  0  0  0  0  0  0  0  0
    4.1443    1.9449    4.8746 H   0  0  0  0  0  0  0  0  0  0  0  0
    2.7121    1.5499    4.2693 H   0  0  0  0  0  0  0  0  0  0  0  0
    0.3519    2.9703    4.3690 C   0  0  2  0  0  0  0  0  0  0  0  0
   -0.4219    3.5077    4.0649 H   0  0  0  0  0  0  0  0  0  0  0  0
    0.7749    2.5618    3.5727 H   0  0  0  0  0  0  0  0  0  0  0  0
    0.6767    3.8243    6.9445 H   0  0  0  0  0  0  0  0  0  0  0  0
    1.2670    5.1241    6.6195 H   0  0  0  0  0  0  0  0  0  0  0  0
   -0.6294    5.0521    6.1844 C   0  0  0  0  0  0  0  0  0  0  0  0
   -0.8200    6.2042    5.4571 C   0  0  0  0  0  0  0  0  0  0  0  0
   -0.0948    6.6100    4.9973 H   0  0  0  0  0  0  0  0  0  0  0  0
   -2.0842    6.7632    5.4072 C   0  0  0  0  0  0  0  0  0  0  0  0
   -2.2414    7.5499    4.8983 H   0  0  0  0  0  0  0  0  0  0  0  0
   -3.1182    6.1651    6.1045 C   0  0  0  0  0  0  0  0  0  0  0  0
   -2.9208    5.0119    6.8210 C   0  0  0  0  0  0  0  0  0  0  0  0
   -3.6424    4.6096    7.2897 H   0  0  0  0  0  0  0  0  0  0  0  0
   -1.6665    4.4420    6.8543 C   0  0  0  0  0  0  0  0  0  0  0  0
   -4.6983    6.8960    6.1209 Cl  0  0  0  0  0  0  0  0  0  0  0  0
```

Table H.2 Mol representation of 2,3-bis[(4-chlorophenyl)amino]butane-1,4-diol as a triflouroacetate salt, continued

```
    3.6508    4.8033    5.7019 H   0  0  0  0  0  0  0  0  0  0  0  0
    4.3845    3.8705    7.1920 C   0  0  0  0  0  0  0  0  0  0  0  0
    5.1664    4.9039    7.7173 C   0  0  0  0  0  0  0  0  0  0  0  0
    5.1391    5.7627    7.3110 H   0  0  0  0  0  0  0  0  0  0  0  0
    5.9763    4.6995    8.8110 C   0  0  0  0  0  0  0  0  0  0  0  0
    6.4867    5.4180    9.1665 H   0  0  0  0  0  0  0  0  0  0  0  0
    6.0474    3.4610    9.3877 C   0  0  0  0  0  0  0  0  0  0  0  0
    5.3444    2.4071    8.8552 C   0  0  0  0  0  0  0  0  0  0  0  0
    5.4230    1.5410    9.2362 H   0  0  0  0  0  0  0  0  0  0  0  0
    4.5198    2.6114    7.7651 C   0  0  0  0  0  0  0  0  0  0  0  0
    4.0393    1.8772    7.4005 H   0  0  0  0  0  0  0  0  0  0  0  0
    7.0782    3.1778   10.7836 Cl  0  0  0  0  0  0  0  0  0  0  0  0
    3.4606   -0.2369    2.0753 C   0  0  0  0  0  0  0  0  0  0  0  0
    5.5468   -1.3001    2.4330 F   0  0  0  0  0  0  0  0  0  0  0  0
    5.3980    0.6705    3.0545 F   0  0  0  0  0  0  0  0  0  0  0  0
    5.5195    0.2331    0.9981 F   0  0  0  0  0  0  0  0  0  0  0  0
    4.9772   -0.1176    2.1327 C   0  0  2  0  0  0  0  0  0  0  0  0
    0.7124    4.4735    6.3078 N   0  3  1  0  0  0  0  0  0  0  0  0
   -1.6417    3.7665    6.9065 H   0  0  0  0  0  0  0  0  0  0  0  0
    3.4802    4.1570    6.1709 N   0  0  1  0  0  0  0  0  0  0  0  0
    2.9894    0.7459    1.4730 O   0  5  0  0  0  0  0  0  0  0  0  0
    3.0751   -1.5286    1.3305 O   0  0  0  0  0  0  0  0  0  0  0  0
  1  2  1  0  0  0  0
  1 12  1  0  0  0  0
  3  4  1  0  0  0  0
  3  9  1  0  0  0  0
  5  6  1  0  0  0  0
  5  7  1  0  0  0  0
```

Table H.2 Mol representation of 2,3-bis[(4-chlorophenyl)amino]butane-1,4-diol as a triflouroacetate salt, continued

```
  5 12  1  0  0  0  0
  7  8  1  0  0  0  0
  7  9  1  0  0  0  0
  9 10  1  0  0  0  0
  9 11  1  0  0  0  0
 12 13  1  0  0  0  0
 12 14  1  0  0  0  0
 17 18  1  0  0  0  0
 17 25  2  0  0  0  0
 18 19  1  0  0  0  0
 18 20  2  0  0  0  0
 20 21  1  0  0  0  0
 20 22  1  0  0  0  0
 22 23  2  0  0  0  0
 22 26  1  0  0  0  0
 23 24  1  0  0  0  0
 23 25  1  0  0  0  0
 28 29  2  0  0  0  0
 28 36  1  0  0  0  0
 29 30  1  0  0  0  0
 29 31  1  0  0  0  0
 31 32  1  0  0  0  0
 31 33  2  0  0  0  0
 33 34  1  0  0  0  0
 33 38  1  0  0  0  0
 34 35  1  0  0  0  0
 34 36  2  0  0  0  0
 36 37  1  0  0  0  0
```

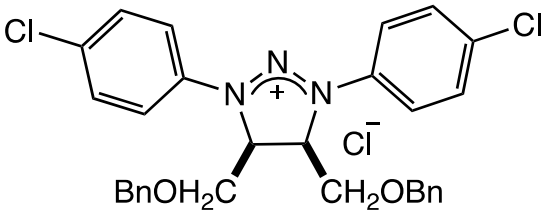
Table H.2 Mol representation of 2,3-bis[(4-chlorophenyl)amino]butane-1,4-diol as a triflouroacetate salt, continued

```
 39 43  1  0  0  0  0
 40 43  1  0  0  0  0
 41 43  1  0  0  0  0
 42 43  1  0  0  0  0
  5 44  1  0  0  0  0
 44 15  1  0  0  0  0
 44 16  1  0  0  0  0
 44 17  1  0  0  0  0
  7 46  1  0  0  0  0
 46 27  1  0  0  0  0
 46 28  1  0  0  0  0
 25 45  1  0  0  0  0
 39 47  1  0  0  0  0
 39 48  2  0  0  0  0
M  CHG  2  44   1  47  -1
M  END
```

Crystal data for 4,5-bis[(benzyloxy)methyl]-1,3-bis(4-chlorophenyl)-4,5-dihydro-3H-1,2,3-triazol-1-ylium chloride

CCDC reference number: 2179888

UK Chem reference number: m21256



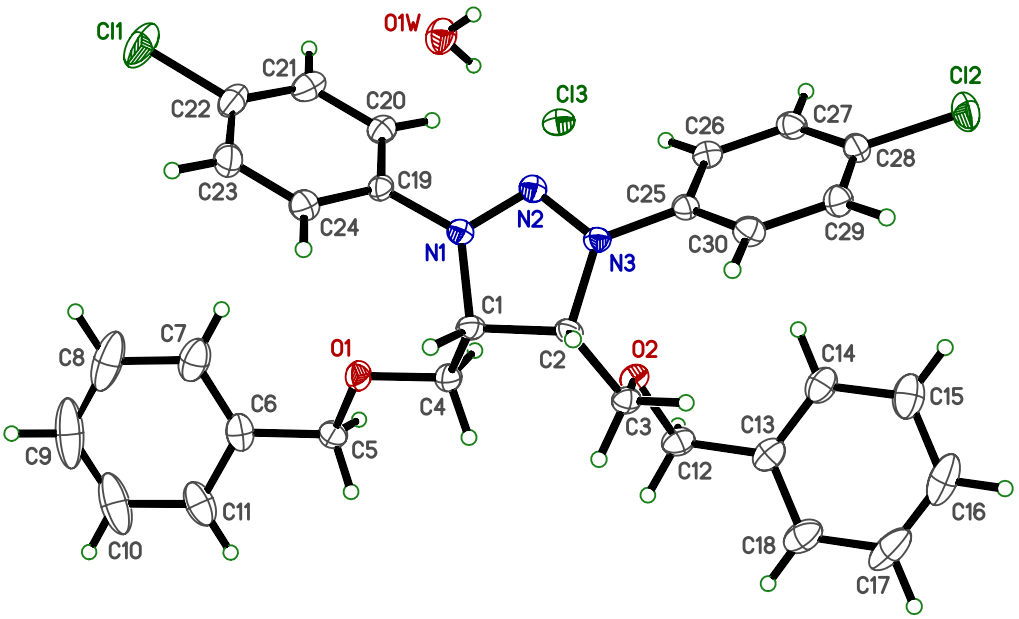


Table I.1 Crystal data and structure refinement for 4,5-bis[(benzyloxy)methyl]-1,3-bis(4-chlorophenyl)-4,5-dihydro-3H-1,2,3-triazol-1-ylium chloride.

Empirical formula	C_{30} H_{30} C_{13} N_3 O_3
Formula weight	586.92
Temperature	90.0(2) K
Wavelength	0.71073 Å
Crystal system, space group	Monoclinic, P2(1)/c
Unit cell dimensions	a = 17.0530(4) Å alpha = 90 deg. b = 10.1884(2) Å beta = 111.656(1) deg. c = 17.7313(5) Å gamma = 90 deg.
Volume	2863.24(12) Å^3
Z, Calculated density	4, 1.362 Mg/m^3
Absorption coefficient	0.357 mm^-1
F(000)	1224
Crystal size	0.280 x 0.120 x 0.080 mm
Theta range for data collection	2.327 to 27.496 deg.
Limiting indices	-22<=h<=22, -13<=k<=13, -23<=l<=23
Reflections collected / unique	38931 / 6579 [R(int) = 0.0485]
Completeness to theta = 25.242	100.0 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.971 and 0.856
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	6579 / 0 / 359
Goodness-of-fit on F^2	1.030
Final R indices [I>2sigma(I)]	R1 = 0.0379, wR2 = 0.0836
R indices (all data)	R1 = 0.0528, wR2 = 0.0919
Extinction coefficient	0.0014(3)
Largest diff. peak and hole	0.577 and -0.388 e.Å^-3

Table I.2 Mol representation of 4,5-bis[(benzyloxy)methyl]-1,3-bis(4-chlorophenyl)-4,5-dihydro-3H-1,2,3-triazol-1-ylium chloride.

```
  Mrv2211 05162214093D

 69 71  0  0  0  0            999 V2000
   11.0474    7.0565   10.9463 Cl  0  0  0  0  0  0  0  0  0  0  0  0
   -1.0436    8.2652    6.9867 Cl  0  0  0  0  0  0  0  0  0  0  0  0
    6.5210    2.8330   11.1636 O   0  0  0  0  0  0  0  0  0  0  0  0
    2.3378    3.7309   10.3683 O   0  0  0  0  0  0  0  0  0  0  0  0
    5.7295    5.0474    9.3606 N   0  3  0  0  0  0  0  0  0  0  0  0
    4.8420    5.8985    8.9752 N   0  0  0  0  0  0  0  0  0  0  0  0
    3.7857    5.2752    8.5794 N   0  0  0  0  0  0  0  0  0  0  0  0
    5.2616    3.6349    9.3388 C   0  0  2  0  0  0  0  0  0  0  0  0
    5.8921    3.0823    8.7935 H   0  0  0  0  0  0  0  0  0  0  0  0
    3.9246    3.7898    8.5827 C   0  0  1  0  0  0  0  0  0  0  0  0
    4.0549    3.4810    7.6404 H   0  0  0  0  0  0  0  0  0  0  0  0
    2.7048    3.1020    9.1488 C   0  0  2  0  0  0  0  0  0  0  0  0
    1.9567    3.1594    8.5028 H   0  0  0  0  0  0  0  0  0  0  0  0
    2.9029    2.1456    9.3101 H   0  0  0  0  0  0  0  0  0  0  0  0
    5.1864    3.0771   10.7481 C   0  0  2  0  0  0  0  0  0  0  0  0
    4.7506    3.7279   11.3535 H   0  0  0  0  0  0  0  0  0  0  0  0
    4.6632    2.2367   10.7587 H   0  0  0  0  0  0  0  0  0  0  0  0
    6.5507    2.0190   12.3330 C   0  0  2  0  0  0  0  0  0  0  0  0
    6.0858    1.1628   12.1573 H   0  0  0  0  0  0  0  0  0  0  0  0
    6.0828    2.4795   13.0740 H   0  0  0  0  0  0  0  0  0  0  0  0
    7.9777    1.7530   12.7196 C   0  0  0  0  0  0  0  0  0  0  0  0
    8.9810    2.6774   12.4710 C   0  0  0  0  0  0  0  0  0  0  0  0
    8.7806    3.4989   12.0380 H   0  0  0  0  0  0  0  0  0  0  0  0
   10.2919    2.3871   12.8654 C   0  0  0  0  0  0  0  0  0  0  0  0
   10.9862    3.0119   12.6930 H   0  0  0  0  0  0  0  0  0  0  0  0
   10.5835    1.1957   13.5039 C   0  0  0  0  0  0  0  0  0  0  0  0
```

Table I.2 Mol representation of 4,5-bis[(benzyloxy)methyl]-1,3-bis(4-chlorophenyl)-4,5-dihydro-3H-1,2,3-triazol-1-ylium chloride, continued

11.4745	1.0077	13.7742	H	0	0	0	0	0	0	0	0	0	0	0	0
9.5866	0.2860	13.7475	C	0	0	0	0	0	0	0	0	0	0	0	0
9.7887	-0.5321	14.1866	H	0	0	0	0	0	0	0	0	0	0	0	0
8.2847	0.5559	13.3546	C	0	0	0	0	0	0	0	0	0	0	0	0
7.5992	-0.0805	13.5205	H	0	0	0	0	0	0	0	0	0	0	0	0
1.2560	3.0344	11.0124	C	0	0	2	0	0	0	0	0	0	0	0	0
1.0713	3.4622	11.8858	H	0	0	0	0	0	0	0	0	0	0	0	0
1.5319	2.0994	11.1856	H	0	0	0	0	0	0	0	0	0	0	0	0
-0.0112	3.0294	10.1881	C	0	0	0	0	0	0	0	0	0	0	0	0
-0.4375	4.1830	9.5380	C	0	0	0	0	0	0	0	0	0	0	0	0
0.0771	4.9785	9.6074	H	0	0	0	0	0	0	0	0	0	0	0	0
-1.6077	4.1854	8.7878	C	0	0	0	0	0	0	0	0	0	0	0	0
-1.8888	4.9770	8.3439	H	0	0	0	0	0	0	0	0	0	0	0	0
-2.3608	3.0288	8.6910	C	0	0	0	0	0	0	0	0	0	0	0	0
-3.1635	3.0257	8.1830	H	0	0	0	0	0	0	0	0	0	0	0	0
-1.9467	1.8832	9.3309	C	0	0	0	0	0	0	0	0	0	0	0	0
-2.4671	1.0910	9.2617	H	0	0	0	0	0	0	0	0	0	0	0	0
-0.7728	1.8727	10.0787	C	0	0	0	0	0	0	0	0	0	0	0	0
-0.4928	1.0760	10.5136	H	0	0	0	0	0	0	0	0	0	0	0	0
7.0180	5.5134	9.7787	C	0	0	0	0	0	0	0	0	0	0	0	0
7.1005	6.6460	10.5672	C	0	0	0	0	0	0	0	0	0	0	0	0
6.3131	7.0925	10.8554	H	0	0	0	0	0	0	0	0	0	0	0	0
8.3534	7.1200	10.9300	C	0	0	0	0	0	0	0	0	0	0	0	0
8.4341	7.8977	11.4696	H	0	0	0	0	0	0	0	0	0	0	0	0
9.4822	6.4498	10.4990	C	0	0	0	0	0	0	0	0	0	0	0	0
9.3942	5.3061	9.7211	C	0	0	0	0	0	0	0	0	0	0	0	0
10.1814	4.8533	9.4418	H	0	0	0	0	0	0	0	0	0	0	0	0
8.1441	4.8304	9.3549	C	0	0	0	0	0	0	0	0	0	0	0	0

Table I.2 Mol representation of 4,5-bis[(benzyloxy)methyl]-1,3-bis(4-chlorophenyl)-4,5-dihydro-3H-1,2,3-triazol-1-ylium chloride, continued

