Generation of Diverse Molecular Complexity from Simple Hydrocarbons

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GENERATION OF DIVERSE MOLECULAR COMPLEXITY FROM SIMPLE HYDROCARBONS

by

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ABSTRACT

GENERATION OF DIVERSE MOLECULAR COMPLEXITY FROM SIMPLE HYDROCARBONS

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In an effort to make diverse molecular complexity from simple hydrocarbons, tricarbonyl(cyclohexadienyl)iron(+1) cation was prepared in two steps from 1, 3-cycloxehadiene. Reactivity of the symmetric iron cation with heteroatom nucleophiles and stabilized carbon nucleophiles was studied. Nucleophilic attack of potassium phthalimide at the dienyl terminus of the cation followed by oxidative decomplexation with Ce^{4+} provided the ligand N-(2,4-cyclohexadiene-1-yl)phthalimide. A series of stereochemically diverse polyhydroxyl aminocyclohexane "aminocyclitols" derivatives and a number of racemic and optically active hydroxy-and polyhydroxy 1,3-diaminocyclohexane derivatives have been synthesized from N-(2,4-cyclohexadiene-1-yl)phthalimide. The relative stereochemistries of the compounds ware assigned on the basis of the ^{1}H NMR data as well as X-ray single crystal diffraction analysis.

In a similar attempt tricabonyl(η^5-6-styrylcyclohepta-2,4-diene-1-yl)iron(+1) cation was synthesized in three steps from 1, 3, 5, 7-cyclooctatetraene. Reactivity with various nucleophiles was studied. Nucleophilic attack of lithium dimethylallyl malonate at the less hindered pentadienyl terminus of the cation, decomplexation by Ce^{4+} followed by rearranged ring closing metathesis using 1st generation Grubbs catalyst gave skeletally unusual (5E, 7Z, 9Z)-dimethylbicyclo[4.4.1]undeca-5,7,9-triene-2,2-dicarboxylate.

Reaction of potassium phthalimide with tricabonyl(η^5-6-styrylcyclohepta-2,4-diene-1-yl)iron(+1) cation in a similar fashion, followed by decomplexation with Ce^{4+} gave racemic 2-(1S, 6R)-6-((E)-styryl)cyclohepta-2, 4-diene-1-yl)isoindoline-1, 3-dione. Asymmetric dihydroxylation of the iron free ligand with ADmix-β followed by cycloaddition with singlet oxygen generated two optically active separable diastereomeric endoperoxides, which led to the synthesis of a number of racemic and optically active functionalized endoperoxides.

Acknowledgements

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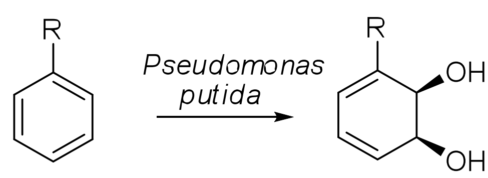
Chapter I

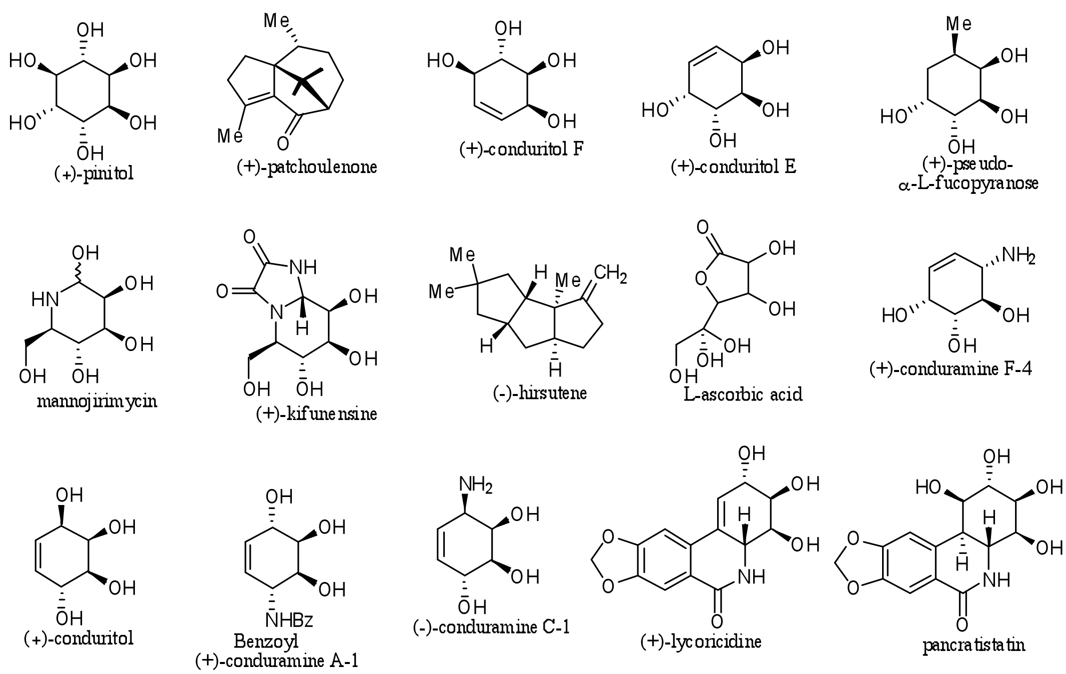
IA. General Introduction

Building complex molecularity starting from simple molecules is a continuing challenging task in organic synthesis. Many researchers have already made complex molecules starting from simple hydrocarbons like benzene (Scheme 2),[1-8] cyclopentadiene, (Scheme 3)[9] and cycloheptatriene (Scheme 4).[10] These synthetic successes have very much relied on the efficient oxidation and/or functionalization of the hydrocarbons. The detailed *in vivo* and *in vitro* study of oxidation of benzene and substituted benzene derivatives by the microorganism *Pseudomonas putida* unfolded a key *syn* dihydroxylation method (Scheme 1). Over a period of time, many researchers have used this *syn* dihydroxylation method successfully and made diverse complex molecules (Scheme 2), such as conduritols, conduramines, sugars, azasugars, *Amaryllidaceae* alkaloids and sesquiterpenes.

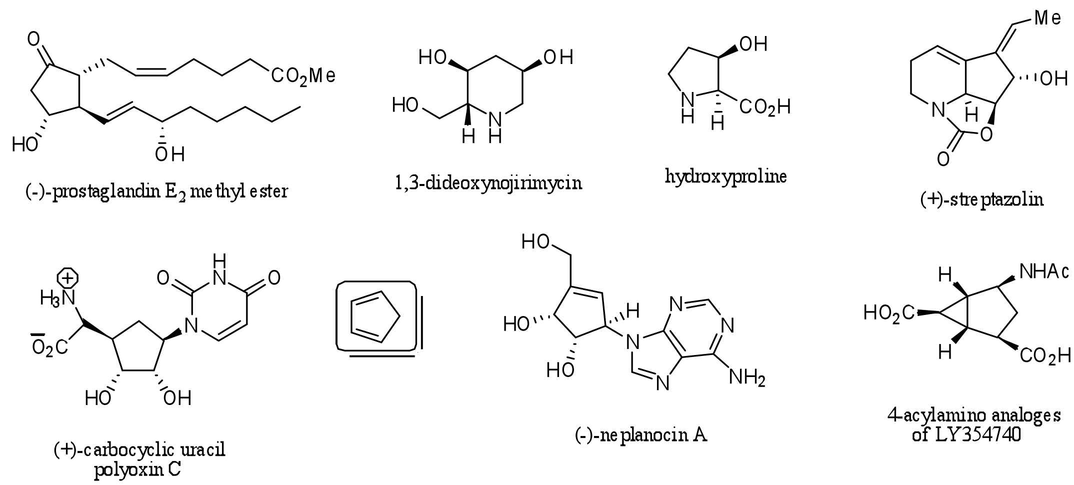


Scheme 1. *syn* Dihydroxylation of benzene derivatives by *P. putida.*

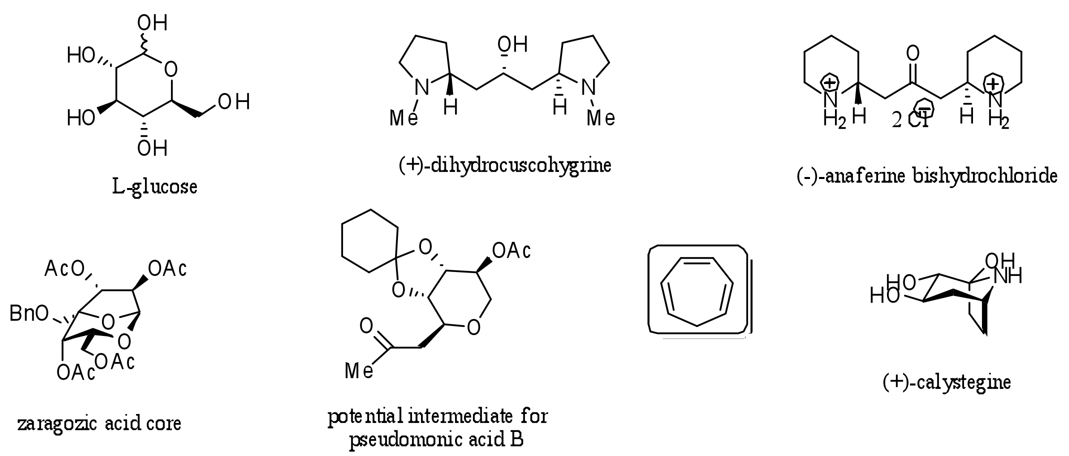
Elegant and efficient synthetic strategies helped to make a wide variety of drug candidates and natural products from simple chemical building blocks, such as cyclopentadiene (Scheme 3) and cycloheptatriene (Scheme 4).



Scheme 2. Partial list of targets prepared by *P. putida* dihydroxylation of benzene and substituted benzene.

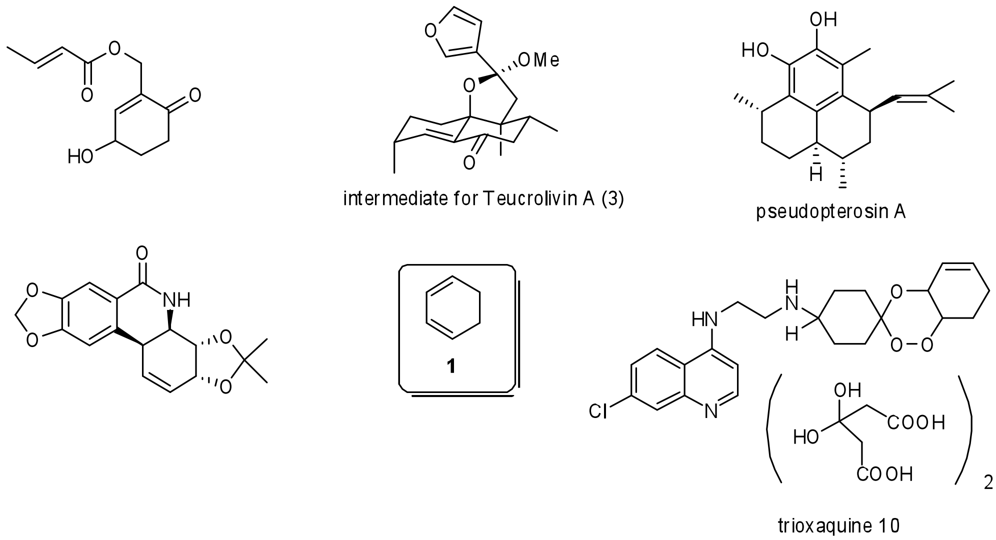


Scheme 3. Partial list of targets prepared from cyclopentadiene.



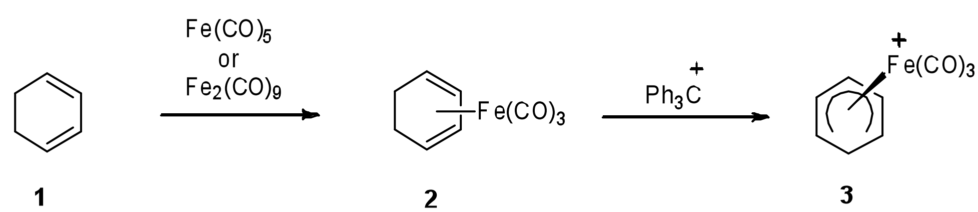
Scheme 4. Partial list of targets prepared from cycloheptatriene.

The use of 1,3-cyclohexadiene (**1**) as a diene in [4 + 2] cycloaddition reactions, as well as a substrate in 1,4-additions, selective dihydroxylations, or selective epoxidations is well known in organic synthesis. Many researchers have used the above protocols to prepare diverse molecular complexity (Scheme 5) from 1,3-cyclohexadiene.[11]



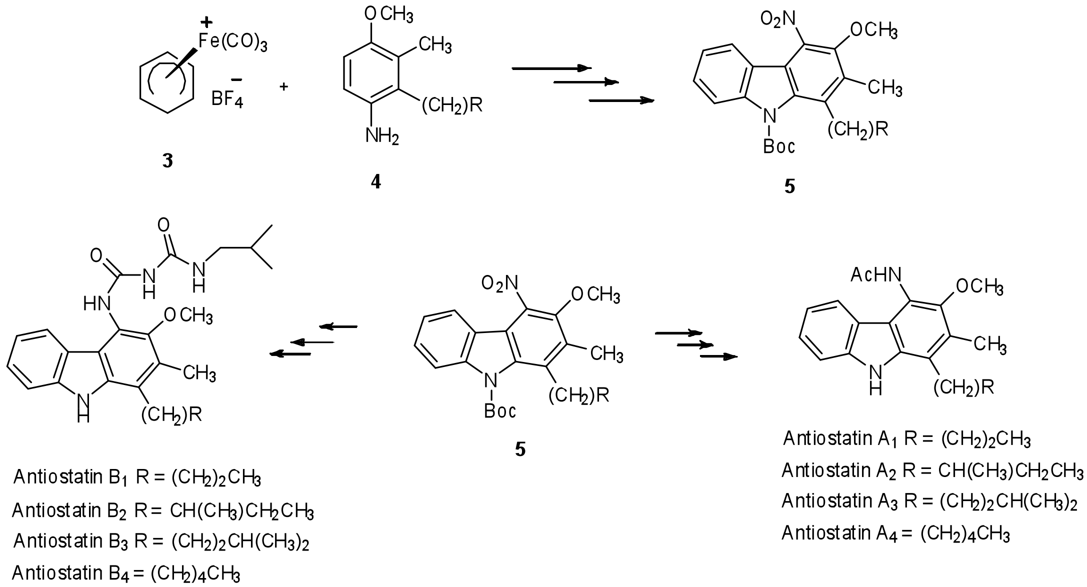
Scheme 5. Partial list of targets prepared from 1,3-cyclohexadiene **1**.

Pioneering work by Birch[12] and Pearson[13] have demonstrated the utility of the $[(\eta^5\text{-cyclohexadienyl})Fe(CO)_3]^+$ cation **3** and its ring substituted derivatives in stoichiometric organic synthesis. The cation **3** can easily be synthesized from 1,3-cyclohexadiene (Scheme 6).[14]



Scheme 6. Synthesis of $[(\eta^5\text{-cyclohexadienyl})Fe(CO)_3]^+$ cation **3**.

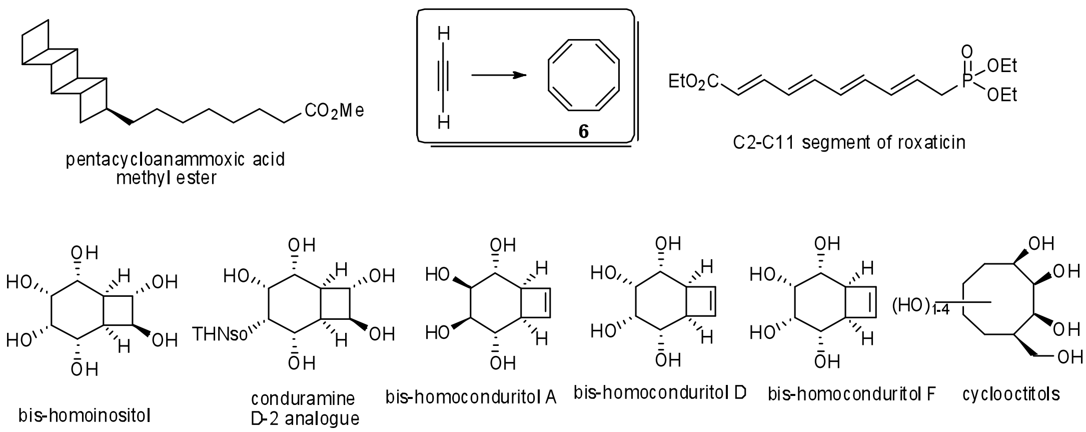
Very recently the synthesis of antiostatins, carbazoles known for their pharmacological potential, was reported by Knolker's group[15] based on the reaction of the cation **3** with arylamines **4** (Scheme 7).



Scheme 7. Synthesis of antiosotatins from cation **3**.

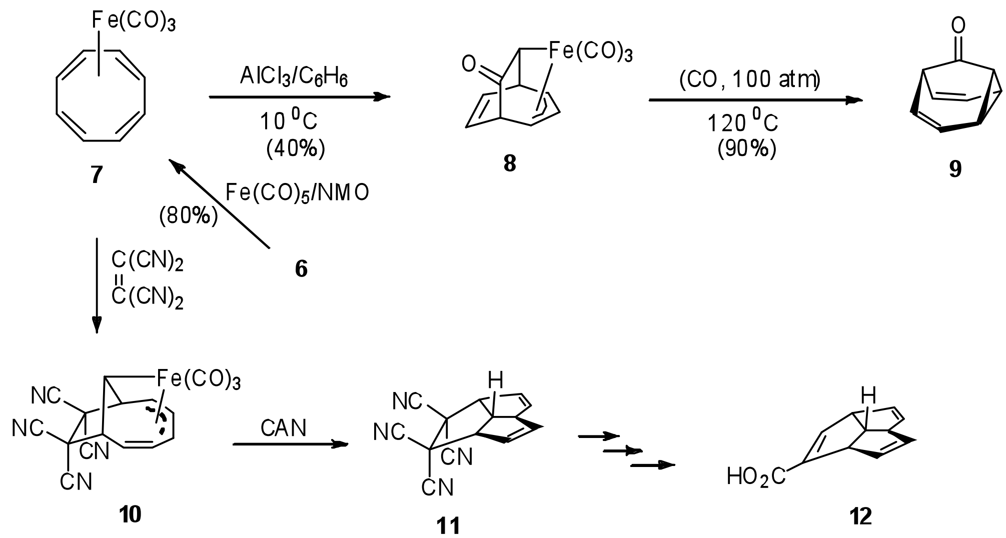
Electrophilic substitution of the arylamines **4** by reaction with cation **3** followed by series of reactions gave the carbazole **5**. Reaction of common precursor **5** in a divergent way leads to the synthesis of all antiosotatins.

Recently researchers have used cyclooctatetraene (**6**), a simple hydrocarbon which can be made by the Ni-catalyzed cyclotetramerization of acetylene,[16] to make complex molecules. Compounds such as aminocyclitols,[17a] bis-homoconduritols,[17b] bis-homoinositol,[17c] pentacycloanammoxic acid methyl ester,[17d] the polyene segment of roxaticin,[17e] and cyclooctitols[17f] (Scheme 8) are made very recently from cyclooctatetraene **6**.



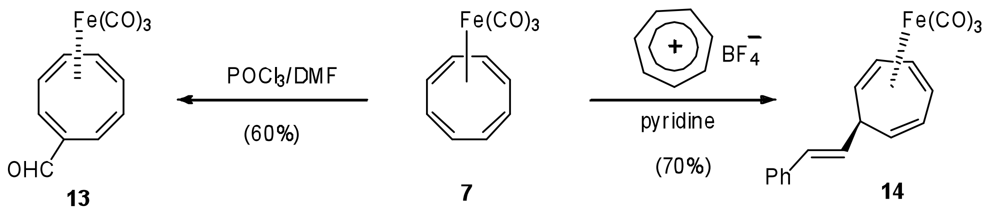
Scheme 8. Synthesis of cyclooctatetraene and target recently prepared from this hydrocarbon.

Complexation of cyclooctatetraene **6** gives tricarbonyl(cyclooctatetraene)iron **7** [(COT)Fe(CO)$_3$] (Scheme 9).[18] Synthetic applications of **7** by other research groups are limited. A σ-alkyl-π-allyl complex **8**[19] forms through rearrangement of **7** on treatment with a Lewis acid. Barbaralone **9** can be made on decomplexation of **8** under high pressure of CO. The synthesis of triquinacene-2-carboxylic acid **12**, [20] was reported by Paquette's group based on the reaction of **7** with tetracyanoethylene to give bicyclic σ-alkyl-π-allyl complex **10**. Oxidative decomplexation followed by C-C bond formation led to tricyclo[5.2.1.0^{4,10}]deca-2,5-diene **11**. Further manipulation of **11** gave the final product **12.**

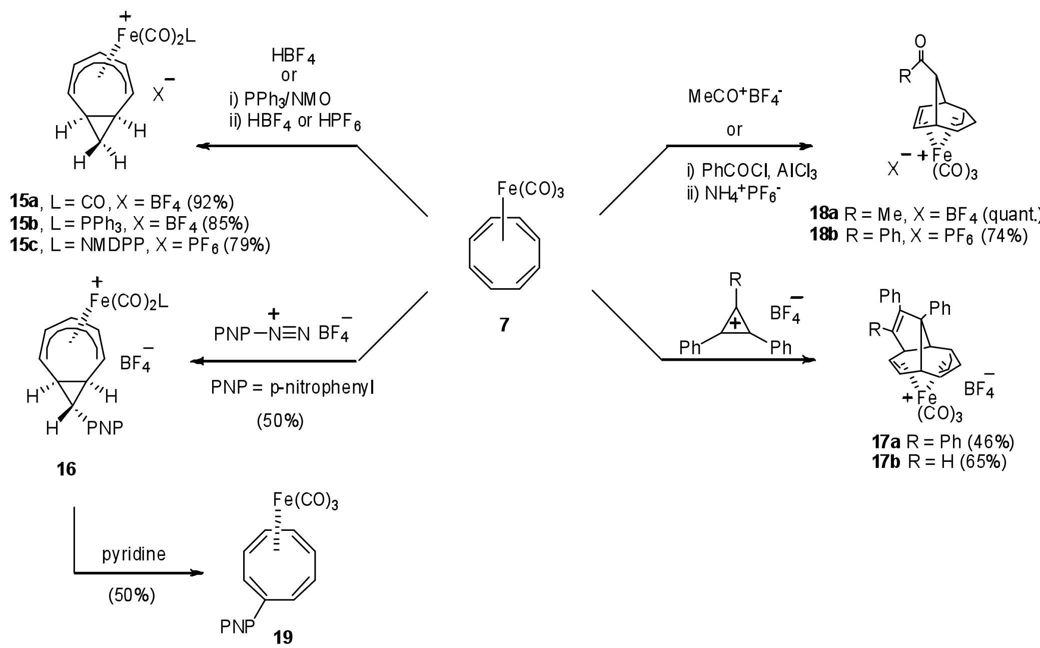


Scheme 9. Preparation of (COT)Fe(CO)$_3$ and previous synthetic applications.

Reported attacks on **7** by a variety of electrophiles are shown in Schemes 10 and 11. The neutral compounds, complexed aldehyde **13** or styrylcycloheptatriene complex **14** were prepared by the Vilsmeyer-Hack formylation of **7** or upon electrophilic attack of tropylium cation in presence of pyridine on **7** (Scheme 10).[21a]



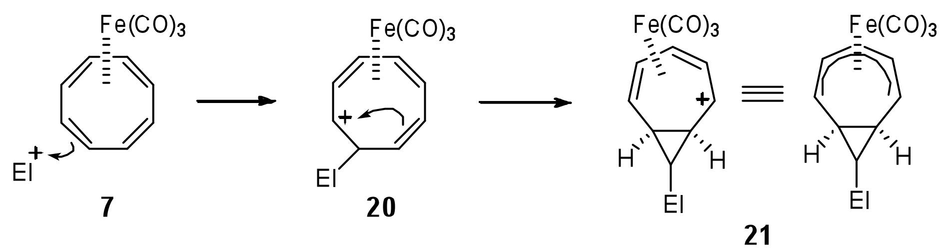
Scheme 10. Reaction of (COT)Fe(CO)$_3$ with electrophiles.



Scheme 11. Reactions of (COT)Fe(CO)$_3$ with electrophiles, generation of cationic compounds.

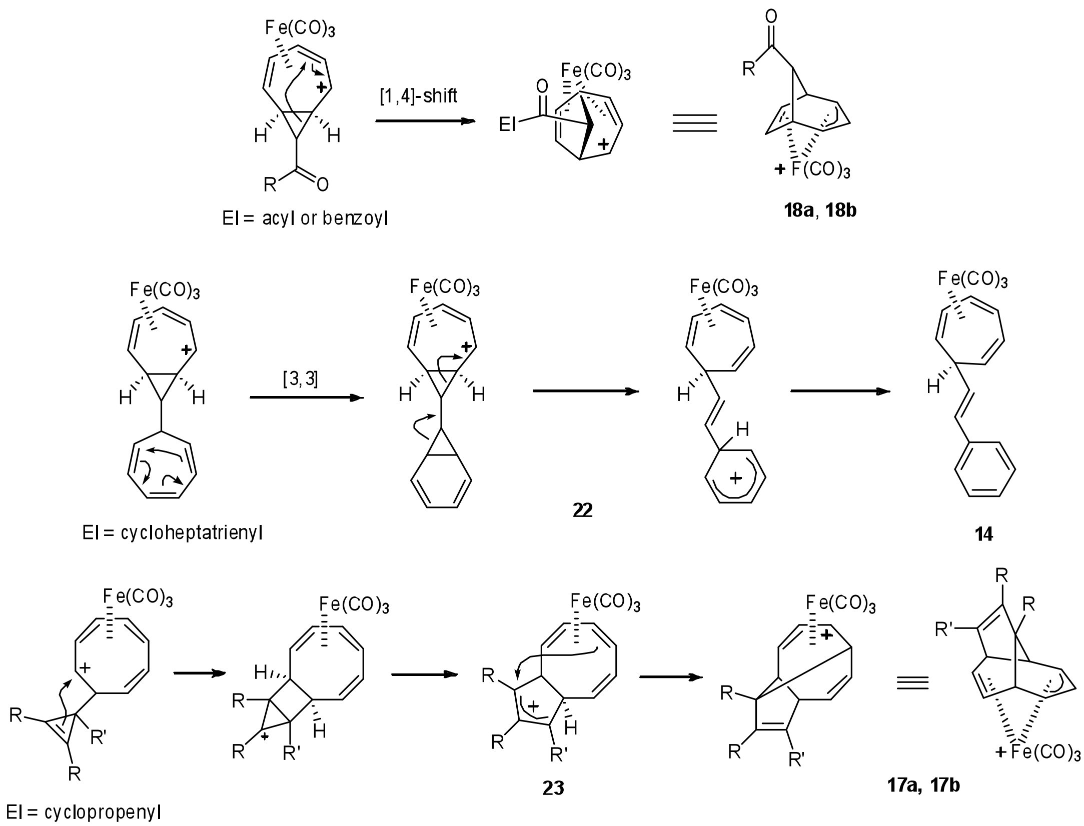
In contrast, a wide variety of skeletally rearranged cationic complexes (**15, 16, 17,** and **18)**[21b-f] were formed by the attack of other electrophiles on **7** (Scheme 11).

A mechanistic rationale for the formation of these rearranged structures is given in Schemes 12 and 13. The generic addition of an electrophile to a non-coordinated olefin of **7** generates a homobutyl cation **20** (Scheme 12). The homobutyl cation **20** rearranges into a cyclopropylcarbinyl cation of structure **21.** The bicyclo[5.1.0]octadienyl cation **21** was stable and isolable (i.e. products **15/16**) when the electrophile was H^+ or p-nitrophenyl$^+$.[21b-d]



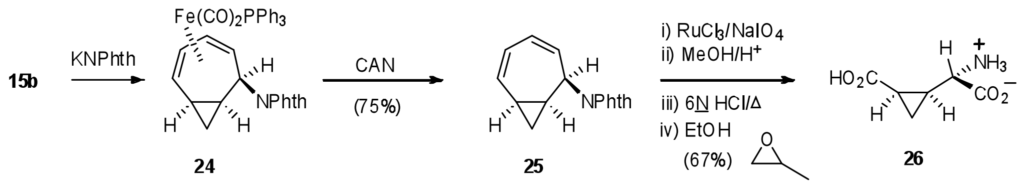
Scheme 12. generic attack of electrophile on (COT)$Fe(CO)_3$.

On the other hand, for El^+ = acylium ion, the acyl group present at C7 of **21** makes the adjacent cyclopropane bond weak and a subsequent [1,4]-shift relieves the strain to form the bicyclo[3.2.1]octadienyl cation **18** (Scheme 13)**.**[21e,f] In the case of tropylium cation as an electrophile, **21** undergoes a [3,3] Cope rearrangement to generates the norcaradiene intermediate **22,** which upon deprotonation gives the styrylcycloheptatriene complex **14**.[21a] Finally, for cyclopropenyl cation as electrophile, **20** rearranges to a bicyclo[6.3.0]nonatetraenyl cation **23**. The cation **23** transforms into a tricyclic cation **17** through an intramolecular bond formation.



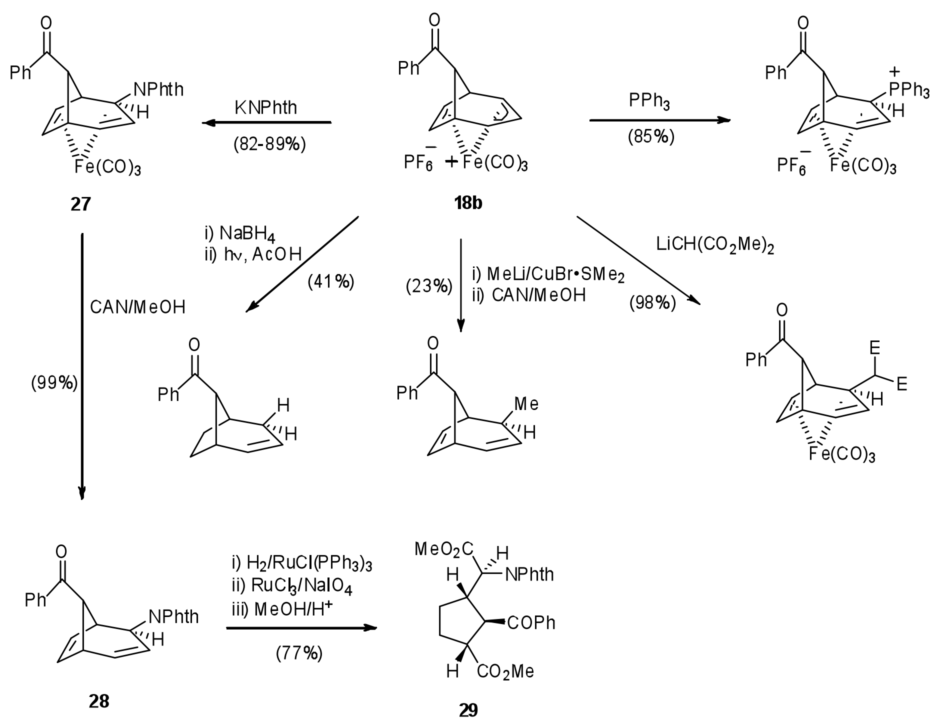
Scheme 13. Proposed mechanism for the generation of the skeletal rearranged products.

The reactivity of the cationic compounds **15a/b/c** & **18b** with several nucleophiles has been studied by Donaldson *et al.* In case of **15a/b** most of the times *exo* attack of nucleophiles on the terminal carbon was observed. The (±)-cis-2-(2'-carboxycyclopropyl)glycine, believed to be a common feature for inhibitors of glutamate transport, has been synthesized upon nucleophilic attack of potassium phthalimide on cation **15b** followed by few more steps (Scheme 14).[22]



Scheme 14. Synthesis of (±)-cis-2-(2'-carboxycyclopropyl)glycine from **15b**.

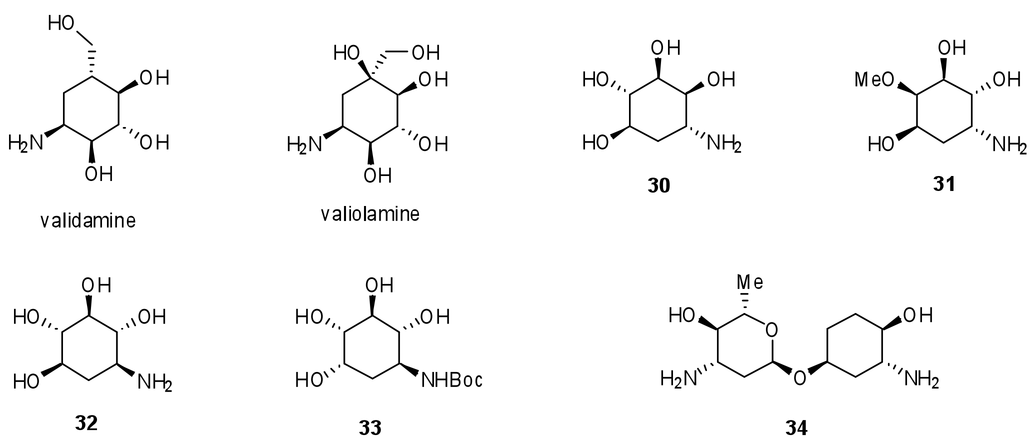
The reactivity of **18b** with various nucleophiles is given in Scheme 15. Attack of the nucleophiles at the η^3–allyl fragment gave several diene complexes (Scheme 15). This relatively unpredicted reactivity was utilized to synthesize the protected amino acid analog **29**.[23]



Scheme 15. Reactivity of **18b** with various nucleophiles, synthesis of protected amino acid analog **29**.

IB. Aminocyclitols

Polyhydroxylated cyclohexanes are popularly known as cyclitols, and a subclass cyclohexanepentols are trivially known as the quercitols (six member carbasugar). These classes of compounds are biologically relevant because of their sugar-mimetic structure. Aminocyclitols, another subclass of cyclitols, possess important biological activity like inhibitory activity against various glycosidases. Aminocyclitols are also present as non-sugar (aglycon) units of numerous aminoglycoside antibiotics, e.g., streptomycin and fortimycin,[24] which possess inhibitory activity against various glycosidases as a single structural unit. Examples of naturally occurring and synthetic aminocyclitols possessing various biological activities are given in Scheme 16.

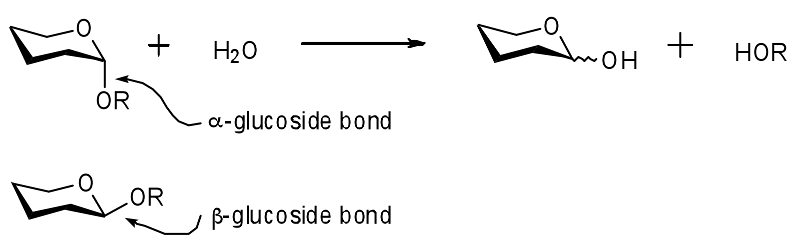


Scheme 16. Partial list of naturally occurring and synthetic aminocyclitols and derivatives.

Naturally occurring polyhydroxyl aminocyclohexanes, such as validamine and valiolamine shows inhibitory activity against various glycosidases.[25] Similarly, synthetic analogues like **30**[26] and **31**[27] were found to be inhibitors of α-glucoside and α-galactosides (IC_{50} = 12.5 and 20 μM, respectively). 2-Deoxy-scyllo-inosamine **32** is an intermediate in the biosynthesis of deoxystreptamine, an aglycon unit of the aminoglycosidase antibiotics.[28]

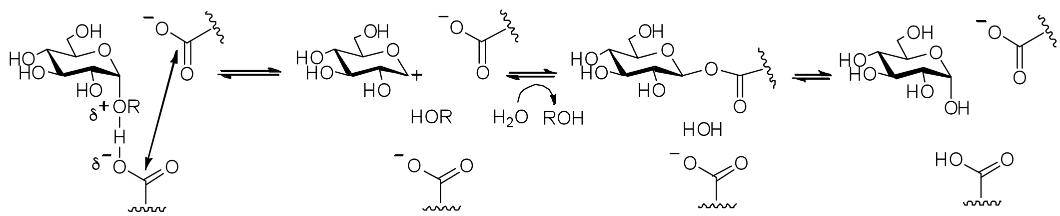
IC. Mode of Action of Aminocyclitols as Glycosidase Inhibitors

The glycosidic bond, shown in Scheme 17, is the mixed acetal linkage between two sugar residues. This bond is very stable towards hydrolysis; in particular, the linkage between two sugar residues is known to be the most stable within naturally occurring biopolymers. The half life for the hydrolysis of glycosidic bond between cellulose and starch (β-glucoside) is in the range of 5 million years.



Scheme 17. Glycosidic bond between two sugar residues.

Glycosidase enzymes catalyze the hydrolysis reaction accelerating the cleavage reaction with rate constant up to 1000 s^{-1} and have the reputation of being among the most efficient enzyme catalysts. Several mechanisms have been proposed for the hydrolysis of the glycosidic linkage.[29] One such mechanism with retention of configuration at the anomeric carbon is shown in Scheme 18.



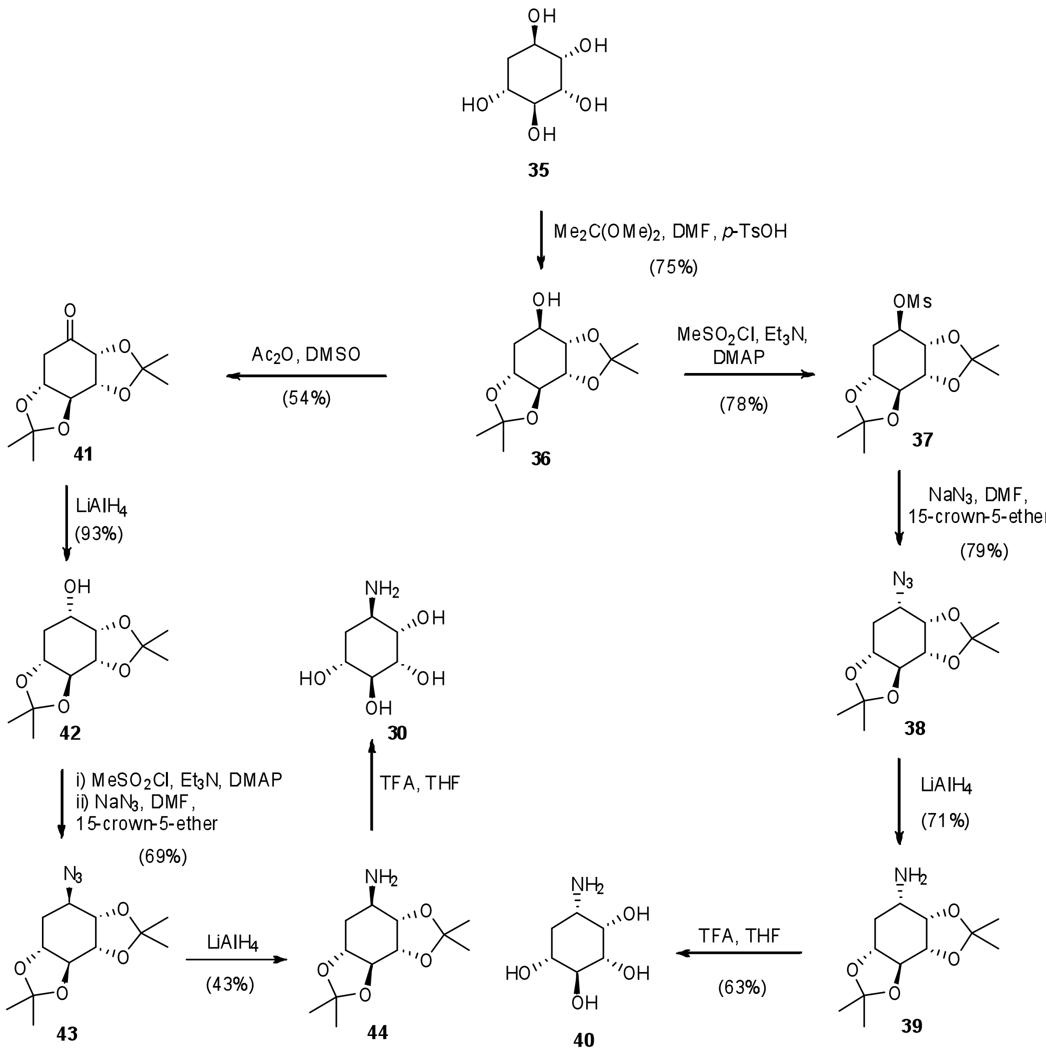
Scheme 18. Mechanism of the hydrolysis of glycosidic bond with retention of configuration at anomeric carbon.

The mechanism for enzymatic glycolysis involves the presence of two carboxylic acid residues. In this particular case (retention at the anomeric carbon), the distance between the two acid residues is ~ 5.5 Å. In the first step, one of the acid groups functions as a general acid catalyst and protonates the glycosidic oxygen with subsequent bond cleavage forming the oxonium ion. The oxonium ion may be stabilized by the other acid residue by forming a covalent glycosyl–enzyme intermediate. In the final step, the water molecule is directed to attack the anomeric center by the carboxylate general base.

The cleavage of the glycoside bonds is an important biological process. There are numerous natural and non-natural sugar mimics having a protonated nitrogen functionality under physiological pH which may form tight a ion pair within the active site of the acid residues of glycosidase enzymes and subsequently inhibiting the enzyme. These inhibitors may be of importance as potential antiviral, antitumor and antidiabetic agents. For example, inhibition of intestinal α-glycosidase lowers blood sugar levels and as such these inhibitors may be of use for the treatment of diabetes. Additionally, inhibition of glycosidase can disrupt the synthesis of oligosaccharides which are involved in cell-cell or cell-virus recognition.

