CATIONIC ZIRCONOCENE-MEDIATED CASCADE SYNTHESIS OF TETRAHYDROFURANS

by

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Tetrahydrofurans and tetrahydropyrans are common structural features of numerous natural products, most notably the marine toxins and the polyether antibiotics, such as brevetoxin and monensin. Despite the structural complexity of these two classes of compounds, a similarity arises when comparing the structural cores. The framework of all polyether antibiotics contains 2,5-disubstituted tetrahydrofurans, substituted tetrahydropyrans and spiroketal systems. A characteristic feature in the core of marine toxins is a *trans*-fused polycyclic ether moiety. Because of these similarities, it is believed that polycyclic ether compounds have a similar biogenetic origin, and many groups have postulated that Nature synthesizes these compounds via a polyene→polyepoxide→polyether pathway.

Based on previous Wipf group methodology, enantiomerically pure diepoxide substrates with electronically different ester terminating groups were subjected to 10 mol% Cp_2ZrCl_2 and 20 mol% $AgClO_4$. It was found that the 2-furyl and 2-benzofuryl ester moieties furnished the best yields and diastereoselectivities of the desired highly functionalized tetrahydrofurans.

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ABBREVIATIONS

Ac	acetyl
Bn	benzyl
BTF	trifluorobenzene
CSA	10-camphorsulphonic acid
DBU	1,8-diazabicyclo[5.4.0]undec-7-ene
DCC	1,3-dicyclohexylcarbodiimide
DIBAL-H	diisobutylaluminum hydride
DMAP	4-dimethylaminopyridine
DMS	dimethyl sulfide
DMSO	dimethyl sulfoxide
DSS	sodium 3-(trimethylsily)-1-propanesulfonate
HMPA	hexamethylphosphoramide
Imid	imidazole
IPA	isopropyl alcohol
KHMDS	potassium bis(trimethylsilyl)amide
LiHMDS	lithium bis(trimethylsilyl)amide
m-CPBA	3-chloroperoxybenzoic acid
MOM	methoxymethyl
Ms	methanesulfonyl
NaHMDS	sodium bis(trimethylsilyl)amide

ABBREVIATIONS

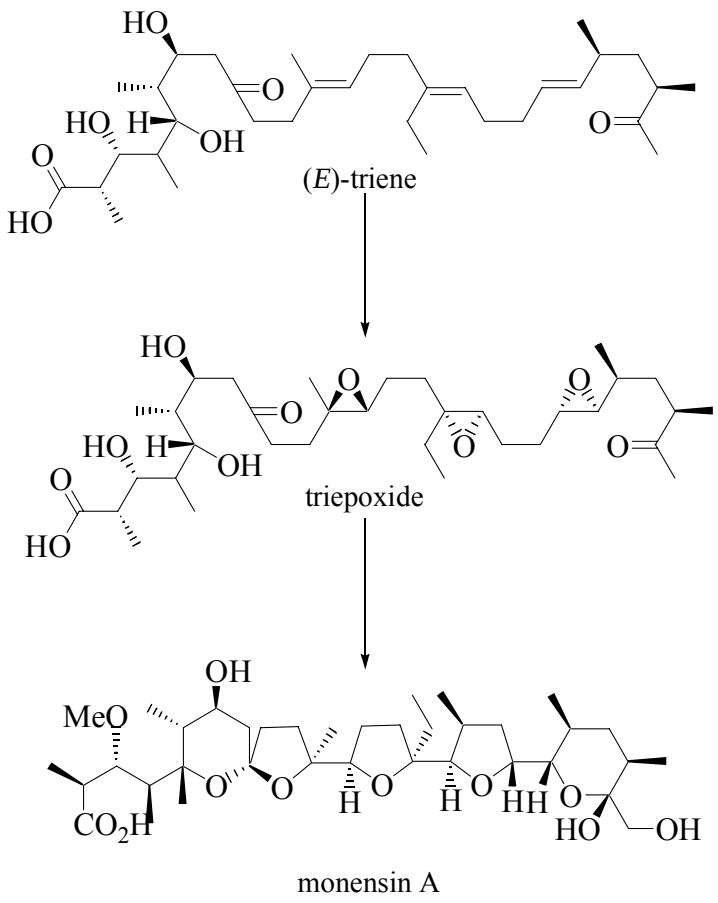
Py or Pyrid	pyridine
TBAF	tetra-*n*-butylammonium fluoride
TBDPS	*tert*-butyldiphenylsilyl
TBME	*tert*-butylmethyl ether
TBS	*tert*-butyldimethylsilyl
THP	tetrahydropyranyl
TIPS	triisopropylsilyl
TMEDA	N,N,N',N'-tetramethylethylenediamine
TMS	trimethylsilyl
Ts	*para*-toluenesulfonyl