```
    8.0623    4.0483    8.8217 H   0  0  0  0  0  0  0  0  0  0  0  0
    2.6382    6.0165    8.1749 C   0  0  0  0  0  0  0  0  0  0  0  0
    2.2668    7.1386    8.9016 C   0  0  0  0  0  0  0  0  0  0  0  0
    2.7805    7.4223    9.6488 H   0  0  0  0  0  0  0  0  0  0  0  0
    1.1359    7.8373    8.5199 C   0  0  0  0  0  0  0  0  0  0  0  0
    0.8666    8.6111    9.0007 H   0  0  0  0  0  0  0  0  0  0  0  0
    0.3971    7.3994    7.4294 C   0  0  0  0  0  0  0  0  0  0  0  0
    0.7756    6.2851    6.6956 C   0  0  0  0  0  0  0  0  0  0  0  0
    0.2632    6.0035    5.9467 H   0  0  0  0  0  0  0  0  0  0  0  0
    1.9130    5.5889    7.0727 C   0  0  0  0  0  0  0  0  0  0  0  0
    2.1933    4.8260    6.5806 H   0  0  0  0  0  0  0  0  0  0  0  0
    4.4502    7.4435   12.8849 Cl  0  5  0  0  0  0  0  0  0  0  0  0
    6.2263    9.0672   12.5584 O   0  0  0  0  0  0  0  0  0  0  0  0
    5.5016    8.8757   13.0373 H   0  0  0  0  0  0  0  0  0  0  0  0
    5.8871    9.3290   11.8006 H   0  0  0  0  0  0  0  0  0  0  0  0
  1 51  1  0  0  0  0
  2 61  1  0  0  0  0
  3 15  1  0  0  0  0
  3 18  1  0  0  0  0
  4 12  1  0  0  0  0
  4 32  1  0  0  0  0
  5  6  2  0  0  0  0
  5  8  1  0  0  0  0
  5 46  1  0  0  0  0
  6  7  1  0  0  0  0
  7 10  1  0  0  0  0
  7 56  1  0  0  0  0
  8  9  1  0  0  0  0
```

Table I.2 Mol representation of 4,5-bis[(benzyloxy)methyl]-1,3-bis(4-chlorophenyl)-4,5-dihydro-3H-1,2,3-triazol-1-ylium chloride, continued

```
  8 10  1  0  0  0  0
  8 15  1  0  0  0  0
 10 11  1  0  0  0  0
 10 12  1  0  0  0  0
 12 13  1  0  0  0  0
 12 14  1  0  0  0  0
 15 16  1  0  0  0  0
 15 17  1  0  0  0  0
 18 19  1  0  0  0  0
 18 20  1  0  0  0  0
 18 21  1  0  0  0  0
 21 22  2  0  0  0  0
 21 30  1  0  0  0  0
 22 23  1  0  0  0  0
 22 24  1  0  0  0  0
 24 25  1  0  0  0  0
 24 26  2  0  0  0  0
 26 27  1  0  0  0  0
 26 28  1  0  0  0  0
 28 29  1  0  0  0  0
 28 30  2  0  0  0  0
 30 31  1  0  0  0  0
 32 33  1  0  0  0  0
 32 34  1  0  0  0  0
 32 35  1  0  0  0  0
 35 36  1  0  0  0  0
 35 44  2  0  0  0  0
 36 37  1  0  0  0  0
```

Table I.2 Mol representation of 4,5-bis[(benzyloxy)methyl]-1,3-bis(4-chlorophenyl)-4,5-dihydro-3H-1,2,3-triazol-1-ylium chloride, continued

```
 36 38  2  0  0  0  0
 38 39  1  0  0  0  0
 38 40  1  0  0  0  0
 40 41  1  0  0  0  0
 40 42  2  0  0  0  0
 42 43  1  0  0  0  0
 42 44  1  0  0  0  0
 44 45  1  0  0  0  0
 46 47  2  0  0  0  0
 46 54  1  0  0  0  0
 47 48  1  0  0  0  0
 47 49  1  0  0  0  0
 49 50  1  0  0  0  0
 49 51  2  0  0  0  0
 51 52  1  0  0  0  0
 52 53  1  0  0  0  0
 52 54  2  0  0  0  0
 54 55  1  0  0  0  0
 56 57  1  0  0  0  0
 56 64  2  0  0  0  0
 57 58  1  0  0  0  0
 57 59  2  0  0  0  0
 59 60  1  0  0  0  0
 59 61  1  0  0  0  0
 61 62  2  0  0  0  0
 62 63  1  0  0  0  0
 62 64  1  0  0  0  0
 64 65  1  0  0  0  0
```

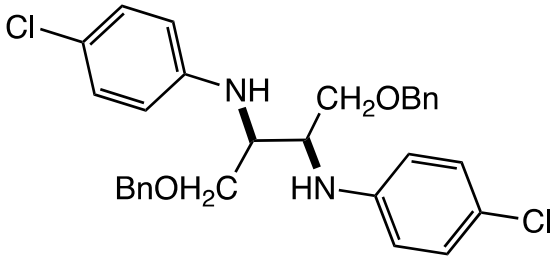
Table I.2 Mol representation of 4,5-bis[(benzyloxy)methyl]-1,3-bis(4-chlorophenyl)-4,5-dihydro-3H-1,2,3-triazol-1-ylium chloride, continued

```
 67 68  1  0  0  0  0
  67 69  1  0  0  0  0
M  CHG  2   5   1  66  -1
M  END
```

Crystal data for (1,4-bis(benzyloxy)-N^2,N^3-bis(4-chlorophenyl)butane-2,3-diamine

CCDC reference number: 2179884

UK Chem reference number: m21244



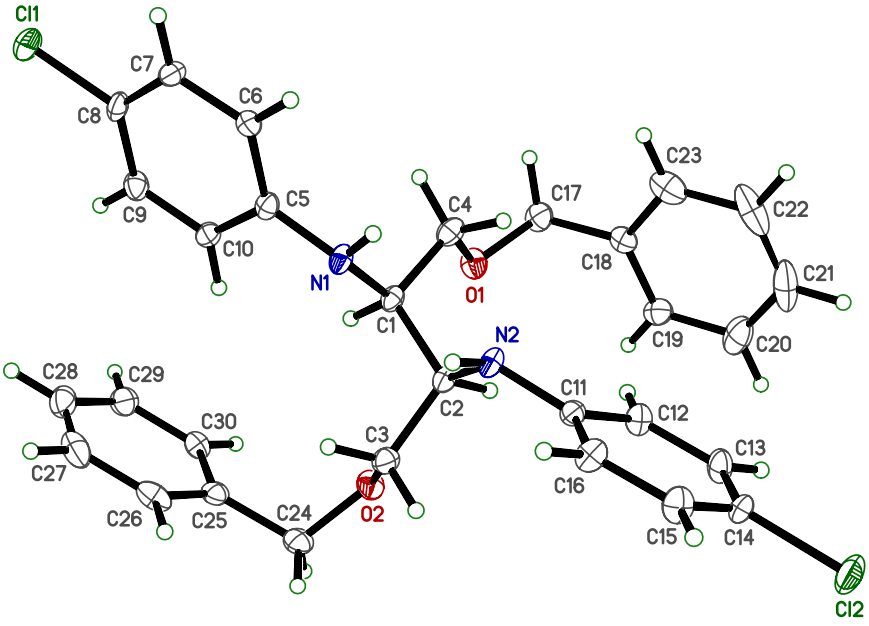


Table J.1 Crystal data and structure refinement for (1,4-bis(benzyloxy)-N^2,N^3-bis(4-chlorophenyl)butane-2,3-diamine.

Empirical formula	C_{30} H_{30} C_{12} N_2 O_2
Formula weight	521.46
Temperature	90.0(2) K
Wavelength	0.71073 Å
Crystal system, space group	Monoclinic, Pc
Unit cell dimensions	a = 5.4017(2) Å alpha = 90 deg. b = 14.7962(7) Å beta = 90.494(2) deg. c = 16.4297(8) Å gamma = 90 deg.
Volume	1313.09(10) Å^3
Z, Calculated density	2, 1.319 Mg/m^3
Absorption coefficient	0.278 mm^-1
F(000)	548
Crystal size	0.300 x 0.070 x 0.040 mm
Theta range for data collection	2.479 to 27.525 deg.
Limiting indices	-7<=h<=6, -19<=k<=19, -21<=l<=17
Reflections collected / unique	19432 / 5173 [R(int) = 0.0365]
Completeness to theta = 25.242	99.8 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.959 and 0.787
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	5173 / 2 / 333
Goodness-of-fit on F^2	1.162
Final R indices [I>2sigma(I)]	R1 = 0.0353, wR2 = 0.0722
R indices (all data)	R1 = 0.0421, wR2 = 0.0771
Absolute structure parameter	0.00(2)
Extinction coefficient	n/a
Largest diff. peak and hole	0.219 and -0.269 e.Å^-3

Table J.2 Mol representation of (2*R*,3*R*)-1,4-bis(benzyloxy)-*N*2,*N*3-bis(4-chlorophenyl)butane-2,3-diamine.

```
Mrv2211 05162214213D

 66 69  0  0  0  0            999 V2000
   -3.6979   -0.8800    7.6813 Cl  0  0  0  0  0  0  0  0  0  0  0  0
    8.0883    7.5223    5.6553 Cl  0  0  0  0  0  0  0  0  0  0  0  0
    2.7521    2.8283   10.3338 O   0  0  0  0  0  0  0  0  0  0  0  0
    1.0319    6.2132    8.9205 O   0  0  0  0  0  0  0  0  0  0  0  0
    1.0125    2.6879    7.0895 N   0  0  2  0  0  0  0  0  0  0  0  0
    1.5660    2.3502    6.6140 H   0  0  0  0  0  0  0  0  0  0  0  0
    3.1874    4.3292    6.6600 N   0  0  2  0  0  0  0  0  0  0  0  0
    2.6923    4.2697    5.9024 H   0  0  0  0  0  0  0  0  0  0  0  0
    1.6168    3.3179    8.2695 C   0  0  2  0  0  0  0  0  0  0  0  0
    0.8786    3.5919    8.8865 H   0  0  0  0  0  0  0  0  0  0  0  0
    2.3854    4.5800    7.8583 C   0  0  2  0  0  0  0  0  0  0  0  0
    3.0083    4.8197    8.6031 H   0  0  0  0  0  0  0  0  0  0  0  0
    1.4436    5.7517    7.6359 C   0  0  2  0  0  0  0  0  0  0  0  0
    1.9077    6.4751    7.1441 H   0  0  0  0  0  0  0  0  0  0  0  0
    0.6587    5.4645    7.1063 H   0  0  0  0  0  0  0  0  0  0  0  0
    2.5100    2.3289    9.0097 C   0  0  2  0  0  0  0  0  0  0  0  0
    2.0676    1.4447    9.0577 H   0  0  0  0  0  0  0  0  0  0  0  0
    3.3677    2.2222    8.5269 H   0  0  0  0  0  0  0  0  0  0  0  0
   -0.0802    1.8239    7.2742 C   0  0  0  0  0  0  0  0  0  0  0  0
   -0.1657    0.6336    6.5539 C   0  0  0  0  0  0  0  0  0  0  0  0
    0.5510    0.3778    5.9849 H   0  0  0  0  0  0  0  0  0  0  0  0
   -1.2831   -0.1806    6.6563 C   0  0  0  0  0  0  0  0  0  0  0  0
   -1.3374   -0.9810    6.1470 H   0  0  0  0  0  0  0  0  0  0  0  0
   -2.3125    0.1721    7.4993 C   0  0  0  0  0  0  0  0  0  0  0  0
   -2.2552    1.3483    8.2131 C   0  0  0  0  0  0  0  0  0  0  0  0
   -2.9719    1.5915    8.7874 H   0  0  0  0  0  0  0  0  0  0  0  0
```

Table J.2 Mol representation of (2*R*,3*R*)-1,4-bis(benzyloxy)-*N*2,*N*3-bis(4-chlorophenyl)butane-2,3-diamine, continued

-1.1504	2.1757	8.0942	C	0	0	0	0	0	0	0	0	0	0	0	0
-1.1224	2.9930	8.5778	H	0	0	0	0	0	0	0	0	0	0	0	0
4.3357	5.1148	6.4443	C	0	0	0	0	0	0	0	0	0	0	0	0
5.2756	5.3179	7.4613	C	0	0	0	0	0	0	0	0	0	0	0	0
5.1209	4.9481	8.3226	H	0	0	0	0	0	0	0	0	0	0	0	0
6.4243	6.0487	7.2294	C	0	0	0	0	0	0	0	0	0	0	0	0
7.0505	6.1965	7.9275	H	0	0	0	0	0	0	0	0	0	0	0	0
6.6492	6.5654	5.9620	C	0	0	0	0	0	0	0	0	0	0	0	0
5.7545	6.3667	4.9312	C	0	0	0	0	0	0	0	0	0	0	0	0
5.9286	6.7243	4.0684	H	0	0	0	0	0	0	0	0	0	0	0	0
4.5969	5.6429	5.1669	C	0	0	0	0	0	0	0	0	0	0	0	0
3.9769	5.5005	4.4617	H	0	0	0	0	0	0	0	0	0	0	0	0
3.8189	2.1230	10.9929	C	0	0	2	0	0	0	0	0	0	0	0	0
3.7259	1.1523	10.8164	H	0	0	0	0	0	0	0	0	0	0	0	0
3.7474	2.2619	11.9705	H	0	0	0	0	0	0	0	0	0	0	0	0
5.1793	2.5872	10.5205	C	0	0	0	0	0	0	0	0	0	0	0	0
5.6769	3.7861	10.9738	C	0	0	0	0	0	0	0	0	0	0	0	0
5.1558	4.3163	11.5658	H	0	0	0	0	0	0	0	0	0	0	0	0
6.9298	4.2314	10.5772	C	0	0	0	0	0	0	0	0	0	0	0	0
7.2694	5.0572	10.9040	H	0	0	0	0	0	0	0	0	0	0	0	0
7.6786	3.4714	9.7065	C	0	0	0	0	0	0	0	0	0	0	0	0
8.5324	3.7791	9.4237	H	0	0	0	0	0	0	0	0	0	0	0	0
7.1978	2.2693	9.2457	C	0	0	0	0	0	0	0	0	0	0	0	0
7.7233	1.7412	8.6562	H	0	0	0	0	0	0	0	0	0	0	0	0
5.9357	1.8233	9.6460	C	0	0	0	0	0	0	0	0	0	0	0	0
5.5960	0.9988	9.3186	H	0	0	0	0	0	0	0	0	0	0	0	0
-0.1435	7.0325	8.8416	C	0	0	2	0	0	0	0	0	0	0	0	0
-0.0724	7.6306	8.0562	H	0	0	0	0	0	0	0	0	0	0	0	0

Table J.2 Mol representation of (2*R*,3*R*)-1,4-bis(benzyloxy)-*N*2,*N*3-bis(4-chlorophenyl)butane-2,3-diamine, continued

