THE APPLICATION OF UMPOLUNG AMIDE SYNTHESIS TO THE ENANTIOSELECTIVE SYNTHESIS OF DIHYDROXYAMIDES

By

DAIN B. BEEZER

Thesis

Submitted to the Faculty of the

Graduate School of Vanderbilt University

in partial fulfillment of the requirements

for the degree of

MASTER OF SCIENCE

in

Chemistry

December, 2013

Nashville, Tennessee

Approved:

Jeffrey N. Johnston, Ph.D.

Gary A. Sulikowski, Ph.D.

ACKNOWLEDGMENT

This work would not have been possible without the financial support of the National Institutes of Health (GM 063557), the D. Stanley and Ann T. Tarbell Endowment Fund, and the Vanderbilt University Chemistry Department.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF SCHEMES

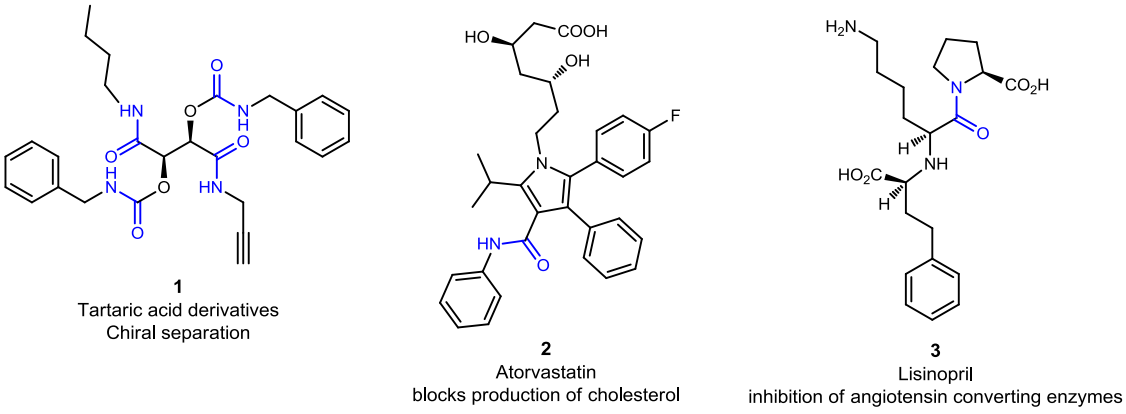
Chapter 1

Background and Introduction

1.1 Importance of Amides

The amide bond is one of the most important linkages in organic chemistry and constitutes the key functional group in peptides, polymers, and many natural products and pharmaceuticals (Figure 1). Purely chemical methods have been developed for the preparation of amides, but most utilize a dehydrative approach, some involving the use of coupling reagents. However, there are drawbacks to this methodology, and although other

Figure 1. Examples of important molecules containing amide bonds illustrating the importance of this functional group.

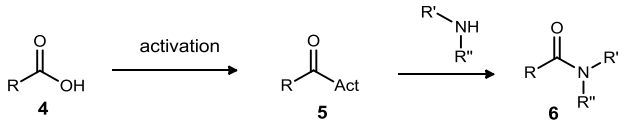


conceptually innovative alternatives exist, there is still a need for alternative methods to target an increasing list of complex problems in amide synthesis.

1.2 Methods of Amide Bond Formation

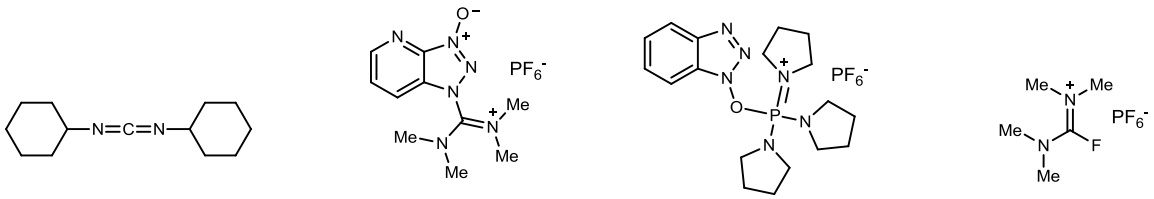
As a result of the importance of amides, much research has been done to find convenient and mild ways for amide synthesis. In its simplest form, an amide can be prepared by the reaction of an amine with an acyl chloride, anhydride, or similar active ester.[1] All of these reactions involve nucleophilic addition-elimination by the amine at the acyl carbon. Carboxylic acids react with amines to give amides. However because of the low reactivity of carboxylate intermediate toward nucleophilic acyl substitution, high

Scheme 1. Dehydrative amide synthesis.



temperatures are required. A much better method, developed by Sheehan and Hess[2] in 1955, involves the use of a dialkylcarbodiimide coupling reagent (for example DCC (**7**)) to promote amide bond formation by reacting with the carboxyl group of an acid and activating it toward nucleophilic acyl substitution (Scheme 1). Since that time, a variety of coupling reagents have been developed.[3] These include uronium salts such as HATU

Figure 2. Amide bond forming reagents.

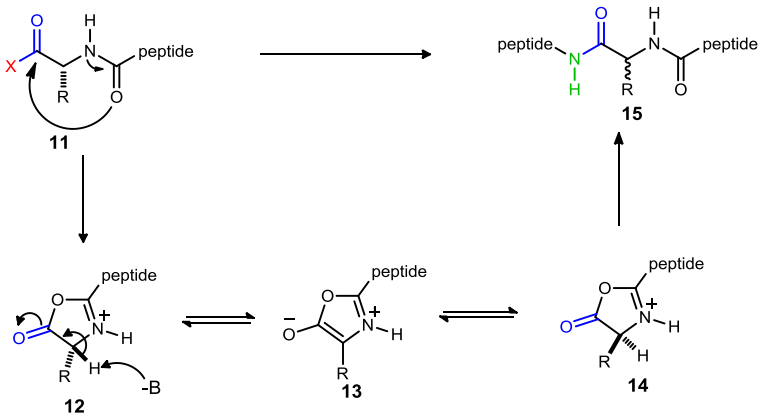


7 DCC | **8** HATU | **9** PyBOP | **10** TFFH

[1] Carey, F.; Giuliano, B. *Organic Chemistry*, McGraw-Hill Companies: New York, 2011
[2] Sheehan, J. C.; Hess, G. P. *J. Am. Chem. Soc*. **1955**, *77*, 1067
[3] For recent reviews, see Montalbetti, C. A. G. N.; Falque, V. *Tetrahedron* **2005**, *61*, 10827; Valeur, E.; Bradley, M. *Chem. Soc. Rev*. **2009**, *38*, 606.

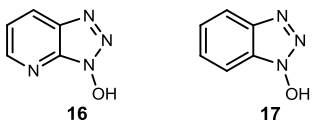
(**8**), phosphonium salts such as PyBOP (**9**) and acid halogenating reagents such as TFFH (**10**) among others (Figure 2). With the widespread availability of a variety of carboxylic acids and amines, this became the preferred method for the synthesis of amides.

Scheme 2. Racemization at the α-carbon of activated carboxylic acids via azlactone formation.



However, as the targets became larger and more complex, new challenges arose. Reactions involving disubstituted amines, peptidic amines or peptidic carboxylic acids resulted in low conversion. In addition, epimerization at the α-carbon of activated α-amino acids became increasingly problematic when using hindered amines. This phenomenon is thought to occur due to the formation of an intermediate azlactone or ketene and commonly occurs with acidic and peptidic carboxylic acids (Scheme 2).[4]

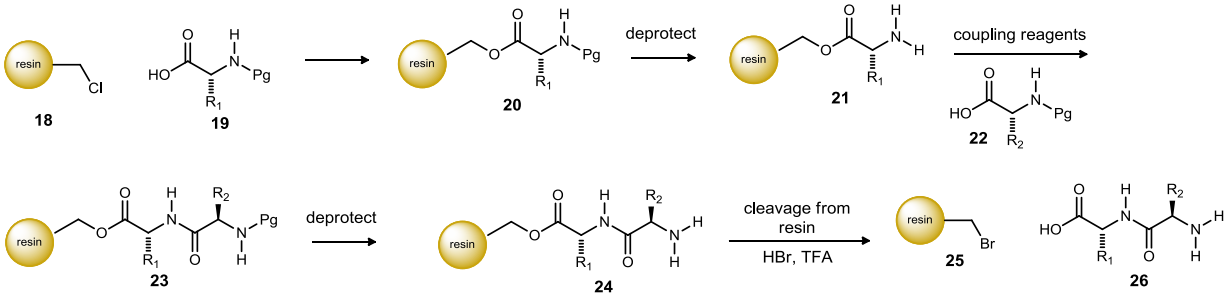
Figure 3. Benzotriazole additives used to reduce epimerization in dehydrative amide synthesis.



[4] Benoiton, N. L. *Chemistry of Peptide Synthesis*; Taylor and Francis Group: Boca Raton, Florida, 2006.

Efforts have been made to overcome the epimerization issue. These involve the use 'racemization suppressants' (Figure 3) such as 1-hydroxy-7-azabenzotriazole (HOAt, **16**)

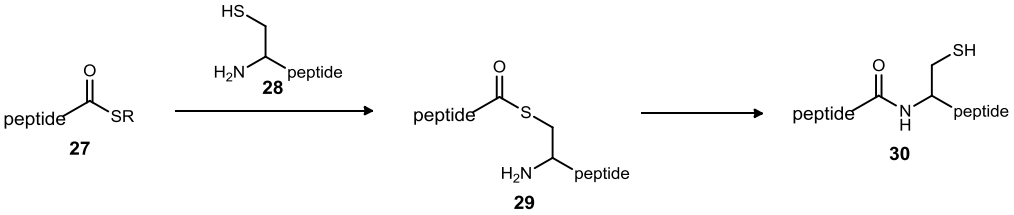
Scheme 3. Solid phase peptide synthesis.



or 1-hydroxy-1*H*-benzotriazole (HOBt, **17**) which minimizes the extent of epimerization, but often fails to eliminate it.[3]

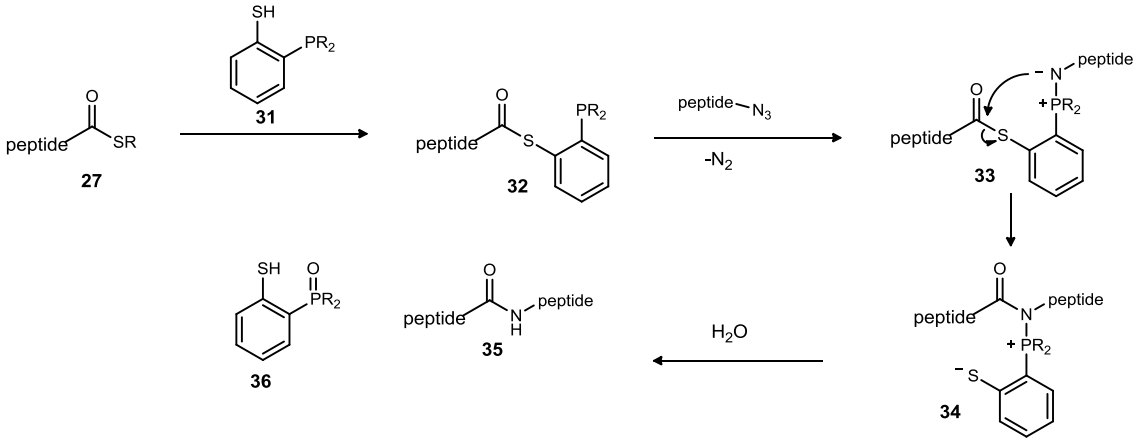
The development of solid phase synthesis addressed the issue of conversion insofar as it allowed the use of excess reagents to drive condensation to completion, while simplifying the purification.[5,6] The desired product is immobilized on a solid support (**18**) and the excess reagents and byproducts are removed by thorough washing.

Scheme 4. Native chemical ligation.



[5] Merrifield, R. B. *J. Am. Chem. Soc.* **1963**, *85*, 2149.
[6] Merrifield R. B. *J. Am. Chem. Soc.* **1964**, *86*, 304.

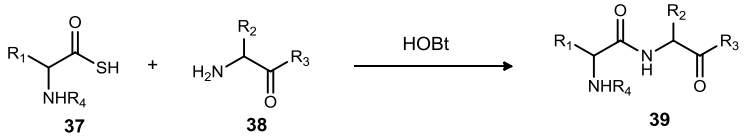
Scheme 5. Staudinger ligation.



New methods have emerged as alternatives to conventional amide synthesis, addressing these practical challenges by conceptual novelty in some cases. Kent and coworkers[7] have developed "native chemical ligation". In this method, the thiolate of an *N*-terminal cysteine residue in one peptide (**28**) reacts with the acyl carbon of a C-terminal thioester in another peptide (**27**) to produce, ultimately, an amide bond between the two peptides (Scheme 4). One limitation of this method is that there is general reliance on the formation of a peptide bond to a cysteine residue at the ligation junction.

Raines and others[8] have developed a new chemical ligation method which

Scheme 6. HOBT-mediated peptide coupling.

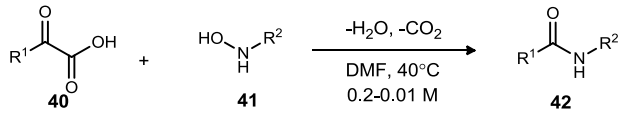


[7] Dawson, P. E.; Muir, T. W.; Clark-lewis, I.; Kent, S. B. *Science* **1994**, *266*, 776

[8] a) Nilsson, B. L.; Kiessling, L. L.; Raines, R. T. *Org. Lett*. **2000**, *2*, 1939. b) Saxon, E.; Armstrong, J.I.; Bertozzi, C. R. *Org. lett.* **2000**, *2*, 2141. c) For a recent review see: Kohn, M.; Breinbauer, R. *Angew. Chem. Int. Ed.* **2004**, *43*, 3106

overcomes the limitation of native chemical ligation (Scheme 5). This method uses a phosphinobenzenethiol (**31**) to link a thioester and an azide and is based on the Staudinger reaction.

Scheme 7. Chemoselective α-ketoacid-hydroxylamine (KAHA) ligation.



Danishefsky and coworkers[9] have also developed a method of peptide ligation that addresses the restrictions of native chemical ligation. They accomplished the coupling of C-terminal thio acids **37** with N-terminal peptides **38** in the presence of HOBt **17** (Scheme 6).

Another method of chemical ligation was developed by the Bode laboratory.[10] Their novel approach involves the decarboxylative condensation of *N*-alkyl hydroxylamines **41** and α-keto acids **40** (Scheme 6). This reaction proceeds in the presence of reactive functional groups, requires no reagents or catalyst, and produces only water and carbon dioxide as byproducts.

Another environmentally friendly method of amide synthesis is the direct amidation of amines with alcohols[11] where two molecules of dihydrogen are liberated (Scheme 8). This unique transformation uses a ruthenium pincer complex **45** for the direct coupling of sterically unhindered primary amines and alcohols.

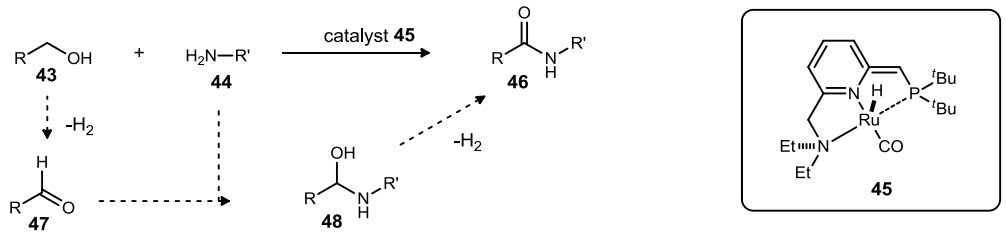
---

[9] a) Li. X.; Danishefsky, S. J. *J. Am. Chem. Soc.* **2008**, *130*, 5446. b) Li. X.; Yuan, Y.; Kan, C.; Danishefsky, S. J. *J. Am. Chem. Soc.* **2008**, *130*, 13225. c) Wang. P.; Danishefsky, S. J. *J. Am. Chem. Soc.* **2010**, *132*, 17045.

[10] Bode, J. W.; Fox, R. M.; Baucom, K. D. *Angew. Chem. Int. Ed*. **2006**, *45*, 1248.

[11] a) Gunanathan, C.; Ben-David, Y.; Milstein, D. *Science* **2007**, *317*, 790. b) Nordstrom, L. U.; Vogt, H.; Madsen, R. *J. Am. Chem. Soc.* **2008**, *130*, 17672

Scheme 8. Oxidative amidation of alcohols.



The concept of using transition metals to catalyze amide bond formation has been applied to other functional groups. The scope includes amidation of nitriles,[12] aldehydes,[13] alkenes,[14] and alkynes[15] with amines. Though powerful, the applications are limited by the use of relatively expensive transition metal catalysts.

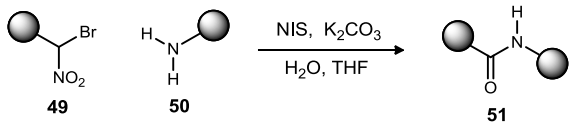
In summary, amide formation is a fundamental reaction in organic chemistry. The importance of amides in chemistry and biology has spurred several different innovative methods for their synthesis. However, as the complexity of biologically active molecules is ever increasing, so is the need for an increase in the depth and scope of amide synthesis to increase the accessibility to various classes of highly complex biological molecules. To do this under mild aqueous conditions and without the generation of waste is a challenging goal.

[12] Cobley, C. J.; van den Heuvel, M.; Abbadi, A.; de Vries, J. G. *Tet. Lett*. **2000**, *41*, 2467.
[13] a) Yoo, W. J.; Li, C. J. *J. Am. Chem. Soc*. **2006**, *128*, 13064. b) Gao, J.; Wang, G.-W. *J. Org. Chem.* **2008**, *73*, 2955.
[14] Beller, M.; Cornilis, B.; Frohning, C. D. *J. Mol. Catal. A: Chem*. **1995**, *104*, 17.
[15] Chan, W. K.; Ho, C. M.; Wong, M. K.; Che, C. M. *J. Am. Chem. Soc*. **2006**, *128*, 14796.

1.3 Umpolung Reactivity in Amide Synthesis.

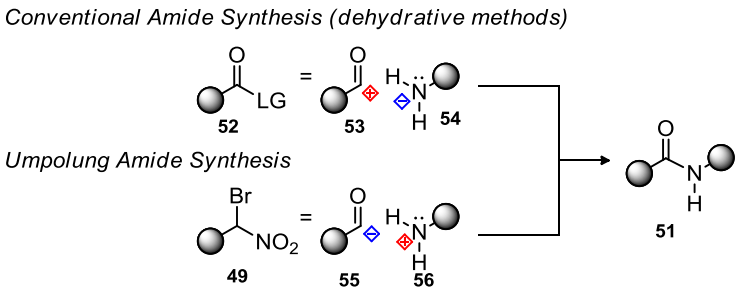
A conceptually new approach to amide synthesis was developed in our lab.[16] Instead of a conventional approach which involves the nucleophilic addition-elimination

Scheme 9. Umpolung amide synthesis.



reaction by the amine on an electrophilic active ester derivative, our approach uses an α-bromo nitroalkane **49** as an acyl donor for a variety of amines (Scheme 9). *N*-Iodosuccinimide **60** is used to activate the amine, and potassium carbonate is used to maintain mildly alkaline condition. Contrary to traditional methods, the amine played the role of the electrophile and the bromonitroalkane played the role of the nucleophile. For this reason the term umpolung[17] (reversed) applies (Scheme 10).

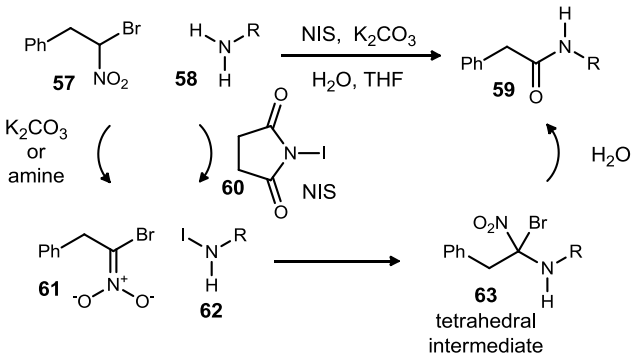
Scheme 10. Umpolung reactivity applied to amide synthesis**.**



[16] Shen, B; Makley, D. M.; Johnston, J. N. *Nature* **2010**, *465*, 1027.
[17] Seebach, D. *Angew. Chem. Int. Ed*. **1979**, *18*, 239

The coupling between an α-bromonitroalkane **57** and an amine **58** was first thought to occur by the initial iodination of the amine and the deprotonation of the α-bromonitroalkane to form the nitronate **61**, followed by subsequent attack of the *N*-iodo amine **62** by the nucleophilic nitronate which forms the key carbon nitrogen bond. Hydrolysis of the tetrahedral intermediate **63** constituted one possible pathway to form the final amide product (Scheme 11).

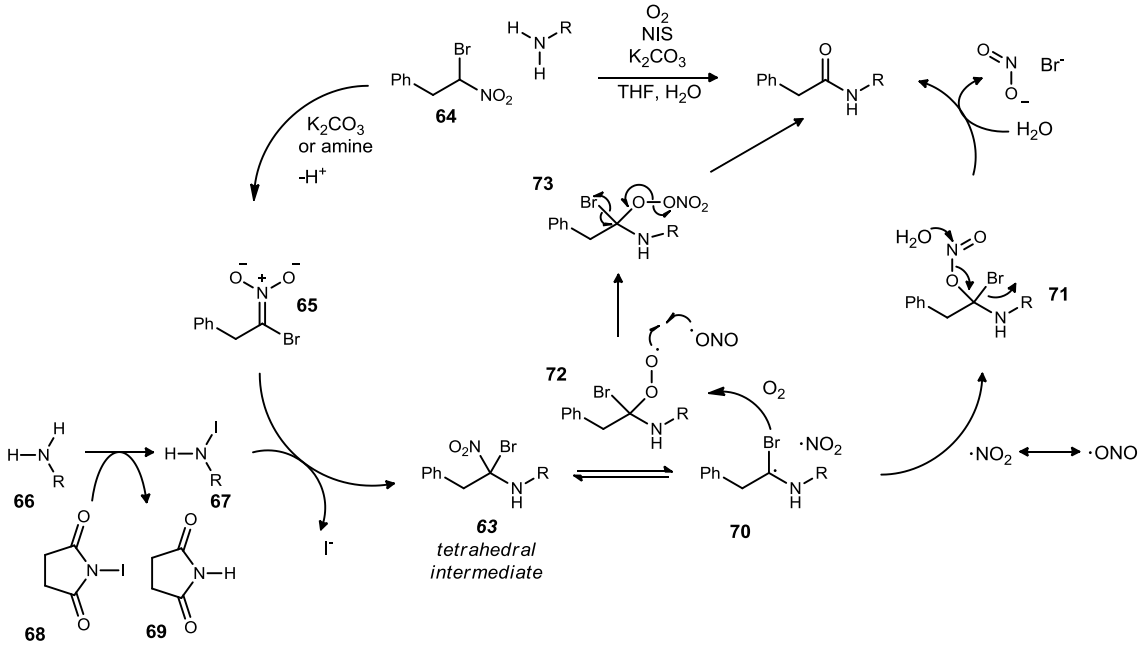
Scheme 11. Umpolung amide synthesis proposed mechanism.



Through a series of experiments designed to gain additional mechanistic insight in the proposed pathway outline above, it was found that two pathways, aerobic and anaerobic, exist that can lead to amide bond formation.[18]

[18] Shackleford, J. P.; Shen, B.; Johnston, J. N. *Proc. Natl. Acad. Sci.* **2012**, *109*, 44-46

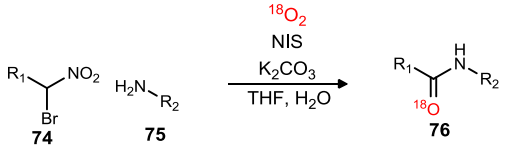
Scheme 12. Proposed aerobic and anaerobic pathways of amide bond synthesis.



In the aerobic pathway (Scheme 12), the tetrahedral intermediate **63** undergoes homolytic bond cleavage to produce an alkyl and a nitro radical. The alkyl radical **70** traps triplet oxygen to give a peroxide radical **72**. The peroxide radical combines with the nitrogen dioxide radical to give **73**, followed by homolytic cleavage of the oxygen-oxygen bond and the bromine-carbon bond to give the desired amide. In the anaerobic pathway, following the homolysis of the tetrahedral intermediate, the nitro radical recombines with the alkyl radical forming a new carbon-oxygen bond **71**. Subsequent attack by water followed by elimination of bromine gives the desired amide. This method allows for the synthesis of amides without epimerization or extensive protection and deprotection.

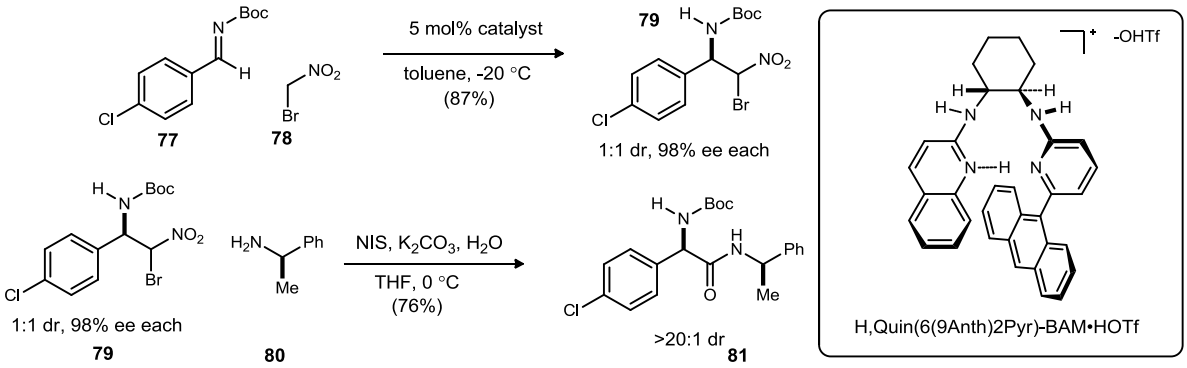
The scope of the umpolung amide synthesis includes the enantioselective synthesis of aryl glycines and α-oxy amides. It can also be used for site selective amide ^{18}O-labeling[17] (Scheme 13). All this and more is possible through the ability to access the

Scheme 14. ^{18}O-labeled amide synthesis.



chiral α-bromo nitroalkane precursor necessary to provide the desired amide. Our group has reported the highly enantioselective aza-Henry reaction with commercially available bromonitromethane **78** utilizing chiral proton catalysis to prepare the required chiral α-bromo nitroalkane **79** for aryl glycine amide synthesis **81** (Scheme 14).

Scheme 13. Enantioselective aryl glycine homologation.

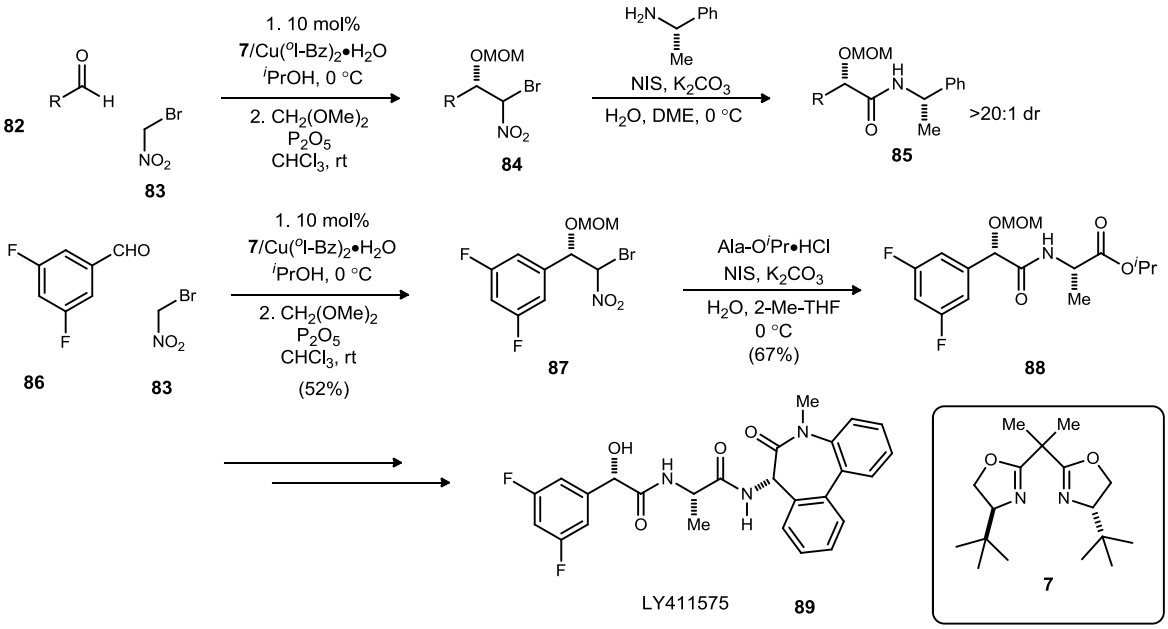


Additionally, our group recently developed an enantioselective Henry reaction using bromonitromethane and a copper bis(oxazoline) system **7** to furnish the chiral α-bromo nitroalkane precursor **84** required for the synthesis of α-oxy amides **85**.[19]

[19] Leighty, M. W.; Shen, B.; Johnston, J. N. *J. Am. Chem. Soc*. **2012**, *134*, 15233

Umpolung amide synthesis can also be applied to the synthesis of biologically active molecules as demonstrated by the synthesis of LY411575 **89** (Scheme 15), a potent γ-secretase inhibitor developed for the treatment of Alzheimer's disease. This combination of entirely enantioselective methods with α-bromo nitroalkane-amine couplings may ultimately enable the efficient fully chemical synthesis of chiral non-racemic unnatural peptides and other biologically active natural products.

Scheme 15. Enantioselective mandelamide synthesis and its application to the synthesis of LY411575.

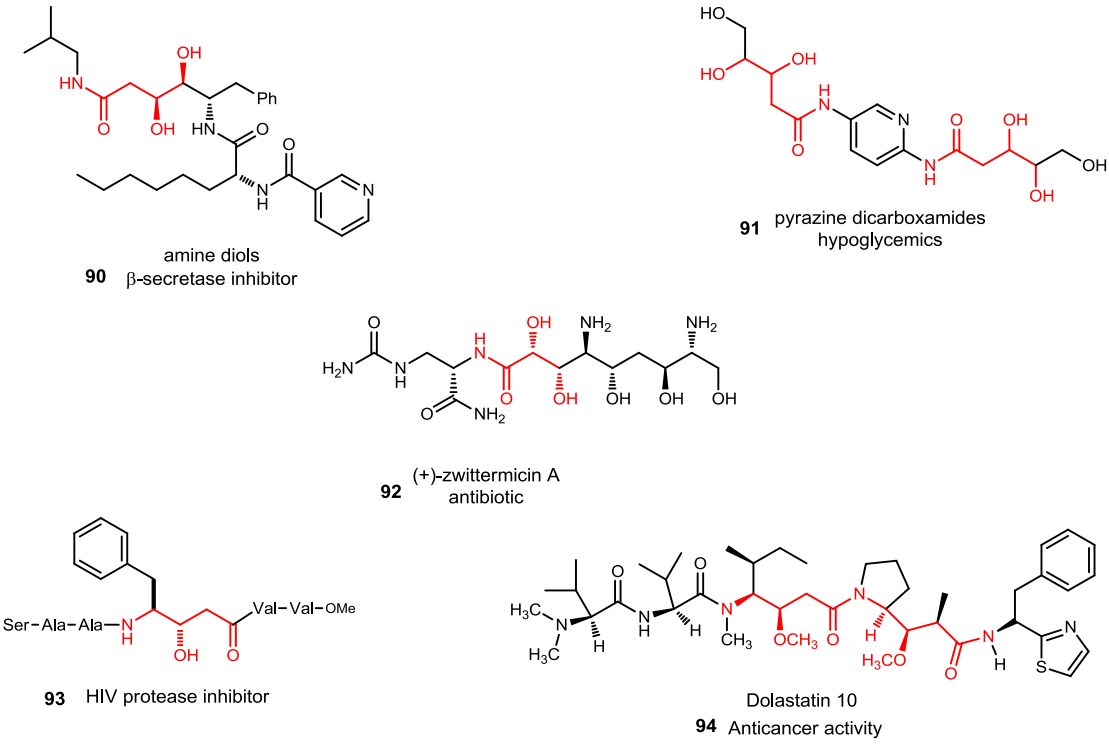


1.4 Dihydroxyamides and Aminohydroxyamides

The scope of the umpolung amide synthesis can be further expanded by demonstrating its utility to synthesize aminohydroxy and dihydroxyamides. These are present as standalone molecules or structural motif of many biologically active natural

products (Figure 4).[20] The chemical synthesis of these motifs is challenging and so there are very few synthetic methods that can provide access to these types of molecules. We envision that by combining the enantioselective synthesis of the requisite aminohydroxy and dihydroxy α-bromonitroalkane with Umpolung Amide Synthesis, a variety of chiral non-racemic aminohydroxy and dihydroxyamides can be accessed, hence opening doors that will lead to the chemical synthesis of complex biologically active natural products and pharmaceuticals.