1. INTRODUCTION

1.1. Biosynthetic Synthesis of Tetrahydrofurans and Tetrahydropyrans

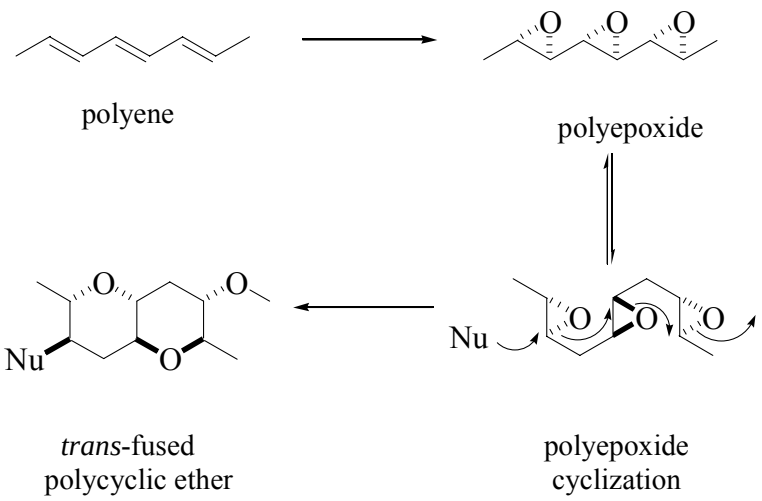
Tetrahydrofurans and tetrahydropyrans are common structural features of numerous natural products, most notably the marine toxins and the polyether antibiotics, such as the brevetoxins and monensin.[1] Despite the structural complexity of the two classes of compounds, a similarity arises when comparing their structural cores. The framework of all polyether antibiotics contains 2,5-disubstituted tetrahydrofurans, substituted tetrahydropyrans and spiroketal systems. A characteristic feature in the core of marine toxins is a *trans*-fused polycyclic ether moiety.[2] Because of these similarities, it is believed that polycyclic ether compounds have a similar biogenetic origin, and many groups have postulated that Nature synthesizes these compounds via a cascade cyclization of a polyepoxide subunit where structural differences may be due to different modes of epoxide openings.

In the early 1980's Westley and Cane proposed a biosynthetic model for polyether antibiotics.[3] Scheme 1 shows their hypothetical explanation of the biosynthesis of monensin. In this model, an all-(*E*) triene is initially formed which undergoes epoxidation at each double bond to give a triepoxide. Attack of the C5 hyroxyl group at the C9 carbonyl position would initiate a cascade of ring closures generating the tetrahydrofuran rings of monensin with the observed stereochemistry. The most important aspect of this model is that with basic manipulation of the starting triene, one could extend it to account for all polyether antibiotics.[4]



Scheme 1: Hypothetical biosynthesis of monensin A.

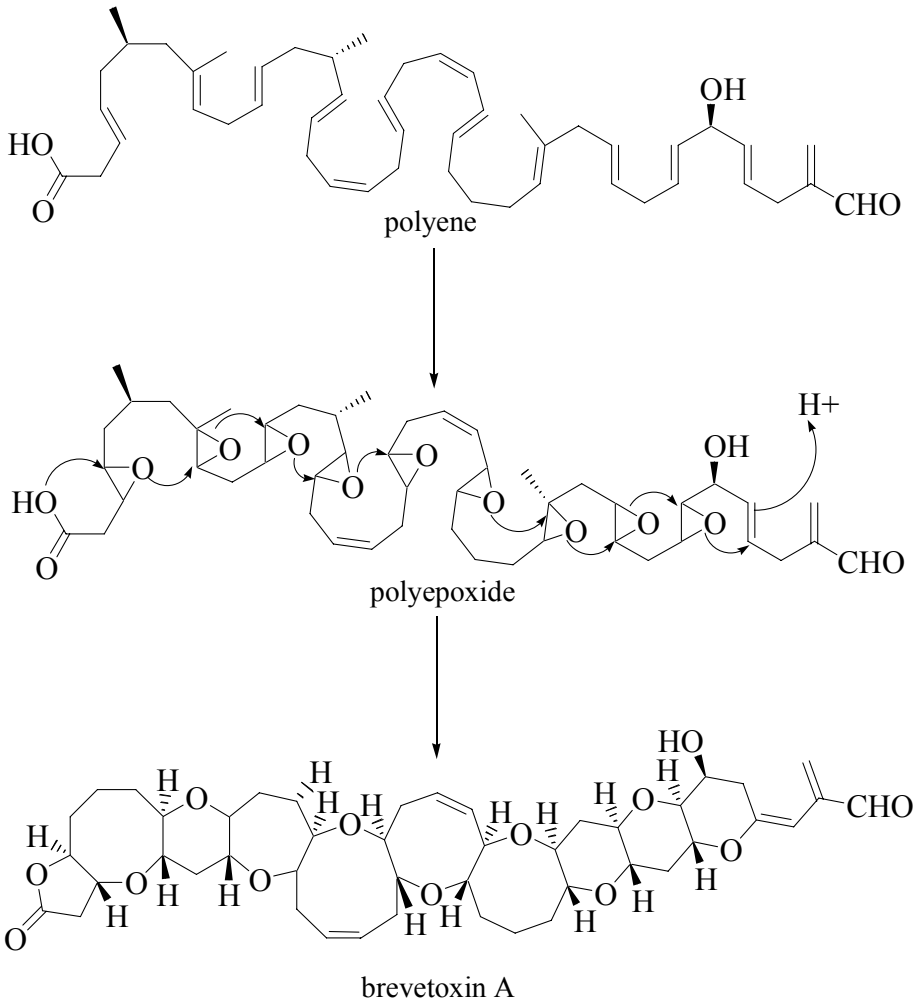
In 1985, Nakanishi proposed a similar model to account for the biosynthesis of the *trans*-fused cyclic ether moiety present in marine toxins. Nakanishi hypothesized that a polyene synthesis occurs via iterative chain homologation followed by asymmetric epoxidation and a series of subsequent *endo*-selective epoxide openings (Scheme 2).[5] Nakanishi extended this hypothesis further and proposed that Nature might synthesize brevetoxin A in a manner similar to the Westley-Cane model used for monensin (Scheme 3). In each of the aforementioned hypotheses lies a central unifying concept which is that the biosynthesis of polyether natural products involves a polyene→polyepoxide→polyether pathway.[6,7,8,9,10]