ID. Recent Synthetic Studies of Aminocyclitols

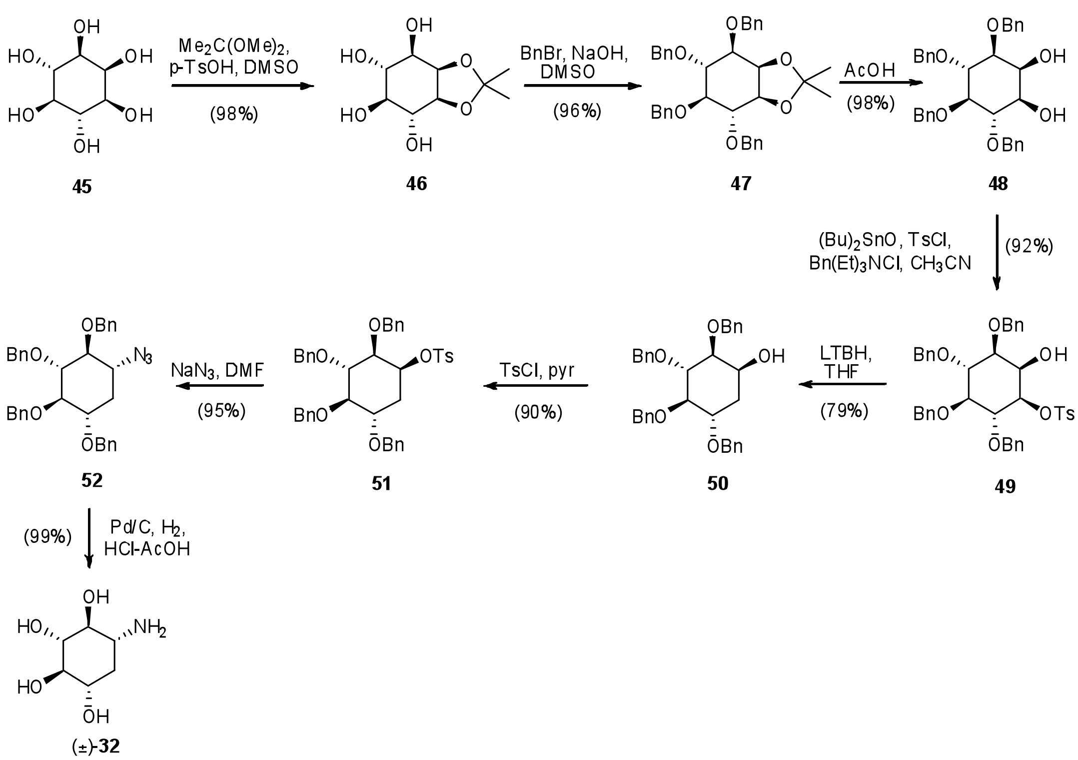
Several synthesis of aminocyclitols and derivatives have been reported starting from quercitols (deoxyinositols),[26,27] from inositols via deoxygenation,[30] from carbohydrates via Ferrier carbocyclic ring-closure,[31,32] via 6-exo radical cyclization of carbohydrate derived from oximes,[33] and from chiral 1,7-octadienes via ring closing metathesis.[34]



Scheme 19. Synthesis of aminocyclitols from (+)-proto-Quercitol.

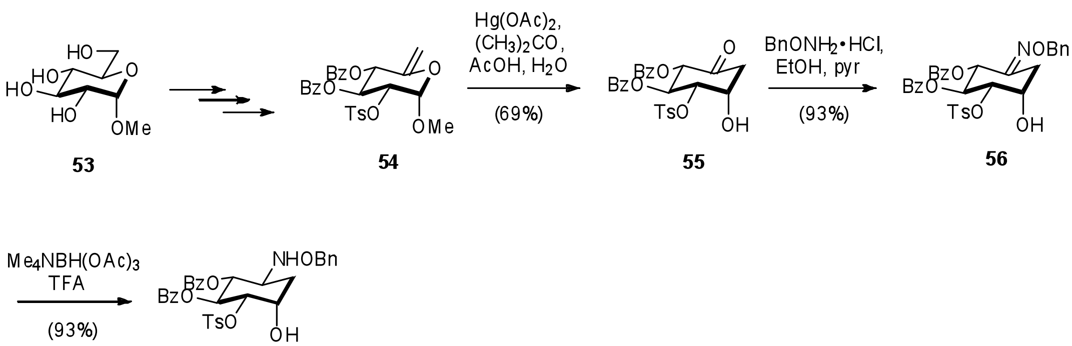
Synthesis of 5-amino-1,2,3,4-cyclohexanetetrols **40** and **30**, found to be α-glucosidase inhibitors, from naturally occurring (+)-proto-quercitol **35** was reported by Phuwapraisirisan, *et al.* (Scheme 19).[26] The (+)-proto-quercitol **35**, isolated from the stems of *Arfeuillea arborescene* was converted into bis-acetonide **36** (Scheme 19). A series of functional groups transformations of common precursor **36** in a divergent way leads to the generation of two isomeric 5-amino-1,2,3,4-cyclohexanetetrols (**40** and **30**).

Spencer, *et al.,* reported the synthesis of (±)-2-deoxy-scyllo-inosamine (±)-**32** from myo-inositol via deoxygenation (Scheme 20).[30] Two of the cis-hydroxyls of myo-inositol **45** were protected as the acetonide to give **46**. Protection of the remaining hydroxyls followed by chemo-selective deprotection gave **48**. Regioselective tosylation of the equatorial hydroxyl of **48** generated the monotosylate **49**. The displacement of the tosyl group by lithium trimethylborohydride (LTBH) gave deoxygenated product **50**. Three more standard functional group transformation leads to the generation of 2-deoxy-scyllo-inosamine (±)-**32**.



Scheme 20. Synthesis of (±)- 2-deoxy-scyllo-inosamine from myo-inositol.

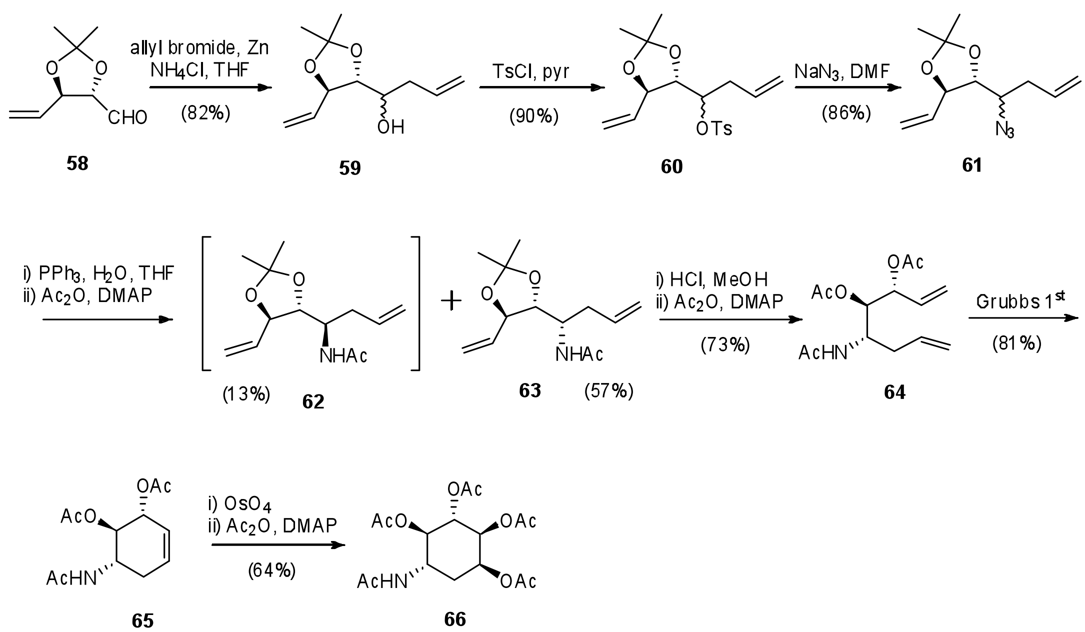
Many researchers have also synthesized aminocyclitols using chiral pool strategies starting from optically active carbohydrates. The synthesis of orthogonally protected 2-deoxystreptamine (2-DOS) from methyl-α-D glucopyranoside was reported by Claude Bauder (Scheme 21).[32]



Scheme 21. Synthesis of aminocyclitol from methyl-α-D glucopyranoside.

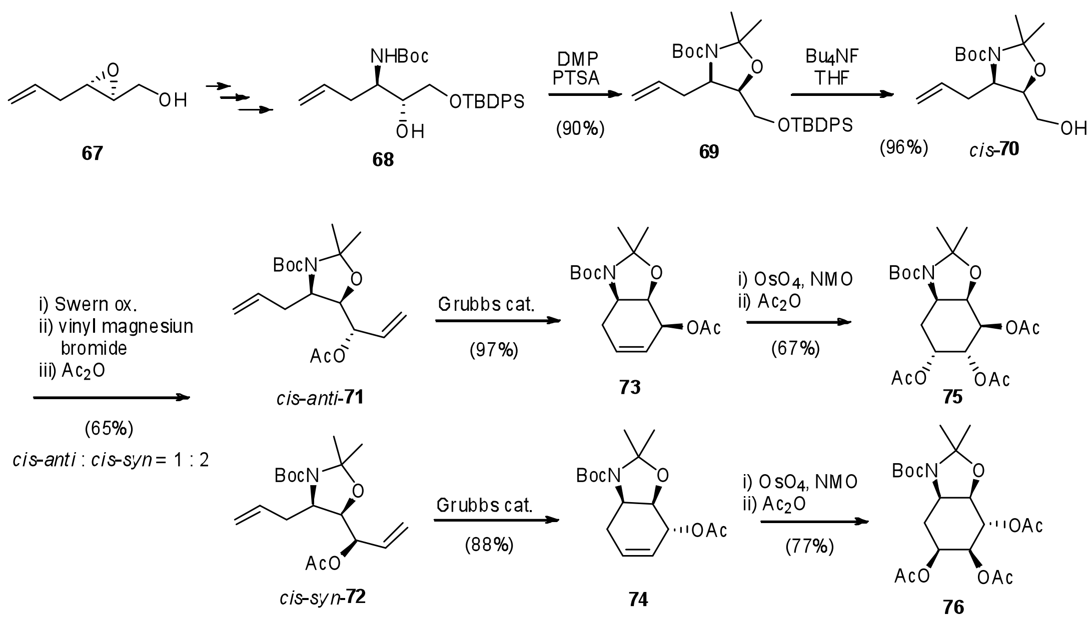
Methyl α-D glucopyranoside **53** was converted into **54** in four steps following literature procedure.[32] Ferrier carbocyclic ring-closure[31, 32] of **54** gave exclusively a single epimeric β-hydroxy-cyclohexanone **55**. Treatment of **55** with O-benzylhydroxylamine hydrochloride in EtOH-pyr gave benzyloxime **56**. Diastereoselective reduction of oxime functionality by tetramethylammonium triacetoxyborohydride/TFA gave a derivative of 2-DOS **57**.

Vankar, *et al.,* reported the synthesis of 5-amino-5-deoxy-D-vibo-quercitol starting from commercially available D-mannitol (Scheme 22).[34a] Reaction of D-mannitol derived aldehyde **58** with allyl magnesium bromide in the presence of zinc gave a diastereomeric mixture (81:19 anti : syn) of homoallyl alcohols **59**. Tosylation followed by treatment with NaN_3 gave the corresponding diastereomeric azides **61**. Reduction/acetylation of the mixture gave a chromatographically separable mixture of two diastereomeric acetates **62** and **63**. Acetonide deprotection followed by acetate formation of the major acetonide **63** gave the dienetriacetate **64** suitable for metathesis. Ring-closing metathesis of **64**, syn-dihydroxylation and acetate formation gave a derivative of 5-amino-5-deoxy-D-vibo-quercitol **66**.



Scheme 22. Synthesis of aminocyclitols from D-mannitol.

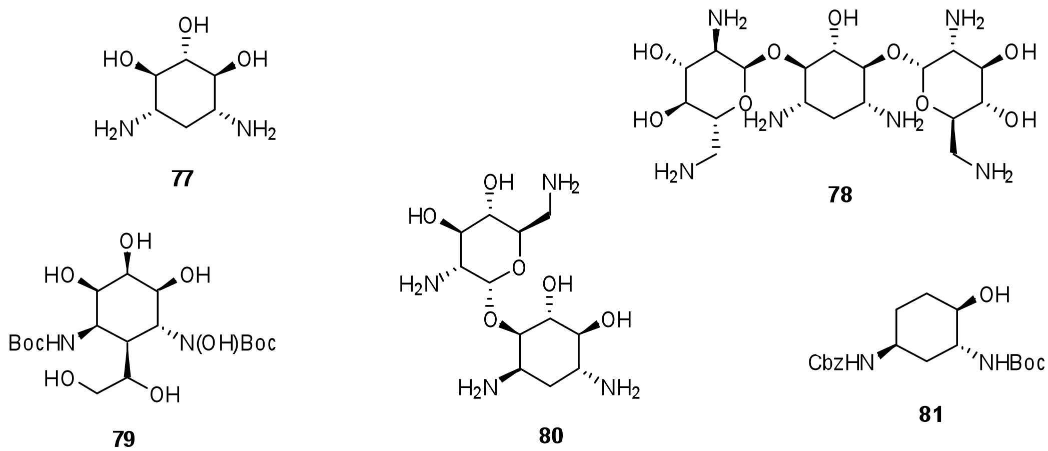
Riera, *et al.,* reported the synthesis of a series of aminocyclitols derivatives starting from readily available epoxy alcohol **67** via a ring closing metathesis protocol.[34b] Synthesis of two of the several isomers are shown in Scheme 23. Epoxy alcohol **67** was converted to amino alcohol **68** with anti configuration following literature procedure (epoxide ring opening, azide reduction, protection).[35] Protection followed by chemoselective deprotection gave the alcohol **70**. Oxidation of the alcohol **70** followed by addition of vinyl magnesium bromide and acetate formation gave a chromatographically separable mixture of *cis-anti*-**71** and *cis-syn*-**72**. Ring closing metathesis of both **71** and **72** using first generation Grubbs catalyst gave **73** and **74** respectively. Catalytic *syn* dihydroxylation of **73** or **74** followed by acetate formation gave two isomeric aminocyclitols derivatives **75** or **76** respectively.



Scheme 23. Synthesis of aminocyclitols from epoxy alcohol.

1E. 1,3-Diaminocyclohexanes

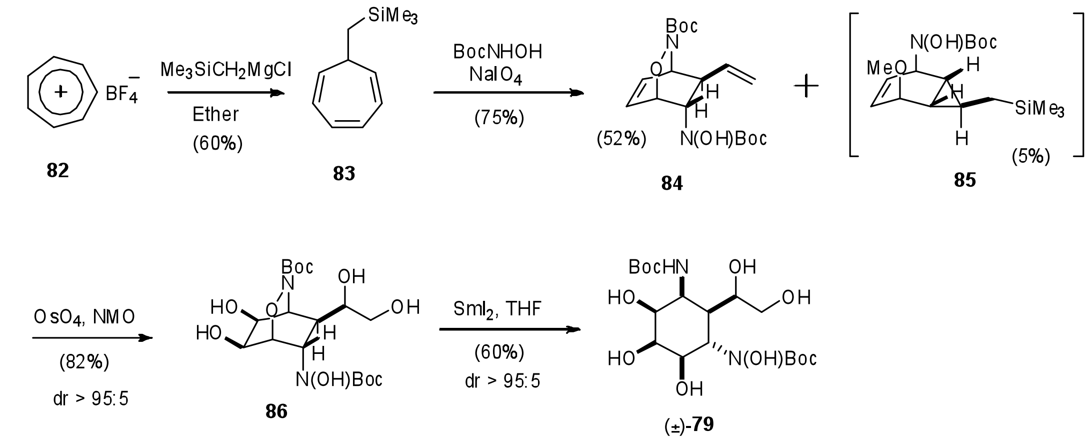
Just like aminocyclohexanes, trihydroxy-1,3-diaminocyclohexanes and their derivatives are important biological entities. Examples of biologically relevant 1,3-diaminocyclohexanes derivatives are given in Scheme 24. Compound **77**[36] is present as an important structural unit in kanamycin A **78** (an aminoglucoside antibiotic which binds to bacterial 16S ribosomal RNA). While the relative orientation of the two amino functionalities in the 1,3 positions in majority of the aminoglucoside antibiotics is *cis*, some synthetic analogue like **79**, **80**[37] and **81** possess a *trans*-1,3-diaminocyclohexane subunit. Compound **79**[38] is a sugar mimic and **81** was utilized as an intermediate in the synthesis of CC chemokine receptor 2 antagonists.[39]



Scheme 24. Partial list of biologically relevant 1,3-diaminocyclohexanes.

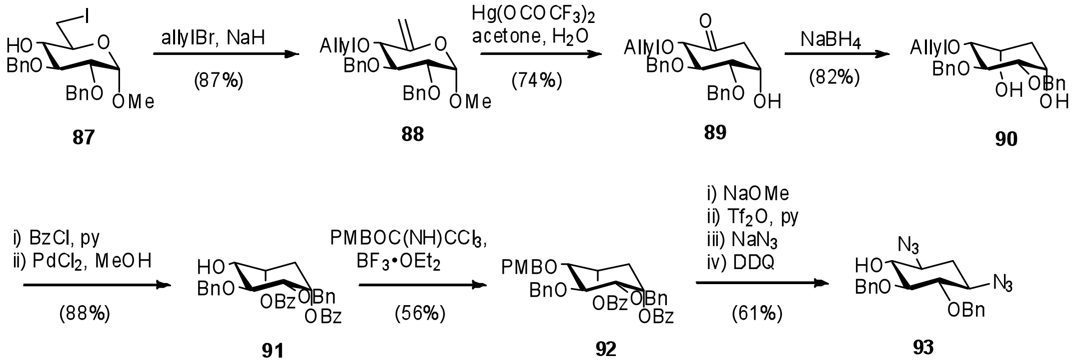
1F. Recent Synthetic Studies of 1,3-diaminocyclohexanes

Synthesis of (±)-**79** was reported by Landais, *et al.,* from commercially available tropylium fluoroborate **82** (Scheme 25).[38] Silylcycloheptatriene **83** was synthesized from tropylium fluoroborate using trimethylsilyl methyl-magnesium chloride as nucleophile. Cycloaddition of **83** with an acyl-nitroso reagent gave a separable mixture of **84** and **85**. Catalytic dihydroxylation of **84** followed by N-O bond reduction of **86** by SmI_2 gave (±)-**79**.



Scheme 25. Synthesis of sugar mimic (±)-**79** from tropylium fruoroborate.

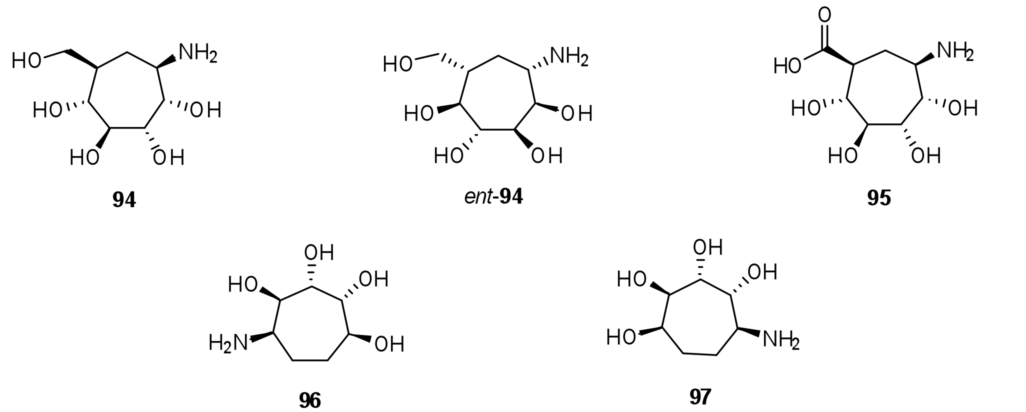
The synthesis of a derivative of **77** has been reported by Xin-Shan Ye, *et al.* (Scheme 26).[37] The iodo precursor **87** was synthesized from methyl-α-D glucopyranoside **53** following the literature procedure. Reaction of **87** with allylbromide and sodium hydride gave the allyl protected *exo*-alkene **88**. Ferrier II rearrangement of **88** gave the hydroxyl ketone **89**. Reduction of **89** by $NaBH_4$ gave exclusively **90**. Benzylation, deprotection of allyl ether and reprotection followed by nucleophilic displacement of the axial benzoates by azide anion gave the final compound **93**.



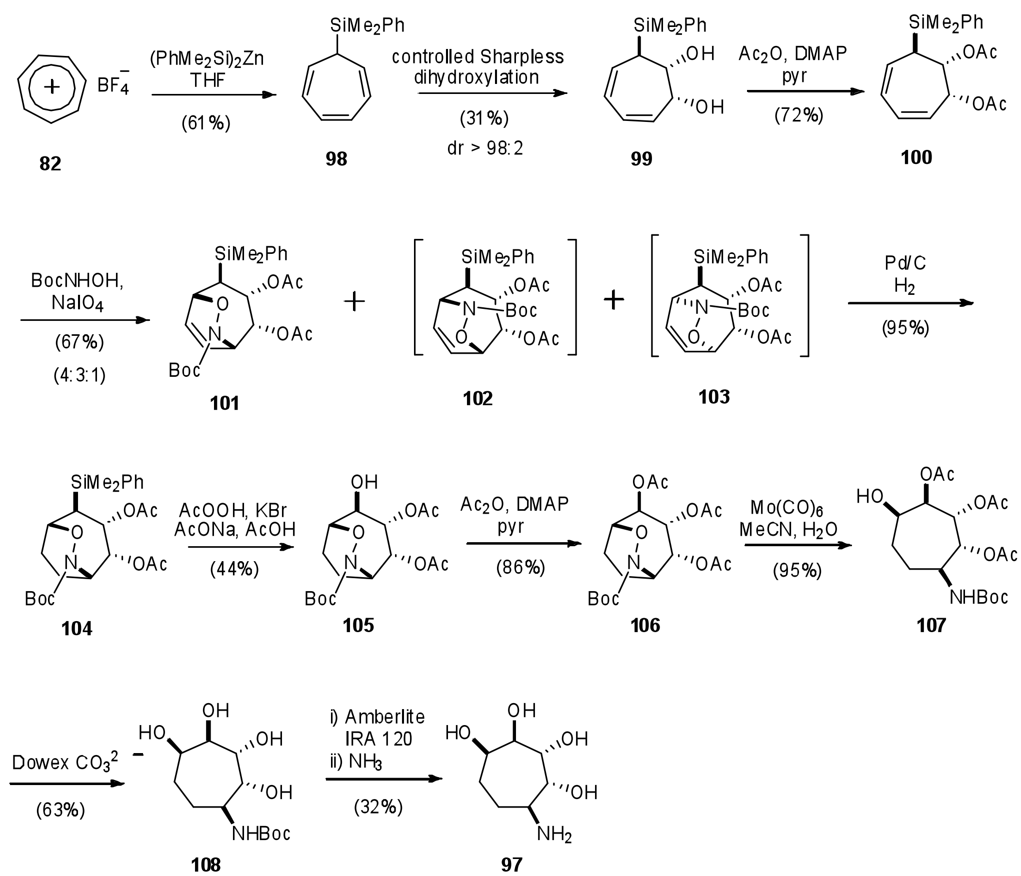
Scheme 26. Synthesis if 1,3-diaminocyclohexane derivative from sugar.

1G. Ring-expanded Homologs of Aminocyclitols

Nature has always favored five- and six-membered ring monosaccharides as essential structural motifs over the ring-expanded homologues. Similarly, synthetic chemists are also interested in making five- and six-membered carbasugars, because of their sugar-mimetic structure, leaving preparation of the higher carbocycles largely untouched. Very recently Casiraghi, *et al.,* [40]and Landais, *et al.,*[41]have reported the synthesis of 7-membered carbocycles, shown in Scheme 27.



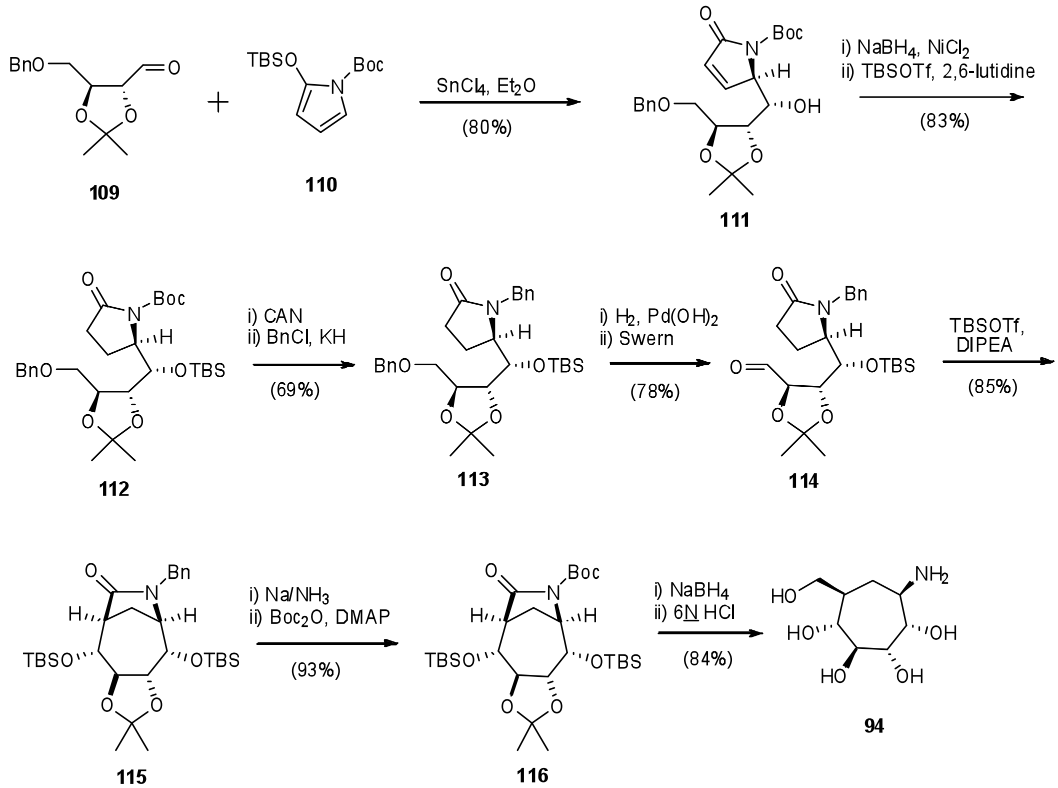
Scheme 27. Partial list of recently synthesized seven-membered carbasugars.



Scheme 28. Synthesis of **97** from commercially available tropylium fluoroborate.

Commercially available tropylium fluoroborate **82** was converted into silylcycloheptatriene **98** using a bis-silyl zinc reagent (Scheme 28). Sharpless dihydroxylation followed by acetylation gave **100**. Cycloaddition of **100** with an acyl-nitroso reagent generated three isomeric compounds **101**, **102** and **103**. The major acyl-nitroso adduct **101** was transformed into the final product **97** following several standard functional groups manipulations.

Lewis acid catalyzed intermolecular aldol condensation between aldehyde **109** (readily available from (+)-tartrate) and pyrrole derivative **110** furnished the unsaturated lactam **111** as a single diastereomer (Scheme 29). Chemoselective reduction of the carbon-carbon double bond followed by protection of hydroxyl group gave **112**. Exchange of the *N*-protecting group, selective deprotection and Swern oxidation gave the aldehyde **114**. The silylative intramolecular aldol condensation of **114** gave compound **115** as a single diastereoisomer. Again, exchange of N-protecting group followed by reductive cleavage of the amide bond and acid hydrolysis leads to the isolation of **94**.



Scheme 29. Synthesis of **94** from (+)-tartrate.

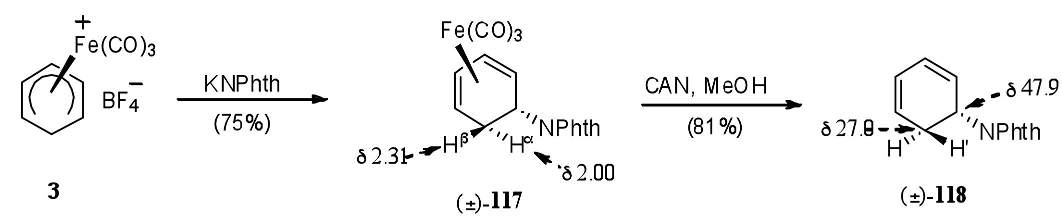
As part of our long term interest in the generation of molecular complexity from simple hydrocarbons, we have synthesized a series of racemic polyhydroxyl aminocyclohexane derivatives, a number of racemic and optically active *trans*-1,3-diaminocyclohexane derivatives and some of their amine salts from commercially available 1,3 cyclohexadiene. In a similar attempt, a number of racemic and optically active functionalized endoperoxides were prepered from readily available cyclooctatetraene.

Chapter II

Polyhydroxyl Aminocyclohexanes

II A. Synthesis of Aminocyclitols from Cyclohexadiene

In an effort to synthesis stereochemically diverse polyhydroxylaminocyclohexanes like **30** or its isomeric derivatives**,** the iron cation **3** was prepared from 1,3-cyclohexadiene **1** following literature procedure (Scheme 6).[14] Nucleophilic attack of potassium phthalimide (KNPhth) at the dienyl terminus of the symmetric cation **3** gave (±)-**117**. Oxidative decomplexation of (±)-**117** with CAN/MeOH gave the iron free ligand (±)-**118** (Scheme 30).

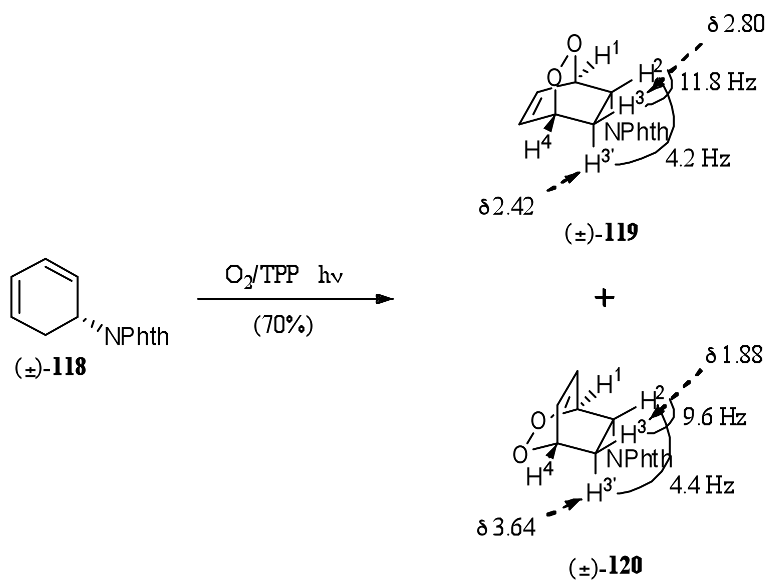


Scheme 30. Synthesis of iron free ligand (±)-**118** from the cation **3**.

The structure of the η^4-bonded iron complex (±)-**117** was assigned based on its ^{1}H and ^{13}C NMR spectral data. Signals at δ 2.77, 3.13, 5.53, and 5.67 ppm in its ^{1}H NMR spectrum and at δ 57.1, 58.2, 86.0, 86.7 in its ^{13}C NMR spectrum are consistent with the η^4-attachment of the iron with the diene portion of the ligand.[42] Assignment of the diastereotopic methylene protons 6-H$^{\alpha}$ (δ 2.00, br d, *J* = 15.1 Hz) and 6-H$^{\beta}$ (δ 2.31, ddd, *J* = 4.2, 11.4 and 15.1 Hz) was based on the magnitude of their geminal coupling and splitting pattern.

The structure of (±)-**118** was similarly assigned on the basis of its NMR spectral data. Signals at δ 2.38 ppm (ddd, *J* = 5.6, 10.0 and 17.2 Hz, 6-H), 2.78 ppm (tdd, *J* = 3.1, 15.2, 17.6, 6-H') and 5.20 (tdd, *J* = 2.9, 9.6, 15.2 1H) in the ^{1}H NMR spectrum and at δ 27.0 and 47.9 ppm in its ^{13}C NMR spectrum corresponded to the two sp^{3} hybridized carbons and their attached hydrogens.

Cycloaddition of (±)-**118** with singlet oxygen gave a separable mixture of endoperoxides (±)-**119** and (±)-**120** (Scheme 31) (Fig. 1 and 2).



Scheme 31. Synthesis of isomeric endoperoxides (±)-**119** and (±)-**120**.

The major product comes from approach of singlet oxygen on the face opposite to the phthalimide substituent. This facial selectivity was similar to that previously reported for cycloaddition of nitrosobenzene with 3-methyl-5-phenyl-1,3-cyclohexadiene.[43] The structural assignments of the two endoperoxides were based on their ^{1}H NMR spectral data. The assignment of the two diastereotopic methylene protons of (±)-**119**, $H^{3'}$ (δ 2.42, ddd, *J* = 2.0, 4.4, 13.6 Hz) and H^3 (δ 2.80, ddd, *J* = 4.0, 9.6, 13.6) were based on the magnitude of their coupling with H^2. Two diastereotopic protons of (±)-**120**, $H^{3'}$ (δ 3.64, td, *J* = 4.2, 13.8 Hz) and H^3 (δ 1.88, ddd, *J* = 1.9, 11.8, 13.8 Hz) was assigned on the same basis. The upfield shift for $H^{3'}$ for (±)-**119** compared to $H^{3'}$ for (±)-**120** and H^3 for (±)-**120** compared to H^3 of (±)-**119** were due to the anisotropic effect of the olefin functionality. The structural assignments were finally confirmed from single crystal X-ray diffraction analysis (Fig. 1 and Fig. 2).

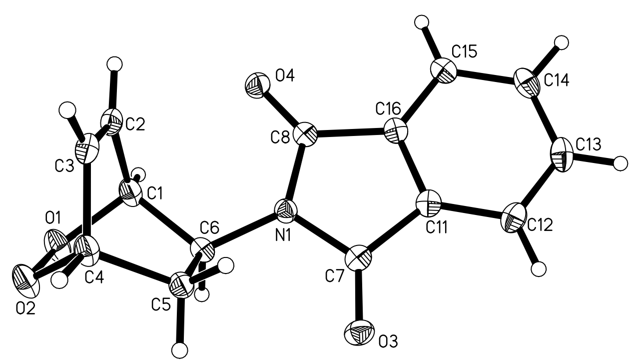


Figure 1. X-ray crystal structure of (±)-**119**.

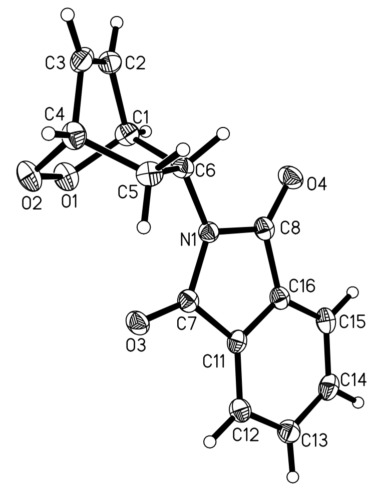
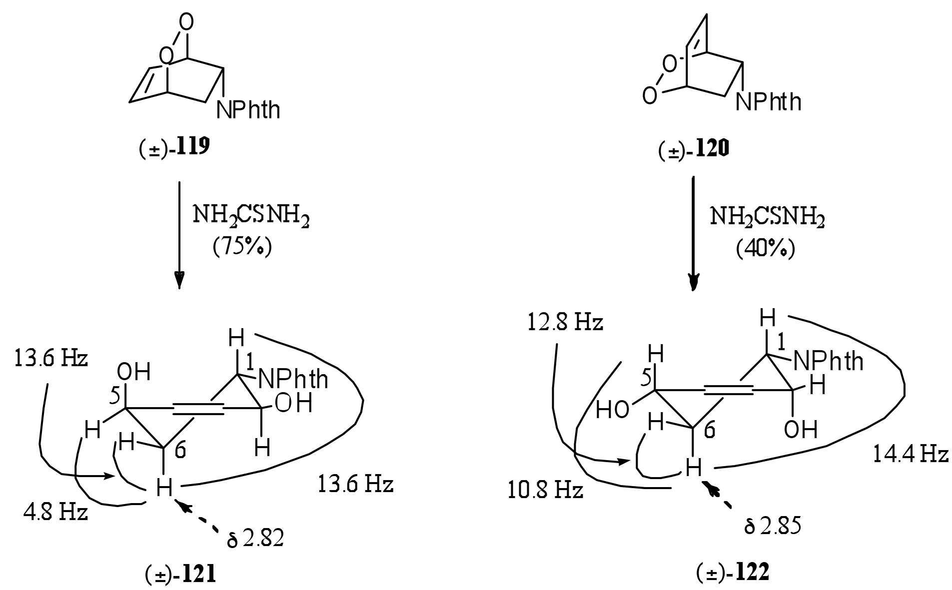


Figure 2. X-ray crystal structure of (±)-**120**.

The major endoperoxide (±)-**119** was reduced to diol (±)-**121** using thiourea-methanol. In a similar fashion (±)-**120** was reduced to (±)-**122** (Scheme 32).

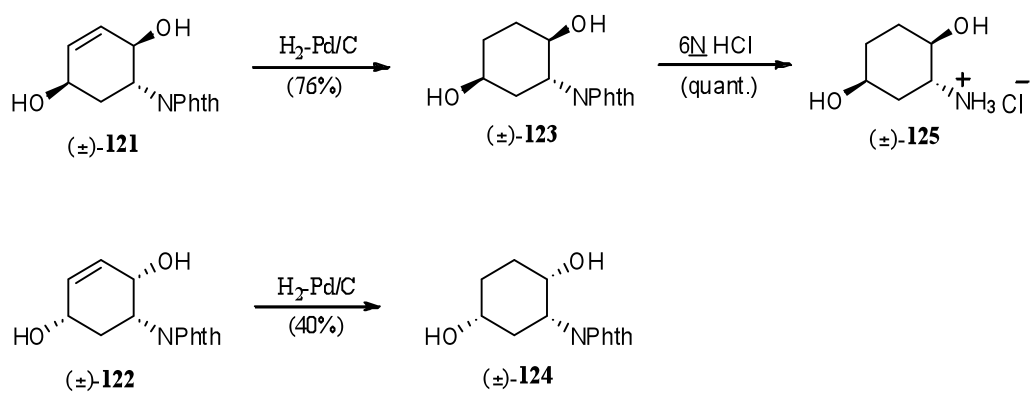


Scheme 32. Thiourea/methanol reduction of (±)-**119** and (±)-**120**.

The structural characterization of each was based on their ^{1}H NMR spectral data. For (±)-**121**, the signal at δ 5.92 (m, 2H) indicates that the olefinic double bond was intact after the thiourea reduction. The relative *trans*-orientation of two substituents at C-1/C-5 was assigned on the basis of the coupling patterns as well as the magnitude of the couplings of the two diastereotopic methylene protons H-6_{eq} (δ 1.97 ppm, br d, *J* = 14.0 Hz) and 6-H_{ax} (δ 2.82 ppm, dt, *J* = 4.8 and 13.6 Hz). Similarly, the *trans*-orientation of substituents at C-1/C-2 was confirmed from the magnitude of the coupling between 1-H_{ax} (4.58, ddd, J = 3.2, 10.0 and 13.6 Hz) and 2-H_{ax} (4.84, br d, J = 9.2 Hz).

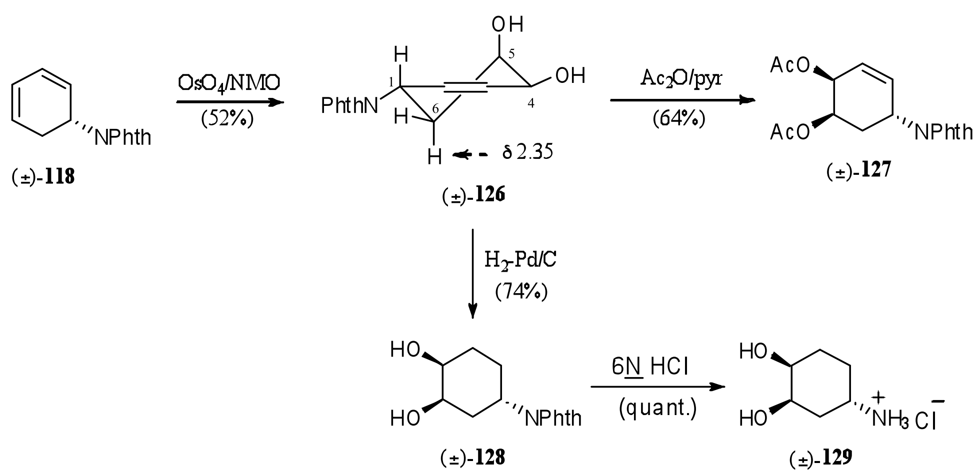
The structure of (±)-**122** was assigned based on its ^{1}H NMR spectral data. The splitting pattern and the magnitude of the coupling of the two-diastereotopic methylene protons 6-H_{ax} (δ 2.85 ppm, ddd, J = 10.8, 12.8 and 14.4 Hz) and 6-H_{eq} (δ 2.21 ppm, br d, J = 12.8 Hz) indicate that the substituents at C-1/C-5 are *cis* to each other. In particular, three large couplings for the 6-H_{ax} were due to two diaxial vicinal coupling of 6-H_{ax} with 5-H_{ax} and 1-H_{ax} and a geminal coupling with 6-H_{eq}. Signals around δ 5.96-5.97 (m, 2H) were assigned to the CH=CH functionality.

Catalytic hydrogenation of enediols (±)-**121** and (±)-**122** gave the corresponding saturated *N*-(dihydroxycyclohexyl)phthalimides (±)-**123** and **(±)-124** (Scheme 33). The structures were assigned based on the the structures of their precursors. Their ^{1}H NMR spectral data were consistent with these assignments. The saturated diol (±)-**123** was converted to its amine salt (±)-**125**.



Scheme 33. Catalytic hydrogenation of (±)-**121** and (±)-**122**.

A brief exposure (30 min) of (±)-**118** to OsO_4/NMO (Scheme 34) gave a diol (±)-**126**. Acetylation of the diol (±)-**126** using acetic anhydride/pyridine gave the corresponding diacetate (±)-**127**. The structure of the diacetate was assigned based on the single crystal X-ray diffraction analysis (Fig. 3), which consequently corroborated the structural assignment of (±)-**126**. Dihydroxylation of (±)-**118** occurs more rapidly at the olefin remote to the electron withdrawing phthalimide substituent.



Scheme 34. Dihydroxylation of (±)-**118** and related reactions.

Catalytic hydrogenation of (±)-**126** gave a saturated diol (±)-**128**, whose structure was assigned based on the structure of its precursor. The saturated diol (±)-**128** was converted to its amine salt (±)-**129**.