```
   -0.2015    7.5986    9.6518 H   0  0  0  0  0  0  0  0  0  0  0  0
   -1.3981    6.2045    8.7238 C   0  0  0  0  0  0  0  0  0  0  0  0
   -2.1121    6.1043    7.5301 C   0  0  0  0  0  0  0  0  0  0  0  0
   -1.8110    6.5736    6.7605 H   0  0  0  0  0  0  0  0  0  0  0  0
   -3.2536    5.3322    7.4571 C   0  0  0  0  0  0  0  0  0  0  0  0
   -3.7335    5.2697    6.6403 H   0  0  0  0  0  0  0  0  0  0  0  0
   -3.7019    4.6410    8.5843 C   0  0  0  0  0  0  0  0  0  0  0  0
   -4.4854    4.1062    8.5338 H   0  0  0  0  0  0  0  0  0  0  0  0
   -2.9996    4.7350    9.7797 C   0  0  0  0  0  0  0  0  0  0  0  0
   -3.3061    4.2682   10.5483 H   0  0  0  0  0  0  0  0  0  0  0  0
   -1.8571    5.5082    9.8496 C   0  0  0  0  0  0  0  0  0  0  0  0
   -1.3784    5.5675   10.6683 H   0  0  0  0  0  0  0  0  0  0  0  0
  1 24  1  0  0  0  0
  2 34  1  0  0  0  0
  3 16  1  0  0  0  0
  3 39  1  0  0  0  0
  4 13  1  0  0  0  0
  4 53  1  0  0  0  0
  5  6  1  0  0  0  0
  5  9  1  0  0  0  0
  5 19  1  0  0  0  0
  7  8  1  0  0  0  0
  7 11  1  0  0  0  0
  7 29  1  0  0  0  0
  9 10  1  0  0  0  0
  9 11  1  0  0  0  0
  9 16  1  0  0  0  0
 11 12  1  0  0  0  0
```

Table J.2 Mol representation of (2*R*,3*R*)-1,4-bis(benzyloxy)-*N*2,*N*3-bis(4-chlorophenyl)butane-2,3-diamine, continued

```
 11 13  1  0  0  0  0
 13 14  1  0  0  0  0
 13 15  1  0  0  0  0
 16 17  1  0  0  0  0
 16 18  1  0  0  0  0
 19 20  2  0  0  0  0
 19 27  1  0  0  0  0
 20 21  1  0  0  0  0
 20 22  1  0  0  0  0
 22 23  1  0  0  0  0
 22 24  2  0  0  0  0
 24 25  1  0  0  0  0
 25 26  1  0  0  0  0
 25 27  2  0  0  0  0
 27 28  1  0  0  0  0
 29 30  2  0  0  0  0
 29 37  1  0  0  0  0
 30 31  1  0  0  0  0
 30 32  1  0  0  0  0
 32 33  1  0  0  0  0
 32 34  2  0  0  0  0
 34 35  1  0  0  0  0
 35 36  1  0  0  0  0
 35 37  2  0  0  0  0
 37 38  1  0  0  0  0
 39 40  1  0  0  0  0
 39 41  1  0  0  0  0
 39 42  1  0  0  0  0
```

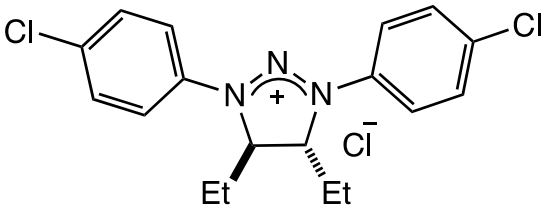
Table J.2 Mol representation of (2*R*,3*R*)-1,4-bis(benzyloxy)-*N*2,*N*3-bis(4-chlorophenyl)butane-2,3-diamine, continued

```
 42 43  2  0  0  0  0
 42 51  1  0  0  0  0
 43 44  1  0  0  0  0
 43 45  1  0  0  0  0
 45 46  1  0  0  0  0
 45 47  2  0  0  0  0
 47 48  1  0  0  0  0
 47 49  1  0  0  0  0
 49 50  1  0  0  0  0
 49 51  2  0  0  0  0
 51 52  1  0  0  0  0
 53 54  1  0  0  0  0
 53 55  1  0  0  0  0
 53 56  1  0  0  0  0
 56 57  2  0  0  0  0
 56 65  1  0  0  0  0
 57 58  1  0  0  0  0
 57 59  1  0  0  0  0
 59 60  1  0  0  0  0
 59 61  2  0  0  0  0
 61 62  1  0  0  0  0
 61 63  1  0  0  0  0
 63 64  1  0  0  0  0
 63 65  2  0  0  0  0
 65 66  1  0  0  0  0
M  END
```

Crystal data for 1,3-bis(4-chlorophenyl)-4,5-diethyl-4,5-dihydro-3H-1,2,3-triazol-1-ylium chloride

CCDC reference number: 2179886

UK Chem reference number: m21296



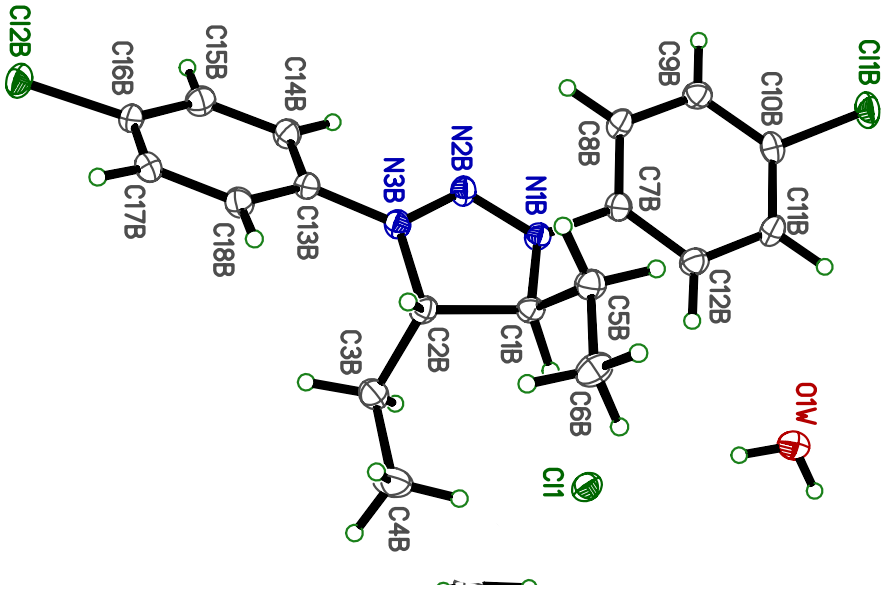


Table K.1 Crystal data and structure refinement for 1,3-bis(4-chlorophenyl)-4,5-diethyl-4,5-dihydro-3H-1,2,3-triazol-1-ylium chloride.

Empirical formula	C18 H22 Cl3 N3 O
Formula weight	402.73
Temperature	90.0(2) K
Wavelength	0.71073 Å
Crystal system, space group	Triclinic, P-1
Unit cell dimensions	a = 9.8582(5) Å alpha = 102.900(2) deg. b = 11.6717(6) Å beta = 104.709(2) deg. c = 18.1996(11) Å gamma = 93.563(3) deg.
Volume	1958.59(19) Å^3
Z, Calculated density	4, 1.366 Mg/m^3
Absorption coefficient	0.479 mm^-1
F(000)	840
Crystal size	0.210 x 0.200 x 0.140 mm
Theta range for data collection	1.901 to 27.525 deg.
Limiting indices	-12<=h<=12, -15<=k<=15, -23<=l<=23
Reflections collected / unique	16919 / 16919 [R(int) = ?]
Completeness to theta = 25.242	99.8 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.970 and 0.840
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	16919 / 6 / 469
Goodness-of-fit on F^2	1.022
Final R indices [I>2sigma(I)]	R1 = 0.0375, wR2 = 0.0758
R indices (all data)	R1 = 0.0571, wR2 = 0.0837
Extinction coefficient	n/a
Largest diff. peak and hole	0.291 and -0.254 e.Å^-3

Table K.2 Mol representation of 1,3-bis(4-chlorophenyl)-4,5-diethyl-4,5-dihydro-3H-1,2,3-triazol-1-ylium chloride.

```
Mrv2211 05162212243D

 94 94  0  0  0  0            999 V2000
   12.7650    0.3415   14.7292 Cl  0  0  0  0  0  0  0  0  0  0  0  0
    3.4316    8.9507   12.8442 Cl  0  0  0  0  0  0  0  0  0  0  0  0
    7.2997    2.5136   15.1307 N   0  3  0  0  0  0  0  0  0  0  0  0
    6.9777    3.5982   14.5119 N   0  0  0  0  0  0  0  0  0  0  0  0
    5.7158    3.8307   14.6730 N   0  0  0  0  0  0  0  0  0  0  0  0
    6.1443    1.8053   15.7555 C   0  0  1  0  0  0  0  0  0  0  0  0
    6.3237    1.6488   16.7267 H   0  0  0  0  0  0  0  0  0  0  0  0
    5.0394    2.8636   15.5883 C   0  0  1  0  0  0  0  0  0  0  0  0
    4.2399    2.4630   15.1407 H   0  0  0  0  0  0  0  0  0  0  0  0
    4.6322    3.5381   16.8957 C   0  0  1  0  0  0  0  0  0  0  0  0
    5.4441    3.8041   17.3959 H   0  0  0  0  0  0  0  0  0  0  0  0
    4.1131    4.3571   16.6960 H   0  0  0  0  0  0  0  0  0  0  0  0
    3.7907    2.6017   17.7557 C   0  0  0  0  0  0  0  0  0  0  0  0
    2.9963    2.3231   17.2539 H   0  0  0  0  0  0  0  0  0  0  0  0
    3.5151    3.0672   18.5722 H   0  0  0  0  0  0  0  0  0  0  0  0
    4.3206    1.8118   17.9926 H   0  0  0  0  0  0  0  0  0  0  0  0
    5.8776    0.4790   15.0548 C   0  0  1  0  0  0  0  0  0  0  0  0
    5.5921    0.6482   14.1220 H   0  0  0  0  0  0  0  0  0  0  0  0
    6.7103   -0.0559   15.0295 H   0  0  0  0  0  0  0  0  0  0  0  0
    4.7952   -0.2978   15.7856 C   0  0  0  0  0  0  0  0  0  0  0  0
    5.0380   -0.3859   16.7308 H   0  0  0  0  0  0  0  0  0  0  0  0
    4.7070   -1.1889   15.3867 H   0  0  0  0  0  0  0  0  0  0  0  0
    3.9429    0.1795   15.7100 H   0  0  0  0  0  0  0  0  0  0  0  0
    8.6391    2.0377   15.0633 C   0  0  0  0  0  0  0  0  0  0  0  0
    9.0686    1.1222   16.0096 C   0  0  0  0  0  0  0  0  0  0  0  0
    8.4877    0.8417   16.7069 H   0  0  0  0  0  0  0  0  0  0  0  0
```

Table K.2 Mol representation of 1,3-bis(4-chlorophenyl)-4,5-diethyl-4,5-dihydro-3H-1,2,3-triazol-1-ylium chloride, continued

10.3581	0.6212	15.9245	C	0	0	0	0	0	0	0	0	0	0	0	0
10.6740	-0.0032	16.5671	H	0	0	0	0	0	0	0	0	0	0	0	0
11.1792	1.0392	14.8955	C	0	0	0	0	0	0	0	0	0	0	0	0
10.7657	1.9887	13.9798	C	0	0	0	0	0	0	0	0	0	0	0	0
11.3578	2.2877	13.2999	H	0	0	0	0	0	0	0	0	0	0	0	0
9.4864	2.4999	14.0612	C	0	0	0	0	0	0	0	0	0	0	0	0
9.1890	3.1568	13.4427	H	0	0	0	0	0	0	0	0	0	0	0	0
5.1648	5.0421	14.1726	C	0	0	0	0	0	0	0	0	0	0	0	0
3.7885	5.2109	14.1712	C	0	0	0	0	0	0	0	0	0	0	0	0
3.2192	4.5025	14.4476	H	0	0	0	0	0	0	0	0	0	0	0	0
3.2520	6.4163	13.7645	C	0	0	0	0	0	0	0	0	0	0	0	0
2.3116	6.5517	13.7739	H	0	0	0	0	0	0	0	0	0	0	0	0
4.1012	7.4263	13.3441	C	0	0	0	0	0	0	0	0	0	0	0	0
5.4690	7.2421	13.2966	C	0	0	0	0	0	0	0	0	0	0	0	0
6.0325	7.9376	12.9781	H	0	0	0	0	0	0	0	0	0	0	0	0
6.0144	6.0459	13.7127	C	0	0	0	0	0	0	0	0	0	0	0	0
6.9541	5.9084	13.6862	H	0	0	0	0	0	0	0	0	0	0	0	0
4.6140	-7.9362	11.7892	Cl	0	0	0	0	0	0	0	0	0	0	0	0
-6.3013	-1.1282	12.6160	Cl	0	0	0	0	0	0	0	0	0	0	0	0
0.8906	-3.5440	10.4707	N	0	0	0	0	0	0	0	0	0	0	0	0
-0.2549	-3.4656	11.0607	N	0	0	0	0	0	0	0	0	0	0	0	0
-0.8342	-2.3554	10.7456	N	0	3	0	0	0	0	0	0	0	0	0	0
1.2543	-2.3196	9.6921	C	0	0	1	0	0	0	0	0	0	0	0	0
1.4584	-2.5611	8.7435	H	0	0	0	0	0	0	0	0	0	0	0	0
-0.0651	-1.5260	9.7680	C	0	0	1	0	0	0	0	0	0	0	0	0
0.1073	-0.6205	10.1557	H	0	0	0	0	0	0	0	0	0	0	0	0
-0.8118	-1.3864	8.4417	C	0	0	1	0	0	0	0	0	0	0	0	0
-0.7571	-2.2377	7.9400	H	0	0	0	0	0	0	0	0	0	0	0	0

Table K.2 Mol representation of 1,3-bis(4-chlorophenyl)-4,5-diethyl-4,5-dihydro-3H-1,2,3-triazol-1-ylium chloride, continued

-1.7671	-1.1948	8.6189	H	0	0	0	0	0	0	0	0	0	0	0	0
-0.2153	-0.2657	7.6071	C	0	0	0	0	0	0	0	0	0	0	0	0
-0.1701	0.5532	8.1440	H	0	0	0	0	0	0	0	0	0	0	0	0
-0.7790	-0.1090	6.8204	H	0	0	0	0	0	0	0	0	0	0	0	0
0.6861	-0.5173	7.3182	H	0	0	0	0	0	0	0	0	0	0	0	0
2.4441	-1.5966	10.3210	C	0	0	1	0	0	0	0	0	0	0	0	0
2.1952	-1.2733	11.2230	H	0	0	0	0	0	0	0	0	0	0	0	0
3.2002	-2.2281	10.4190	H	0	0	0	0	0	0	0	0	0	0	0	0
2.8750	-0.4195	9.4616	C	0	0	0	0	0	0	0	0	0	0	0	0
3.1445	-0.7425	8.5765	H	0	0	0	0	0	0	0	0	0	0	0	0
3.6311	0.0364	9.8871	H	0	0	0	0	0	0	0	0	0	0	0	0
2.1273	0.2070	9.3670	H	0	0	0	0	0	0	0	0	0	0	0	0
1.7379	-4.6616	10.7280	C	0	0	0	0	0	0	0	0	0	0	0	0
2.8842	-4.8311	9.9651	C	0	0	0	0	0	0	0	0	0	0	0	0
3.0637	-4.2501	9.2351	H	0	0	0	0	0	0	0	0	0	0	0	0
3.7656	-5.8550	10.2763	C	0	0	0	0	0	0	0	0	0	0	0	0
4.5544	-5.9818	9.7623	H	0	0	0	0	0	0	0	0	0	0	0	0
3.4847	-6.6904	11.3435	C	0	0	0	0	0	0	0	0	0	0	0	0
2.3090	-6.5577	12.0649	C	0	0	0	0	0	0	0	0	0	0	0	0
2.1135	-7.1621	12.7711	H	0	0	0	0	0	0	0	0	0	0	0	0
1.4242	-5.5476	11.7561	C	0	0	0	0	0	0	0	0	0	0	0	0
0.6106	-5.4565	12.2382	H	0	0	0	0	0	0	0	0	0	0	0	0
-2.1275	-2.0568	11.2552	C	0	0	0	0	0	0	0	0	0	0	0	0
-2.6309	-0.7725	11.1091	C	0	0	0	0	0	0	0	0	0	0	0	0
-2.0941	-0.0896	10.7243	H	0	0	0	0	0	0	0	0	0	0	0	0
-3.9179	-0.4929	11.5267	C	0	0	0	0	0	0	0	0	0	0	0	0
-4.2738	0.3823	11.4278	H	0	0	0	0	0	0	0	0	0	0	0	0
-4.6838	-1.4970	12.0898	C	0	0	0	0	0	0	0	0	0	0	0	0

Table K.2 Mol representation of 1,3-bis(4-chlorophenyl)-4,5-diethyl-4,5-dihydro-3H-1,2,3-triazol-1-ylium chloride, continued