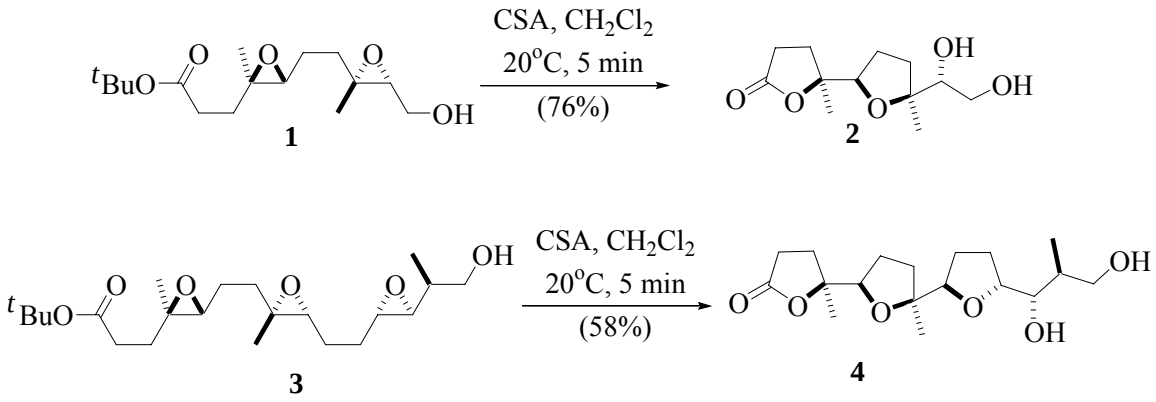
Scheme 2: Nakanishi's biosynthetic hypothesis for *trans*-fused polyethers.

1.2. Polyepoxide Cascade Cyclizations in Natural Product Synthesis

In attempts to synthetically support the biosynthetic model proposed for the formation of polyether antibiotics and marine ladder toxins, many groups have explored the polyene→polyepoxide→polyether pathway. Kishi,[11,12,] Corey,[13] and Mori[14] have all employed polyepoxide cascade cyclizations in their syntheses of polyether natural products. Most notably are Paterson's approach towards the cyclic ether skeleton of etheromycin and McDonald's efficient synthesis of the *trans*-fused moiety of brevetoxin. Paterson's preliminary studies began with diepoxy *tert*-butyl ester **1**, which upon exposure to CSA in CH_2Cl_2 at 0 ^oC rapidly lead to the formation of cyclized product **2** in 76% yield.



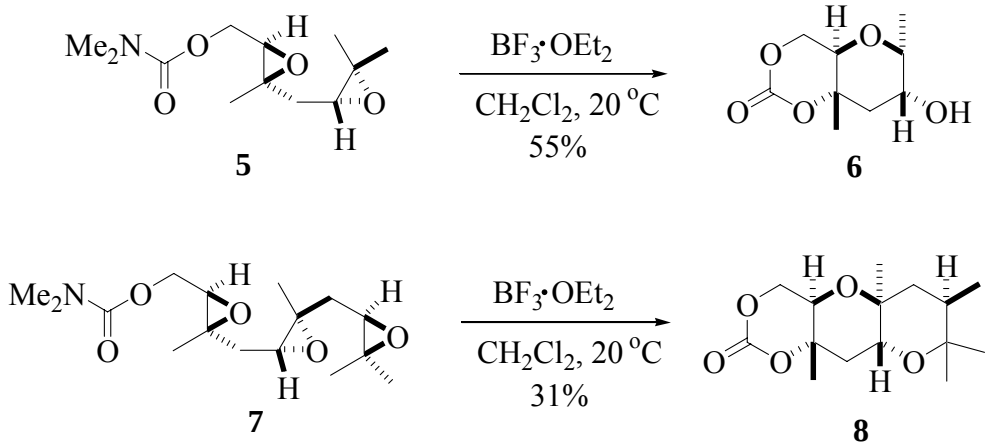
Scheme 3: Hypothetical biosynthesis of brevetoxin A.