Figure 4. Examples of biologically active molecules containing aminohydroxy or dihydroxy amides.



[20] He, H.; Silo-Suh, L. A.; Handelsman, J.; Clardy, J. *Tetrahedron Lett*. **1994**, *35*, 2499-2502. Bashiardes, G.; Carry, J.; Evers, M.; Filoche, B.; Mignani, S. WO 99/03844, 1999. Schostarez, H. J.; Chrusciel, R. A. WO 2003/006453, 2003; *Synthesis* **1996**, *6*, 719-725

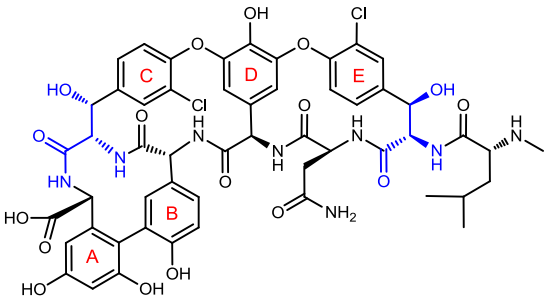
Chapter 2

Synthesis of α,β-Dihydroxy Amides

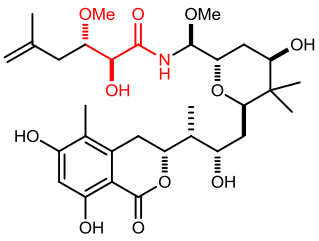
2.1 Importance of α,β-Dihydroxy and Aminohydroxy amides.

α,β-Dihydroxy amides and aminohydroxy amides are found as constituents of

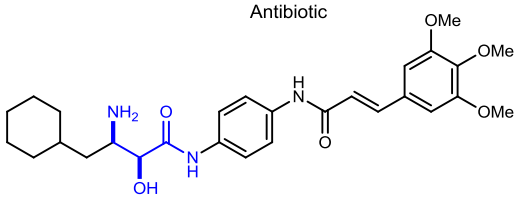
Figure 5. Examples of molecules containing α,β-dihydroxy and amino hydroxy amides.



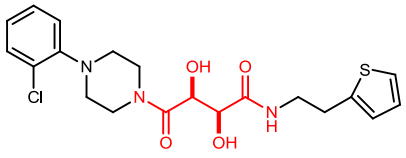
95 Vancomycin Aglycon
Antibiotic



96 Psymberin
anticancer



97 Bestatin-based derivatives
potent anti-angiogenic activity



Bis-amides of tartrate
98 Tumor necrosis factor-α convertase (TACE)

various biologically active natural products and pharmaceuticals (Figure 5). For example, vancomycin **95**, a glycopeptide antibiotic, is currently in use, and is mainly used for the treatment of various acute infections due to gram-positive bacteria.[21] This antibiotic has an α-amino β-hydroxy amide as part of its molecular structure. Psymberin **96** is a potent and selective cancer cell growth inhibitor, isolated from the extracts of deep water

[21] Malabarba, A.; Nicas, T. I.; Thompson, R. C. *Med. Res. Rev.* **1997**, *17*, 69.

sponges.[22] Its molecular structure includes an α-hydroxy β-oxy amide moiety. Bestatin-based derivatives **97** often include α-hydroxy β-amino amides, and have been shown to possess potent anti-angiogenic activity, which is related to the treatment of cancer.[23] Bisamide derivatives of tartrate **98** have also been shown to have anti-cancer activity. Furthermore, the presence of the dihydroxy groups has been shown to play a key role in the mechanism of action of these derivatives.[24] Given the biological significance of these types of amides, a number of reactions have been developed to provide access to these motifs.

2.2 Preparation of α,β-Dihydroxy and Aminohydroxy Amides

The most common synthetic method used to access these types of amides employs the use of dehydrative amide synthesis. Typically the requisite dihydroxy or aminohydroxy acid or ester is synthesized through a multi-step process, and peptide coupling reagents are used to form the amide bond. An example of this can be seen in the synthesis of bis(amide) derivatives of tartrate **98**.[25] Esterification of L-tartaric acid followed by acetonide protection and partial hydrolysis yields the requisite protected dihydroxy acid needed for amide bond formation. Two methods are commonly used to install the dihydroxy groups. The first is an aldol reaction. One example of this is within Crimmins' synthesis of psymberin **96**.[26] The second is Sharpless asymmetric

[22] Cichewicz, R. H.; Valeriote, F. A.; Crews, P. *Org. Lett.* **2004**, *6*, 1951
[23] Sendzik, M.; Janc, J. W.; Cabuslay, R.; Honigberg, L.; Mackman, R. L.; Magill, C.; Squires, N.; Waldeck, N. *Bioorg. Med. Chem. Lett*. **2004**, *14*, 3180-3184.
[24] Rosner, K. E. et al. *Bioorg. Med. Chem. Lett*. **2010**, *20*, 1189-1193
[25] Rosner, K. E. et al. *Bioorg. Med. Chem. Lett*. **2010**, *20*, 1189-1193
[26] Crimmins, M. T.; Stevens, J. M.; Schaaf, G. M. *Org. Lett*. **2009**, *11*, 3990-3993

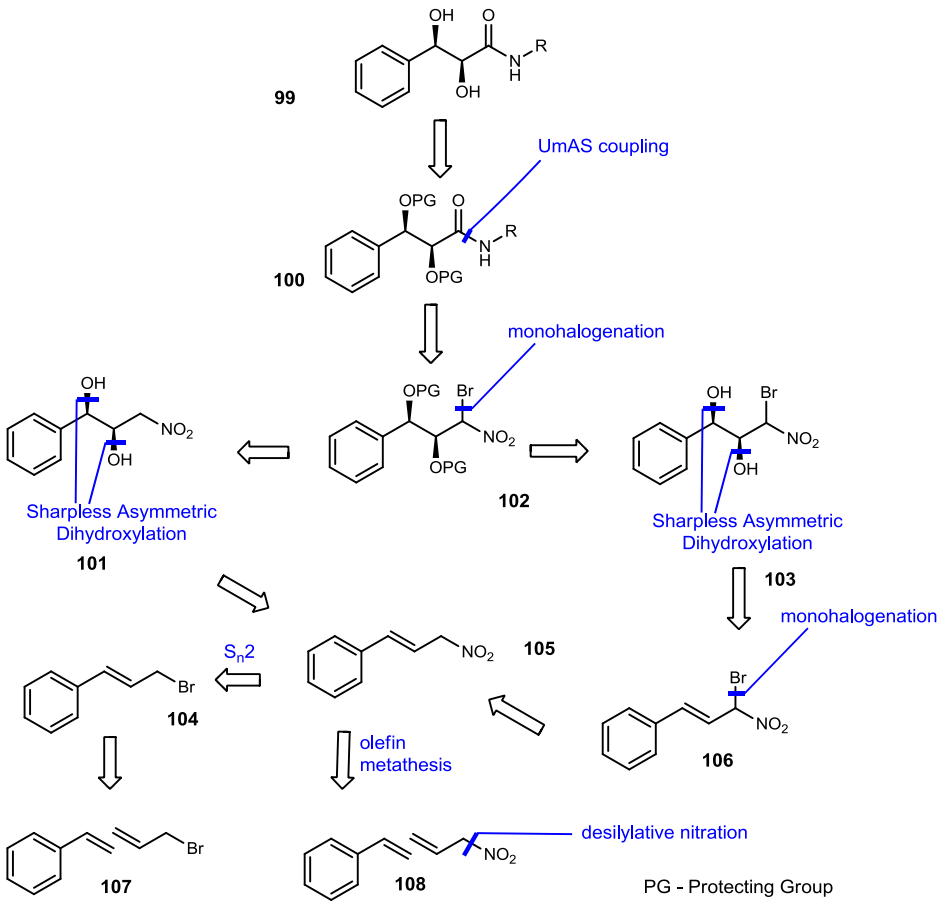
dihydroxylation. One example is in the Hruby synthesis of serine derivatives.[27] Sharpless asymmetric aminohydroxylation has been used to access aminohydroxy amides via a traditional route. An example of this is in the synthesis of vancomycin **95**.[28] One of the major drawbacks of these synthetic methodologies is epimerization. With the number of complex targets on the rise, there exists a need for more convenient and effective methodologies to access these molecules.

2.3 Enantioselective Synthesis of α,β-Dihydroxy Amides via Umpolung Amide Synthesis

To further expand the current scope of the umpolung amide synthesis to include synthesis of dihydroxyamides, an enantioselective synthesis of the requisite amide donor had to be developed. Synthesis of chiral non-racemic dihydroxy α-bromonitroalkane has not been published in the literature and there is very little done on the dihydroxylation of nitroalkenes. Hence it was hypothesized that the desired β,γ-dihydroxy α-bromonitroalkane **103** could be synthesized by a short sequence of reactions starting with alkene cross-metathesis, followed by asymmetric dihydroxylation. Subjecting the β,γ-dihydroxy α-bromonitroalkane to UmAS conditions will furnish the desired amide **99** (Scheme 16). It was also envisioned that aminohydroxy amides could be accessed through this route by substituting Sharpless asymmetric dihydroxylation with Sharpless asymmetric aminohydroxylation.

[27] Xiong, C.; Wang, W.; Hruby, V. J. *J. Org. Chem*. **2002**, *67*, 3514-3517
[28] Evans, D. A. *et. al Angew. Chem., Int. Ed.* **1998,** *37*, 2700. Nicolaou, K. C. *et. al. Angew. Chem., Int. Ed.* **1998,** *37*, 2717 and the references cited therein

Scheme 16. Retrosynthetic analysis for the synthesis of α,β-dihydroxyamides.

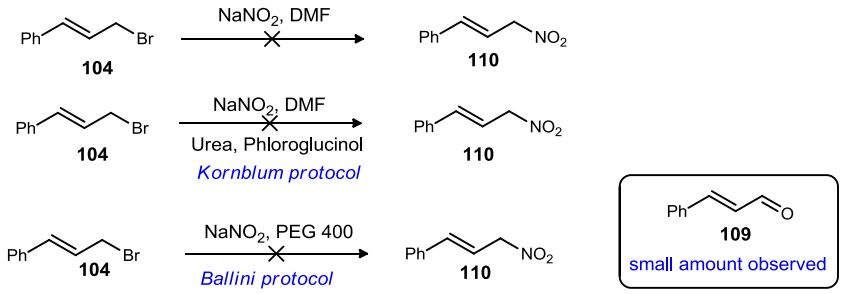


2.3.1 Synthesis of β,γ-unsaturated bromonitroalkene

Initial attempts to prepare β,γ-unsaturated nitroalkenes started with the nucleophilic substitution reaction between cinnamyl bromide **104** and sodium nitrite. Cinnamyl bromide was stirred with sodium nitrite in dimethylformamide for 24 h according to Kornblum's protocol.[29] Analysis of the crude reaction mixture by ^{1}H NMR showed that no reaction had occurred, as only peaks corresponding to the starting material were

[29] Kornblum, N.; Larson, H. O.; Blackwood, R. K.; Moonberry, D. D.; Graham, G. E. *J. Am. Chem. Soc.* **1956**, *78*, 1497

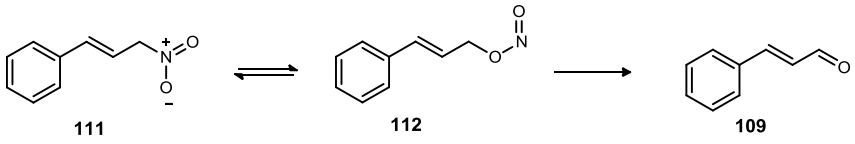
Scheme 17. Synthesis of 1-phenyl-3-nitropropene via nucleophilic substitution.



present in the spectrum. The same reaction was repeated using Ballini's protocol,[30] in which a different solvent was used. However, no conversion of starting material was observed by NMR (Scheme 17). There was however, a trace amount of cinnamaldehyde **109** observed ^{1}H NMR. The formation of this undesired product is thought to occur by the decomposition of the nitrite byproduct **112** of this reaction, or by an isomerization of the nitroalkane **111** to the nitrite[31] followed by decomposition (Scheme 18).

As a result of previously failed attempts, it was hypothesized that the β,γ-unsaturated α-bromonitroalkene could be accessed directly through a Henry reaction between the desired aldehyde and bromonitromethane followed by dehydration to give the desired product. The ultimate goal would be to develop conditions that would favor

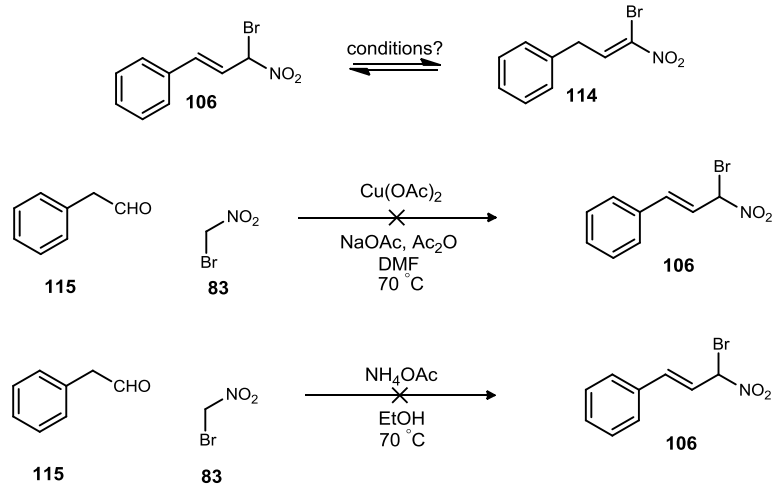
Scheme 18. Isomerization of nitroalkene to nitrite followed by decomposition to the aldehyde.



[30] Ballini, R.; Barboni, L.; Palmieri, A. *Green Chem.* **2008**, *10*, 1004
[31] Hochstein, W.; Schollkopf U. *Liebigs Ann. Chem.* **1978**, *11*, 1823-1834

formation of the β,γ-unsaturated **106** over the α,β-unsaturated α-bromonitroalkene **114**. To this end, benzaldehyde **115** and bromonitromethane **83** was stirred in the presence of copper acetate, sodium acetate and acetic anhydride in dimethyl formamide at 70 °C. Analysis of the crude ^{1}H NMR spectrum showed no conversion of starting materials. The reaction conditions were changed to ammonium acetate in ethanol at 70 °C. However, no conversion of starting material to product was observed (Scheme 19).

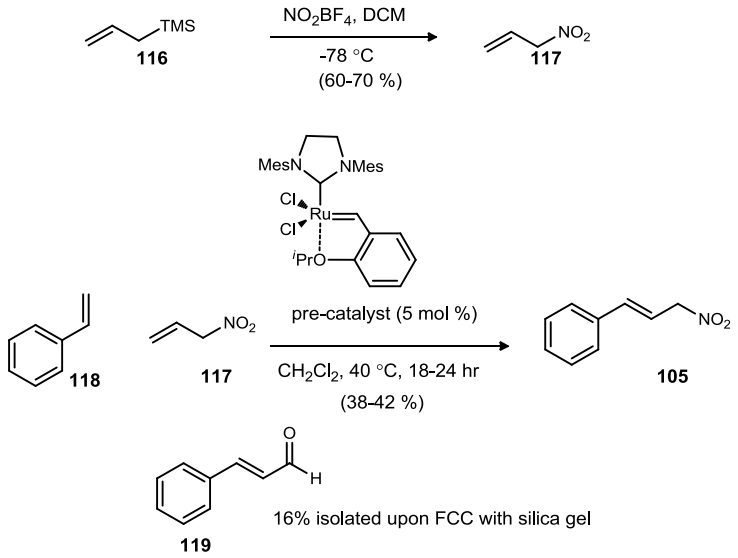
Scheme 19. Synthesis of β,γ-unsaturated α-bromonitroalkene via Henry reaction.



Taking into consideration previous failed attempts, it was hypothesized that the desired β,γ-unsaturated α-bromonitroalkene could be accessed by alkene metathesis followed by α-monobromination. To this end, 3-nitropropene **117** was synthesized by the desilylative nitration of allyltrimethylsilane.[32] Alkene cross-metathesis of styrene with 3-nitropropene[33] furnished the desired nitroalkene in moderate yield. The yield was affected by the decomposition of the nitroalkene upon silica gel chromatography (Scheme 20).

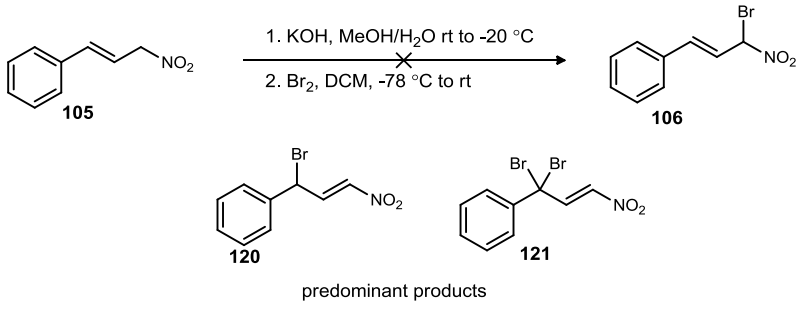
[32] Olah, G.; Rochin, C. *J. Org. Chem*. **1987**, *52*, 701-702.
[33] Wdowik, T.; Samojlowicz, C.; Jawiczuk, M.; Zarecki, A.; Grela, K. *Synlett* **2010**, *19*, 2931-2935.

Scheme 20. Desilylative nitration followed by alkene cross-metathesis.



The desired nitroalkene was then subjected to α-monobromination according to literature procedures[34] (). Analysis of the crude ^{1}H NMR spectrum showed that two undesired products were formed in this reaction, as a result of brominating at the benzylic carbon

Scheme 21. Monobromination of 1-phenyl-3-nitropropene**.**

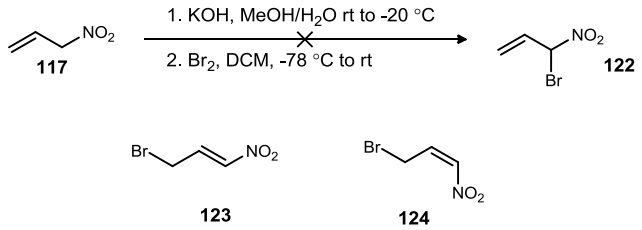


instead of the α-carbon. In light of these results, a different approach was explored. This approach involves the α-monobromination of 3-nitropropene followed by alkene cross-

[34] Erickson, A. S.; Kornblum, N. *J. Org. Chem.* **1977**, *42*, 3764-3765

metathesis to provide the desired β,γ-unsaturated α-bromonitroalkene. When 3-nitropropene was subjected to α-monobromination, the desired product was not observed. Instead, bromination at the γ-position occurred to give a geometric mixture of nitroalkene isomers **123** and **124** (Scheme 22).

Scheme 22. Monobromination of 3-nitropropene.

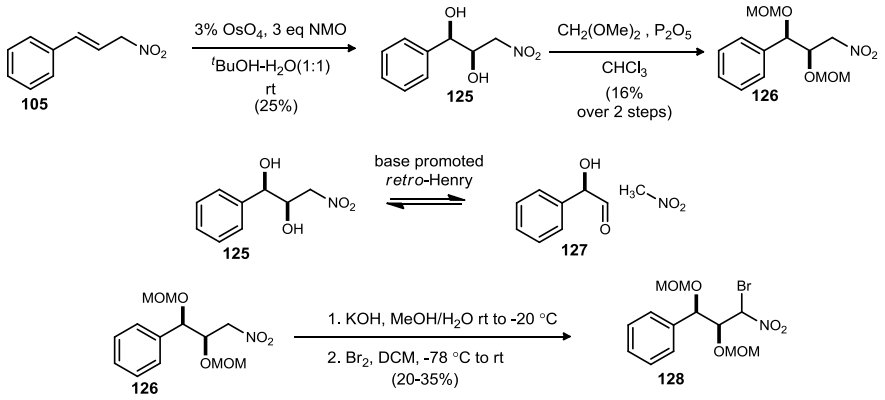


2.3.2 Synthesis of Racemic β,γ-Dioxy α-Bromonitroalkane

At this point, it became clear that the presence of the double bond was problematic and that we would not be able to access the desired β,γ-unsaturated α-bromonitroalkene. Hence an alternate route was developed. This involves the dihydroxylation of the β,γ-nitroalkene **105** followed by α-monobromination. Hence, the desired nitroalkene was subjected to Upjohn dihydroxylation[35] which provided the desired racemic *cis*-diol in moderate yield. The *cis*-diol **125** was subjected to methoxymethyl ether protection to prevent the decomposition of the *cis*-diol by a *retro*-Henry pathway. The protected *cis*-diol **126** was then subjected to α-monobromination, which provided the desired β,γ-dihydroxy-α-bromonitroalkane **128** (Scheme 23).

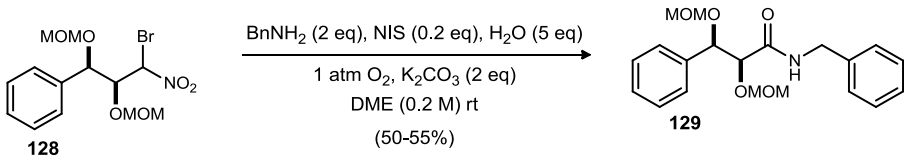
[35] VanRheenen, V.; Kelly, R. C.; Cha, D. Y. *Tetrahedron. Lett*. **1987**, *17*, 1973-1976

Scheme 23. Upjohn dihydroxylation, followed by MOM protection to prevent *retro*-Henry, and subsequent monobromination.



The β,γ-dihydroxy-α-bromonitroalkane was then subjected to Umpolung Amide Synthesis conditions which furnished the desired amide **128** in good yield (Scheme 24). In summary, the synthesis of α,β-dihydroxyamide has been achieved in four steps from commercially available materials.

Scheme 24. Umpolung amide coupling with β,γ-dioxy α-bromonitroalkane and benzyl amine.

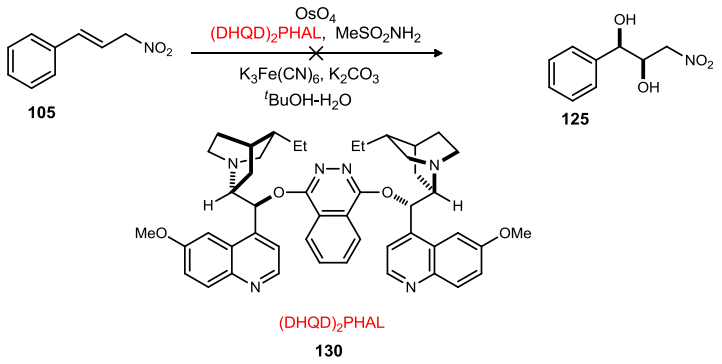


2.3.3 Synthesis of Chiral Non-Racemic β,γ-Dihydroxy α-Bromonitroalkane.

The Sharpless asymmetric dihydroxylation was utilized to synthesize the requisite enantioenriched diols. Using the commercially available premixed asymmetric

dihydroxylation reagent (AD-mix-α), the nitroalkene **105** was subjected to asymmetric dihydroxylation conditions.[36] Analysis of the crude reaction mixture by ^{1}H NMR, showed that the starting material had been consumed but there was no sign to the desired product (Scheme 25).

Scheme 25. Sharpless asymmetric dihydroxylation of β,γ-unsaturated nitroalkenes.



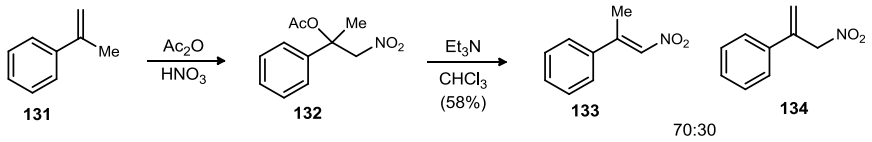
It was very challenging to identify the decomposition products of the reaction as it appears that these byproducts are water soluble. The reaction condition was modified by increasing the amount of osmium tetroxide and decreasing the amount of potassium carbonate. It was envisioned that this would increase the rate of the desirable reaction over a possible background reaction that could be responsible for the decomposition of the substrate. However, no product or byproducts were isolated. The temperature of the reaction was lowered in an effort to reduce decomposition of the nitroalkene. After a period of 24 hours, analysis by ^{1}H NMR showed that the rate of decomposition had slowed, but no diol formation was observed. Decomposition of the starting nitroalkene was investigated, by exposing the racemic diol to the reaction conditions. After 24 hours, most of the diol was recovered. This indicates that the alkene is decomposing before the

[36] Sharpless, K. B.; Amberg, W.; Bennani, Y.; Crispino, G. A.; Hartung, J.; Jeong, K.; Kwong, H.;, Morikawa, K.; Wang, Z. Xu, D.; Zhang, X. *J. Org. Chem* **1992**, *57*, 2768-2771.

diol is formed. This led to an investigation of the individual reagents in the reaction mixture. The alkene was stirred with each reagent separately. Analysis of ^{1}H NMR showed that in the presence of the ligand and potassium carbonate, the alkene decomposed. This led to the conclusion that the nitroalkene is base-sensitive. An investigation of the influence of pH on the dihydroxylation of this base-sensitive substrate followed. The reaction was examined in various buffer solutions ranging from pH 5 to pH 12. However, this only affected the rate of disappearance of the nitroalkene. Acetic acid was added as an additive to the reaction based on a literature protocol,[37] however no product was observed.

At this stage, it was hypothesized that changes to the substrate might help to identify the decomposition pathway for these β,γ-unsaturated nitroalkenes. The use of a 1,1-disubstituted nitroalkene was explored. 3-Nitro-2-phenylpropene **134** was

Scheme 26. Synthesis of 3-nitro-2-phenylpropene.

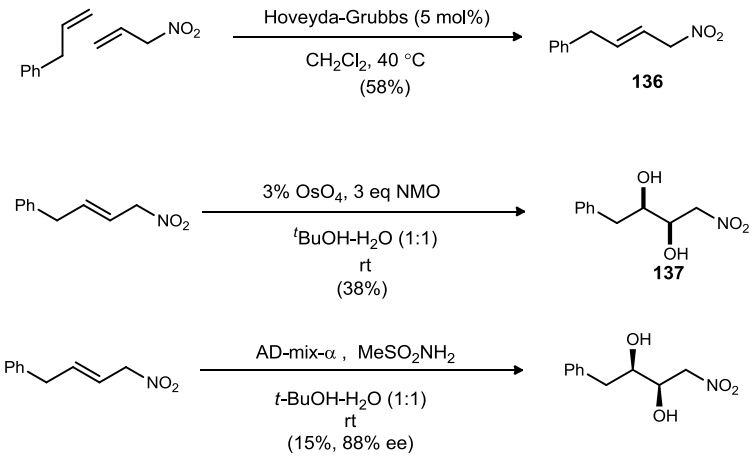


synthesized in two steps by literature[38] procedure (Scheme 26). 3-Nitro-2-phenylpropene **134** was subjected to asymmetric dihydroxylation conditions. The ^{1}H NMR spectrum of the reaction mixture exhibited no peaks corresponding to the desired product or the starting alkene. Further attempts to synthesize the desired non-racemic diol from the above-mentioned substrates were unsuccessful.

[37] Budzinska, A.; Sas, W. *Tetrahedron Lett.* **2001**, *42*, 105-107
[38] Ohta, H.; Kobayashi, N.; Ozaki, K. *J. Org. Chem.* **1989**, *54*, 1820-1804

To investigate whether further modification of the substrate would yield any desirable results, an aliphatic β,γ-unsaturated nitroalkene was explored. 1-Nitro-4-phenyl-2-butene **136** was synthesized using a previously described procedure (Scheme 27). The aliphatic β,γ-unsaturated nitroalkene was subjected to asymmetric dihydroxylation for 10 minutes. Upon analysis of the ^{1}H NMR, it was determined that the reaction was somewhat successful as the spectrum had peaks corresponding to both product diol and starting alkene. The desired product was isolated and analyzed by chiral high pressure liquid chromatography (HPLC), and found to be 88% ee. This led to the conclusion that this methodology might not be immediately applicable to aliphatic nitroalkenes.

Scheme 27. Synthesis of aliphatic β,γ-dihydroxy nitroalkane.



Further work is needed to optimize the asymmetric dihydroxylation of aliphatic nitroalkene and its application to synthesize nonracemic aliphatic α,β-dihydroxyamides via umpolung amide synthesis.

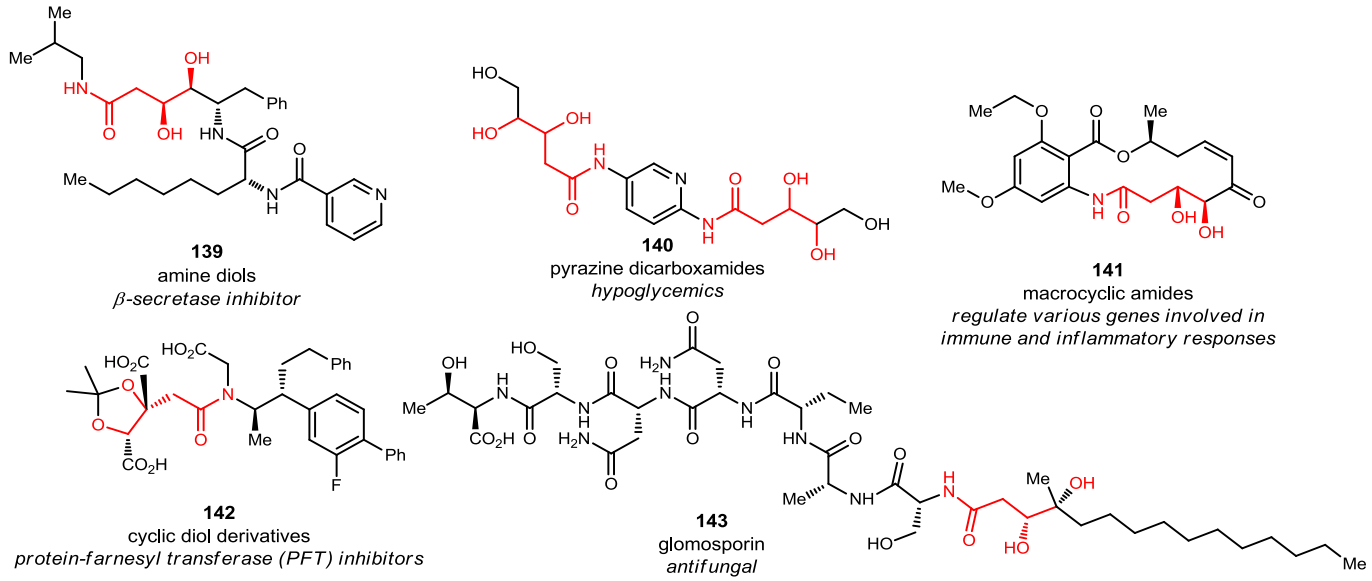
Chapter 3

Synthesis of β,γ-Dihydroxy Amides

3.1 Importance of β,γ-Dihydroxy Amides

β,γ-Dihydroxy amides are present in a wide variety of biologically active molecules (Figure 6). For example, amine diols of amides (e.g. **139**) have been shown to inhibit β-secretase,[39] a target for the treatment of Alzheimer's disease among other illnesses. The

Figure 6. Biologically active compounds containing β,γ-dihydroxy amides.



presence of the diol in its molecular structure is essential for the interaction of the molecule with its target. Pyrazine dicarboxamides **140** contain β,γ-dihydroxyamides and

[39] Schostarez, H. J.; Chrusciel, R. A. WO 2003/006453, 2003.

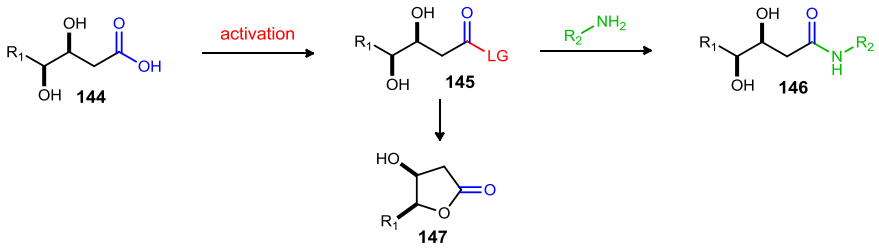
have been shown to inhibit glycemia in Swiss albino mice and have low toxicity.[40] These compounds have been investigated for the treatment of various types of diabetes. Cyclic amic acid derivatives **142**, also containing β,γ-dihydroxyamides as part of their structure, have been shown to inhibit protein-farnesyl transferase for antitumor and anti-HIV agents.[41] β,γ-Dihydroxy amides are also found in macrocyclic compounds[42] and peptidic substrates[43] that have noted biological activity. The biological significance of β,γ-dihydroxyamides has generated much interest in creating effective synthetic methods to readily access these molecules. The most common synthetic strategies utilize a dehydrative approach. While this approach has been successful, there are limitations that create the need for more innovative approaches.