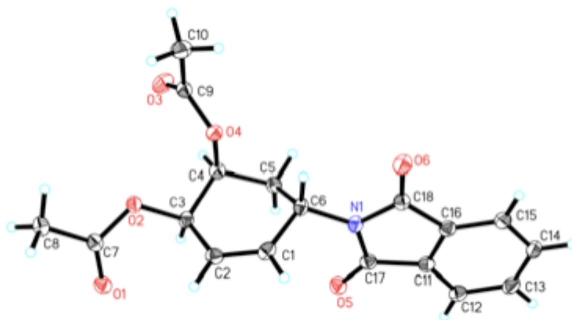
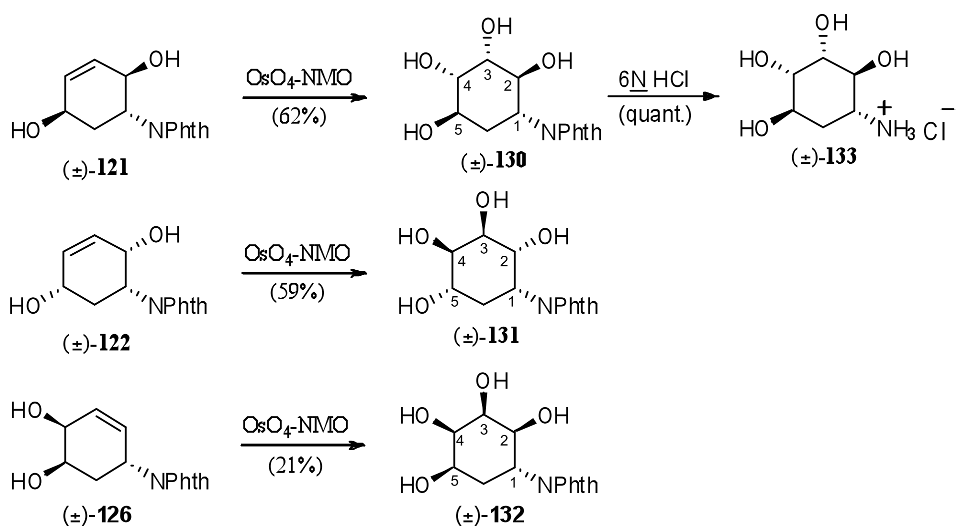


Figure 3. X-ray crystal structure of (±)-**127**.

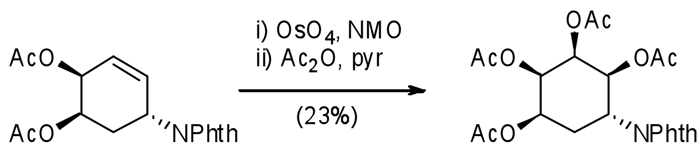
Catalytic dihydroxylation of enediols (±)-**121,** (±)-**122** and (±)-**126** with OsO_4/ NMO is shown in Scheme 35.



Scheme 35. Dihydroxylation of (±)-**121,** (±)-**122** and (±)-**126.**

The structures of the tetraols (±)-**130** and (±)**-131** were assigned based on their ^{1}H NMR spectral data. For (±)-**130**, the assignment of the C-1 phthalimide and the C-5 hydroxyl as *trans* is based on the appearance of the H-6_{ax} signal and magnitude of its coupling (dt, J = 2.8, 13.2 Hz). The one smaller coupling is due to an axial-equatorial disposition of H-6_{ax} and H-5_{eq}. The *trans* relationship between the hydroxyls at C-2 and C-3 was evidenced by the large coupling between the H-2_{ax} and H-3_{ax} protons (J = 9.6 Hz). For (±)-**131**, the *cis* relationship of the C-1 phthalimide and C-5 hydroxyl was based on the appearance of the H-6_{ax} signal and magnitude of its couplings (q, J = 12.4 Hz). These three large couplings are due to the axial-axial couplings to H-1 and H-5 and the geminal coupling to H-6_{eq}. The *trans*-diequatorial relationship of the C-4 and C-5 hydroxyls was evidenced by the axial-axial coupling between H-4_{ax} and H-5_{ax} (J = 9.8 Hz). These structural assignments were consistent with the *syn*-dihydroxylation and the selectivity noted by Kishi, *et al*.,[44] On the other hand, the structure of (±)**-132** was assigned based on the single crystal X-ray diffraction analysis (Fig. 4), which indicated that the C-1 phthalimide and the C-2 and C-5 hydroxyl are equatorial and C-3 and C-5 hydroxyls are axial. Tetraol (±)-**130** was shown to be diastereomeric with (±)**-132** by NMR spectroscopy. For diol (±)**-126,** dihydroxylation occurs on the face opposite to phthalimide substituent. It has been noticed that the directing influence of the phthalimide group towards hydroxylation was greater than the C-4 hydroxyl group.

Due to the low yield for dihydroxylation of (±)-**126**, the diacetate (±)-**127** was converted into tetraacetate (±)-**134** (Eq. 1). Compound (±)-**134** was shown to be the tetraacetate of **(**±)-**132** by NMR spectroscopy.



(±)-**127** (±)-**134** (1)

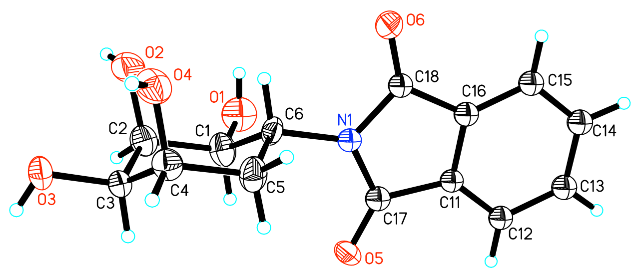
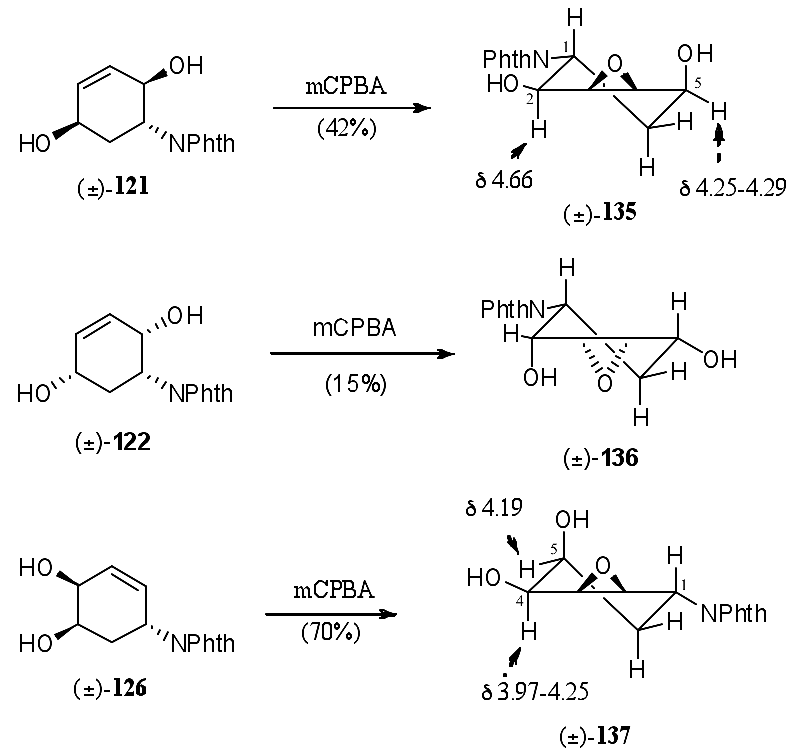


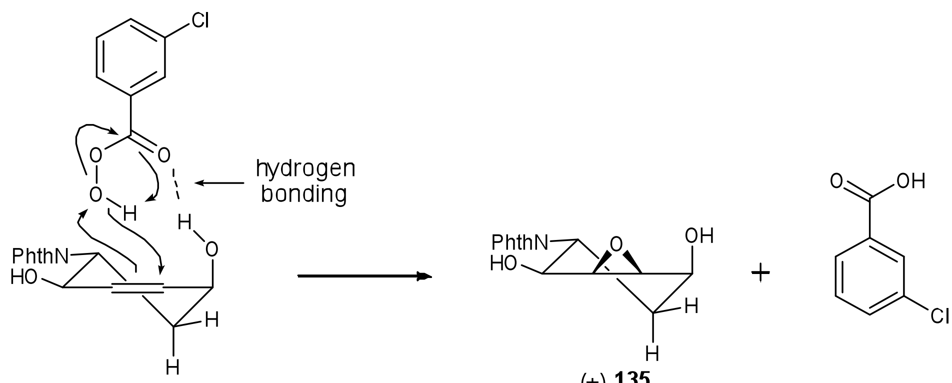
Figure 4. X-ray crystal structure of (±)-**132**.

Treatment of endiols (±)-**121**, (±)-**122** and (±)-**126** with mCPBA gave corresponding epoxides (±)-**135**, (±)-**136** and (±)-**137** (Scheme 36).



Scheme 36. Epoxidation of (±)-**121**, (±)-**122** and (±)-**126**.

The structure of epoxides (±)-**135** and (±)-**137** were assigned based on their single crystal X-ray diffraction analysis (Fig. 5 and Fig. 6). In both the crystsl structures, the cyclohexane ring is in the half chair form and the phthalimide group is pseudo equatorially oriented. Structure of (±)-**136** was assigned based on the comparison of its ^{1}H NMR spectrum with that of isomeric (±)-**135**. In all of these cases, epoxidation occurs on the same face of the olefin as the adjacent hydroxyl groups. The facial selectivity of epoxidation could be explained on the basis of hydrogen bonded association between the hydroxyl group of the endiol and the carbonyl group of the *m*-chloroperbenzoic acid (Scheme 37).[45] The relative low yield (15%) of (±)-**136** could be potentially explained on the basis of the steric hindrances due to the *syn* orientation of all the substituents, including the epoxide ring.



Scheme 37. Rational for the facial selectivity of epoxidation.

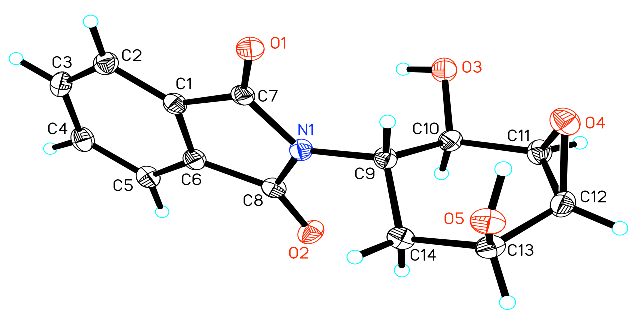


Figure 5. X-ray crystal structure of (±)-**135**.

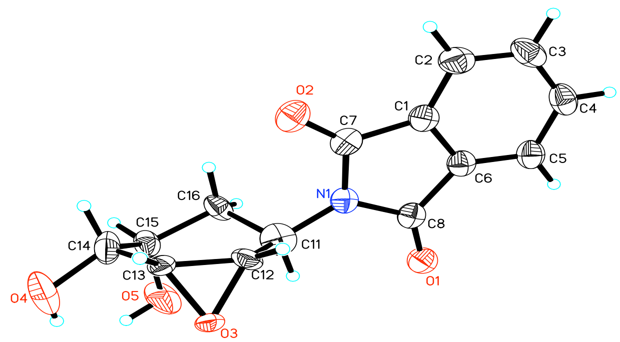
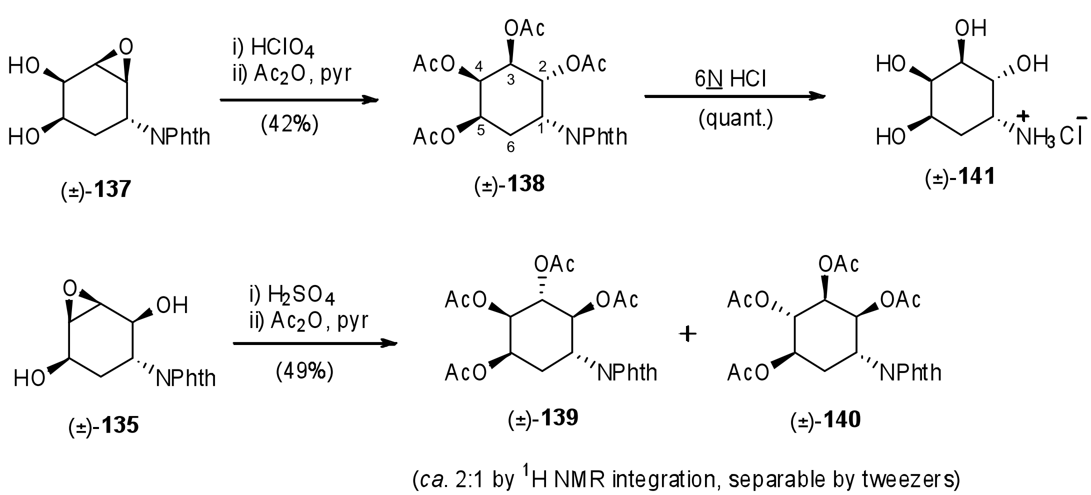


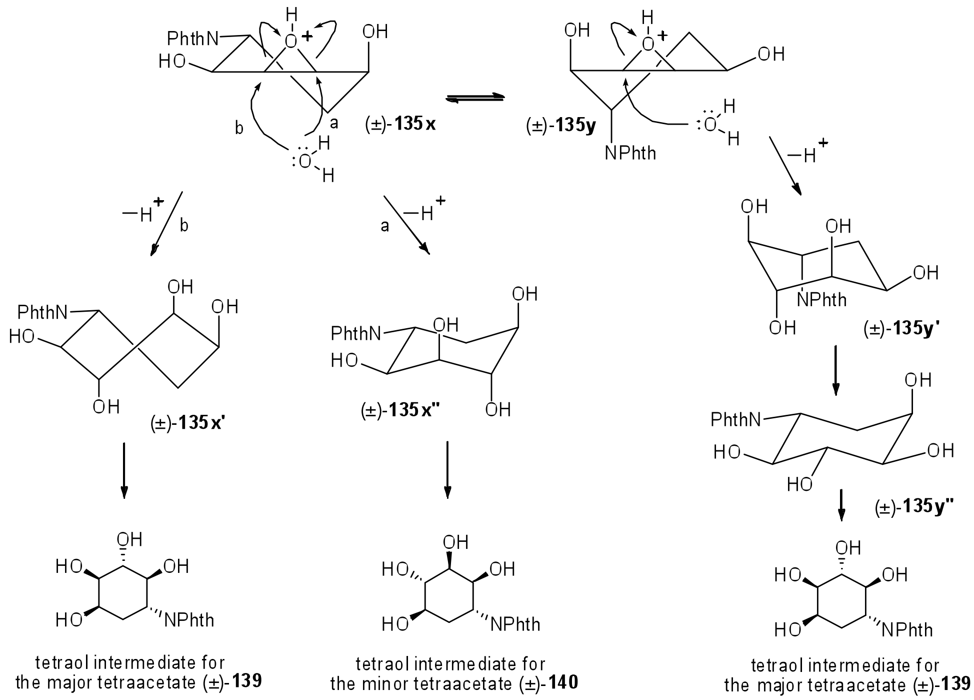
Figure 6. X-ray crystal structure of (±)-**137**.

Hydrolysis followed by acetylation of epoxides (±)-**135** and (±)-**137** required using different acid conditions for the hydrolysis steps as is shown in Scheme 38. Epoxide (±)-**137** gave a single tetraacetate (±)-**138**. On the contrary, epoxide (±)-**135** gave a mixture of two tetraacetates (±)-**139** and (±)-**140** (ca. 2:1 ratio by ^{1}H NMR integration). Slow recrystallization of the mixture (**139** and **140**) from ethyl acetate generated two distinct crystalline forms of the two tetraacetates, which allowed them to be separated by tweezers.



Scheme 38. Hydrolysis of epoxide (±)-**137** and (±)-**135**.

The structures of tetraacetates (±)-**139** and (±)-**140** were assigned based on their single crystal X-ray diffraction analysis (Fig. 7 and Fig. 8). The structure of (±)-**138** was assigned based on its ^{1}H NMR spectral data. For (±)-**138**, the *trans* relationship between the C-1 phthalimide and C-5 acetoxy group was assigned on the appearance and the coupling magnitude of H-6_{ax} (br t, J = 11.0 Hz). The two large couplings are due to the vicinal coupling to H-1_{ax} and geminal coupling to H-6_{eq}. The absence of the third large coupling is consistent with H-5 being equatorial (i.e. a small ax-eq coupling). Furthermore the appearance of H-1 (ddd, J = 3.3, 4.5, 11.1 Hz) indicates that the C-2 hydroxyl is axial/H-2 equatorial. The two smaller coupling are due to H-1_{ax}/H-6_{eq} and H-1_{ax}/H-2_{eq}. As anticipated, products **138** arise by a diaxial ring opening of the epoxide ring. On the contrary, the ring opening of epoxide (±)-**135** (Scheme 39), could be rationalized by considering two active conformers of (±)-**135.** Product (±)-**139** (the major tetraacetate) could arise either by the diaxial ring opening (path b) of the epoxide from conformer (±)-**135x,** *via* a twist boat-like transition state (±)-**135x'** or by diaxial ring opening of epoxide from conformer (±)-**135y**, *via* a chair-like transition state (±)-**135y'** followed by a chair-chair inversion. The rational for the formation of the minor tetraacetate (±)-**140** is also given in Scheme 39.



Scheme 39. Rational for epoxide hydrolysis.

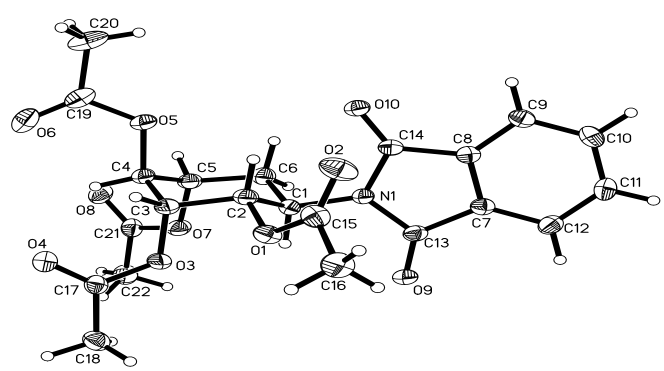


Figure 7. X-ray crystal structure of (±)-**140**.

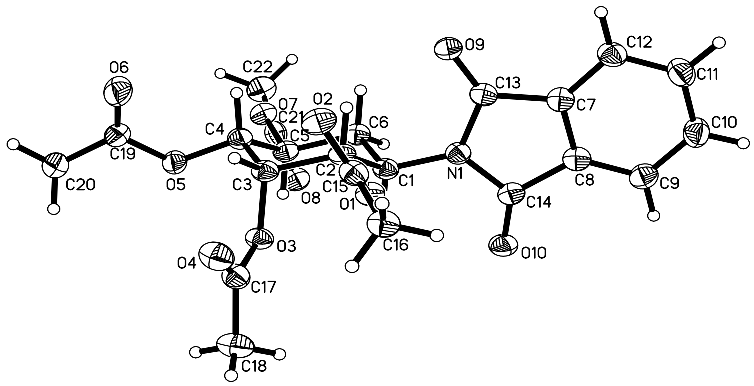
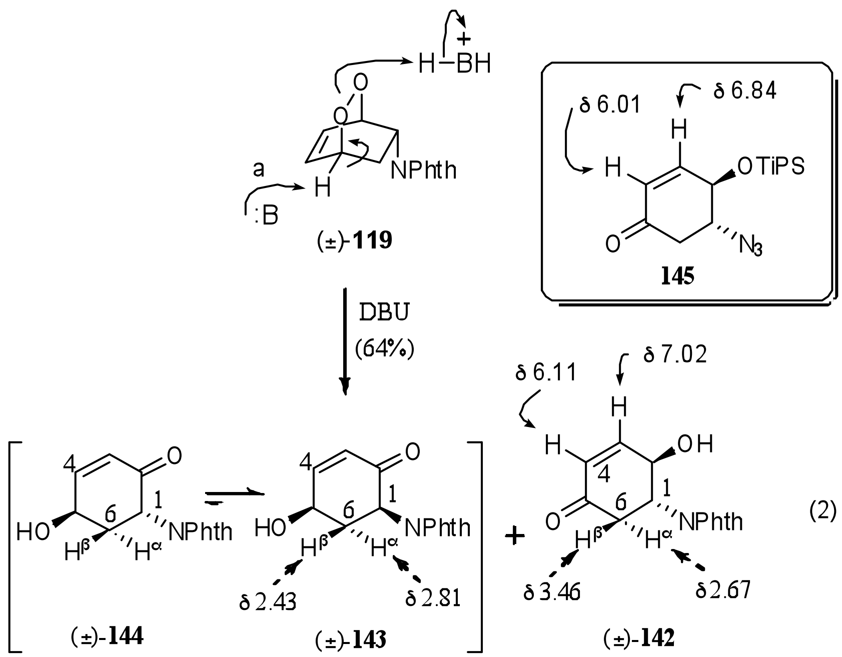


Figure 8. X-ray crystal structure of (±)-**139**.

Reaction of the major endoperoxide (±)-**119** with diazabicyclo[5.4.0]undecene (DBU) (Kornblum-DeLaMare rearrangement)[46] (Eq. 2) gave a mixture of (±)-**142**, (±)-**143** and (±)-**144**. Purification by column chromatography gave (±)-**142** as a pure compound and (±)-**143** and (±)-**144** as an inseparable mixture. The major cyclohexenone (±)-**142** arises due to the deprotonation of the sterically less hindered proton of (±)-**119** by DBU (pathway a). The structure of (±)-**142** was assigned by the comparison of its NMR spectral data with that of 5-azido-4-(triisopropylsolyloxy)-2-cyclohexene-1-one (**145**).[47] In particular, signals for (±)-**142** at δ 6.11 (d) and 7.02 (dd) ppm in the ^{1}H NMR spectrum and δ 129.6 and 152.3 ppm in the ^{13}C NMR spectrum are a close match for the corresponding olefinic protons and carbons of **145** which appear at δ 6.01 (d), 6.84 (dd), 129.1 and 150.5 ppm respectively. The two diastereotopic methylene protons 6-Hα (δ

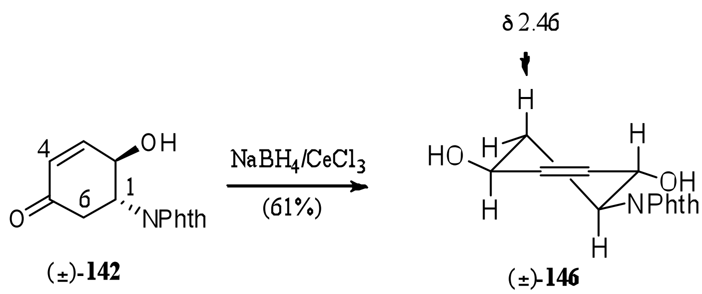
2.67 ppm, dd, J = 4.8 and 16.4 Hz) and 6-Hβ (δ 3.43 ppm, dd, J = 13.6 and 16.4 Hz) were assigned based on the magnitude of their geminal coupling.



(2)

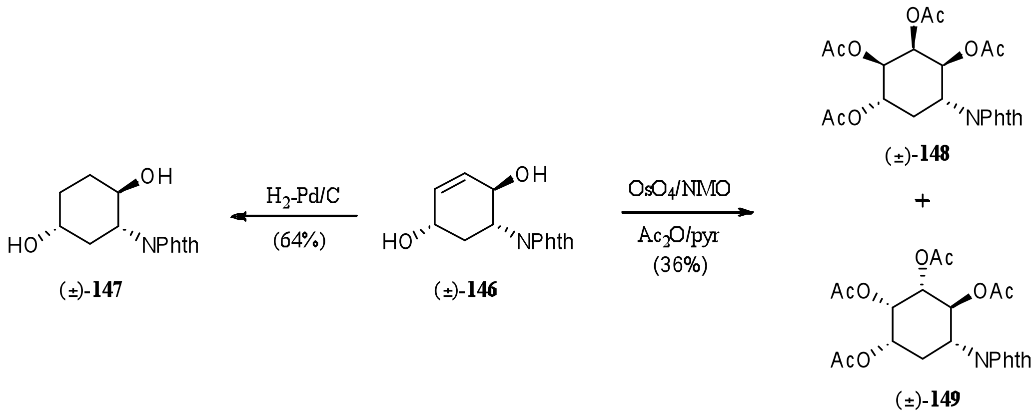
The structures of the other two cyclohexenones were also assigned based on their ^{1}H NMR spectral data. The magnitude of the coupling of H-6β (δ 2.81, td, J = 11.4, 14.4 Hz) in (±)-**143** indicates that the substituents at C-1/C-5 are *cis*. On the other hand, the presence of only a single large coupling (J = 13.2 Hz) for H-6β (δ 2.26) in (±)-**144** indicates that the C-1/C-5 substituents are *trans*. The stereoisomer (±)-**143** presumably is the result of base catalyzed epimerization of the proton α to the carbonyl of (±)-**144**; the diequatorial stereoisomer (±)-**143** being more stable than the axial-equatorial stereoisomer (±)-**144**.

Reduction of (±)-**142** under Luche conditions ($NaBH_4/CeCl_3$) [48] gave a single diol (±)-**146** (Eq. 3). The structure of the (±)-**146** was assigned based on its ^1H NMR spectral data. In particular, the signal for the 6-H_{ax} (δ 2.46 ppm, ddd, J = 10.0, 12.0, 13.2 Hz) was a doublet of doublet of doublets. These three large couplings are due to the diaxial relative orientations of 6-H_{ax} with respect to 1-H and 5-H as well as the geminal coupling to 6-H_{eq}. This also confirms that the substituents at C-1 and C-5 are *cis* to each other.



(3)

The double bond of the diol (±)-**146** was reduced catalytically using H_2-Pd/C (Scheme 38) to afford (±)-**147**; the structure was assigned based on the structure of its precursor. The catalytic dihydroxylation of (±)-**146** with OsO_4 and NMO followed by acetylation with acetic anhydride/pyridine (Scheme 40) gave an equimolar mixture of two tetraacetates (±)-**148** and (±)-**149**.[44] The structures of these two tetraacetates were assigned based on the ^1H NMR spectral data of the mixture. In particular, the 6-H_{ax} signals of each evidences three large couplings. Fortuitously, the structural assignment of (±)-**149** was confirmed from single crystal X-ray diffraction analysis of a crystal selected from a recrystallization of the mixture (Fig. 9).



Scheme 40. Catalytic hydrogenation/hydroxylation of (±)-**146**.

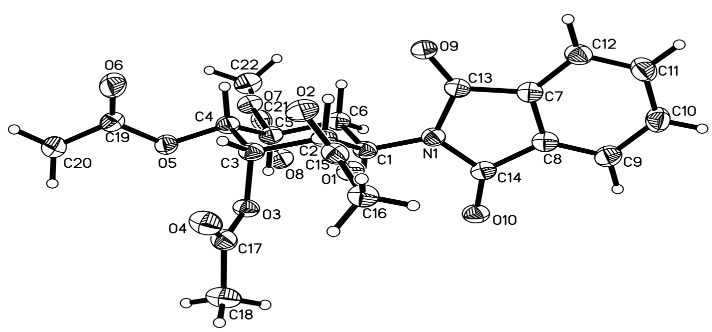
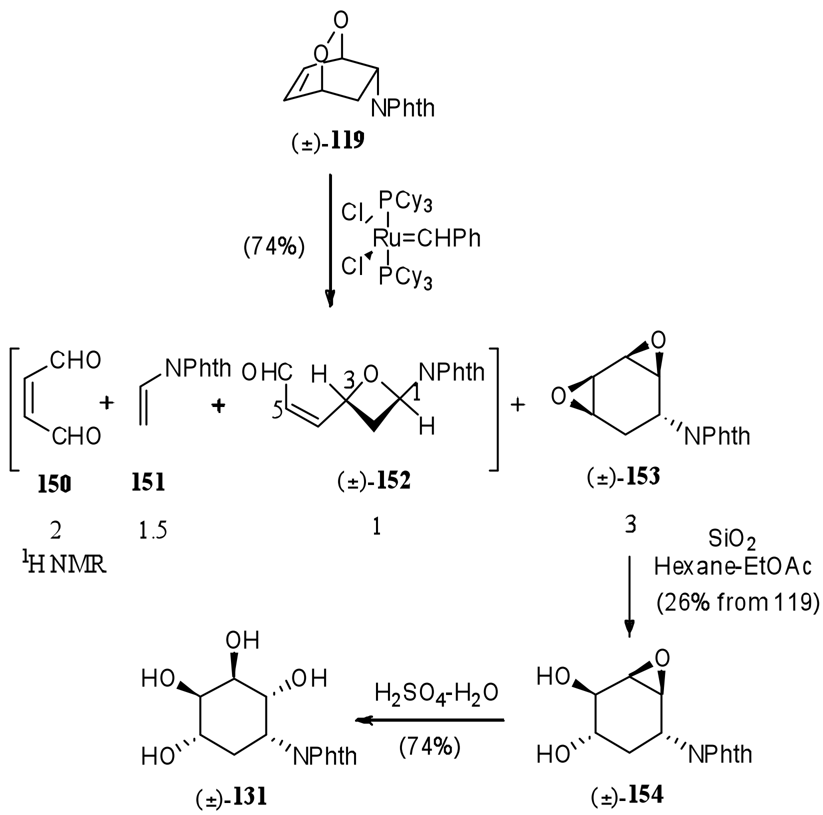


Figure 9. X-ray crystal structure of (±)-**149**.

Treatment of the major endoperoxide (±)-**119** with Grubbs 2nd generation catalyst[49] in absence of any external olefin led to the fragmentation of the endoperoxide into a mixture of **150**, **151**, (±)-**152** and (±)-**153** (Scheme 41). Chromatographic separation of the mixture gave **151**, (±)-**152** and (±)-**153** as pure fractions. The structure of **150** was assigned based on comparison of the ^{1}H NMR spectral data of the crude to the literature data.[50] *N*-vinylphthalimide **151** was identified by comparison of its literature mp and ^{1}H NMR spectral data with literature values.[51] The structure of (±)-**153** was assigned based on its ^{1}H NMR spectral data. In particular, the four relatively narrow one-proton signals at δ 3.26, 3.30, 3.54-3.56 and 3.58-3.60 ppm corresponds to the four epoxide methine protons; these signals are similar to those of other cyclohexene diepoxides.[52] The structural assignment of the oxetane (±)-**152** was also based on its ^{1}H NMR spectral data. In particular, signals at δ 10.15 (d, *J* = 7.2 Hz), 6.88 (ddd, 0.8, 6.8, and 11.5) and 6.07 (dd, *J* = 7.2 and 11.6 Hz) were indicative of the presence of the 3-oxo-1-Z-butenyl sidechain. The signals at 6.33 (q, *J* = 7.2 Hz) and 6.40 (ddd, J = 1.2, 5.0, and 8.3 Hz) correspond to 3-H and 1-H, and are similar to those of a 2,4-*trans* substituted oxetone ring.[53]



Scheme 41. Reaction of (±)-**119** with Grubbs 2nd generation catalyst.

The hydrolysis of the bisepoxide (±)-**153** in an unusual fashion on column (SiO_2-H_2O/EtOAc) gave the epoxydiol (±)-**154**. The structure was assigned based on its single crystal X-ray diffraction analysis (Fig. 10). The ^{1}H NMR spectral data of (±)-**154** were consistent with the structure. Further hydrolysis of (±)-**154** using H_2O-H_2SO_4 gave a single tetraol (±)-**131**. The structure (±)-**131** was identified by comparison of its spectral data with the sample prepared by dihydroxylation of (±)-**122**.

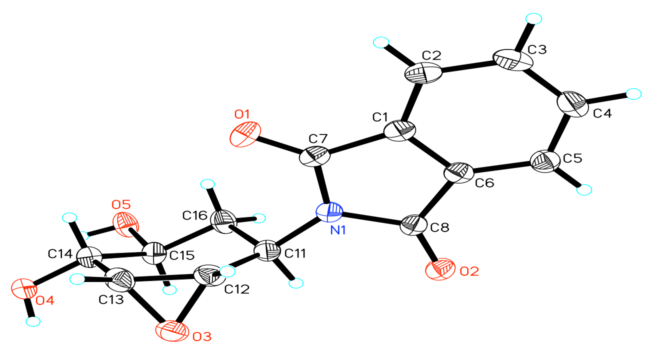
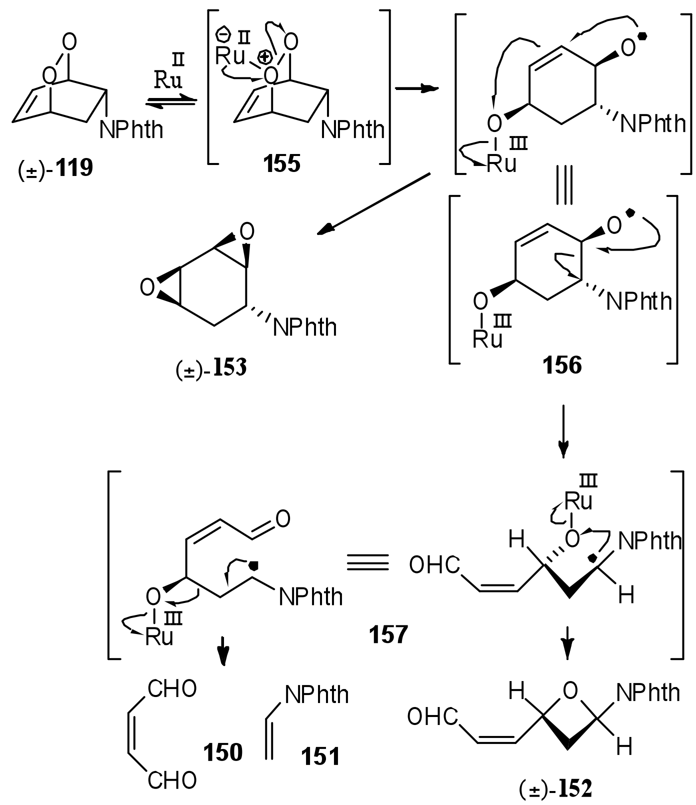


Figure 10. X-ray crystal structure of (±)-**154.**

The transition metal-mediated fragmentation of 1,4-epiperoxides (endoperoxides), including the use of Ru(II) reagents, has been reported.[54] An inner-sphere radical mechanism can be proposed to explain the formation of the products. Coordination of coordinatively unsaturated Ru(II) with the sterically less hindered oxygen of the endoperoxide (±)-**119** followed by a single electron exchange leads to the breaking of weak O-O bond and generating an oxyradical **156**. Interaction of oxyradical with the internal double bond gave the bisepoxide (±)-**153**. Alternatively, the oxyradical rearranges into a more stable nitrogen stabilized radical species **157** through a homolytic C-C bond breaking. Reaction of the carbon radical at oxygen gave the oxetane (±)-**152** and further homolytic C-C bond cleavage of **157** gave **150** and **151**. A similar mechanistic explanation was reported for the formation of β-lactones from the keto endoperoxide of phenol.[55]

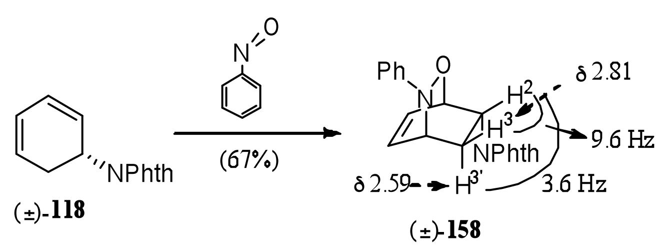


Scheme 42. Proposed mechanistic explanation for the formation of four different products upon treatment of (±)-**119** with Grubbs 2nd generation catalyst.

In conclusion, we were able to synthesize a number of stereochemically diverse polyhydroxyl aminocyclohexanes derivatives and some of their amine salts from a single precursor (±)-**118**.

II B. Synthesis of *trans*-1,3-Diaminocyclohexanes from Cyclohexadiene

In an attempt to synthesis structurally diverse 1,3-diaminocyclohexane, the cycloaddition reaction of (±)-**118** with nitrosobenzene was studied (Eq. 4).[56]



(4)

The cycloaddition was regio as well as diastereoselective and gave a single isomer 8-aza-7-oxabicyclo[2.2.2]oct-5-ene (±)-**158**. The structure of (±)-**158** was assigned based on its ^{1}H NMR spectral data. The assignment of the two diastereotopic methylene protons [H^3 (δ 2.81) and $H^{3'}$ (δ 2.59)] was done based on the magnitude of their vicinal coupling with H^2, the *syn*-coupling 9.6 Hz (ca. 0^0 dihedral angle) is larger than the *anti*-coupling 3.6 Hz (ca. 120^0 dihedral angle). The upfield shift of $H^{3'}$ (δ 2.59) compared to that of H^3 (δ 2.81) was due to the anisotopic effect of the olefin functionality on $H^{3'}$. The assignment was confirmed from its single crystal X-ray diffraction analysis (Fig. 11).

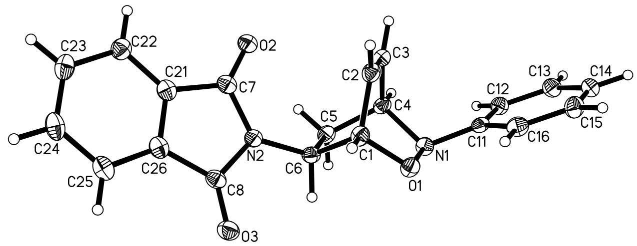
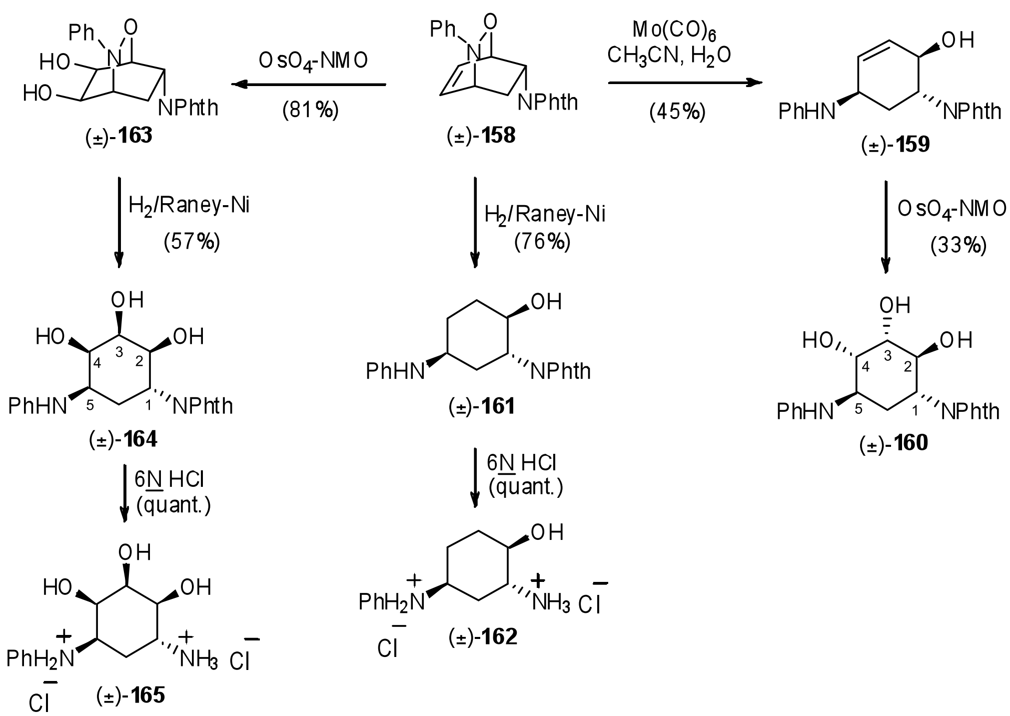


Figure 11. X-ray crystal structure of (±)-**158**.

To achieve the goal of synthesizing stereochemically diverse 1,3-diaminocyclohexanes, several reactions were studied with the nitroso adduct (±)-**158**, the results are shown in Scheme 43.



Scheme 43. Reactions of nitroso adduct (±)-**158**.

The N-O bond of (±)-**158** was selectively reduced by heating at reflux with $Mo(CO)_6$ in CH_3CN for one hour (Scheme 43).[57] The structure of (±)-**159** was assigned based on its ^1H NMR spectral data. In particular, signals at δ 4.39 and δ 4.84 (downfield compare to its precursor) are consistent with the N-O bond cleavage. This structural assignment was further confirmed by derivatization. Catalytic dihydroxylation of the olefin (±)-**159** by OsO_4/*N*-methylmorpholine *N*-oxide gave the triol (±)-**160**. Dihydroxylation occurred on the face of the olefin opposite to the C-2 hydroxyl. The *anti*- orientation of C-2 and C-3 hydroxyl groups was confirmed based on the magnitude of the coupling (J = 9.6 Hz) between 2-H_{ax} and 3-H_{ax}.

The olefinic double bond and the N-O bond of (±)-**158** were catalytically reduced in a single step by H_2/Raney-Ni (Scheme 43). The structure of (±)-**161** was assigned based on its ^1H NMR spectral data and subsequently confirmed from its single crystal X-ray diffraction analysis (Fig. 12).

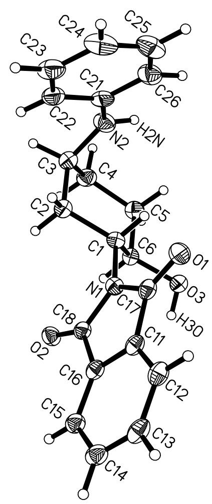
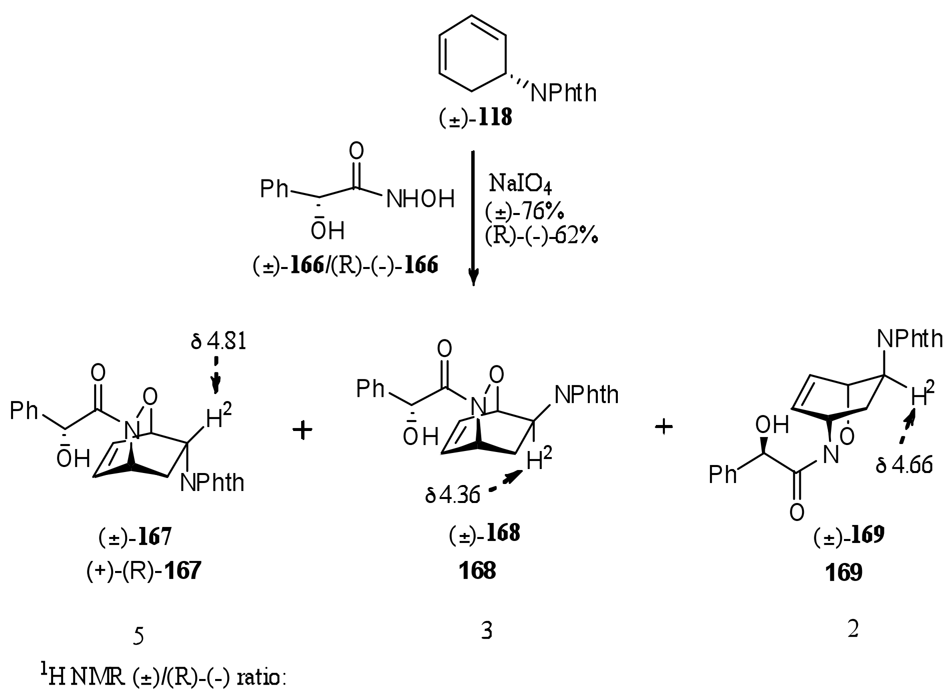


Figure 12. X-ray crystal structure of (±)-**161**.