Scheme 4: Paterson's cyclizations of polyepoxides **1** and **3**.

Subunit **2** is a common bicyclic portion of a large number of polyether natural products. Exposure of triepoxide **3** to similar reaction conditions afforded tricyclic polyether fragment **4** in 58% yield (Scheme 4)[15]

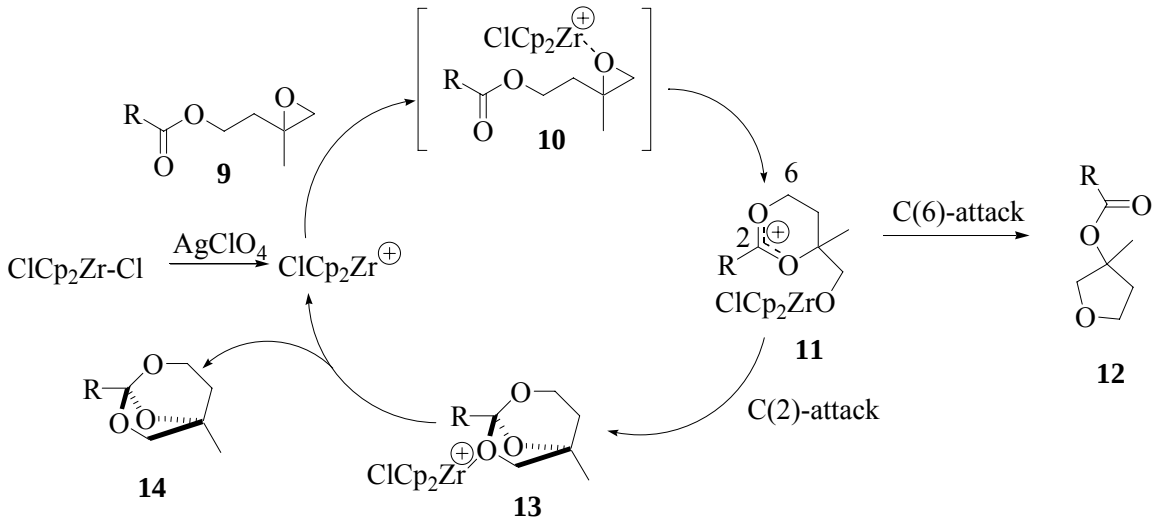
McDonald explored the Lewis acid initiated tandem *endo*-selective oxacyclization of diepoxide *tert*-butyl carbonate **5**. Reaction of **5** with 1 equivalent of BF_3•OEt_2 at 20 °C afforded the *trans*-fused product **6** in 55% yield. The formation of all-fused *trans,trans*-tricyclic species **8** was achieved by the BF_3•OEt_2 promoted cyclization of triepoxide **7** in 31% yield (Scheme 5).[16]



Scheme 5: McDonald's oxacyclizations of **5** and **7.**

1.3. Previous Wipf Group Methodology

In the early 1990's, Wipf and coworkers reported the novel synthesis of ortho esters and tetrahydrofurans via epoxide opening cascades mediated by cationic zirconocene (Scheme 6).[17] Intermediate-activated epoxide **10** is then formed which undergoes an epoxide rearrangement initiated by neighboring group participation of the terminal ester carbonyl group, generating dioxycarbenium ion **11**.