[40] Bashiardes, G.; Carry, J.; Evers, M.; Filoche, B.; Mignani, S. WO 99/03844, 1999
[41] Aoyama, T.; Kawakami, K.; Arai, S.; satoh, T.; Monden, Y. WO 9729078, 1997
[42] Boivin, R.; Chiba, K.; Davis, H. A.; Diepitro, L.; Du, H.; Eguchi, Y.; Fujita, M.; Gilbert. S.; Goto, M.; Harmange, J. C.; et al WO 2003076424
[43] Ishiyama, D.; Sato, T.; Honda, R.; Senda, H.; Konno, H.; Kanazawa, S. *J. Antibiotics*, **2000**, *53*, 525-531

3.2 Current Methods used to access β,γ-Dihydroxy Amides

The synthesis of amides using dehydrative methods is perhaps the most widely used method of amide synthesis. However, accessing β,γ-dihydroxyamides via this approach is somewhat challenging. One of the challenges encountered is the formation of

Scheme 28. Formatiom of hydroxy γ-lactone.

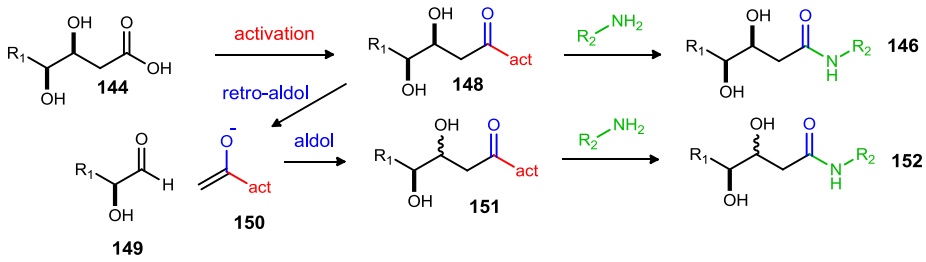


the hydroxy γ-lactone **147** from the activated acyl intermediate (Scheme 28). Sharpless and co-workers[44] have shown that β-hydroxy γ-lactones can be formed through dihydroxylation of β,γ-unsaturated esters.

[44] Wang, Z.; Zhang X.; Sharpless, K. B. *Tetrahedron lett.* **1992**, *33*, 6407-6410

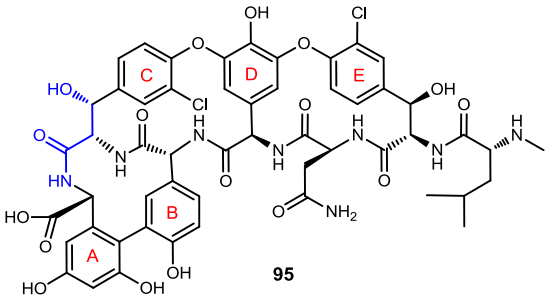
Another challenge encountered, is the competing *retro*-aldol reaction, resulting in degradation or epimerization at the β-hydroxy position (Scheme 29). In the synthesis of vancomycin **95** (Figure 7), Evans,[45] Nicolaou[46] and others observed *retro*-aldol opening

Scheme 29. Competing retro-aldol pathway.



of the CD ring system during amide coupling with different peptide coupling reagents.

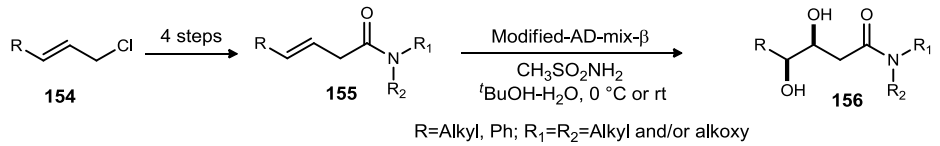
Figure 7. Vancomycin aglycon.



To overcome these challenges, a few innovative approaches have been developed. One such approach is the Sharpless asymmetric dihydroxylation of β,γ-unsaturated amides.[47] This approach affords the corresponding diols in good yields and high enantiomeric excesses (Scheme 30).

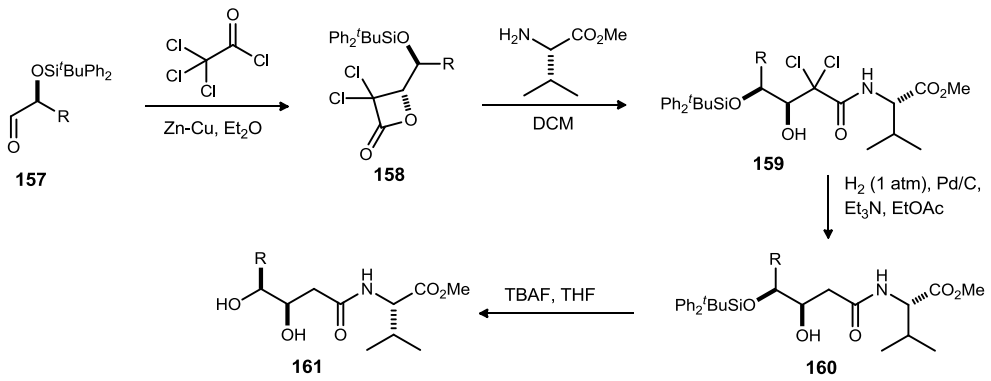
[45] Evans, D. A. *et. al Angew. Chem., Int. Ed.* **1998,** *37,* 2700.
[46] Nicolaou, K. C. *et. al. Angew. Chem., Int. Ed.* ***1998,*** *37, 2717 and the references cited therein.*
[47] Bennani, Y. L.; Sharpless, K. B. *Tetrahedron Lett.* **1993**, *34*, 2079-2082.

Scheme 30. Sharpless asymmetric dihydroxylation of unsaturated amides.



Another approach is the coupling of α,α-dichloro β-lactones **158** with α-amino acid esters.[48] α,α-Dichloro β-lactones, obtained by the diastereoselective cycloaddition of dichloroketene to α-(silyloxy) aldehydes, coupled efficiently with α-amino acid esters leading, after dehalogenation with H_2 over Pd on charcoal, to β,γ-dihydroxy amides under mild reaction conditions (Scheme 31).

Scheme 31. Coupling of α,α-dichloro β-lactones with α-amino acid esters.



These alternative approaches offer solutions to some, but not all, of the challenges encountered. With the increasing complexity of a rising number of biologically significant molecules, there remains a need for greater innovation in synthetic methods to

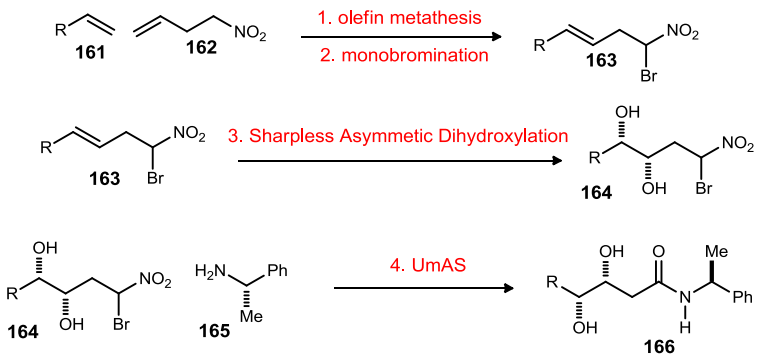
[48] Palomo, C. Miranda, J. I.; Linden, A. *J. Org. Chem*. **1996**, *61*, 9196-9201

access this common structural motif. Toward this end, the enantioselective synthesis of β,γ-dihydroxy amides via umpolung amide synthesis was explored.

3.3 Entioselective Synthesis of β,γ-Dihydroxy Amides via Umpolung Amide Synthesis

Efforts toward the synthesis of α,β-dihydroxy amides have provided insight to a viable synthetic route to access β,γ-dihydroxy amides. It was envisioned that the position of the double bond will no longer be problematic and so synthesis of the requisite amide donor will be possible using the route that was investigated for the synthesis of α,β-dihydroxyamides. A modified route was proposed (Scheme 32). This sequence of reactions starts with the synthesis of the γ,δ-unsaturated nitroalkenes **163** via alkene cross-metathesis followed by monobromination and asymmetric dihydroxylation to afford the desired γ,δ-dihydroxy α-bromonitroalkane **164**. The desired amide **166** is then synthesized by umpolung amide synthesis using the γ,δ-dihydroxy α-bromonitroalkane with the desired amine.

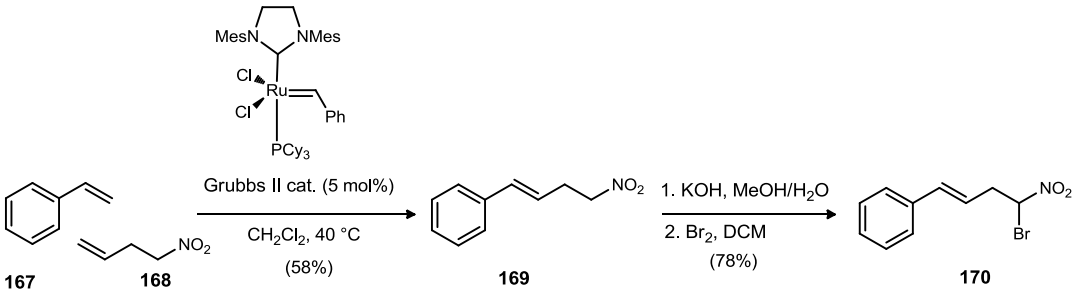
Scheme 32. Proposed enantioselective synthesis of β,γ-dihydroxy amides via umpolung amide synthesis.



3.3.1 Synthesis of γ,δ-Unsaturated Bromonitroalkene.

4-Nitro-1-butene **168** was synthesized by known literature procedures.[49] This nitroalkene was then subjected to alkene cross-metathesis with styrene to furnish the desired 1-phenyl-4-nitrobutene **169**. This substrate was then subjected to α-monobromination to furnish the desired bromonitroalkane **170** in good yield (Scheme 33).

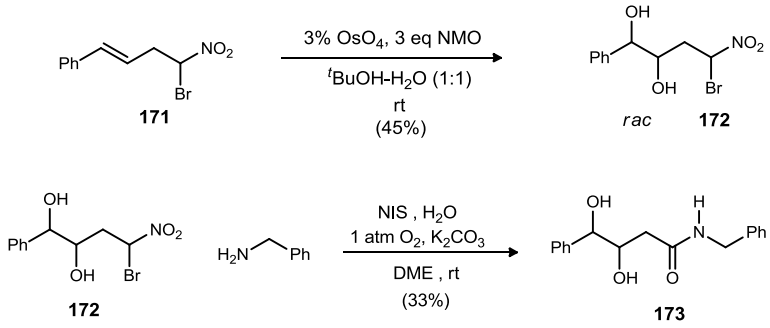
Scheme 33. Synthesis of γ,δ-unsaturated bromonitroalkane.



3.3.2 Synthesis of Racemic β,γ-Dihydroxy Amide.

The γ,δ-unsaturated α-bromonitroalkene was subjected to Upjohn dihydroxylation. The desired racemic γ,δ-dihydroxy α-bromonitroalkane **172** was isolated in moderate

Scheme 34. Synthesis of racemic β,γ-dihydroxyamide.



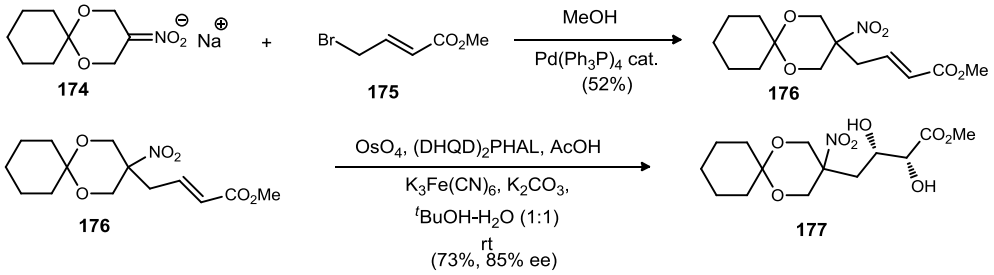
[49] Kornblum, N.; Larson, H. O.; Blackwood, R. K.; Moonberry, D. D.; Graham, G. E. *J. Am. Chem.* **1956**, *78*, 1497

yield (Scheme 34). This compound was then subjected to UmAS conditions which furnished the desired amide in moderate yield.

3.3.3 Synthesis of Nonracemic β,γ-Dihydroxy Amide.

In order to synthesize β,γ-dihydroxyamide in an enantioselective fashion, Sharpless asymmetric dihydroxylation was utilized. Although previous attempts to dihydroxylate nitroalkenes in an enantioselective fashion were mostly unsuccessful, there was precedence in the literature[50] for this type of transformation with electron deficient γ,δ-unsaturated nitroalkenes (Scheme 35).

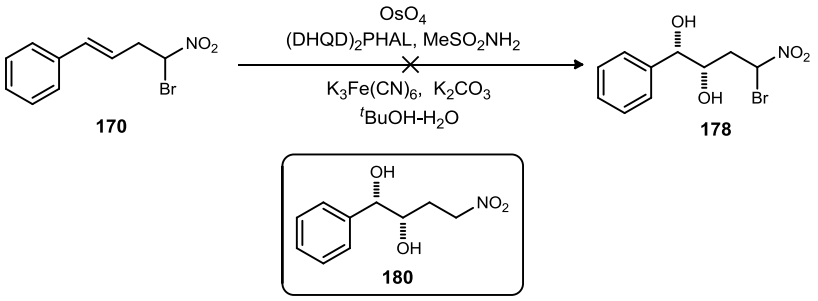
Scheme 35. Asymmetric synthesis of a branched-chain analogue of azapyranoses from a 5-allylic derivative of 5-nitro-1,3-dioxane.



The proposed synthetic strategy was tested by subjecting the γ,δ-unsaturated α-bromonitroalkene **170** to asymmetric dihydroxylation. Analysis of the ^{1}H NMR spectrum showed that the starting alkene was fully consumed in this reaction, but the desired product was not observed. Additionally, the ^{1}H NMR also showed that while the alkene was converted to the diol, the bromine at the α position was lost (Scheme 36). Attempts

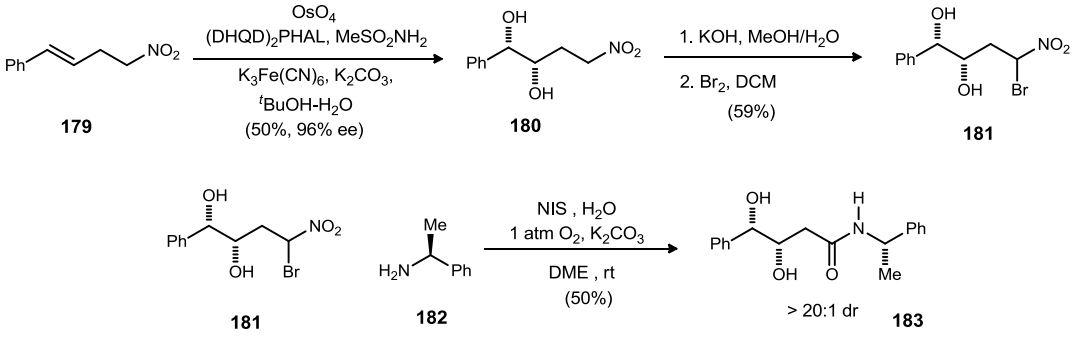
[50] Budzinska, A.; Sas, W. *Tetrahedron Lett.* **2001**, *42*, 105-107

Scheme 36. Asymmetric dihydroxylation of γ,δ-unsaturated α-bromonitroalkene.



were made to engineer the reaction to prevent debromination, including running the reaction under buffered conditions.[51] However they were unsuccessful. At this point it became clear that bromination had to occur after asymmetric dihydroxylation. These changes were applied to the proposed synthetic route. Gratifyingly, the desired amide was isolated in four steps from commercially available materials (Scheme 37). The advantages of the proposed synthetic route include no epimerization, no hydroxy γ-lactone formation, and no extensive protection and deprotection schemes.

Scheme 37. Modified synthesis of non-racemic β,γ-dihydroxy amide.



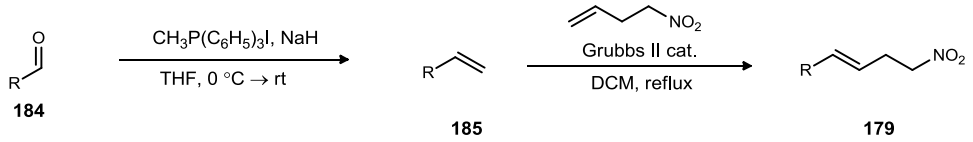
[51] Vanhessche, K. P. M.; Wabg, Z. M.; Sharpless, K. B. *Tetrahedron Lett.* **1994**, *35*, 3469-3472

3.3.4 Reaction Substrate Scope

The scope of each reaction in this four-step synthetic pathway design to access β,γ-dihydroxyamides was explored. Each reaction was evaluated using a variety of aromatic and aliphatic substrates. A variety of aromatic and aliphatic styrene derivatives were accessed by a Wittig olefination using methyl triphenylphosphonium iodide according to literature procedures.[52,53] The substituted styrene derivatives were isolated in high yields and their ^{1}H NMR was consistent with literature data. The alkene cross-metathesis protocol showed broad tolerance for aromatic and aliphatic styrene derivatives (Table 1). Predominantly *E*-isomers were isolated for all electron-donating and electron-withdrawing substituents in the *para* and *meta* position. *ortho*-Substituted substrates had *E*/*Z* ratios >13:1, and aliphatic substrates had *E*/*Z* ratios >11:1.

[52] Faler, C. A.; Joullie, M. M. *Org. Lett.* **2007**, *10*, 1987-1990
[53] Zhang, C.-P.; Wang, Z.-L.; Chen, Q.-Y.; Gu, Y.-C.; Xiao, J.-C. *Chem. Commun.* **2011**, *47*, 6632-6634

Table 1. Wittig olefination followed by alkene cross-metathesis: substrate scope.



entry	R	185[a]	yield (%)[b]	179[c]	yield (%)[b]
1	C_6H_5	a	89	a	69
2	$^{p}MeC_6H_4$	b	95	b	64
3	$^{p}PhC_6H_4$	c	90	c	65
4	$^{p}MeOC_6H_4$	d	85	d	65
5	$^{p}MeSC_6H_4$	e	90	e	40
6	$^{p}FC_6H_4$	f	70	f	58
7	$^{p}F_3CC_6H_4$	g	85	g	63
8	$^{p}ClC_6H_4$	h	94	h	58
9	$^{p}BrC_6H_4$	i	92	i	62
10	$^{m}MeC_6H_4$	j	97	j	67
11	$^{m}MeOC_6H_4$	k	70	k	60
12	$^{m}FC_6H_4$	l	66	l	53
13	$^{m}F_3CC_6H_4$	m	58	m	58
14	$^{m}ClC_6H_4$	n	91	n	36
15	$^{m}BrC_6H_4$	o	74	o	64
16	$^{o}MeC_6H_4$	p	96	p	62
17	$^{o}MeOC_6H_4$	q	93	q	58
18	$^{o}ClC_6H_4$	r	91	r	50
19	$^{o}BrC_6H_4$	s	70	s	68
20	$^{o,p}FC_6H_3$	t	90	t	60
21	$^{o,p}MeC_6H_4$	u	80	u	55
22	C_6H_{10}	v	75	v	55
23	$PhCH_2$	w	-[d]	w	60

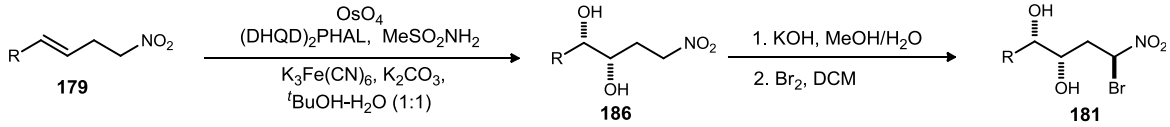
[a]All reactions were conducted using aldehyde (10 mmol, 0.5M in THF), methyltriphenylphosphonium iodide (12 mmol), and dry sodium hydride (45 mmol) at rt. [b]Isolated yield. [c]All reactions were conducted using styrene (9 mmol, 0.5M in DCM), 4-nitrobut-1-ene (2.5 mmol), and Grubbs' 2nd generation catalyst (5 mol %) at 40 °C. [d]Purchased from Sigma Aldrich.

It was gratifying to see that the asymmetric dihydroxylation of various aromatic and aliphatic alkenes proceeded in moderate to good yield and excellent enantioselection (Table 2). Reaction times varied from 6-12 hours at ambient temperature. Longer reaction times resulted in diminished yields. Electron-donating and electron-withdrawing substituents at the *para*-, *meta*- and *ortho*-positions of aromatic substrates provided the

desired products in moderate yield and high enantioselection. Yields were consistent, leading to the conclusion that this reaction is relatively unaffected by substitution on the aromatic ring. This trend extends to aliphatic substrates which delivered the desired γ,δ-dihydroxy nitroalkane with high enantioselection.

Various substituted aromatic γ,δ-dihydroxy nitroalkanes exhibited similar reactivity toward α-monobromination (Table 2). In each case the desired γ,δ-dihydroxy α-bromonitroalkane was isolated in moderate to good yield. The major byproduct of this reaction is γ,δ-dihydroxy α,α-dibromonitroalkane which has an impact on the isolated yield of the desired α-bromonitroalkane. Electrophilic aromatic substitution was observed when an electron-donating substituent was in the *meta*-position. However, shortening the reaction time reduced this byproduct to a minimum while still achieving full conversion of the starting nitroalkane. Aliphatic substrates were converted to the corresponding γ,δ-dihydroxy α-bromonitroalkane in good yield. The major byproduct was the corresponding γ,δ-dihydroxy α,α-dibromo nitroalkane. The amount of the byproduct produced was reduced by decreasing reaction time and using 0.9 equivalent of the potassium hydroxide.

Table 2. Asymmetric dihydroxylation followed by α-monobromination.



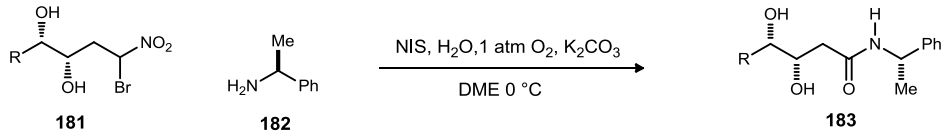
entry	R	186[a]	ee (%)[b]	yield (%)[c]	181[d]	yield (%)[c]
1	C_6H_5	a	96	40	a	59
2	$^{p}MeC_6H_4$	b	94	51	b	71
3	$^{p}PhC_6H_4$	c	95	53	c	60
4	$^{p}MeOC_6H_4$	d	96	49	d	62
5	$^{p}MeSC_6H_4$	e	96	55	e	65
6	$^{p}FC_6H_4$	f	99	49	f	72
7	$^{p}F_3CC_6H_4$	g	98	45	g	65
8	$^{p}ClC_6H_4$	h	99	45	h	78
9	$^{p}BrC_6H_4$	i	97	50	i	67
10	$^{m}MeC_6H_4$	j	97	66	j	80
11	$^{m}MeOC_6H_4$	k	99	51	k	65
12	$^{m}FC_6H_4$	l	98	49	l	68
13	$^{m}F_3CC_6H_4$	m	96	40	m	63
14	$^{m}ClC_6H_4$	n	99	50	n	73
15	$^{m}BrC_6H_4$	o	97	55	o	75
16	$^{o}MeC_6H_4$	p	95	58	p	68
17	$^{o}MeOC_6H_4$	q	96	46	q	56
18	$^{o}ClC_6H_4$	r	99	52	r	66
19	$^{o}BrC_6H_4$	s	95	43	s	65
20	$^{o,p}FC_6H_3$	t	96	55	t	63
21	$^{o,p}MeC_6H_4$	u	96	62	u	70
22	C_6H_{10}	v	96	49	v	58
23	$PhCH_2$	w	95	55	w	60

[a]All reactions were conducted using β,γ-unsaturated nitroalkene (1 equiv, 0.1 M in $^{t}BuOH:H_2O$ (1:1)), K_3FeCN_6 (3 equiv), K_2CO_3 (3 equiv), $(DHQD)_2PHAL$ (10 mol%), $CH_3SO_2NH_2$ (1 equiv) and OsO_4 (3 mol%) at rt. [b]Determined by chiral HPLC using chiral stationary phase. [c]Isolated yield. [d]All reactions were conducted using β,γ-dihydroxy nitroalkane (1 equiv), KOH (0.95 equiv) and Br_2 (0.95 equiv).

Finally, our investigation concluded with the synthesis of various aromatic and aliphatic β,γ-dihydroxy amides via umpolung Amide Synthesis (UmAS) (Table 3). Enantioenriched (>98% ee) α-methyl benzyl amine was used to provide confirmation that

the diastereomers are homochiral at the γ and δ carbon and remain enriched as the various γ,δ-dihydroxy nitroalkanes were transformed into β,γ-dihydroxy amides. Each of the aromatic and aliphatic substrates provided the corresponding amide in moderate to good yields and as a single diastereomer. This is consistent with the proposed mechanism of UmAS, which does not allow for hydroxy γ-

Table 3. Synthesis of various β,γ-dihydroxy amides via umpolung amide synthesis.



entry	R	183[a]	yield (%)[b]
1	C_6H_5	a	50
2	$^{p}MeC_6H_4$	b	58
3	$^{p}PhC_6H_4$	c	56
4	$^{p}MeOC_6H_4$	d	50
5	$^{p}MeSC_6H_4$	e	48
6	$^{p}FC_6H_4$	f	56
7	$^{p}F_3CC_6H_4$	g	55
8	$^{p}ClC_6H_4$	h	54
9	$^{p}BrC_6H_4$	i	56
10	$^{m}MeC_6H_4$	j	55
11	$^{m}MeOC_6H_4$	k	48
12	$^{m}FC_6H_4$	l	55
13	$^{m}F_3CC_6H_4$	m	49
14	$^{m}ClC_6H_4$	n	58
15	$^{m}BrC_6H_4$	o	61
16	$^{o}MeC_6H_4$	p	55
17	$^{o}MeOC_6H_4$	q	45
18	$^{o}ClC_6H_4$	r	53
19	$^{o}BrC_6H_4$	s	55
20	$^{o,p}FC_6H_3$	t	54
21	$^{o,p}MeC_6H_4$	u	62
22	C_6H_{10}	v	50
23	$PhCH_2$	w	56

[a]All reactions were conducted using bromonitroalkane (1 equiv), H_2O (5 equiv), (*S*)-*α*-Me-benzylamine (1.2 equiv), K_2CO_3 (2 equiv), NIS (2 mol%) in DME (0.2 M). [b]Isolated yield.

lactone formation and formation of α-hydroxy aldehyde via a retro-aldol pathway.

In summary, a new approach to β,γ-dihydroxy amides has been developed using a sequence of reactions starting with an alkene cross-metathesis and followed by asymmetric dihydroxylation, α-monobromination, and finally umpolung amide synthesis. This allows for the synthesis of various β,γ-dihydroxy amides without the need for protection/deprotection schemes. The selectivity achieved in the asymmetric dihydroxylation was translated throughout the sequence to furnish the desired enantiopure amides. This methodology represents one of the few innovative approaches to chiral non-racemic β,γ-dihydroxy amides that avoids the use of the corresponding carboxylic acid intermediate, which is prone to hydroxy γ-lactone formation and formation of α-hydroxy aldehyde via a *retro*-aldol pathway.

Chapter 4

Experimental

All reagents and solvents were commercial grade and purified prior to use when necessary. Methyltriphenylphosphonium iodide was synthesized according to literature procedure.[54] Dichloromethane (CH_2Cl_2) and tetrahydrofuran (THF) was dried by passage through a column of activated alumina as described by Grubbs.[55] *N*-Iodosuccinimide was recrystallized from dioxane and carbon tetrachloride. All organic layers collected from extractions were dried over $MgSO_4$. Thin layer chromatography (TLC) was performed using glass-backed silica gel (250 μm) plates and flash chromatography utilized 230–400 mesh silica gel from Sorbent Technologies. UV light, and/or the use of CAM and potassium permanganate solutions were used to visualize products.

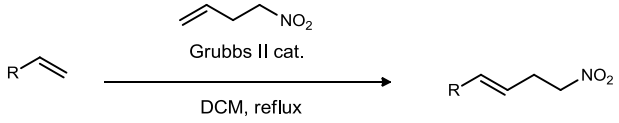
Melting points were measured on a Meltemp melting point apparatus and were not corrected. Nuclear magnetic resonance spectra (NMR) were acquired on a Bruker DRX-500 (500 MHz), Bruker AV-400 (400 MHz) or Bruker AV II-600 (600 MHz) instrument. Chemical shifts are measured relative to residual solvent peaks as an internal standard set to δ 7.26 and δ 77.0 ($CDCl_3$), δ 2.05 and δ 206 ($(CD_3)_2CO$), and δ 3.31 and δ 49.0 (CD_3OD). IR spectra were recorded on a Thermo Nicolet IR100 spectrophotometer and are reported in wavenumbers (cm^{-1}). Compounds were analyzed as neat films on a

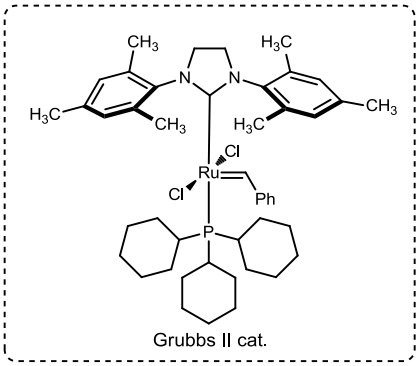
[54] Vikse, K. L.; Ahmad, Z.; Manning, C. C.; Harrington, D. A.; McIndoe, J. S. *Angew. Chem. Int. Ed.* **2011**, 50(*36*), 8304-8306

[55] Pangborn, A. B.; Giardello, M. A.; Grubbs, R. H.; Rosen, R. K.; Timmers, F. J. *Organometallics* **1996**, *15*, 1518-1520.

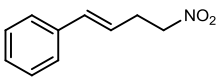
NaCl plate (transmission). Mass spectra were recorded on a Waters LCT spectrometer by use of the ionization method noted.

Synthesis of Substituted 4-Nitro-1-Aryl Butene Derivatives





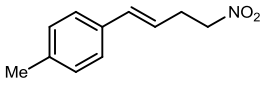
General procedure: To a stirred solution of the styrene (9 mmol) and 4-nitrobut-1-ene (260 mg, 250 µmol) in dichloromethane (20 mL) was added Grubbs' 2nd generation catalyst (100 mg, 120 µmol). The mixture was then heated to reflux temperature for 18 h, after which the mixture was cooled and concentrated under reduced pressure. Purification by MPLC yielded the desired compound.



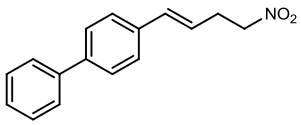
(4-Nitrobut-1-en-1-yl)benzene (179a)[56]**.** Styrene (936 mg, 9.00 mmol) was stirred with 4-nitrobut-1-ene according to the general procedure. The title compound was isolated as a pale yellow oil

[56] Marsh, G. P.; Parsons, P. J.; McCarthy, C.; Corniquet, X. G. *Org. Lett.* **2007**, *9*, 2613-2616

(305 mg, 69%) after purification by MPLC (SiO_2, 0-5% diethyl ether in hexanes, 30 min, 210 nm). R_f = 0.55 (20% EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40–7.27 (m, 5H), 6.56 (d, *J* = 15.8 Hz, 1H), 6.15 (dt, *J* = 15.7, 7.2 Hz, 1H), 4.51 (t, *J* = 7.2 Hz, 2H), 2.91 (ddt, *J* = 7.2, 7.2, 1.3 Hz, 2H). Values were consistent with literature reference.