```
  -4.1794   -2.7744   12.2540 C   0  0  0  0  0  0  0  0  0  0  0  0
  -4.7185   -3.4544   12.6409 H   0  0  0  0  0  0  0  0  0  0  0  0
  -2.8880   -3.0570   11.8531 C   0  0  0  0  0  0  0  0  0  0  0  0
  -2.5231   -3.9244   11.9840 H   0  0  0  0  0  0  0  0  0  0  0  0
   2.6583    1.7502   13.1748 Cl  0  5  0  0  0  0  0  0  0  0  0  0
  -2.0734    3.3589   12.1748 Cl  0  5  0  0  0  0  0  0  0  0  0  0
   0.4516    1.5860   11.6035 O   0  0  0  0  0  0  0  0  0  0  0  0
  -0.1115    2.1448   11.8326 H   0  0  0  0  0  0  0  0  0  0  0  0
   1.1443    1.7460   12.0180 H   0  0  0  0  0  0  0  0  0  0  0  0
   0.7905    4.3537   13.1324 O   0  0  0  0  0  0  0  0  0  0  0  0
   0.0655    4.1279   12.8083 H   0  0  0  0  0  0  0  0  0  0  0  0
   1.2953    3.7086   13.0056 H   0  0  0  0  0  0  0  0  0  0  0  0
 1 29  1  0  0  0  0
 2 39  1  0  0  0  0
 3  4  2  0  0  0  0
 3  6  1  0  0  0  0
 3 24  1  0  0  0  0
 4  5  1  0  0  0  0
 5  8  1  0  0  0  0
 5 34  1  0  0  0  0
 6  7  1  0  0  0  0
 6  8  1  0  0  0  0
 6 17  1  0  0  0  0
 8  9  1  0  0  0  0
 8 10  1  0  0  0  0
10 11  1  0  0  0  0
10 12  1  0  0  0  0
10 13  1  0  0  0  0
```

Table K.2 Mol representation of 1,3-bis(4-chlorophenyl)-4,5-diethyl-4,5-dihydro-3H-1,2,3-triazol-1-ylium chloride, continued

```
 13 14  1  0  0  0  0
 13 15  1  0  0  0  0
 13 16  1  0  0  0  0
 17 18  1  0  0  0  0
 17 19  1  0  0  0  0
 17 20  1  0  0  0  0
 20 21  1  0  0  0  0
 20 22  1  0  0  0  0
 20 23  1  0  0  0  0
 24 25  2  0  0  0  0
 24 32  1  0  0  0  0
 25 26  1  0  0  0  0
 25 27  1  0  0  0  0
 27 28  1  0  0  0  0
 27 29  2  0  0  0  0
 29 30  1  0  0  0  0
 30 31  1  0  0  0  0
 30 32  2  0  0  0  0
 32 33  1  0  0  0  0
 34 35  1  0  0  0  0
 34 42  2  0  0  0  0
 35 36  1  0  0  0  0
 35 37  2  0  0  0  0
 37 38  1  0  0  0  0
 37 39  1  0  0  0  0
 39 40  2  0  0  0  0
 40 41  1  0  0  0  0
 40 42  1  0  0  0  0
```

Table K.2 Mol representation of 1,3-bis(4-chlorophenyl)-4,5-diethyl-4,5-dihydro-3H-1,2,3-triazol-1-ylium chloride, continued

```
 42 43  1  0  0  0  0
 44 72  1  0  0  0  0
 45 82  1  0  0  0  0
 46 47  1  0  0  0  0
 46 49  1  0  0  0  0
 46 67  1  0  0  0  0
 47 48  2  0  0  0  0
 48 51  1  0  0  0  0
 48 77  1  0  0  0  0
 49 50  1  0  0  0  0
 49 51  1  0  0  0  0
 49 60  1  0  0  0  0
 51 52  1  0  0  0  0
 51 53  1  0  0  0  0
 53 54  1  0  0  0  0
 53 55  1  0  0  0  0
 53 56  1  0  0  0  0
 56 57  1  0  0  0  0
 56 58  1  0  0  0  0
 56 59  1  0  0  0  0
 60 61  1  0  0  0  0
 60 62  1  0  0  0  0
 60 63  1  0  0  0  0
 63 64  1  0  0  0  0
 63 65  1  0  0  0  0
 63 66  1  0  0  0  0
 67 68  1  0  0  0  0
 67 75  2  0  0  0  0
```

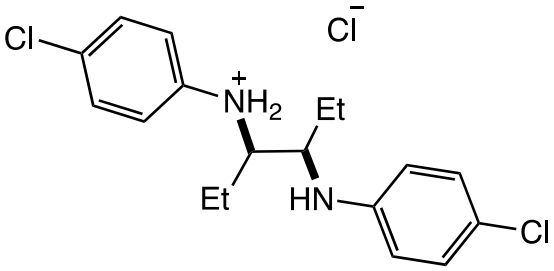
Table K.2 Mol representation of 1,3-bis(4-chlorophenyl)-4,5-diethyl-4,5-dihydro-3H-1,2,3-triazol-1-ylium chloride, continued

```
 68 69  1  0  0  0  0
 68 70  2  0  0  0  0
 70 71  1  0  0  0  0
 70 72  1  0  0  0  0
 72 73  2  0  0  0  0
 73 74  1  0  0  0  0
 73 75  1  0  0  0  0
 75 76  1  0  0  0  0
 77 78  1  0  0  0  0
 77 85  2  0  0  0  0
 78 79  1  0  0  0  0
 78 80  2  0  0  0  0
 80 81  1  0  0  0  0
 80 82  1  0  0  0  0
 82 83  2  0  0  0  0
 83 84  1  0  0  0  0
 83 85  1  0  0  0  0
 85 86  1  0  0  0  0
 89 90  1  0  0  0  0
 89 91  1  0  0  0  0
 92 93  1  0  0  0  0
 92 94  1  0  0  0  0
M  CHG  4   3   1  48   1  87  -1  88  -1
M  END
```

Crystal data for N^3,N^4-bis(4-chlorophenyl)hexane-3,4-diamine as a HCl salt

CCDC reference number: 2179890

UK Chem reference number: m21319



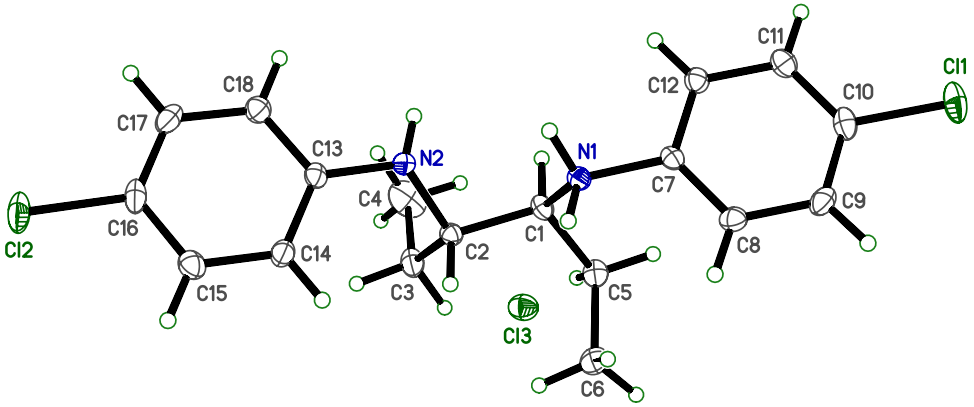


Table L.1 Crystal data and structure refinement for N^3,N^4-bis(4-chlorophenyl)hexane-3,4-diamine as a HCl salt.

Empirical formula	C_{18} H_{23} C_{13} N_2
Formula weight	373.73
Temperature	90.0(2) K
Wavelength	0.71073 Å
Crystal system, space group	Monoclinic, C2/c
Unit cell dimensions	a = 25.2703(9) Å alpha = 90 deg. b = 6.2514(3) Å beta = 100.076(1) deg. c = 24.4235(9) Å gamma = 90 deg.
Volume	3798.8(3) Å^3
Z, Calculated density	8, 1.307 Mg/m^3
Absorption coefficient	0.483 mm^-1
F(000)	1568
Crystal size	0.330 x 0.020 x 0.010 mm
Theta range for data collection	2.140 to 27.899 deg.
Limiting indices	-33<=h<=32, -8<=k<=8, -32<=l<=31
Reflections collected / unique	27875 / 4513 [R(int) = 0.0758]
Completeness to theta = 25.242	99.9 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.971 and 0.892
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4513 / 0 / 219
Goodness-of-fit on F^2	1.029
Final R indices [I>2sigma(I)]	R1 = 0.0435, wR2 = 0.0801
R indices (all data)	R1 = 0.0790, wR2 = 0.0900
Extinction coefficient	n/a
Largest diff. peak and hole	0.355 and -0.294 e.Å^-3

Table L.2 Mol representation for N^3,N^4-bis(4-chlorophenyl)hexane-3,4-diamine as a HCl salt.

```
Mrv2211 05162213363D

 46 46  0  0  0  0            999 V2000
   13.1846    4.5095   13.4995 Cl  0  5  0  0  0  0  0  0  0  0  0  0
    8.1259    7.3873   19.7414 Cl  0  0  0  0  0  0  0  0  0  0  0  0
   18.8050    1.3342   12.2125 Cl  0  0  0  0  0  0  0  0  0  0  0  0
   12.2999    4.4307   16.7257 N   0  3  1  0  0  0  0  0  0  0  0  0
   12.9534    4.9969   16.4503 H   0  0  0  0  0  0  0  0  0  0  0  0
   11.9588    4.1066   15.9236 H   0  0  0  0  0  0  0  0  0  0  0  0
   14.7959    3.4443   16.0359 N   0  0  2  0  0  0  0  0  0  0  0  0
   15.1587    3.9555   16.6235 H   0  0  0  0  0  0  0  0  0  0  0  0
   12.8919    3.2865   17.5363 C   0  0  2  0  0  0  0  0  0  0  0  0
   13.4503    3.6820   18.2660 H   0  0  0  0  0  0  0  0  0  0  0  0
   13.8202    2.5071   16.6013 C   0  0  2  0  0  0  0  0  0  0  0  0
   13.2660    2.1529   15.8479 H   0  0  0  0  0  0  0  0  0  0  0  0
   14.4863    1.3103   17.2946 C   0  0  1  0  0  0  0  0  0  0  0  0
   13.7774    0.7102   17.6369 H   0  0  0  0  0  0  0  0  0  0  0  0
   15.0054    0.8047   16.6201 H   0  0  0  0  0  0  0  0  0  0  0  0
   15.4070    1.6679   18.4400 C   0  0  0  0  0  0  0  0  0  0  0  0
   15.8345    0.8549   18.7817 H   0  0  0  0  0  0  0  0  0  0  0  0
   14.8886    2.0902   19.1564 H   0  0  0  0  0  0  0  0  0  0  0  0
   16.0950    2.2904   18.1241 H   0  0  0  0  0  0  0  0  0  0  0  0
   11.8090    2.4290   18.1843 C   0  0  2  0  0  0  0  0  0  0  0  0
   11.1907    3.0277   18.6735 H   0  0  0  0  0  0  0  0  0  0  0  0
   12.2394    1.8387   18.8526 H   0  0  0  0  0  0  0  0  0  0  0  0
   10.9841    1.5588   17.2384 C   0  0  0  0  0  0  0  0  0  0  0  0
   10.2383    1.1574   17.7310 H   0  0  0  0  0  0  0  0  0  0  0  0
   11.5511    0.8500   16.8690 H   0  0  0  0  0  0  0  0  0  0  0  0
   10.6342    2.1112   16.5085 H   0  0  0  0  0  0  0  0  0  0  0  0
   11.2668    5.2055   17.4242 C   0  0  0  0  0  0  0  0  0  0  0  0
```

Table L.2 Mol representation for N^3,N^4-bis(4-chlorophenyl)hexane-3,4-diamine as a HCl salt, continued