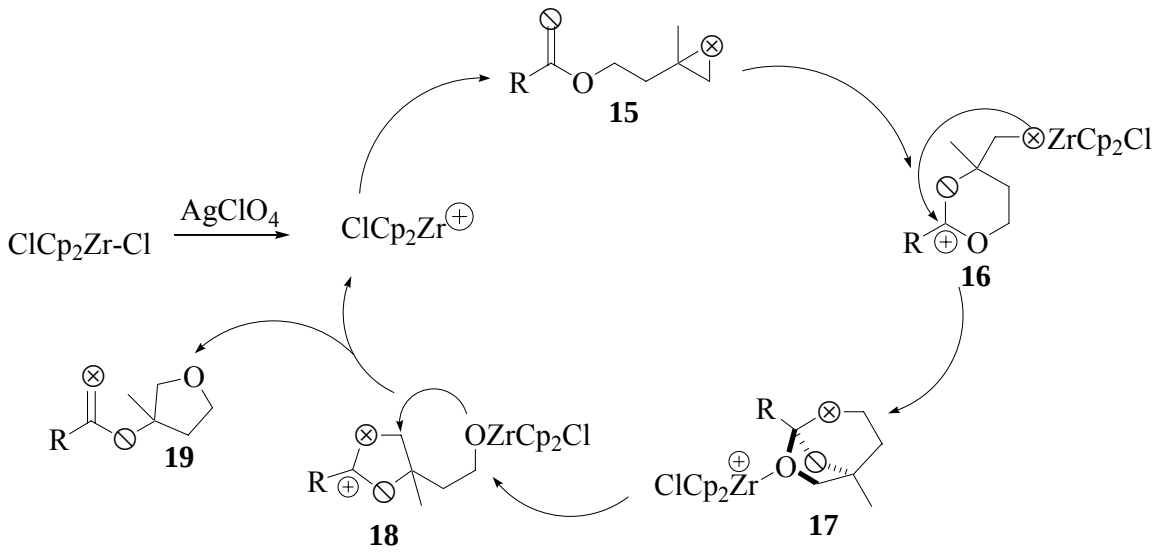


Scheme 6: Proposed mechanism for tetrahydrofuran and ortho ester formation.

At this point, C2 attack leads to ortho ester **14** while tetrahydrofuran **12** is generated via C6 attack. Product distribution is a consequence of the nature of the R substituent on intermediate **11**. If the dioxycarbenium ion is stabilized by the R substituent, an equilibrium is established between **12** and **13** followed by irreversible attack at C6 providing tetrahydrofuran **12**. Alternatively, if species **11** is not stabilized, ortho ester formation is observed.

In 2003, ^{18}O-labeling experiments were performed by Giner and coworkers to provide further insight into the mechanism of tetrahydrofuran formation using epoxy-ester **15**.[18] The results of this work are shown in Scheme 7. Similar to Wipf's proposed mechanism, dioxycarbenium ion **16** is formed via acid induced epoxide rearrangement of ^{18}O-labeled **15**. Subsequent C2 attack provides orthoester **17**. In contradiction to Wipf's mechanism, Giner discovered that tetrahydrofuran formation proceeds entirely through five-membered dioxycarbenium ion **18** which is formed by the ring-opening of ortho ester **17**. Alkoxide attack leads to tetrahydrofuran **19** and the regeneration of cationic zirconocene.

Although the results of this labeling experiment exclude the pathway originally proposed by Wipf and coworkers, it by no means proves that the transformation proceeds via a five membered dioxycarbenium ion. Rather it demonstrates that the desired tetrahydrofuran is formed in a less direct, slightly more complex sequence.

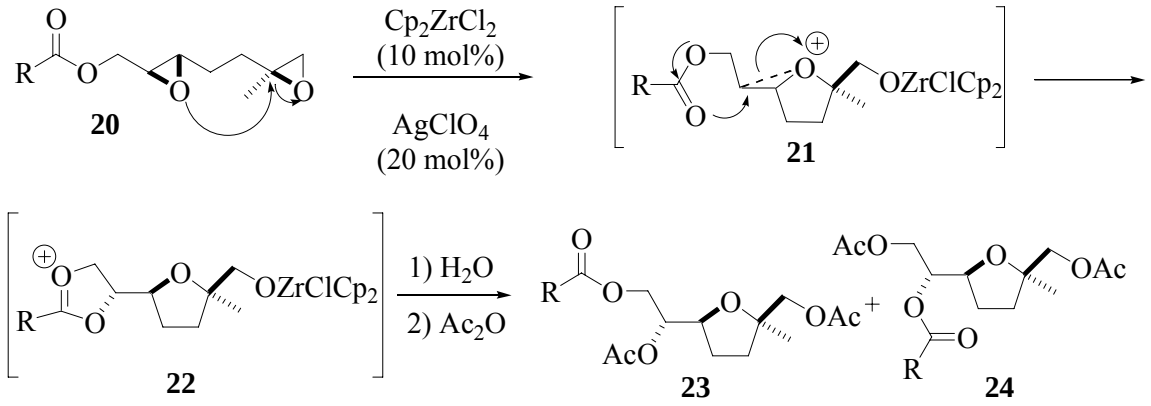


Scheme 7: Alternate mechanism for tetrahydrofuran formation.