Catalytic dihydroxylation of (±)-**158** by OsO_4 in presence of *N*-methylmorpholine *N*-oxide gave a single diol (±)-**163** (Scheme 43). The dihydroxylation was anticipated to occur on the face of the olefin opposite to the sterically bulky phthalimide group. This relative stereochemistry was further confirmed by derivatization of (±)-**163**. The N-O bond of (±)-**163** was successfully cleaved using H_2 (40 psi)/Raney-Ni. The relative stereochemistry of (±)-**164** was assigned based on its ^{1}H NMR spectral data, which also confirmed the structural assignment of (±)-**163**. The different splitting pattern and the magnitude of coupling of the two diastereotopic methylene protons 6-H_{ax} (dt, J = 3.2, 13.2 Hz) and 6-H_{eq} (td, J = 3.8, 13.2 Hz) indicates that the C-1 phthalimide and C-5 phenylamino substituents are *trans*. The small coupling between 2-H_{ax} (δ 4.34, dd, J = 2.6, 10.8 Hz) and 3-H_{eq} (δ 4.21, t, J = 2.6 Hz) is consistent with an axial-equatorial relationship between these two protons and thus indicates that the C-2 and C-3 hydroxyl groups are *cis* to each other. Compounds (±)-**161** and (±)-**164** were converted to their respective amine salts (±)-**162** and (±)-**165** by treatment by 6N HCl.

To explore the preparation of optically active 1,3-diaminocyclohexanes, the cycloaddition reaction of (±)-**118** with chiral acylnitroso compounds were studied (Scheme 44).[58]



Scheme 44. Cycloaddition of (±)-**118** with acylnitroso compounds.

Racemic and optically active mandelohydroxamic acid, (±)-**166** and (-)-R-**166** was prepared from corresponding racemic and optically active methyl mandelate following literature procedure.[58] In the case of racemic mandelohydroxamic acid (±)-**166**, cycloaddition of the *in situ* generated acylnitroso intermediate with (±)-**118** gave a chromatographically inseparable mixture of diastereomers (±)-**167**, (±)-**168** and (±)-**169** (*ca*. 5:3:2 from ^{1}H NMR integration). Fractional crystallization from CH_3CN gave (±)-**167** as a pure compound (25%, isolated yield). The structural assignment of (±)-**167** was based on its ^{1}H NMR spectral data and was confirmed by single crystal X-ray diffraction analysis (Fig. 13). Similarly, structural assignments for (±)-**168** and (±)-**169** were based on the ^{1}H NMR spectral data of the mixture. The upfield chemical shift of H^2 of (±)-**168** (δ 4.36 ppm), relative to that of H^2 of (±)-**167** or (±)-**169** (δ 4.81 or 4.68 ppm respectively) was due to the anisotopic effect of the olefin functionality.

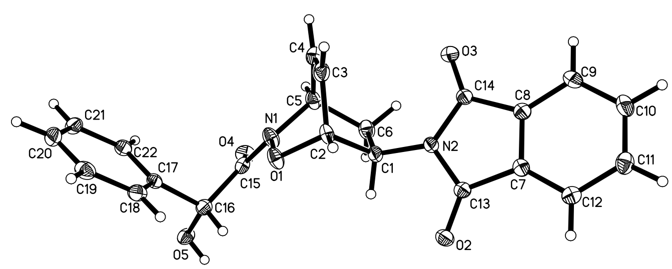
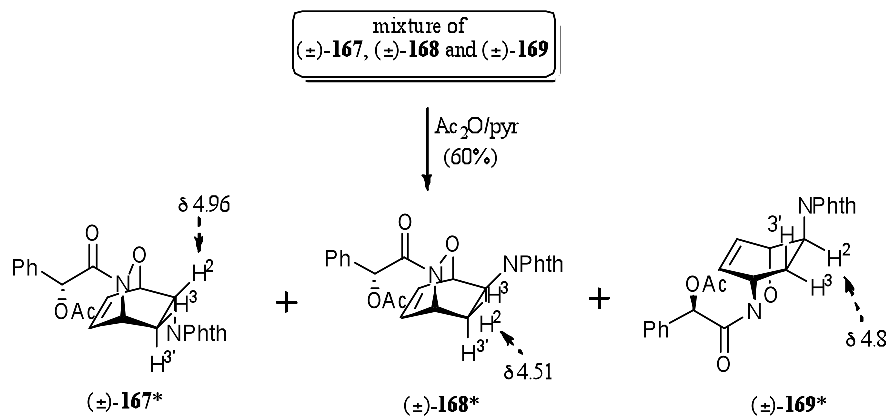


Figure 13. X-ray crystal structure of (±)-**168**.

In a similar fashion optically active mandelohydroxamic acid (-)-**166** gave a chromatographically inseparable optically active mixture of diastereomeric (+)-**167**, **168** and **169** (*ca*.5:3:2 from ^{1}H NMR integration). Pure (+)-**167** (11%, isolated yield) was isolated by fractional crystallization from CH_3CN and as expected the ^{1}H and ^{13}C NMR spectral data of (+)-**167** was identical with the racemic compound (±)-**167**.

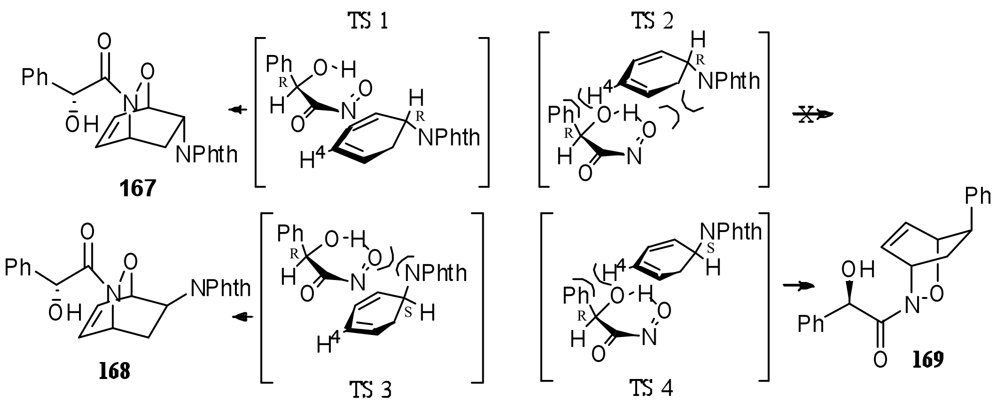
In an effort to purify more isomers, the mixture of racemic compounds (±)-**167**, (±)-**168** and (±)-**169** was acetylated using acetic anhydride and pyridine (Eq. 5). Pure (±)-

168* (19%, isolated yield) was separated by preparative TLC from the mixture of (±)-**167***, (±)-**168*** and (±)-**169***. The chemical shifts for the signals of the 8-aza-7-oxo-bicyclo[2.2.2]octane core of acetates (±)-**167*** and (±)-**169*** were relatively similar to those for the alcohols (±)-**167** and (±)-**169.**



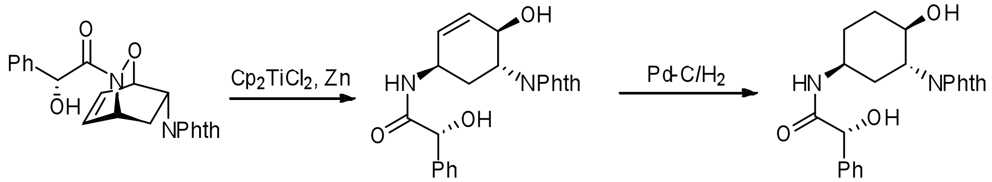
(5)

The diastereoselectivity for the cycloaddition (Scheme 44) could be rationalized on the basis of the energy of the transition states leading to the products. It has been proposed that the six-membered cyclic hydrogen bonded conformer of the nitrosoacyl dienophile derived from the mandelohydroxamic acid is the active form of the dienophile in the cycloaddition reaction with the diene.[58a] Keeping this proposal in consideration, different transition states can be drawn (Scheme 45). In TS 1, i.e. the approach of (R)-nitroso dienophile on the *exo*-face of the (R)-**118** does not have any major steric repulsion, leading to the major product **167**. On the other hand, approach of (R)-nitroso dienophile on the *endo*-face of the (R)-**118** (TS 2) has major steric repulsion between 4-H and the phenyl substituent and nitroso oxygen and the phthalimide substituent leading to no cycloaddition. In comparison, approach of (R)-nitroso dienophile on the exo-face of the (S)-**118** (TS 3) and endo-face of (S)-**118** (TS 4) has minor steric repulsion or equally matched in energy leading to the products **168** and **169** respectively.



Scheme 45. Proposed transition state explanation for the selectivity of cycloaddition of acylnitroso reagents with (±)-**118**.

The "N-O" bond of the racemic (±)-**167** and optically active (+)-**167** was reduced using titanocene (III) chloride (Scheme 46).[59] The structures of the products (±)-**170** and (-)-**170** were assigned based on the comparison of their ^{1}H NMR spectral data with that of previously prepared (±)-**159**. The "C=C" bonds of the (±)-**170** and (-)-**170** was catalytically reduced by H_2-Pd/C. The structures of (±)-**171** and (-)-**171** were assigned based on the comparison of their ^{1}H NMR spectral data with that of their precursors.



(±)-**167** (±)-**170** (66%) (±)-**171** (76%)

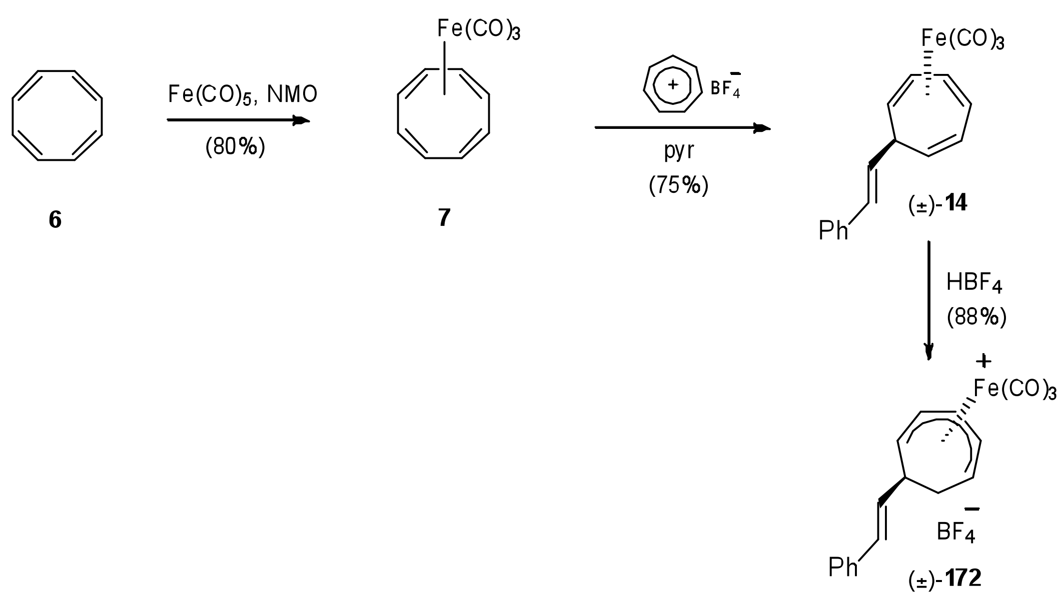
(+)-**167** (-)-**170** (53%) (-)-**171** (80%)

Scheme 46. Selective reduction of “N-O” bond of (±)-**167** and (-)-**167.**

Chapter III

III A. Synthesis of Tricarbonyl(η^5-6-styrylcyclohepta-2,4-dien-1-yl)iron(+1) from Cyclooctatetraene and its Reactivity study

The synthesis of tricarbonyl(η^5-6-styrylcyclohepta-2,4-dien-1-yl)iron(+1) tetrafluoroborate (±)-**172** from cyclooctatetraene **(6)** was first reported by Woodward, *et al.,* in 1984.[60] Despite the structural diversity represented by this transformation an examination of the reactivity of (±)-**14** and its application in organic synthesis is not known. To study the reactivity of tricarbonyl(η^5-6-styrylcyclohepta-2,4-dien-1-yl)iron(+1) cation, it was synthesized in three steps from cyclooctatetraene following the literature procedure. (Scheme 47).[18,60]



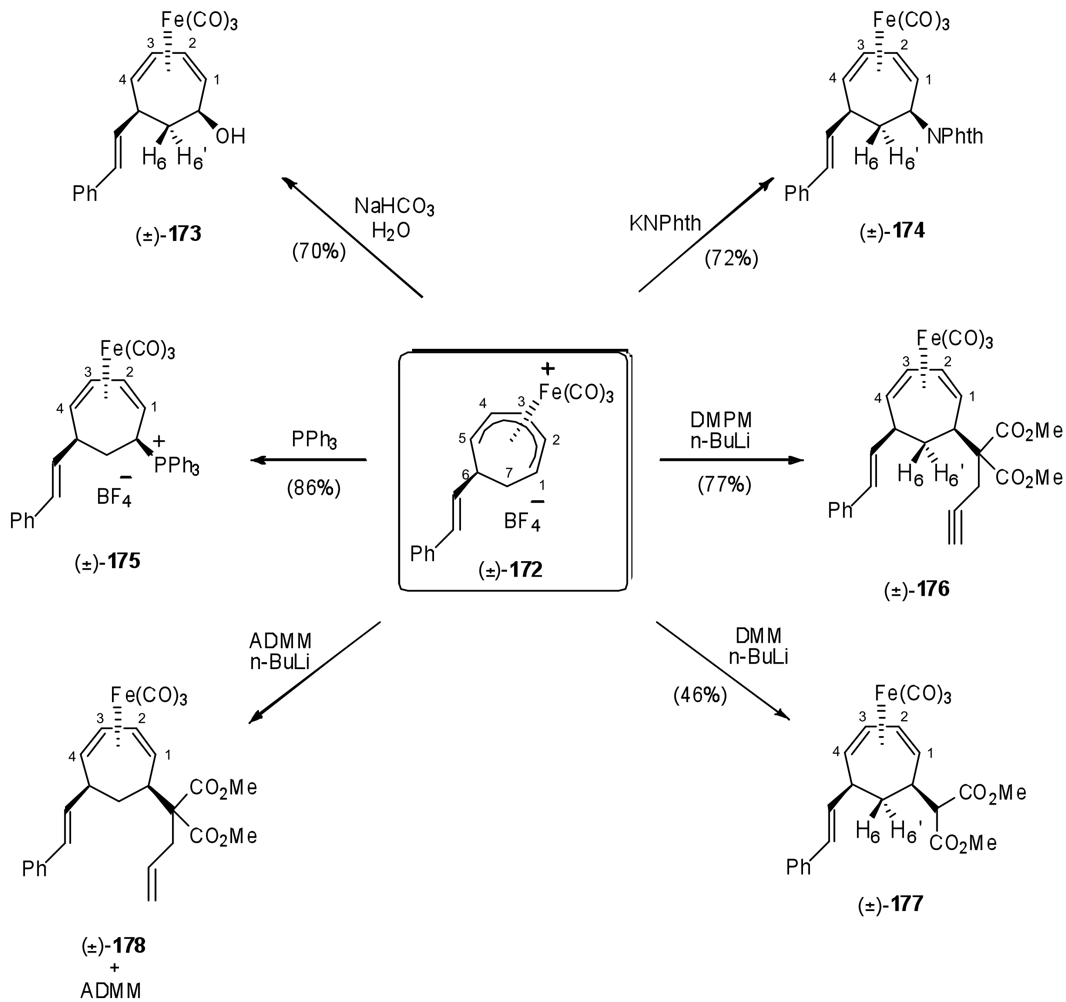
Scheme 47. Synthesis of cation (±)-**172** from cyclooctatetraene **6**.

The complexation of cyclooctatetraene with iron(pentacarbonyl) (Scheme 47) in the presence of trimethylamine *N*-oxide gave **7**. Compound **7** was characterized based on its ^{1}H and ^{13}C NMR spectral data. A single peak at 5.25 ppm in ^{1}H NMR and two peaks at 212.5 and 100.1 ppm in ^{13}C NMR indicated the fluxional nature of **7** on the NMR time scale at ambient temperature and was consistent with the literature.[61]

Compound (±)-**14** was prepared by the reaction of tricarbonyl(cyclooctatetraene)iron **7** with tropylium tetrafluoroborate in the presence of pyridine following literature procedure.[60] A slight modification in the literature procedure using one equivalent of pyridine and repeated extraction of the reaction mixture resulted in an improvement from 41% to 75% yield. The structure was assigned based on comparison of its ^{1}H and ^{13}C NMR spectral data with the literature[60] values.

Protonation of the **14** by fluoroboric acid followed by precipitation from co-solvent ether gave the cation (±)-**172**. The cation was characterized by the comparison of its ^{1}H and ^{13}C spectral data with the literature values.[60]

The reactivity of (±)-**172** with various heteroatom and stabilized carbon based nucleophiles was studied and the results are shown in the Scheme 48.



Scheme 48. Reactivity of cation (±)-**172** with various nucleophiles**.**

In all the above cases nucleophilic attack at the less hindered dienyl terminus (C-1) of the cation was observed. Nucleophilic attack occurs *exo* to the tricarbonyliron moiety. Evidence in support of exo-attack (i.e. 5,7-*cis*-disubstituted cycloheptadiene) was present in the NMR spectra of (±)-**173** (±)-**176** and (±)-**177**. In particular, two signals at ca. δ 87-91 ppm in their ^{13}C NMR spectra and multiplets integrating to two protons at ca. δ 4.9-5.6 ppm in their ^{1}H NMR spectra are consistent with the two internal carbons (C-2/C-3) and their attached protons. In addition, an apparent quartet at ca. 0.9-2.0 ppm (J =

ca. 12 Hz) in the ^{1}H NMR spectra for (±)-**173** (±)-**174** (±)-**176** and (±)-**177** was assigned to H-6. The three large couplings are due to diaxial vicinal coupling of H-6 with H-5 and H-7 and a geminal coupling to H-6' (Fig. 14).

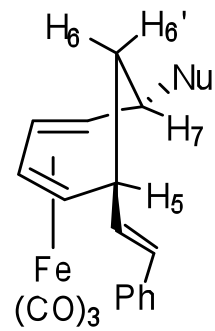
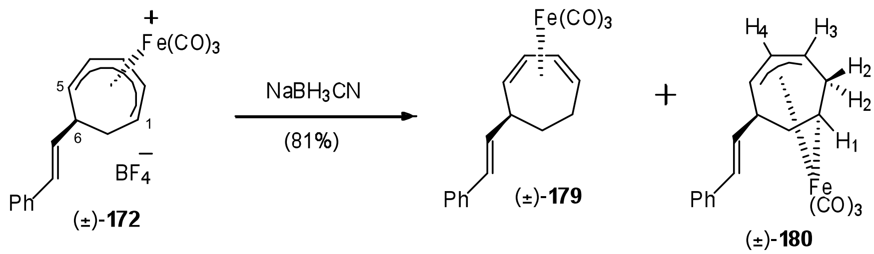


Figure 14. Generic structure of (±)-**173**, (±)-**174**, (±)-**176** and (±)-**177.**

For the reaction of (±)-**172** with the anion from dimethyl allylmalonate, the product was isolated as an inseparable mixture of (±)-**178** and unreacted dimethyl allylmalonate. The stereochemistry of (±)-**174**, (±)-**176**, and (±)-**178** are eventually corroborated by decomplexation.

The reaction of cation (±)-**172** with sodium cyanoborohydride gave an inseparable mixture of (±)-**179** and (±)-**180** in a nearly equimolar ratio (Eq. 6).

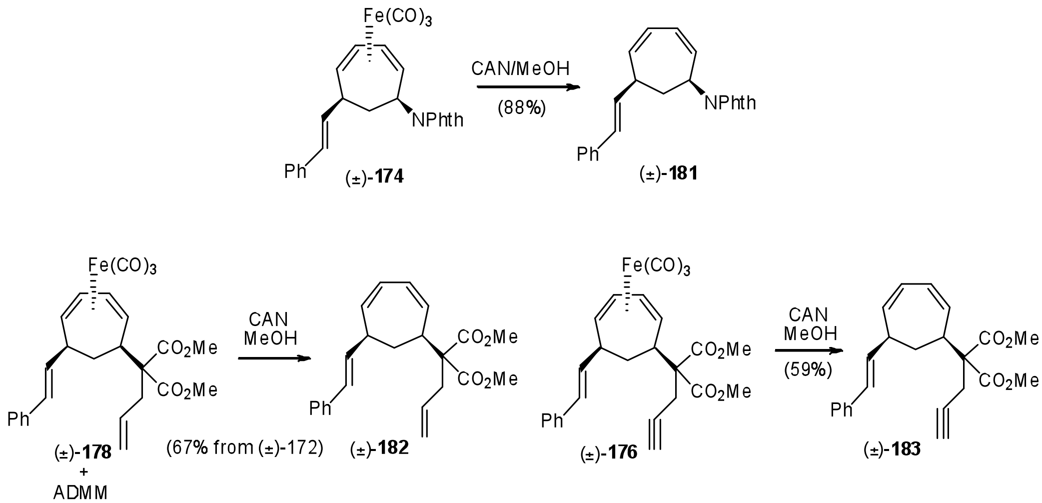


(6)

Diene complex (±)-**179** was formed by hydride attack at the less sterically hindered dienyl terminus (C-1). The structure of diene complex (±)-**179** was clearly identified as non-symmetrical by the presence of two signals at δ 87.1 and 89.0 ppm in the ^{13}C NMR spectrum. The structure of cycloheptene-1,5-diyl complex (±)-**180** was assigned on the basis of its NMR spectral data. In particular, the signal at δ 97.2 ppm in the ^{13}C NMR spectrum and the triplet at δ 4.97 ppm in the ^{1}H NMR spectrum were assigned to the central allyl carbon (C-4) and its attached proton. One of the overlapping signals at δ 4.38-4.49 ppm which appears as a quartet, was assigned to H-3. The nearly equivalent couplings (ca. J = 8.4 Hz) are due to vicinal couplings to H-4 and H-2 and H-2'.

III B. Decomplexation of Iron Coordinated Compounds

Successful decomplexation reactions of iron coordinated compounds (±)-**174**, (±)-**176** and (±)-**178** are shown in Scheme 49.



Scheme 49. Decomplexation of iron coordinated cyclic dienes.

The structures of the products (±)-**181**, (±)-**182** and (±)-**183** were assigned based on their NMR spectral data. In particular, signals in the range of 5.5-6.0 ppm which integrated to four protons correspond to the olefinic protons of conjugated diene portion of the molecule. The structural assignment of (±)-**181** was further confirmed from its single crystal X-ray diffraction analysis (Fig. 15).

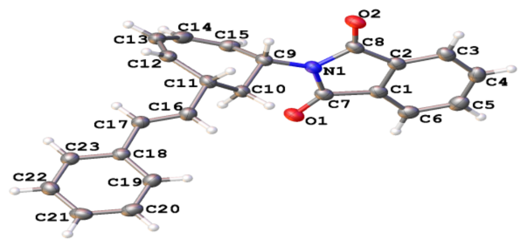
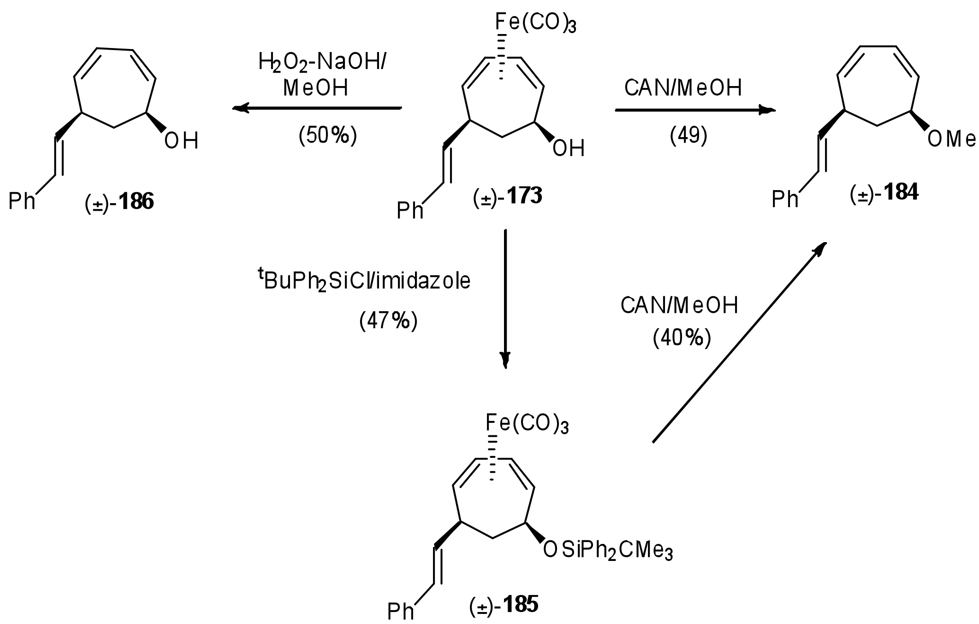


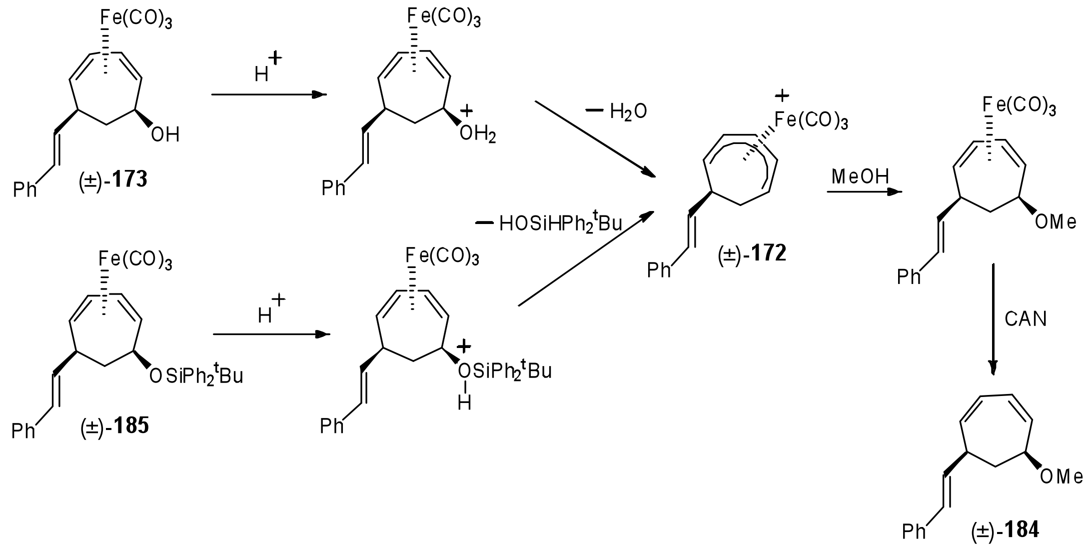
Figure 15. X-ray crystal structure of (±)-**181**.

Removal of iron from the cycloheptadienol complex (±)-**173** was attempted using a variety of oxidizing agent/solvent conditions and the results are shown in Scheme 50. Use of ceric ammonium nitrate (CAN) in methanol gave the methyl ether (±)-**184**. Protection of cycloheptadienol complex (±)-**173** as its silyl ether gave (±)-**185**. Attempted decomplexation of (±)-**185** likewise gave the methyl ether (±)-**184**. Since we speculated that the methoxy group present in (±)-**184** came from the solvent, decomplexation of (±)-**173** with CAN in either DMF or CH_3CN was attempted. In each case, starting material and a complex mixture of unidentified pruducts were obtained. Similarly attempted decomplexation of (±)-**173** with trimethylamine *N*-oxide gave a complex mixture of unidentified products. Finally decomplexation of (±)-**173** with alkaline hydrogen peroxide afforded the desire cycloheptadienol (±)-**186**.



Scheme 50. Decomplexation of (±)-**173**.

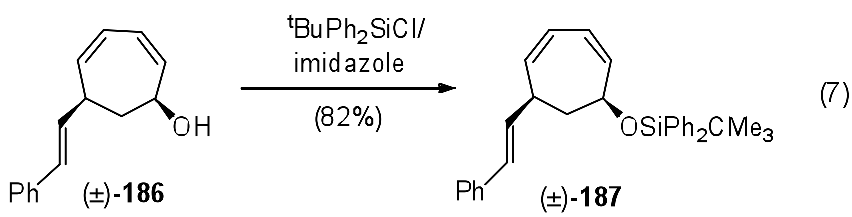
The formation of methyl ether (±)-**184** from alcohol (±)-**173** or silyl ether (±)-**185** was rationalized on the basis of an S_N1-like substitution from the solvent methanol (Scheme 51). As the oxidation reaction proceeds with CAN, the solution becomes acidic. Protonation of the hydroxyl of (±)-**173** or the silyl ether of (±)-**185**, followed by ionization regenerates the cycloheptadienyl cation (±)-**172**. Reaction of the cation thus formed with solvent gives the methyl ether complex which upon decomplexation gives (±)-**184** (Scheme 51).



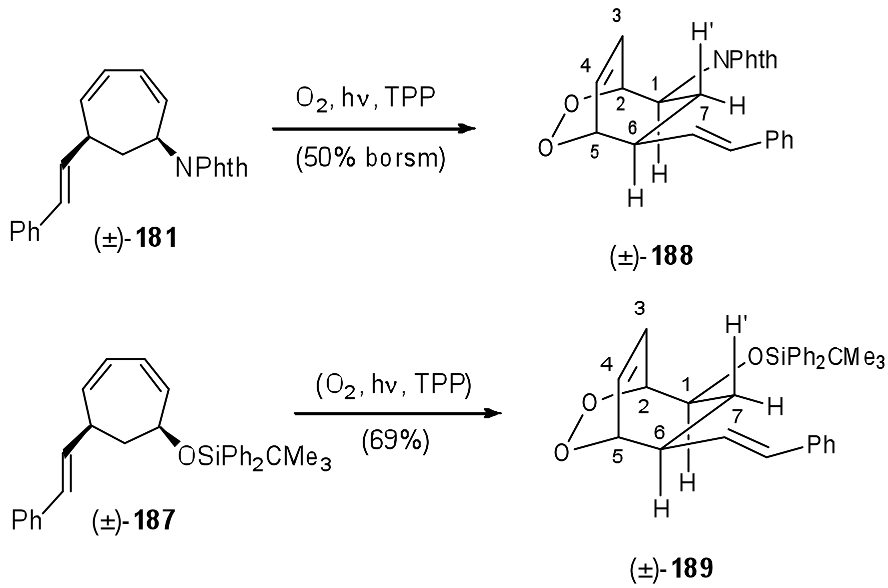
Scheme 51. Mechanistic rational for the formation of (±)-**184** upon decomplexation of (±)-**173** or (±)-**185** with CAN/MeOH.

III C. Singlet oxygen cycloaddition of iron free ligands

To study singlet oxygen cycloaddition reactions of some iron free ligands, compound (±)-**187** was prepared from (±)-**176** (Eq. 7)**.**



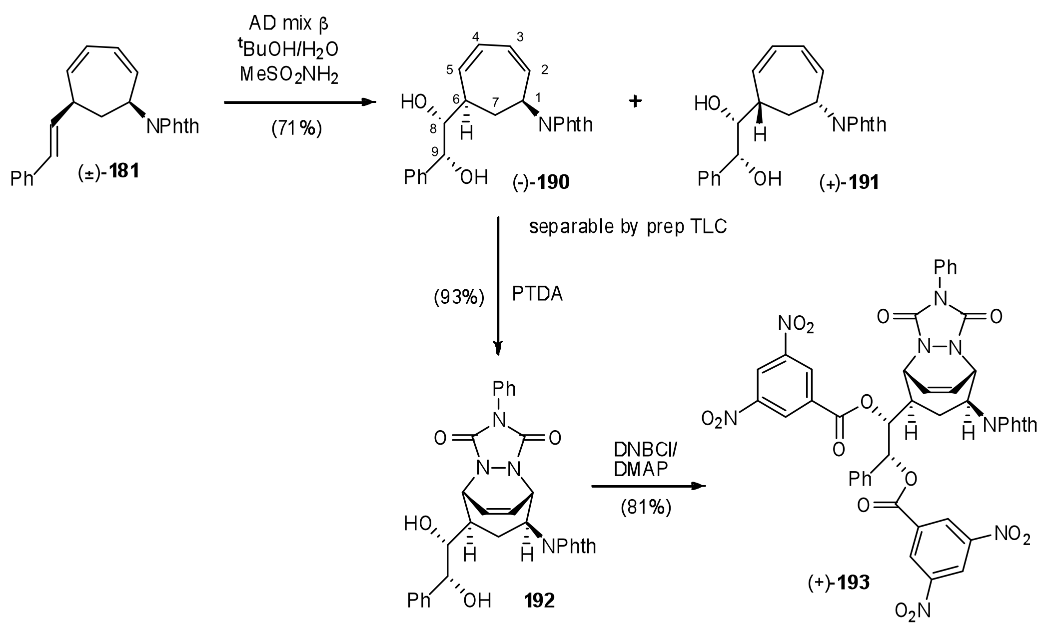
Exposure of the iron free ligand (±)-**181** or (±)-**187** to singlet oxygen cycloaddition condition generated a single endoperoxide (±)-**188** or (±)-**189** respectively (Scheme 52).



Scheme 52. Cycloaddition of (±)-**181** and (±)-**187** with singlet oxygen.

Structural assignment of endoperoxides (±)-**188** and (±)-**189** were based on their ^{1}H NMR spectral data. Cycloaddition occurs on the diene face opposite to *syn*- C-1/C-6 substituents. Similar facial selectivity was also observed by Pearson, *et al.*,[62] , Seitz, *et al.*,[63] and others for substituted cycloheptadiene systems. In particular, peaks at δ 4.53 (narrow m, 2H) for (±)-**189** and at δ 4.79 (m, 2H) for (±)-**188** corresponds to H-2 and H-5 protons. Upfield shifts of H-7' protons compare to H-7 in both (±)-**188** and (±)-**189** was due to the anisotopic effect of olefin functionality on H7'.

To resolve the racemic cycloheptadienes, asymmetric dihydroxylation of (±)-**181** with commercially available AD-mix β was studied (Scheme 53). Dihydroxylation occurs on the *trans* styryl double bond and gave a mixture of two diastereomeric diols (-)-**190** and (+)-**191**; the mixture was separable by preparative thin layer chromatography. The absolute configuration of the diol chiral centers of (-)-**190** and (+)-**191** were assigned based on the Sharpless mnemonic device.[64] Cycloaddition of less polar cycloheptadiene diastereomer (-)-**190**, with *N*-phenyl-1,3,5-triaza-2,4-dione (PTAD), followed by reaction with 3,5-dinitrobenzoyl chloride gave (+)-**193**. The relative stereochemistry of all chiral centers of (+)-**193** were assigned based on its single crystal X-ray diffraction analysis (Fig. 16), which also allowed assignment of the C-1 and C-6 stereocenters configurations of (-)-**190** and (+)-**191** as indicated.



Scheme 53. Resolution of (±)-**181** by asymmetric dihydroxylation.

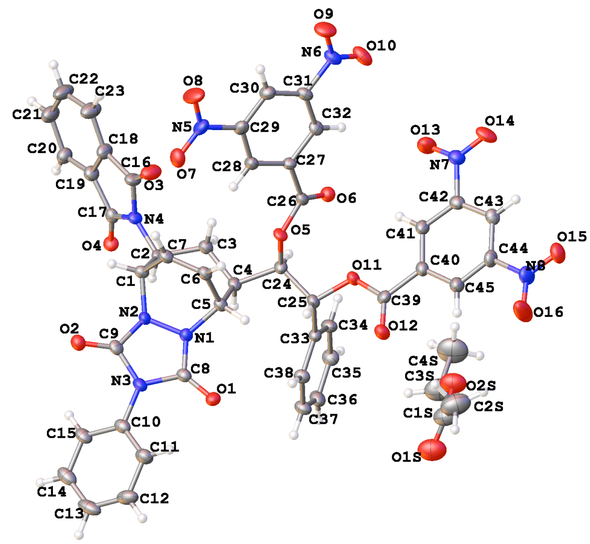
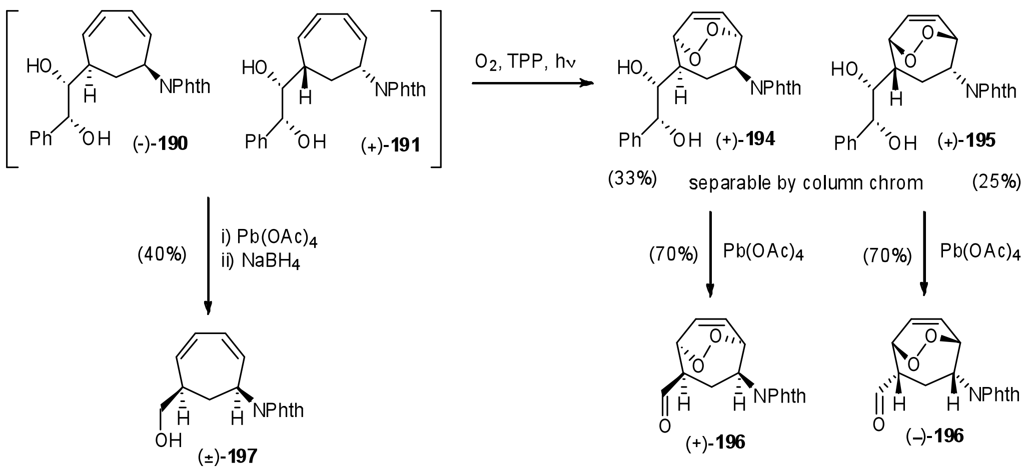


Figure 16. X-ray crystal structure (+)-**193**.

Due to difficulties in large scale chromatographic separation of the mixture of two diastereomeric diols (-)-**190** and (+)-**191**, the mixture was exposed to the singlet oxygen cycloaddition conditions (Scheme 54) which gave a mixture of two chromatographically separable diastereomeric endoperoxides (+)-**194** and (+)-**195**. Notably the optical rotation attributed to of the (1’,2’-dihydroxyphenyl) side chain is presumably greater in magnitude compared to the 6,7-dioxabicyclo[3.2.2]octane. Treatment of (+)-**194** and (+)-**195** with $Pb(OAc)_4$ separately, gave the corresponding diol-cleavage proructs enantiomeric aldehydes (+)-**196** and (-)-**196**. On the other hand, treatment of the mixture of (-)-**190** and (+)-**191** with $Pb(OAc)_4$ followed by reduction of intermediate aldehyde by $NaBH_4$ gave a primary alcohol (±)-**197**.

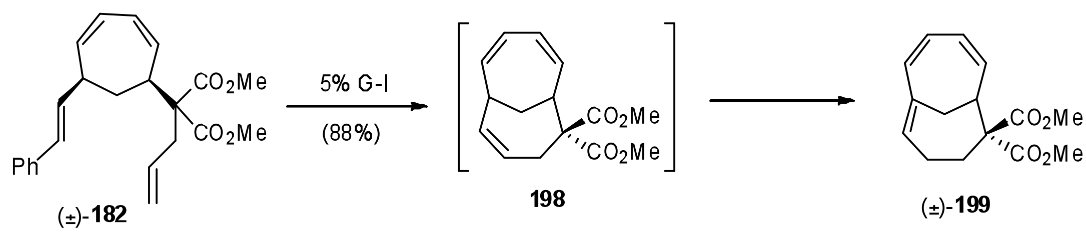


Scheme 54. Treatment of mixture of (-)-**190** and (+)-**191** with singlet oxygen.

The structures of (+)-**194** and (+)-**195** were assigned on the basis of the structures of their precursors and also confirmed by the independent treatment of pure (-)-**190** with singlet oxygen, which generated the corresponding endoperoxide (+)-**194**. The structures of enantiomeric aldehydes (+)-**196** and (-)-**196** were assigned based on the structures of their precursors. In particular, the peak at δ 9.63 ppm in the ^{1}H NMR spectrum of each indicates the presence of the aldehyde functionality in the diol cleavage products (+)/(-)-**196**. The structure of (±)-**197** was assigned on the basis of its ^{1}H NMR spectral data. A multiplate peak at 3.55-3.76 (m, 2H) in the ^{1}H NMR spectra was assigned to the hydroxy methylene portion of the primary alcohol (±)-**197**.

III D. Synthesis of Bicyclo[4.4.1]undecatriene

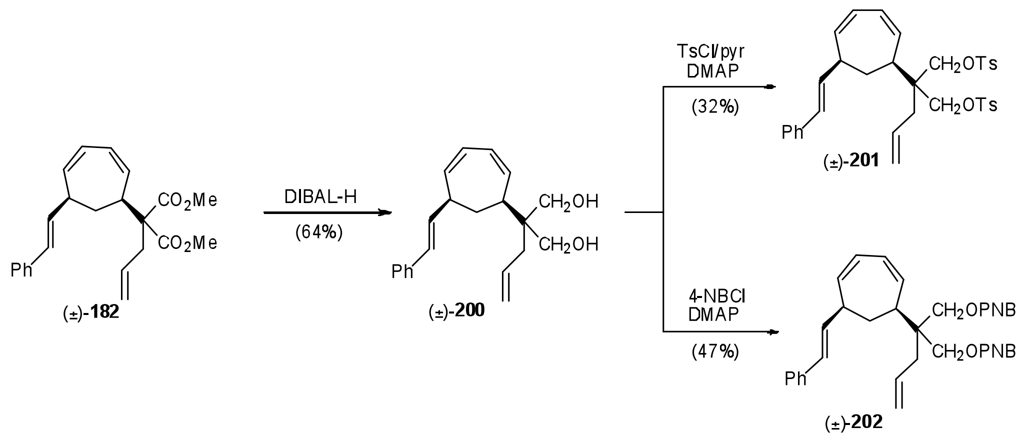
Treatment of (±)-**182** with 1st generation Grubbs catalyst gave the ring-closed product (±)-**199** (Scheme 55). The structure of (±)-**199** was assigned based on its ^{1}H and ^{13}C NMR spectral data. In particular, the ^{1}H NMR spectrum of (±)-**199** integrates to 18 Hs; five of which were olefinic. Furthermore, the ^{13}C NMR spectrum of (±)-**199** consisted of 15 signals with five olefinic methine carbons and one quaternary olefinic carbon. Olefin isomerization has previously been reported as a competitive side reaction of Ru-catalyzed olefin metathesis.[65] The thermodynamically favored (±)-**199** (because of extended conjugation) might form by the isomerization of initially formed **198** isomer.



Scheme 55. Generation of bicyclo[4.4.1]undecatriene from (±)-**182**.

Attempts to prepare crystalline derivatives of (±)-**199** were made. In that direction, reduction of the two ester functional groups of (±)-**199** was unsuccessful. In an different attempt, the ester functional groups of (±)-**182** were reduced to the corresponding diol (±)-**200** by diisobutylaluminium hydride (DIBAL-H) (Scheme 56). Conversion of the two primary alcohol groups of (±)-**200** to different functional groups

(Scheme 54) gave (±)-**201**, and (±)-**202**. Attempted ring closing metathesis of solid (±)-**201** and (±)-**202** were unsuccessful.