```
     9.9412    4.9474   17.1625 C   0  0  0  0  0  0  0  0  0  0  0  0
     9.6953    4.3089   16.5031 H   0  0  0  0  0  0  0  0  0  0  0  0
     8.9672    5.6341   17.8759 C   0  0  0  0  0  0  0  0  0  0  0  0
     8.0458    5.4743   17.7089 H   0  0  0  0  0  0  0  0  0  0  0  0
     9.3534    6.5474   18.8265 C   0  0  0  0  0  0  0  0  0  0  0  0
    10.6811    6.8358   19.0665 C   0  0  0  0  0  0  0  0  0  0  0  0
    10.9240    7.4901   19.7110 H   0  0  0  0  0  0  0  0  0  0  0  0
    11.6571    6.1542   18.3504 C   0  0  0  0  0  0  0  0  0  0  0  0
    12.5779    6.3369   18.4953 H   0  0  0  0  0  0  0  0  0  0  0  0
    15.7226    2.9554   15.1046 C   0  0  0  0  0  0  0  0  0  0  0  0
    15.3600    2.0492   14.1109 C   0  0  0  0  0  0  0  0  0  0  0  0
    14.4584    1.7556   14.0505 H   0  0  0  0  0  0  0  0  0  0  0  0
    16.2960    1.5699   13.2091 C   0  0  0  0  0  0  0  0  0  0  0  0
    16.0415    0.9475   12.5382 H   0  0  0  0  0  0  0  0  0  0  0  0
    17.6071    2.0075   13.2956 C   0  0  0  0  0  0  0  0  0  0  0  0
    17.9842    2.9297   14.2408 C   0  0  0  0  0  0  0  0  0  0  0  0
    18.8790    3.2462   14.2722 H   0  0  0  0  0  0  0  0  0  0  0  0
    17.0464    3.3926   15.1460 C   0  0  0  0  0  0  0  0  0  0  0  0
    17.3093    4.0207   15.8089 H   0  0  0  0  0  0  0  0  0  0  0  0
  2 32  1  0  0  0  0
  3 42  1  0  0  0  0
  4  5  1  0  0  0  0
  4  6  1  0  0  0  0
  4  9  1  0  0  0  0
  4 27  1  0  0  0  0
  7  8  1  0  0  0  0
  7 11  1  0  0  0  0
  7 37  1  0  0  0  0
  9 10  1  0  0  0  0
```

Table L.2 Mol representation for N^3,N^4-bis(4-chlorophenyl)hexane-3,4-diamine as a HCl salt, continued

```
  9 11  1  0  0  0  0
  9 20  1  0  0  0  0
 11 12  1  0  0  0  0
 11 13  1  0  0  0  0
 13 14  1  0  0  0  0
 13 15  1  0  0  0  0
 13 16  1  0  0  0  0
 16 17  1  0  0  0  0
 16 18  1  0  0  0  0
 16 19  1  0  0  0  0
 20 21  1  0  0  0  0
 20 22  1  0  0  0  0
 20 23  1  0  0  0  0
 23 24  1  0  0  0  0
 23 25  1  0  0  0  0
 23 26  1  0  0  0  0
 27 28  1  0  0  0  0
 27 35  2  0  0  0  0
 28 29  1  0  0  0  0
 28 30  2  0  0  0  0
 30 31  1  0  0  0  0
 30 32  1  0  0  0  0
 32 33  2  0  0  0  0
 33 34  1  0  0  0  0
 33 35  1  0  0  0  0
 35 36  1  0  0  0  0
 37 38  1  0  0  0  0
 37 45  2  0  0  0  0
 38 39  1  0  0  0  0
```

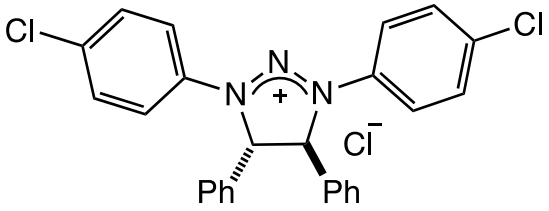
Table L.2 Mol representation for N^3,N^4-bis(4-chlorophenyl)hexane-3,4-diamine as a HCl salt, continued

```
 38 40  2  0  0  0  0
 40 41  1  0  0  0  0
 40 42  1  0  0  0  0
 42 43  2  0  0  0  0
 43 44  1  0  0  0  0
 43 45  1  0  0  0  0
 45 46  1  0  0  0  0
M  CHG  2   1  -1   4   1
M  END
```

Crystal data 1,3-bis(4-chlorophenyl)-4,5-diphenyl-4,5-dihydro-3H-1,2,3-triazol-1-ylium chloride

CCDC reference number: 2179896

UK Chem reference number: m21331s



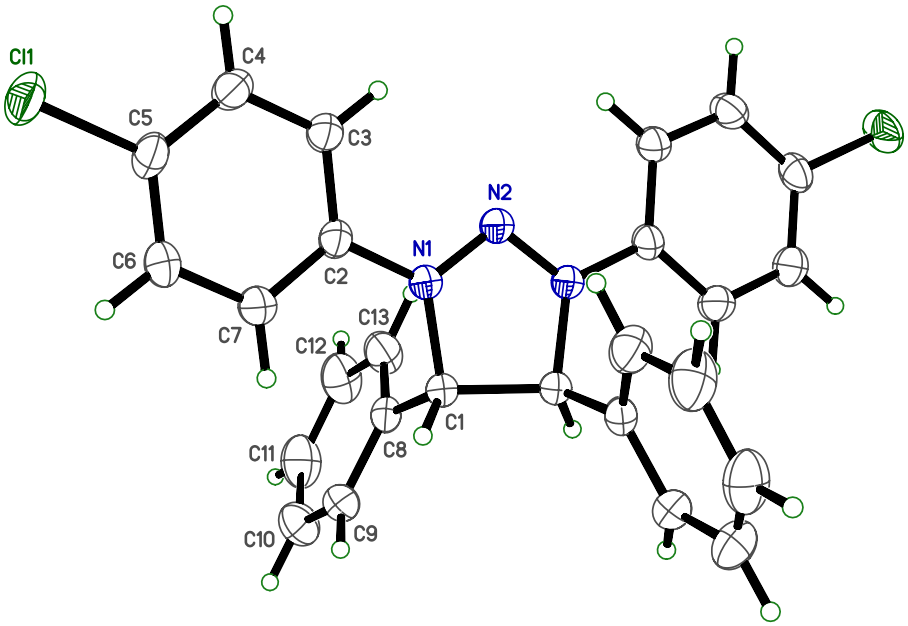


Table M.1 Crystal data and structure refinement for 1,3-bis(4-chlorophenyl)-4,5-diphenyl-4,5-dihydro-3H-1,2,3-triazol-1-ylium chloride.

Empirical formula	C_{26} H_{20} C_{12} N_3
Formula weight	445.35
Temperature	250(2) K
Wavelength	0.71073 Å
Crystal system, space group	Monoclinic, C2/c
Unit cell dimensions	a = 8.8145(7) Å alpha = 90 deg. b = 17.6901(15) Å beta = 95.622(3) deg. c = 15.6982(12) Å gamma = 90 deg.
Volume	2436.0(3) Å^3
Z, Calculated density	4, 1.214 Mg/m^3
Absorption coefficient	0.283 mm^-1
F(000)	924
Crystal size	0.130 x 0.110 x 0.080 mm
Theta range for data collection	2.592 to 27.496 deg.
Limiting indices	-11<=h<=11, -22<=k<=22, -20<=l<=20
Reflections collected / unique	35778 / 2807 [R(int) = 0.0379]
Completeness to theta = 25.242	99.9 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.000 and 0.000
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	2807 / 0 / 141
Goodness-of-fit on F^2	1.032
Final R indices [I>2sigma(I)]	R1 = 0.0411, wR2 = 0.1012
R indices (all data)	R1 = 0.0555, wR2 = 0.1118
Extinction coefficient	n/a
Largest diff. peak and hole	0.264 and -0.303 e.Å^-3

Table M.2 Mol representation for 1,3-bis(4-chlorophenyl)-4,5-diphenyl-4,5-dihydro-3H-1,2,3-triazol-1-ylium chloride.

```
Mrv2211 05162212193D

 52 55  0  0  0  0            999 V2000
    5.5736    9.1311    0.4379 Cl  0  0  0  0  0  0  0  0  0  0  0  0
    0.6286    7.9304    3.3960 N   0  3  0  0  0  0  0  0  0  0  0  0
   -0.0919    8.8655    3.9413 N   0  0  0  0  0  0  0  0  0  0  0  0
    0.1396    6.5631    3.7147 C   0  0  1  0  0  0  0  0  0  0  0  0
    0.1877    5.9746    2.9199 H   0  0  0  0  0  0  0  0  0  0  0  0
    1.8235    8.2428    2.7010 C   0  0  0  0  0  0  0  0  0  0  0  0
    2.2315    9.5579    2.5628 C   0  0  0  0  0  0  0  0  0  0  0  0
    1.7240   10.2572    2.9332 H   0  0  0  0  0  0  0  0  0  0  0  0
    3.3933    9.8250    1.8741 C   0  0  0  0  0  0  0  0  0  0  0  0
    3.6890   10.7116    1.7727 H   0  0  0  0  0  0  0  0  0  0  0  0
    4.1235    8.7844    1.3316 C   0  0  0  0  0  0  0  0  0  0  0  0
    3.7131    7.4864    1.4567 C   0  0  0  0  0  0  0  0  0  0  0  0
    4.2207    6.7919    1.0775 H   0  0  0  0  0  0  0  0  0  0  0  0
    2.5469    7.2008    2.1435 C   0  0  0  0  0  0  0  0  0  0  0  0
    2.2498    6.3133    2.2307 H   0  0  0  0  0  0  0  0  0  0  0  0
    0.9447    6.0229    4.8839 C   0  0  0  0  0  0  0  0  0  0  0  0
    1.2820    4.6537    4.8363 C   0  0  0  0  0  0  0  0  0  0  0  0
    1.0688    4.1245    4.0891 H   0  0  0  0  0  0  0  0  0  0  0  0
    1.9456    4.0962    5.9163 C   0  0  0  0  0  0  0  0  0  0  0  0
    2.1793    3.1858    5.9017 H   0  0  0  0  0  0  0  0  0  0  0  0
    2.2634    4.8626    7.0057 C   0  0  0  0  0  0  0  0  0  0  0  0
    2.7026    4.4755    7.7413 H   0  0  0  0  0  0  0  0  0  0  0  0
    1.9386    6.2035    7.0234 C   0  0  0  0  0  0  0  0  0  0  0  0
    2.1676    6.7327    7.7656 H   0  0  0  0  0  0  0  0  0  0  0  0
    1.2921    6.7976    5.9815 C   0  0  0  0  0  0  0  0  0  0  0  0
    1.0664    7.6787    5.9721 H   0  0  0  0  0  0  0  0  0  0  0  0
   -5.0862   11.4632    7.5120 Cl  0  0  0  0  0  0  0  0  0  0  0  0
```

Table M.2 Mol representation for 1,3-bis(4-chlorophenyl)-4,5-diphenyl-4,5-dihydro-3H-1,2,3-triazol-1-ylium chloride, continued

```
   -1.1584    8.3245    4.4517 N   0  0  0  0  0  0  0  0  0  0  0  0
   -1.3243    6.8979    4.0673 C   0  0  1  0  0  0  0  0  0  0  0  0
   -1.6370    6.3573    4.8354 H   0  0  0  0  0  0  0  0  0  0  0  0
   -2.0975    9.1036    5.1725 C   0  0  0  0  0  0  0  0  0  0  0  0
   -1.8804   10.4555    5.3733 C   0  0  0  0  0  0  0  0  0  0  0  0
   -1.1114   10.8725    5.0293 H   0  0  0  0  0  0  0  0  0  0  0  0
   -2.8099   11.1799    6.0855 C   0  0  0  0  0  0  0  0  0  0  0  0
   -2.6820   12.1000    6.2295 H   0  0  0  0  0  0  0  0  0  0  0  0
   -3.9318   10.5488    6.5886 C   0  0  0  0  0  0  0  0  0  0  0  0
   -4.1393    9.2106    6.4014 C   0  0  0  0  0  0  0  0  0  0  0  0
   -4.9066    8.7976    6.7547 H   0  0  0  0  0  0  0  0  0  0  0  0
   -3.2143    8.4676    5.6904 C   0  0  0  0  0  0  0  0  0  0  0  0
   -3.3414    7.5454    5.5607 H   0  0  0  0  0  0  0  0  0  0  0  0
   -2.2796    6.7889    2.9047 C   0  0  0  0  0  0  0  0  0  0  0  0
   -3.1841    5.7467    2.8737 C   0  0  0  0  0  0  0  0  0  0  0  0
   -3.2359    5.1452    3.5943 H   0  0  0  0  0  0  0  0  0  0  0  0
   -4.0150    5.5907    1.7769 C   0  0  0  0  0  0  0  0  0  0  0  0
   -4.6288    4.8793    1.7533 H   0  0  0  0  0  0  0  0  0  0  0  0
   -3.9479    6.4663    0.7261 C   0  0  0  0  0  0  0  0  0  0  0  0
   -4.5055    6.3477   -0.0213 H   0  0  0  0  0  0  0  0  0  0  0  0
   -3.0611    7.5227    0.7648 C   0  0  0  0  0  0  0  0  0  0  0  0
   -3.0235    8.1311    0.0494 H   0  0  0  0  0  0  0  0  0  0  0  0
   -2.2353    7.6853    1.8463 C   0  0  0  0  0  0  0  0  0  0  0  0
   -1.6355    8.4086    1.8718 H   0  0  0  0  0  0  0  0  0  0  0  0
    0.1688    9.4875   -0.3132 Cl  0  5  0  0  0  0  0  0  0  0  0  0
  1 11  1  0  0  0  0
  2  3  2  0  0  0  0
  2  4  1  0  0  0  0
  2  6  1  0  0  0  0
```

Table M.2 Mol representation for 1,3-bis(4-chlorophenyl)-4,5-diphenyl-4,5-dihydro-3H-1,2,3-triazol-1-ylium chloride, continued

```
  3 28  1  0  0  0  0
  4  5  1  0  0  0  0
  4 16  1  0  0  0  0
  4 29  1  0  0  0  0
  6  7  2  0  0  0  0
  6 14  1  0  0  0  0
  7  8  1  0  0  0  0
  7  9  1  0  0  0  0
  9 10  1  0  0  0  0
  9 11  2  0  0  0  0
 11 12  1  0  0  0  0
 12 13  1  0  0  0  0
 12 14  2  0  0  0  0
 14 15  1  0  0  0  0
 16 17  1  0  0  0  0
 16 25  2  0  0  0  0
 17 18  1  0  0  0  0
 19 20  1  0  0  0  0
 19 21  1  0  0  0  0
 21 22  1  0  0  0  0
 21 23  2  0  0  0  0
 23 24  1  0  0  0  0
 23 25  1  0  0  0  0
 25 26  1  0  0  0  0
 27 36  1  0  0  0  0
 28 29  1  0  0  0  0
 28 31  1  0  0  0  0
 29 30  1  0  0  0  0
 29 41  1  0  0  0  0
```

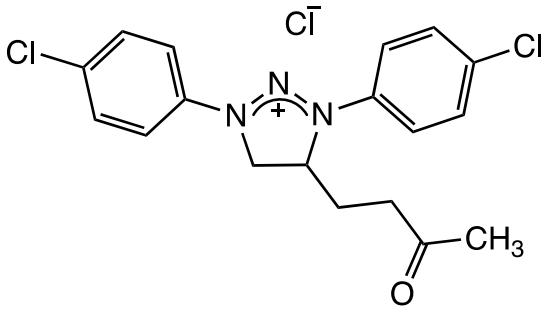
Table M.2 Mol representation for 1,3-bis(4-chlorophenyl)-4,5-diphenyl-4,5-dihydro-3H-1,2,3-triazol-1-ylium chloride, continued