2. STRATEGY AND GOALS

In spite of numerous literature examples of polyepoxide cascade cyclizations initiated by Lewis acids, no groups have explored the powerful Lewis acidity of zirconium based Lewis acids in synthesizing highly functionalized tetrahydrofurans and tetrahydropyrans. Our goal was to use $Cp_2ZrCl_2/AgClO_4$ to initiate a cascade cyclization of an enantiomerically pure diepoxide, forming a highly functionalized tetrahydrofuran.[19] Based on previous work in the Wipf group, the mechanism is believed to first involve coordination of cationic zirconocence to the 1,1-disubstituted epoxide, thus activating the proximal carbon for attack by the internal epoxide to generate cationic intermediate **20**. Neighboring group participation by the ester carbonyl group is then expected to lead to attack on intermediate **21**, resulting in dioxycarbenium ion **22**. Upon quenching with H_2O, intermediate **22** is converted into tetrahydrofurans **23** and **24**, with **23** being the major regioisomer and **24** the minor. These two regioisomers can be rationalized by hydrolysis of dioxycarbenium ion **22** occuring in a non-regioselective manner (Scheme 8). The structure of these regioisomers were deduced via 1D and 2D NMR spectroscopy (*vide infra*). Subunits of this type are common in polyether natural products such as cationomycin (Figure 1).[20]

Due to the important role the ester moiety plays in the proposed mechanism, it is believed a strongly electron donating ester group will facilitate the desired cyclization. To explore this concept, a variety of differently substituted, enantiomerically pure diepoxides were first synthesized and then subjected to our cationic zirconocene conditions.



Scheme 8: Proposed mechanism for tetrahydrofuran formation.

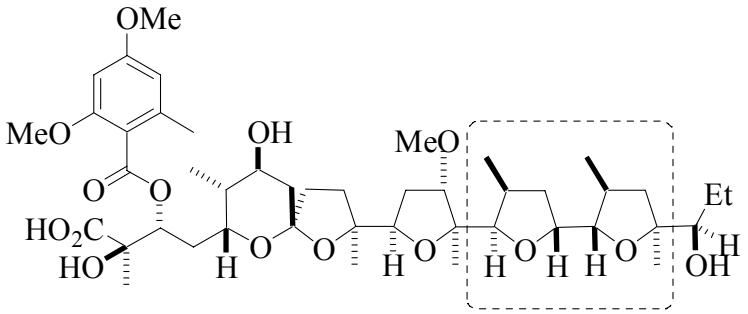


Figure 1: Structure of cationomycin.