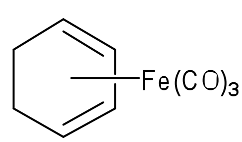
Scheme 56. Reduction of (±)-**182** by DIBAL-H**.**

In conclution, synthesis of tricarbonyl(η^5-6-styrylcyclohepta-2,4-dien-1-yl)iron(+1) from cyclooctatetraene and its reactivity study was achieved. Based on the reactivity pattern structural diversities were created in the forms of functionalized endoperoxides and bicyclo[4.4.1]undecatriene**.**

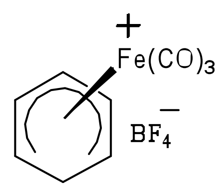
Experimental

General Data:

All non-aqueous reactions were carried out under a nitrogen atmosphere. Spectroscopic grade solvents were used without further purification with the exception of ether and tetrahydrofuran which were distilled from sodium, using benzophenone as indicator. Methylene chloride was distilled from phosphorous pentaoxide and hexane was distilled before use. Column chromatography was performed using silica gel 62 grade (60-200 mesh and 200-400 mesh, Dynamic Adsorbents Inc). Melting points were recorded using a Mel-Temp apparatus and are uncorrected. Carbon and proton NMR were recorded in Varian Mercury 300 and 400 spectrometer. Elemental analyses were obtained from Midwest Microlabs, Indianapolis. IN, and high resolution mass spectra were obtained from the University of Nebraska center for Mass Spectrometry, Lincoln, NE.

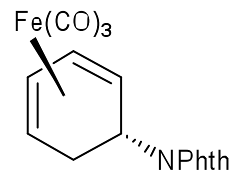


Tricarbonyl (1,3-cyclohexadiene)iron (2): To a 500 mL round-bottomed flask equipped with a condenser, was charged 1,3-cyclohexadiene (4.20 g, 52.4 mmol), benzene (250 mL) and $Fe_2(CO)_9$ (50.00 g 137.4 mmol). After stirring for few minutes, the mixture was heated at reflux for 3 h under nitrogen. The mixture was cooled to room temperature and additional $Fe_2(CO)_9$ (26.0 g, 71.4 mmol) was added. The mixture was heated at reflux for another 4 h. After cooling to room temperature, the dark reaction mixture was filtered through celite using CH_2Cl_2 as eluent. The filtrate and the washings were concentrated. The crude mixture was purified by column chromatography (SiO_2, 100% hexane) to afford the product as a yellow orange oil (10.05 g, 87%). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.54-1.64 (m, 2H), 1.66-1.76 (m, 2H), 3.19-3.24 (m, 2H), 5.27-5.30 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 23.8, 62.4, 85.4, 212.3.

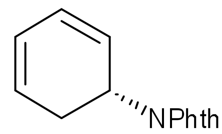


Tricarbonyl(η^5-cyclohexadienyl)iron(1+) tetrafluoroborate (3): To a 100 mL round-bottomed flask was charged triphenylcarbenium tetrafluoroborate (7.64 g, 23.2 mmol), dry CH_2Cl_2 (25 mL) and stirred for few min at room temperature under nitrogen. A solution of iron complex **2** (4.25 g, 19.3 mmol) in dry CH_2Cl_2 (25 mL) was added. After 5 min, an orange solid compound began to separate from the greenish-blue solution. The reaction mixture was stirred for 1 h and then whole mixture was poured into ether (350 mL). The yellow solid cation was isolated by filtration and dried under high vacuum

(5.96 g, 100%). mp 207-210 ^{0}C; ^{13}C NMR (CD_3NO_2, 100 MHz) δ 26.0, 67.4, 91.9, 104.6, 210.9.

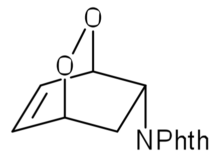


Tricarbonyl(5-phthalimido-1,3-cyclohexadiene)iron (±)-117: In a 100 mL Schlenk flask, iron cation **3** (920 mg, 2.95 mmol) was dissolved in dry CH_2Cl_2 (40 mL) with stirring at room temperature under nitrogen. Solid potassium phthalimide (820 mg, 4.43 mmol) was added and the mixture was stirred for 5 h. The reaction mixture was quenched with water and extracted several times with CH_2Cl_2. The combined extracts were washed with brine, dried (Na_2SO_4) and concentrated. The residue was purified by column chromatography (SiO_2, hexane-ethyl acetate = 6:1) to afford a light yellow solid (807 mg, 75%). mp 166-169 ^{0}C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.00 (br d, *J* = 15.1 Hz, 1H), 2.31 (ddd, *J* = 4.2, 11.4, 15.1 Hz, 1H), 2.77 (ddd, *J* = 1.0, 3.2, 6.3 Hz, 1H), 3.11-3.15 (m, 1H), 4.80 (td, *J* = 3.7, 11.5 Hz, 1H), 5.53 (t, *J* = 5.6 Hz, 1H), 5.67 (t, *J* = 5.7 Hz, 1H), 7.60-7.83 (m, 4H, NPhth); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 27.3, 48.1, 57.1, 58.2, 86.0, 86.7, 123.3, 132.1, 134.2, 168.2, 211.4. Anal. Calcd. for $C_{17}H_{11}NO_5Fe$: C, 55.92; H, 3.04. Found: C, 56.10; H, 3.18.

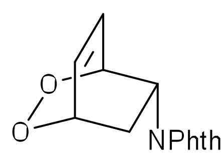


***N*-(2,4-cyclohexadien-1-yl)phthalimide (±)-118**: In a 250 mL round-bottom flask, iron complex (±)-**117** (800 mg, 2.19 mmol) was dissolved in methanol (110 mL) with stirring. Solid ceric ammonium nitrate (360 mg, 6.56 mmol) was added and the mixture was stirred for 2 h. The reaction mixture was quenched with water and extracted several times with CH_2Cl_2. The combined extracts were washed with brine, dried (Na_2SO_4) and concentrated. The residue was purified by column chromatography (SiO_2, hexane-ethyl acetate = 4:1) to give a colorless solid (400 mg, 81%). mp 138–140 ^{0}C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.38 (ddd, *J* = 5.6, 10.0, 17.2 Hz, 1H), 2.78 (tdd *J* = 3.1, 15.2, 17.7 Hz, 1H), 5.20 (tdd, *J* = 2.9, 9.6, 15.2 Hz, 1H), 5.68 (dd, *J* = 3.0, 9.6 Hz, 1H), 5.89-6.10 (m, 3H), 7.71-7.86 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 27.5, 45.9, 123.2, 123.7, 125.3, 125.5, 125.6, 132.1, 133.9, 176.2. Anal. Calcd. for $C_{14}H_{11}NO_2$: C, 74.65; H, 4.92; N, 6.22. Found: C, 74.60; H, 4.94; N, 6.24.

Reaction of (±)-118 with singlet oxygen: To a 25 mL two necked round-bottomed flask, equipped with a condenser, was charged diene (±)-**118** (1.0 gm, 4.4 mmol), dry $CHCl_3$ (50 mL) and tetraphenylporphine (138 mg, 5 mol%). The deep purple solution was stirred at 0 ^{0}C while irradiated with a 60 W tungsten-halogen lamp for 8 h. The reaction mixture was concentrated under vacuum. The residue was purified through column chromatography (SiO_2, hexane-ethyl acetate = 4:1) to give a colorless solid (±)-**119** (593 mg, 52%). Further elution (hexane–ethyl acetate = 3:1) gave a colorless solid (±)-**120** (257 mg, 18%).

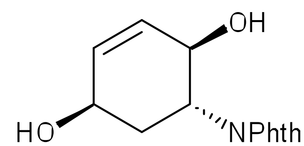


***N*-(8,9-Dioxobicyclo[2.2.2]oct-5-en-2-yl)phthalimide (±)-119**: mp 155–157 ^{0}C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.42 (ddd, *J* = 2.0, 4.4, 13.6, Hz, 1H), 2.80 (ddd, *J* = 4.0, 9.6, 13.6 Hz, 1H), 4.84-4.98 (m, 3H), 6.65 (ddd, *J* = 1.6, 6.0, 8.0 Hz, 1H), 6.88 (ddd, *J* = 1.6. 6.0, 8.0 Hz, 1H), 7.71-7.74 and 7.79-7.8 (AA'BB', 4H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 28.5, 45.9, 71.2, 123.5, 129.5, 131.6, 134.0, 134.5, 168.3 (one peak observed by solvent). Anal. Calcd. for $C_{14}H_{11}O_4N$: C, 65.36; H, 4.31. Found: C, 65.45; H, 4.39.

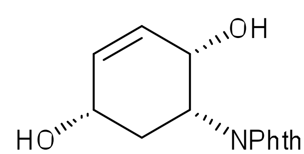


***N*-(8,9-Dioxobicyclo[2.2.2]oct-5-en-2-yl)phthalimide (±)-120**: mp 216–219 ^{0}C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.88 (ddd, *J* = 1.9, 11.8, 13.8 Hz, 1H), 3.64 (td, *J* = 4.2, 13.8 Hz, 1H), 4.41 (ddd, *J* = 1.8, 4.5, 12.0 Hz, 1H), 4.67 (qd, *J* = 1.7, 6.3 Hz, 1H), 4.89 (qdd, *J* = 1.8, 3.6, 5.7 Hz, 1H), 6.75-6.87 (m, 2H), 7.70-7.74 and 7.78-7.83 (AA'BB', 4H); ^{13}C

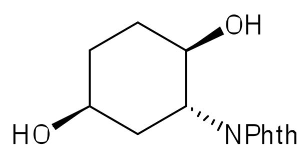
NMR ($CDCl_3$, 75 MHz) δ 21.0, 47.2, 70.9, 75.2, 123.5, 130.8, 132.0, 134.0, 134.3, 168.9. Anal. Calcd. for $C_{14}H_{11}O_4N$: C, 65.36; H, 4.31. Found: C, 65.46; H, 4.34.



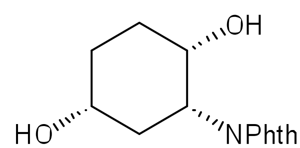
***N*-(2R*,5S*-Dihydroxy-3-cyclohexene-1S*-yl) phthalimide (±)-121**: To a 5 mL round-bottom flask was charged with the major endoperoxide (±)-**119** (25 mg, 0.097 mmol) in methanol (1.5 mL) at room temperature under nitrogen was added solid thiourea (7.0 mg, 0.097 mmol). The mixture was stirred for 15 h. The reaction mixture was concentrated under vacuum and the residue was purified by column chromatography (SiO_2, hexane-ethyl acetate = 1:3) to afford a colorless solid (19 mg, 75%). mp 180–183 ^{0}C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.97 (br d, *J* = 14.0 Hz, 1H), 2.28 (br s, OH, 1H), 2.35 (br s, OH, 1H), 2.82 (dt, *J* = 4.8, 13.6, Hz, 1H), 4.42 (br s, 1H), 4.58 (ddd, *J* = 3.2, 10.0, 13.6 Hz, 1H), 4.84 (br d, *J* = 9.2 Hz, 1H), 5.92 (s, 2H), 7.70-7.74 and 7.81-7.85 (4H, Phth); ^{13}C NMR (CD_3OD, 100 MHz) δ 35.1, 51.1, 65.2, 68.5, 124.1, 130.1, 133.5, 134.8, 135.4, 170.2. Anal. Calcd. for $C_{14}H_{13}NO_4$: C, 64.86; H, 5.05. Found: C, 64.92; H, 5.11.



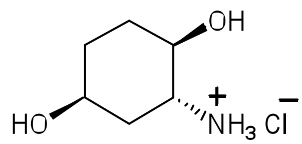
***N*-(2S*,5R*-Dihydroxy-3-cyclohexen-1S*-yl)phthalimide (±)-122**: To a 25 mL round-bottom flask charged with the minor endoperoxide (±)-**120** (0.10 gm, 0.40 mmol) in methanol (4 mL) at room temperature under nitrogen was added solid thiourea (40 mg, 0.48 mmol). The mixture was stirred for 15 h. The reaction mixture was concentrated under vacuum and the residue was purified by column chromatography (SiO_2, hexane-ethyl acetate = 1:4) to afford a colorless solid (40 mg, 40%). mp 168-171 ^{0}C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.21 (br d, *J* = 12.8 Hz, 1H), 2.26 (d, *J* = 7.2 Hz, OH, 1H), 2.81 (d, *J* = 8.8 Hz, OH, 1H), 2.85 (ddd, *J* = 10.8, 12.8, 14.4 Hz, 1H), 4.17-4.23 (m, 1H), 4.43-4.45 (m, 2H), 5.96-5.97 (m, 2H), 7.70-7.74 and 7.81-7.85 (4H, Phth); ^{13}C NMR (CD_3OD, 100 MHz) δ 31.2, 52.7, 65.8, 69.1, 124.1, 128.3, 133.4, 135.4, 136.8, 170.3. Anal. Calcd. for $C_{14}H_{13}NO_4$: C, 64.86; H, 5.05. Found: C, 64.77; H, 5.08.



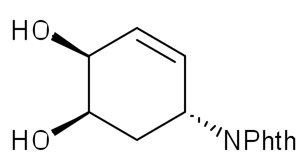
***N*-(2R*,5R*,-Dihydroxycyclohex-1S*-yl)phthalimide (±)-123**: In a hydrogenation container, olefin (±)-**121** (0.20 g, 0.77 mmol) was dissolved in methanol (20 mL) at room temperature. To the mixture was added 10% Pd/C (60 mg) and the suspension was stirred under hydrogen (40 psi) for 5 h. The reaction mixture was filtered through celite. The filtrate was concentrated, adsorbed to silica and applied to a column of silica. Elution (hexane-ethyl acetate = 1:4) gave a colorless solid (143 mg, 76%). mp 198–200 ^{0}C; ^{1}H NMR (CD_3OD, 400 MHz) δ 1.60-1.72 (m, 1H), 1.84-1.91 (m, 4H), 2.42 (dt, *J* = 13.2, 2.4 Hz, 1H), 4.14 (pent, *J* = 2.6 Hz, 1H), 4.26 (dt, *J* = 6.4, 9.8, Hz, 1H), 4.47 (ddd, *J* = 4.0, 10.0, 12.8 Hz, 1H), 7.75-7.88 (m, 4H); ^{13}C NMR (CD_3OD, 100 MHz) δ 29.8, 31.9, 36.3, 53.5, 66.7, 70.2, 124.0, 133.5, 135.3, 170.3. Anal. Calcd. for $C_{14}H_{15}NO_4$: C, 64.36; H, 5.79. Found: C, 64.20; H, 5.73.



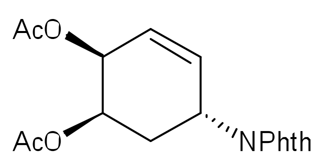
***N*-(2S*,5S*-Dihydroxycyclohex-1S*-yl)phthalimide (±)-124**: In a small hydrogenation container, olefin (±)-**122** (40.0 mg, 0.154 mmol) was dissolved in methanol (7 mL) at room temperature. To the mixture was added 10% Pd/C catalyst (ca. 5 mg) and the suspension was stirred under hydrogen (40 psi) for 7 h. The reaction mixture was filtered through celite. The filtrate was concentrated, adsorbed to silica gel and applied to a column of silica. Elution (hexane-ethyl acetate = 1:4) gave a colorless solid (25 mg, 62%). mp 175–177 ^{0} C; ^{1}H NMR (CD_3OD, 400 MHz) δ 1.60-1.95 (m, 5H), 2.88 (td, *J* = 11.7, 13.5 Hz, 1H), 3.60-3.72 (m, 1H), 3.98 (s, 1H), 4.18 (ddd, *J* = 2.2, 3.8, 13.5 Hz, 1H), 7.75-7.90 (m, 4H); ^{13}C NMR (CD_3OD, 100 MHz) δ 29.5, 30.4, 33.6, 55.4, 68.5, 70.8, 124.2, 133.3, 135.5, 170.6. Anal. Calcd. for $C_{14}H_{15}NO_4.1/2H_2O$: C, 62.21; H, 5.96. Found: C, 62.03; H, 5.70.



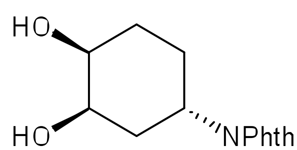
1S*-(2R*,5R*-Dihydroxycyclohexyl)ammoinium chloride (±)-125: To a 10 mL round-bottomed flask was charged diol (±)-**123** (0.10 g, 0.38 mmol) and aqueous HCl (6N, 6 mL). The mixture was heated at reflux for 15 h. The reaction mixture was dried, re-dissolved in deionized water (8 mL) and then extracted with ethyl acetate (8 mL X 3). The aqueous solution was concentrated, dried under high vacuum to afford a light brown gummy compound (64 mg, 100%). ^{1}H NMR (CD_3OD, 400 MHz) δ 1.53-1.64 (m, 2H), 1.72-1.86 (m, 3H), 2.11 (br m, *J* = 13.4 Hz, 1H), 3.18-3.27 (m, 1H), 3.42-3.51 (m, 1H), 4.08-4.11 (m, 1H); ^{13}C NMR (CD_3OD, 100 MHz) δ 29.2, 31.4, 36.4, 53.5, 65.8, 72.1.



***N*-(4R*,5S*-Dihydroxy-2-cyclohexane-1S*-yl)phthalimide (±)-126:** To a solution of diene (±)-**118** (750 mg, 3. 33 mmol) in acetone (15 mL) was added a solution of *N*-methylmorpholine *N*-oxide (960 mg, 8.19 mmol) in water (4 mL) followed by a solution of OsO_4 in toluene (2 mL, 10 mol%). The reaction mixture was stirred for 30 min at room temperature and then solid $Na_2S_2O_4$ (0.6 g) was added and the mixture stirred for another 30 min. The crude reaction mixture was purified by column chromatography (hexane-ethyl acetate = 1:4) to give a colorless solid (447 mg, 52%). mp 178-181 ^{0}C; ^{1}H NMR (CD_3OD, 400 MHz) δ 2.12 (dtd, *J* = 1.6, 5.8, 13.4 Hz, 1H), 2.35 (ddd, *J* = 2.0, 10.2, 13.6 Hz, 1H), 4.17-4.22 (m, 1H), 4.30-4.34 (m, 1H), 5.11-5.17 (m, 1H), 5.63 (dtd, *J* = 1.6, 2.4, 10.2 Hz, 1H), 5.73 (dt, *J* = 1.6, 2.0, 10.4 Hz, 1H), 7.78-7.85 (AA'BB', 4H); ^{13}C NMR (CD_3OD, 100 MHz) δ 33.4, 45.4, 68.6, 69.5, 124.2, 129.1, 131.9, 133.4, 135.5, 169.6. Anal. Calcd. for $C_{14}H_{13}NO_4$: C, 64.86; H, 5.05. Found: C, 64.87; H, 5.02.

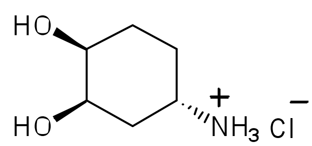


***N*-(4R*,5S*-Diacetoxy-2-cyclohexen-1S*-yl)phthalimide (±)-127:** To a 10 mL round-bottom flask was charged diol (±)-**126** (30 mg, 0.12 mmol) and CH_2Cl_2 (0.8 mL) at room temperature. To the stirring suspension was added dropwise pyridine (0.10 mL, 1.2 mmol). Upon addition of pyridine the mixture became clear. Acetic anhydride (0.10 mL, 1.2 mmol) was added and the mixture stirred for 12 h. The reaction mixture was quenched with 1M HCl (5 mL) and extracted several times with CH_2Cl_2, washed with brine, dried (Na_2SO_4) and concentrated. The residue was purified by column chromatography (hexane-ethyl acetate = 1:1) to afford a colorless solid (27 mg, 68%). mp 151-154 ^{0}C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.07 (s, 3H), 2.15 (s, 3H), 2.19-2.28 (m, 1H), 2.54 (ddd, *J* = 2.1, 9.3, 13.8 Hz, 1H), 5.17 (ddd, *J* = 2.9, 6.3, 9.3 Hz, 1H), 5.62-5.67 (m, 1H), 5.68-5.72 (m, 1H), 5.78 (s, 2H), 7.72-7.77 and 7.82-7.88 (4H, Phth); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.1, 21.3, 30.0, 44.1, 67.9, 68.3, 123.6, 127.1, 129.9, 132.0, 134.4, 168.0, 170.7, 170.4. Anal. Calcd. for $C_{18}H_{17}NO_6$: C, 62.97; H, 4.99. Found: C, 63.64; H, 5.12.

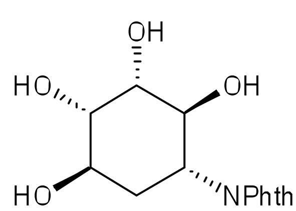


***N*-(3S*,4R*-Dihydroxycyclohex-1R*-yl)phthalimide (±)-128**: In a hydrogenation container, cyclohexenylphthalimide (±)-**126** (0.10 mg, 0.38 mmol) was dissolved in methanol (10 mL) at room temperature. To the mixture 10% Pd/C catalyst (ca. 5 mg) was added and the mixture was stirred under hydrogen (40 psi) for 4 h. The reaction mixture was filtered through celite. The filtrate was concentrated, adsorbed onto silica gel and then applied to a column of silica. Elution (hexane-ethyl acetate = 1:4) gave a colorless solid (75 mg, 74%). mp 243–247 ^{0}C; ^{1}H NMR (CD_3OD, 400 MHz) δ 1.60-1.80 (m, 2H), 1.84-1.96 (m, 2H), 2.28 (dq, *J* = 4.2, 13.0 Hz, 1H), 2.52 (dt, *J* = 2.4, 12.8 Hz, 1H), 3.67 (ddd, *J* = 2.9, 4.5, 11.5 Hz, 1H), 4.03-4.04 (m, 1H), 4.58 (tt, *J* = 4.1, 12.6 Hz

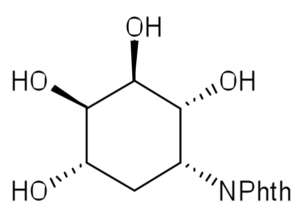
1H), 7.75-7.88 (m, 4H); ^{13}C NMR (d_6-DMSO, 100 MHz) δ 27.3, 27.6, 34.3, 44.3, 68.6, 70.2, 122.9, 131.5, 134.3, 168.0. FAB-HRMS m/z 268.1157 (calcd. for $C_{14}H_{15}NO_4Li$ (M+Li) m/z 268.1161).



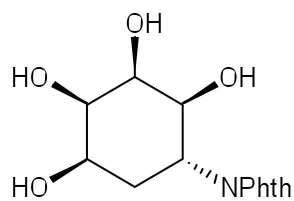
1R*-(3S*,4R*-Dihydroxycyclohexyl)ammonium chloride (±)129: To a 10 mL round-bottomed flask was charged diol (±)-**128** (40.0 mg, 0.153 mmol) and aqueous HCl (6N, 3 mL). The mixture was heated at reflux for 15 h. The reaction mixture was dried, re-dissolved in deionized water (6 mL) and then extracted with ethyl acetate (5 mL X 3). The aqueous solution was concentrated and dried under high vacuum to afford a light yellow foamy solid (26 mg, 100%). ^{1}H NMR (CD_3OD, 400 MHz) δ 1.34- 2.15 (m, 6H), 3.29-3.39 (m, 1H), 3.49-3.58 (m, 1H), 3.92-3.98 (m, 1H); ^{13}C NMR (CD_3OD, 75 MHz) δ 27.1, 29.3, 36.5, 46.5, 69.3, 71.2.



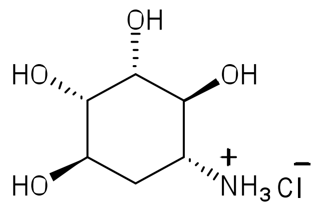
***N*-(2R*,3S*,4R*,5S*-Tetrahydroxycyclohex-1S*-yl)phthalimide (±)-130**: To a stirring solution of olefin (±)-**121** (60 mg, 0.23 mmol) in acetone (1 mL) was added a solution of *N*-methylmorpholine *N*-oxide (70 mg, 0.58 mmol) in water (0.3 mL) followed by a solution of OsO_4 in toluene (0.1 mL, 10 mol%). The reaction mixture was stirred for 20 h at room temperature and then $Na_2S_2O_4$ (35 mg) was added and stirred for another 30 min. The mixture was concentrated, adsorbed to silica using methanol and applied to a column of silica. Elution (CH_2Cl_2-methanol = 9:1) gave a colorless solid (42 g, 62%). mp 267–270 ^{0}C; ^{1}H NMR (CD_3OD, 400 MHz) δ 1.69 (td, *J* = 2.8, 13.2 Hz, 1H), 2.82 (dt, *J* = 2.8, 13.2 Hz, 1H), 3.73 (dd, *J* = 3.2, 9.6 Hz, 1H), 3.93-4.00 (m, 2H), 4.43-4.50 (m, 2H), 7.78-7.87 (m, 4H); ^{13}C NMR (CD_3OD, 100 MHz) δ 31.2, 51.6, 70.4, 70.7, 74.0, 74.4, 124.1, 133.5, 135.4, 170.2. Anal. Calcd. for $C_{14}H_{15}NO_6$: C, 57.33; H, 5.15. Found: C, 57.29; H, 5.34.



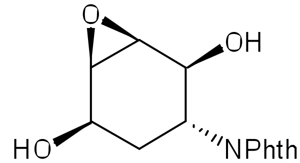
***N*-(2S*,3R*,4S*,5R*-Tetrahydroxycyclohex-1S*-yl)phthalimide (±)-131**: To a stirring solution of olefin (±)-**122** (30.0 mg, 0.115 mmol) in acetone (1 mL) was added a solution of *N*-methylmorpholine *N*-oxide (30.0 mg, 0.240 mmol) in water (0.25 mL) followed by a solution of OsO_4 in toluene (0.1 mL, 10 mol%). The reaction mixture was stirred for 15 h at room temperature and then $Na_2S_2O_4$ (0.02 g) was added and stirring continued for another 30 min. The reaction mixture was dried, re-dissolved in ethyl acetate, adsorbed to silica gel and applied to a column of silica. Elution (100% ethyl acetate) gave a colorless solid (20 mg, 59%). mp 253-255 ^{0} C; ^{1}H NMR (CD_3OD, 400 MHz) δ 1.89 (td, *J* = 3.8, 12.4 Hz, 1H), 2.86 (q, *J* = 12.4, Hz, 1H), 3.71 (dd, *J* = 2.8, 9.6 Hz, 1H), 3.82 (ddd, *J* = 4.8, 10.0, 11.6 Hz, 1H), 3.94-3.99 (m, 2H), 4.69 (ddd, *J* = 2.0, 4.4, 14.0 Hz, 1H), 7.78-7.87 (m, 4H); ^{13}C NMR (CD_3OD, 100 MHz) δ 31.3, 50.1, 70.5, 74.0, 74.1, 74.2, 124.2, 133.3, 135.5, 170.7. Anal. Calcd. for $C_{14}H_{15}NO_6$: C, 57.33; H, 5.15. Found: C, 57.53; H, 5.11.



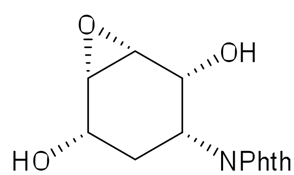
***N*-(2S*,3S*,4R*5R*-Tetrahydroxycyclohex-1R*-yl)phthalimide (±)-132**: To a stirring solution of olefin (±)-**126** (0.10 g, 0.38 mmol) in acetone (4 mL) was added a solution of *N*-methylmorpholine *N*-oxide (0.07 gm 0.57 mmol) in water (1 mL) followed by a solution of OsO_4 in toluene (0.2 mL, 10 mol%). The reaction mixture was stirred for 8 h at room temperature. The reaction mixture was filtered and the residue was dissolved in a mixture of methanol and CH_2Cl_2 and adsorbed to silica gel and then applied to a column of silica. Elution (methanol:CH_2Cl_2 = 1:4, few drops of NH_4OH) gave a colorless solid (22 mg, 21%). mp 243–245 ^{0}C; ^{1}H NMR (d_6-DMSO, 300 MHz) δ 1.79 (td, *J* = 3.6, 13.2 Hz, 1H), 2.19 (dt, *J* = 1.8, 13.2 Hz, 1H), 3.46 (td, *J* = 2.7, 6.3 Hz, 1H), 3.86-3.96 (br m, 2H), 4.02-4.10 (br m, 1H), 4.55 (dt, *J* = 4.2, 12.0 Hz, 1H), 4.84-4.94 (m, 3H), 5.03 (d, *J* = 5.7 Hz 1H), 7.80-7.92 (m, 4H); ^{13}C NMR (d_6-DMSO, 75 MHz) δ 32.4, 46.5, 68.3, 69.2, 70.4, 75.3, 122.8, 131.6, 134.3, 168.4. FAB-HRMS m/z 300.1067 (calcd. for $C_{14}H_{15}NO_6Li$ (M+Li) m/z 300.1059).



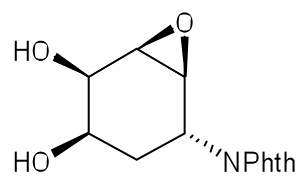
1S*-(2R*,3S*,4R*,5S*-Tetrahydroxycyclohexyl)ammonium chloride (±)-133: To a 10 mL round-bottomed flask was charged tetraol (±)-**130** (50 mg, 0.17 mmol) and HCl (6N, 4 mL). The mixture was heated at reflux for 15 h. The reaction mixture was dried, re-dissolved in deionized water (6 mL) and then extracted with ethyl acetate (6 mL X 3). The aqueous solution was concentrated, dried under high vacuum to afford a light yellow solid (33 mg, 100%). mp 92–95 ^{0}C; ^{1}H NMR (CD_3OD, 400 MHz) δ 1.91-2.02 (m, 2H), 3.19-3.28 (m, 1H), 3.62-3.69 (m, 2H), 3.86-3.89 (m, 1H), 3.93-3.96 (m, 1H); ^{13}C NMR (CD_3OD, 100 MHz) δ 31.46, 51.94, 69.56, 72.39, 73.02, 74.01.



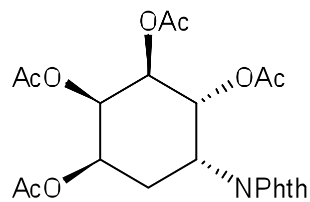
***N*-(3,4-Epoxy-2S*,5R*-dihydroxycyclohex-1R*-yl)phthalimide (±)-135**: To a stirring solution of diol (±)-**121** (50.0 mg, 0.193 mmol) and CH_2Cl_2 (1mL) was added a solution of mCPBA (0.1 g, 0.4 mmol, 70 wt%,) in CH_2Cl_2 (1 mL) at room temperature under nitrogen. After stirring for 7 h, the reaction mixture was quenched with a mixture of Et_3N and water (1:9, 10 mL) and then extracted with ethyl acetate (8 mL X 3). The combined extracts were washed with brine, dried (Na_2SO_4) and concentrated. The residue was re-dissolved in CH_2Cl_2, adsorbed to silica gel, and then applied to a column of silica. Elution (100% ethyl acetate) gave a colorless solid (22.0 g, 42%). mp 203–206 ^{0}C; ^{1}H NMR (CD_3OD, 400 MHz) δ 1.68 (br d, J = 14.0 Hz, 1H), 2.52 (ddd, J = 6.0, 12.4, 14.4 Hz, 1H), 3.47-3.49 (narrow m, 2H), 4.25-4.29 (m, 1H), 4.52 (ddd, J = 3.2, 9.6, 13.0 Hz, 1H), 4.66 (d, J = 9.2 Hz, 1H), 7.78-7.89 (m, 4H); ^{13}C NMR (CD_3OD, 100 MHz) δ 36.1, 48.8, 57.3, 59.0, 64.9, 68.6, 124.1, 133.4, 135.5, 170.1. Anal. Calcd. for $C_{14}H_{13}NO_5$: C, 61.09; H, 4.76. Found: C, 60.58; H, 4.80.



***N*-(3,4-Epoxy-2R*,5S*-dihydroxycyclohex-1R*-yl)phthalimide (±)-136**: To a stirring solution of diol (±)-**122** (53 mg, 0.20 mmol) and CH_2Cl_2 (2 mL) was added a solution of mCPBA (0.1 g, 70 wt%, 0.4 mmol) in CH_2Cl_2 (2 mL) at room temperature under nitrogen and stirred for 15 h. The reaction mixture was quenched with a mixture of Et_3N and water (1:9, 7 mL) and then extracted several times with CH_2Cl_2. The combined CH_2Cl_2 solution was washed with sat. $NaHCO_3$ solution followed by brine, dried (Na_2SO_4) and concentrated. The residue was redissolved in CH_2Cl_2, adsorbed to silica gel, and then applied to a column of silica. Elution (100% ethyl acetate) gave a colorless solid (8 mg, 15%). mp 180–182 ^{0}C; ^{1}H NMR (CD_3OD, 300 MHz) δ 1.79 (br d, *J* = 12.4 Hz, 1H), 2.78-2.92 (m, 1H), 3.39-3.48 (m, 3H), 3.97-4.15 (m, 4H), 7.77-7.86 (m, 4H); ^{13}C NMR (CD_3OD, 75 MHz) δ 27.3, 52.5, 55.6, 58.1, 65.4, 69.9, 124.1, 133.4, 135.5, 170.2. Due to the low yield for this epoxide, hydrolysis was not attempted.



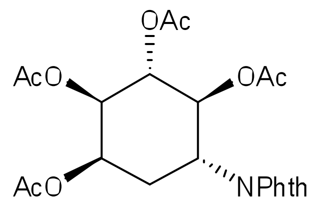
***N*-(2,3-Epoxy-4R*,5R*-dihydroxycyclohex-1R*yl)phthalimide (±)-137:** To a stirring solution of diol (±)-**126** (100 mg, 0.400 mmol) and CH_2Cl_2 (2 mL) was added a solution of mCPBA (0.2 g, 0.8 mmol) in CH_2Cl_2 (2 mL) at room temperature and stirred for 12 h. The reaction mixture was quenched with a mixture of Et_3N and water (1:10, 10 mL) and then extracted several times with CH_2Cl_2. The combined extracts were washed with brine, dried (Na_2SO_4) and concentrated. The excess Et_3N was removed under high vacuum to give a colorless solid (73 mg, 70%). mp 167-170 ^{0}C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.03 (ddd, *J* = 2.0, 10.7, 13.7 Hz, 1H), 2.25 (dddd, *J* = 1.6, 4.2, 6.9, 13.7 Hz, 1H), 2.89 (d, *J* = 11.6 Hz, 1H, OH), 3.05 (d, *J* = 10.0 Hz, 1H, OH), 3.48 (dd, *J* = 1.6, 3.6 Hz, 1H), 3.65-3.68 (narrow m, 1H), 3.97-4.25 (m, 1H), 4.19 (ddd, *J* = 1.6, 4.3, 9.5 Hz, 1H), 4.88 (dd, *J* = 6.9, 10.6 Hz, 1H), 7.75-7.80 and 7.85-7.89 (4H, Phth); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 32.3, 41.7, 58.7, 58.9, 67.2, 68.4, 123.8, 131.9, 134.7, 167.8. Anal. Calcd. for $C_{14}H_{13}NO_5.1/4H_2O$: C, 60.10; H, 4.86. Found: C, 59.95; H, 4.69.



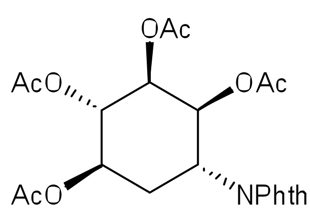
***N*-(2R*,3S*,4R*,5R*-Tetraacetoxycyclohex-1R*-yl)phthalimide (±)-138**: To a 25 mL round-bottom flask was charged with epoxide (±)-**137** (137 mg, 0.498 mmoL) and water (10 mL). To the suspension was added $HClO_4$ (6 drops) and the suspension was heated at reflux. After 20 min of reflux the suspension turned clear. The reflux was continued for another 30 min at which time a colorless solid compound began to separate out. The mixture was stirred for 20 more min, cooled to room temperature and filtered. The colorless solid residue was dried under high vacuum (86 mg, 59%). mp 265–267 ^{0} C. The crude product was used in the follow step without further characterization. A 25 mL round-bottom flask was charged with tetraol (70 mg, 0.24 mmol) at room temperature. Acetic anhydride (0.20 mL) was added followed by pyridine (0.15 mL). The suspension was stirred overnight. The clear reaction mixture was diluted with ethyl acetate (5 mL), quenched with 1M HCl (10 mL) and extracted with ethyl acetate (10 mL X 2). The combined extracts were washed with brine, dried (Na_2SO_4) and concentrated. The residue was purified by column chromatography (hexane-ethyl acetate = 1:1) to afford a colorless solid (79 mg, 71%). mp 67–70 ^{0} C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.70-7.86 (m, 4H), 5.70-5.64 (m, 1H), 5.43-5.38 (narrow m, 2H), 5.36-5.31 (narrow m, 1H), 5.04 (ddd, *J* =

11.1, 4.5, 3.3 Hz, 1H), 3.18 (br t, J = 11.0 Hz, 1H), 2.02, 2.06, 2.11, 2.17 (m & OAc, 13H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 20.95, 21.0, 21.2, 27.4, 44.8, 67.9, 68.2, 69.3, 70.0, 123.6, 131.7, 134.5, 168.6, 169.7, 170.1, 170.2. Anal. Calcd. for $C_{22}H_{23}NO_{10}$: C, 57.26; H, 5.02. Found: C, 57.15; H, 5.04.

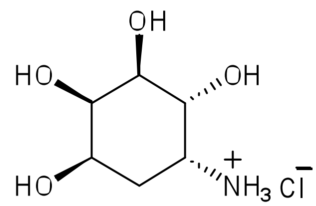
Hydrolysis of epoxide (±)-135: To a 25 mL round-bottomed flask was charged epoxide (±)-**135** (160 mg, 0.582 mmoL) and water (7 mL). To the suspension was added H_2SO_4 (14 drops) and the suspension was heated at reflux. After 30 min the suspension turned clear. The reflux was continued for another 30 min and during which time a colorless solid compound began to separate out. The mixture was stirred for an additional 20 min, cooled to room temperature and filtered. The colorless solid residue was dried under high vacuum (119 mg, 70%). mp 270–272 ^{0} C. The product was used in the next step without further characterization. To a 5 mL round-bottom flask was charged crude tetraol (136 mg, 0.464 mmol) at room temperature. Acetic anhydride (0.5 mL) was added followed by pyridine (0.4 mL). The suspension was stirred overnight. The clear reaction mixture was diluted with ethyl acetate (10 mL) and quenched with 1M HCl solution (20 mL). The mixture was extracted with ethyl acetate (10 mL X 2) and the combined extracts were washed with brine, dried (Na_2SO_4) and concentrated. The residue was purified by column chromatography (hexane-ethyl acetate = 1:1) to afford a colorless solid (137 mg, 70%). The colorless solid was determined to be a mixture of two tetra-acetates by ^{1}H NMR spectroscopy. Slow recrystallization of the mixture (ethyl acetate) gave two crystalline forms, which were manually separated (tweezers) to afford the pure diastereomers.



***N*-(2S*,3R*,4R*,5R*-Tetraacetoxycyclohex-1R*-yl)phthalimide (±)-139**: mp 215–217 ^{0}C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ1.85, 2.02, 2.21 (13H, 4Xs and m, OAc), 2.93 (dt, *J* = 2.1, 14.0 Hz, 1H), 4.70 (ddd, *J* = 4.8, 10.5, 13.2 Hz, 1H), 5.11 (dd, *J* = 2.8, 10.7 Hz, 1H), 5.51-5.58 (m, 2H), 5.73 (dd, *J* = 9.6, 10.5 Hz, 1H), 7.70-7.88 (m 4H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 20.6, 20.8, 20.7, 21.3, 28.7, 47.4, 67.5, 70.4, 71.6, 71.7, 123.8, 131.6, 134.6, 168.0, 170.0, 170.1, 170.15, 170.17. Anal. Calcd. for $C_{22}H_{23}NO_{10}$: C, 57.26; H, 5.04. Found: C, 57.18; H, 4.96.

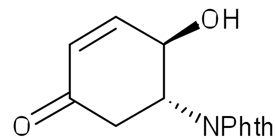


***N*-(2S*,3S*,4S*,5R*-Tetraacetoxycyclohex-1R*-yl)phthalimide (±)-140**: mp 218–221 ^{0}C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.85 (s, OAc, 3H), 2.00-2.13 (br d, *J* = 14.4 Hz, 1H), 2.15, 2.17, 2.21 (3Xs, OAc, 9H), 2.99 (ddd, *J* = 3.6, 12.5, 14.4 Hz, 1H), 4.92 (ddd, *J* = 4.2, 10.9, 12.2 Hz, 1H), 5.10-5.13 (narrow m, 1H), 5.16 (dt, *J* = 1.5, 3.0 Hz, 1H), 5.48 (dt, *J* = 1.2, 3.5 Hz, 1H), 5.87 (dd, *J* = 3.6, 10.8 Hz, 1H), 7.73-7.90 (m, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 20.8, 21.0, 21.1, 21.2, 29.2, 44.5, 68.1, 68.6, 68.7, 69.0, 123.7, 131.7, 134.5, 168.2, 169.0, 169.7, 169.74, 169.9. Anal. Calcd. for $C_{22}H_{23}NO_{10}$: C, 57.3; H, 5.0. Found: C, 57.17; H, 4.98.



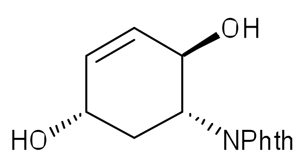
1R*-(2R*,3S*,4R*,5R*-Tetrahydroxycyclohexyl)ammonium choloride (±)-141: To a 25 mL round-bottomed flask was charged tetra-acetate (±)-**138** (67 mg, 0.15 mmol) and 6N HCl (4 mL). The mixture was heated at reflux for 4 h. The reaction mixture was dried, re-dissolved in deionized water (6 mL) and then extracted with ethyl acetate (6 mL X 3). The aqueous solution was concentrated, dried under high vacuum to afford a light yellow solid (27 mg, 93%). mp 57–60 ^{0}C; ^{1}H NMR (CH_3OD, 400 MHz) δ 2.00-2.22 (m, 2H), 3.80-3.87 (m, 1H), 3.89-3.95 (m, 1H), 3.97-4.03 (m, 1H), 4.08-4.17 (m, 2H).

Reaction of (±)-119 with DBU: To a stirring solution of the major endoperoxide (±)-**119** (690 mg, 2.68 mmol) in CH_2Cl_2 (25 mL) at room temperature was added dropwise 1,8-diazabicyclo[5.4.0]undec-7-ene (0.70 mL, 4.03 mmol). The mixture was stirred for 15 min, then diluted with CH_2Cl_2 (20 mL), and finally neutralized with amberlite IRC-76. The mixture was filtered and the filtrate concentrated and applied to a column of silica. Elution (hexane-ethyl acetate = 1: 1) gave the 5-phthalimidocyclohexenone (±)-**142** as a colorless compound (278 mg, 40%). Further elution gave a mixture of epimeric 6-phthalimidocyclohexenone (±)-**144** and (±)-**143** as a colorless solid (155 mg, 24%).