```
 31 32  2  0  0  0  0
 31 39  1  0  0  0  0
 32 33  1  0  0  0  0
 32 34  1  0  0  0  0
 34 35  1  0  0  0  0
 34 36  2  0  0  0  0
 36 37  1  0  0  0  0
 37 38  1  0  0  0  0
 37 39  2  0  0  0  0
 39 40  1  0  0  0  0
 41 42  1  0  0  0  0
 41 50  2  0  0  0  0
 42 43  1  0  0  0  0
 42 44  2  0  0  0  0
 44 45  1  0  0  0  0
 44 46  1  0  0  0  0
 46 47  1  0  0  0  0
 46 48  2  0  0  0  0
 48 49  1  0  0  0  0
 48 50  1  0  0  0  0
 50 51  1  0  0  0  0
 17 19  2  0  0  0  0
M  CHG  2   2   1  52  -1
M  END
```

Crystal data for (1,3-bis(4-chlorophenyl)-5-(3-oxobutyl)-4,5-dihydro-3H-1,2,3-triazol-1-ylium chloride

CCDC reference number: 2179897

UK Chem reference number: m22100



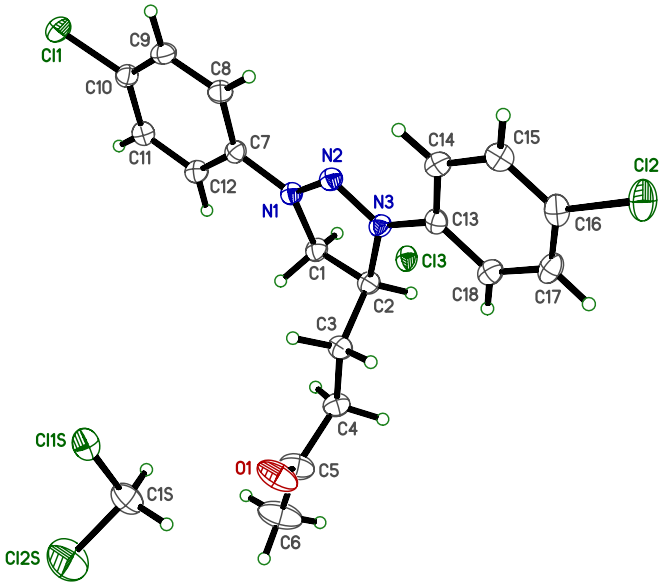


Table N.1 Crystal data and structure refinement for (1,3-bis(4-chlorophenyl)-5-(3-oxobutyl)-4,5-dihydro-3H-1,2,3-triazol-1-ylium chloride.

Empirical formula	$C_{18.77}$ $H_{19.55}$ $C_{14.55}$ N_3 O
Formula weight	464.43
Temperature	90.0(2) K
Wavelength	0.71073 Å
Crystal system, space group	Monoclinic, P2(1)/n
Unit cell dimensions	a = 6.9028(3) Å alpha = 90 deg. b = 15.0459(6) Å beta = 94.982(2) deg. c = 20.6434(6) Å gamma = 90 deg.
Volume	2135.90(14) Å^3
Z, Calculated density	4, 1.444 Mg/m^3
Absorption coefficient	0.637 mm^-1
F(000)	954
Crystal size	0.220 x 0.200 x 0.150 mm
Theta range for data collection	2.399 to 27.537 deg.
Limiting indices	-8<=h<=8, -19<=k<=19, -24<=l<=26
Reflections collected / unique	34400 / 4892 [R(int) = 0.0337]
Completeness to theta = 25.242	99.8 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.928 and 0.834
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4892 / 203 / 372
Goodness-of-fit on F^2	1.039
Final R indices [I>2sigma(I)]	R1 = 0.0328, wR2 = 0.0747
R indices (all data)	R1 = 0.0388, wR2 = 0.0782
Extinction coefficient	n/a
Largest diff. peak and hole	0.370 and -0.385 e.Å^-3

Table N.2 Mol representation for 1,3-bis(4-chlorophenyl)-5-(3-oxobutyl)-4,5-dihydro-3H-1,2,3-triazol-1-ylium chloride.

```
Mrv2211 05162214483D

 47 47  0  0  0  0            999 V2000
   -3.4403   13.8953   15.3735 Cl  0  0  0  0  0  0  0  0  0  0  0  0
    6.2800   15.6984    7.0103 Cl  0  0  0  0  0  0  0  0  0  0  0  0
    1.2410   12.4144   12.0946 N   0  3  0  0  0  0  0  0  0  0  0  0
    1.8934   13.3004   11.4108 N   0  0  0  0  0  0  0  0  0  0  0  0
    2.8856   12.7247   10.8066 N   0  0  0  0  0  0  0  0  0  0  0  0
    1.7259   11.0351   11.8790 C   0  0  2  0  0  0  0  0  0  0  0  0
    1.1227   10.5266   11.2809 H   0  0  0  0  0  0  0  0  0  0  0  0
    1.8283   10.5474   12.7342 H   0  0  0  0  0  0  0  0  0  0  0  0
    4.2274   11.1893   12.2234 C   0  0  2  0  0  0  0  0  0  0  0  0
    5.0355   11.6213   11.8490 H   0  0  0  0  0  0  0  0  0  0  0  0
    3.9841   11.6646   13.0573 H   0  0  0  0  0  0  0  0  0  0  0  0
    4.5322    9.7322   12.5412 C   0  0  1  0  0  0  0  0  0  0  0  0
    3.6847    9.2623   12.7436 H   0  0  0  0  0  0  0  0  0  0  0  0
    4.9314    9.3050   11.7423 H   0  0  0  0  0  0  0  0  0  0  0  0
    5.4720    9.5698   13.7047 C   0  0  0  0  0  0  0  0  0  0  0  0
    6.0709   10.5121   14.1855 O   0  0  0  0  0  0  0  0  0  0  0  0
    5.5909    8.1622   14.2499 C   0  0  0  0  0  0  0  0  0  0  0  0
    6.3665    8.1072   14.8462 H   0  0  0  0  0  0  0  0  0  0  0  0
    5.7044    7.5327   13.5074 H   0  0  0  0  0  0  0  0  0  0  0  0
    4.7784    7.9356   14.7489 H   0  0  0  0  0  0  0  0  0  0  0  0
    0.0946   12.7785   12.8503 C   0  0  0  0  0  0  0  0  0  0  0  0
   -0.3665   14.0940   12.8378 C   0  0  0  0  0  0  0  0  0  0  0  0
    0.0618   14.7492   12.2991 H   0  0  0  0  0  0  0  0  0  0  0  0
   -1.4569   14.4322   13.6205 C   0  0  0  0  0  0  0  0  0  0  0  0
   -1.7741   15.3274   13.6375 H   0  0  0  0  0  0  0  0  0  0  0  0
   -2.0811   13.4562   14.3782 C   0  0  0  0  0  0  0  0  0  0  0  0
   -1.6321   12.1475   14.3903 C   0  0  0  0  0  0  0  0  0  0  0  0
```

Table N.2 Mol representation for 1,3-bis(4-chlorophenyl)-5-(3-oxobutyl)-4,5-dihydro-3H-1,2,3-triazol-1-ylium chloride, continued

```
   -2.0771   11.4903   14.9124 H   0  0  0  0  0  0  0  0  0  0  0  0
   -0.5218   11.8086   13.6285 C   0  0  0  0  0  0  0  0  0  0  0  0
   -0.1866   10.9198   13.6399 H   0  0  0  0  0  0  0  0  0  0  0  0
    3.7368   13.4709    9.9475 C   0  0  0  0  0  0  0  0  0  0  0  0
    3.5242   14.8343    9.7612 C   0  0  0  0  0  0  0  0  0  0  0  0
    2.8392   15.2836   10.2423 H   0  0  0  0  0  0  0  0  0  0  0  0
    4.3201   15.5278    8.8685 C   0  0  0  0  0  0  0  0  0  0  0  0
    4.1808   16.4558    8.7204 H   0  0  0  0  0  0  0  0  0  0  0  0
    5.3255   14.8514    8.1910 C   0  0  0  0  0  0  0  0  0  0  0  0
    5.5626   13.5080    8.4091 C   0  0  0  0  0  0  0  0  0  0  0  0
    6.2782   13.0723    7.9610 H   0  0  0  0  0  0  0  0  0  0  0  0
    4.7544   12.7968    9.2831 C   0  0  0  0  0  0  0  0  0  0  0  0
    4.8935   11.8678    9.4246 H   0  0  0  0  0  0  0  0  0  0  0  0
    2.0832   14.2704    8.5986 Cl  0  5  0  0  0  0  0  0  0  0  0  0
   -0.3444    8.6907   13.8195 C   0  0  2  0  0  0  0  0  0  0  0  0
    0.4125    9.1439   13.3701 H   0  0  0  0  0  0  0  0  0  0  0  0
   -0.9913    9.3848   14.1017 H   0  0  0  0  0  0  0  0  0  0  0  0
    0.2399    7.8549   15.2163 Cl  0  0  0  0  0  0  0  0  0  0  0  0
   -1.1325    7.5832   12.6714 Cl  0  0  0  0  0  0  0  0  0  0  0  0
    3.0771   11.3000   11.2189 C   0  0  2  0  0  0  0  0  0  0  0  0
  1 26  1  0  0  0  0
  2 36  1  0  0  0  0
  3  4  2  0  0  0  0
  3  6  1  0  0  0  0
  3 21  1  0  0  0  0
  4  5  1  0  0  0  0
  5 31  1  0  0  0  0
  6  7  1  0  0  0  0
  6  8  1  0  0  0  0
```

Table N.2 Mol representation for 1,3-bis(4-chlorophenyl)-5-(3-oxobutyl)-4,5-dihydro-3H-1,2,3-triazol-1-ylium chloride, continued

```
  9 10  1  0  0  0  0
  9 11  1  0  0  0  0
  9 12  1  0  0  0  0
 12 13  1  0  0  0  0
 12 14  1  0  0  0  0
 12 15  1  0  0  0  0
 15 16  2  0  0  0  0
 15 17  1  0  0  0  0
 17 18  1  0  0  0  0
 17 19  1  0  0  0  0
 17 20  1  0  0  0  0
 21 22  1  0  0  0  0
 21 29  2  0  0  0  0
 22 23  1  0  0  0  0
 22 24  2  0  0  0  0
 24 25  1  0  0  0  0
 24 26  1  0  0  0  0
 26 27  2  0  0  0  0
 27 28  1  0  0  0  0
 27 29  1  0  0  0  0
 29 30  1  0  0  0  0
 31 32  1  0  0  0  0
 31 39  2  0  0  0  0
 32 33  1  0  0  0  0
 32 34  2  0  0  0  0
 34 35  1  0  0  0  0
 34 36  1  0  0  0  0
 36 37  2  0  0  0  0
 37 38  1  0  0  0  0
```

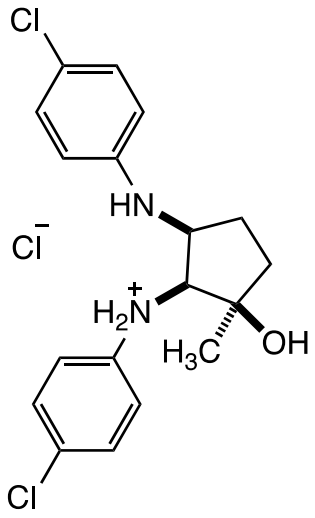
Table N.2 Mol representation for 1,3-bis(4-chlorophenyl)-5-(3-oxobutyl)-4,5-dihydro-3H-1,2,3-triazol-1-ylium chloride, continued

```
 37 39  1  0  0  0  0
 39 40  1  0  0  0  0
 42 43  1  0  0  0  0
 42 44  1  0  0  0  0
 42 45  1  0  0  0  0
 42 46  1  0  0  0  0
  5 47  1  0  0  0  0
  6 47  1  0  0  0  0
 47  9  1  0  0  0  0
M  CHG  2   3   1  41  -1
M  END
```

Crystal data and structure refinement for 2,3-bis[(4-chlorophenyl)amino]-1-methylcyclopentan-1-ol as a HCl salt

CCDC reference number: 2179893

UK Chem reference number: m22070



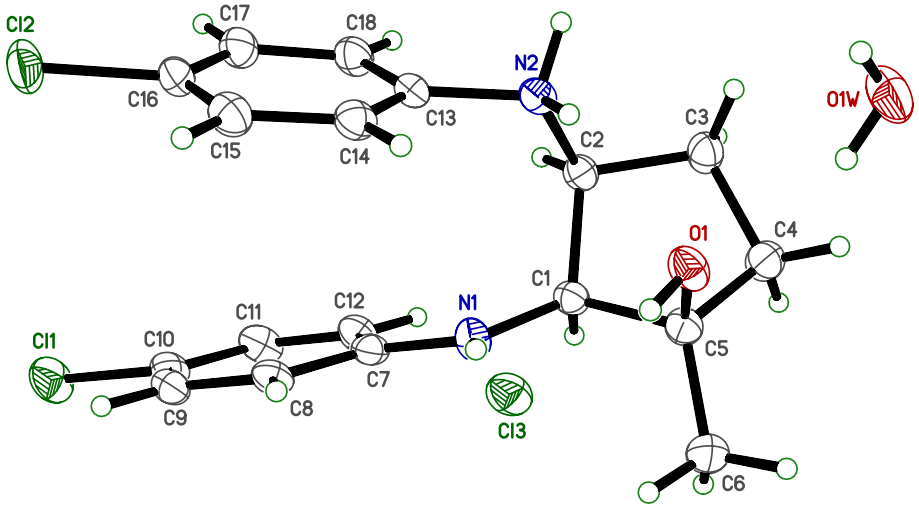


Table O.1 Crystal data and structure refinement for 2,3-bis[(4-chlorophenyl)amino]-1-methylcyclopentan-1-ol as a HCl salt.

Empirical formula	C_{18} $H_{22.50}$ C_{13} N_2 $O_{1.75}$
Formula weight	401.23
Temperature	90.0(2) K
Wavelength	0.71073 Å
Crystal system, space group	Monoclinic, P2(1)/c
Unit cell dimensions	a = 13.8925(8) Å alpha = 90 deg. b = 7.5000(4) Å beta = 107.043(2) deg. c = 19.2509(10) Å gamma = 90 deg.
Volume	1917.74(18) Å^3
Z, Calculated density	4, 1.390 Mg/m^3
Absorption coefficient	0.490 mm^-1
F(000)	838
Crystal size	0.310 x 0.160 x 0.020 mm
Theta range for data collection	2.213 to 27.516 deg.
Limiting indices	-18<=h<=17, -9<=k<=9, -25<=l<=25
Reflections collected / unique	38495 / 4407 [R(int) = 0.0938]
Completeness to theta = 25.242	100.0 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.971 and 0.740
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4407 / 3 / 243
Goodness-of-fit on F^2	1.063
Final R indices [I>2sigma(I)]	R1 = 0.0452, wR2 = 0.1007
R indices (all data)	R1 = 0.0785, wR2 = 0.1155
Extinction coefficient	n/a
Largest diff. peak and hole	0.358 and -0.343 e.Å^-3

Table O.2 Mol representation for (2,3-bis[(4-chlorophenyl)amino]-1-methylcyclopentan-1-ol as a HCl salt.