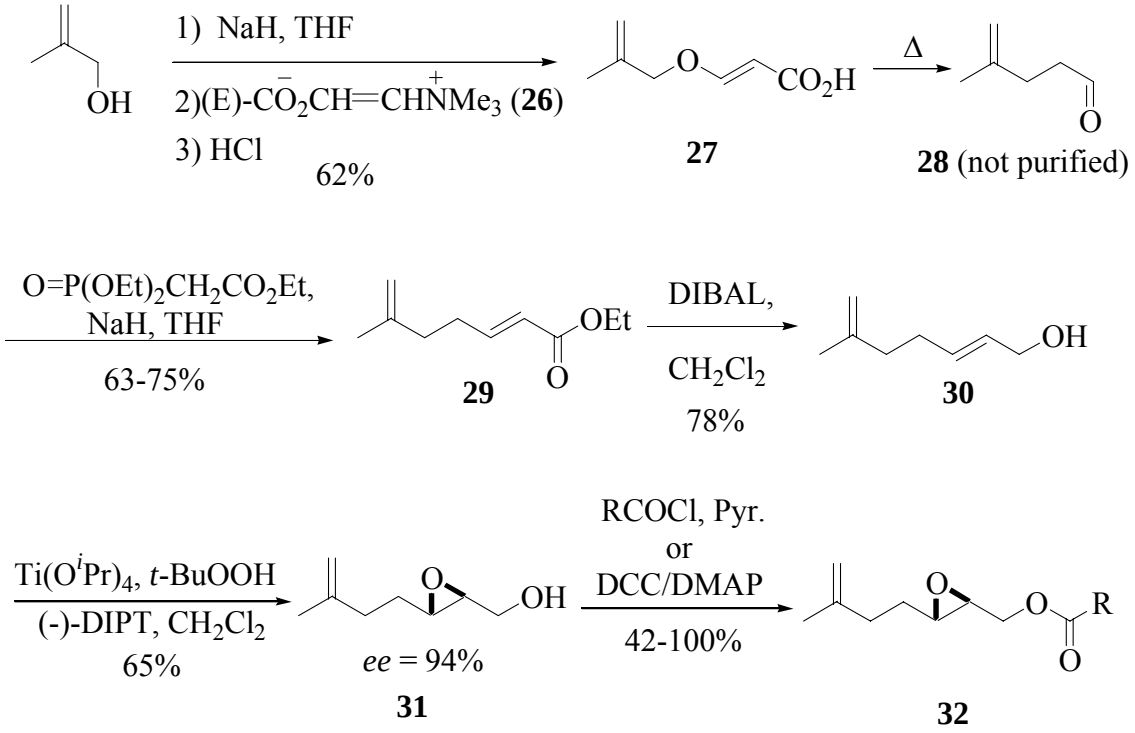
3. RESULTS AND DISCUSSION

3.1. Route to Enantiomerically Pure Diepoxides

The diepoxides were synthesized in a linear fashion starting from commercially available β-methallyl alcohol which underwent reaction with (*E*)-(carboxyvinyl)trimethylammonium betaine **26** to give carboxylic acid **27** (Scheme 9). This acid was subjected to thermal Claisen rearrangement conditions to provide **28**.[21] Subsequent Horner-Wadsworth-Emmons reaction gave the conjugated ester **29** which was reduced with DIBAL-H to give the allylic alcohol **30**.[22] Sharpless asymmetric epoxidation provided epoxide **31** in 94% ee based on comparison with a literature $[\alpha]_D$.[23] The terminal hydroxyl group was acylated with a variety of ester moieties via DCC coupling with the appropriate carboxylic acid or reaction with an acid chloride in pyridine. As shown in Table 1, we were able to prepare a number of ester substrates with different terminating groups (i.e., R = Me, C_6H_5, (4-OMe)C_6H_4, (3,4-OMe)C_6H_3, (2,4-OMe)C_6H_3, (3,4,5-OMe)C_6H_2, furan and benzofuran) in a moderate to high yield (42-100%). Due to the difficulty in separating the resulting *m*-chloroperoxybenzoic acid from the desired diepoxide, some yields were substantially lower.

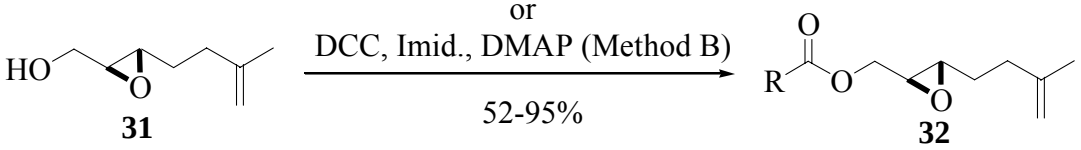
With intermediate **32** in hand, our initial goal was to epoxidize the terminal, 1,1-disubstituted alkene in an asymmetric manner. Attempts to epoxidize this alkene proved unsuccessful using either the Shi epoxidation or a two step protocol involving Sharpless asymmetric dihydroxylation followed by tosylation and subsequent ring closure. The Shi

epoxidation yielded a 1.8:1 ratio of products which quickly decomposed, allowing the isolation of < 10% of the desired product. Sharpless asymmetric dihyroxylation resulted in a disappointing 1.5:1 ratio of products. Attempts to generate the epoxide via tosylation and ring closure were not pursued (Table 2). It should be noted that there is limited literature precedence for the asymmetric epoxidation of terminal 1,1-disubstituted alkenes by way of the methods previously described.

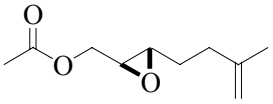
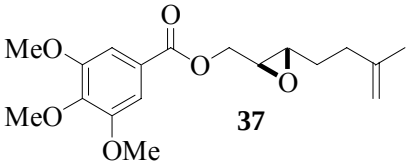
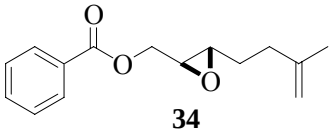
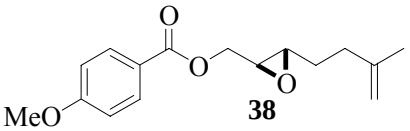
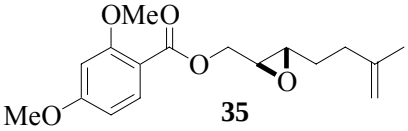
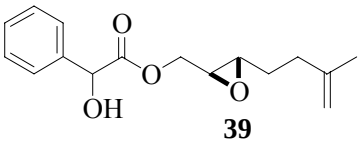
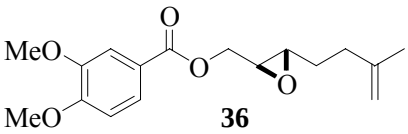
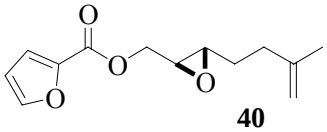
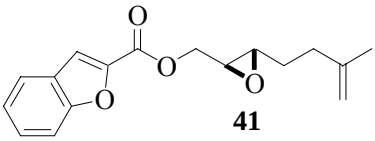