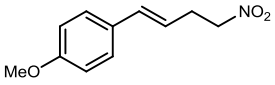


1-Methyl-4-(4-nitrobut-1-en-1-yl)benzene (179b). 1-Methyl-4-vinylbenzene (1.1 g, 9.0 mmol) was stirred with 4-nitrobut-1-ene according to the general procedure. The title compound was isolated as a colorless oil (310 mg, 64%) after purification by MPLC (SiO_2, 0-5% diethyl ether in hexanes, 30 min, 210 nm). R_f = 0.52 (20% EtOAc/hexanes); IR (film) 3026, 2921, 1551, 1513, 1431, 1379, 969, 794 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.25 (d, *J* = 8.2 Hz, 2H), 7.14 (d, *J* = 7.9 Hz, 2H), 6.49 (d, *J* = 15.9 Hz, 1H), 6.06 (dt, *J* = 15.6, 7.2 Hz, 1H), 4.49 (t, *J* = 7.2 Hz, 2H), 2.88 (ddt, *J* = 7.2, 7.2, 1.3 Hz, 2H), 2.35 (s, 3H); ^{13}C NMR (600 MHz, $CDCl_3$) ppm 137.6, 133.7, 129.2, 126.1, 121.8, 74.9, 30.7, 21.07; HRMS (ESI): Exact mass calcd for $C_{11}H_{13}NO_2$ $[M]^+$ 191.0941, found 191.0950.

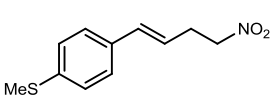


4-(4-Nitrobut-1-en-1-yl)-1,1'-biph0enyl (179c). 4-Vinyl-1,1'-biphenyl (1.6 g, 9.0 mmol) was stirred with 4-nitrobut-1-ene according to the general procedure. The title compound was isolated as a white solid (411 mg, 65%) after purification by MPLC (SiO_2, 0-5% diethyl ether in hexanes, 30 min, 210 nm). Mp = 111-113 °C; R_f =

0.58 (20% EtOAc/hexanes); IR (film) 3027, 2918, 1553, 1538, 1380, 972 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.62 (d, *J* = 7.4 Hz, 2H), 7.58 (d, *J* = 8.3 Hz, 2H), 7.47 (dd, *J* = 7.9, 7.9 Hz, 2H), 7.42 (d, *J* = 8.3 Hz, 2H), 7.38 (dd, *J* = 7.3, 7.3 Hz, 1H), 6.57 (d, *J* = 15.9 Hz, 1H), 6.17 (dt, *J* = 15.5, 7.1 Hz, 1H), 4.50 (t, *J* = 7.0 Hz, 2H), 2.93 (ddt, *J* = 7.0, 7.0, 1.1 Hz, 2H); ^{13}C NMR (500 MHz, $CDCl_3$) ppm 140.5, 135.5, 133.5, 128.8, 127.4, 127.2, 126.9, 126.7, 123.0, 74.9, 30.8; HRMS (CI): Exact mass calcd for $C_{16}H_{15}NO_2$ $[M]^+$ 253.1103, found 253.1100.



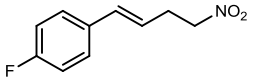
1-Methoxy-4-(4-nitrobut-1-en-1-yl)benzene (179d)[57]. 1-Methoxy-4-vinylbenzene (1.2 g, 9.0 mmol) was stirred with 4-nitrobut-1-ene according to the general procedure. The title compound was isolated as an off-white solid (336 mg, 65%) after purification by MPLC (SiO_2, 0-5% diethyl ether in hexanes, 30 min, 210 nm). R_f = 0.48 (20% EtOAc/hexanes); ^1H NMR (400 MHz, $CDCl_3$) δ 7.30 (d, *J* = 9.3 Hz, 2H), 6.87 (d, *J* = 9.0 Hz, 2H), 6.48 (d, *J* = 16 Hz, 1H), 5.98 (dt, *J* = 15.9, 7.0 Hz, 1H), 4.50 (t, *J* = 7.0 Hz, 2H), 3.82 (s, 3H), 2.88 (ddt, *J* = 7.0, 7.0, 1.0 Hz, 2H). Values were consistent with literature reference.



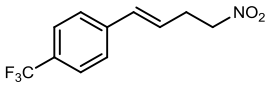
1-(Methylthio)-4-(4-nitrobut-1-en-1-yl)benzene (179e). 1-(Methylthio)-4-vinylbenzene (1.4 g, 9.0 mmol) was stirred with 4-nitrobut-1-ene according to the general procedure. The title

[57] Uozumi, Y.; Suzuka, T. *J. Org. Chem.* **2006**, *71*, 8644-8646

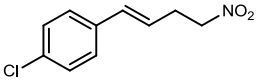
compound was isolated as a white solid (223 mg, 40%) after purification by MPLC (SiO_2, 0-5% diethyl ether in hexanes, 30 min, 210 nm). Mp = 53-54 °C; R_f = 0.45 (20% EtOAc/hexanes); IR (film) 2920, 1546, 1429, 1381, 1218, 1091, 976, 791 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.25 (d, *J* = 8.4 Hz, 2H), 7.19 (d, *J* = 8.4 Hz, 2H), 6.47 (d, *J* = 15.9 Hz, 1H), 6.07 (dt, *J* = 15.6, 7.1 Hz, 1H), 4.48 (t, *J* = 7.1 Hz, 2H), 2.88 (ddt, *J* = 7.1, 7.1, 1.3 Hz, 2H), 2.48 (s, 3H); ^{13}C NMR (600 MHz, $CDCl_3$) ppm 138.1, 133.4, 133.3, 126.6, 126.5, 122.2, 75.0, 30.7, 15.7; HRMS (CI): Exact mass calcd for $C_{11}H_{13}NO_2S$ $[M]^+$ 223.0662, found 223.0657.



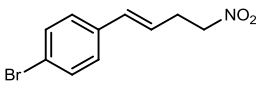
1-Fluoro-4-(4-nitrobut-1-en-1-yl)benzene (179f). 1-Fluoro-4-vinylbenzene (1.1 g, 9.0 mmol) was stirred with 4-nitrobut-1-ene according to the general procedure. The title compound was isolated as a colorless oil (280 mg, 58%) after purification by MPLC (SiO_2, 0-5% diethyl ether in hexanes, 30 min, 210 nm). R_f = 0.50 (20% EtOAc/hexanes); IR (film) 3039, 2921, 1552, 1509, 1228 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.30 (dd, *J* = 8.8, 5.5 Hz, 2H), 6.99 (dd, *J* = 8.8, 8.8 Hz, 2H), 6.47 (d, *J* = 15.8 Hz, 1H), 6.03 (dt, *J* = 15.7, 7.2 Hz, 1H), 4.49 (t, *J* = 7.2 Hz, 2H), 2.88 (ddt, *J* = 7.2, 7.2, 1.3 Hz, 2H); ^{13}C NMR (600 MHz, $CDCl_3$) ppm 162.3 (d, $^1J_{CF}$ = 247 Hz), 132.7, 132.6 (d, $^4J_{CF}$ = 3.0 Hz), 127.7 (d, $^3J_{CF}$ = 7.7 Hz), 122.7 (d, $^5J_{CF}$ = 1.5 Hz), 115.5 (d, $^2J_{CF}$ = 21.5 Hz), 74.9, 30.6; HRMS (ESI): Exact mass calcd for $C_{10}H_{10}FNO_2$ $[M]^+$ 195.0690, found 195.0690.



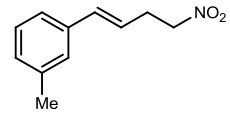
1-(4-Nitrobut-1-en-1-yl)-4-(trifluoromethyl)benzene (179g). 1-(Trifluoromethyl)-4-vinylbenzene (1.6 g, 9.0 mmol) was stirred with 4-nitrobut-1-ene according to the general procedure. The title compound was isolated as a colorless oil (210 mg, 34%) after purification by MPLC (SiO_2, 0-10% diethyl ether in hexanes, 40 min, 210 nm). R_f = 0.43 (20% EtOAc/hexanes); IR (film) 3040, 2922, 1554, 1326, 1164, 1115, 1067 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.56 (d, *J* = 8.1 Hz, 2H), 7.43 (d, *J* = 8.1 Hz, 2H), 6.56 (d, *J* = 15.8 Hz, 1H), 6.23 (dt, *J* = 15.7, 7.0 Hz, 1H), 4.53 (t, *J* = 6.9 Hz, 2H), 2.88 (ddt, *J* =7.0, 7.0, 1.1 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) ppm 139.8, 132.8, 129.6 (q, $^2J_{CF}$ = 33.0 Hz), 126.5, 125.8, 125.6 (q, $^3J_{CF}$ = 3.6 Hz), 124.1 (q, $^1J_{CF}$ = 273 Hz), 74.7, 30.6; HRMS (ESI): Exact mass calcd for $C_{11}H_{10}F_3NO_2$ $[M]^+$ 245.0658, found 245.0658.



1-Chloro-4-(4-nitrobut-1-en-1-yl)benzene (179h). 1-Chloro-4-vinylbenzene (1.3 g, 9.0 mmol) was stirred with 4-nitrobut-1-ene according to the general procedure. The title compound was isolated as a white solid (310 mg, 58%) after purification by MPLC (SiO_2, 0-5% diethyl ether in hexanes, 30 min, 210 nm). Mp = 53-54 °C; R_f = 0.51 (20% EtOAc/hexanes); IR (film) 3029, 2964, 2918, 1555, 1539, 1380, 972, 793 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.25 (m, 4H), 6.46 (d, *J* = 15.8 Hz, 1H), 6.08 (dt, *J* = 15.8, 7.0 Hz, 1H), 4.50 (t, *J* = 7.0 Hz, 2H), 2.89 (ddt, *J* = 7.0, 7.0, 1.3 Hz, 2H); ^{13}C NMR (600 MHz, $CDCl_3$) ppm 134.8, 133.4, 132.8, 128.7, 127.4, 123.6, 74.8, 30.7; HRMS (APCI): Exact mass calcd for $C_{10}H_{10}ClNO_2$ $[M]^+$ 211.6449, found 211.0404.

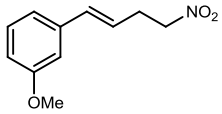


1-Bromo-4-(4-nitrobut-1-en-1-yl)benzene (179i). 1-Bromo-4-vinylbenzene (1.7 g, 9.0 mmol) was stirred with 4-nitrobut-1-ene according to the general procedure. The title compound was isolated as a white solid (400 mg, 62%) after purification by MPLC (SiO_2, 0-5% diethyl ether in hexanes, 30 min, 210 nm). Mp = 71-72 °C; R_f = 0.58 (20% EtOAc/hexanes); IR (film) 3027, 2918, 1553, 1538, 1380, 972 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.42 (d, *J* = 8.5 Hz, 2H), 7.20 (d, *J* = 8.5 Hz, 2H), 6.45 (d, *J* = 15.9 Hz, 1H), 6.12 (dt, *J* = 15.8, 7.1 Hz, 1H), 4.50 (t, *J* = 7.0 Hz, 2H), 2.88 (ddt, *J* = 7.0, 7.0, 1.3 Hz, 2H); ^{13}C NMR (600 MHz, $CDCl_3$) ppm 135.4, 132.9, 131.7, 127.8, 123.8, 121.6, 74.8, 30.7; HRMS (ESI): Exact mass calcd for $C_{10}H_{10}BrNO_2$ $[M]^+$ 256.9869, found 256.9864.

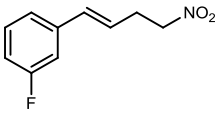


1-Methyl-3-(4-nitrobut-1-en-1-yl)benzene (179j). 1-Methyl-3-vinylbenzene (1.1 g, 9.0 mmol) was stirred with 4-nitrobut-1-ene according to the general procedure. The title compound was isolated as a pale yellow oil (320 mg, 67%) after purification by MPLC (SiO_2, 0-5% diethyl ether in hexanes, 30 min, 210 nm). R_f = 0.51 (20% EtOAc/hexanes); IR (film) 3027, 2920, 1550, 1487, 1430, 1379, 968 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.20 (dd, *J* = 7.6, 7.6 Hz, 1H), 7.16 (s, 1H), 7.15 (dd, *J* = 7.6, 7.6 Hz, 1H), 7.06 (d, *J* = 7.4 Hz, 1H), 6.49 (d, *J* = 15.8 Hz, 1H), 6.10 (dt, *J* = 15.8, 7.1 Hz, 1H), 4.50 (t, *J* = 7.0 Hz, 2H), 2.90 (ddt, *J* =7.0, 7.0, 1.4 Hz, 2H), 2.34 (s, 3H); ^{13}C NMR (600 MHz, $CDCl_3$) ppm 138.1, 136.4, 134.1, 128.6, 128.5, 126.9, 123.4, 122.6, 75.0, 30.8,

21.3; HRMS (ESI): Exact mass calcd for $C_{11}H_{13}NNaO_2$ $[M+Na]^+$ 214.0844, found 214.0854.

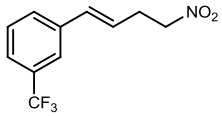


1-Methoxy-3-(4-nitrobut-1-en-1-yl)benzene (179k). 1-Methoxy-3-vinylbenzene (1.2 g, 9.0 mmol) was stirred with 4-nitrobut-1-ene according to the general procedure. The title compound was isolated as a pale yellow oil (310 mg, 60%) after purification by MPLC (SiO_2, 0-5% diethyl ether in hexanes, 30 min, 210 nm). R_f = 0.49 (20% EtOAc/hexanes); IR (film) 3004, 2957, 2837, 1580, 1552, 1489, 1431, 1379, 1264, 1158, 1044, 969 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.23 (dd, *J* = 7.9, 7.9 Hz, 1H), 6.93 (d, *J* = 7.7 Hz, 1H), 6.87 (dd, *J* = 2.2, 2.2 Hz, 1H), 6.80 (dd, *J* = 8.3, 2.3 Hz, 1H), 6.49 (d, *J* = 15.8 Hz, 1H), 6.11 (dt, *J* = 15.8, 7.1 Hz, 1H), 4.50 (t, *J* = 7.0 Hz, 2H), 3.81 (s, 3H), 2.90 (ddt, *J* = 7.0, 7.0, 1.4 Hz, 2H); ^{13}C NMR (600 MHz, $CDCl_3$) ppm 159.8, 137.8, 133.9, 129.6, 123.2, 118.9, 113.4, 111.6, 74.9, 55.2, 30.7; HRMS (ESI): Exact mass calcd for $C_{11}H_{13}NNaO_3$ $[M+Na]^+$ 230.0793, found 230.0792.

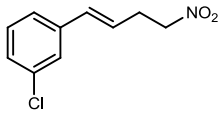


1-Fluoro-3-(4-nitrobut-1-en-1-yl)benzene (179l). 1-Fluoro-3-vinylbenzene (1.1 g, 9.0 mmol) was stirred with 4-nitrobut-1-ene according to the general procedure. The title compound was isolated as a colorless oil (200 mg, 40%) after purification by MPLC (SiO_2, 0-5% diethyl ether in hexanes, 30 min, 210 nm). R_f = 0.51 (20% EtOAc/hexanes); IR (film) 3035, 2920, 1581, 1441, 1379, 1253, 1143 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.27 (ddd, *J* = 8.0, 8.0, 6.1 Hz, 1H), 7.16 (m, 1H), 7.11 (ddd, *J* =

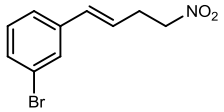
3.9, 3.9, 2.1 Hz, 1H), 6.94 (dddd, *J* = 8.4, 8.4, 2.3, 0.6 Hz, 1H) 6.49 (d, *J* = 15.8 Hz, 1H), 6.13 (dt, *J* = 15.7, 7.1 Hz, 1H), 4.51 (t, *J* = 7.0 Hz, 2H), 2.91 (ddt, *J* = 7.0, 7.0, 1.3 Hz, 2H); ^{13}C NMR (600 MHz, $CDCl_3$) ppm 163.0 (d, $^1J_{CF}$ = 246 Hz), 138.7 (d, $^3J_{CF}$ = 7.7 Hz), 132.9 (d, $^4J_{CF}$ = 2.2 Hz) 130.1 (d, $^3J_{CF}$ = 8.5 Hz), 124.4, 122.2 (d, $^4J_{CF}$ = 2.3 Hz), 114.6 (d, $^2J_{CF}$ = 21.2 Hz), 112.7 (d, $^2J_{CF}$ = 21.2 Hz), 74.8, 30.6; HRMS (ESI): Exact mass calcd for $C_{10}H_{10}FNO_2$ $[M]^+$ 195.0690, found 195.0689.



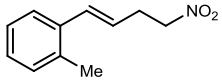
1-(4-Nitrobut-1-en-1-yl)-3-(trifluoromethyl)benzene (179m). 1-(Trifluoromethyl)-3-vinylbenzene (1.6 g, 9.0 mmol) was stirred with 4-nitrobut-1-ene according to the general procedure. The title compound was isolated as a colorless oil (355 mg, 58%) after purification by MPLC (SiO_2, 0-10% diethyl ether in hexanes, 40 min, 210 nm). R_f = 0.42 (20% EtOAc/hexanes); IR (film) 3039, 2923, 1554, 1434, 1332, 1164, 1125, 1073, 967 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (s, 1H), 7.49 (m, 2H), 7.41 (dd, *J* = 7.7, 7.7 Hz, 1H), 6.53 (d, *J* = 15.8 Hz, 1H), 6.20 (dt, *J* = 15.7, 7.0 Hz, 1H), 4.53 (t, *J* = 7.0 Hz, 2H), 2.88 (ddt, *J* = 7.0, 7.0, 1.1 Hz, 2H); ^{13}C NMR (400 MHz, $CDCl_3$) ppm 137.2, 132.6, 130.9 (q, $^2J_{CF}$ = 32.8 Hz), 129.4, 129.0, 125.1, 124.2 (q, $^3J_{CF}$ = 3.6 Hz), 124.1 (q, $^1J_{CF}$ = 273 Hz), 122.8 (q, $^3J_{CF}$ = 3.6 Hz), 74.6, 30.5; HRMS (CI): Exact mass calcd for $C_{11}H_{10}F_3NO_2$ $[M]^+$ 245.0658, found 245.0669.



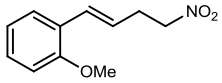
1-Chloro-3-(4-nitrobut-1-en-1-yl)benzene (179n). 1-Chloro-3-vinylbenzene (1.3 g, 9.0 mmol) was stirred with 4-nitrobut-1-ene according to the general procedure. The title compound was isolated as a pale yellow oil (190 mg, 36%) after purification by MPLC (SiO_2, 0-5% diethyl ether in hexanes, 30 min, 210 nm). R_f = 0.47 (20% EtOAc/hexanes); IR (film) 3029, 2919, 1550, 1474, 1428, 1378, 966 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.33 (s, 1H), 7.25–7.19 (m, 3H), 6.46 (d, *J* = 15.8 Hz, 1H), 6.13 (dt, *J* = 15.8, 7.1 Hz, 1H), 4.51 (t, *J* = 7.2 Hz, 2H), 2.91 (ddt, *J* = 7.1, 7.1, 1.4 Hz, 2H); ^{13}C NMR (600 MHz, $CDCl_3$) ppm 138.2, 134.5, 132.7, 129.8, 127.7, 126.2, 124.5, 124.4, 74.7, 30.6; HRMS (ESI): Exact mass calcd for $C_{10}H_{10}ClNNaO_2$ $[M+Na]^+$ 234.0298, found 234.0308.



1-Bromo-3-(4-nitrobut-1-en-1-yl)benzene (179o). 1-Bromo-3-vinylbenzene (1.7 g, 9.0 mmol) was stirred with 4-nitrobut-1-ene according to the general procedure. The title compound was isolated as a colorless viscous oil (410 mg, 64%) after purification by MPLC (SiO_2, 0-5% diethyl ether in hexanes, 30 min, 210 nm). R_f = 0.49 (20% EtOAc/hexanes); IR (film) 3059, 3029, 2919, 1558, 1474, 1426, 1380, 967 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.47 (dd, *J* = 1.9, 1.9 Hz, 1H), 7.36 (ddd, *J* = 7.9, 1.8, 1.0 Hz, 1H), 7.24 (m, 1H), 7.16 (dd, *J* = 8.0, 8.0 Hz, 1H), 6.43 (d, *J* = 15.9 Hz, 1H), 6.11 (dt, *J* = 15.8, 7.1 Hz, 1H), 4.49 (t, *J* = 7.2 Hz, 2H), 2.88 (ddt, *J* = 7.1, 7.1, 1.4 Hz, 2H); ^{13}C NMR (600 MHz, $CDCl_3$) ppm 138.5, 132.4, 130.5, 130.0, 129.0, 124.9, 124.6, 122.7, 74.7, 30.5; HRMS (ESI): Exact mass calcd for $C_{10}H_{10}BrNO_2$ $[M]^+$ 256.9869, found 256.9858.

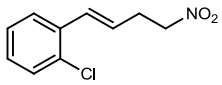


1-Methyl-2-(4-nitrobut-1-en-1-yl)benzene (179p). 1-Methyl-2-vinylbenzene (1.1 g, 9.0 mmol) was stirred with 4-nitrobut-1-ene according to the general procedure. The title compound was isolated as a pale yellow oil (296 mg, 62%) after purification by MPLC (SiO_2, 0-5% diethyl ether in hexanes, 30 min, 210 nm). R_f = 0.51 (20% EtOAc/hexanes); IR (film) 3022, 2920, 1551, 1484, 1431, 1379, 969, 749 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.41 (m, 1H), 7.20-7.16 (m, 3H), 6.76 (d, *J* = 15.6 Hz, 1H), 6.13 (dt, *J* = 15.7, 7.2 Hz, 1H), 4.52 (t, *J* = 7.3 Hz, 2H), 2.93 (ddt, *J* = 7.1, 7.1, 1.3 Hz, 2H), 2.36 (s, 3H); ^{13}C NMR (600 MHz, $CDCl_3$) ppm 135.7, 135.3, 132.0, 127.7, 126.1, 125.7, 124.4, 75.1, 31.0, 19.7; HRMS (CI): Exact mass calcd for $C_{11}H_{13}NO_2$ $[M]^+$ 191.0946, found 191.0944.

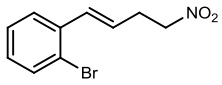


1-Methoxy-2-(4-nitrobut-1-en-1-yl)benzene (179q). 1-Methoxy-2-vinylbenzene (1.2 g, 9.0 mmol) was stirred with 4-nitrobut-1-ene according to the general procedure. The title compound was isolated as a pale yellow oil (300 mg, 58%) after purification by MPLC (SiO_2, 0-5% diethyl ether in hexanes, 30 min, 210 nm). R_f = 0.49 (20% EtOAc/hexanes); IR (film) 3006, 2942, 2839, 1596, 1550, 1489, 1434, 1379, 1026, 974 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.39 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.23 (ddd, *J* = 7.8, 7.8, 1.6 Hz, 1H), 6.93 (dd, *J* = 7.7, 7.7 Hz, 1H), 6.87 (d, *J* = 7.8 Hz, 1H), 6.85 (d, *J* = 15.8 Hz, 1H), 6.13 (dt, *J* = 15.8, 7.1 Hz, 1H), 4.49 (t, *J* = 7.1 Hz, 2H), 3.84 (s, 3H), 2.91 (ddt, *J* = 7.1, 7.1, 1.4 Hz, 2H); ^{13}C NMR (600 MHz, $CDCl_3$) ppm 156.5, 128.8, 128.8, 126.8,

125.5, 123.5, 120.6, 110.9, 75.1, 55.4, 31.2; HRMS (ESI): Exact mass calcd for $C_{11}H_{13}NNaO_3$ $[M+Na]^+$ 230.0793, found 230.0790.

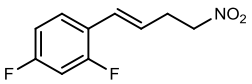


1-Chloro-2-(4-nitrobut-1-en-1-yl)benzene (179r). 1-Chloro-2-vinylbenzene (1.3 g, 9.0 mmol) was stirred with 4-nitrobut-1-ene according to the general procedure. The title compound was isolated as a pale yellow oil (264 mg, 50%) after purification by MPLC (SiO_2, 0-5% diethyl ether in hexanes, 30 min, 210 nm). R_f = 0.47 (20% EtOAc/hexanes); IR (film) 3060, 2920, 1551, 1469, 1434, 1378, 1035, 967 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.47 (dd, *J* = 7.6, 1.9 Hz, 1H), 7.34 (dd, *J* = 7.6, 1.5 Hz, 1H), 7.23-7.17 (m, 2H), 6.91 (d, *J* = 15.8 Hz, 1H), 6.11 (dt, *J* = 15.8, 7.1 Hz, 1H), 4.54 (t, *J* = 7.1 Hz, 2H), 2.96 (ddt, *J* = 7.1, 7.1, 1.4 Hz, 2H); ^{13}C NMR (600 MHz, $CDCl_3$) ppm 134.6, 132.9, 130.3, 129.7, 128.8, 126.9, 126.8, 125.9, 74.8, 30.8; HRMS (ESI): Exact mass calcd for $C_{10}H_{10}ClNNaO_2$ $[M+Na]^+$ 234.0298, found 234.0300.

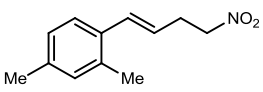


1-Bromo-2-(4-nitrobut-1-en-1-yl)benzene (179s). 1-Bromo-2-vinylbenzene (1.7 g, 9.0 mmol) was stirred with 4-nitrobut-1-ene according to the general procedure. The title compound was isolated as a colorless viscous oil (435 mg, 68%) after purification by MPLC (SiO_2, 0-5% diethyl ether in hexanes, 30 min, 210 nm). R_f = 0.45 (20% EtOAc/hexanes); IR (film) 3006, 2919, 2839, 1597, 1551, 1489, 1435, 1380, 1245, 974 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.54 (d, *J* = 8.2 Hz, 1H), 7.45 (d, *J* = 7.9 Hz, 1H), 7.26 (dd, *J* = 7.1, 7.1 Hz, 1H), 7.10 (dd, *J* = 7.9, 7.9 Hz, 1H), 6.86 (d, *J* = 15.7 Hz, 1H),

6.07 (dt, *J* = 15.8, 7.1 Hz, 1H), 4.54 (t, *J* = 7.1 Hz, 2H), 2.88 (ddt, *J* = 7.0, 7.0, 1.2 Hz, 2H); ^{13}C NMR (400 MHz, $CDCl_3$) ppm 136.4, 132.8, 132.4, 129.1, 127.6, 127.1, 126.5, 123.3, 74.7, 30.6; HRMS (ESI): Exact mass calcd for $C_{10}H_{10}BrNNaO_2$ $[M+Na]^+$ 277.9793, found 277.9796.

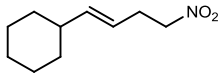


2,4-Difluoro-1-(4-nitrobut-1-en-1-yl)benzene (179t). 2,4-Difluoro-1-vinylbenzene (1.3 g, 9.0 mmol) was stirred with 4-nitrobut-1-ene according to the general procedure. The title compound was isolated as a pale yellow oil (320 mg, 60%) after purification by MPLC (SiO_2, 0-5% diethyl ether in hexanes, 30 min, 210 nm). R_f = 0.50 (20% EtOAc/hexanes); IR (film) 3082, 3050, 2922, 2853, 1612, 1553, 1502, 1429, 1380, 1274, 1140, 1103, 968, 853 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.47 (dd, *J* = 7.6, 1.9 Hz, 1H), 7.34 (dd, *J* = 7.6, 1.5 Hz, 1H), 7.23-7.17 (m, 2H), 6.91 (d, *J* = 15.8 Hz, 1H), 6.11 (dt, *J* = 15.8, 7.1 Hz, 1H), 4.54 (t, *J* = 7.1 Hz, 2H), 2.96 (ddt, *J* = 7.1, 7.1, 1.4 Hz, 2H); ^{13}C NMR (600 MHz, $CDCl_3$) ppm 162.3 (dd, *J* = 249, 12.0 Hz), 160.0 (dd, *J* = 252, 12.0 Hz), 128.2 (dd, *J* = 9.5, 5.2 Hz), 125.6, 125.4 (dd, *J* = 5.0, 1.8 Hz), 120.6 (dd, *J* = 12.2, 3.8 Hz), 111.4 (dd, *J* = 21.3, 3.5 Hz), 103.9 (dd, *J* = 25.9, 25.9 Hz), 74.8, 30.9; HRMS (CI): Exact mass calcd for $C_{10}H_8F_2NO_2$ $[M-H]^+$ 212.0529, found 212.0532.

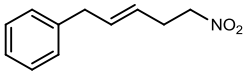


(E)-2,4-Dimethyl-1-(4-nitrobut-1-en-1-yl)benzene (179u). 2,4-dimethyl-1-vinylbenzene (1.2 g, 9.0 mmol) was stirred with 4-nitrobut-1-ene according to the general procedure. The title

compound was isolated as a pale yellow oil (343 mg, 67%) after purification by MPLC (SiO_2, 0-5% diethyl ether in hexanes, 30 min, 210 nm). R_f = 0.53 (20% EtOAc/hexanes); IR (film) 3080, 3050, 2920, 1551, 1502, 1380, 1274, 969 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.32 (d, *J* = 7.8 Hz, 1H), 7.01 (d, *J* = 8.1 Hz, 1H), 7.00 (s, 1H), 6.74 (d, *J* = 15.7 Hz, 1H), 5.97 (dt, *J* = 15.7, 7.2 Hz, 1H), 4.51 (t, *J* = 7.4 Hz, 2H), 2.93 (ddd, *J* = 14.3, 7.1, 1.4 Hz, 2H), 2.34 (s, 3H), 2.33 (s, 3H); ^{13}C NMR (600 MHz, $CDCl_3$) ppm 137.3, 135.0, 132.7, 131.7, 130.9, 126.7, 125.4, 123.3, 75.0, 30.9, 20.9, 19.5; HRMS (CI): Exact mass calcd for $C_{12}H_{15}NO_2$ $[M]^+$ 205.1103, found 205.1105.

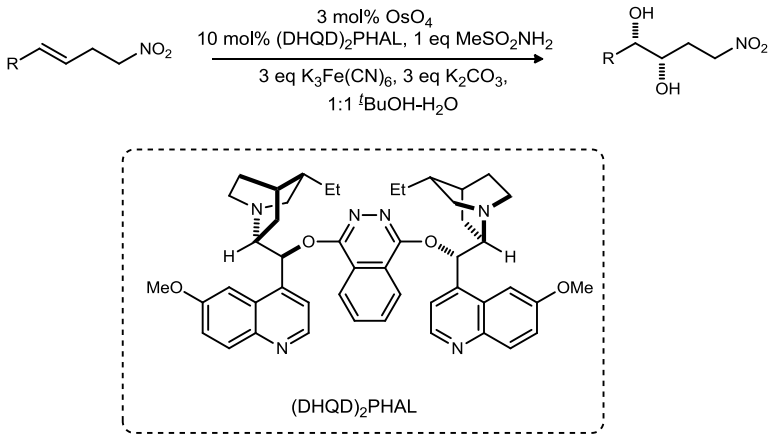


(4-Nitrobut-1-en-1-yl)cyclohexane (179v). Vinylcyclohexane (990 mg, 9.0 mmol) was stirred with 4-nitrobut-1-ene according to the general procedure. The title compound was isolated as a colorless oil (252 mg, 55%) after purification by MPLC (SiO_2, 0-10% diethyl ether in hexanes, 30 min, 210 nm). R_f = 0.42 (20% EtOAc/hexanes); IR (film) 2924, 2851, 1553, 1447, 1378, 970 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 5.52 (dd, *J* = 15.4, 6.5 Hz, 1H), 5.29 (dt, *J* = 15.4, 6.8 Hz, 1H), 4.37 (t, *J* = 7.2 Hz, 2H), 2.65 (dt, *J* = 7.1, 7.1 Hz, 2H), 1.91 (m, 1H), 1.71-0.98 (m, 10H); ^{13}C NMR (600 MHz, $CDCl_3$) ppm 141.2, 120.4, 75.5, 40.5, 32.7, 30.5, 26.0, 25.9; HRMS (ESI): Exact mass calcd for $C_{10}H_{16}NO_2$ $[M-H]^+$ 182.1176, found 182.1170.



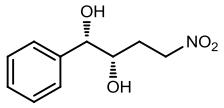
(5-Nitropent-2-en-1-yl)benzene (179w). Allylbenzene (1.1 g, 9.0 mmol) was stirred with 4-nitrobut-1-ene according to the general procedure. The title compound was isolated as a pale yellow oil (287 mg, 60%) after purification by MPLC (SiO_2, 0-10% diethyl ether in hexanes, 30 min, 210 nm). R_f = 0.42 (20% EtOAc/hexanes); IR (film) 3060, 3026, 2917, 1551, 1430, 1379, 971, 745, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.36-7.17 (m, 5H), 5.78 (dt, *J* = 15.1, 7.1 Hz, 1H), 5.46 (dt, *J* = 15.2, 6.9 Hz, 1H), 4.41 (t, *J* = 7.1 Hz, 2H), 3.37 (d, *J* = 6.9 Hz, 2H), 2.73 (ddt, *J* = 7.1, 7.1, 1.1 Hz, 2H); ^{13}C NMR (400 MHz, $CDCl_3$) ppm 139.8, 133.8, 128.5, 126.2, 124.6, 75.2, 38.8, 30.4; HRMS (ESI): Exact mass calcd for $C_{11}H_{13}NO_2$ $[M]^+$ 191.0941, found 191.0941.