```
Mrv2211 05162214333D

 48 48  0  0  0  0            999 V2000
    2.4002    1.5675    9.3764 Cl  0  0  0  0  0  0  0  0  0  0  0  0
    1.3701    3.7588   13.5606 Cl  0  0  0  0  0  0  0  0  0  0  0  0
    8.0129    0.1192   15.9843 O   0  0  0  0  0  0  0  0  0  0  0  0
    7.3721   -0.4183   16.0653 H   0  0  0  0  0  0  0  0  0  0  0  0
    6.3879    0.3048   13.5675 N   0  0  0  0  0  0  0  0  0  0  0  0
    6.0706   -0.1114   14.2611 H   0  0  0  0  0  0  0  0  0  0  0  0
    6.9838    2.6933   15.2082 N   0  3  1  0  0  0  0  0  0  0  0  0
    6.9726    2.0955   15.8688 H   0  0  0  0  0  0  0  0  0  0  0  0
    7.3138    3.5271   15.5224 H   0  0  0  0  0  0  0  0  0  0  0  0
    7.7321    0.7988   13.6688 C   0  0  1  0  0  0  0  0  0  0  0  0
    8.1544    0.7001   12.7677 H   0  0  0  0  0  0  0  0  0  0  0  0
    7.9484    2.2678   14.1231 C   0  0  2  0  0  0  0  0  0  0  0  0
    7.8791    2.8843   13.3391 H   0  0  0  0  0  0  0  0  0  0  0  0
    9.3880    2.2873   14.6914 C   0  0  1  0  0  0  0  0  0  0  0  0
    9.9803    2.8346   14.1179 H   0  0  0  0  0  0  0  0  0  0  0  0
    9.3946    2.6653   15.6066 H   0  0  0  0  0  0  0  0  0  0  0  0
    9.8592    0.8234   14.7109 C   0  0  1  0  0  0  0  0  0  0  0  0
   10.4310    0.6302   13.9260 H   0  0  0  0  0  0  0  0  0  0  0  0
   10.3738    0.6326   15.5348 H   0  0  0  0  0  0  0  0  0  0  0  0
    8.5850   -0.0101   14.6668 C   0  0  1  0  0  0  0  0  0  0  0  0
    8.7608   -1.4578   14.2841 C   0  0  0  0  0  0  0  0  0  0  0  0
    7.8890   -1.9054   14.2895 H   0  0  0  0  0  0  0  0  0  0  0  0
    9.3568   -1.8957   14.9270 H   0  0  0  0  0  0  0  0  0  0  0  0
    9.1509   -1.5136   13.3867 H   0  0  0  0  0  0  0  0  0  0  0  0
    5.5011    0.6163   12.5562 C   0  0  0  0  0  0  0  0  0  0  0  0
    4.1627    0.2123   12.6935 C   0  0  0  0  0  0  0  0  0  0  0  0
    3.8991   -0.2702   13.4684 H   0  0  0  0  0  0  0  0  0  0  0  0
```

Table O.2 Mol representation for (2,3-bis[(4-chlorophenyl)amino]-1-methylcyclopentan-1-ol as a HCl salt, continued

```
  3.2240    0.5011   11.7259 C   0  0  0  0  0  0  0  0  0  0  0  0
  2.3223    0.2252   11.8386 H   0  0  0  0  0  0  0  0  0  0  0  0
  3.6007    1.1956   10.5898 C   0  0  0  0  0  0  0  0  0  0  0  0
  4.9074    1.6058   10.4192 C   0  0  0  0  0  0  0  0  0  0  0  0
  5.1596    2.0816    9.6368 H   0  0  0  0  0  0  0  0  0  0  0  0
  5.8569    1.3182   11.4010 C   0  0  0  0  0  0  0  0  0  0  0  0
  6.7554    1.6024   11.2826 H   0  0  0  0  0  0  0  0  0  0  0  0
  5.5869    2.9340   14.8020 C   0  0  0  0  0  0  0  0  0  0  0  0
  4.5711    2.2016   15.3746 C   0  0  0  0  0  0  0  0  0  0  0  0
  4.7622    1.5436   16.0325 H   0  0  0  0  0  0  0  0  0  0  0  0
  3.2586    2.4414   14.9729 C   0  0  0  0  0  0  0  0  0  0  0  0
  2.5436    1.9317   15.3352 H   0  0  0  0  0  0  0  0  0  0  0  0
  3.0110    3.4300   14.0410 C   0  0  0  0  0  0  0  0  0  0  0  0
  4.0294    4.1789   13.4908 C   0  0  0  0  0  0  0  0  0  0  0  0
  3.8371    4.8679   12.8657 H   0  0  0  0  0  0  0  0  0  0  0  0
  5.3405    3.9113   13.8630 C   0  0  0  0  0  0  0  0  0  0  0  0
  6.0589    4.3967   13.4745 H   0  0  0  0  0  0  0  0  0  0  0  0
 13.8407    1.8704   17.8451 O   0  0  0  0  0  0  0  0  0  0  0  0
 13.2982    2.4679   18.0801 H   0  0  0  0  0  0  0  0  0  0  0  0
 13.3898    1.1581   17.8862 H   0  0  0  0  0  0  0  0  0  0  0  0
  6.6015    3.9440   17.8465 Cl  0  5  0  0  0  0  0  0  0  0  0  0
 1 30  1  0  0  0  0
 2 40  1  0  0  0  0
 3  4  1  0  0  0  0
 3 20  1  0  0  0  0
 5  6  1  0  0  0  0
 5 10  1  0  0  0  0
 5 25  1  0  0  0  0
 7  8  1  0  0  0  0
```

Table O.2 Mol representation for (2,3-bis[(4-chlorophenyl)amino]-1-methylcyclopentan-1-ol as a HCl salt, continued

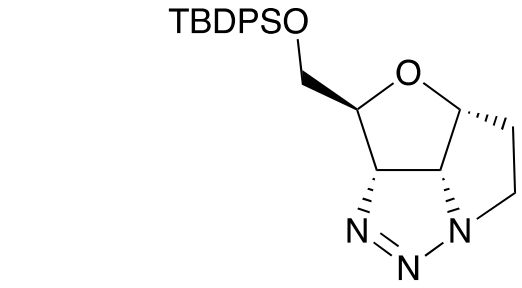
```
  7  9  1  0  0  0  0
  7 12  1  0  0  0  0
  7 35  1  0  0  0  0
 10 11  1  0  0  0  0
 10 12  1  0  0  0  0
 10 20  1  0  0  0  0
 12 13  1  0  0  0  0
 12 14  1  0  0  0  0
 14 15  1  0  0  0  0
 14 16  1  0  0  0  0
 14 17  1  0  0  0  0
 17 18  1  0  0  0  0
 17 19  1  0  0  0  0
 17 20  1  0  0  0  0
 20 21  1  0  0  0  0
 21 22  1  0  0  0  0
 21 23  1  0  0  0  0
 21 24  1  0  0  0  0
 25 26  2  0  0  0  0
 25 33  1  0  0  0  0
 26 27  1  0  0  0  0
 26 28  1  0  0  0  0
 28 29  1  0  0  0  0
 28 30  2  0  0  0  0
 30 31  1  0  0  0  0
 31 32  1  0  0  0  0
 31 33  2  0  0  0  0
 33 34  1  0  0  0  0
 35 36  2  0  0  0  0
```

Table O.2 Mol representation for (2,3-bis[(4-chlorophenyl)amino]-1-methylcyclopentan-1-ol as a HCl salt, continued

```
 35 43  1  0  0  0  0
 36 37  1  0  0  0  0
 36 38  1  0  0  0  0
 38 39  1  0  0  0  0
 38 40  2  0  0  0  0
 40 41  1  0  0  0  0
 41 42  1  0  0  0  0
 41 43  2  0  0  0  0
 43 44  1  0  0  0  0
 45 46  1  0  0  0  0
 45 47  1  0  0  0  0
M  CHG  2   7   1  48  -1
M  END
```

Crystal data for (4*S*,5*S*,7*R*,10*R*)-5-{[(tert-butyldiphenylsilyl)oxy]methyl}-6-oxa-1,2,3 triazatricyclo[5.2.1.0^{4,10}]dec-2-ene

UK Chem reference number: m20253



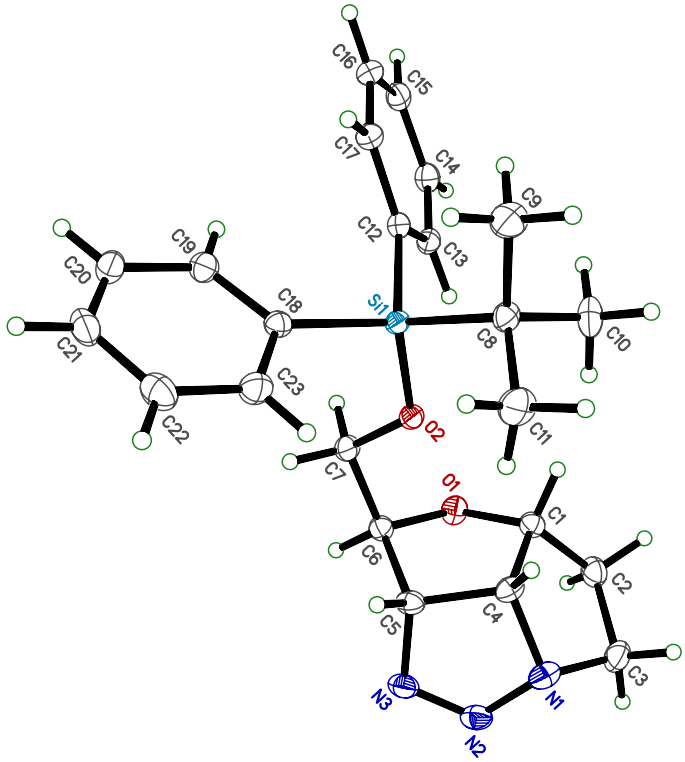


Table P.1 Crystal data and structure refinement for (4*S*,5*S*,7*R*,10*R*)-5-{[(tert-butyldiphenylsilyl)oxy]methyl}-6-oxa-1,2,3 triazatricyclo[5.2.1.$0^{4,10}$]dec-2-ene.

Empirical formula	C_{23} H_{29} N_3 O_2 Si
Formula weight	407.58
Temperature	90.0(2) K
Wavelength	0.71073 Å
Crystal system, space group	Orthorhombic, P2(1)2(1)2(1)
Unit cell dimensions	a = 7.7480(3) Å alpha = 90 deg. b = 11.2484(5) Å beta = 90 deg. c = 25.0666(8) Å gamma = 90 deg.
Volume	2184.62(15) Å^3
Z, Calculated density	4, 1.239 Mg/m^3
Absorption coefficient	0.131 mm^-1
F(000)	872
Crystal size	0.300 x 0.260 x 0.240 mm
Theta range for data collection	1.984 to 27.526 deg.
Limiting indices	-10<=h<=10, -14<=k<=14, -32<=l<=32
Reflections collected / unique	29798 / 5000 [R(int) = 0.0325]
Completeness to theta = 25.242	99.7 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.942 and 0.892
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	5000 / 0 / 265
Goodness-of-fit on F^2	1.057
Final R indices [I>2sigma(I)]	R1 = 0.0264, wR2 = 0.0678
R indices (all data)	R1 = 0.0279, wR2 = 0.0691
Absolute structure parameter	-0.03(3)
Extinction coefficient	n/a
Largest diff. peak and hole	0.217 and -0.210 e.Å^-3

Table P.2 Mol representation for (4*S*,5*S*,7*R*,10*R*)-5-{[(tert-butyldiphenylsilyl)oxy]methyl}-6-oxa-1,2,3 triazatricyclo[5.2.1.$0^{4,10}$]dec-2-ene.

```
Mrv2211 05162214533D

 58 62  0  0  0  0            999 V2000
    4.0812    4.8699    8.3055 Si  0  0  1  0  0  0  0  0  0  0  0  0
    5.8124    6.7893   11.9527 O   0  0  0  0  0  0  0  0  0  0  0  0
    4.7168    5.9465    9.3870 O   0  0  0  0  0  0  0  0  0  0  0  0
    7.9460    8.8078   10.6117 N   0  0  1  0  0  0  0  0  0  0  0  0
    7.2270    9.7535   11.3554 N   0  0  0  0  0  0  0  0  0  0  0  0
    5.9955    9.6872   11.1719 N   0  0  0  0  0  0  0  0  0  0  0  0
    7.0227    6.6560   11.1850 C   0  0  2  0  0  0  0  0  0  0  0  0
    7.0831    5.7589   10.7473 H   0  0  0  0  0  0  0  0  0  0  0  0
    8.2516    6.9356   12.0749 C   0  0  1  0  0  0  0  0  0  0  0  0
    7.9713    7.1772   12.9933 H   0  0  0  0  0  0  0  0  0  0  0  0
    8.8402    6.1407   12.1195 H   0  0  0  0  0  0  0  0  0  0  0  0
    8.9763    8.1137   11.3979 C   0  0  2  0  0  0  0  0  0  0  0  0
    9.3652    8.7204   12.0767 H   0  0  0  0  0  0  0  0  0  0  0  0
    9.7021    7.7856   10.8104 H   0  0  0  0  0  0  0  0  0  0  0  0
    6.9825    7.7924   10.1428 C   0  0  1  0  0  0  0  0  0  0  0  0
    7.1411    7.4864    9.2043 H   0  0  0  0  0  0  0  0  0  0  0  0
    5.6487    8.4847   10.3455 C   0  0  1  0  0  0  0  0  0  0  0  0
    5.1977    8.7205    9.4847 H   0  0  0  0  0  0  0  0  0  0  0  0
    4.8304    7.5186   11.2017 C   0  0  1  0  0  0  0  0  0  0  0  0
    4.2639    8.0461   11.8346 H   0  0  0  0  0  0  0  0  0  0  0  0
    3.9363    6.6101   10.3805 C   0  0  2  0  0  0  0  0  0  0  0  0
    3.5057    5.9415   10.9703 H   0  0  0  0  0  0  0  0  0  0  0  0
    3.2245    7.1439    9.9462 H   0  0  0  0  0  0  0  0  0  0  0  0
    5.5239    4.4708    7.1579 C   0  0  2  0  0  0  0  0  0  0  0  0
    5.1085    3.4233    6.1164 C   0  0  0  0  0  0  0  0  0  0  0  0
```

Table P.2 Mol representation for (4*S*,5*S*,7*R*,10*R*)-5-{[(tert-butyldiphenylsilyl)oxy]methyl}-6-oxa-1,2,3 triazatricyclo[5.2.1.$0^{4,10}$]dec-2-ene, continued

5.8780	3.2016	5.5514	H	0	0	0	0	0	0	0	0	0	0	0	0
4.3877	3.7846	5.5592	H	0	0	0	0	0	0	0	0	0	0	0	0
4.7947	2.6150	6.5728	H	0	0	0	0	0	0	0	0	0	0	0	0
6.6496	3.8875	8.0287	C	0	0	0	0	0	0	0	0	0	0	0	0
6.3196	3.0958	8.5025	H	0	0	0	0	0	0	0	0	0	0	0	0
6.9414	4.5598	8.6791	H	0	0	0	0	0	0	0	0	0	0	0	0
7.4060	3.6350	7.4584	H	0	0	0	0	0	0	0	0	0	0	0	0
6.0716	5.7118	6.4347	C	0	0	0	0	0	0	0	0	0	0	0	0
6.9187	5.4870	5.9958	H	0	0	0	0	0	0	0	0	0	0	0	0
6.2212	6.4296	7.0847	H	0	0	0	0	0	0	0	0	0	0	0	0
5.4245	6.0102	5.7617	H	0	0	0	0	0	0	0	0	0	0	0	0
3.5506	3.3276	9.2295	C	0	0	0	0	0	0	0	0	0	0	0	0
3.9868	3.1132	10.5467	C	0	0	0	0	0	0	0	0	0	0	0	0
4.5705	3.7430	10.9533	H	0	0	0	0	0	0	0	0	0	0	0	0
3.5793	1.9933	11.2674	C	0	0	0	0	0	0	0	0	0	0	0	0
3.8843	1.8696	12.1585	H	0	0	0	0	0	0	0	0	0	0	0	0
2.7318	1.0586	10.6947	C	0	0	0	0	0	0	0	0	0	0	0	0
2.4393	0.3063	11.1954	H	0	0	0	0	0	0	0	0	0	0	0	0
2.3150	1.2316	9.3803	C	0	0	0	0	0	0	0	0	0	0	0	0
1.7495	0.5852	8.9743	H	0	0	0	0	0	0	0	0	0	0	0	0
2.7217	2.3464	8.6586	C	0	0	0	0	0	0	0	0	0	0	0	0
2.4328	2.4479	7.7594	H	0	0	0	0	0	0	0	0	0	0	0	0
2.5715	5.6169	7.4773	C	0	0	0	0	0	0	0	0	0	0	0	0
1.2754	5.1760	7.7628	C	0	0	0	0	0	0	0	0	0	0	0	0
1.1499	4.4848	8.4027	H	0	0	0	0	0	0	0	0	0	0	0	0
0.1624	5.7290	7.1294	C	0	0	0	0	0	0	0	0	0	0	0	0
-0.7086	5.4116	7.3380	H	0	0	0	0	0	0	0	0	0	0	0	0
0.3244	6.7369	6.1995	C	0	0	0	0	0	0	0	0	0	0	0	0

Table P.2 Mol representation for (4*S*,5*S*,7*R*,10*R*)-5-{[(tert-butyldiphenylsilyl)oxy]methyl}-6-oxa-1,2,3 triazatricyclo[5.2.1.$0^{4,10}$]dec-2-ene, continued