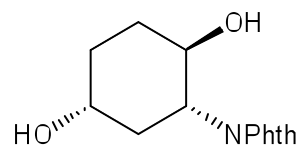


***N*-(2S*-Hydroxy-5-oxo-3-cyclohexene-1S*-yl)phthalimide (±)-142**: mp 175–177 ^{0}C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.67 (dd, *J* = 4.8, 16.4 Hz, 1H), 3.43 (dd, *J* = 13.6, 16.4 Hz, 1H), 4.65 (ddd, *J* = 4.8, 10.0, Hz, 1H), 5.33 (br d, *J* = 10.4 Hz, 1H), 6.11 (d, *J* = 10.0 Hz, 1H), 7.02 (dd, *J* = 1.6, 10.3 Hz, 1H) 7.78-7.89 (AA'BB', 4H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 40.2, 53.6, 67.7, 123.8, 129.6, 131.8, 134.8, 152.4, 168.5, 196.4. Anal. Calcd for $C_{14}H_{11}NO_4$: C, 65.36; H, 4.31. Found: C, 65.01, H, 4.31.

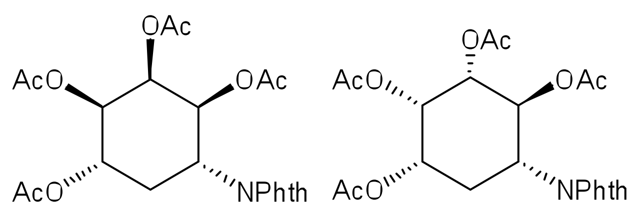
***N*-(5-Hydroxy-2-oxo-3-cyclohexen-1-yl)phthalimide (±)-143/(±)-144**. mp 192-195 ^{0}C; δ (CD_3OD, 400 MHz) 2.51-2.43 (m, 1H), 2.81 (td, *J* = 14.4, 11.4 Hz, 1H), 4.84-4.75 (m, 1H), 4.98 (dd, *J* = 14.6, 5.0 Hz, 1H), 6.09 (dd, *J* = 10.8, 2.4 Hz, 1H), 7.12 (d, *J* = 10.4 Hz, 1H), 7.96-7.78 (m, 4H) and δ (partial, CD_3OD, 400 MHz) 2.26 (br d, *J* = 13.2 Hz, 1H), 3.02 (dt, *J* = 13.2, 3.6 Hz, 1H), 4.60-4.58 (m, 1H), 5.35 (dd, *J* = 13.2, 4.8 Hz, 1H).



***N*-(2R*,5R*-Dihydroxy-3-cyclohexene-1S*-yl)phthalimide(±)-146**: To a stirring solution of the major cyclohexenone (±)-**142** (270 mg, 1.05 mmol) in methanol (22 mL) at room temperature was added $CeCl_3.7H_2O$ (0.391 gm, 1.05 mmol) followed by solid $NaBH_4$ (80 mg, 2.1 mmol). The reaction mixture was stirred for 45 min and then quenched with water (10 mL). The mixture was concentrated under vacuum to removed methanol. The concentrated mixture was diluted with water (20 mL) and then extracted with ethyl acetate (20 mL X 5). The combined extracts were washed with saturated $NaHCO_3$ and dried (Na_2SO_4). The solution was concentrated and dried under high vacuum to afford a colorless solid (167 mg, 61%). mp 187–190 ^{0}C; ^{1}H NMR (CD_3OD, 400 MHz) δ 2.09-2.15 (m, 1H), 2.46 (ddd, *J* = 10.0, 12.0, 13.2 Hz, 1H), 4.19 (ddd, *J* = 3.0, 9.2, 13.6 Hz, 1H), 4.39-4.46 (m, 1H), 4.85-4.95 (m, 1H), 5.73 (td, *J* = 1.6, 10.4 Hz, 1H), 5.78 (dq, *J* =1.9, 10.4, Hz, 1H), 7.78-7.89 (m, 4H); ^{13}C NMR (CD_3COCD_3, 75 MHz) δ 36.8, 54.5, 67.5, 67.7, 123.7, 131.8, 133.1, 134.0, 135.0, 169.0. Anal. Calcd. for $C_{14}H_{13}NO_4$: C, 64.86; H, 5.05. Found: C, 64.93; H, 5.27.

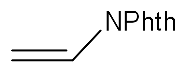


***N*-(2R*,5S*-Dihydroxycyclohex-1S*-yl)phthalimide (±)-147**: To a Parr apparatus was charged olefin (±)-**146** (56 mg, 0. 22 mmol), methanol (10 mL) and 10% of Pd/C (ca. 5 mg) catalyst. The mixture was stirred at room temperature under hydrogen (40 psi) for 5 h. The reaction mixture was filtered through celite and the filtrate was concentrated and applied to a wet column of silica. Elution (100% ethyl acetate) gave a colorless compound (36 mg, 64%). mp 243–245 ^{0}C; ^{1}H NMR (CD_3OD, 300 MHz) δ 1.38-1.55 (m, 2H), 1.93-2.18 (m, 3H), 2.25 (q, J = 12.0 Hz, 1H), 3.64-3.76 (m, 1H), 4.02 (ddd, J = 4.4, 9.3, 13.5 Hz, 1H), 4.21-4.31 (m, 1H), 7.78-7.90 (m, 4H); ^{13}C NMR (CD_3OD, 75 MHz) δ 32.4, 34.3, 38.2, 55.9, 69.6, 70.0, 124.1, 133.4, 135.4, 170.1. Anal. Calcd. for $C_{14}H_{15}NO_4$: C, 64.36; H, 5.79. Found: C, 64.01; H, 5.76.

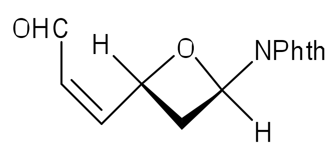


***N*-(2S*,3S*,4R*,5S*-Tetraacetoxycyclohex-1R*-yl)phthalimide (±)-148 and *N*-(2S*,3R*,4S*,5S*-Tetraacetoxycyclohex-1R*-yl)phthalimide (±)-149**: To a stirring solution of olefin (±)-**146** (160 mg, 0.620 mmol) in acetone (4 mL) was added a solution of *N*-methylmorpholine *N*-oxide (0.150 gm, 1.24 mmol) in water (0.8 mL) followed by a solution of OsO_4 in toluene (0.4 mL, 10 mol%). The reaction mixture was stirred at room temperature for 30 h and then solid $Na_2S_2O_4$ (0.10 gm, 0.62 mmol) was added and stirred for another 30 min. The crude reaction mixture was adsorbed on silica and then layered onto a column of silica gel. Elution (ethyl acetate-methanol = 9:1) gave a colorless mixture of two tetraols (82 mg, 45%). To a round-bottom flask was charged the mixture of tetraols (82 mg, 0.27 mmol) and acetic anhydride (0.6 mL) at room temperature. To the stirring mixture pyridine (0.4 mL) was added dropwise and the mixture was stirred overnight. The reaction mixture was diluted with ethyl acetate (6 mL) and quenched with aqueous HCl (1M, 7 mL) solution. The aqueous layer was extracted with ethyl acetate (6 mL X 3). The combined ethyl acetate layers were washed with brine, dried (Na_2SO_4) and concentrated. The residue was re-dissolved in CH_2Cl_2 and applied to a column of wet silica gel. Elution (hexane-ethyl acetate = 1:1) gave a colorless mixture of two tetraacetates (104 mg, 82%). Anal. Calcd. for $C_{22}H_{23}NO_{10}$: C, 57.26; H, 5.02. Found: C, 57.27; H, 5.3. mp 150-160 ^{0}C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ (mixture) 2.56 (dt, *J* = 12.9, 10.9 Hz, 0.45H), 3.14 (q, *J* = 12.7 Hz, 0.55H), 4.40 (ddd, *J* = 13.6, 10.4, 4.8 Hz, 0.55H), 4.77 (ddd, *J* = 13.4, 11.0, 4.8 Hz, 0.45H), 5.04 (ddd, *J* = 12.0, 4.4, 2.0 Hz, 0.55H), 5.07 (dd, *J* = 10.4, 2.8 Hz, 0.55H), 5.24-5.22 (dd, *J* = 10.2, 2.6 Hz, 0.45H), 5.33 (m, 0.45H), 5.63 (narrow m, 0.55H), 5.71 (t, *J* = 2.8 Hz, 0.45H), 5.77 (dd, *J* = 11.0, 2.6 Hz, 0.45H), 5.92 (t, *J* = 10.4 Hz, 0.55H), 7.88-7.70 (m, 4H).

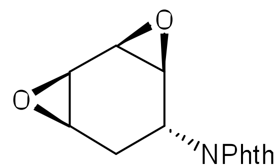
Rearrangement of major endoperoxide (±)-119 with Grubb's catalyst. In a 10 mL round-bottomed flask, major endoperoxide (±)-**119** (50 mg, 0.19 mmol) was dissolved in dry CH_2Cl_2 (1.5 mL) at room temperature. To the stirring solution Grubb's II catalyst (1.6 mg 10 mol%) was added and the mixture was stirred for 30 min. The mixture was concentrated under reduced pressure. Analysis of the crude product by ^{1}H NMR indicated this to be a mixture of (±)-**153** : **151** : **150** : (±)-**152** ratio = 3 : 1.5 : 2 : 1. Separation of the mixture by column chromatography (hexane-ethyl acetate = 10:1 to 1:4) gave colorless solid **151** (8 mg, 24%). oxetane (7 mg, 14%) and diepoxide (29%)



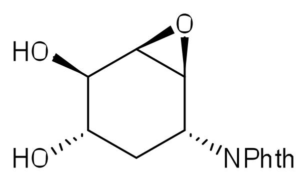
***N*-Vinylphthalimide (151)**: mp 84–86 ^{0} C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 5.06 (d, *J* = 10.3 Hz 1H), 6.10 (d, *J* = 16.3 Hz, 1H), 6.89 (dd, *J* = 9.9, 16.5 Hz, 1H), 7.76 (dd, *J* = 3.5, 5.5 Hz, 2H), 7.89 (dd, *J* = 3.4, 5.6 Hz, 2H); ^{13}C NMR ($CDCl_3$ 75 MHz) δ 104.8, 123.9, 124.0, 131.8, 134.9, 166.7. This spectral data are consistent with the literarute values.[50]



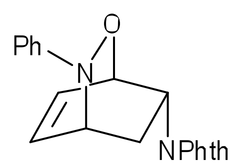
Oxetane (±)-152: (7 mg, 14%); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.04 (td, *J* = 8.0, 12.0 Hz, 1H), 3.82 (ddd, *J* = 4.6, 7.6, 12.0 Hz, 1H), 6.07 (dd, *J* = 7.2, 11.6 Hz, 1H), 6.33 (q, *J* = 7.2 Hz, 1H), 6.40 (ddd, *J* = 1.2, 5.0, 8.3 Hz, 1H), 6.88 (ddd, *J* = 0.8, 6.8, 11.5 Hz 1H), 7.78-7.80 (m, 2H), 7.92-7.94 (m 2H), 10.15 (d, *J* = 7.2 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 33.8, 74.9, 77.8, 123.9, 129.8, 131.9, 134.9, 150.5, 167.4, 191.3.



***N*-(2,4-Cyclohexadien-1-yl)phthalimide bisepoxide (±)-153**: (14 mg, 29%); mp 205–207 ^{0}C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.13 (ddd, *J* = 2.6, 6.6, 15.0 Hz, 1H), 2.40 (ddd, *J* = 2.4, 9.2, 14.8 Hz 1H), 3.26 (dd, *J* = 2.6, 3.8, Hz, 1H), 3.30 (td, *J* = 2.4, 4.0 Hz, 1H), 3.54-3.56 (m, 1H), 3.58-3.60 (m, 1H), 4.59 (ddd, *J* = 2.4, 6.8, 9.4 Hz, 1H), 7.75-7.77 (AA'BB'. 2H), 7.86-7.88 (AA'BB' 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 26.0, 43.5, 47.3, 49.3, 49.7, 50.7, 123.7, 131.9, 134.6, 168.0. Anal. Calcd. for $C_{14}H_{11}NO_4$: C, 65.36; H, 4.31. Found: C, 65.15; H, 4.36.

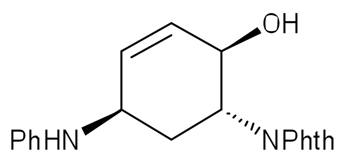


***N*-(2,3-Epoxy-4R*,5S*-dihydroxycyclohex-1R*-yl)phthalimide (±)-154**: In a 10 mL round-bottom flask, endoperoxide (±)-**119** (150 mg, 0.584 mmol) was dissolved in dry CH_2Cl_2 (5 mL) at room temperature. To the stirring solution Grubb's II catalyst (50 mg 10 mol%) was added and the mixture was stirred for 30 min. The mixture was concentrated under reduced pressure and applied to a wet (hexane) column of silica. The column was eluted with ethyl acetate and hexane mixture (1:4) for a while and then left to stand overnight. Further elution, (100% ethyl acetate) gave a colorless solid (40 mg, 26%). mp 215–218 ^{0}C; ^{1}H NMR (CH_3OD, 400 MHz) δ 1.81-1.91 (m, 1H), 1.98 (q, *J* = 12.0 Hz, 1H), 3.38 (dd, *J* = 1.5, 3.6 Hz, 1H), 3.45 (dd, *J* = 1.5, 3.6 Hz, 1H), 3.64 (ddd, J = 3.6, 8.4, 12.0 Hz, 1H), 3.87 (dd, *J* = 1.5, 8.5 Hz, 1H), 4.58 (dd, *J* = 6.9, 11.4 Hz, 1H), 7.78-7.90 (m, 4H); ^{13}C NMR (CH_3OD, 75 MHz) δ 35.3, 46.6, 58.8, 59.8, 68.3, 74.8, 124.4, 133.3, 135.8, 169.1. FAB-HRMS m/z 276.0875 (Calcd. for $C_{14}H_{14}NO_5$ (M+H) m/z 276.0872). Hydrolysis of this epoxide in a fashion similar to that previously describe gave *N*-(2S*,3R*,4S*,5R*-tetrahydroxycyclohex-1S*-yl)phthalimide (74%).

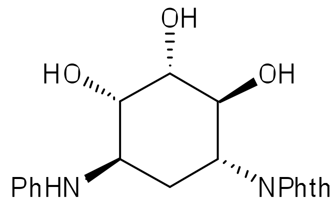


3-Phenyl-7-phthalimido-2-oxa-3-azabicyclo[2.2.2]oct-5-ene (±)-158: In a 25 mL round-bottom flask, nitrosobenzene (220 mg, 2.04 mmol) was dissolved in dry CH_2Cl_2 (8 mL) at room temperature under nitrogen. Diene (±)-**118** (230 mg, 1.02 mmol) was added in one portion and the mixture was stirred for 2 h. The reaction mixture was concentrated under reduced pressure. The residue was purified by column chromatography (SiO_2, hexane-ethyl acetate = 4:1) to afford a colorless solid (224 mg, 67%). mp = 148 – 151 ^{0}C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.59 (td, *J* = 3.6, 13.6 Hz, 1H), 2.81 (ddd, *J* = 3.2, 9.6, 13.2 Hz, 1H), 4.63-4.67 (m, 1H), 4.90 (td, *J* = 4.0, 9.6 Hz, 1H), 5.01 (dt, *J* = 1.6, 5.2 Hz, 1H), 6.38 (ddd, *J* = 1.8, 6.4, 8.2 Hz, 1H), 6.53 (ddd, *J* = 1.6, 5.6, 8.4 Hz, 1H), 6.96 (t, *J* =

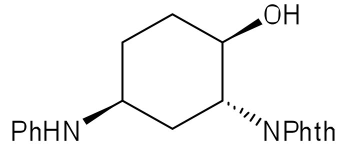
7.6 Hz, 1H), 7.03 (d, *J* = 7.6 Hz, 2H), 7.24 (t, *J* = 7.6, Hz, 2H), 7.70-7.84 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 27.6, 48.2, 57.1, 69.4, 117.7, 122.5, 123.3, 128.4, 128.7, 131.7, 132.6, 134.3, 151.8, 168.5. Anal. Calcd. for $C_{20}H_{16}N_2O_3$: C, 72.28; H, 4.85; N, 8.43. Found: C, 72.11, H, 4.89, N, 8.46.



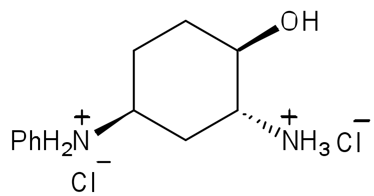
***N*-[(1S*,2S*,5S*)-2-Hydroxy-5-(phenylamino)cyclohex-3-enyl]phthalimide (±)-159**: To a stirring solution of olefin (±)-**158** (200 mg, 0.600 mmol) in a mixture of CH_3CN (8 mL) and water (0.7 mL) was added $Mo(CO)_6$ (158 mg, 0.600 mmol) and the mixture was heated at reflux for 1 h. The reaction mixture was concentrated under reduced pressure and applied to a column of silica. Elution (hexane-ethyl acetate = 1:1) gave a light yellow foamy solid (90 mg, 45%). mp 73-75 ^{0} C; ^{1}H NMR (CD_3OD, 400 MHz) δ 2.05 (br d, *J* = 13.2 Hz, 1H), 2.77 (dt, *J* = 4.8, 13.2 Hz, 1H), 4.23 (br s, 1H), 4.39 (ddd, *J* = 3.4, 9.8, 13.2 Hz 1H), 4.84 (dd, *J* = 1.4, 9.8, Hz, 1H), 5.82-5.95 (m, 2H), 6.64 (d, *J* = 7.6 Hz, 2H), 6.71 (d, *J* = 7.2 Hz, 1H), 7.17 (dd, *J* = 7.0, 8.6 Hz, 2H), 7.65-7.80 (m, 4H); ^{13} C NMR ($CDCl_3$, 100 MHz) δ 29.9, 48.0, 51.2 68.4, 113.3, 117.9, 123.4, 128.4, 129.6, 131.9, 133.8, 134.2, 146.7, 169.0. FAB-HRMS m/z 334.1321 (calcd for $C_{20}H_{18}N_2O_3$ (M+) m/z 334.1317).



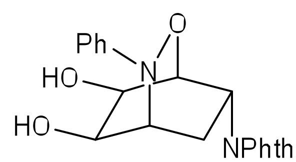
***N*-[(1S*,2R*,3R*4R*,5S*)-2,3,4-Trihydroxy-5-phenylamino)cyclohexyl]phthalimide (±)-160**: To a stirring solution of olefin (±)-**159** (50 mg, 0.15 mmol) in acetone (0.8 mL) was added a solution of *N*-methylmorpholine *N*-oxide (30.0 mg, 0.230 mmol) in water (0.3 mL) followed by a solution of OsO_4 in toluene (0.1 mL, 10 mol%). The reaction mixture was stirred for 15 h at room temperature and then $Na_2S_2O_4$ (26 mg) was added and stirred for another 30 min. The reaction mixture was concentrated under reduced pressure and applied to a column of silica. Elution (hexane-ethyl acetate = 1:4) gave a colorless solid (18 mg, 33%). mp 253-255 ^{0} C; ^{1}H NMR (CD_3OD, 300 MHz) δ 1.78 (br d, *J* = 13.3 Hz, 1H), 3.00 (dt, *J* = 3.9, 13.3 Hz, 1H), 3.70-3.78 (m and dd *J* = 2.7, 9.3, Hz, 2H), 4.11 (narrow t, *J* = 2.6 Hz, 1H), 4.43 (ddd, *J* = 4.2, 10.8, 13.2 Hz, 1H), 4.55 (d, *J* = 9.6, 10.2 Hz, 1H), 6.62 (t, *J* = 7.2 Hz, 1H), 6.72 (d, *J* = 8.4 Hz, 2H), 7.11 (dd, *J* = 7.5, 8.4 Hz, 2H), 7.76-7.83 (m, 4H); ^{13}C NMR (CD_3COCD_3, 75 MHz) δ 28.1, 51.6, 53.3, 69.9, 71.9, 73.7, 113.6, 117.4, 123.7, 129.8, 132.7, 135.1, 148.6, 168.8. FAB-HRMS m/z 369.1447 (calcd for $C_{20}H_{21}N_2O_5$ (M+H) m/z 369.1450).



***N*-[(1S*,2S*,5R*)-2-Hydroxy-5-(phenylamino)cyclohexyl]phthalimide (±)-161**: In a hydrogenation container olefin (±)-**158** (0.3 g, 0.9 mmol) was dissolved in methanol (30 mL) at room temperature. To the reaction mixture was added an aqueous slurry of Raney-Ni (0.5 mL) catalyst and the mixture was stirred under hydrogen (40 psi) for 4 h. The reaction mixture was filtered through celite and concentrated under reduced pressure. The residue was re-dissolved in ethyl acetate, adsorbed to silica and then applied to a column of silica. Elution (hexane-ethyl acetate = 1:1) gave a light yellow solid (225 mg, 74%). mp 242–245 ^{0}C; ^{1}H NMR (CD_3OD, 400 MHz) δ 1.74-2.05 (m, 5H), 2.51 (dt, *J* = 3.6, 13.1 Hz 1H), 3.80 (br s, 1H), 4.27-4.40 (m, 2H), 6.59 (t, *J* = 7.6 Hz, 1H), 6.69 (d, *J* = 7.6 Hz, 2H), 7.09 (t, *J* = 7.6 Hz, 2H) 7.74-7.83 (m, 4H); ^{13}C NMR (CD_3OD, 100 MHz) δ 29.4, 30.3, 33.4, 54.1, 70.3, 114.6, 118.1, 124.1, 130.2, 133.5, 135.3, 149.2, 170.4, one signal obscured by solvent. Anal. Calcd for $C_{20}H_{20}N_2O_3$: C, 71.41; H, 5.99. Found: C, 71.50; H, 6.04.

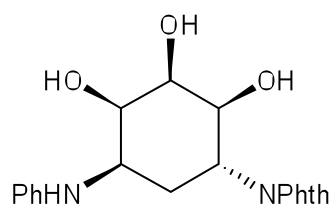


(±)-162: A round-bottomed flask was charged with diamino alcohol (±)-**161** (50.0 mg, 0.148 mmol) and 6N HCl (3 mL). The mixture was heated at reflux for 15 h. The reaction mixture was dried, redissolved in deionized water (6 mL) and then extracted with ethyl acetate (5 X 3 mL). The aqueous solution was concentrated and dried under high vacuum to afford a colorless foamy solid (43 mg, 100%). ^{1}H NMR (CD_3OD, 400 MHz) δ 1.62-1.89 (m, 5H), 2.16-2.26 (m, 1H), 3.35-3.43 (m, 1H), 3.50-3.58 (m, 1H), 3.76-3.83 (m, 1H), 7.35-7.46 (m, 5H); ^{13}C NMR (CD_3OD, 75 MHz) δ 24.8, 28.3, 29.4, 52.3, 59.3, 69.4, 125.1, 131.4, 131.7, 134.9.

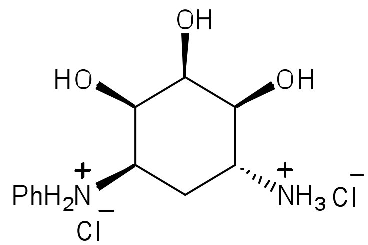


3-Phenyl-7-phthalimido-2-oxa-3-azabicyclo[2.2.2]oct-5-ene-5,6-diol (±)-163: To a stirring solution of olefin (±)-**158** (70 mg, 0.21 mmol) in acetone (2.5 mL) was added a solution of *N*-methylmorpholine *N*-oxide (73 mg, 0.62 mmol) in water (0.5 mL) followed by a solution of OsO_4 in toluene (0.2mL, 15 mol%). The reaction mixture was stirred for 10 h at room temperature and then $Na_2S_2O_4$ (52 mg) was added and stirred for another 30 min. The mixture was concentrated and adsorbed to silica using CH_2Cl_2. This was layered onto a silica gel column. Elution (hexane-ethyl acetate = 1:1) gave a colorless solid (63 mg, 81%). mp 183–186 ^{0}C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.29 (ddd, *J* = 4.8, 11.6, 14.4 Hz, 1H), 2.72 (ddd, *J* = 1.2, 7.6, 14.4 Hz, 1H), 3.44 (d, *J* = 7.6 Hz, 1H, OH), 3.71 (d, *J* = 10.0 Hz, 1H, OH), 3.98-4.13 (m, 2H), 4.34 (t, *J* = 7.6 Hz, 1H), 4.58 (dt, *J* =

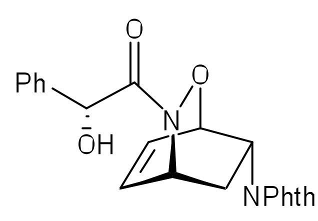
3.2, 9.2 Hz, 1H), 4.88 (ddd, *J* = 4.0, 8.0, 11.2 Hz, 1H), 7.04 (t, *J* = 7.2 Hz, 1H), 7.22 (d, *J* = 8.0 Hz, 2H), 7.24 (dd, *J* = 7.2, 8.8 Hz, 2H), 7.73-7.86 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 19.7, 45.0, 59.5, 64.1, 66.0, 76.6, 116.1, 122.8, 123.8, 129.4, 131.5, 134.7, 149.8, 168.6. Anal. Calcd. for $C_{20}H_{18}N_2O_5.0.6H_2O$: C, 63.69; H, 5.13. Found: C, 63.66; H, 4.93.



***N*-[(1S*,2R*,3S*,5S*)-2,3,4-Trihydroxy-5-(phenylamino)cyclohexyl]phthalimide (±)-164**: In a hydrogenation container, diol (±)-**163** (0.160 g, 0.437 mmol) was dissolved in methanol (30 mL) at room temperature. To the reaction mixture, aqueous slurry of Raney-Ni (0.3 mL) catalyst was added and the mixture was stirred under hydrogen (40 psi) for 2 h. The reaction mixture was filtered through celite. The filtrate was concentrated, adsorbed to silica gel and then applied to a column of silica. Elution (100% ethyl acetate) gave a colorless solid (91 mg, 57%). mp 233–235 ^{0}C; ^{1}H NMR (CD_3OD, 400 MHz), δ 2.03 (td, *J* = 3.8, 13.2 Hz, 1H), 2.31 (dt, *J* = 3.2, 13.2 Hz, 1H), 3.84 (dd, *J* = 3.0, 4.3, Hz, 1H), 3.99-4.03 (m, 1H), 4.21 (t, *J* = 2.6 Hz, 1H), 4.34 (dd, *J* = 2.6, 10.8, Hz, 1H), 4.64 (ddd, J = 3.8, 10.8, 13.2 Hz, 1H), 6.57 (t, *J* = 7.6 Hz, 1H), 6.62 (d, *J* = 8.0 Hz, 2H), 7.08 (t, *J* = 7.6 Hz, 2H), 7.75-7.83 (m, 4H); ^{13}C NMR (CD_3OD, 100 MHz) δ 30.1, 48.3, 54.9, 70.2, 70.7, 76.4, 114.2, 117.9, 124.1, 130.3, 133.4, 135.4, 149.4, 170.3. FAB-HRMS m/z 369.1448 (Calcd for $C_{20}H_{21}N_2O_5$ (M+H) m/z 369.1450)

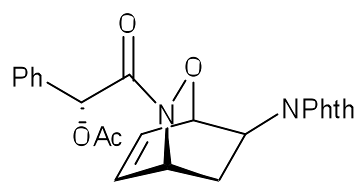


(±)-165: In a 10 mL round-bottomed flask was charged triol (±)-**164** (35.0 mg, 0.095 mmol) and 6N HCl (3 mL). The mixture was heated at reflux for 15 h. The reaction mixture was dried re-dissolved in deionized water (6 mL) and then extracted with ethyl acetate (5 mL X 3). The aqueous solution was concentrated, dried under high vacuum to afford a colorless solid (17 mg, 57%). ^{1}H NMR (CD_3OD, 300 MHz), δ 1.74-1.89 (m, 1H), 2.20 (d, *J* = 13.8 Hz, 1H), 3.56-3.69 (m, 2H), 3.87-3.94 (s, 1H), 3.98-4.04 (s, 1H), 4.13-4.18 (s, 1H), 7.48-7.61 (m, 5H); ^{13}C NMR (CD_3OD, 75 MHz) δ 26.4, 47.8, 65.4, 68.5, 71.9, 74.9, 125.0, 131.1, 131.7, 136.4.



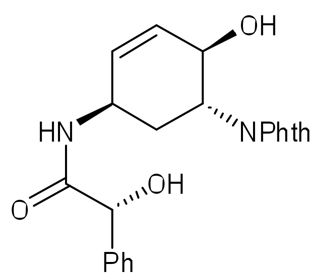
3-Mandeloyl-7-phthalimido-2-oxa-3-azabicyclo[2.2.2]oct-5-enes (±)-167: To a rapidly stirring solution of (±)-**118** (0.600 g, 2.67 mmol) and $NaIO_4$ (0.683 g, 3.19 mmol) in CH_2Cl_2 (10 mL), DMF (10 mL) and water (5 mL) was added, over a period of 45 min, a solution of (±)-mandelohydroxamic acid (0.441 g, 2.64 mmol) in DMF (10 mL). The mixture was stirred for an additional 3 h, then poured into water and extracted several times with CH_2Cl_2. The combined extracts were washed with brine, dried (Na_2SO_4) and concentrated. The residue was purified by column chromatography (SiO_2, hexane-ethyl acetate, 1:1) to afford a colorless solid (0.795 g, 77%). From ^{1}H NMR, mixture of (±)-**167**, (±)-**168** and (±)-**169** (5:3:2). Recrystallization (MeCN) of two batches gave (±)-**167** (0.513 g, 25%). mp 160-162 ^{0}C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.49 (ddd, *J* = 2.7, 4.5, 13.5, 1H), 2.60 (ddd, *J* = 3.3, 9.0, 13.5 Hz, 1H), 4.15 (d, *J* = 7.5 Hz, 1H), 4.73 (t, *J* = 3.9 Hz, 1H), 4.81 (td, *J* = 4.5, 9.0 Hz, 1 H), 5.25-5.36 (m and d, *J* = 6.6 Hz, 2 H total), 5.79 (t, *J* = 6.6 Hz, 1 H), 6.57 (t, *J* = 6.6 Hz, 1 H), 7.19-7.30 (m, 5 H), 7.65-7.80 (m, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 26.6, 47.6, 48.6, 71.6, 71.8, 123.5, 127.8, 128.08, 128.12, 128.2, 131.4, 134.47, 134.51, 137.5, 168.1, 173.1. Anal. Calcd for $C_{22}H_{18}N_2O_5$: C, 67.69; H, 4.64. Found: C, 67.48; H, 4.65.

(7*S*)-3-[(*R*)-Mandeloyl]-7-phthalimido-2-oxa-3-azabicyclo[2.2.2]oct-5-ene [(+)-167]: Reaction of (±)-**118** (0.300 g, 1.33 mmol) with the nitrosoacyl generated from (*R*)-mandelohydroxamic acid (0.212 g, 1.27 mmol) was carried out in a fashion similar to the typical procedure for 14-16 using (±)-mandelohydroxamic acid. Purification of the residue by column chromatography (silica gel, hexanes-EtOAc, 1:1) gave a colorless solid (0.316 g, 62%). Recrystallization (MeCN) gave (+)-**167** (57 mg, 11%); mp 180-183 ˚C; $[\alpha]_D$ = +126.5 (c 0.429, CH_2Cl_2). The ^{1}H NMR spectrum of this product was identical to that of the racemic compound.

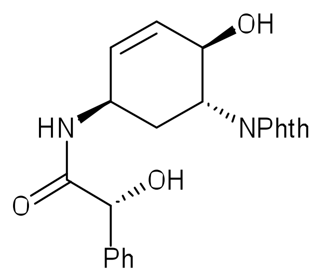


Reaction of 3-Mandeloyl-7-phthalimido-2-oxa-3-azabicyclo[2.2.2]oct-5-ene with Acetic Anhydride(±)-168*: To a mixture of **(±)-167, (±)-168**, and (±)-**179** (80 mg, 0.20 mmol) in CH_2Cl_2 (1 mL), at r.t. was added dropwise pyridine (0.10 mL, 1.0 mmol) followed by Ac_2O (0.10 mL, 1.1 mmol). The mixture was stirred for 12 h, diluted with CH_2Cl_2 and quenched with 1 M HCl. The mixture was extracted several times with CH_2Cl_2 and the combined extracts were washed with brine, dried (Na_2SO_4), and concentrated. Purification of the residue by preparative TLC (hexane-EtOAc = 7:3) gave

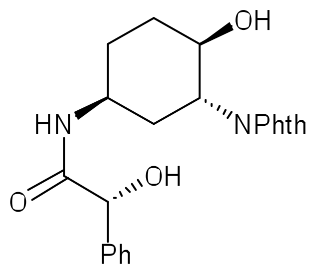
(±)-**168*** (17 mg, 19%) as a colorless oil, followed by a mixture of (±)-**167*** and (±)-**169*** (ca. 8:3 ratio, 39 mg, 41%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.16 (s, 3 H), 2.38-2.43 (m, 2 H), 4.47-4.55 (m, 1 H), 5.00-5.05 (m, 1 H), 5.33-5.38 (br s, 1 H), 6.13 (s, 1 H), 6.55 (br t, J = 6.8 Hz, 1 H), 6.89 (br t, J = 7.2 Hz, 1 H), 7.39-7.55 (m, 5 H), 7.70-7.80 (m, 4 H);^{13}C NMR (75 MHz, $CDCl_3$) δ 20.9, 26.9, 47.3, 48.9, 72.2, 73.7, 123.5, 128.4, 128.5, 128.9, 129.2, 131.5, 134.3, 134.5, 135.0, 168.2, 170.7; one CO signal not observed.HRMS (ESI): m/z [M + Na]$^+$ calcd for $C_{24}H_{20}N_2NaO_6$: 455.1219; found: 455.1216.



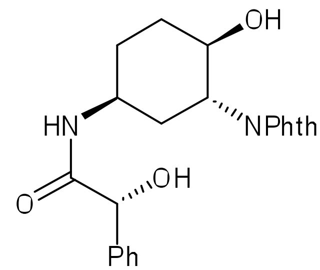
(2R*)-2-Hydroxy-N-[(1R*,4R*,5R*)-4-hydroxy-5-phthalimidocyclohex-2-enyl]-2-phenylacetamide (±)-170: To a flame dried 10 mL Schlenk flask under nitrogen at room temperature was charged titanocene dichloride (93 mg, 0.38 mmol), activated zinc dust (50 mg, 0.75 mmol) and freshly distilled THF (1.2 mL). The mixture was stirred for 45 min. The mixture turned red to olive green. The green mixture was cooled to - 30°C and to the cooled mixture was added a solution of (±)-**167** (60 mg, 0.15 mmol) in methanol (1.5 mL). The reaction mixture was stirred for 1 h maintaining the temperature between -15 to -30 °C. The reaction mixture was warmed to room temperature and quenched with sat. NH_4Cl (5 mL) solution. The whole mixture was filtered through celite and aqueous layer was extracted with ethyl acetate (3 X 5 mL). The combined ethyl acetate extracts were washed with brine, dried (Na_2SO_4), concentrated and applied to a column of silica. Elution (100% ethyl acetate) gave a colorless solid (40 mg, 66%). mp = 223-225 °C; ^{1}H NMR (CD_3OD, 400 MHz) δ 1.75 (tdd, *J* = 1.6, 3.2, 14.0 Hz, 1H), 2.64 (dt, *J* = 4.8, 14.0 Hz, 1H), 4.40 (ddd, J = 3.1, 9.4, 13.9 Hz, 1H), 4.49-4.54 (m, 1H), 4.98 (s, 1H), 5.75-5.81 (m, 1H), 5.94 (br d, *J* = 10.0 Hz, 1H), 7.24 (t, *J* = 7.6 Hz, 1H), 7.31 (t, *J* = 8.0 Hz, 2H), 7.45 (d, *J* = 7.6 Hz, 1H), 7.74-7.78 (m, 2H), 7.81-7.84 (m, 2H), one signal obscured by solvent; ^{13}C NMR (CD_3OD, 100 MHz) δ 32.4, 45.8, 52.1, 67.9, 75.8, 124.2, 127.4, 128.4, 129.4, 129.7, 133.4, 135.6, 136.5, 141.8, 170.1, 175.2; HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{22}H_{20}N_2NaO_5$: 415.1270; found: 415.1274.



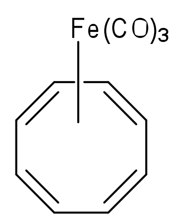
(2R)-2-Hydroxy-N-[(1R,4R,5R)-4-hydroxy-5-phthalimidocyclohex-2-enyl]-2-phenylacetamide (-)-170: The reduction of (+)-**167** (50 mg, 0.13 mmol) in methanol (1.5 mL) with titanium was carried out in a fashion similar to the reduction of (±)-167. Purification by column chromatography (100% ethyl acetate) gave a colorless foamy solid (27 mg, 54%). mp = 193-195 °C; $[\alpha]_D$ = - 106 (c 0.270, MeOH); The ^{1}H NMR spectrum was identical to the racemic compound.



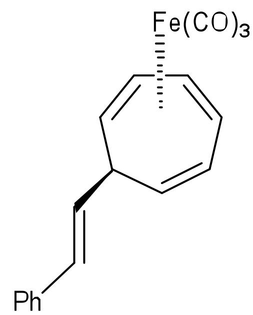
(2R*)-2-Hydroxy-*N*-[(1S*,4R*,5R*)-4-hydroxy-5-phthalimidocyclohexyl]-2-phenylacetamide (±)-171: To a parr apparatus was charged olefin (±)-**170** (30 mg, 0.077 mmol), methanol (6 mL) and 10% of Pd/C (ca. 2.5 mg) catalyst. The mixture was stirred at room temperature under hydrogen (40 psi) for 2 h. The reaction mixture was filtered through celite. The filtrate was concentrated and applied to a column of silica. Elution (100% ethyl acetate) gave a colorless solid (23 mg, 76%). mp = 150-152 °C; ^{1}H NMR (CD_3OD, 300 MHz) δ 1.50-2.05 (m, 6H), 2.43 (dt, J = 3.0, 12.3 Hz, 1H), 4.04-4.34 (m, 3H), 5.03 (br s, 1H), 7.23-7.51 (5H, Ar), 7.71-7.84 (m, 4H, Ar), one signal obscured by the solvent; ^{13}C NMR (CD_3OD, 75 MHz) δ 29.0, 30.7, 33.3, 46.4, 54.1, 69.7, 75.6, 124.1, 128.4, 129.4, 129.8, 133.4, 135.4, 141.8, 170.2, 175.1. HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{22}H_{22}N_2NaO_5$: 417.1426; found 417.1422



(2R)-2-Hydroxy-*N*-[(1S,4R,5R)-4-hydroxy-5-phthalimidocyclohexyl]-2-phenylacetamide (-)-171: The reduction of (-)-170 (25 mg, 0.064 mmol) with H_2 in the presence of 10% Pd/C was carried out in a fashion similar to the reduction of (±)-170. Purification by column chromatography (100% ethyl acetate) gave colorless oil (20 mg, 80%). $[\alpha]_D$ = - 84 (c 0.20, MeOH); The ^{1}H NMR spectral data was identical to the racemic compound.

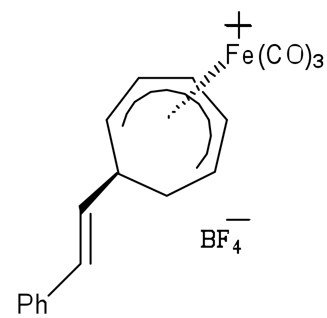


Tricarbonyl(η^4-cyclooctatetraene)iron(0) (7): To a 500 mL round-bottomed flask was added cyclooctatetraene (5.0 mL, 48 mmol) dissolved in benzene (200 mL). Iron pentacarbonyl (14 mL, 96 mmol) was added followed by the addition of trimethylamine N-oxide dihydrate (21.33 g, 191.9 mmol). The reaction mixture was heated at reflux for 2 h then filtered and concentrated. The solid residue was washed several times with benzene and the washings were filtered and concentrated. The deep-brownish residue was purified by column chromatography (SiO_2, hexane-ethyl acetate = 20:1) to afford a deep brown crystal like solid (9.83 g, 100%). mp 82 - 86^{0}C (lit.[27], 92 – 93.5^{0}C); IR (KBr, cm^{-1}) 2043, 1960; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 5.25 (s, 8H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 100.1, 212.5.