Synthesis of Substituted 4-Nitro-1-Aryl Butane-1,2-diols Derivatives

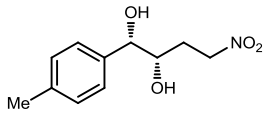


General Procedure. To a mixture of $K_3Fe(CN)_6$ (988 mg, 3.00 mmol), K_2CO_3 (415 mg, 3.00 mmol), and $(DHQD)_2PHAL$ (78 mg, 100 µmol) in ^{t}BuOH-H_2O (1:1, 10 mL) cooled to 0 °C was added OsO_4 as a 7.6 M solution in ^{t}BuOH (3 mol%) followed by

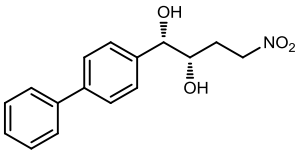
$CH_3SO_2NH_2$ (95 mg, 1.0 mmol). After stirring for 10 min at 0 °C, the alkene was added in one portion. The reaction mixture was stirred at room temperature for 6-12 h. Once all starting material was consumed (as indicated by TLC analysis), Na_2SO_3 was added and the mixture was stirred for 10 min. Ethyl acetate was added to the mixture, and after separation of the layers, the aqueous phase was further extracted with ethyl acetate. The combined organic extracts were dried and concentrated. The residue was purified by flash column chromatography (silica gel, ethyl acetate in hexanes).



(1*S*,2*S*)-4-Nitro-1-phenylbutane-1,2-diol (186a). (4-Nitrobut-1-en-1-yl)benzene (177 mg, 1.00 mmol) was treated utilizing the general procedure. The title compound was isolated as a pale yellow viscous oil (80 mg, 40%) after purification (SiO_2, 10-40% ethyl acetate in hexanes). The product was determined to be 96% ee by chiral HPLC analysis (Chiralcel OJ, 25% ^{i}PrOH/hexanes, 1.0 mL/min, $t_r(e_{1,}$ minor) = 11.4 min, $t_r(e_{2,}$ major) = 14.1 min); R_f = 0.42 (60% EtOAc/hexanes); IR (film) 3399, 3033, 2922, 1551, 1430, 1382, 1053, 765, 704 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41-7.32 (m, 5H), 4.51 (dd, *J* = 7.1, 7.1 Hz, 2H), 4.49 (d, *J* = 6.7 Hz, 1H), 3.83 (ddd, *J* = 9.7, 6.8, 3.8 Hz, 1H), 2.71 (s, 1H), 2.45 (s, 1H), 2.10-1.99 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) ppm 140.0, 128.9, 128.7, 126.6, 77.7, 72.7, 72.3, 30.1; HRMS (CI): Exact mass calcd for $C_{10}H_{12}NO_3$ $[M\text{-}OH]^+$ 194.0823, found 194.0826.

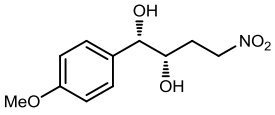


(1*S*,2*S*)-1-(4-Methylphenyl)-4-nitrobutane-1,2-diol (186b). 1-Methyl-4-(4-nitrobut-1-en-1-yl)benzene (191 mg, 1.00 mmol) was stirred utilizing the general procedure. The title compound was isolated as a white solid (108 mg, 48%) after purification (SiO_2, 10-40 % ethyl acetate in hexanes). The product was determined to be 95% ee by chiral HPLC analysis (Chiralcel OJ-H, 15% EtOH/hexanes, 0.6 mL/min, $t_r(e_1,$ minor) = 26.7 min, $t_r(e_2,$ major) = 34.3 min); mp = 78-80 °C; R_f = 0.44 (60% EtOAc/hexanes); IR (film) 3324, 3038, 2925, 1551, 1432, 1382, 1323, 1055, 924, 824 cm^{-1}; ^1H NMR (400 MHz, $(CD_3)_2CO$) δ 7.30 (d, *J* = 8.0 Hz, 2H), 7.17 (d, *J* = 7.9 Hz, 2H), 4.60 (dd, *J* = 7.1, 7.1 Hz, 2H), 4.58 (s, 1H), 4.49 (d, *J* = 6.3 Hz, 1H), 4.19 (s, 1H), 3.77 (m, 1H), 2.88 (s, 3H), 2.10-1.92 (m, 2H); ^{13}C NMR (125 MHz, $(CD_3)_2CO$) ppm 139.4, 137.3, 129.0, 127.3, 77.3, 73.0, 72.9, 30.8, 20.6; HRMS (ESI): Exact mass calcd for $C_{11}H_{13}NO_3$ $[M-H_2O]^+$ 207.0890, found 207.0891.

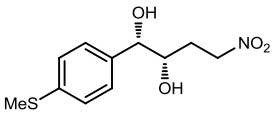


(1*S*,2*S*)-1-([1,1'-Biphenyl]-4-yl)-4-nitrobutane-1,2-diol (186c). 4-(4-Nitrobut-1-en-1-yl)-1,1'-biphenyl (253 mg, 1.00 mmol) was treated utilizing the general procedure. The title compound was isolated as a white solid (144 mg, 50%) after purification (SiO_2, 10-40% ethyl acetate in hexanes). The product was determined to be 95% ee by chiral HPLC analysis (Chiralcel OJ, 25% ^{i}PrOH/hexanes, 1.0 mL/min, $t_r(e_1,$ minor) = 39.9 min, $t_r(e_2,$ major) = 47.6 min); mp = 126-128 °C; R_f = 0.46 (60% EtOAc/hexanes); IR (film) 3403, 2913, 1541, 1420, 1379, 1242, 1045, 831, 759, 725, 687 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.62 (d, *J* = 8.3 Hz, 2H), 7.60 (d, *J* = 8.4 Hz, 2H), 7.47 (dd, *J* = 7.5, 7.5 Hz,

2H), 7.42 (d, *J* = 8.2 Hz, 2H), 7.38 (ddd, *J* = 7.5, 7.5, 1.2 Hz, 1H), 4.55 (m, 3H), 3.77 (ddd, *J* = 8.7, 6.5, 4.3 Hz, 1H), 2.13-2.08 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) ppm 141.6, 140.3, 139.0, 129.0, 128.9, 128.8, 127.6, 127.1, 127.0, 77.5, 72.7, 72.3, 30.2; HRMS (ESI): Exact mass calcd for $C_{16}H_{16}NO_3$ $[M\text{-}OH]^+$ 270.1136, found 270.1121.

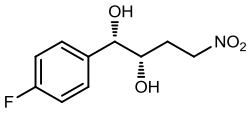


(1*S*,2*S*)-1-(4-Methoxyphenyl)-4-nitrobutane-1,2-diol (187d). 1-Methoxy-4-(4-nitrobut-1-en-1-yl)benzene (207 mg, 1.00 mmol) was treated utilizing the general procedure. The title compound was isolated as a white solid (118 mg, 49%) after purification (SiO_2, 10-40% ethyl acetate in hexanes). The product was determined to be 96% ee by chiral HPLC analysis (Chiralcel OJ, 30% EtOH/hexanes, 0.8 mL/min, $t_r(e_1$, minor) = 16.5 min, $t_r(e_2$, major) = 22.9 min); mp = 60-62 °C; R_f = 0.38 (60% EtOAc/hexanes); IR (film) 3368, 3019, 2936, 1550, 1433, 1383, 1031, 837 cm^{-1}; ^{1}H NMR (400 MHz, $(CD_3)_2CO$) δ 7.33 (d, *J* = 8.7 Hz, 2H), 6.91 (d, *J* = 8.7 Hz, 2H), 4.60 (dd, *J* = 7.2, 7.2 Hz, 2H), 4.54 (s, 1H), 4.47 (d, *J* = 6.6 Hz, 1H), 4.17 (s, 1H), 3.80 (s, 3H), 3.76 (m, 1H), 2.10-1.90 (m, 2H); ^{13}C NMR (125 MHz, $(CD_3)_2CO$) ppm 159.6, 134.3, 128.5, 113.8, 77.1, 73.0, 72.9, 55.0, 30.8; HRMS (ESI): Exact mass calcd for $C_{11}H_{15}NO_5$ $[M]^+$ 241.0945, found 241.0945.



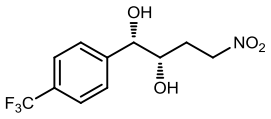
(1*S*,2*S*)-1-(4-(Methylthio)phenyl)-4-nitrobutane-1,2-diol (186e). 1-(Methylthio)-4-(4-nitrobut-1-en-1-yl)benzene (223 mg, 1.00 mmol) was treated utilizing the general procedure. The title compound was isolated as a dark yellow viscous oil (141 mg, 55%) after purification (SiO_2, 10-40% ethyl acetate in hexanes). The product was

determined to be 96% ee by chiral HPLC analysis (Chiralcel IA, 15% EtOH/hexanes, 0.6 mL/min, $t_r(e_{1,}$ minor) = 21.0 min, $t_r(e_{2,}$ major) = 25.1 min); R_f = 0.39 (60% EtOAc/hexanes); IR (film) 3397, 2923, 1551, 1430, 1383, 1092, 822 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.25 (d, *J* = 8.8 Hz, 2H), 7.22 (d, *J* = 8.8 Hz, 2H), 4.60 (dd, *J* = 7.3, 7.3 Hz, 2H), 4.47 (d, *J* = 6.8 Hz, 1H), 3.76 (m, 1H), 3.12 (s, 2H), 2.50 (s, 3H), 2.02-1.94 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) ppm 139.0, 136.7, 127.1, 126.6, 77.3, 72.6, 72.3, 30.1, 15.5; HRMS (CI): Exact mass calcd for $C_{11}H_{15}NO_{4S}$ $[M]^+$ 257.0722, found 257.0716.



(1*S*,2*S*)-1-(4-Fluorophenyl)-4-nitrobutane-1,2-diol (186f). 1-Fluoro-4-(4-nitrobut-1-en-1-yl)benzene (195 mg, 1.00 mmol) was treated utilizing the general procedure. The title compound was isolated as a white solid (80 mg, 35%) after purification (SiO_2, 10-40% ethyl acetate in hexanes). The product was determined to be 99% ee by chiral HPLC analysis (Chiralcel OJ, 25% ^{i}PrOH/hexanes, 1.0 mL/min, $t_r(e_{1,}$ minor) = 11.4 min, $t_r(e_{2,}$ major) = 14.1 min); mp = 104-106 °C; R_f = 0.42 (60% EtOAc/hexanes); IR (film) 3315, 2922, 1547, 1427, 1377, 1225, 1038, 957, 762, 682 cm^{-1}; ^1H NMR (500 MHz, $(CD_3)_2CO$) δ 7.44 (dd, *J* = 8.6, 5.8 Hz, 2H), 7.08 (dd, *J* = 8.8, 8.8 Hz, 2H), 4.64 (s, 1H), 4.59 (dd, *J* = 7.0, 7.0 Hz, 2H), 4.56 (d, *J* = 6.7 Hz, 1H), 4.16 (s, 1H), 3.76 (m, 1H), 2.10-1.91 (m, 2H); ^{13}C NMR (125 MHz, $(CD_3)_2CO$) ppm 162.8 (d, $^1J_{CF}$ = 243 Hz), 138.9 (d, $^4J_{CF}$ = 3.3 Hz), 129.4 (d, $^3J_{CF}$ = 8.2 Hz), 115.2 (d, $^2J_{CF}$ = 21.5 Hz), 76.8, 73.3, 73.1, 31.0; HRMS (ESI): Exact mass calcd for $C_{10}H_{12}FNNaO_4$ $[M+Na]^+$ 252.0648, found 252.0643.

(1*S*,2*S*)-1-(4-(Trifluoromethyl)phenyl)-4-nitrobutane-1,2-diol

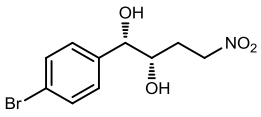


(186g). 1-(4-Nitrobut-1-en-1-yl)-4-(trifluoromethyl)benzene (245 mg, 1.00 mmol) was treated utilizing the general procedure. The title compound was isolated as a white solid (126 mg, 45%) after purification (SiO_2, 10-40% ethyl acetate in hexanes). The product was determined to be 98% ee by chiral HPLC analysis (Chiralcel IA, 15% EtOH/hexanes, 0.6 mL/min, $t_r(e_1$, minor) = 16.9 min, $t_r(e_2$, major) = 19.8 min); mp = 123-125 °C; R_f = 0.45 (60% EtOAc/hexanes); IR (film) 3407, 2924, 2854, 1552, 1416, 1380, 1327, 1063, 817 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$)[58] δ 7.65 (d, *J* = 8.3 Hz, 2H), 7.48 (d, *J* = 8.3 Hz, 2H), 4.60 (d, *J* = 6.0 Hz, 1H), 4.54 (dd, *J* = 7.0, 7.0 Hz, 2H), 3.84 (ddd, *J* = 9.8, 6.0, 3.5 Hz, 1H), 2.15-2.01 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) ppm 144.2, 130.8 (q, $^2J_{CF}$ = 33.0 Hz), 127.0, 125.7 (q, $^3J_{CF}$ = 3.6 Hz), 123.7 (q, $^1J_{CF}$ = 273 Hz), 76.9, 72.5, 72.1, 30.2; HRMS (ESI): Exact mass calcd for $C_{11}H_{12}F_2NO_4$ $[M-F]^+$ 260.0729, found 260.0723.

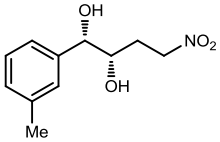
(1*S*,2*S*)-1-(4-Chlorophenyl)-4-nitrobutane-1,2-diol (186h). 1-Chloro-4-(4-nitrobut-1-en-1-yl)benzene (212 mg, 1.00 mmol) was treated utilizing the general procedure. The title compound was isolated as a white solid (79 mg, 32%) after purification (SiO_2, 10-40% ethyl acetate in hexanes). The product was determined to be 99% ee by chiral HPLC analysis (Chiralcel OJ, 25% ^{i}PrOH/hexanes, 1.0 mL/min, $t_r(e_1$, minor) = 11.4 min, $t_r(e_2$, major) = 14.1 min); mp = 99-101 °C; R_f = 0.42 (60% EtOAc/hexanes); IR (film) 3281, 2943, 1546, 1425, 1370, 1041, 930 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 (d, *J* = 8.5

[58] No OH peaks observed

Hz, 2H), 7.27 (d, *J* = 8.8 Hz, 2H), 4.51 (dd, *J* = 7.0, 7.0 Hz, 2H), 4.47 (d, *J* = 6.6 Hz, 1H), 3.77 (ddd, *J* = 9.7, 5.5, 3.4 Hz, 1H), 2.74 (br s, 1H), 2.61 (br s, 1H), 2.10-1.97 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) ppm 138.6, 134.4, 129.0, 127.9, 76.9, 72.6, 72.2, 30.1; HRMS (ESI): Exact mass calcd for $C_{10}H_{12}ClNNaO_4$ $[M+Na]^+$ 268.0353, found 268.0343.

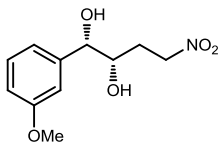


(1*S*,2*S*)-1-(4-Bromophenyl)-4-nitrobutane-1,2-diol (186i). 1-Bromo-4-(4-nitrobut-1-en-1-yl)benzene (256 mg, 1.00 mmol) was treated utilizing the general procedure. The title compound was isolated as a white solid (145 mg, 50%) after purification (SiO_2, 10-40% ethyl acetate in hexanes). The product was determined to be 97% ee by chiral HPLC analysis (Chiralcel IA, 15% EtOH/hexanes, 0.6 mL/min, $t_r(e_{1,}$ minor) = 25.8 min, $t_r(e_{2,}$ major) = 28.4 min); mp = 88-90 °C; R_f = 0.48 (60% EtOAc/hexanes); IR (film) 3412, 2910, 1541, 1484, 1439, 1370, 1040, 928, 793 cm^{-1}; ^{1}H NMR (400 MHz, $(CD_3)_2CO$) δ 7.52 (d, *J* = 8.5 Hz, 2H), 7.39 (d, *J* = 8.5 Hz, 2H), 4.75 (d, *J* = 4.0 Hz, 1H), 4.63 (dd, *J* = 7.0, 7.0 Hz, 2H), 4.59 (d, *J* = 6.5 Hz, 1H), 4.25 (d, *J* = 3.9 Hz, 1H), 3.77 (ddd, *J* = 9.7, 5.5, 3.4 Hz, 1H), 2.13-1.96 (m, 2H); ^{13}C NMR (125 MHz, $(CD_3)_2CO$) ppm 141.8, 131.3, 131.2, 129.3, 120.9, 76.3, 72.9, 72.5, 30.6; HRMS (CI): Exact mass calcd for $C_{10}H_{12}BrNO_4$ $[M]^-$ 288.9955, found 288.9954.



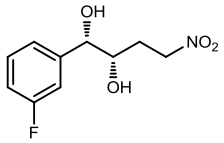
(1*S*,2*S*)-1-(3-Methylphenyl)-4-nitrobutane-1,2-diol (186j). 1-Methyl-3-(4-nitrobut-1-en-1-yl)benzene (191 mg, 1.00 mmol) was treated utilizing the general procedure. The title compound was

isolated as a clear viscous oil (148 mg, 66%) after purification (SiO_2, 10-40% ethyl acetate in hexanes). The product was determined to be 95% ee by chiral HPLC analysis (Chiralcel OJ-H, 15% EtOH/hexanes, 0.6 mL/min, $t_r(e_1$, minor) = 28.5 min, $t_r(e_2$, major) = 33.6 min); R_f = 0.44 (60% EtOAc/hexanes); IR (film) 3324, 3038, 2925, 1551, 1432, 1382, 1323, 1055, 924, 824 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.26 (dd, *J* = 7.7, 7.7 Hz, 1H), 7.15 (d, *J* = 7.7 Hz, 1H), 7.11 (s, 1H), 7.09 (d, *J* = 7.9 Hz, 1H), 4.44 (dd, *J* = 7.0, 7.0 Hz, 2H), 4.35 (d, *J* = 6.9 Hz, 1H), 3.78-3.73 (br m, 1H), 3.50-3.35 (br m, 2H), 2.37 (s, 3H), 2.03-1.92 (m, 2H); ^{13}C NMR (150 MHz, $(CD_3)_2CO$) ppm 142.4, 137.8, 128.5, 128.3, 127.9, 124.4, 77.4, 73.0, 72.9, 30.8, 20.9; HRMS (ESI): Exact mass calcd for $C_{11}H_{15}NNaO_4$ $[M+Na]^+$ 248.0899, found 248.0905.

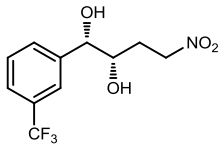


(1*S*,2*S*)-1-(3-Methoxyphenyl)-4-nitrobutane-1,2-diol (186k). 1-Methoxy-3-(4-nitrobut-1-en-1-yl)benzene (207 mg, 1.00 mmol) was stirred utilizing the general procedure. The title compound was isolated as a white solid (123 mg, 51%) after purification (SiO_2, 10-40% ethyl acetate in hexanes). The product was determined to be 99% ee by chiral HPLC analysis (Chiralcel OJ, 25% ^{i}PrOH/hexanes, 1.0 mL/min, $t_r(e_1$, minor) = 31.5 min, $t_r(e_2$, major) = 35.7 min); mp = 78-80 °C; R_f = 0.38 (60% EtOAc/hexanes); IR (film) 3402, 2922, 2841, 1551, 1434, 1382, 1262, 1044, 786 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.28 (dd, *J* = 8.8, 8.8 Hz, 1H), 6.88-6.83 (m, 3H), 4.47 (dd, *J* = 7.0, 7.0 Hz, 2H), 4.40 (d, *J* = 6.6 Hz, 1H), 3.80 (s, 3H), 3.78-3.75 (m, 1H), 2.97 (br s, 2H), 2.06-1.98 (m, 2H); ^{13}C NMR (150 MHz, $(CD_3)_2CO$) ppm 160.3, 144.4, 129.6, 119.8, 113.4, 113.1,

77.5, 73.3, 73.1, 55.1, 31.1; HRMS (ESI): Exact mass calcd for $C_{11}H_{15}NaNO_5$ $[M+Na]^+$ 264.0848, found 264.0838.

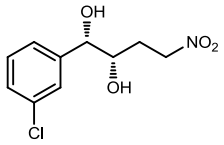


(1*S*,2*S*)-1-(3-Fluorophenyl)-4-nitrobutane-1,2-diol (186l). 1-Fluoro-3-(4-nitrobut-1-en-1-yl)benzene (195 mg, 1.00 mmol) was treated utilizing the general procedure. The title compound was isolated as a white solid (112 mg, 49%) after purification (SiO_2, 10-40% ethyl acetate in hexanes). The product was determined to be 98% ee by chiral HPLC analysis (Chiralcel IA, 15% EtOH/hexanes, 0.6 mL/min, $t_r(e_{1,}$ minor) = 23.4 min, $t_r(e_{2,}$ major) = 28.4 min); mp = 83-85 °C; R_f = 0.42 (60% EtOAc/hexanes); IR (film) 3315, 2922, 1547, 1427, 1377, 1225, 1038, 957, 762, 682 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.37 (dd, *J* = 14.5, 7.8 Hz, 1H), 7.12 (d, *J* = 7.8 Hz, 1H), 7.09 (d, *J* = 9.7 Hz, 1H), 7.05 (dd, *J* = 8.5, 8.5 Hz, 1H), 4.54 (dd, *J* = 7.0, 7.0 Hz, 2H), 4.51 (d, *J* = 6.2 Hz, 1H), 3.81 (m, 1H), 2.75 (br s, 2H), 2.13-2.03 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) ppm 162.8 (d, $^1J_{CF}$ = 243 Hz), 142.8 (d, $^3J_{CF}$ = 6.7 Hz), 130.4 (d, $^3J_{CF}$ = 8.2 Hz), 122.2 (d, $^4J_{CF}$ = 2.6 Hz), 115.5 (d, $^2J_{CF}$ = 21.5 Hz), 113.6 (d, $^2J_{CF}$ = 22.0 Hz), 76.9, 72.5, 72.1, 30.1; HRMS (ESI): Exact mass calcd for $C_{10}H_{12}FNNaO_4$ $[M+Na]^+$ 252.0648, found 252.0643.

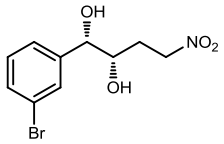


(1*S*,2*S*)-1-(3-(Trifluoromethyl)phenyl)-4-nitrobutane-1,2-diol (186m). 1-(4-Nitrobut-1-en-1-yl)-3-(trifluoromethyl)benzene (245 mg, 1.00 mmol) was treated utilizing the general procedure. The title compound was isolated as a white solid (112 mg, 40%) after purification (SiO_2, 10-40% ethyl acetate in hexanes). The product was determined to be

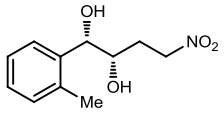
96% ee by chiral HPLC analysis (Chiralcel OJ-H, 10% EtOH/hexanes, 0.6 mL/min, $t_r(e_1$, minor) = 28.9 min, $t_r(e_2$, major) = 30.6 min); mp = 118-120 °C; R_f = 0.42 (60% EtOAc/hexanes); IR (film) 3276, 2917, 1542, 1430, 1369, 1327, 1042, 793 cm^{-1}; ^1H NMR (500 MHz, CD_3OD) δ 7.74 (s, 1H), 7.65 (d, *J* = 7.3 Hz, 1H), 7.58 (d, *J* = 7.5 Hz, 1H), 7.53 (dd, *J* = 7.5, 7.5 Hz, 1H), 4.64 (d, *J* = 4.9 Hz, 1H), 4.57 (dd, *J* = 7.0, 7.0 Hz, 2H), 3.78 (ddd, *J* = 9.8, 6.0, 3.5 Hz, 1H), 2.14-1.97 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) ppm 143.2, 130.4 (q, $^2J_{CF}$ = 31.9 Hz), 128.4, 124.3 (q, $^1J_{CF}$ = 272 Hz), 123.8 (q, $^3J_{CF}$ = 3.9 Hz), 123.2 (q, $^3J_{CF}$ = 3.9 Hz), 75.7, 72.1, 71.7, 30.3; HRMS (CI): Exact mass calcd for $C_{11}H_{11}F_3NO_4$ $[M-H]^+$ 278.0646, found 278.0648.



(1*S*,2*S*)-1-(3-Chlorophenyl)-4-nitrobutane-1,2-diol (186n). 1-Chloro-3-(4-nitrobut-1-en-1-yl)benzene (212 mg, 1.00 mmol) was treated utilizing the general procedure. The title compound was isolated as a white solid (123 mg, 50%) after purification (SiO_2, 10-40% ethyl acetate in hexanes). The product was determined to be 99% ee by chiral HPLC analysis (Chiralcel IA, 15% EtOH/hexanes, 0.6 mL/min, $t_r(e_1$, minor) = 21.0 min, $t_r(e_2$, major) = 25.1 min); mp = 109-111 °C; R_f = 0.42 (60% EtOAc/hexanes); IR (film) 3281, 2943, 1546, 1425, 1370, 1041, 930 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.35 (s, 1H), 7.33-7.29 (m, 2H), 7.23-7.19 (m, 1H), 4.52 (dd, *J* = 7.0, 7.0 Hz, 2H), 4.47 (d, *J* = 6.2 Hz, 1H), 3.80 (ddd, *J* = 9.7, 6.2, 3.9 Hz, 1H), 2.70 (br s, 2H), 2.13-2.00 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) ppm 142.2, 134.8, 130.1, 128.7, 126.7, 124.7, 76.9, 72.5, 72.2, 30.2; HRMS (ESI): Exact mass calcd for $C_{10}H_{12}ClNNaO_4$ $[M+Na]^+$ 268.0353, found 268.0346.

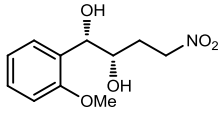


(1*S*,2*S*)-1-(3-Bromophenyl)-4-nitrobutane-1,2-diol (186o). 1-Bromo-3-(4-nitrobut-1-en-1-yl)benzene (256 mg, 1.00 mmol) was treated utilizing the general procedure. The title compound was isolated as a white solid (160 mg, 55%) after purification (SiO_2, 10-40% ethyl acetate in hexanes). The product was determined to be 97% ee by chiral HPLC analysis (Chiralcel IA, 15% EtOH/hexanes, 0.6 mL/min, $t_r(e_1$, minor) = 21.3 min, $t_r(e_2$, major) = 24.4 min); mp = 113-115 °C; R_f = 0.48 (60% EtOAc/hexanes); IR (film) 3268, 2912, 1544, 1423, 1369, 1040, 927, 737 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.50 (s, 1H), 7.48-7.45 (m, 1H), 7.26-7.24 (m, 2H), 4.52 (dd, *J* = 6.9, 6.9 Hz, 2H), 4.63 (d, *J* = 6.2 Hz, 1H), 3.79 (ddd, *J* = 9.7, 5.5, 3.9 Hz, 1H), 2.79 (s, 2H), 2.12-2.02 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) ppm 145.2, 130.4, 130.1, 129.9, 126.0, 121.9, 76.0, 72.8, 72.3, 30.6; HRMS (ESI): Exact mass calcd for $C_{10}H_{12}BrNNaO_4$ $[M+Na]^+$ 311.9858, found 311.9847.

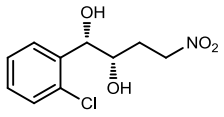


(1*S*,2*S*)-1-(2-Methylphenyl)-4-nitrobutane-1,2-diol (186p). 1-Methyl-2-(4-nitrobut-1-en-1-yl)benzene (191 mg, 1.00 mmol) was treated utilizing the general procedure. The title compound was isolated as a pale yellow viscous oil (131 mg, 58%) after purification (SiO_2, 10-40% ethyl acetate in hexanes). The product was determined to be 95% ee by chiral HPLC analysis (Chiralcel OJ-H, 15% EtOH/hexanes, 0.6 mL/min, $t_r(e_1$, minor) = 23.3 min, $t_r(e_2$ major) = 25.3 min); R_f = 0.48 (60% EtOAc/hexanes); IR (film) 3400, 3025, 2928, 1551, 1431, 1382, 1101, 1055, 762 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$)

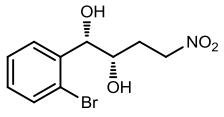
δ 7.38 (dd, *J* = 6.5, 6.5 Hz, 1H), 7.27-7.17 (m, 3H), 4.79 (dd, *J* = 5.8, 5.8 Hz, 1H), 4.52 (dd, *J* = 7.0, 7.0 Hz, 2H), 3.88 (ddd, *J* = 13.1, 6.4, 3.3 Hz, 1H), 2.65 (d, *J* = 3.5 Hz, 1H), 2.37 (s, 3H), 2.28 (d, *J* = 4.3 Hz, 1H), 2.18-2.00 (m, 2H); ^{13}C NMR (125 MHz, $(CD_3)_2CO$) ppm 140.6, 135.4, 130.5, 127.5, 127.4, 126.1, 73.6, 73.0, 72.3, 30.9, 19.1; HRMS (ESI): Exact mass calcd for $C_{11}H_{14}NO_3$ $[M\text{-}OH]^+$ 208.0968, found 208.0962.



(1*S*,2*S*)-1-(2-Methoxyphenyl)-4-nitrobutane-1,2-diol (186q). 1-Methoxy-2-(4-nitrobut-1-en-1-yl)benzene (207 mg, 1.00 mmol) was treated utilizing the general procedure. The title compound was isolated as a pale yellow viscous oil (84 mg, 32%) after purification (SiO_2, 10-40% ethyl acetate in hexanes). The product was determined to be 97% ee by chiral HPLC analysis (Chiralcel OJ-H, 15% EtOH/hexanes, 0.6 mL/min, $t_r(e_1$, minor) = 27.6 min, $t_r(e_2$, major) = 30.9 min); R_f = 0.39 (60% EtOAc/hexanes); IR (film) 3401, 2929, 2843, 1551, 1439, 1382, 1243, 1042, 1027, 759 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 (ddd, *J* = 7.7, 7.7, 1.8 Hz, 1H), 7.28 (d, *J* = 7.7 Hz, 1H), 6.97 (dd, *J* = 7.7, 7.7 Hz, 1H), 6.90 (d, *J* = 8.5 Hz, 1H), 4.70 (d, *J* = 6.6 Hz, 1H), 4.51 (dd, *J* = 7.1, 7.1 Hz, 2H), 3.89 (m, 1H), 3.84 (s, 3H), 3.15 (br s, 1H), 2.99 (br s, 1H), 2.12-1.98 (m, 2H); ^{13}C NMR (150 MHz, $(CD_3)_2CO$) ppm 156.9, 130.9, 128.8, 128.1, 120.9, 110.9, 73.3, 72.6, 70.9, 55.4, 31.3; HRMS (ESI): Exact mass calcd for $C_{11}H_{15}NNaO_5$ $[M+Na]^+$ 264.0848, found 264.0849.

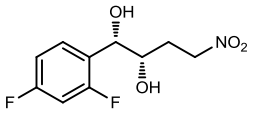


(1*S*,2*S*)-1-(2-Chlorophenyl)-4-nitrobutane-1,2-diol (186r). 1-Chloro-2-(4-nitrobut-1-en-1-yl)benzene (212 mg, 1.00 mmol) was treated utilizing the general procedure. The title compound was isolated as a white solid (128 mg, 52%) after purification (SiO_2, 10-40% ethyl acetate in hexanes). The product was determined to be 99% ee by chiral HPLC analysis (Chiralcel IA, 15% EtOH/hexanes, 0.6 mL/min, $t_r(e_{1,}$ minor) = 19.0 min, $t_r(e_{2,}$ major) = 23.5 min); mp = 66-68 °C; R_f = 0.42 (60% EtOAc/hexanes); IR (film) 3399, 2926, 1552, 1432, 1382, 1103, 1062, 757 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) 7.50 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.39 (dd, *J* = 7.8, 1.3 Hz, 1H), 7.34 (ddd, *J* = 7.5, 7.5, 1.3 Hz, 1H), 7.28 (ddd, *J* = 7.6, 7.6, 1.9 Hz, 1H), 5.03 (d, *J* = 5.2 Hz, 1H), 4.55 (dd, *J* = 7.1, 7.1 Hz, 2H), 3.89 (ddd, *J* = 9.7, 5.2, 3.3 Hz, 1H), 2.83 (br s, 2H), 2.30-2.09 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) ppm 137.9, 132.2, 129.6, 129.3, 127.9, 127.3, 72.8, 72.3, 71.7, 30.2; HRMS (ESI): Exact mass calcd for $C_{10}H_{12}ClNNaO_4$ $[M+Na]^+$ 268.0353, found 268.0360.