```
   -0.4305    7.0890    5.7425 H   0  0  0  0  0  0  0  0  0  0  0  0
    1.5874    7.2323    5.9352 C   0  0  0  0  0  0  0  0  0  0  0  0
    1.6983    7.9516    5.3244 H   0  0  0  0  0  0  0  0  0  0  0  0
    2.6937    6.6773    6.5640 C   0  0  0  0  0  0  0  0  0  0  0  0
    3.5570    7.0238    6.3711 H   0  0  0  0  0  0  0  0  0  0  0  0
  1  3  1  0  0  0  0
  1 24  1  0  0  0  0
  1 37  1  0  0  0  0
  1 48  1  0  0  0  0
  2  7  1  0  0  0  0
  2 19  1  0  0  0  0
  3 21  1  0  0  0  0
  4  5  1  0  0  0  0
  4 12  1  0  0  0  0
  4 15  1  0  0  0  0
  5  6  2  0  0  0  0
  6 17  1  0  0  0  0
  7  8  1  0  0  0  0
  7  9  1  0  0  0  0
  7 15  1  0  0  0  0
  9 10  1  0  0  0  0
  9 11  1  0  0  0  0
  9 12  1  0  0  0  0
 12 13  1  0  0  0  0
 12 14  1  0  0  0  0
 15 16  1  0  0  0  0
 15 17  1  0  0  0  0
 17 18  1  0  0  0  0
```

Table P.2 Mol representation for (4*S*,5*S*,7*R*,10*R*)-5-{[(tert-butyldiphenylsilyl)oxy]methyl}-6-oxa-1,2,3 triazatricyclo[5.2.1.$0^{4,10}$]dec-2-ene, continued

```
 17 19  1  0  0  0  0
 19 20  1  0  0  0  0
 19 21  1  0  0  0  0
 21 22  1  0  0  0  0
 21 23  1  0  0  0  0
 24 25  1  0  0  0  0
 24 29  1  0  0  0  0
 24 33  1  0  0  0  0
 25 26  1  0  0  0  0
 25 27  1  0  0  0  0
 25 28  1  0  0  0  0
 29 30  1  0  0  0  0
 29 31  1  0  0  0  0
 29 32  1  0  0  0  0
 33 34  1  0  0  0  0
 33 35  1  0  0  0  0
 33 36  1  0  0  0  0
 37 38  1  0  0  0  0
 37 46  2  0  0  0  0
 38 39  1  0  0  0  0
 38 40  2  0  0  0  0
 40 41  1  0  0  0  0
 40 42  1  0  0  0  0
 42 43  1  0  0  0  0
 42 44  2  0  0  0  0
 44 45  1  0  0  0  0
 44 46  1  0  0  0  0
 46 47  1  0  0  0  0
```

Table P.2 Mol representation for (4*S*,5*S*,7*R*,10*R*)-5-{[(tert-butyldiphenylsilyl)oxy]methyl}-6-oxa-1,2,3 triazatricyclo[5.2.1.$0^{4,10}$]dec-2-ene, continued

```
 48 49  1  0  0  0  0
 48 57  2  0  0  0  0
 49 50  1  0  0  0  0
 49 51  2  0  0  0  0
 51 52  1  0  0  0  0
 51 53  1  0  0  0  0
 53 54  1  0  0  0  0
 53 55  2  0  0  0  0
 55 56  1  0  0  0  0
 55 57  1  0  0  0  0
 57 58  1  0  0  0  0
M  END
```

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Vita

Setareh Saryazdi

EDUCATION

Ph.D. Candidate, Organic Chemistry [Aug. 2015- expected July 2022]
University of Kentucky, Lexington, KY.
Advisor: Prof. Robert B. Grossman
Dissertation Title: 1,2-diamination of alkenes *via* reduction of 1,2,3-triazolinium ions

Master of Science, Organic Chemistry [Sep. 2010-Sep. 2012]
Sharif University of Technology, Tehran, Iran.
Advisor: Prof. Firouz Matloubi Moghaddam
Thesis Title: Investigation of alcohols and thiols oxidation *via* DABCO-tribromide catalyst supported on silica and magnetic iron oxide nanoparticles.

Bachelor of Science, Chemistry [Sep. 2004- Sep. 2008]
Islamic Azad University, Tehran, Iran.

RESEARCH EXPERIENCES

Research Assistant, Prof. Grossman's Organic Chemistry Laboratory, Department of Chemistry, University of Kentucky, Lexington, KY [May 2016–Present]

- Designed a new methodology for 1,2-diamination of alkenes *via* low-pressure reduction of 1,2,3-triazolinium ions. Synthesized triazolinium ions in two different ways:
  1. Inter- and intramolecular 1,3-dipolar cycloaddition of alkene-azide to form 1,2,3-triazolines and further *N*-alkylation of the triazolines.
  2. Intermolecular 1,3-dipolar cycloaddition of alkenes with azidium ions (our neologism) to form triazolinium ions.
- Synthesized isotopically labeled intermediates to study oxacyclization catalyzed by LolO, the iron- and 2-oxoglutarate-dependent oxygenase, in biosynthesis of loline alkaloids.
- Purified LolO enzyme to study its mechanism in oxidative cyclization.

Research Assistant, Organic Synthesis and Natural Products Laboratory, Department of Chemistry, Sharif University of Technology, Tehran, Iran [Oct. 2010–Sep. 2012]

- Synthesized immobilized DABCO–tribromide on silica as a recoverable reagent in oxidation of alcohols to carbonyl compounds.
- Synthesized a magnetically recyclable manganese complex to selectively oxidize sulfur-containing organic molecules, such as thiols and sulfides to disulfides.

PUBLICATIONS (*H-INDEX= 2*)

1. Bagherzadeh, M., Haghdoost, M. M., Matloubi Moghaddam, F., Koushki Foroushani, B., **Saryazdi**, **S.**, Payab, E. Mn (III) Complex Supported on Fe_3O_4 Nanoparticles: Magnetically

Separable Nanocatalyst for Selective Oxidation of Thiols to Disulfides, *Journal of Coordination Chemistry,* 2013, 66, 3025-3026.
2. Matloubi Moghaddam, F., Masoud, N., Koushki Foroushani, B., **Saryazdi**, **S.**, Ghonouei, N., Daemi, E. Silica Supported DABCO–tribromide: A Recoverable Reagent for Oxidation of Alcohols to Corresponding Carbonyl Compounds, *Scientica Iranica*, 2013, 20, 598-602.

PUBLICATIONS IN PREPARATION

1. **Saryazdi**, **S.**, Parkin, S., Grossman, R. B. 1,2-Diamination of Alkenes *via* Reduction of 1,2,3-Triazolinium Ions, *Organic Letters*.
2. Gukathasan, S., **Saryazdi**, **S.**, Parkin, s., Grossman, R. B., Awuah, S. Gold(III) Bearing Diamine Complexes for Anticancer Activities, *Inorganic Chemistry*.

ORAL PRESENTATION

1. **Saryazdi, S.**, Grossman, R. B. Use of 1D and 2D NMR to Monitor the Reaction Time and Assign the Stereochemistry, NMR Flash Talk Symposium, 2021, Lexington, KY.

POSTER PRESENTATIONS

1. **Saryazdi, S.**, Grossman, R. B. Syn 1,2-Diamination of Alkenes *via* Reduction of 1,2,3-Triazolinium Ions, ACS National Meeting & Exposition, 2021, Atlanta, GA.
2. **Saryazdi**, S., Grossman R. B. Intramolecular Azide–Alkene Cycloaddition: A Novel Pathway towards Loline Alkaloid Synthesis, 45th Annual Naff Symposium, 2019, University of Kentucky, Lexington, KY.
3. Pan, J., Bhardwaj, M., **Saryazdi, S.**, Zhang, B., Chang, W.C., Schardle, C.L., Grossman, R. B., Krebs, C., JM Bollinger, J. M. Mechanistic Study of Oxacyclization Catalyzed by the Fe(II)/2-oxoglutarate (2OG) Dependent Oxygenase LolO in Loline Alkaloid Biosynthesis, Bioinorganic Workshop, 2018, Pennsylvania State University, State College, PA.
4. Patwardhan, M. A., French, A. N., **Saryazdi, S.**, Riddle, A. Undergraduate Laboratory Assistants in Large Enrollment Organic Chemistry Laboratories, 25th Biennial Conference on Chemical Education, 2018, University of Notre Dame, Notre Dame, IN.
5. Bagherzadeh, M., Haghdoost, M. M., Matloubi Moghaddam, F., Koushki Foroushani, B., **Saryazdi, S.** Immobilization of DABCO–tribromide on Magnetic Iron Oxide Nanoparticles, and its Application in Oxidation of Alcohols to Carbonyl Compounds, 4th International Congress on Nanoscience and Nanotechnology, 2012, Kashan, Iran.
6. Matloubi Moghaddam, F., Koushki Foroushani, B., **Saryazdi, S.** Using 1-(1-buthyl sulfonic) -3-Methylimidazolium Nitrate and Phosphorouspentoxide as a Green Solvent for Oxidation of Benzylic Alcohols to the Corresponding Carbonyl Compound, 18th Iranian Seminar of Organic Chemistry, 2012, Zahedan, Iran.

MEMBERSHIP

- American Chemical society (ACS)
- American Chemical Society Division of Organic Chemistry

TEACHING EXPERIENCES

Advanced Organic Chemistry Teaching Assistant, Department of Chemistry, University of Kentucky, Lexington, KY. [Jan. 2022–May 2022]

- Taught a research-based capstone organic chemistry lab, for which TA's are chosen to serve essentially as research mentors.

Organic Chemistry Instructor, Organic Chemistry I, Department of Chemistry, University of Kentucky, Lexington, KY. [May 2020–Aug. 2020]

- *Independently* taught an online sophomore undergrad O-Chem course
- Designed syllabus, created multimedia course materials, and administered online exams *via* Canvas.

Recitation Teaching Assistant, General Chemistry I, Department of Chemistry, University of Kentucky. Lexington, KY. [Aug. 2019– Dec. 2019 & Aug. 2021– Fall 2021]

- Taught recitation sessions for CHE 105, CHE 109, and CHE 110).
- Taught CHE110 in Fall 2019 as a required practicum course for the completion of the Graduate Certificate in College Teaching and Learning.

Organic Chemistry Super Teaching Assistant, Organic Chemistry Laboratory I and II, Department of Chemistry, University of Kentucky, Lexington, KY. [Aug. 2016–Dec. 2017]

- Helped the laboratory supervisor in CHE231 & CHE233 to organize the course materials on Canvas, to create assignments and exams, and to assist the TAs with running the labs.

Organic Chemistry Teaching Assistant, Organic Chemistry Laboratory I and II, Department of Chemistry, University of Kentucky, Lexington, KY. [Aug. 2015–May 2017]

- Taught CHE231 & CHE233 laboratory courses

ChemCamp Instructor, University of Kentucky, Lexington KY. [Jul. 2019, Jul. 2021 & June 2022]

HONORS & AWARDS

- Research Challenge Trust Fund Fellowship, Department of Chemistry, University of Kentucky, Lexington, KY. [May 2020–Aug. 2021 & May 2018–Aug. 2019]
- 100% Plus Award, Department of Chemistry, University of Kentucky, Lexington, KY. [May 2021]
- A&S Outstanding Teaching Assistant Award, College of Art & Sciences, University of Kentucky, Lexington, KY. [May 2020]

LEADERSHIP

- Treasurer of Chemistry Graduate Student Association, University of Kentucky, Lexington, KY. [Jul. 2019–Jul. 2020]

OUTREACH

- Volunteer, Kentucky Refugee Ministries, Lexington, KY. [Nov. 2021]
- Scientific Judge, Central Kentucky Regional Science & Engineering Fair (CKRSEF), Lexington, KY. [Mar. 2018]
- Scientific Judge, Kentucky Junior Academy of Science (KJAS), Lexington, KY. [April 2019]

PERSONAL DEVELOPMENT

- Certificate of College Teaching and Learning, Graduate School, University of Kentucky, Lexington, KY. [Feb. 2020]
- Certificate of Inclusive Pedagogies in Graduate Student Learning Community, University of Kentucky, Lexington, KY. [Aug. 2018– May 2019]

SERVICES

- Technical NMR Assistant, University of Kentucky, Lexington KY. [Jan. 2021– May 2021]
- Microteaching Leader, University of Kentucky, Lexington, KY. [Aug. 2019 & Jan. 2020 & Aug. 2020]
- Graduate Student Recruitment Representative, University of Kentucky, Lexington, KY. [Oct 2019]