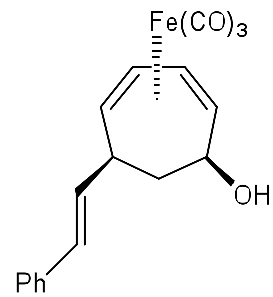


Tricarbonyl(η^4–6-styrylcyclohepta-1,3,5-triene)iron (0) (±)-14: To a 1 L round-bottomed flask, (cyclooctatetraene)$Fe(CO)_3$ (10.0 g, 40.9 mmol) was dissolved in dry acetone (50 mL) at -23 ^{0}C under N_2. Dry pyridine (3 mL, 40.9 mmol) was added and mixture stirred for 5 min. A solution/suspension of tropylium tetrafluoroborate (8.73 g, 49.1 mmol) in dry acetone (400 mL) was added and the reaction mixture was stirred for 8 h maintaining the temperature at -23 ^{0}C. The reaction mixture was warmed to room temperature and stirred overnight. The clear reddish solution was concentrated under reduced pressure and dried. To the solid residue was added ether (200 mL) and the slurry stirred for 2 h and filtered. The above process was repeated three times with the solid residue. The combined filtrates were concentrated and the residue was purified by column chromatography (100% hexane) to give a bright yellow solid (10.42 g, 75%). mp 43–47 ^{0}C (lit. 60, mp 64-66 ^{0}C); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.10-3.03 (m, 1H), 3.34-

3.21 (m, 2H), 5.18-5.10 (m, 1H), 5.43-5.33 (m, 2H), 5.92-5.82 (m, 2H), 6.46 (d, *J* = 16.0 Hz, 1H), 7.37-7.19 (m, 5H); ^{13}C NMR (CDCl$_3$, 75 MHz) δ 46.9, 55.8, 64.9, 87.6, 95.3, 126.4, 127.4, 127.6, 128.9, 129.1, 130.4, 134.2, 137.6, 211.3. The NMR spectral data obtained for the product were consistent with the literature values.[60]

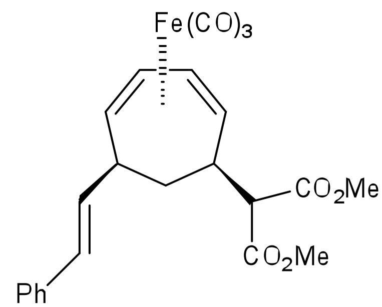


Tricarbonyl(η^5-6-styrylcyclohepta-2,4-dien-1-yl)iron(+1) tetrafluoroborate (±)-172: To a 250 mL round-bottomed flask, (7-styrenyl-1,3,5-cycloheptatriene)Fe(CO)$_3$ (8.0 g, 24 mmol) was dissolved in acetic anhydride (150 mL) at 0 ^{0}C with stirring. An ice-cold solution of fluoroboric acid (60 wt%, 23.40 mL, 240.0 mmol) in acetic anhydride (25 mL) was added dropwise to the stirring mixture. After 20 min of stirring a yellow-gray precipitate began to form. The reaction mixture was added dropwise into a large excess of ether (3.5 L). The solid yellow cation was isolated by filtration and dried under high vacuum (8.88 g, 88%). IR (KBr) 2112, 2067, 760, 697 cm^{-1}; ^{1}H NMR (d$_6$-acetone, 300 MHz) δ 1.23-1.34 (m, 1H), 2.50-2.63 (m, 1H), 4.25 (br d, *J* = 8.0 Hz, 1H), 4.80-4.96 (m, 2H), 5.93 (dd, *J* = 16.0, 8.0 Hz, 1H), 6.29 (m, 1H), 6.62 (m, *J* = 16.0 Hz, 2H), 7.33 (m, 5H), 7.47 (tq, *J* = 6.0, 1.0 Hz, 1H). The NMR spectral data obtained for the product were consistent with the literature values.[60]

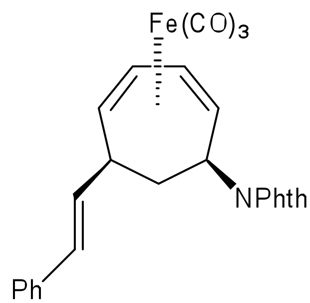


Tricarbonyl(η^4-6-styrylcyclohepta-2,4-diene-1-ol)iron (±)-173: In a 500 mL round bottomed flask, solid cation (±)-**172** (4.10 g, 9.71 mmol) was dissolved in water (250 mL) and the mixture was stirred for 20 min. To the clear light yellow solution was added solid sodium bicarbonate (8.07 g, 95.2 mmol). After a few minutes, a yellow colored solid began to precipitate. The reaction mixture was stirred for 45 min, at which time it was extracted several times with dichloromethane. The combined extracts were washed with brine, dried ($MgSO_4$) and concentrated. The yellow sticky, foamy residue was purified by column chromatography (Al_2O_3, hexane-ethyl acetate = 4:1) to give the product as a yellow solid (2.37 g, 70%). mp 122 - 126^{0}C; IR (KBr) 3200-3400, 2049, 1979, 746, 693 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.04 (br d, *J* = 12.0 Hz, 1H), 1.64 (d, *J* = 6.0 Hz, 1H), 1.75 (br d, *J* = 12.0 Hz, 1H), 2.81-2.96 (m, 3H), 4.12 (pentet, *J* = 5.5 Hz, 1H), 5.30-5.37 (m, 1H), 5.38-5.45 (m, 1H), 5.98 (dd, *J* = 8.0, 16.0 Hz, 1H), 6.37 (d, *J* =

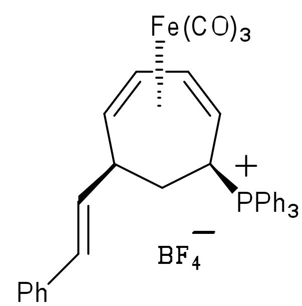
16.0 Hz, 1H), 7.17-7.38 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 38.6, 43.1, 62.0, 62.2, 70.8, 88.17, 88.2, 126.4, 127.6, 128.8, 128.9, 135.7, 137.4, 210.0.



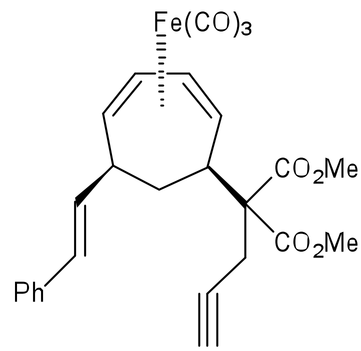
Tricarbonyl[dimethyl 2-(6-styryl-2-4-cycloheptadien-1-yl)propanedioate]iron (±)-177: To a stirring solution of dimethyl malonate (0.060 mL, 0.43 mmol) in THF (6 mL) at 0 ^{0}C under nitrogen was added a solution of n-BuLi (0.20 mL, 1.6M in hexane, 0.43 mmol) and stirred for 30 min. To the stirring mixture was added cation (±)-**172** (100 mg, 0.24 mmol) and the mixture was stirred for an additional 45 min and gradually warmed to room temperature. The reaction was quenched with water and extracted several times with ether, washed with brine, dried (Na_2SO_4) and concentrated. The residue was purified by column chromatography (SiO_2, hexane - ethyl acetate = 7:3) to give a yellow oil (50 mg, 46%). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.83-0.85 (m, 1H), 1.05 (q, J = 12.4 Hz, 1H), 2.74-2.84 (m, 3H), 2.90 (d, J = 6.8 Hz, 1H), 3.29 (d, J = 5.6 Hz, 1H), 3.72 (s, OMe, 3H), 3.74 (s, OMe, 3H), 5.30 (pentet, J = 4.4 Hz, 2H), 5.93 (dd, J = 8.8, 16.0 Hz, 1H), 6.33 (d, J = 16.0 Hz, 1H), 7.18-7.32 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 33.5, 39.1, 42.9, 52.7, 58.6, 59.8, 61.6, 87.9, 88.3, 126.2, 127.4, 128.7, 128.8, 136.3, 137.3, 168.6. The signal for the metal carbonyl was not observed. FAB-HRMS (calcd for $C_{23}H_{22}O_7$ Fe(M^+) 466.0715), m/z 466.0707.



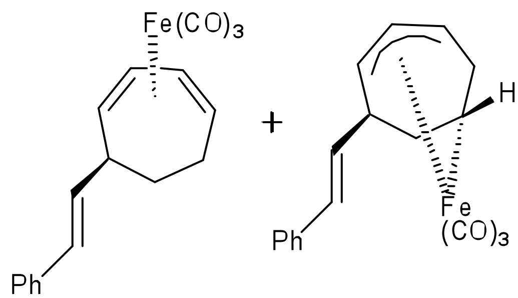
Tricarbonyl[(6-styryl-2,4-cycloheptadien-1-yl)phthalimide]iron (±)-174: To a stirring suspension of cation (±)-**172** (1.00 g, 2.37 mmol) in dry CH_2Cl_2 (100 mL) under N_2 at room temperature was added solid potassium phthalimide (0.659 g, 3.56 mmol). The reaction mixture was stirred for 12 h and then quenched with water. The mixture was extracted several times with CH_2Cl_2, dried (Na_2SO_4) and concentrated. The residue was purified by column chromatography (SiO_2, hexane-ethyl acetate = 4:1) to afford a light yellow solid (820 mg, 72%). mp 185 – 188 ^{0}C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.62-1.68 (m, *J* = 12.6 Hz, 1H), 2.13 (q, *J* = 12.6 Hz, 1H), 2.87 (br d, *J* = 7.5 Hz, 1H), 3.07-3.14(m, *J* = 3.9, 8.1 Hz, 2H), 4.88 (dd, *J* = 3.6, 12.6 Hz, 1H), 5.56 (dd, *J* = 5.1, 7.5 Hz, 1H), 5.69 (dd, *J* = 5.1, 7.5 Hz, 1H), 6.13 (dd, *J* = 8.1, 15.9 Hz, 1H), 6.50 (d, *J* = 16.0 Hz, 1H), 7.33-7.46 (m, 5H), 7.84 (dd, *J* = 3.0, 5.5 Hz, 2H), 7.94 (dd, *J* = 3.1, 5.6 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 33.8, 43.7, 50.8, 56.5, 61.9, 88.6, 89.6, 123.4, 126.4, 127.6, 128.8, 129.2, 132,2, 134.3, 135.5, 137.4, 168.2, 210.1. Anal. Calcd for $C_{26}H_{19}NO_5Fe$: C, 64.88; H, 3.98. Found: C, 64.85; H, 3.97.



Tricarbonyl[(6-styryl-2,4-cycloheptadien-1-yl)triphenylphosponium (1+) tetrafluoroborate]iron (±)-175: To a suspension of the iron cation (±)-**172** (300 mg, 0.710 mmol) in dichloromethane (15 mL) was added triphenylphosphine (0.186 g, 0.710 mmol) at room temperature under nitrogen. The mixture was stirred for 45 min, the clear light yellow solution was concentrated and dried. The glassy solid residue was washed with pentane and dried under high vacuum to afford a glassy light yellow solid (410 mg, 83%). mp 155-158 ^{0}C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.04-1.10 (m, *J* = 5.2, 12.0 Hz, 1H), 1.86 (br s, 1H), 2.72 (dd, *J* = 7.2, 15.6 Hz, 1H), 3.02 (d, *J* = 7.2 Hz, 1H), 3.13 (br t, *J* = 8.8 Hz, 1H), 4.22 (t, *J* = 12.4 Hz, 1H), 4.99 (br t, *J* = 5.2 Hz, 1H), 5.31 (m, 1H), 5.88 (dd, *J* = 8.4, 15.6 Hz, 1H), 6.44 (d, *J* = 15.6 Hz, 1H), 7.15-7.31 (m, 5H), 7.76-7.81 (m, 15H); ^{13}C NMR (CD_3COCD_3, 75 MHz) δ 30.1, 34.5 (d, J_{PC} = 35.8), 42.8 (d, J_{PC} = 14.1), 49.4 (d, J_{PC} = 6.4), 62.5, 88.4, (d, J_{PC} = 1.7), 90.9, 118.5, (d, J_{PC} = 81.3), 127.1, 128.3, 129.4, 129.5 (d, J_{PC} = 6.6), 130.0 (d, J_{PC} = 44.0), 131.4 (d, J_{PC} = 11.9), 134.4 (d, J_{PC} = 19.6), 135.1 (d, J_{PC} = 9.2), 136.0 (d, J_{PC} = 2.8), 206.4.

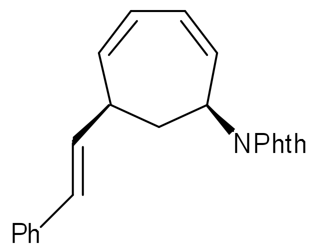


Tricarbonyl[dimethyl 2-propargyl-2-(6-styrenyl-2-4-cycloheptadien-1-yl)propanedioate]iron (±)-176: To a flame-dried 10 mL Schlenk flask was charged THF (4 mL), dimethyl propagyl malonate (0.100 mL, 0.462 mmol) and n-BuLi (0.200 mL, 2.5M in hexane, 0.497 mmol) at 0 ^{O}C under nitrogen. The mixture was stirred for 45 min, iron cation (±)-**172** (150 mg, 0.355 mmol) was added and stirred for another 3 h. The reaction mixture was quenched with water, extracted several times with ether, and the combined ether extracts were washed with brine, dried (Na_2SO_4) and concentrated. The residue was purified by column chromatography (SiO_2, hexane-ethyl acetate, 4:1) to afford a light yellow oil (136 mg, 77%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.90 (br m, *J* = 12.3 Hz, 1H), 1.38 (d, *J* = 12.4 Hz, 1H), 2.07 (narrow t, *J* = 2.1 Hz, 1H), 2.71-2.91 (m, 4H), 2.99-3.08 (m, 2H), 3.76 (s, OMe, 3H), 3.77 (s, OMe, 3H), 5.28 (m, *J* = 6.9 Hz, 2H), 5.93 (dd, *J* = 8.4, 15.9 Hz, 1H), 6.34 (d, *J* = 15.6 Hz, 1H), 7.19-7.35 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 22.7, 31.2, 42.3, 43.4, 52.9, 53.0, 58.2, 61.2, 62.9, 71.9, 79.3, 88.0, 89.2, 126.3, 127.5, 128.7, 136.4, 137.3, 169.8, 170.0. The signal for the metal carbonyl was not observed.

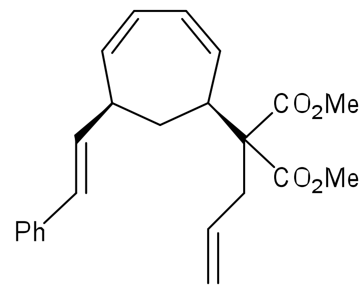


(±)-179 and (±)-180: A flame-dried 10 mL Schlenk flask was charged THF (2.5 mL), iron cation (±)-**172** (100 mg, 0.237 mmol) at 0 ^{0}C under nitrogen. To the stirring suspension was added $NaBH_3CN$ (0.023 g, 0.360 mmol) and the mixture was stirred for 30 min. The reaction mixture was warmed to room temperature and stirred for another 30 min. The light yellow mixture was quenched with water, extracted several times with ether, and the combined ether extracts were washed with brine, dried (Na_2SO_4) and concentrated. The residue was purified by column chromatography (SiO_2, hexane-ethyl acetate, 4:1) to afford a yellow oily fraction (64 mg, 81%). ^{1}H NMR ($CDCl_3$, 300 MHz) mixture, δ 1.11-1.19 (bm, 1H), 1.27 (dd, *J* = 4.5, 12.6 Hz, 1H), 1.57-1.70 (m, 1H), 2.03-2.30 (m, 3H), 2.43-2.62 (m, 1H), 2.72-2.87 (m, 3H), 3.01 (d, *J* = 7.5 Hz, 1H), 3.10 (md, *J* = 9.9 Hz, 1H), 3.22 (t, *J* = 6.6 Hz, 1H), 4.38-4.49 (m, 2H), 4.97 (bt, *J* = 8.4 Hz, 1H), 5.38-5.51 (m, 2H), 6.03-6.17 (m, *J* = 9 Hz, 2H), 6.40 (d, *J* = 15.6 Hz, 1H), 6.46 (d, *J* =

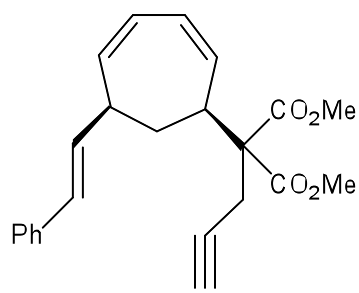
15.9 Hz, 1H), 7.27-7.49 (m, 10H); ^{13}C NMR ($CDCl_3$, 300 MHz) δ 16.4, 27.8, 29.9, 30.1, 30.3, 42.7, 58.1, 59.4, 61.3, 62.3, 74.6, 87.1, 88.9, 97.2, 126.1, 126.3, 127.1, 127.3, 128.3, 128.7, 128.73, 128.8, 137.4, 137.6, 137.8.



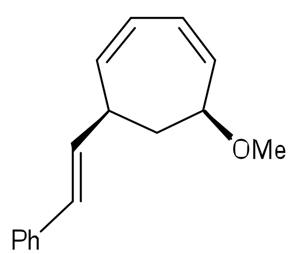
(6-Styrenyl-2,4-cyclohepta-1-yl)phthalimide (±)-181: In a 200 mL Schlenk flask, iron complex (±)-**174** (500 mg, 1.04 mmol) was dissolved in MeOH (75 mL) at room temperature under N_2. Solid ceric ammonium nitrate (1.71 g, 3.12 mmol) was added and the mixture was stirred for 1 h. After 2 h of stirring a white insoluble compound began to separate from the clear brown solution. The reaction mixture was stirred overnight and then quenched with water and extracted several times with CH_2Cl_2. The combined extracts were washed with brine, dried (Na_2SO_4) and concentrated. The residue was purified by column chromatography (SiO_2, hexane-ethyl acetate=3:1) to afford a light yellow solid. (315 mg, 88%). mp 110-112 ^{0}C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.05 (md, *J* = 13.2 Hz, 1H), 2.86 (td, *J* = 11.1, 13.2 Hz, 1H), 3.56-3.58 (m, 1H), 5.29 (d, *J* = 10.5 Hz, 1H), 5.78-5.89 (m, 4H), 6.18 (dd, *J* = 8.4, 15.9 Hz, 1H), 6.48 (d, *J* = 15.9 Hz, 1H), 7.21-7.35 (m, 5H), 7.72 (dd, *J* = 3.1, 5.4 Hz, 2H), 7.87 (dd, *J* = 3.1, 5.4 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 38.2, 44.0, 50.5, 123.3, 123.9, 124.0, 126.2, 127.3, 128.6, 129.8, 132.0, 132.2, 133.6, 134.1, 136.9, 137.2, 167.7. Anal. calcd for $C_{23}H_{19}NO_2$: C, 80.91; H, 5.61. Found: C, 80.61; H, 5.67.



Dimethyl 2-allyl-2-(6-styryl-2-4-cycloheptadien-1-yl)propanedioate (±)-182: A flame-dried 200 mL Schlenk flask was charged with freshly distilled ether (120 mL) at 0 °C under nitrogen. Dimethyl allylmalonate (1.00 mL, 6.16 mmol) was added followed by dropwise addition of a solution of n-butyl lithium (4.5 mL, 7.1 mmol, 1.6M in hexane). The mixture was stirred for 1 h. Solid iron cation (±)-**172** (2.0 g, 4.7 mmol) was added and stirred for 3 h at room temperature. The reaction mixture was quenched with water and extracted several times with ether. The combined ether extracts were washed with brine, dried (Na_2SO_4), and concentrated. The residue was purified by column chromatography (SiO_2, hexane-ethyl acetate = 4:1) to afford a mixture of product and dimethyl allylmalonate (2.608 g). The mixture (2.608 g) was dissolved in methanol (100 mL) and ceric ammonium nitrate (7.50 gm, 13.7 mmol) was added, and the mixture stirred for 1 h at room temperature. The mixture was concentrated, diluted with water and extracted several times with ether. The combined ether extracts were washed with brine, dried (Na_2SO_4), and concentrated. The residue was purified by column chromatography (SiO_2, hexane-ethyl acetate = 20:1) to give the product as a colorless oil (1.17 gm, 67%). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.68-1.55 (m, 1H), 2.09 (dd, J = 5.4, 13.3 Hz, 1H), 2.60 - 2.78 (dd, J = 8.2, 10.4 Hz, 2H), 3.11 (bd, J = 8.7 Hz, 1H), 3.38-3.48 (bm, 1H), 3.72 (s, 6H), 5.05 (br s, 1H), 5.08 (d, J = 7.5 Hz, 1H), 5.69-5.87 (br m, 5H), 6.11 (ddd, J = 1.1, 8.1, 15.7 Hz, 1H), 6.41 (d, J = 15.9 Hz, 1H), 7.34-7.15 (5H, Ar); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 37.9, 38.8, 43.0, 47.4, 52.5, 61.7, 119.1, 124.4, 124.7, 126.3, 127.3, 128.7, 129.6, 132.8, 133.2, 134.3, 137.0, 137.6, 171.4. ESI-HRMS m/z 389.1728 (calcd for $C_{23}H_{26}O_4Na$ m/z 389.1729).

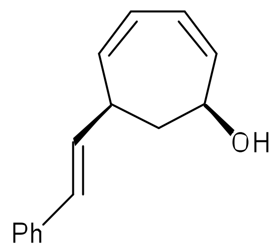


Dimethyl 2-propargyl-2-(6-styryl-2-4-cycloheptadien-1-yl)propanedioate (±)-183: To a stirring solution of iron complex (±)-**176** (136 mg, 0.270 mmol) in methanol (4 mL) at room temperature under nitrogen was added ceric ammonium nitrate (0.44 g, 0.81 mmol). The mixture was stirred for 2 h, and then concentrated. Water was added to the residue and the mixture was extracted several times with CH_2Cl_2. The combined CH_2Cl_2 extracts were washed with brine, dried (Na_2SO_4) and concentrated. The residue was purified by column chromatography (SiO_2, hexane-ethyl acetate, 4:1) to afford a yellowish liquid (42 mg, 59%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.69 (md, *J* = 12.0 Hz, 1H), 2.06 (narrow t, *J* = 2.7 Hz, 1H), 2.19 (dd, *J* = 5.7, 13.2 Hz, 1H), 2.94 (d, *J*= 2.4 Hz, 2H), 3.41 (bd, *J* = 9.3 Hz, 1H), 3.52 (bm, 1H), 3.76 (s, 6H), 5.76-5.85 (m, 4H), 6.14 (dd, *J* = 7.8, 15.9 Hz, 1H), 6.46 (d, *J* = 15.9 Hz, 1H), 7.17-7.36 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 23.8, 27.0, 37.4, 42.5, 47.2, 52.8, 60.2, 71.9, 79.1, 124.5, 124.8, 126.2, 127.3, 128.6, 129.6, 132.6, 133.4, 137.1, 137.5, 170.3

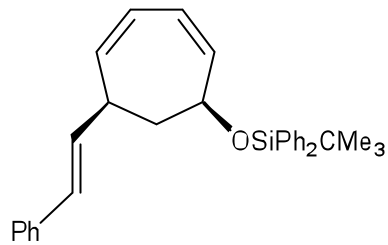


Methyl 6**-Styryl-2,4-cycloheptadienyl ether (±)-184**: To a 100 mL round-bottomed flask complexed alcohol (±)-**173** (820 mg, 2.34 mmol) was charged. Methanol (30 mL) was added at room temperature followed by the addition of solid ceric ammonium nitrate (2.56 gm, 4.66 mmol). The reaction mixture was stirred for 30 min, and then water (15 mL) was added. The mixture was extracted several times with ether, washed with brine, dried ($MgSO_4$) and concentrated. The residue was purified by column chromatography (SiO_2, hexane-ethyl acetate = 20:1) to give a colorless oil (0.26 g, 49.0%). IR 1098, 747, 691 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.05 (q, *J* = 12.0 Hz, 1H), 2.24 (d, *J* = 12.0 Hz, 1H), 3.39 (s, 4H), 4.15 (d, *J* = 10.0 Hz, 1H), 5.74 (m, 3H), 5.88 (d, *J* = 11.0 Hz, 1H), 6.19 (dd, *J* = 8, 16 Hz, 1H), 6.46 (d, *J* = 16.0 Hz, 1H), 7.33 (m, 5H); ^{13}C NMR ($CDCl_3$, 75

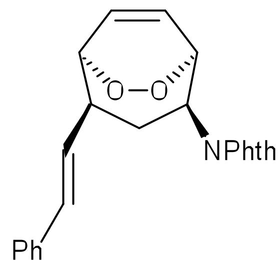
MHz) δ 38.1, 42.8, 56.5, 79.8, 122.7, 124.2, 126.3, 127.5, 128.8, 129.6, 132.8, 136.6, 136.7, 137.7.



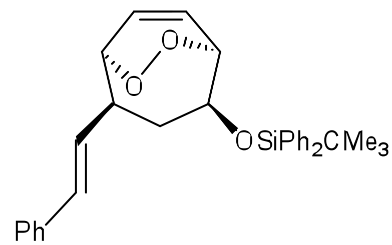
6-Styryl-2,4-cycloheptadiene-1-ol (±)-186: To a 100 mL round-bottomed flask alcohol (±)-**173** (0.30 g, 0.85 mmol) was dissolved into methanol (12 mL) with slight warming. A solution of H_2O_2 (5.70 mL, 51.0 mmol, 30 wt %) was added to the reaction mixture at 0 ^{0}C under N_2. A solution of NaOH (240.0 mg, 5.950 mmol) in methanol (8 mL) was added to the reaction mixture dropwise. The reaction mixture immediately turned deep brown in color. The mixture was stirred for 30 min at 0 ^{0}C followed by another 30 min at room temperature. The mixture was quenched with water (30 mL) and extracted several times with ether. The combined extracts were washed with brine, dried ($MgSO_4$) and concentrated. The residue was purified by column chromatography (SiO_2, hexane-ethyl acetate = 4:1) to give the product as a colorless foamy solid (90.0 mg, 50%). mp 59 - 63^{0}C; IR (KBr) 3200-3400, 746, 692 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.64 (d, *J* = 6.0 Hz, 1H), 2.13-2.27 (m, 2H), 3.40-3.48 (m, 1H), 4.61 (d, *J* = 8.0 Hz, 1H), 5.66-5.87 (m, 4H), 6.18 (dd, *J* = 8.0, 16.0, Hz, 1H), 6.42 (d, *J* = 16.0 Hz, 1H), 7.19-7.37 (m, 5H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 41.9, 42.0, 71.1, 122.7, 124.3, 126.4, 127.5, 128.8, 129.6, 132.7, 136.9, 137.5, 138.1.



[t]Butyldiphenylsilyl 6-**Styryl-2,4-cycloheptadienyl ether (±)-187**: In a 25 mL oven dried round-bottomed flask was dissolved alcohol (±)-**187** (0.11 g, 0.51 mmol) into dry dichloromethane (5 mL) at room temperature under N_2. Solid imidazole (80.0 mg, 1.17 mmol) was added and stirred the mixture for 30 min. t-Butyldiphenylsilyl chloride (0.20 mL, 0.76 mmol) was added dropwise and the resultant mixture stirred for 3 h, at which time additional imidazole (40.0 mg, 0.58 mmol) was added followed by additional t-butyldiphenylsilyl chloride (0.10 mL, 0.38 mmol). The reaction mixture was stirred for 14 h. Water (10 mL) was added, and the mixture was extracted several times with dichloromethane. The light yellow solution was washed with brine, dried (Na_2SO_4) and concentrated. The oily residue was purified by column chromatography (SiO_2, hexane-ethyl acetate = 20:1), to give the product as colorless oil (0.19 g, 82%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.07 (s, 9H), 1.93 (d, J = 12.9 Hz, 1H), 2.09-2.25 (m, J = 12.6 Hz, 1H), 2.91 (m, 1H), 4.62 (d, J = 8.1 Hz, 1H), 5.54-5.65 (m, 2H), 5.66-5.77 (m, 1H), 5.93-6.12 (m, 2H), 6.18 (dd, J = 3.0, 16.0 Hz, 1H), 7.18-7.52 (m, 10H), 7.67-7.79 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 19.4, 27.24, 42.5, 42.7, 72.6, 121.3, 124.2, 126.3, 127.3, 127.87, 127.9, 128.7, 129.4, 129.88, 129.9, 132.9, 134.2, 134.5, 136.09, 136.1, 136.6, 137.7, 140.0.

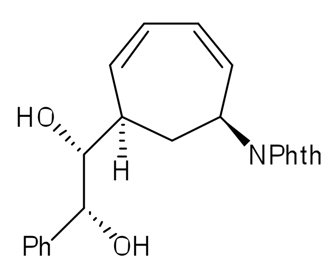


(±)-188: To a 50 mL two-necked round-bottomed flask, equipped with a condenser, was charged diene (±)-**181** (200 mg, 0.5 80 mmol), dry $CHCl_3$ (10 mL) and tetraphenylporphine (35 mg, 10 mol%). The deep purple solution was irradiated with a 60 W tungsten-halogen lamp for 10 h, while ultra-pure O_2 was bubbled through the solution. The reaction mixture was concentrated under vacuum. The residue was purified through column chromatography (SiO_2, hexane-ethyl acetate = 1:1) to give a colorless solid (70 mg, 50% based on the recovered starting material). mp 175-177 ^{0}C, ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.77 (md, *J* = 9.6 Hz, 1H), 2.11 (q, *J* = 10.1 Hz, 1H), 3.01 (q, *J* = 3.3 Hz, 1H), 4.66-4.81 (m, 2H), 4.84 (dd, *J* = 3, 9.9 Hz, 1H), 5.98 (dd, *J* = 6.3, 11.1 Hz, 1H), 6.43-6.51 (m, 2H), 6.89 (dd, *J* = 6.3, 6.1 Hz, 1H), 7.21-7.33 (m, 5H), 7.75 (dd, *J* = 3.6, 5.6 Hz, 2H), 7.86 (dd, *J* = 3.5, 5.6 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 29.8, 45.8, 52.0, 80.4, 81.1, 123.6, 123.8, 126.4, 127.9, 128.7, 128.8, 130.8, 131.8, 131.9, 134.5, 136.8, 167.8. Anal. Calcd. for $C_{23}H_{19}NO_4$: C, 73.98; H, 5.13. Found: C, 73.87; H, 5.27

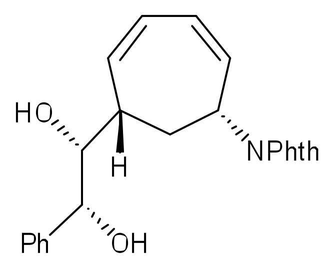


Cycloaddition product with oxygen (±)-189: To a 50 mL oven dried - necked round-bottomed flask fitted with a condenser, was added a solution of diene (±)-**187** (70.0 mg, 0.15 mmol) in dry dichloromethane (4 mL). Solid tetraphenylporphine (0.9 mg, 1 mol%) was added to the reaction mixture. The deep purple solution was irradiated with a 60 W tungsten-halogen lamp for 8 h, while ultra-pure O_2 was bubbled through the solution. The reaction mixture was evaporated under reduced pressure, re-dissolved in methanol (10 mL) and filtered through celite. The filtration was repeated several times to remove tetraphenylporphine and then finally the solution was concentrated. The residue was purified to give a colorless oil column chromatography (SiO_2, hexane-ethyl acetate = 20:1), (50 mg, 69%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.08 (s, 9H), 1.43-1.65 (m, 1H), 1.75-2.10 (m, 1H), 2.55-2.73 (m, 1H), 4.03-4.21 (m, 1H), 4.43-4.67 (m, 2H), 5.99 (dd, *J* = 16, 8 Hz, 1H), 6.38 (d, *J* = 16 Hz, 1H), 6.41-6.63 (m, 2H), 7.15-7.39 (m, 5H), 7.40-7.55 (m, 5H), 7.59-7.73 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 19.4, 27.1, 34.6, 41.9, 73.4, 80.9, 81.2, 126.3, 127.2, 127.7, 127.9, 127.93, 128.0, 128.8, 130.0, 130.2, 130.3, 130.7, 133.7, 133.8, 135.8, 135.9, 137.0.

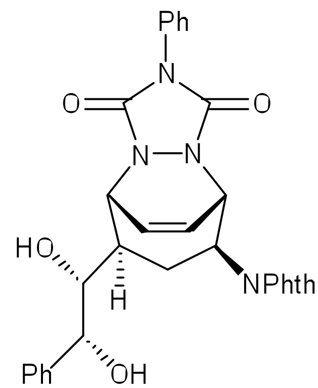
Asymmetric dihydroxylation of (±)-181: To a 25 mL round-bottomed flask was charged a mixture of ^{t}BuOH (3 mL) and water (3 mL) and stirred for 5 min at room temperature. Solid AD mix-β (0.826 g) was added to the stirring solution followed by the addition of methylsulfonamide (60 mg, 0.59 mmol). The mixture was stirred until the two layers were separated. The mixture was cooled to 0 ^{0}C upon which inorganic salt was precipitated out. Alkene (200 mg, 0.59 mmol) was added in one portion and the mixture was stirred for 72 h maintaining the temperature at 0 ^{0}C. The reaction mixture was quenched with water, extracted several times with ethyl acetate, and the combined extracts were washed with brine. The organic layer was concentrated under reduced pressure. The residue was purified by column chromatography (SiO_2, hexane-ethyl acetate=1:1) to give a mixture of diastereomers as colorless oily liquid (149 mg, 71%). The diastereomers could be separated by preparative TLC (SiO_2, hexane-ethyl ether = 1:1).



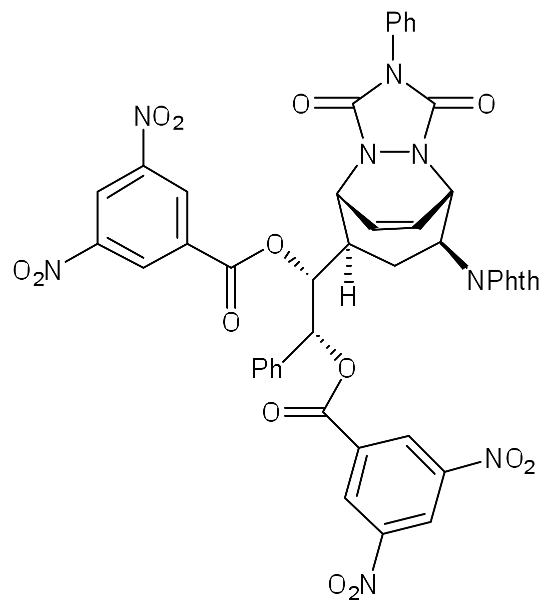
<u>Less polar diol (F1) (-)-190:</u> $[\alpha]_D$ = - 5.1 (c, 0.500, CH_2Cl_2), ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.89 (d, *J* = 12.9 Hz, 1H), 2.66 (d , *J* = 11.9 Hz, 1H), 2.76 (OH, 1H), 2.93 (q, *J* = 11.4 Hz, 1H), 2.99 (OH 1H), 3.71 (m, *J* = 3.0 Hz, 1H), 4.71 (d, *J* = 6.6 Hz, 1H), 5.05 (dd, *J* = 3, 11.1 Hz, 1H), 5.63 (dd, *J* = 1.5, 11.4 Hz, 1H), 5.77-5.90 (m, 3H), 7.29-7.35 (m, 5H), 7.68 (dd, *J* = 3, 5.4 Hz, 2H), 7.80 (dd, *J* = 3.1, 5.5 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 35.4, 41.5, 50.9, 75.1, 79.2, 123.4, 124.6, 125.8, 126.9, 128.5, 128.9, 132.1, 132.9, 133.1, 134.2, 140.9, 167.9. Anal. Calcd for $C_{23}H_{21}O_4N.3/4H_2O$: C, 71.02; H, 5.83. Found: C, 71.19; H, 5.83.



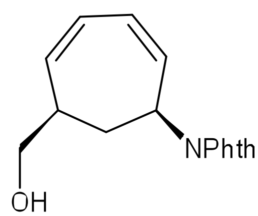
<u>More polar diol (F2) (+)-191:</u> $[\alpha]_D$ = + 74.1 (c, 0.486, CH_2Cl_2), ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.99 (d, *J* = 10.8 Hz, 1H), 2.51 (d, *J* = 10.8 Hz, 1H), 2.64 (q, *J* = 11.1 Hz, 1H), 2.72 (OH, 1H), 2.91 (OH, 1H), 3.73 (dd, *J* = 3.6, 6.6 Hz, 1H), 4.61 (d, *J* = 6.9 Hz, 1H), 4.99 (dd, *J* = 11.4, 1.5 Hz, 1H), 5.61 (d, *J* = 10.2 Hz, 1H), 5.70-5.83 (m, 3H), 7.22-7.34 (m, 5H), 7.65 (dd, *J* = 3.3, 5.5 Hz, 2H), 7.77 (dd, *J* = 3.1, 5.6 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 31.5, 41.2, 51.2, 75.3, 79.3, 123.5, 124.5, 125.4, 126.7, 128.5, 128.9, 132.2, 132.9, 134.2, 136.5, 141.0, 167.9.



PTAD adduct 192: To a colorless solution of less polar diol (-)-**190** (69.0 mg, 0.184 mmoL) in CH_2Cl_2 (1.5 mL) at room temperature was added dropwise a solution of 4-phenyl-1,2,4-triazoline-3,5-dione in CH_2Cl_2 and the mixture was occasionally stirred. The process was continued until the light red color of unreacted 4-phenyl-1,2,4-triazoline-3,5-dione persisted. The mixture was concentrated and applied to a column of silica. Elution: (hexane-ethyl acetate, 1:4) gave a color less solid (94 mg, 93%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.58 (td, *J* = 3.9, 12.9 Hz, 1H), 2.09 (td, *J* = 3.9, 12.3 Hz, 1H), 2.28 (q, *J* = 12.3 Hz, 1H), 3.49 (bs, 1H), 4.51 (dd, *J* = 4.2, 12.3 Hz, 1H), 4.81 (d, *J* = 6.0 Hz, 1H), 5.02 (d, *J* = 6.6 Hz, 1H), 5.40 (d, *J* = 6.6 Hz, 1H), 6.35 (dd, *J* = 7.2 Hz, 1H), 6.61 (dd, *J* = 7.5 Hz, 1H), 7.33-7.49 (m, 10H), 7.72-7.84 (m, 4H).



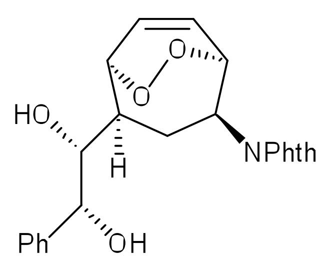
Bis(dinitrobenzoate) PTAD adduct (+)-193: To a stirring solution of 4-phenyl-1,2,4-triazoline-3,5-dione adduct (**192**) (94.0 mg, 0.171 mmoL) in dry CH_2Cl_2 (2 mL) at room temperature under nitrogen was added 4-(dimethylamino)pyridine (0.045 g, 0.376 mmoL) and the mixture was stirred for 15 min. To the stirring reaction mixture was added 3,5-dinitrobenzoyl chloride (0.085 g, 0.376 mmoL) and the mixture was stirred for 3 h. The reaction mixture was diluted with CH_2Cl_2 (4 mL) and washed with 0.1 M HCl solution. The combined CH_2Cl_2 washings were washed with brine, dried (Na_2SO_4) and concentrated. The residue was purified by column chromatography (SiO_2, hexane-ethyl acetate, 1:1) to afforded a light yellow solid (131 mg, 81%). mp = 240-242 ^{0}C; $[\alpha]_D$ = + 50.1, CH_2Cl_2)^{1}H NMR ($CDCl_3$, 300 MHz) δ, 1.74 (td, *J* = 3.9, 12.3 Hz, 1H), 2.11-2.27 (m, 1H), 2.35 (bd, *J* = 12.6 Hz, 1H), 4.55 (dd, *J* = 4.2, 12.0 Hz, 1H), 5.06 (d, *J* = 6.9 Hz, 1H), 5.55 (d, *J* = 6.9 Hz, 1H), 5.86 (dd, *J* = 2.4, 9 Hz, 1H), 6.48 (dd, *J* = 6.9 Hz, 1H), 6.59 (d, *J* = 8.7 Hz, 1H), 6.68 (dd, *J* = 8.7 Hz, 1H), 7.31-7.53 (m, 8H), 7.65-7.84 (m, 6H), 8.97-9.35 (m, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 28.7, 41.4, 50.7, 51.3, 54.9, 78.3, 78.7, 123.0, 123.4, 123.7, 124.6, 125.6, 127.4, 128.6, 129.4, 129.5, 129.6, 130.5, 131.3, 131.4, 132.2, 132.8, 134.2, 134.7, 148.8, 148.9, 151.6, 152.4, 161.6, 162.5, 167.4. Anal. Calcd. for $C_{45}H_{30}N_8O_{16}$ · 1/2 H_2O: C, 57.57; H, 3.22. Found: C, 57.04; H, 3.58



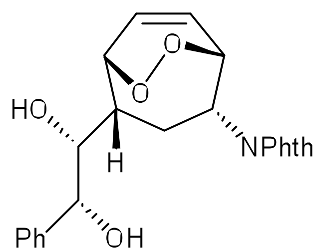
***N*-(6-Hyroxymethylene-2,4-heptadien-1-yl)phthalimide** **(±)-197**: In a 25 mL round-bottom flask the mixture of diastereomeric diols (-)-**190** and (+)-**191** (300 mg, 0.808 mmol) was dissolved in dry CH_2Cl_2 (12 mL) at 0 ^{0}C under N_2. After 5 min of stirring solid $Pb(OAc)_4$ (0.43 g, 0.97 mmol) was added and the mixture was stirred for 1 h. The reaction mixture was quenched with water, extracted several times with CH_2Cl_2, and the combined extracts were washed with brine, dried (Na_2SO_4) and concentrated. The crude mixture (204 mg) was re-dissolved in a mixture of MeOH (5 mL) and CH_2Cl_2 (2 mL) at 0^0 C and solid $NaBH_4$ (1.0 mg, O.26 mmol) was added. After stirring for 1 h, the reaction mixture was quenched with water, extracted several times with ethyl acetate and the combined extracts were washed with brine, dried (Na_2SO_4) and concentrated. The residue was purified by column chromatography (SiO_2, hexane-ethyl acetate=1:1) to afford the product as a colorless liquid (88 mg, 40%). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.95-1.84 (m, 1H), 2.03-1.96 (m, 1H), 2.66-2.56 (m, 1H), 2.86-2.77 (m, 1H), 3.67-3.55 (m, 2H), 5.19

(dd, J = 3.0, 11.2 Hz, 1H), 5.75-5.65 (m, 2H), 5.88-5.77 (m, 2H), 7.71 (dd, J = 5.5, 3.0 Hz, 2H), 7.83 (dd, J = 5.1, 3.2 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 33.9, 42.5, 50.7, 66.5, 123.3, 124.1, 124.9, 131.9, 132.9, 134.0, 134.6, 167.9.

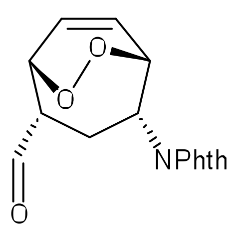
Singlet oxygen cycloaddition of the mixture of (-)-190 and (+)-191: To a 100 mL two-necked round-bottomed flask, equipped with a condenser, was charged dienediol mixture **190** and **191** (500 mg, 1.33 mmol), dry $CHCl_3$ (40 mL) and tetraphenylporphine (82 mg, 10 mol%). The deep purple solution was irradiated with a 60 W tungsten-halogen lamp for 72 h to consume all the starting material, while ultra-pure O_2 was bubbled through the solution. The reaction mixture was concentrated under vacuum, and the residue was purified by column chromatography (SiO_2, hexane-ethyl acetate = 1:1) to afford a less polar (F1) foamy endoperoxide **194** (179 mg, 33%) and a more polar (F2) foamy endoperoxide **195** (133 mg, 25%).



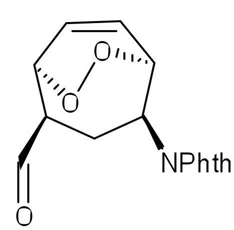
Less polar endoperoxide (+)-194: $[\alpha]_D$ = + 46.0 (c, 0.214, CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.60 (md, J = 12.6 Hz, 1H), 2.03-2.10 (m, 1H), 2.29 (dd, J = 5.7, 12.3 Hz, 1H), 2.48 (d, J = 4.8 Hz, OH), 2.68 (d, J = 3.9 Hz, OH), 3.43 (m, 1H), 4.68-4.73 (m, 3H), 5.18 (d, *J* = 7.2 Hz, 1H), 6.41 (dd, *J* = 7.5, 8.4 Hz, 1H), 6.71 (dd, *J* = 7.2, 9.1 Hz, 1H), 7.26-7.39 (m, 5H), 7.73 (dd, *J* = 2.7, 5.1 Hz, 2H), 7.82 (dd, *J* = 3.3, 5.7 Hz, 2H); ($CDCl_3$, 75 MHz) δ 27.6, 43.8, 52.2, 74.0, 76.9, 78.1, 79.8, 123.6, 125.8, 126.5, 128.4, 128.8, 128.9, 131.8, 134.5, 141.0, 167.8.