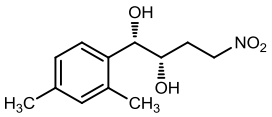


(1*S*,2*S*)-1-(2-Bromophenyl)-4-nitrobutane-1,2-diol (186s). 1-Bromo-2-(4-nitrobut-1-en-1-yl)benzene (256 mg, 1.00 mmol) was treated utilizing the general procedure. The title compound was isolated as a white solid (124 mg, 43%) after purification (SiO_2, 10-40% ethyl acetate in hexanes). The product was determined to be 99% ee by chiral HPLC analysis (Chiralcel IA, 15% EtOH/hexanes, 0.6 mL/min, $t_r(e_{1,}$ major) = 20.1 min, $t_r(e_{2,}$ major) = 23.5 min); mp = 75-78 °C; R_f = 0.48 (60% EtOAc/hexanes); IR (film) 3397, 2926, 1551, 1433, 1382, 1103, 1058, 954, 756 cm^{-1}; ^1H NMR (400 MHz,

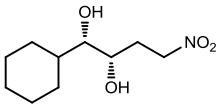
$(CD_3)_2CO$) δ 7.62 (dd, *J* = 7.7, 1.4 Hz, 1H), 7.57 (dd, *J* = 8.0, 0.8 Hz, 1H), 7.39 (dd, *J* = 7.8, 7.8 Hz, 1H), 7.22 (ddd, *J* = 7.9, 7.9, 1.6 Hz, 1H), 4.97 (dd, *J* = 5.0, 5.0 Hz, 1H), 4.83 (d, *J* = 5.0 Hz, 1H), 4.67 (dd, *J* = 7.0, 7.0 Hz, 2H), 4.10 (d, *J* = 6.2 Hz, 1H), 3.85 (m, 1H), 2.31-2.11 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) ppm 142.2, 132.8, 129.9, 129.6, 129.0, 122.5, 75.2, 73.2, 71.9, 31.6; HRMS (ESI): Exact mass calcd for $C_{10}H_{12}BrNNaO_4$ $[M+Na]^+$ 311.9858, found 311.9849.



(1*S*,2*S*)-1-(2,4-Difluorophenyl)-4-nitrobutane-1,2-diol (186t). 2,4-difluoro-1-(4-nitrobut-1-en-1-yl)benzene (213 mg, 1.00 mmol) was treated utilizing the general procedure. The title compound was isolated as a white solid (125 mg, 51%) after purification (SiO_2, 10-40% ethyl acetate in hexanes). The product was determined to be 94% ee by chiral HPLC analysis (Chiralcel OJ-H, 15% EtOH/hexanes, 0.6 mL/min, $t_r(e_{1,}$ minor) = 21.8 min, $t_r(e_{2,}$ major) = 23.5 min); mp = 80-82 °C; R_f = 0.46 (60% EtOAc/hexanes); IR (film) 3270, 2921, 1547, 1429, 1378, 1266, 1094, 1040, 962 cm^{-1}; ^1H NMR (400 MHz, CD_3OD) δ 7.58 (ddd, *J* = 8.5, 8.5, 6.7 Hz, 1H), 6.99 (ddd, *J* = 8.5, 8.5, 2.2 Hz, 1H), 6.93 (ddd, *J* = 10.7, 9.3, 2.5 Hz, 1H), 4.83 (d, *J* = 5.4 Hz, 1H), 4.69-4.53 (m, 2H), 3.76 (ddd, *J* = 9.2, 4.7, 4.7 Hz, 1H), 2.12-1.98 (m, 2H); ^{13}C NMR (150 MHz, CD_3OD) ppm 163.6 (dd, J_{CF} = 247, 12.0 Hz), 161.1 (dd, J_{CF} = 247, 12.0 Hz), 131.0 (dd, J_{CF} = 9.7, 6.3 Hz), 126.4 (dd, J_{CF} = 13.8, 3.4 Hz), 112.2 (dd, J_{CF} = 21.2, 3.5 Hz), 103.9 (dd, J_{CF} = 25.7, 25.7 Hz), 73.4, 72.6, 70.9, 31.6; HRMS (ESI): Exact mass calcd for $C_{10}H_{11F2}NNaO_4$ $[M+Na]^+$ 270.1832, found 270.1849.



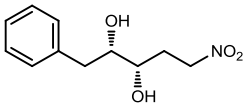
(1*S*,2*S*)-1-(2,4-Dimethylphenyl)-4-nitrobutane-1,2-diol (186u). (*E*)-2,4-Dimethyl-1-(4-nitrobut-1-en-1-yl)benzene (205 mg, 1.00 mmol) was treated utilizing the general procedure. The title compound was isolated as a white solid (148 mg, 62%) after purification (SiO_2, 10-40% ethyl acetate in hexanes). The product was determined to be 97% ee by chiral HPLC analysis (Chiralcel OJ-H, 15% EtOH/hexanes, 0.6 mL/min, $t_r(e_1$, minor) = 27.3 min, $t_r(e_2$, major) = 31.6 min); mp = 75-78 °C; R_f = 0.49 (60% EtOAc/hexanes); IR (film) 3394, 2924, 1552, 1429, 1381, 1102, 1051, 821 cm^{-1}; ^1H NMR (600 MHz, CD_3OD)[59] δ 7.28 (d, *J* = 7.8 Hz, 1H), 7.01 (d, *J* = 7.9 Hz, 1H), 6.98 (s, 1H), 4.70 (d, *J* = 6.5 Hz, 1H), 4.54-4.47 (m, 2H), 3.76 (ddd, *J* = 7.8, 6.4, 6.4 Hz, 1H), 2.33 (s, 3H), 2.27 (s, 3H), 1.97-1.94 (m, 2H); ^{13}C NMR (150 MHz, CD_3OD) ppm 138.1, 137.8, 136.3, 132.1, 128.0, 127.7, 74.5, 73.6, 73.3, 31.8, 21.1, 19.6; HRMS (ESI): Exact mass calcd for $C_{12}H_{17}NNaO_4$ $[M+Na]^+$ 262.1055, found 262.1044.



(1*S*,2*S*)-1-Cyclohexyl-4-nitrobutane-1,2-diol (186v). (4-Nitrobut-1-en-1-yl)cyclohexane (183 mg, 1.00 mmol) was treated utilizing the general procedure. The title compound was isolated as a white solid (126 mg, 58%) after purification (SiO_2, 10-40% ethyl acetate in hexanes). The product was determined to be 96% ee by chiral HPLC analysis (Chiralcel IA, 15% EtOH/hexanes, 0.6 mL/min, $t_r(e_1$, minor) = 22.8 min, $t_r(e_2$ major) = 27.4 min); Mp = 45-48 °C; R_f = 0.44 (60% EtOAc/hexanes); IR (film) 3334, 2912, 2851, 1536, 1437, 1377, 1117, 1032, 909, 729 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ

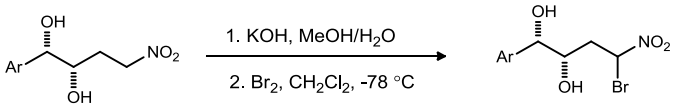
[59] OHs' not visible in ^1H NMR. See IR.

4.65-4.52 (m, 2H), 3.77 (m, 1H), 3.17 (m, 1H), 2.32 (br s, 1H), 2.21-2.15 (m, 2H), 1.96 (br s, 1H), 1.81-1.64 (m, 4H), 1.53-1.45 (m, 1H), 1.31-1.01 (m, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) ppm 78.3, 72.5, 68.0, 40.0, 31.6, 29.6, 27.7, 26.2, 26.1, 25.9; HRMS (ESI): Exact mass calcd for $C_{10}H_{19}NNaO_4$ $[M+Na]^+$ 240.1212, found 240.1220.

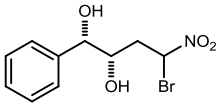


(2*S*,3*S*)-5-Nitro-1-phenylpentane-2,3-diol (186w). (5-Nitropent-2-en-1-yl)benzene (191 mg, 1.00 mmol) was treated utilizing the general procedure. The title compound was isolated as a white solid (124 mg, 55%) after purification (SiO_2, 10-40% ethyl acetate in hexanes). The product was determined to be 95% ee by chiral HPLC analysis (Chiralcel IA, 15% EtOH/hexanes, 0.6 mL/min, $t_r(e_1$, minor) = 36.5 min, $t_r(e_2$, major) = 42.5 min); mp = 55-57 °C; R_f = 0.42 (60% EtOAc/hexanes); IR (film) 3398, 3029, 2922, 1551, 1431, 1383, 1112, 1061, 750, 702 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 (dd, *J* = 7.4, 7.4 Hz, 2H), 7.28 (dd, *J* = 6.8, 6.8 Hz, 1H), 7.23 (d, *J* = 7.1 Hz, 2H), 4.63-4.54 (m, 2H), 3.71 (ddd, *J* = 8.7, 4.2, 4.2 Hz, 1H), 3.63 (ddd, *J* = 9.7, 4.0, 4.0 Hz, 1H), 2.90 (dd, *J* = 13.7, 4.2 Hz, 1H), 2.77 (dd, *J* = 13.7, 9.0 Hz, 1H), 2.29-2.18 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) ppm 137.2, 129.3, 128.8, 126.9, 74.7, 72.4, 70.4, 40.1, 31.3; HRMS (ESI): Exact mass calcd for $C_{11}H_{16}NO_4$ $[M+H]^+$ 226.1085, found 226.1084.

Synthesis of γ,δ-Dihydroxy-α-Bromonitroalkanes



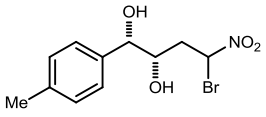
General Procedure[60]. The nitroalkane was added to a solution of KOH in 25% MeOH:H_2O (0.95 eq, 100 mM) and allowed to stir until the nitroalkane completely dissolved. The reaction was cooled to -22 °C and transferred to a separatory funnel. Simultaneously, a solution of bromine in DCM (0.95 eq, 200 mM) was cooled to -78 °C and quickly added to the separatory funnel, which was shaken vigorously until the orange color disappeared. The reaction mixture was separated, and the aqueous layer was extracted with DCM. The combined organic extract was dried and concentrated. The residue was purified by flash column chromatography (silica gel, ethyl acetate in hexanes).



(1*S*,2*S*)-4-Bromo-4-nitro-1-phenylbutane-1,2-diol (181a). (1*S*,2*S*)-4-Nitro-1-phenylbutane-1,2-diol (73 mg, 350 μmol) was treated utilizing the general procedure. The title compound was isolated as a white solid (60 mg, 59%) after purification (SiO_2, 5-30% ethyl acetate in hexanes). Mp = 85-88 °C; R_f = 0.65 (60% EtOAc/hexanes); IR (film) 3396, 3031, 2919, 1563, 1453, 1355, 1057, 702 cm^{-1}; (major) ^1H NMR (600 MHz, $CDCl_3$) δ 7.42-7.35 (m, 3H), 7.32 (d, *J* = 7.7 Hz, 2H), 6.13 (dd, *J* = 9.7, 4.0 Hz, 1H), 4.52

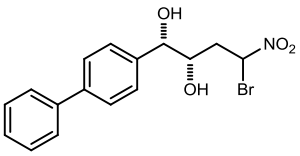
[60] Procedure adapted from Erickson, A.S.; Kornblum, N. *J. Org. Chem.* **1977**, *42*, 3764

(d, *J* = 6.4, 1H), 3.96 (ddd, *J* = 10.7, 6.4, 2.5 Hz, 1H), 2.89 (br s, 1H), 2.57 (br s, 1H), 2.58 (ddd, *J* = 14.6, 10.6, 4.1 Hz, 1H), 2.12 (ddd, *J* = 14.4, 9.8, 2.5 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) ppm 139.6, 129.0, 128.8, 126.5, 78.1, 77.2, 72.6, 39.9; (minor) ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.42-7.35 (m, 3H), 7.29 (d, *J* = 7.7 Hz, 2H), 6.18 (dd, *J* = 10.4, 3.3 Hz, 1H), 4.46 (d, *J* = 6.1 Hz, 1H), 3.74 (ddd, *J* = 10.2, 6.1, 2.6 Hz, 1H), 2.84 (br s, 1H), 2.57 (br s, 1H), 2.46 (ddd, *J* = 14.6, 10.4, 2.7 Hz, 1H), 2.36 (ddd, *J* = 14.6, 10.3, 3.3 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) ppm 139.4, 129.0, 128.9, 126.5, 77.3, 75.6, 72.1, 40.8; HRMS (ESI): Exact mass calcd for $C_{10}H_{12}BrNNaO_4$ $[M+Na]^+$ 311.9847, found 311.9844.



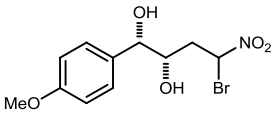
(1*S*,2*S*)-4-Bromo-4-nitro-1-(p-tolyl)butane-1,2-diol (181b). (1*S*,2*S*)-1-(4-Bromophenyl)-4-nitrobutane-1,2-diol (68 mg, 300 μmol) was treated utilizing the general procedure. The title compound was isolated as a white solid (73 mg, 80%) after purification (SiO_2, 5-30% ethyl acetate in hexanes). Mp = 74-76 °C; R_f = 0.65 (60% EtOAc/hexanes); IR (film) 3389, 3027, 2923, 1565, 1356, 1061, 819 cm^{-1}; (major) ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.20 (d, *J* = 8.7 Hz, 2H), 7.18 (d, *J* = 8.7 Hz, 2H), 6.10 (dd, *J* = 9.9, 4.2 Hz, 1H), 4.43 (d, *J* = 6.9 Hz, 1H), 3.92-3.89 (m, 1H), 3.16 (br s, 1H), 2.89 (br s, 1H) 2.48 (ddd, *J* = 14.7, 14.7, 4.1 Hz, 1H), 2.36 (s, 3H), 2.20 (ddd, *J* = 14.4, 12.4, 2.4 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) ppm 138.7, 136.5, 129.7, 126.5, 78.1, 77.3, 72.6, 39.8, 21.1; (minor) ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.19 (d, *J* = 8.1 Hz, 2H), 7.15 (d, *J* = 8.1 Hz, 2H), 6.16 (dd, *J* = 10.5, 3.3 Hz, 1H), 4.36 (d, *J* = 6.5 Hz, 1H), 3.71-3.67 (m, 1H), 3.16 (br s, 1H), 2.85 (br s, 1H) 2.48 (ddd, *J* = 14.9, 10.5, 2.8 Hz, 1H), 2.35 (s, 3H), 2.20

(ddd, *J* = 14.7, 10.3, 3.3 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) ppm δ 138.7, 136.3, 129.7, 126.5, 77.1, 75.3, 72.1, 40.7, 21.1; HRMS (ESI): Exact mass calcd for $C_{11}H_{14}BrNNaO_4$ $[M+Na]^+$ 326.0004, found 325.9990.



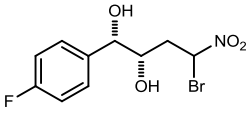
(1*S*,2*S*)-1-([1,1'-Biphenyl]-4-yl)-4-bromo-4-nitrobutane-1,2-diol (181c). (1*S*,2*S*)-1-([1,1'-Biphenyl]-4-yl)-4-nitrobutane-1,2-diol (86 mg, 0.30 mmol) was treated utilizing the general procedure. The title compound was isolated as a white solid (66 mg, 60%) after purification (SiO_2, 5-30% ethyl acetate in hexanes). Mp = 117-120 °C; R_f = 0.62 (60% EtOAc/hexanes); IR (film) 3316, 3029, 2918, 1564, 1352, 1071, 1031, 835 cm^{-1}; (major) ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.62 (d, *J* = 8.1 Hz, 2H), 7.59 (d, *J* = 8.3 Hz, 2H), 7.46 (dd, *J* = 7.5, 7.5 Hz, 2H), 7.42-7.37 (m, 3H), 6.17 (dd, *J* = 9.9, 4.1 Hz, 1H), 4.58 (d, *J* = 6.4 Hz, 1H), 4.01 (ddd, *J* = 10.1, 6.4, 2.3 Hz, 1H), 2.81 (br s, 1H), 2.61 (ddd, *J* = 14.5, 10.6, 4.0 Hz, 1H), 2.53 (br s, 1H), 2.20 (ddd, *J* = 14.9, 9.9, 4.1 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) ppm 141.8, 104.2, 138.5, 128.8127.7, 127.1, 127.1, 126.9, 78.1, 77.1, 72.1, 39.9; (minor) ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.62 (d, *J* = 8.1 Hz, 2H), 7.59 (d, *J* = 8.3 Hz, 2H), 7.46 (dd, *J* = 7.6, 7.6 Hz, 2H), 7.42-7.37 (m, 3H), 6.22 (dd, *J* = 10.5, 3.2 Hz, 1H), 4.53 (d, *J* = 6.1 Hz, 1H), 3.79 (ddd, *J* = 9.9, 6.0, 2.7 Hz, 1H), 2.79 (br s, 1H), 2.54 (ddd, *J* = 14.8, 10.6, 2.7 Hz, 1H), 2.53 (br s, 1H), 2.41 (ddd, *J* = 14.8, 10.4, 3.2 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) ppm 141.8, 140.3, 138.3, 128.8, 127.7, 127.6, 127.1, 126.9, 76.9, 75.6, 72.6, 40.8; HRMS (ESI): Exact mass calcd for $C_{16}H_{16}BrNNaO_4$ $[M]^+$ 388.0160, found 388.0161.

(1*S*,2*S*)-4-Bromo-1-(4-methoxyphenyl)-4-nitrobutane-1,2-diol



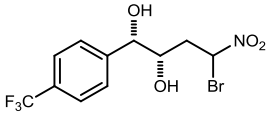
(181d). (1*S*,2*S*)-1-(4-Methoxyphenyl)-4-nitrobutane-1,2-diol (72 mg, 300 µmol) was treated utilizing the general procedure. The title compound was isolated as a pale yellow viscous oil (60 mg, 62%) after purification (SiO_2, 5-30% ethyl acetate in hexanes). R_f = 0.58 (60% EtOAc/hexanes); IR (film) 3402, 3008, 2910, 1564, 1356, 1031, 834 cm^{-1}; (major) ^1H NMR (600 MHz, $CDCl_3$) δ 7.24 (d, *J* = 8.6 Hz, 2H), 6.91 (d, *J* = 8.7 Hz, 2H), 6.10 (dd, *J* = 9.8, 4.1 Hz, 1H), 4.44 (d, *J* = 6.9 Hz, 1H), 3.93-3.90 (m, 1H), 3.82 (s, 3H), 3.00 (br s, 1H), 2.65 (br s, 1H), 2.49 (ddd, *J* = 14.5, 10.5, 4.1 Hz, 1H), 2.08 (ddd, *J* = 14.5, 9.9, 2.5 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) ppm 159.9, 131.5, 127.8, 114.5, 78.1, 77.0, 72.6, 55.3, 39.8; (minor) ^1H NMR (600 MHz, $CDCl_3$) δ 7.20 (d, *J* = 8.6 Hz, 2H), 6.91 (d, *J* = 8.7 Hz, 2H), 6.17 (dd, *J* = 10.6, 3.3 Hz, 1H), 4.38 (d, *J* = 6.6 Hz, 1H), 3.81 (s, 3H), 3.70-3.68 (m, 1H), 3.00 (br s, 1H), 2.61 (br s, 1H), 2.42 (ddd, *J* = 14.8, 10.7, 2.7 Hz, 1H), 2.28 (ddd, *J* = 14.7, 10.4, 3.3 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) ppm 159.9, 131.4, 127.8, 114.3, 76.9, 75.6, 72.1, 55.3, 40.7; HRMS (ESI): Exact mass calcd for $C_{11}H_{14}BrNNaO_5$ $[M+Na]^+$ 341.9953, found 341.9955.

(1*S*,2*S*)-4-Bromo-1-(4-fluorophenyl)-4-nitrobutane-1,2-diol



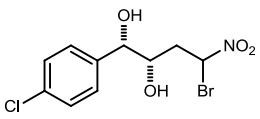
(181f). (1*S*,2*S*)-1-(4-Fluorophenyl)-4-nitrobutane-1,2-diol (30 mg, 130 µmol) was treated utilizing the general procedure. The title compound was isolated as a white solid (29 mg, 72%) after purification (SiO_2, 5-30% ethyl acetate in hexanes). Mp = 104-106 °C; R_f = 0.60 (60% EtOAc/hexanes); IR (film) 3399, 2922, 1547, 1427, 1377, 1225, 1038, 840 cm^{-1}; (major)

^{1}H NMR (600 MHz, $(CD_3)_2CO$) δ 7.47 (dd, *J* = 8.6, 5.6 Hz, 2H), 7.11 (dd, *J* = 8.8, 8.8 Hz, 2H), 6.32 (dd, *J* = 9.2, 4.7 Hz, 1H), 4.82-4.80 (m, 1H), 4.68 (dd, *J* = 5.3, 5.3 Hz, 1H), 4.40-4.39 (m, 1H), 3.94 (ddd, *J* = 10.6, 5.5, 2.6 Hz, 1H), 2.58 (ddd, *J* = 14.9, 10.6, 4.7 Hz, 1H), 2.20 (ddd, *J* = 14.4, 9.1, 2.5 Hz, 1H); ^{13}C NMR (150 MHz, $(CD_3)_2CO$) ppm 162.9 (d, $^{1}J_{CF}$ = 243 Hz), 138.5 (d, $^{4}J_{CF}$ = 3.3 Hz), 129.4 (d, $^{3}J_{CF}$ = 8.2 Hz), 115.2 (d, $^{2}J_{CF}$ = 21.5 Hz), 79.6, 76.1, 75.9, 40.7; (minor) ^{1}H NMR (600 MHz, $(CD_3)_2CO$) δ 7.45 (dd, *J* = 8.6, 5.6 Hz, 2H), 7.11 (dd, *J* = 8.8, 8.8 Hz, 2H), 6.38 (dd, *J* = 10.3, 3.4 Hz, 1H), 4.79-4.77 (m, 1H), 4.64 (dd, *J* = 5.3, 5.3 Hz, 1H), 4.43-4.41 (m, 1H), 3.70 (ddd, *J* = 10.6, 5.5, 2.6 Hz, 1H), 2.53 (ddd, *J* = 14.3, 10.3, 2.9 Hz, 1H), 2.20 (ddd, *J* = 14.2, 10.1, 3.2 Hz, 1H); ^{13}C NMR (150 MHz, $(CD_3)_2CO$) ppm 162.9 (d, $^{1}J_{CF}$ = 243 Hz), 138.3 (d, $^{4}J_{CF}$ = 3.3 Hz), 129.4 (d, $^{3}J_{CF}$ = 8.2 Hz), 115.2 (d, $^{2}J_{CF}$ = 21.5 Hz), 77.3, 73.1, 72.6, 41.2; HRMS (ESI): Exact mass calcd for $C_{10}H_{11}BrFNNaO_4$ $[M+Na]^+$ 329.9753, found 329.9750.

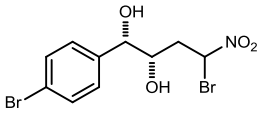


(1*S*,2*S*)-4-Bromo-4-nitro-1-(4-(trifluoromethyl)phenyl)butane-1,2-diol (181g). (1*S*,2*S*)-1-(4-(Trifluoromethyl)phenyl)-4-nitrobutane-1,2-diol (110 mg, 400 μmol) was treated utilizing the general procedure. The title compound was isolated as a white solid (93 mg, 65%) after purification (SiO_2, 5-30% ethyl acetate in hexanes). Mp = 117-120 °C; R_f = 0.58 (60% EtOAc/hexanes); IR (film) 3398, 2921, 1566, 1327, 1166, 1124, 1067, 843 cm^{-1}; (major) ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.67 (d, *J* = 6.3 Hz, 2H), 7.48 (d, *J* = 8.2 Hz, 2H), 6.21 (dd, *J* = 10.2, 3.3 Hz, 1H), 4.62 (d, *J* = 5.8 Hz, 1H), 3.97 (ddd, *J* = 10.1, 5.6, 2.1 Hz, 1H), 2.74 (br s, 2H), 2.63 (ddd, *J* = 14.6, 10.5, 4.1 Hz, 1H), 2.17 (ddd, *J* = 14.5, 9.8, 2.5 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) ppm 143.7, 131.0 (q, $^{2}J_{CF}$ = 32.7

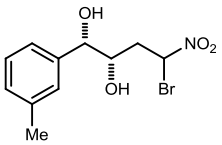
Hz), 126.9, 125.9 (q, $^{3}J_{CF}$ = 3.4 Hz), 123.7 (q, $^{1}J_{CF}$ = 273 Hz), 77.8, 76.5, 72.4, 39.9; (minor) ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.66 (d, *J* = 6.2 Hz, 2H), 7.44 (d, *J* = 8.2 Hz, 2H), 6.15 (dd, *J* = 9.8, 4.1 Hz, 1H), 4.57 (d, *J* = 5.5 Hz, 1H), 3.75 (ddd, *J* = 9.9, 5.4, 2.7 Hz, 1H), 2.74 (br s, 1H), 2.70 (br s, 1H), 2.63 (ddd, *J* = 14.8, 10.3, 2.8 Hz, 1H), 2.50 (ddd, *J* = 14.8, 10.3, 3.3 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) ppm 143.5, 130.9 (q, $^{2}J_{CF}$ = 32.7 Hz), 126.9, 125.9 (q, $^{3}J_{CF}$ = 3.4 Hz), 123.7 (q, $^{1}J_{CF}$ = 273 Hz), 76.3, 75.4, 71.9, 40.8; HRMS (CI): Exact mass calcd for $C_{11}H_{10}BrF_3NO_4$ $[M-H]^+$ 339.9791, found 339.9805.

(1*S*,2*S*)-4-Bromo-1-(4-chlorophenyl)-4-nitrobutane-1,2-diol (181h). 

(1*S*,2*S*)-1-(4-Chlorophenyl)-4-nitrobutane-1,2-diol (80 mg, 327 μmol) was treated according to the general procedure. The title compound was isolated as a white solid (82 mg, 78%) after purification (SiO_2, 10-40% ethyl acetate in hexanes). Mp = 99-101 °C; R_f = 0.62 (60% EtOAc/hexanes); IR (film) 3281, 2943, 1546, 1425, 1370, 1041, 930 cm^{-1};(major) ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40-7.36 (m, 2H), 7.29-7.22 (m, 2H), 6.13 (dd, *J* = 9.7, 4.2 Hz, 1H), 4.50 (d, *J* = 4.3 Hz, 1H), 3.92-3.87 (br m, 1H), 2.89 (br s, 1H), 2.75 (br s, 1H), 2.56 (ddd, *J* = 14.2, 10.6, 4.1 Hz, 1H), 2.14 – 2.08 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm 138.1, 134.7, 129.2, 127.9, 77.9, 76.5, 72.5, 39.9; (minor) ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40-7.36 (m, 2H), 7.29-7.22 (m, 2H), 6.19 (dd, *J* = 10.3, 3.4 Hz, 1H), 4.44 (d, *J* = 2.7 Hz, 1H), 3.71-3.66 (br m, 1H), 2.89 (br s, 1H), 2.75 (br s, 1H), 2.45-2.31 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm 138.1, 134.7, 129.2, 127.9, 76.4, 75.5, 71.9, 40.7; HRMS (ESI): Exact mass calcd for $C_{10}H_{11}BrClNNaO_4$ $[M+Na]^+$ 345.9458, found 345.9454.

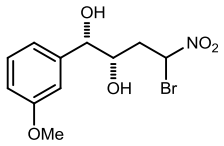
(1*S*,2*S*)-4-Bromo-1-(4-bromophenyl)-4-nitrobutane-1,2-diol (181i). 

(1*S*,2*S*)-1-(4-Bromophenyl)-4-nitrobutane-1,2-diol (90 mg, 310 µmol) was treated utilizing the general procedure. The title compound was isolated as a white solid (77 mg, 67%) after purification (SiO_2, 5-30% ethyl acetate in hexanes). Mp = 92-94 °C; R_f = 0.60 (60% EtOAc/hexanes); IR (film) 3396, 2922, 1563, 1404, 1355, 1069, 825 cm^{-1}; (major) ^1H NMR (600 MHz, $CDCl_3$) δ 7.53 (d, *J* = 8.4 Hz, 2H), 7.23 (d, *J* = 8.4 Hz, 2H), 6.14 (dd, *J* = 9.9, 4.0 Hz, 1H), 4.51 (d, *J* = 6.3 Hz, 1H), 3.92 (ddd, *J* = 10.5, 8.8, 2.5 Hz, 1H), 2.71 (br s, 2H), 2.57 (ddd, *J* = 14.4, 14.4, 4.0 Hz, 1H), 2.20 (ddd, *J* = 14.4, 12.4, 2.5 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) ppm 138.7, 132.1, 128.2, 122.8, 77.9, 76.6, 72.4, 39.9; (minor) ^1H NMR (600 MHz, $CDCl_3$) δ 7.53 (d, *J* = 8.4 Hz, 2H), 7.20 (d, *J* = 8.4 Hz, 2H), 6.20 (dd, *J* = 10.5, 3.2 Hz, 1H), 4.46 (d, *J* = 6.0 Hz, 1H), 3.92 (ddd, *J* = 10.4, 6.1, 2.8 Hz, 1H), 2.57 (ddd, *J* = 14.9, 10.5, 2.8 Hz, 1H), 2.55 (br s, 2H), 2.20 (ddd, *J* = 14.8, 10.5, 3.3 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) ppm 138.5, 132.1, 128.2, 122.8, 76.4, 75.4, 71.9, 40.7; HRMS (CI): Exact mass calcd for $C_{10}H_{10}Br_2NO_3$ $[M\text{-}OH]^+$ 349.9023, found 349.9023.

(1*S*,2*S*)-4-Bromo-4-nitro-1-(m-tolyl)butane-1,2-diol (181j). 

(1*S*,2*S*)-1-(3-Methylphenyl)-4-nitrobutane-1,2-diol (50 mg, 220 µmol) was treated utilizing the general procedure. The title compound was isolated as a white solid (53 mg, 80%) after purification (SiO_2, 5-30% ethyl acetate in hexanes). Mp = 98-100 °C; R_f = 0.67 (60%

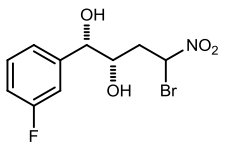
EtOAc/hexanes); IR (film) 3390, 2925, 1550, 1359, 1040, 923 cm^{-1}; (major) ^{1}H NMR (600 MHz, $(CD_3)_2CO$) δ 7.25-7.18 (m, 3H), 7.19 (d, *J* = 7.1 Hz, 1H), 6.31 (dd, *J* = 9.2, 4.6 Hz, 1H), 4.68 (d, *J* = 4.4 Hz, 1H), 4.58 (dd, *J* = 5.6, 5.6 Hz, 1H), 4.34 (d, *J* = 5.1 Hz, 1H), 3.94 (dddd, *J* = 10.7, 5.7, 5.7, 3.6 Hz, 1H), 2.59 (ddd, *J* = 14.6, 10.6, 4.8 Hz, 1H), 2.32 (s, 3H), 2.16 (ddd, *J* = 14.4, 9.2, 2.6 Hz, 1H); ^{13}C NMR (150 MHz, $(CD_3)_2CO$) ppm 142.2, 138.1, 128.8, 128.6, 128.1, 124.6, 79.6, 77.1, 73.2, 40.8, 21.2; (minor) ^{1}H NMR (600 MHz, $(CD_3)_2CO$) δ 7.25-7.18 (m, 3H), 7.19 (d, *J* = 7.1 Hz, 1H), 6.36 (dd, *J* = 10.4, 3.5 Hz, 1H), 4.66 (d, *J* = 4.5 Hz, 1H), 4.55 (dd, *J* = 5.5, 5.5 Hz, 1H), 4.37 (d, *J* = 5.0 Hz, 1H), 3.71 (dddd, *J* = 10.1, 5.5, 5.5, 3.1 Hz, 1H), 2.51 (ddd, *J* = 14.5, 10.5, 3.0 Hz, 1H), 2.33 (ddd, *J* = 14.4, 9.2, 2.6 Hz, 1H), 2.32 (s, 3H); ^{13}C NMR (150 MHz, $(CD_3)_2CO$) ppm 142.0, 138.0, 128.8, 128.6, 128.1, 124.6, 77.2, 76.9, 72.6, 41.4, 21.2; HRMS (CI): Exact mass calcd for $C_{11}H_{14}BrNNaO_4$ $[M+Na]^+$ 326.0004, found 326.0000.



(1*S*,2*S*)-4-Bromo-1-(3-methoxyphenyl)-4-nitrobutane-1,2-diol (181k). (1*S*,2*S*)-1-(3-Methoxyphenyl)-4-nitrobutane-1,2-diol (73 mg, 300 μmol) was treated utilizing the general procedure. The title compound was isolated as a white solid (62 mg, 65%) after purification (SiO_2, 5-30% ethyl acetate in hexanes). Mp = 80-83 °C; R_f = 0.58 (60% EtOAc/hexanes); IR (film) 3390, 2930, 1559, 1255, 1070, 650 cm^{-1}; (major) ^{1}H NMR (600 MHz, $(CD_3)_2CO$) δ 7.27 (dd, *J* = 8.0, 8.0 Hz, 1H), 7.02-6.97 (m, 2H), 6.86 (d, *J* = 8.1 Hz, 1H), 6.33 (dd, *J* = 9.2, 4.7 Hz, 1H), 4.74 (d, *J* = 4.5 Hz, 1H), 4.61 (dd, *J* = 5.3, 5.3 Hz, 1H), 4.34 (d, *J* = 5.1 Hz, 1H), 3.96 (dddd, *J* = 10.7, 5.5, 5.5, 2.6 Hz, 1H), 3.79 (s, 3H), 2.62 (ddd, *J* = 14.9, 10.5, 4.8 Hz, 1H), 2.19 (ddd, *J* = 14.2, 9.0, 2.2 Hz, 1H); ^{13}C

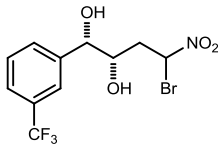
NMR (150 MHz, $(CD_3)_2CO$) ppm 160.4, 143.9, 129.7, 119.7, 113.5, 113.1, 79.6, 76.9, 73.2, 55.2, 40.8; (minor) ^{1}H NMR (600 MHz, $(CD_3)_2CO$) δ 7.27 (dd, *J* = 8.0, 8.0 Hz, 1H), 7.02-6.97 (m, 2H), 6.86 (d, *J* = 8.1 Hz, 1H), 6.39 (dd, *J* = 10.3, 3.4 Hz, 1H), 4.71 (d, *J* = 4.7 Hz, 1H), 4.59 (dd, *J* = 5.2, 5.2 Hz, 1H), 4.38 (d, *J* = 5.1 Hz, 1H), 3.79 (s, 3H), 3.73 (dddd, *J* = 10.1, 5.4, 5.4, 3.1 Hz, 1H), 2.54 (ddd, *J* = 14.5, 10.4, 3.5 Hz, 1H), 2.36 (ddd, *J* = 14.7, 10.0, 3.4 Hz, 1H); ^{13}C NMR (150 MHz, $(CD_3)_2CO$) ppm 160.4, 143.8, 129.7, 119.7, 113.5, 113.1, 77.3, 76.8, 72.7, 55.2, 41.4; HRMS (CI): Exact mass calcd for $C_{11}H_{14}BrNNaO_5$ $[M+Na]^+$ 341.9953, found 341.9965.

(1*S*,2*S*)-4-Bromo-1-(3-fluorophenyl)-4-nitrobutane-1,2-diol (181l).



(1*S*,2*S*)-1-(3-Chlorophenyl)-4-nitrobutane-1,2-diol (36 mg, 156 μmol) was treated utilizing the general procedure. The title compound was isolated as a white solid (33 mg, 63%) after purification (SiO_2, 5-30% ethyl acetate in hexanes). Mp = 96-98 °C; R_f = 0.59 (60% EtOAc/hexanes); IR (film) 3401, 2929, 1555, 1355, 1060, 823 cm^{-1}; (major) ^{1}H NMR (600 MHz, $(CD_3)_2CO$) δ 7.37 (dd, *J* = 7.8, 6.1 Hz, 1H), 7.24 (d, *J* = 8.1 Hz, 1H), 7.23-7.19 (m, 1H), 7.05-7.02 (m, 1H), 6.33 (dd, *J* = 9.1, 4.7 Hz, 1H), 4.89 (d, *J* = 4.8 Hz, 1H), 4.72 (d, *J* = 5.3 Hz, 1H), 4.42 (d, *J* = 5.5 Hz, 1H), 3.99-3.95 (br m, 1H), 2.64-2.56 (m, 1H), 2.36 (ddd, *J* = 13.8, 10.0, 3.3 Hz, 1H); ^{13}C NMR (150 MHz, $(CD_3)_2CO$) ppm 163.1 (d, $^1J_{CF}$ = 243 Hz), 145.5 (d, $^3J_{CF}$ = 6.7 Hz), 130.4 (d, $^3J_{CF}$ = 8.0 Hz), 123.4, 114.7 (d, $^2J_{CF}$ = 21.5 Hz), 114.1 (d, $^2J_{CF}$ = 21.9 Hz), 79.6, 77.3, 68.9, 40.9; (minor) ^{1}H NMR (600 MHz, $(CD_3)_2CO$) δ 7.38 (dd, *J* = 7.8, 6.1 Hz, 1H), 7.26 (d, *J* = 7.9 Hz, 1H), 7.23-7.19 (m, 1H), 7.05-7.02 (m, 1H), 6.39 (dd, *J* = 10.2, 3.4 Hz, 1H), 4.86 (d, *J* = 4.8 Hz, 1H), 4.67 (d, *J* =

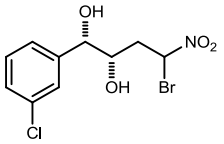
5.2 Hz, 1H), 4.45 (d, *J* = 5.5 Hz, 1H), 3.76-3.72 (br m, 1H), 2.64-2.56 (m, 1H), 2.25 (ddd, *J* = 13.8, 10.0, 3.3 Hz, 1H); ^{13}C NMR (150 MHz, $(CD_3)_2CO$) ppm 163.1 (d, $^1J_{CF}$ = 243 Hz), 145.3 (d, $^3J_{CF}$ = 6.6 Hz), 130.4 (d, $^3J_{CF}$ = 8.0 Hz), 123.4, 114.7 (d, $^2J_{CF}$ = 21.5 Hz), 114.1 (d, $^2J_{CF}$ = 21.9 Hz), 75.9, 72.8, 69.0, 41.3; HRMS (CI): Exact mass calcd for $C_{10}H_{10}BrFNO_4$ $[M-H]^+$ 305.9772, found 345.9765.



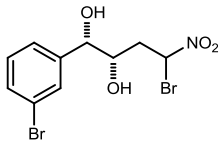
(1*S*,2*S*)-4-Bromo-4-nitro-1-(3-(trifluoromethyl)phenyl)butane-1,2-diol (181m). (1*S*,2*S*)-1-(3-(Trifluoromethyl)phenyl)-4-nitrobutane-1,2-diol (100 mg, 360 μmol) was treated utilizing the general procedure. The title compound was isolated as a white solid (81 mg, 63%) after purification (SiO_2, 5-30% ethyl acetate in hexanes). Mp = 66-68 °C; R_f = 0.58 (60% EtOAc/hexanes); IR (film) 3401, 2921, 1565, 1329, 1166, 1125, 1072, 703 cm^{-1}; (major) ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.64-7.60 (m, 2H), 7.56-7.51 (m, 2H), 6.33 (dd, *J* = 9.8, 4.1 Hz, 1H), 4.64 (d, *J* = 5.7 Hz, 1H), 3.96 (ddd, *J* = 10.5, 5.7, 2.4 Hz, 1H), 2.65 (ddd, *J* = 14.6, 10.5, 4.1 Hz, 1H), 2.62 (br s, 2H), 2.18 (ddd, *J* = 14.5, 9.8, 2.5 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) ppm 140.8, 131.4 (q, $^2J_{CF}$ = 32.4 Hz), 129.9, 129.5, 125.6 (q, $^3J_{CF}$ = 3.7 Hz), 123.9 (q, $^1J_{CF}$ = 273 Hz), 123.2 (q, $^3J_{CF}$ = 3.7 Hz), 77.8, 76.4, 72.4, 40.0; (minor) ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.64-7.60 (m, 2H), 7.56-7.51 (m, 2H), 6.21 (dd, *J* = 10.3, 3.4 Hz, 1H), 4.59 (d, *J* = 5.9 Hz, 1H), 3.77 (ddd, *J* = 10.2, 5.4, 2.9 Hz, 1H), 2.62 (br s, 2H), 2.51 (ddd, *J* = 14.9, 10.3, 3.0 Hz, 1H), 2.45 (ddd, *J* = 14.8, 10.4, 3.5 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) ppm 140.7, 131.0 (q, $^2J_{CF}$ = 32.4 Hz), 129.8, 129.5, 125.6 (q, $^3J_{CF}$ = 3.7 Hz), 123.9 (q, $^1J_{CF}$ = 273 Hz), 123.2 (q, $^3J_{CF}$ = 3.7 Hz),

76.3, 75.3, 71.9, 40.8; HRMS (CI): Exact mass calcd for $C_{11}H_{10}BrF_3NO_4$ $[M-H]^+$ 355.9740, found 355.9726.

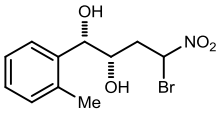
(1*S*,2*S*)-4-Bromo-1-(3-chlorophenyl)-4-nitrobutane-1,2-diol



(181n). (1*S*,2*S*)-1-(3-Chlorophenyl)-4-nitrobutane-1,2-diol (74 mg, 300 μmol) was treated utilizing the general procedure. The title compound was isolated as a white solid (71 mg, 73%) after purification (SiO_2, 5-30% ethyl acetate in hexanes). Mp = 98-100 °C; R_f = 0.61 (60% EtOAc/hexanes); IR (film) 3401, 2929, 1555, 1355, 1060, 823 cm^{-1}; (major) ^1H NMR (600 MHz, $(CD_3)_2CO$) δ 7.48 (s, 1H), 7.40-7.35 (m, 2H), 7.31 (dd, *J* = 1.6, 1.6 Hz, 1H), 6.34 (dd, *J* = 9.1, 4.7 Hz, 1H), 4.90 (d, *J* = 4.8 Hz, 1H), 4.72 (dd, *J* = 4.7, 4.7 Hz, 1H), 4.43 (d, *J* = 5.7 Hz, 1H), 3.99 (dddd, *J* = 10.5, 5.2, 5.2, 2.6 Hz, 1H), 2.64 (ddd, *J* = 15.1, 10.6, 4.7 Hz, 1H), 2.28 (ddd, *J* = 14.4, 9.0, 2.5 Hz, 1H); ^{13}C NMR (150 MHz, $(CD_3)_2CO$) ppm 144.9, 134.0, 130.2, 127.9, 127.4, 125.9, 79.5, 75.8, 72.8, 40.6; (minor) ^1H NMR (600 MHz, $(CD_3)_2CO$) δ 7.47 (s, 1H), 7.40-7.35 (m, 2H), 7.30-7.29 (m, 1H), 6.41 (dd, *J* = 10.2, 3.4 Hz, 1H), 4.88 (d, *J* = 4.9 Hz, 1H), 4.69 (dd, *J* = 4.7, 4.7 Hz, 1H), 4.46 (d, *J* = 5.6 Hz, 1H), 3.79 (dddd, *J* = 10.1, 5.2, 5.2, 3.1 Hz, 1H), 2.61 (ddd, *J* = 14.8, 10.2, 3.4 Hz, 1H), 2.38 (ddd, *J* = 14.8, 10.2, 3.4 Hz, 1H); ^{13}C NMR (150 MHz, $(CD_3)_2CO$) ppm 144.8, 134.0, 130.2, 127.9, 127.4, 125.9, 77.2, 75.6, 72.2, 41.2; HRMS (CI): Exact mass calcd for $C_{10}H_{11}BrClNNaO_4$ $[M+Na]^+$ 345.9458, found 345.9460.

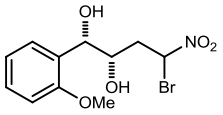
(1*S*,2*S*)-4-Bromo-1-(3-bromophenyl)-4-nitrobutane-1,2-diol (181o). 

(1*S*,2*S*)-1-(3-Bromophenyl)-4-nitrobutane-1,2-diol (87 mg, 300 µmol) was treated utilizing the general procedure. The title compound was isolated as a white solid (83 mg, 75%) after purification (SiO_2, 5-30% ethyl acetate in hexanes). Mp = 82-85 °C; R_f = 0.61 (60% EtOAc/hexanes); IR (film) 3405, 2921, 1558, 1350, 1030, 723 cm^{-1}; (major) ^1H NMR (600 MHz, $(CD_3)_2CO$) δ 7.63 (s, 1H), 7.49-7.43 (m, 2H), 7.31 (dd, *J* = 7.8, 7.8 Hz, 1H), 6.42 (dd, *J* = 10.2, 3.5 Hz, 1H), 4.88 (d, *J* = 4.9 Hz, 1H), 4.69 (dd, *J* = 5.1, 5.1 Hz, 1H), 4.46 (d, *J* = 5.8 Hz, 1H), 3.76 (dddd, *J* = 10.1, 5.7, 5.7, 3.1 Hz, 1H), 2.65 (ddd, *J* = 14.9, 10.6, 4.7 Hz, 1H), 2.40 (ddd, *J* = 14.2, 10.0, 3.3 Hz, 1H); ^{13}C NMR (150 MHz, $(CD_3)_2CO$) ppm 145.2, 130.9, 130.6, 130.4, 126.4, 122.4, 79.6, 77.3, 72.3, 41.3; (minor) ^1H NMR (600 MHz, $(CD_3)_2CO$) δ 7.63 (s, 1H), 7.49-7.43 (m, 2H), 7.31 (dd, *J* = 7.8, 7.8 Hz, 1H), 6.35 (dd, *J* = 9.0, 4.7 Hz, 1H), 4.80 (d, *J* = 5.0 Hz, 1H), 4.73 (dd, *J* = 5.1, 5.1 Hz, 1H), 4.43 (d, *J* = 5.8 Hz, 1H), 4.00 (dddd, *J* = 10.6, 5.7, 5.7, 2.6 Hz, 1H), 2.62 (ddd, *J* = 14.9, 10.6, 4.7 Hz, 1H), 2.29 (ddd, *J* = 14.4, 9.1, 2.5 Hz, 1H); ^{13}C NMR (150 MHz, $(CD_3)_2CO$) ppm 145.4, 130.9, 130.6, 126.4, 122.4, 75.8, 75.6, 72.9, 40.7.

(1*S*,2*S*)-4-Bromo-4-nitro-1-(o-tolyl)butane-1,2-diol (181p). 

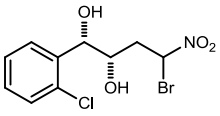
(1*S*,2*S*)-1-(2-Methylphenyl)-4-nitrobutane-1,2-diol (79 mg, 350 µmol) was treated utilizing the general procedure. The title compound was isolated as a clear viscous oil (72 mg, 68%) after purification (SiO_2, 5-30% ethyl acetate in hexanes). R_f = 0.61 (60% EtOAc/hexanes); IR (film) 3398, 3026, 2927, 1565, 1356, 1055, 760 cm^{-1}; (major) ^1H NMR (600 MHz,

$CDCl_3$) δ 7.37 (dd, J = 6.5, 2.5 Hz, 1H), 7.28-7.25 (m, 2H), 7.20 (dd, *J* = 5.3, 5.3 Hz, 1H), 6.13 (dd, *J* = 9.9, 4.1 Hz, 1H), 4.79 (d, *J* = 5.9 Hz, 1H), 3.96 (dddd, *J* = 10.2, 5.9, 5.9, 2.0 Hz, 1H), 3.07 (br s, 1H), 2.80 (br s, 1H), 2.60 (ddd, *J* = 14.6, 10.6, 4.0 Hz, 1H), 2.35 (s, 3H), 2.14 (ddd, *J* = 14.4, 9.9, 2.3 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) ppm 137.7, 135.1, 131.0, 128.4, 126.6, 126.0, 78.2, 73.2, 71.9, 39.9, 19.3; (minor) ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.31 (dd, *J* = 4.6, 4.6 Hz, 1H), 7.28-7.25 (m, 2H), 7.20 (dd, *J* = 5.3, 5.3 Hz, 1H), 6.19 (dd, *J* = 10.4, 3.2 Hz, 1H), 4.73 (d, *J* = 5.8 Hz, 1H), 3.76 (dddd, *J* = 9.9, 5.7, 5.7, 2.6 Hz, 1H), 3.07 (br s, 1H), 2.76 (br s, 1H), 2.49 (ddd, *J* = 14.9, 10.4, 2.8 Hz, 1H), 2.14 (ddd, *J* = 14.4, 9.9, 2.3 Hz, 1H), 2.35 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) ppm 137.6, 135.1, 131.0, 128.4, 126.6, 125.9, 75.6, 73.1, 71.3, 40.8; HRMS (CI): Exact mass calcd for $C_{11}H_{14}BrNNaO_4$ $[M+Na]^+$ 326.0004, found 325.9991.



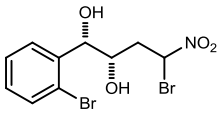
(1*S*,2*S*)-4-Bromo-1-(2-methoxyphenyl)-4-nitrobutane-1,2-diol (181q). (1*S*,2*S*)-1-(2-Methoxyphenyl)-4-nitrobutane-1,2-diol (70 mg, 290 μmol) was treated utilizing the general procedure. The title compound was isolated as a clear viscous oil (52 mg, 56%) after purification (SiO_2, 5-30% ethyl acetate in hexanes). R_f = 0.50 (60% EtOAc/hexanes); IR (film) 3399, 3010, 2936, 1563, 1244, 1026, 757 cm^{-1}; (major) ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.32 (ddd, *J* = 8.0, 8.0, 1.7 Hz, 1H), 7.28 (dd, *J* = 7.5, 1.5 Hz, 1H), 7.01-6.98 (m, 1H), 6.92 (d, *J* = 8.2 Hz, 1H), 6.13 (dd, *J* = 9.3, 4.1 Hz, 1H), 4.73 (d, *J* = 6.0 Hz, 1H), 4.05 (ddd, *J* = 9.6, 6.2, 2.1 Hz, 1H), 3.86 (s, 3H), 2.98 (br s, 2H), 2.59 (ddd, *J* = 14.4, 10.3, 4.1 Hz, 1H), 2.40 (ddd, *J* = 14.4, 9.8, 2.6 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) ppm 156.4, 129.6, 128.0, 127.3, 121.2, 110.8, 78.3, 73.8, 71.3, 55.4, 40.1;

(minor) ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.32 (ddd, *J* = 8.0, 8.0, 1.7 Hz, 1H), 7.28 (dd, *J* = 7.9, 1.9 Hz, 1H), 7.01-6.98 (m, 1H), 6.91 (d, *J* = 8.1 Hz, 1H), 6.19 (dd, *J* = 10.7, 3.3 Hz, 1H), 4.66 (d, *J* = 5.9 Hz, 1H), 3.86 – 3.82 (m, 1H), 3.84 (s, 3H), 3.09 (br s, 2H), 2.49 (ddd, *J* = 14.7, 10.7, 2.9 Hz, 1H), 2.34 (ddd, *J* = 14.9, 9.9, 3.1 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) ppm 137.6, 135.1, 131.0, 128.4, 126.6, 125.9, 75.6, 73.1, 71.3, 40.8; HRMS (ESI): Exact mass calcd for $C_{11}H_{14}BrNNaO_5$ $[M+Na]^+$ 341.9953, found 341.9950.



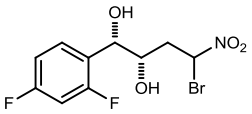
(1*S*,2*S*)-4-Bromo-1-(2-chlorophenyl)-4-nitrobutane-1,2-diol (181r). (1*S*,2*S*)-1-(2-Chlorophenyl)-4-nitrobutane-1,2-diol (74 mg, 300 µmol) was treated utilizing the general procedure. The title compound was isolated as a clear oil (72 mg, 65%) after purification (SiO_2, 5-30% ethyl acetate in hexanes). R_f = 0.61 (60% EtOAc/hexanes); IR (film) 3400, 2928, 1564, 1350, 1056, 1018, 749 cm^{-1}; (major) ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50-7.26 (m, 4H), 6.14 (dd, *J* = 9.9, 4.0 Hz, 1H), 5.06-5.03 (br m, 1H), 4.08-4.04 (br m, 1H), 2.85 (br s, 1H), 2.71 (d, *J* = 4.6 Hz, 1H), 2.56 (ddd, *J* = 9.3, 9.3, 4.3 Hz, 1H), 2.26 (ddd, *J* = 14.3, 9.8, 2.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm 137.4, 132.2, 129.8, 129.6, 127.8, 127.4, 78.1, 72.6, 71.4, 40.1; (minor) ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50-7.26 (m, 4H), 6.20 (dd, *J* = 9.1, 4.5 Hz, 1H), 5.01-4.99 (br m, 1H), 3.84-3.79 (m, 1H), 2.86-2.67 (m (overlapping), 4H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm 137.3, 132.2, 129.8, 127.8, 127.4, 75.6, 72.5, 71.0, 40.8; HRMS (ESI): Exact mass calcd for $C_{10}H_{11}BrClNNaO_4$ $[M+Na]^+$ 345.9458, found 345.9467.

(1*S*,2*S*)-4-Bromo-1-(2-bromophenyl)-4-nitrobutane-1,2-diol



(181s). (1*S*,2*S*)-1-(2-Bromophenyl)-4-nitrobutane-1,2-diol (87 mg, 300 µmol) was treated utilizing the general procedure. The title compound was isolated as a clear oil (72 mg, 65%) after purification (SiO_2, 5-30% ethyl acetate in hexanes). R_f = 0.61 (60% EtOAc/hexanes); IR (film) 3401, 2924, 1564, 1354, 1057, 1022, 753 cm^{-1}; (major) ^1H NMR (600 MHz, $CDCl_3$) δ 7.58 (d, *J* = 7.9 Hz, 1H), 7.49 (dd, *J* = 7.7, 1.5 Hz, 1H), 7.38 (dd, *J* = 8.3, 8.3 Hz, 1H), 7.23-7.19 (m, 1H), 6.15 (dd, *J* = 9.8, 3.8 Hz, 1H), 5.05 (d, *J* = 4.3 Hz, 1H), 4.09 (ddd, *J* = 10.7, 4.1, 5.9 Hz, 1H), 2.83 (ddd, *J* = 14.5, 10.7, 4.1 Hz, 1H), 2.67 (br s, 1H), 2.51 (br s, 1H), 2.31 (ddd, *J* = 14.5, 10.0, 2.5 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) ppm 139.1, 133.1, 129.9, 128.0, 127.9, 122.3, 78.2, 74.6, 71.4, 40.3; (minor) ^1H NMR (600 MHz, $CDCl_3$) δ 7.57 (d, *J* = 7.9 Hz, 1H), 7.44 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.37 (dd, *J* = 8.3, 8.3 Hz, 1H), 7.23-7.19 (m, 1H), 6.22 (dd, *J* = 9.8, 3.8 Hz, 1H), 4.99 (d, *J* = 4.7 Hz, 1H), 3.85 (ddd, *J* = 9.8, 4.1, 3.8 Hz, 1H), 2.67 (br s, 1H), 2.65-2.57 (m, 2H), 2.51 (br s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) ppm 138.8, 133.1, 129.9, 128.0, 127.9, 122.4, 75.6, 74.6, 71.0, 40.9; HRMS (ESI): Exact mass calcd for $C_{10}H_{11}Br_2NNaO_4$ $[M+Na]^+$ 389.8952, found 389.8953.

(1*S*,2*S*)-4-Bromo-1-(2,4-difluorophenyl)-4-nitrobutane-1,2-diol

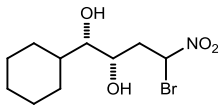


(181t). (1*S*,2*S*)-1-(2,4-Difluorophenyl)-4-nitrobutane-1,2-diol (99 mg, 400 µmol) was treated utilizing the general procedure. The title compound was isolated as a clear oil (72 mg, 63%) after purification (SiO_2, 5-30% ethyl acetate in hexanes). R_f = 0.60 (60% EtOAc/hexanes); IR

(film) 3398, 2922, 1565, 1503, 1356, 1271, 1094, 965 cm^{-1}; (major) ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.45 (ddd, *J* = 8.4, 8.4, 6.4 Hz, 1H), 6.97-6.93 (m, 1H), 6.87-6.83 (m, 1H), 6.16 (dd, *J* = 10.0, 4.0 Hz, 1H), 4.87 (d, *J* = 6.0 Hz, 1H), 4.00-3.96 (m, 1H), 2.72 (br s, 1H), 2.66 (ddd, *J* = 14.6, 10.6, 4.1 Hz, 1H), 2.58 (br s, 1H), 2.18 (ddd, *J* = 14.4, 10.0, 2.3 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) ppm 163.0 (dd, $^{1}J_{CF}$ = 251, 12.0 Hz), 159.8 (dd, $^{1}J_{CF}$ = 251, 12.0 Hz), 128.8 (dd, $^{3}J_{CF}$ = 9.5, 5.7 Hz), 122.9 (dd, $^{3}J_{CF}$ = 13.8, 3.8 Hz), 112.1 (dd, $^{2}J_{CF}$ = 21.4, 4.7 Hz), 104.2 (dd, $^{2}J_{CF}$ = 25.6, 25.6 Hz), 77.9, 71.9, 70.4, 39.8; (minor) ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.40 (ddd, *J* = 8.4, 8.4, 6.6 Hz, 1H), 6.97-6.93 (m, 1H), 6.87-6.83 (m, 1H), 6.22 (dd, *J* = 10.4, 3.2 Hz, 1H), 4.81 (d, *J* = 6.0 Hz, 1H), 3.75 (ddd, *J* = 9.4, 6.1, 2.5 Hz, 1H), 2.77 (br s, 1H), 2.58 (br s, 1H), 2.50 (ddd, *J* = 14.8, 10.3, 2.6 Hz, 1H), 2.43 (ddd, *J* = 13.7, 10.3, 3.2 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) ppm 163.0 (dd, $^{1}J_{CF}$ = 251, 12.0 Hz), 159.8 (dd, $^{1}J_{CF}$ = 251, 12.0 Hz), 128.8 (dd, $^{3}J_{CF}$ = 9.5, 5.7 Hz), 122.8 (dd, $^{3}J_{CF}$ = 13.8, 3.8 Hz), 112.0 (dd, $^{2}J_{CF}$ = 21.4, 4.7 Hz), 104.1 (dd, $^{2}J_{CF}$ = 25.6, 25.6 Hz), 75.3, 71.5, 70.2, 40.5; HRMS (CI): Exact mass calcd for $C_{10}H_9BrF_2NO_4$ $[M-H]^+$ 323.9678, found 323.9680.

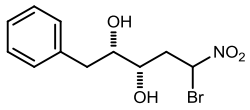
(1*S*,2*S*)-4-Bromo-1-(2,4-dimethylphenyl)-4-nitrobutane-1,2-diol (181u). (1*S*,2*S*)-1-(2,4-Dimethylphenyl)-4-nitrobutane-1,2-diol (140 mg, 585 µmol) was treated utilizing the general procedure. The title compound was isolated as a white solid (132 mg, 71%) after purification (SiO_2, 10-40% ethyl acetate in hexanes). Mp = 95-98 °C; R_f = 0.58 (60% EtOAc/hexanes); IR (film) 3394, 2924, 1565, 1355, 1054, 823 cm^{-1}; (major) ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.20 (d, *J* = 7.8 Hz, 1H), 7.05 (d, *J* = 8.3 Hz, 1H), 7.00 (br s, 1H),

6.09 (dd, *J* = 9.9, 4.0 Hz, 1H), 4.69 (d, *J* = 6.6 Hz, 1H), 3.76 (ddd, *J* = 10.3, 6.6, 1.9 Hz, 1H), 3.41 (br s, 1H), 3.40 (br s, 1H), 2.49 (ddd, *J* = 14.6, 10.7, 4.1 Hz, 1H), 2.32 (s, 3H), 2.28 (s, 3H), 2.06 (ddd, *J* = 16.6, 12.2, 2.3 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) ppm 138.1, 135.0, 134.6, 131.7, 127.3, 126.0, 78.2, 73.2, 72.1, 39.7, 20.9, 19.2; (minor) ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.13 (d, *J* = 7.8 Hz, 1H), 7.03 (d, *J* = 8.6 Hz, 1H), 7.00 (br s, 1H), 6.15 (dd, *J* = 10.5, 3.3 Hz, 1H), 4.63 (d, *J* = 6.3 Hz, 1H), 3.72 (ddd, *J* = 10.4, 6.3, 2.5 Hz, 1H), 3.41 (br s, 1H), 3.06 (br s, 1H), 2.41 (ddd, *J* = 14.8, 10.5, 2.7 Hz, 1H), 2.34-2.24 (m, 1H), 2.31 (s, 3H), 2.27 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) ppm 138.1, 135.0, 134.4, 131.7, 127.3, 125.9, 75.7, 73.2, 71.4, 40.6, 20.9, 19.2; HRMS (EI): Exact mass calcd for $C_{12}H_{15}BrNO_3$ $[M\text{-}OH]^+$ 300.0230, found 300.0226.



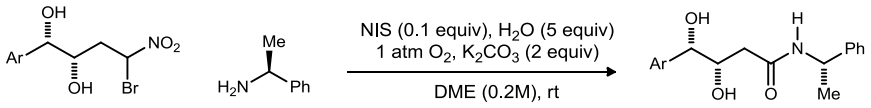
(1*S*,2*S*)-4-Bromo-1-cyclohexyl-4-nitrobutane-1,2-diol (181v). (1*S*,2*S*)-1-Cyclohexyl-4-nitrobutane-1,2-diol (92 mg, 420 μmol) was treated utilizing the general procedure. The title compound was isolated as a white solid (55 mg, 58%) after purification (SiO_2, 5-30% ethyl acetate in hexanes). Mp = 53-55 °C; R_f = 0.62 (60% EtOAc/hexanes); IR (film) 3330, 2923, 2851, 1550, 1343, 1030, 723 cm^{-1}; (major) ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.19 (dd, *J* = 9.9, 3.2 Hz, 1H), 3.94-3.88 (m, 1H), 3.22-3.20 (m, 1H), 2.69 (ddd, *J* = 14.6, 10.5, 4.1 Hz, 1H), 2.31 (ddd, *J* = 14.4, 9.9, 2.5 Hz, 1H), 2.32 (br s, 1H), 1.92 (br s, 1H), 1.81-1.64 (m, 4H), 1.53-1.45 (m, 1H), 1.31-1.01 (m, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) ppm 78.5, 78.0, 68.1, 41.5, 39.9, 29.5, 27.7, 26.2, 25.9, 25.8; ^{1}H NMR (600 MHz, $CDCl_3$) d_1 (minor) δ 6.24 (dd, *J* = 10.5, 3.2 Hz, 1H), 3.69-3.63 (m, 1H), 3.15-3.13 (m, 1H), 2.64 (ddd, *J* = 14.7, 10.6, 2.7 Hz, 1H), 2.47 (ddd, *J* = 14.6, 10.5, 3.4 Hz, 1H), 2.32

(br s, 1H), 1.88 (br s, 1H), 1.81-1.64 (m, 4H), 1.53-1.45 (m, 1H), 1.31-1.01 (m, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) ppm 78.0, 75.9, 67.9, 42.1, 39.9, 29.5, 27.6, 26.2, 25.9, 25.8.

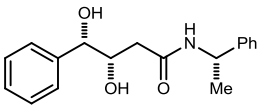


(2*S*,3*S*)-5-Bromo-5-nitro-1-phenylpentane-2,3-diol (181w). (2*S*,3*S*)-5-Nitro-1-phenylpentane-2,3-diol (68 mg, 300 μmol) was treated utilizing the general procedure. The title compound was isolated as a white solid (55 mg, 60%) after purification (SiO_2, 5-30% ethyl acetate in hexanes). Mp = 97-99 °C; R_f = 0.65 (60% EtOAc/hexanes); IR (film) 3337, 3026, 2918, 2851, 1550, 1348, 1028, 696 cm^{-1}; (major) ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.37-7.33 (m, 2H), 7.29-7.27 (m, 1H), 7.22 (d, *J* = 7.2 Hz, 2H), 6.20 (dd, *J* = 9.8, 4.2 Hz, 1H), 3.82-3.78 (m, 1H), 3.76-3.74 (m, 1H), 2.92 (dd, *J* = 13.7, 4.2 Hz, 1H), 2.76 (dd, *J* = 13.7, 9.1 Hz, 1H), 2.75-2.69 (m, 1H), 2.39 (ddd, *J* = 14.2, 9.8, 2.6 Hz, 1H), 2.44 (br s, 1H), 1.94 (br s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) ppm 136.7, 129.3, 128.9, 127.1, 78.2, 74.3, 70.4, 41.2, 40.1; (minor) ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.37-7.33 (m, 2H), 7.29-7.27 (m, 1H), 7.20 (d, *J* = 7.2 Hz, 2H), 6.26 (dd, *J* = 10.5, 3.1 Hz, 1H), 3.71-3.68 (m, 1H), 3.57-3.53 (m, 1H), 2.88 (dd, *J* = 13.7, 4.2 Hz, 1H), 2.80 (dd, *J* = 13.7, 9.2 Hz, 1H), 2.75-2.69 (m, 1H), 2.51 (ddd, *J* = 14.6, 10.4, 3.2 Hz, 1H), 2.42 (br s, 1H), 1.92 (br s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) ppm 136.7, 129.3, 128.9, 127.1, 75.6, 74.2, 70.2, 42.0, 40.0; HRMS (CI): Exact mass calcd for $C_{11}H_{15}BrNO_4$ $[M+H]^+$ 304.0179, found 304.0180.