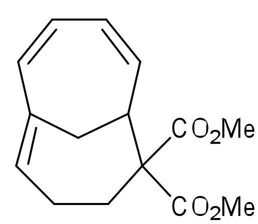
More polar endoperoxide (+)-195: [α] = + 29.9 (c, 1.175, CH_2Cl_2). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.61 (d, *J* = 12.9 Hz, 1H), 1.96 (d, *J* = 12.3 Hz, 1H), 2.19 (q, *J* = 12.6 Hz, 1H), 3.14 (OH, 2H), 3.73 (d, *J* = 3.9 Hz, 1H), 4.45 (d, *J* = 6.9 Hz, 1H), 4.54 (dd, *J* = 3.9, 12.6 Hz, 1H), 4.65 (d, *J* = 7.5 Hz, 2H), 6.43 (dd, *J* = 8.7, 9.0 Hz, 1H), 6.61 (dd, *J* = 8.8, 9.1 Hz, 1H), 7.26-7.36 (m, 5H), 7.72 (dd, *J* = 3.1, 5.7 Hz, 2H), 7.80 (dd, *J* = 3.3, 6.1 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 23.4, 43.9, 52.4, 75.1, 77.0, 79.7, 81.4, 123.5, 126.5, 126.6, 127.3, 128.6, 129.0, 131.7, 134.4, 140.7, 167.8.



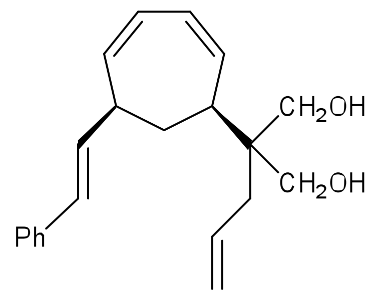
2-Formyl-4-phthalimido-6,7-dioxabicyclo[3.2.2]non-8-ene (-)-196: In a 25 mL round-bottom flask more polar endoperoxide (+)-**195** (46 mg, 0.11 mmol) was dissolved in dry CH_2Cl_2 (3 mL) at room temperature under N_2. After 5 min of stirring solid $Pb(OAc)_4$ (60 mg, 0.14 mmol) was added and the mixture was stirred for 10 min. The reaction mixture was quenched with water, extracted several times with CH_2Cl_2, and the combined extracts were washed with brine, dried (Na_2SO_4) and concentrated. The residue was purified by column chromatography (SiO_2, hexane-ethyl acetate = 1:1) to give the product as a colorless oil (23 mg, 73%). $[\alpha]_D$ = – 100 (c 0.287, CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.11 (q, J = 12.8 Hz, 1H), 3.14 (dd, J = 5.2, 12.8 Hz, 1H), 4.78-4.83 (m, 3H), 5.24 (d, J = 6.8 Hz, 1H), 6.41 (dd, J = 8.4, 8.7 Hz, 1H), 6.75 (dd, J = 8.0, 12.1 Hz, 1H), 7.75 (dd, J = 3.6, 5.8 Hz, 2H), 7.84 (dd, J = 3.4, 5.8 Hz, 2H), 9.63 (s, 1H); ^{13}C ($CDCl_3$, 100 MHz) δ 23.8, 52.1, 54.3, 75.4, 80.0, 123.7, 124.6, 129.7, 131.7, 134.6, 167.7, 199.0.



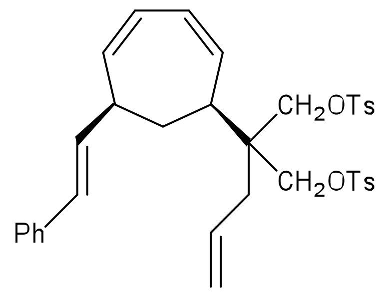
2-Formyl-4-phthalimido-6,7-dioxabicyclo[3.2.2]non-8-ene (+)-196: In a 25 mL round-bottom flask less polar endoperoxide (+)-**194** (190 mg, 0.467 mmol) was dissolved in dry CH_2Cl_2 (15 mL) at room temperature under N_2. After 5 min of stirring solid $Pb(OAc)_4$ (0.248 g, 0.560 mmol) was added and the mixture was stirred for 10 min. The reaction mixture was quenched with water, extracted several times with CH_2Cl_2, and the combined extracts were washed with brine, dried (Na_2SO_4) and concentrated. The residue was purified by column chromatography (SiO_2, hexane-ethyl acetate = 1:1) to give the product as a colorless oil (94 mg, 70%). $[\alpha]_D$ = + 112 (c, 0.424, CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.11 (q, *J* = 12.8 Hz, 1H), 3.14 (dd, *J* = 5.2, 12.8 Hz, 1H), 4.78-4.83 (m, 3H), 5.24 (d, *J* = 6.8 Hz, 1H), 6.41 (dd, *J* = 8.4, 8.7 Hz, 1H), 6.75 (dd, *J* = 8.0, 12.1 Hz, 1H), 7.75 (dd, *J* = 3.6, 5.8 Hz, 2H), 7.84 (dd, *J* = 3.4, 5.8 Hz, 2H), 9.63 (s, 1H); ^{13}C ($CDCl_3$, 100 MHz) δ 23.8, 52.1, 54.3, 75.4, 80.0, 123.7, 124.6, 129.7, 131.7, 134.6, 167.7, 199.0.



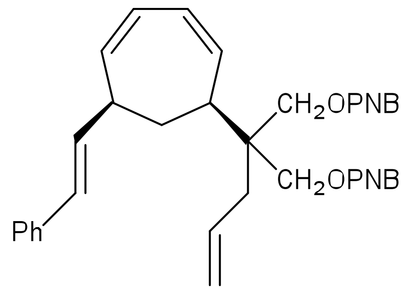
5,5-Bis(methoxycarbonyl) bicyclo[4.4.1]undeca-1,7,9-triene (±)-199: To a stirring solution of (±)-**182** (30.0 mg, 0.080 mmol) in CH_2Cl_2 (2 mL) at room temperature was added Grubbs 1st generation catalyst (3 mg, 5 mol%). The reaction mixture was stirred for 45 min, concentrated and the residue was purified by column chromatography (SiO_2, hexane-ethyl acetate = 20:1) to gave the product as a colorless oil (19 mg, 88%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.27 (dd, *J* = 14.2, 1.2 Hz, 1H), 2.55 (dd, *J* = 14.2, 1.5 Hz, 1H), 2.85-2.75 (m, 1H), 2.96-2.89 (m, 2H), 3.29 (dq, *J* = 17.3, 2 Hz, 1H), 3.75 (s, 3H), 3.66 (s 3H), 3.84-3.76 (m, 1H), 5.66-5.57 (m, 2H), 6.12-6.18 (m, 1H), 6.31-6.26 (m, 1H), 6.44-6.39 (m, 1H); [13]C NMR ($CDCl_3$, 75 MHz) δ 32.8, 40.3, 43.6, 50.6, 52.5, 52.9, 63.0, 127.4, 128.4, 131.4, 132.5, 132.9, 146.8, 171.1, 173.0. ESI-HRMS m/z 262.1198 (calcd for $C_{15}H_{18}O_4$ m/z 262.1205).



(±)-200: A flame dried 100 mL Schlenk flask was charged with (±)-**182** (582 mg, 1.59 mmol) and freshly distilled CH_2Cl_2 (30 mL) at -78 °C under nitrogen. To this was added dropwise a solution of DIBAL-H (10.0 mL, 9.54 mmol, 1M solution in hexane) and the resultant mixture was stirred for 1 h. The reaction mixture was warmed to room temperature and stirred for 2 h. The mixture was cooled to 0 °C and quenched with water (0.4 mL), NaOH solution (0.4 mL, 15% w/v). Water (1 mL) was added and stirred for 15 min at room temperature. $MgSO_4$ was added followed by ethyl acetate (30 mL) and stirred for another 15 min, filtered, concentrated and applied to a column of silica. Elution (hexane-ethyl acetate = 1:1) gave a colorless oil (317 mg, 64%). [1]H NMR ($CDCl_3$, 300 MHz) δ 1.71-1.59 (m, 1H), 2.29-2.03 (m, 3H), 2.55 (s, OH, 1H), 2.67 (s, OH, 1H), 2.84 (dm, J = 8.3 Hz, 1H), 3.43-3.30 (bm, 1H), 3.88-3.67 (m, 4H), 5.07 (bs, 1H), 5.12 (br d, J = 8.6 Hz, 1H), 5.91-5.72 (m, 4H), 6.05-5.96 (dd, J = 4.2, 10.9 Hz, 1H), 6.18 (dd, J = 8.2, 15.9 Hz, 1H), 6.45 (d, J = 15.9 Hz, 1H), 7.38-7.18 (m, Ar, 5H); ^{13}C NMR ($CDCl_3$, 300 MHz) δ 35.4, 35.9, 40.3, 44.2, 47.0, 67.7, 67.8, 118.3, 124.8, 125.1, 126.3, 127.3, 128.7, 129.4, 133.3, 134.4, 135.1, 137.0, 137.6.



(±)-201: To a stirring solution of (±)-**200** (170 mg, 0.540 mmol) in CH_2Cl_2 (8 mL) at room temperature was added pyridine (0.100 mL, 1.37 mmol), DMAP (6 mg, 10 mol%) and TsCl (260 mg, 1.37 mmol). The reaction mixture was stirred overnight, quenched with saturated NH_4Cl solution and the aqueous layer were extracted several times with CH_2Cl_2. The combined CH_2Cl_2 extracts were washed with brine, dried (Na_2SO_4) and concentrated. The residue was purified by column chromatography. (hexane-ethyl acetate = 1:1) to give colorless foamy solid (109 mg, 32%). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.52-1.41 (m, 1H), 1.83 (dd, J = 5.4, 13.1 Hz, 1H), 2.16 (bd, J = 6.7 Hz, 2H), 2.42 (s, 6H), 2.58 (d, J = 9.8 Hz, 1H), 3.20 (br s, 1H), 4.01-3.86 (m, 4H), 5.07-4.96 (m, 2H), 5.82-5.54 (m, 5H), 6.06-5.98 (dd, J = 8.1, 15.5 Hz, 1H), 6.36 (d, J = 15.9 Hz, 1H), 7.36-7.19 (m, 9H, Ar), 7.77-7.72 (m, 4H, Ar); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 21.8, 27.0, 35.3, 35.7, 40.9, 42.9, 46.8, 70.1, 70.4, 120.1, 124.5, 125.3, 126.2, 127.4, 128.08, 128.11, 128.7, 129.7, 130.12, 130.14, 131.8, 131.8, 131.8, 131.8, 132.25, 132.28, 132.3, 132.7, 136.9, 137.4, 145.27, 145.3.



(±)-202: To a stirring solution of (±)-**200** (50 mg, 0.16 mmol) in CH_2Cl_2 (2.5 mL) at room temperature under nitrogen was added DMAP (66.0 mg, 0.352 mmol) and stirred for 10 min. To the stirring solution was added 4-nitrobenzoyl chloride (60 mg, 0.51 mmol). The reaction mixture was stirred for overnight, diluted with CH_2Cl_2 and quenched with sat. $NaHCO_3$. The aqueous layer was extracted several times with CH_2Cl_2. The combined CH_2Cl_2 extracts were washed with brine, dried (Na_2SO_4) and concentrated. The residue was purified by column chromatography (hexane-ethyl acetate = 1:1) to give a light yellow glassy solid (45 mg, 47%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.85-1.72 (m, 1H), 2.25-2.16 (dd, *J* = 5.2, 13.5 Hz, 1H), 2.47-2.21 (m, 2H), 2.84 (bd, *J* = 8.4 Hz, 1H), 3.37-3.25 (bm, 1H), 4.58-4.44 (m, 4H), 5.12 (d, *J* = 3.5 Hz, 1H), 5.16 (s, 1H), 5.92-5.69 (m, 4H), 6.15-5.99 (m, 2H), 6.36 (d, *J* = 15.9 Hz, 1H), 7.28-7.14 (5H, Ar), 8.24-8.08 (8H, Ar); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 36.5, 36.7, 42.1, 43.2, 47.2, 67.1, 67.2, 119.9, 123.9, 124.7, 125.6, 126.2, 127.6, 128.8, 129.9, 130.9, 132.4, 132.5, 133.5, 135.2, 137.1, 137.3, 150.9, 164.6.

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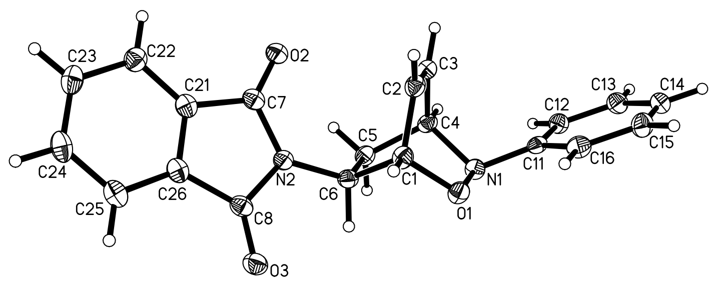
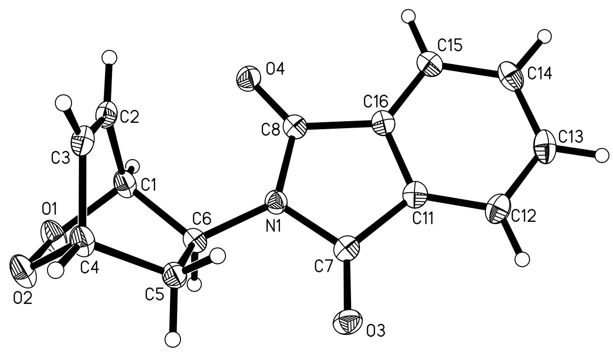
Appendix



Crystal data and structure refinement for (±)-**158**.

Identification code	dont4	
Empirical formula	C20 H16 N2 O3	
Formula weight	332.35	
Temperature	100(2) K	
Wavelength	1.54178 Å	
Crystal system	Monoclinic	
Space group	C 2/c	
Unit cell dimensions	a = 25.6400(13) Å	a= 90°.
	b = 5.4993(3) Å	b= 99.259(3)°.
	c = 22.3486(12) Å	g = 90°.
Volume	3110.1(3) Å^3	
Z	8	
Density (calculated)	1.420 Mg/m^3	
Absorption coefficient	0.789 mm^{-1}	
F(000)	1392	
Crystal size	0.32 x 0.02 x 0.02 mm^3	

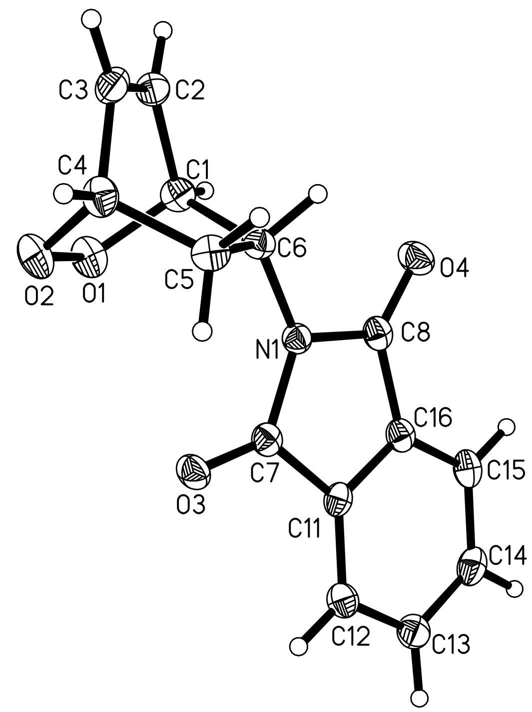
Theta range for data collection	3.49 to 67.88°.
Index ranges	-30<=h<=29, 0<=k<=6, 0<=l<=26
Reflections collected	21439
Independent reflections	2775 [R(int) = 0.0603]
Completeness to theta = 67.88°	97.7 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9844 and 0.7864
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	2775 / 0 / 227
Goodness-of-fit on F^2	1.025
Final R indices [I>2sigma(I)]	R1 = 0.0433, wR2 = 0.1001
R indices (all data)	R1 = 0.0602, wR2 = 0.1064
Extinction coefficient	0.00024(6)
Largest diff. peak and hole	0.262 and -0.202 e.Å^{-3}



Crystal data and structure refinement for (±)-**119**.

Identification code	donu	
Empirical formula	C14 H11 N O4	
Formula weight	257.24	
Temperature	100(2) K	
Wavelength	1.54178 Å	
Crystal system	Monoclinic	
Space group	P 21/c	
Unit cell dimensions	a = 11.2217(2) Å	a= 90°.
	b = 6.91770(10) Å	b= 106.3860(10)°.
	c = 14.8259(2) Å	g = 90°.
Volume	1104.16(3) $Å^3$	
Z	4	
Density (calculated)	1.547 Mg/m^3	
Absorption coefficient	0.962 mm^{-1}	
F(000)	536	

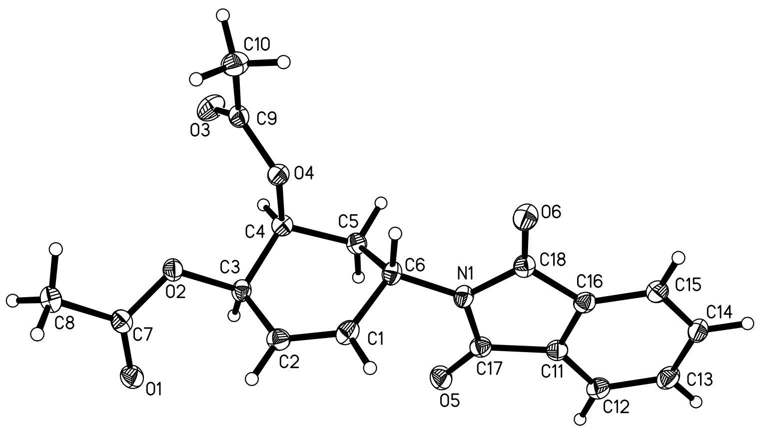
Crystal size	0.20 x 0.15 x 0.09 mm^3
Theta range for data collection	4.11 to 67.93°.
Index ranges	-13<=h<=12, 0<=k<=8, 0<=l<=17
Reflections collected	9222
Independent reflections	1969 [R(int) = 0.0183]
Completeness to theta = 67.93°	97.7 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9184 and 0.8309
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	1969 / 0 / 217
Goodness-of-fit on F^2	1.009
Final R indices [I>2sigma(I)]	R1 = 0.0327, wR2 = 0.0871
R indices (all data)	R1 = 0.0338, wR2 = 0.0881
Extinction coefficient	0.0021(4)
Largest diff. peak and hole	0.256 and -0.197 e.$Å^{-3}$



Crystal data and structure refinement for (±)-**120**.

Identification code	donv	
Empirical formula	C14 H11 N O4	
Formula weight	257.24	
Temperature	100(2) K	
Wavelength	1.54178 Å	
Crystal system	Orthorhombic	
Space group	P 21 21 21	
Unit cell dimensions	a = 6.77800(10) Å	a= 90°.
	b = 8.5059(2) Å	b= 90°.
	c = 19.6445(4) Å	g = 90°.
Volume	1132.56(4) Å^3	

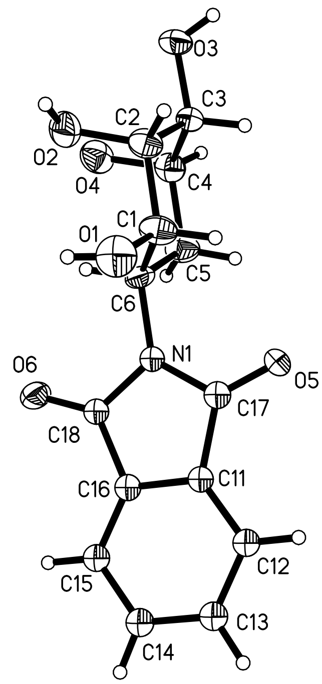
Z	4
Density (calculated)	1.509 Mg/m^3
Absorption coefficient	0.938 mm^{-1}
F(000)	536
Crystal size	0.15 x 0.12 x 0.03 mm^3
Theta range for data collection	4.50 to 67.63°.
Index ranges	0<=h<=8, 0<=k<=10, 0<=l<=23
Reflections collected	9242
Independent reflections	1191 [R(int) = 0.0210]
Completeness to theta = 67.63°	98.6 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9724 and 0.8721
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	1191 / 0 / 172
Goodness-of-fit on F^2	0.994
Final R indices [I>2sigma(I)]	R1 = 0.0290, wR2 = 0.0763
R indices (all data)	R1 = 0.0305, wR2 = 0.0773
Absolute structure parameter	0.6(3)
Largest diff. peak and hole	0.176 and -0.191 e.$Å^{-3}$



Crystal data and structure refinement for (±)-**127**.

Identification code	donw	
Empirical formula	C18 H17 N O6	
Formula weight	343.33	
Temperature	100(2) K	
Wavelength	1.54178 Å	
Crystal system	Monoclinic	
Space group	P 21/c	
Unit cell dimensions	a = 8.4527(2) Å	a= 90°.
	b = 8.9213(2) Å	b= 91.6100(10)°.
	c = 21.1061(5) Å	g = 90°.
Volume	1590.96(6) $Å^3$	
Z	4	
Density (calculated)	1.433 Mg/m^3	
Absorption coefficient	0.912 mm^{-1}	
F(000)	720	
Crystal size	0.53 x 0.41 x 0.07 mm^3	

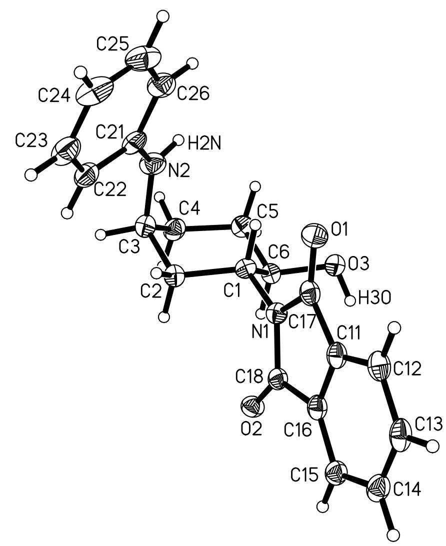
Theta range for data collection	4.19 to 67.86°.
Index ranges	-10<=h<=10, 0<=k<=10, 0<=l<=23
Reflections collected	13190
Independent reflections	2766 [R(int) = 0.0195]
Completeness to theta = 67.86°	95.8 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9389 and 0.6436
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	2766 / 0 / 229
Goodness-of-fit on F^2	1.032
Final R indices [I>2sigma(I)]	R1 = 0.0322, wR2 = 0.0806
R indices (all data)	R1 = 0.0331, wR2 = 0.0812
Extinction coefficient	0.0016(2)
Largest diff. peak and hole	0.268 and -0.188 e.Å^{-3}



Crystal data and structure refinement for (±)-**132**.

Identification code	donx	
Empirical formula	C14 H15 N O6	
Formula weight	293.27	
Temperature	100(2) K	
Wavelength	1.54178 Å	
Crystal system	Monoclinic	
Space group	P 21/n	
Unit cell dimensions	a = 12.0696(6) Å	a= 90°.
	b = 6.9279(4) Å	b= 108.536(2)°.
	c = 15.8178(8) Å	g = 90°.
Volume	1254.02(11) $Å^3$	
Z	4	
Density (calculated)	1.553 Mg/m^3	
Absorption coefficient	1.042 mm^{-1}	

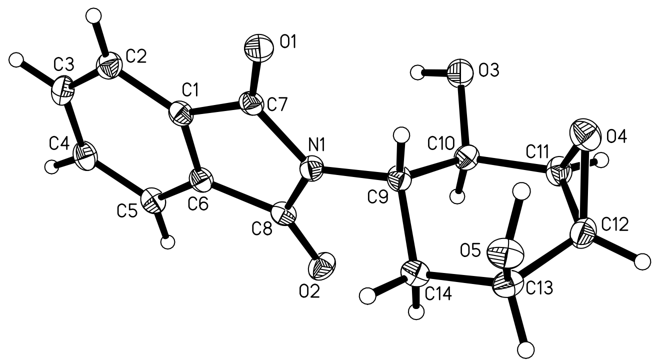
F(000)	616
Crystal size	0.23 x 0.11 x 0.04 mm^3
Theta range for data collection	4.05 to 67.59°.
Index ranges	-14<=h<=13, 0<=k<=8, 0<=l<=18
Reflections collected	10253
Independent reflections	2215 [R(int) = 0.0278]
Completeness to theta = 67.59°	97.6 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9595 and 0.7956
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	2215 / 45 / 185
Goodness-of-fit on F^2	1.013
Final R indices [I>2sigma(I)]	R1 = 0.0891, wR2 = 0.2428
R indices (all data)	R1 = 0.0996, wR2 = 0.2512
Largest diff. peak and hole	0.571 and -0.564 e.$Å^{-3}$



Crystal data and structure refinement for (±)-**161**.

Identification code	dony	
Empirical formula	C20 H20 N2 O3	
Formula weight	336.38	
Temperature	100(2) K	
Wavelength	1.54178 Å	
Crystal system	Monoclinic	
Space group	P 21/c	
Unit cell dimensions	a = 14.9286(4) Å	a= 90°.
	b = 6.8883(2) Å	b= 99.053(2)°.
	c = 16.4514(5) Å	g = 90°.
Volume	1670.67(8) Å^3	
Z	4	
Density (calculated)	1.337 Mg/m^3	
Absorption coefficient	0.735 mm^{-1}	
F(000)	712	
Crystal size	0.24 x 0.16 x 0.05 mm^3	

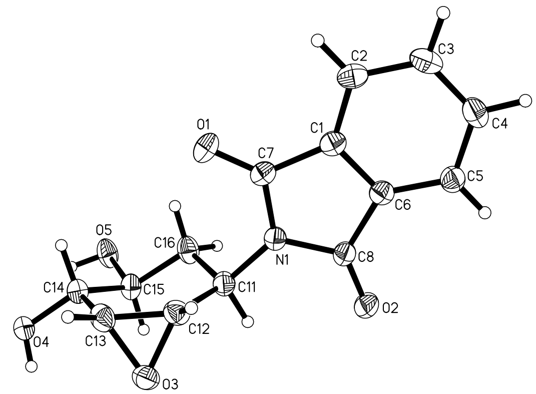
Theta range for data collection	3.00 to 67.49°.
Index ranges	-17<=h<=16, 0<=k<=8, 0<=l<=18
Reflections collected	13354
Independent reflections	2920 [R(int) = 0.0217]
Completeness to theta = 67.49°	96.7 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9642 and 0.8434
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	2920 / 0 / 235
Goodness-of-fit on F^2	1.009
Final R indices [I>2sigma(I)]	R1 = 0.0344, wR2 = 0.0923
R indices (all data)	R1 = 0.0402, wR2 = 0.0969
Extinction coefficient	0.0008(2)
Largest diff. peak and hole	0.232 and -0.167 e.$Å^{-3}$



Crystal data and structure refinement for (±)-**135**.

Identification code	donz	
Empirical formula	C14 H13 N O5	
Formula weight	275.25	
Temperature	100(2) K	
Wavelength	1.54178 Å	
Crystal system	Monoclinic	
Space group	P 21/n	
Unit cell dimensions	a = 5.52500(10) Å	a= 90°.
	b = 17.7359(2) Å	b= 92.8490(10)°.
	c = 12.5209(2) Å	g = 90°.
Volume	1225.42(3) $Å^3$	
Z	4	
Density (calculated)	1.492 Mg/m^3	
Absorption coefficient	0.966 mm^{-1}	
F(000)	576	
Crystal size	0.21 x 0.09 x 0.07 mm^3	

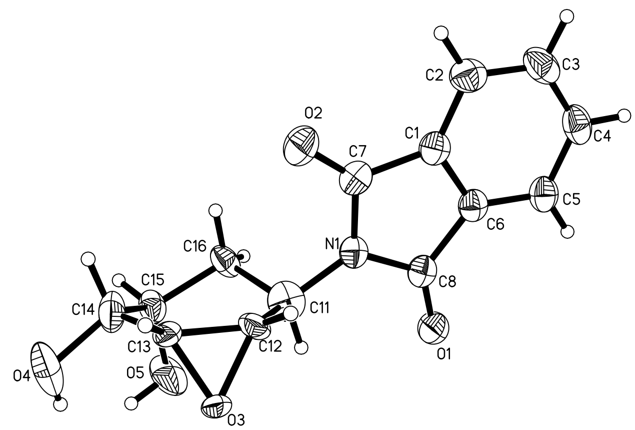
Theta range for data collection	4.33 to 68.17°.
Index ranges	-6<=h<=6, 0<=k<=21, 0<=l<=15
Reflections collected	10319
Independent reflections	2194 [R(int) = 0.0196]
Completeness to theta = 68.17°	97.9 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9354 and 0.8228
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	2194 / 0 / 234
Goodness-of-fit on F^2	0.990
Final R indices [I>2sigma(I)]	R1 = 0.0322, wR2 = 0.0839
R indices (all data)	R1 = 0.0343, wR2 = 0.0858
Extinction coefficient	0.0013(3)
Largest diff. peak and hole	0.266 and -0.173 e.$Å^{-3}$



Crystal data and structure refinement for (±)-**154**.

Identification code	don1a	
Empirical formula	C14 H13 N O5	
Formula weight	275.25	
Temperature	100(2) K	
Wavelength	1.54178 Å	
Crystal system	Monoclinic	
Space group	P 21/n	
Unit cell dimensions	a = 7.2305(4) Å	a= 90°.
	b = 20.6353(11) Å	b= 104.012(4)°.
	c = 8.5115(5) Å	g = 90°.
Volume	1232.16(12) Å^3	
Z	4	
Density (calculated)	1.484 Mg/m^3	
Absorption coefficient	0.961 mm^{-1}	
F(000)	576	
Crystal size	0.24 x 0.15 x 0.04 mm^3	
Theta range for data collection	4.28 to 67.47°.	

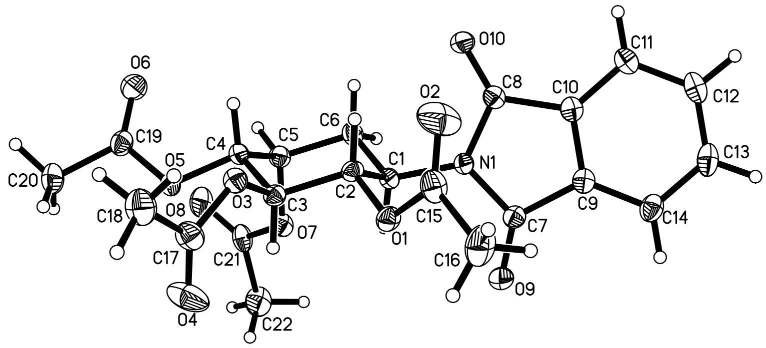
Index ranges	-8<=h<=8, 0<=k<=24, 0<=l<=10
Reflections collected	10020
Independent reflections	2145 [R(int) = 0.0249]
Completeness to theta = 67.47°	98.8 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9626 and 0.8021
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	2145 / 56 / 251
Goodness-of-fit on F^2	1.007
Final R indices [I>2sigma(I)]	R1 = 0.0407, wR2 = 0.0918
R indices (all data)	R1 = 0.0481, wR2 = 0.0959
Extinction coefficient	0.0004(2)
Largest diff. peak and hole	0.211 and -0.200 e.$Å^{-3}$



Crystal data and structure refinement for (±)-**137**.

Identification code	don1b	
Empirical formula	C14 H13 N O5	
Formula weight	275.25	
Temperature	100(2) K	
Wavelength	1.54178 Å	
Crystal system	?	
Space group	?	
Unit cell dimensions	a = 5.4050(3) Å	a= 76.891(3)°.
	b = 7.6853(4) Å	b= 89.431(4)°.
	c = 15.2798(8) Å	g = 78.624(3)°.
Volume	605.62(6) $Å^3$	
Z	2	
Density (calculated)	1.509 Mg/m^3	
Absorption coefficient	0.978 mm^{-1}	
F(000)	288	
Crystal size	0.42 x 0.18 x 0.04 mm^3	

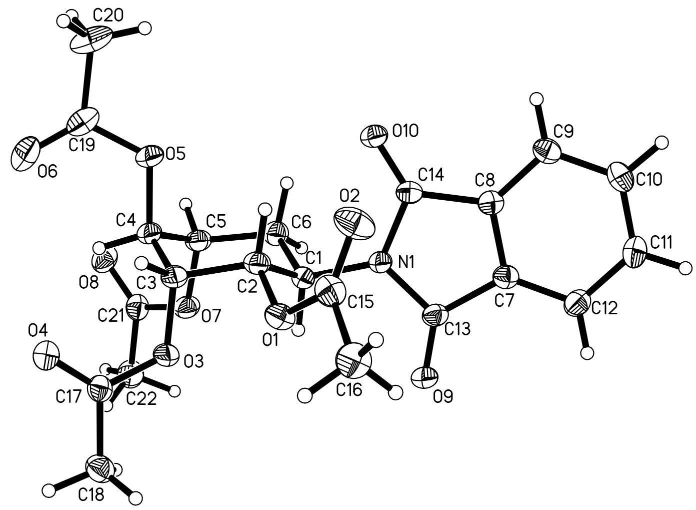
Theta range for data collection	2.97 to 67.23°.
Index ranges	-6<=h<=6, -8<=k<=9, 0<=l<=18
Reflections collected	4840
Independent reflections	2009 [R(int) = 0.0155]
Completeness to theta = 67.23°	98.2 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9619 and 0.6843
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	2009 / 72 / 253
Goodness-of-fit on F^2	1.023
Final R indices [I>2sigma(I)]	R1 = 0.0598, wR2 = 0.1653
R indices (all data)	R1 = 0.0635, wR2 = 0.1689
Extinction coefficient	0.0035(9)
Largest diff. peak and hole	0.368 and -0.546 e.$Å^{-3}$



Crystal data and structure refinement for (±)-**149**.

Identification code	don1c	
Empirical formula	C22 H23 N O10	
Formula weight	461.41	
Temperature	100(2) K	
Wavelength	1.54178 Å	
Crystal system	Monoclinic	
Space group	P 21/n	
Unit cell dimensions	a = 8.8800(3) Å	a= 90°.
	b = 10.6102(3) Å	b= 91.799(2)°.
	c = 23.7595(8) Å	g = 90°.
Volume	2237.48(12) $Å^3$	
Z	4	
Density (calculated)	1.370 Mg/m^3	
Absorption coefficient	0.931 mm^{-1}	
F(000)	968	
Crystal size	0.45 x 0.13 x 0.12 mm^3	
Theta range for data collection	3.72 to 67.79°.	
Index ranges	-10<=h<=10, 0<=k<=12, 0<=l<=28	

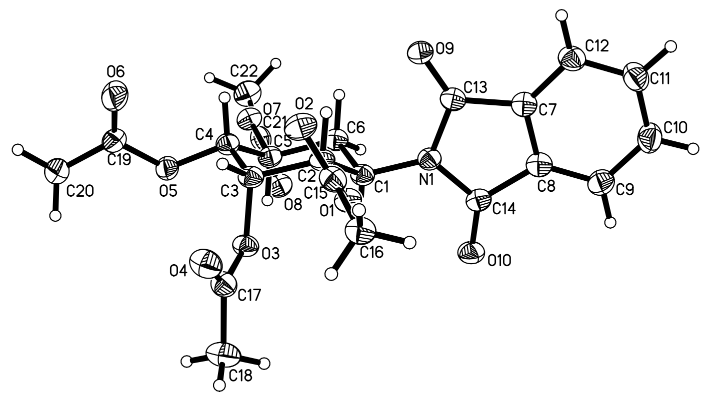
Reflections collected	18364
Independent reflections	3972 [R(int) = 0.0193]
Completeness to theta = 67.79°	98.6 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.8965 and 0.6795
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3972 / 0 / 303
Goodness-of-fit on F^2	1.012
Final R indices [I>2sigma(I)]	R1 = 0.0325, wR2 = 0.0821
R indices (all data)	R1 = 0.0348, wR2 = 0.0839
Extinction coefficient	0.00039(8)
Largest diff. peak and hole	0.271 and -0.198 e.$Å^{-3}$



Crystal data and structure refinement for (±)-**140**.

Identification code	don1d	
Empirical formula	C22 H23 N O10	
Formula weight	461.41	
Temperature	100(2) K	
Wavelength	1.54178 Å	
Crystal system	Monoclinic	
Space group	P 21/c	
Unit cell dimensions	a = 7.3527(2) Å	a= 90°.
	b = 21.4079(7) Å	b= 93.921(2)°.
	c = 14.1359(5) Å	g = 90°.
Volume	2219.87(12) $Å^3$	
Z	4	
Density (calculated)	1.381 Mg/m^3	
Absorption coefficient	0.938 mm^{-1}	
F(000)	968	

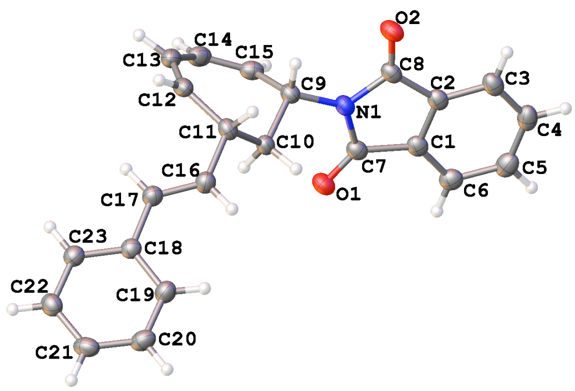
Crystal size	0.20 x 0.18 x 0.18 mm^3
Theta range for data collection	3.75 to 67.16°.
Index ranges	-8<=h<=8, 0<=k<=25, 0<=l<=16
Reflections collected	17338
Independent reflections	3890 [R(int) = 0.0265]
Completeness to theta = 67.16°	98.8 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.8493 and 0.8346
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3890 / 0 / 302
Goodness-of-fit on F^2	0.997
Final R indices [I>2sigma(I)]	R1 = 0.0391, wR2 = 0.0966
R indices (all data)	R1 = 0.0479, wR2 = 0.1019
Largest diff. peak and hole	0.244 and -0.191 e.$Å^{-3}$



Crystal data and structure refinement for (±)-**139**.

Identification code	don1e	
Empirical formula	C22 H23 N O10	
Formula weight	461.41	
Temperature	100(2) K	
Wavelength	1.54178 Å	
Crystal system	Monoclinic	
Space group	C 2/c	
Unit cell dimensions	a = 27.7646(12) Å	a= 90°.
	b = 11.6104(5) Å	b= 123.535(2)°.
	c = 16.3768(7) Å	g = 90°.
Volume	4400.5(3) $Å^3$	
Z	8	
Density (calculated)	1.393 Mg/m^3	
Absorption coefficient	0.946 mm^{-1}	
F(000)	1936	
Crystal size	0.44 x 0.12 x 0.05 mm^3	
Theta range for data collection	3.82 to 67.98°.	
Index ranges	-33<=h<=26, 0<=k<=13, 0<=l<=19	

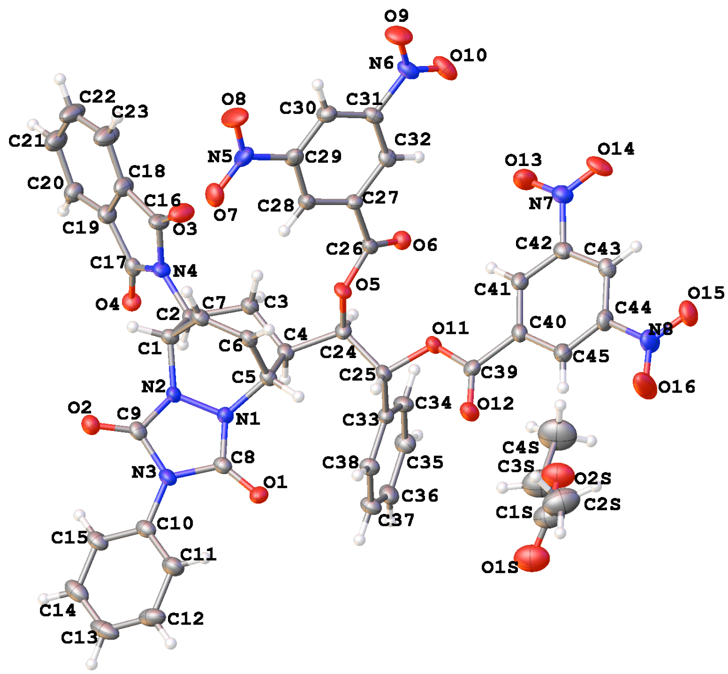
Reflections collected	17563
Independent reflections	3843 [R(int) = 0.0431]
Completeness to theta = 67.98°	98.1 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9542 and 0.6809
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3843 / 0 / 302
Goodness-of-fit on F^2	0.995
Final R indices [I>2sigma(I)]	R1 = 0.0373, wR2 = 0.0972
R indices (all data)	R1 = 0.0464, wR2 = 0.1035
Largest diff. peak and hole	0.236 and -0.200 e.$Å^{-3}$



Crystal data and structure refinement for (±)-**181**.

Identification code	don1g
Empirical formula	$C_{23}H_{19}NO_2$
Formula weight	341.39
Temperature / K	100.0
Crystal system	Triclinic
Space group	P-1
a / Å, b / Å, c / Å	8.8410(3), 9.9197(4), 21.4535(7)
α/°, β/°, γ/°	79.572(3), 89.780(3), 70.498(4)
Volume / $Å^3$	1740.99(12)
Z	4
ρ_{calc} / mg mm^{-3}	1.302
μ / mm^{-1}	0.657
F(000)	720

Crystal size / mm^3	0.15 × 0.08 × 0.05
Theta range for data collection	4.20 to 71.15°
Index ranges	-10 ≤ h ≤ 10, -11 ≤ k ≤ 12, -26 ≤ l ≤ 26
Reflections collected	23107
Independent reflections	6592[R(int) = 0.0283]
Data/restraints/parameters	6592/0/462
Goodness-of-fit on F^2	1.066
Final R indexes [I>2σ (I)]	R_1 = 0.0428, wR_2 = 0.1268
Final R indexes [all data]	R_1 = 0.0505, wR_2 = 0.1334
Largest diff. peak/hole / e $Å^{-3}$	0.273/-0.239



Crystal data and structure refinement for (+)**193**.

Identification code	don1o
Empirical formula	$C_{49}H_{38}N_8O_{18}$
Formula weight	1026.87
Temperature / K	100.6
Crystal system	monoclinic
Space group	$P2_1$
a / Å, b / Å, c / Å	12.2658(2), 12.6155(3), 30.2568(8)
α/°, β/°, γ/°	90.00, 100.078(2), 90.00
Volume / Å^3	4609.66(19)

Z	4
ρ_{calc} / mg mm^{-3}	1.480
μ / mm^{-1}	0.979
F(000)	2128
Crystal size / mm^3	0.33 × 0.08 × 0.03
2Θ range for data collection	7.4 to 147.64°
Index ranges	-11 ≤ h ≤ 14, -14 ≤ k ≤ 15, -37 ≤ l ≤ 37
Reflections collected	25828
Independent reflections	14394[R(int) = 0.0389]
Data/restraints/parameters	14394/1/1355
Goodness-of-fit on F^2	1.072
Final R indexes [I>2σ (I)]	R_1 = 0.0682, wR_2 = 0.1886
Final R indexes [all data]	R_1 = 0.0758, wR_2 = 0.1973
Largest diff. peak/hole / e Å^{-3}	0.570/-0.591