UmAS with γ,δ-Dihydroxy-α-Bromonitroalkanes

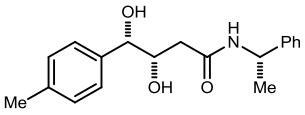


General Procedure. To a 10 mL round-bottom flask containing a solution of the α-bromonitroalkane in dimethoxymethane (200 mM) and water (5 equiv) was added (*S*)-(–)-α-methylbenzyl amine (1.2 equiv, 98% ee) at rt followed by *N*-Iodosuccinimide (0.1 equiv) and potassium carbonate (2 equiv). The flask was fitted with an oxygen balloon. The reaction was stirred at rt until the reaction was determined complete by TLC (EtOAc/hexanes, 6-12 h). The resulting mixture was quenched with 1 M hydrochloric acid solution and diluted with dichloromethane. The biphasic solution was transferred to a separatory funnel, the layers were separated. The aqueous phase was extracted with dichloromethane. The combined organic extracts were further washed with saturated sodium thiosulfate solution. The organic extracts were then dried, filtered, and concentrated to give the crude products which were purified by flash column chromatography on silica gel.

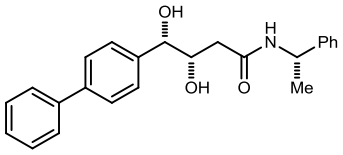


(3*S*,4*S*)-3,4-Dihydroxy-4-phenyl-*N*-((*S*)-1-phenylethyl)butanamide (183a). (1*S*,2*S*)-4-Bromo-4-nitro-1-phenylbutane-1,2-diol (32 mg, 110 μmol) was treated utilizing

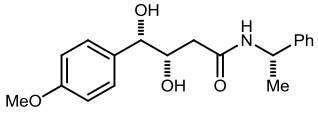
the general procedure. The title compound was isolated as a pale yellow viscous oil (17 mg, 50%) after purification (SiO_2, 20-80% ethyl acetate in hexanes); R_f = 0.40 (85% EtOAc/hexanes); IR (film) 3312, 3063, 2926, 1642, 1547, 1509, 1217, 1074, 1026, 700 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.36-7.26 (m, 10H), 5.98 (d, *J* = 7.3 Hz, 1H), 5.11 (dq, *J* = 14.3, 7.0 Hz, 1H), 4.49 (d, *J* = 7.1 Hz, 1H), 4.23 (br s, 1H), 4.05-4.02 (br m, 1H), 3.16 (br s, 1H), 2.25 (dd, *J* = 15.6, 3.8 Hz, 1H), 2.21 (dd, *J* = 15.7, 7.7 Hz, 1H), 1.46 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) ppm 170.9, 142.8, 140.1, 128.8, 128.6, 128.3, 127.6, 126.9, 126.1, 77.1, 73.1, 48.9, 38.1, 21.7.



(3*S*,4*S*)-3,4-Dihydroxy-*N*-((*S*)-1-phenylethyl)-4-(*p*-tolyl)butanamide (183b). (1*S*,2*S*)-4-Bromo-1-(4-chlorophenyl)-4-nitrobutane-1,2-diol (68 mg, 224 μmol) was treated utilizing the general procedure. The title compound was isolated as a clear oil (40 mg, 58%) after purification (SiO_2, 20-80% ethyl acetate in hexanes). R_f = 0.48 (85% EtOAc/hexanes); IR (film) 3305, 3063, 2925, 1642, 1548, 1065, 700 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.35 (dd, *J* = 7.4, 7.4 Hz, 2H), 7.30-7.27 (m, 3H), 7.18 (d, *J* = 7.9 Hz, 2H), 7.13 (d, *J* = 7.7 Hz, 2H), 6.25 (d, *J* = 7.7 Hz, 1H), 5.09 (dq, *J* = 14.1, 7.0 Hz, 1H), 4.44 (d, *J* = 7.0 Hz, 1H), 4.32 (br s, 1H), 4.02 (ddd, *J* = 7.7, 7.7, 4.0 Hz, 1H), 3.36 (br s, 1H), 2.34 (s, 3H), 2.25-2.18 (m, 2H), 1.45 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) ppm 170.9, 142.9, 137.9, 137.1, 129.2, 128.7, 127.4, 126.8, 126.0, 76.9, 73.0, 48.8, 38.3, 21.7, 21.1; HRMS (ESI): Exact mass calcd for $C_{19}H_{23}NNaO_3$ $[M]^+$ 336.1576, found 336.1563.

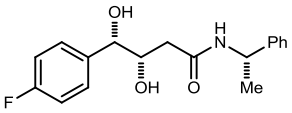


(3*S*,4*S*)-4-([1,1'-Biphenyl]-4-yl)-3,4-dihydroxy-*N*-((*S*)-1-phenylethyl)butanamide (183c). (1*S*,2*S*)-1-([1,1'-Biphenyl]-4-yl)-4-bromo-4-nitrobutane-1,2-diol (50 mg, 137 µmol) was treated utilizing the general procedure. The title compound was isolated as a white solid (28 mg, 56%) after purification (SiO_2, 20-80% ethyl acetate in hexanes). Mp = 99-101 °C; R_f = 0.39 (85% EtOAc/hexanes); IR (film) 3326, 3061, 2927, 1645, 1546, 1075 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.56 (d, *J* = 8.3 Hz, 2H), 7.55 (d, *J* = 8.3 Hz, 2H), 7.43 (dd, *J* = 8.3 Hz, 2H), 7.38-7.33 (m, 5H), 7.31-7.26 (m, 3H), 6.03 (d, *J* = 7.7 Hz, 1H), 5.12 (dq, *J* = 14.4, 7.1 Hz, 1H), 4.54 (d, *J* = 7.1 Hz, 1H), 4.34 (br s, 1H), 4.05 (ddd, *J* = 7.7, 7.7, 3.7 Hz, 1H), 3.24 (br s, 1H), 2.31 (dd, *J* = 15.5, 3.5 Hz, 1H), 2.26 (dd, *J* = 15.5, 7.9 Hz, 1H), 1.45 (d, *J* = 7.3 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) ppm 170.9, 142.8, 141.2, 140.6, 139.1, 128.8, 128.7, 127.6, 127.4, 127.3, 127.2, 127.0, 126.1, 76.8, 73.1, 48.9, 38.2, 21.7, ; HRMS (ESI): Exact mass calcd for $C_{24}H_{25}NNaO_3$ $[M+Na]^+$ 398.1732, found 398.1717.



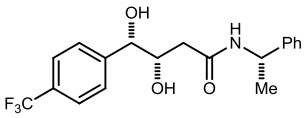
(3*S*,4*S*)-3,4-Dihydroxy-4-(4-methoxyphenyl)-*N*-((*S*)-1-phenylethyl)butanamide (183d). (1*S*,2*S*)-4-Bromo-1-(4-methoxyphenyl)-4-nitrobutane-1,2-diol (39 mg, 120 µmol) was treated utilizing the general procedure. The title compound was isolated as a white solid (20 mg, 50%) after purification (SiO_2, 20-80% ethyl acetate in hexanes). Mp = 104-106 °C; R_f = 0.32 (85% EtOAc/hexanes); IR (film) 3399, 3033, 2922, 1640, 1551, 1053 cm^{-1}; ^1H NMR (600

MHz, $CDCl_3$) [61] δ 7.34 (dd, *J* = 6.7, 6.7 Hz, 2H), 7.29-7.25 (m, 3H), 7.20 (d, *J* = 8.7 Hz, 2H), 6.85 (d, *J* = 8.9 Hz, 2H), 6.05 (d, *J* = 7.6 Hz, 1H), 5.09 (dq, *J* = 14.5, 7.1 Hz, 1H), 4.42 (d, *J* = 7.4 Hz, 1H), 4.02 (ddd, *J* = 7.9, 7.9, 3.3 Hz, 1H), 3.79 (s, 3H), 2.22 (dd, *J* = 15.5, 3.4 Hz, 1H), 2.17 (dd, *J* = 15.5, 8.1 Hz, 1H), 1.45 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) ppm 170.9, 159.5, 142.8, 132.1, 128.7, 128.2, 127.5, 126.1, 113.9, 76.7, 73.2, 55.3, 48.8, 38.2, 21.7.

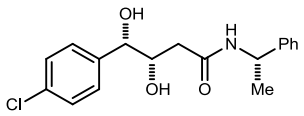


(3*S*,4*S*)-4-(4-Fluorophenyl)-3,4-dihydroxy-*N*-((*S*)-1-phenylethyl)butanamide (183f). (1*S*,2*S*)-4-Bromo-1-(4-fluorophenyl)-4-nitrobutane-1,2-diol (29 mg, 94 μmol) was treated utilizing the general procedure. The title compound was isolated as a white solid (17 mg, 56%) after purification (SiO_2, 20-80% ethyl acetate in hexanes). Mp = 135-138 °C; R_f = 0.41 (85% EtOAc/hexanes); IR (film) 3367, 2922, 2852, 1617, 1536, 1509, 1217, 1085, 1043 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.35 (dd, *J* = 7.7, 7.7 Hz, 2H), 7.30-7.28 (m, 5H), 7.01 (dd, *J* = 8.6, 8.6 Hz, 2H), 5.93 (d, *J* = 7.5 Hz, 1H), 5.11 (dq, *J* = 14.4, 7.1 Hz, 1H), 4.48 (d, *J* = 6.9 Hz, 1H), 4.35 (d, *J* = 2.3 Hz, 1H), 4.00-3.97 (m, 1H), 3.23 (br s, 1H), 2.24 (dd, *J* = 15.6, 3.5 Hz, 1H), 2.19 (dd, *J* = 15.5, 8.0 Hz, 1H), 1.45 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) ppm 170.8, 162.5 (d, $^1J_{CF}$ = 248 Hz), 142.7, 135.9 (d, $^4J_{CF}$ = 3.0 Hz), 128.8, 128.6 (d, $^3J_{CF}$ = 8.2 Hz), 127.6, 126.1 , 115.5 (d, $^2J_{CF}$ = 21.5 Hz), 76.3, 73.1, 48.9, 38.0, 21.7; HRMS (ESI): Exact mass calcd for $C_{18}H_{20}FNNaO_3$ $[M+Na]^+$ 340.1325, found 340.1314.

[61] Hydroxyl protons not visible by ^{1}H NMR

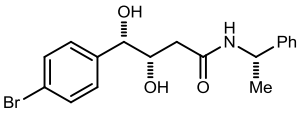


(3*S*,4*S*)-3,4-Dihydroxy-*N*-((*S*)-1-phenylethyl)-4-(4-(trifluoromethyl)phenyl)butanamide (183g). (1*S*,2*S*)-4-Bromo-4-nitro-1-(4-(trifluoromethyl)phenyl)butane-1,2-diol (35 mg, 98 µmol) was treated utilizing the general procedure. The title compound was isolated as a white solid (20 mg, 55%) after purification (SiO_2, 20-80% ethyl acetate in hexanes). Mp = 118-120 °C; R_f = 0.45 (85% EtOAc/hexanes); IR (film) 3312, 3069, 2975, 2927, 1640, 1546, 1326, 1125, 1067 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.58 (d, *J* = 8.0 Hz, 2H), 7.43 (d, *J* = 8.0 Hz, 2H), 7.36-7.34 (m, 2H), 7.30-7.27 (m, 3H), 5.90 (d, *J* = 7.6 Hz, 1H), 5.10 (dq, *J* = 14.3, 7.1 Hz, 1H), 4.57 (d, *J* = 6.3 Hz, 1H), 4.39 (br s, 1H), 4.03 (ddd, *J* = 7.1, 7.1, 3.3 Hz, 1H), 3.45 (br s, 1H), 2.27 (dd, *J* = 15.5, 3.9 Hz, 1H), 2.24 (dd, *J* = 15.5, 7.7 Hz, 1H), 1.47 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) ppm 170.7, 144.3, 142.6, 130.3 (q, $^2J_{CF}$ = 32.1 Hz), 128.8, 127.7, 127.3, 126.1, 125.4 (q, $^3J_{CF}$ = 3.6 Hz), 124.1 (q, $^1J_{CF}$ = 273 Hz), 76.2, 72.8, 48.9, 38.1, 21.7; HRMS (ESI): Exact mass calcd for $C_{19}H_{20}F_3NNaO_3$ $[M+Na]^+$ 390.1293, found 390.1276.

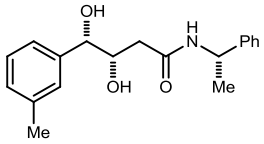


(3*S*,4*S*)-4-(4-Chlorophenyl)-3,4-dihydroxy-*N*-((*S*)-1-phenylethyl)butanamide (183h). (1*S*,2*S*)-4-Bromo-1-(4-chlorophenyl)-4-nitrobutane-1,2-diol (35 mg, 108 µmol) was treated utilizing the general procedure. The title compound was isolated as a white solid (19 mg, 54%) after purification (SiO_2, 20-80% ethyl acetate in hexanes). Mp = 139-141 °C; R_f = 0.48 (85% EtOAc/hexanes); IR (film) 3313, 2925, 1640, 1546, 1087 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.36 (dd, *J* = 8.0, 7.0 Hz, 2H),

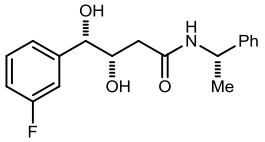
7.31-7.28 (m, 5H), 7.24 (d, *J* = 9.2 Hz, 2H), 5.86 (d, *J* = 7.4 Hz, 1H), 5.11 (dq, *J* = 14.3, 7.1 Hz, 1H), 4.48 (d, *J* = 6.8 Hz, 1H), 4.37 (d, *J* = 3.8 Hz, 1H), 3.99 (ddd, *J* = 10.7, 7.2, 3.3 Hz, 1H), 3.21 (d, *J* = 1.4 Hz, 1H), 2.26 (dd, *J* = 15.6, 3.5 Hz, 1H), 2.20 (dd, *J* = 15.5, 7.9 Hz, 1H), 1.45 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) ppm 170.8, 142.6, 138.7, 133.9, 128.8, 128.7, 128.3, 127.7, 126.1, 76.4, 73.0, 48.9, 37.9, 21.7; HRMS (ESI): Exact mass calcd for $C_{18}H_{20}ClNNaO_3$ $[M+Na]^+$ 356.1029, found 356.1016.



(3*S*,4*S*)-4-(4-Bromophenyl)-3,4-dihydroxy-*N*-((*S*)-1-phenylethyl)butanamide (183i). (1*S*,2*S*)-4-Bromo-1-(4-bromophenyl)-4-nitrobutane-1,2-diol (30 mg, 81 μmol) was treated utilizing the general procedure. The title compound was isolated as a white solid (17 mg, 56%) after purification (SiO_2, 20-80% ethyl acetate in hexanes). Mp = 130-132 °C; R_f = 0.49 (85% EtOAc/hexanes); IR (film) 3306, 2924, 1643, 1547, 1071, 700 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.44 (d, *J* = 8.4 Hz, 2H), 7.37-7.34 (m, 2H), 7.30-7.28 (m, 3H), 7.17 (d, *J* = 9.2 Hz, 2H), 5.90 (d, *J* = 7.4 Hz, 1H), 5.10 (dq, *J* = 14.3, 7.1 Hz, 1H), 4.47 (d, *J* = 6.8 Hz, 1H), 4.37 (br s, 1H), 3.98 (ddd, *J* = 7.6, 7.6, 3.4 Hz, 1H), 3.27 (br s, 1H), 2.26 (dd, *J* = 15.5, 3.5 Hz, 1H), 2.20 (dd, *J* = 15.5, 7.9 Hz, 1H), 1.47 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) ppm 170.8, 142.6, 139.2, 131.6, 128.8, 128.6, 127.6, 126.1, 122.1, 76.3, 72.9, 48.9, 37.9, 21.7; HRMS (ESI): Exact mass calcd for $C_{18}H_{20}BrNNaO_3$ $[M+Na]^+$ 400.0524, found 400.0504.



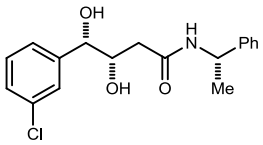
(3*S*,4*S*)-3,4-Dihydroxy-*N*-((*S*)-1-phenylethyl)-4-(*m*-tolyl)butanamide (183j). (1*S*,2*S*)-4-Bromo-4-nitro-1-(*m*-tolyl)butane-1,2-diol (50 mg, 164 µmol) was treated utilizing the general procedure. The title compound was isolated as a white solid (28 mg, 55%) after purification (SiO_2, 20-80% ethyl acetate in hexanes). Mp = 109-111 °C; R_f = 0.48 (85% EtOAc/hexanes); IR (film) 3311, 3063, 2924, 1642, 1546, 1062 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$)[62] δ 7.35-7.32 (m, 2H), 7.29-7.25 (m, 3H), 7.20 (d, *J* = 7.5 Hz, 1H), 7.11 (s, 1H), 7.10 (d, *J* = 7.1 Hz, 1H), 7.06 (d, *J* = 7.4 Hz, 1H), 6.18 (d, *J* = 7.6 Hz, 1H), 5.08 (dq, *J* = 14.4, 7.1 Hz, 1H), 4.42 (d, *J* = 7.11 Hz, 1H), 4.28 (br s, 1H), 4.02 (ddd, *J* = 7.3, 7.3, 4.1 Hz, 1H), 3.31 (br s, 1H), 2.32 (s, 3H), 2.26 (dd, *J* = 15.5, 4.0 Hz, 1H), 2.22 (dd, *J* = 15.5, 7.6 Hz, 1H), 1.44 (dd, *J* = 7.0 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) ppm 170.8, 142.8, 140.0, 138.2, 128.9, 128.7, 128.4, 127.5, 127.5, 126.0, 124.0, 77.1, 73.0, 48.8, 38.3, 21.7, 21.4; HRMS (ESI): Exact mass calcd for $C_{19}H_{23}NNaO_3$ $[M+Na]^+$ 336.1576, found 336.1562.



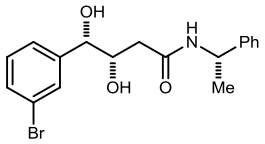
(3*S*,4*S*)-4-(3-Fluorophenyl)-3,4-dihydroxy-*N*-((*S*)-1-phenylethyl)butanamide (183l). (1*S*,2*S*)-4-Bromo-1-(3-fluorophenyl)-4-nitrobutane-1,2-diol (33 mg, 107 µmol) was treated utilizing the general procedure. The title compound was isolated as a white solid (18 mg, 55%) after purification (SiO_2, 20-80% ethyl acetate in hexanes). Mp = 68-70 °C; R_f = 0.48 (85% EtOAc/hexanes); IR (film) 3312, 3067, 2925, 1640, 1547, 1072 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.35 (dd, *J* = 7.6, 7.6 Hz,

[62] Hydroxyl protons not visible by ^1H NMR

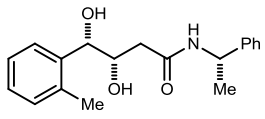
2H), 7.31-7.26 (m, 4H), 7.08-7.04 (m, 2H), 6.98 (dd, *J* = 10.7, 8.5 Hz, 1H), 5.94 (d, *J* = 7.6 Hz, 1H), 5.10 (dq, *J* = 14.3, 7.0 Hz, 1H), 4.50 (d, *J* = 6.9 Hz, 1H), 4.35 (br s, 1H), 4.01 (ddd, *J* = 7.6, 7.6, 3.7 Hz, 1H), 3.28 (br s, 1H), 2.29 (dd, *J* = 15.5, 3.7 Hz, 1H), 2.24 (dd, *J* = 15.5, 7.8 Hz, 1H), 1.48 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) ppm 170.8, 162.9 (d, $^1J_{CF}$ = 247 Hz), 142.8 (d, $^3J_{CF}$ = 6.9 Hz), 142.6, 130.0 (d, $^3J_{CF}$ = 8.1 Hz), 128.8, 127.6, 126.1, 122.6 (d, $^4J_{CF}$ = 2.4 Hz), 115.5 (d, $^2J_{CF}$ = 21.3 Hz), 113.8 (d, $^2J_{CF}$ = 21.3 Hz), 76.4, 72.9, 48.9, 38.1, 21.7; HRMS (ESI): Exact mass calcd for $C_{18}H_{20}FNNaO_3$ $[M+Na]^+$ 340.1325, found 340.1314.



(3*S*,4*S*)-4-(3-Chlorophenyl)-3,4-dihydroxy-*N*-((*S*)-1-phenylethyl)butanamide (183n). (1*S*,2*S*)-4-Bromo-1-(3-chlorophenyl)-4-nitrobutane-1,2-diol (40 mg, 123 µmol) was treated utilizing the general procedure. The title compound was isolated as a white solid (23 mg, 58%) after purification (SiO_2, 20-80% ethyl acetate in hexanes). Mp = 64-66 °C; R_f = 0.42 (85% EtOAc/hexanes); IR (film) 3314, 3066, 2925, 1642, 1546, 1076 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.36-7.32 (m, 3H), 7.30-7.24 (m, 5H), 7.17 (d, *J* = 6.9 Hz, 1H), 6.01 (d, *J* = 7.4 Hz, 1H), 5.09 (dq, *J* = 14.3, 7.0 Hz, 1H), 4.46 (d, *J* = 6.7 Hz, 1H), 4.38 (br s, 1H), 4.00 (ddd, *J* = 7.5, 7.5, 3.7 Hz, 1H), 3.40 (br s, 1H), 2.26 (dd, *J* = 15.5, 3.6 Hz, 1H), 2.22 (dd, *J* = 15.5, 7.8 Hz, 1H), 1.47 (dd, *J* = 6.8 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) ppm 170.8, 142.7, 142.4, 134.5, 129.8, 128.8, 128.3, 127.6, 127.1, 126.1, 125.1, 76.3, 72.8, 48.9, 38.1, 21.7; HRMS (ESI): Exact mass calcd for $C_{18}H_{20}ClNNaO_3$ $[M+Na]^+$ 356.1029, found 356.1014.

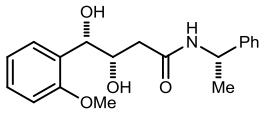


(3*S*,4*S*)-4-(3-Bromophenyl)-3,4-dihydroxy-*N*-((*S*)-1-phenylethyl)butanamide (183o). (1*S*,2*S*)-4-Bromo-1-(3-bromophenyl)-4-nitrobutane-1,2-diol (90 mg, 244 µmol) was treated utilizing the general procedure. The title compound was isolated as a white solid (56 mg, 61%) after purification (SiO_2, 20-80% ethyl acetate in hexanes). Mp = 68-70 °C; R_f = 0.50 (85% EtOAc/hexanes); IR (film) 3312, 3065, 2927, 1643, 1546, 1070 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.46 (s, 1H), 7.40 (d, *J* = 7.9 Hz, 1H), 7.32 (dd, *J* = 7.7, 7.7 Hz, 2H), 7.27-7.24 (m, 3H), 7.20 (d, *J* = 7.7 Hz, 1H), 7.17 (dd, *J* = 7.7, 7.7 Hz, 1H), 6.23 (d, *J* = 7.8 Hz, 1H), 5.04 (dq, *J* = 14.3, 7.1 Hz, 1H), 4.41 (d, *J* = 6.5 Hz, 1H), 4.36 (br s, 1H), 3.97 (ddd, *J* = 7.6, 7.6, 4.0 Hz, 1H), 3.63 (br s, 1H), 2.23 (dd, *J* = 15.4, 7.9 Hz, 1H), 2.19 (dd, *J* = 15.4, 7.9 Hz, 1H), 1.48 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) ppm 170.8, 142.7, 142.7, 131.1, 130.0, 129.9, 128.7, 127.5, 126.1, 125.5, 122.6, 76.1, 72.7, 48.9, 38.3, 21.8; HRMS (ESI): Exact mass calcd for $C_{18}H_{21}BrNO_3$ $[M+H]^+$ 378.0705, found 378.0688.

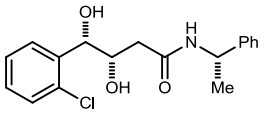


(3*S*,4*S*)-3,4-Dihydroxy-*N*-((*S*)-1-phenylethyl)-4-(*o*-tolyl)butanamide (183p). (1*S*,2*S*)-4-Bromo-4-nitro-1-(*o*-tolyl)butane-1,2-diol (50 mg, 164 µmol) was treated utilizing the general procedure. The title compound was isolated as a white solid (27 mg, 55%) after purification (SiO_2, 20-80% ethyl acetate in hexanes). Mp = 62-64 °C; R_f = 0.49 (85% EtOAc/hexanes); IR (film) 3282, 3066, 2926, 1643, 1547, 1083 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.40 (d, *J* = 7.6 Hz, 1H), 7.34 (dd, *J* = 7.6, 7.6 Hz, 2H), 7.29-7.26 (m, 3H), 7.23-7.18 (m, 2H), 7.14 (d, *J* = 7.6 Hz, 1H), 6.23 (d, *J* = 7.6

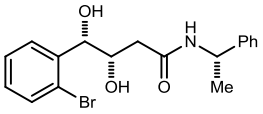
Hz, 1H), 5.09 (dq, *J* = 14.4, 7.0 Hz, 1H), 4.80 (d, *J* = 6.6 Hz, 1H), 4.19 (br s, 1H), 4.12 (ddd, *J* = 7.7, 7.7, 4.0 Hz, 1H), 3.27 (br s, 1H), 2.32 (dd, *J* = 15.3, 9.1 Hz, 1H), 2.31 (s, 3H), 2.22 (dd, *J* = 15.5, 3.1 Hz, 1H), 1.46 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) ppm 170.8, 142.8, 138.2, 135.5, 130.6, 128.6, 127.9, 127.4, 126.6, 126.3, 126.0, 72.9, 72.4, 48.9, 38.4, 21.8, 19.5; HRMS (ESI): Exact mass calcd for $C_{19}H_{23}NNaO_3$ $[M+Na]^+$ 336.1576, found 336.1561.



(3*S*,4*S*)-3,4-Dihydroxy-4-(2-methoxyphenyl)-*N*-((*S*)-1-phenylethyl)butanamide (183q). (1*S*,2*S*)-4-Bromo-1-(2-methoxyphenyl)-4-nitrobutane-1,2-diol (40 mg, 125 µmol) was treated according to the general procedure. The title compound was isolated as a yellow viscous oil (27 mg, 45%) after purification (SiO_2, 20-80% ethyl acetate in hexanes). R_f = 0.23 (85% EtOAc/hexanes); IR (film) 3313, 3066, 2929, 1643, 1545, 1242, 1028, 756 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.35-7.30 (m, 5H), 7.28-7.24 (m, 2H), 6.96 (dd, *J* = 7.7, 7.7 Hz, 1H), 6.86 (d, *J* = 7.8 Hz, 1H), 6.44 (d, *J* = 7.7 Hz, 1H), 5.10 (dq, *J* = 14.3, 7.0 Hz, 1H), 4.79 (d, *J* = 6.6 Hz, 1H), 4.12 (ddd, *J* = 9.2, 6.7, 3.0 Hz, 1H), 3.93 (br s, 1H), 3.78 (br s, 3H), 3.42 (br s, 1H), 2.37 (dd, *J* = 15.4, 8.8 Hz, 1H), 2.25 (dd, *J* = 15.4, 3.2 Hz, 1H), 1.46 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) ppm 170.9, 156.5, 143.1, 129.1, 128.7, 128.2, 128.1, 127.3, 126.1, 121.0, 110.7, 72.9, 71.9, 55.4, 48.8, 39.0, 21.9.

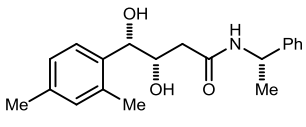


(3*S*,4*S*)-4-(2-Chlorophenyl)-3,4-dihydroxy-*N*-((*S*)-1-phenylethyl)butanamide (183r). (1*S*,2*S*)-4-Bromo-1-(2-chlorophenyl)-4-nitrobutane-1,2-diol (54 mg, 166 μmol) was treated utilizing the general procedure. The title compound was isolated as a white solid (29 mg, 53%) after purification (SiO_2, 20-80% ethyl acetate in hexanes). Mp = 118-120 °C; R_f = 0.48 (85% EtOAc/hexanes); IR (film) 3323, 3065, 2924, 1621, 1544, 1058 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.56 (d, *J* = 7.8 Hz, 1H), 7.35-7.21 (m, 8H), 6.11 (d, *J* = 7.2 Hz, 1H), 5.10 (dq, *J* = 14.2, 7.0 Hz, 1H), 5.03 (d, *J* = 5.3 Hz, 1H), 4.11 (ddd, *J* = 8.6, 5.3, 3.1 Hz, 1H), 2.52 (dd, *J* = 15.8, 8.8 Hz, 1H), 2.31 (dd, *J* = 15.4, 3.1 Hz, 1H), 1.48 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) ppm 171.0, 142.7, 138.2, 132.4, 129.4, 128.9, 128.7, 128.4, 127.5, 127.1, 126.1, 72.4, 71.9, 48.9, 38.7, 21.7; HRMS (ESI): Exact mass calcd for $C_{18}H_{20}ClNNaO_3$ $[M+Na]^+$ 356.1029, found 356.1018.



(3*S*,4*S*)-4-(2-Bromophenyl)-3,4-dihydroxy-*N*-((*S*)-1-phenylethyl)butanamide (183s). (1*S*,2*S*)-4-Bromo-1-(2-bromophenyl)-4-nitrobutane-1,2-diol (37 mg, 100 μmol) was treated utilizing the general procedure. The title compound was isolated as a clear viscous oil (21 mg, 55%) after purification (SiO_2, 20-80% ethyl acetate in hexanes). R_f = 0.38 (85% EtOAc/hexanes); IR (film) 3409, 3277, 3066, 2927, 1644, 1545, 1051, 742 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.49 (dd, *J* = 5.8, 1.3 Hz, 1H), 7.45 (dd, *J* = 5.7, 1.2 Hz, 1H), 7.31-7.27 (m, 3H), 7.12 (ddd, *J* = 7.9, 7.9, 1.8 Hz, 1H), 6.51 (d, *J* = 7.9 Hz, 1H), 5.03 (dq, *J* = 14.4, 7.1 Hz, 1H), 4.94 (d, *J* = 4.9 Hz, 1H),

4.22 (br s, 1H), 4.11-4.07 (m, 1H), 4.02 (br s, 1H), 2.50 (dd, *J* = 15.3, 9.0 Hz, 1H), 2.29 (dd, *J* = 15.3, 3.4 Hz, 1H), 1.41 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) ppm 170.9, 142.8, 139.8, 132.5, 129.



(3*S*,4*S*)-4-(2,4-Dimethylphenyl)-3,4-dihydroxy-*N*-((*S*)-1-phenylethyl)butanamide (183u). (1*S*,2*S*)-4-Bromo-1-(2,4-dimethylphenyl)-4-nitrobutane-1,2-diol (60 mg, 189 µmol) was treated according to the general procedure. The title compound was isolated as a pale yellow viscous oil (38 mg, 62%) after purification (SiO_2, 20-80% ethyl acetate in hexanes). R_f = 0.40 (85% EtOAc/hexanes); IR (film) 3318, 3030, 2926, 1644, 1543, 1450, 1031, 700 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.32 (dd, *J* = 7.7, 7.7 Hz, 2H), 7.27-7.24 (m, 4H), 6.99 (d, *J* = 8.2 Hz, 1H), 6.94 (s, 1H), 6.30 (d, *J* = 7.9 Hz, 1H), 5.09 (dq, *J* = 14.4, 7.2 Hz, 1H), 4.73 (d, *J* = 6.7 Hz, 1H), 4.09 (ddd, *J* = 9.6, 6.7, 2.9 Hz, 1H), 2.29 (dd, *J* = 15.5, 4.1 Hz, 1H), 2.28 (s, 3H), 2.26 (s, 3H), 2.19 (dd, *J* = 15.4, 3.1 Hz, 1H), 1.43 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) ppm 170.9, 142.8, 137.5, 135.4, 135.2, 131.4, 128.6, 127.4, 126.9, 126.6, 126.0, 72.9, 72.5, 48.8, 38.5, 21.8, 20.9, 19.3.