Scheme 9: Route to intermediate **32.**

Table 1: Acylated monoepoxide substrates



31 **32**

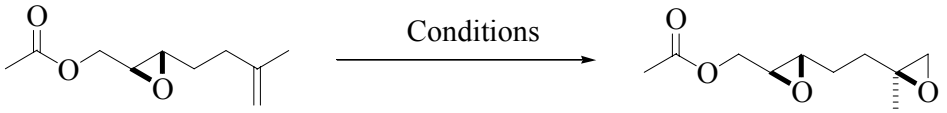
entry	product	yield (%)	entry	product	yield (%)
1[a]	 **33**	92	5[a]	 **37**	70
2[a]	 **34**	60	6[a]	 **38**	100
3[a]	 **35**	84	7[a]	 **39**	55
4[a]	 **36**	42	8[a]	 **40**	95
			9[b]	 **41**	94

[a] Prepared via Method A. [b] Prepared via Method B

This problem was circumvented by epoxidizing **32** with *m*-CPBA, giving a 1:1 mixture of inseparable diastereomers in 44-80% yield (Table 3). A late stage Jacobsen kinetic resolution gave our desired enantiomerically pure diepoxide (Table 4).[24] The ^{1}H NMR of the diastereomeric mixtures contains singlets at 1.34 and 1.33 ppm arising from the terminal methyl group of each diastereomer. After performing the kinetic resolution, the only observable peak in that region of the spectrum occurs at 1.33 ppm, therefore, the kinetic resolution was determined to afford a single diastereomer.

Depending on the substrate used, a 19-44% yield was obtained for the final, kinetically resolved diepoxide. This was lower than expected when compared to literature examples. Unfortunately, 5-15% of a cyclized product was isolated, presumably arising from a cascade cyclization promoted by Jacobsen's chiral cobalt (III) catalyst **60**. Diepoxide **59** was analyzed by X-ray diffraction to confirm the configuration of the major isomer (Figure 2).

Table 2: Epoxidation of the terminal 1,1-disubstituted epoxide.



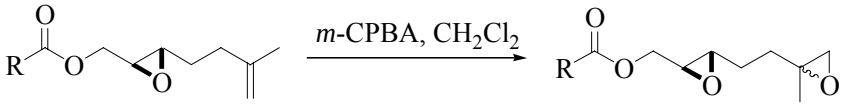
entry	conditions	d.r.[a]	yield (%)
1	1) *t*-BuOH, H_2O, AD-mix α, 0 °C 2) MsCl, NEt_3, CH_2Cl_2, 0 °C	1.5:1	----
2	Na_2EDTA (aq.), Bu_4NH_4OH (cat.) CH_3CN, oxone, $NaHCO_3$, ketone	1.8:1	<10 decomp.
3	1) *m*-CPBA, CH_2Cl_2, $NaHCO_3$ 2) Jacobsen's Kinetic Resolution	1:1 single product	80-90 19-44

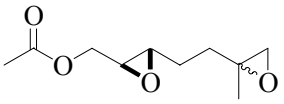
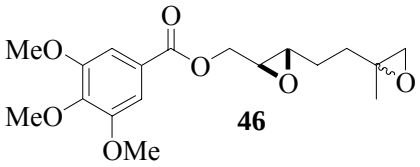
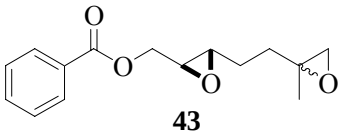
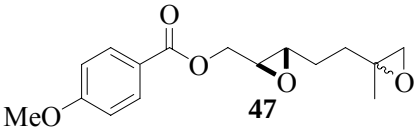
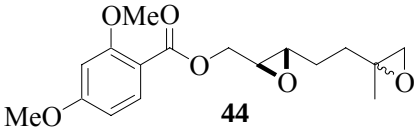
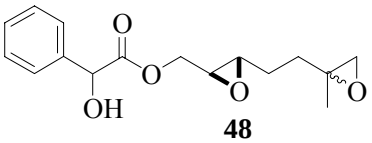
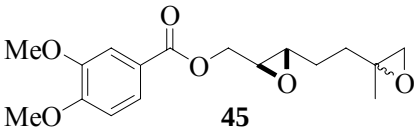
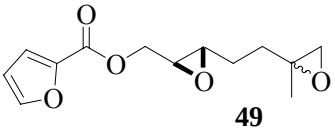
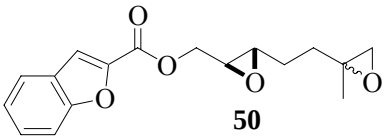
[a] Diastereomeric ratios based on ^{1}H NMR analysis of the crude reaction mixture.

3.2. Initial Cyclizations Using Cp_2ZrCl_2 /$AgClO_4$

Based Wipf group methodology, the enantiomerically pure diepoxides listed in Table 4 were subjected to 10 mol% Cp_2ZrCl_2 and 20 mol% $AgClO_4$ in CH_2Cl_2 at ambient temperature. It should be noted that pre-absorbing $AgClO_4$ on Celite was tried but the results were comparable to those obtained without Celite.[20] The addition of $P(OPh)_3$ to the reaction mixture was also explored but there were no observable advantages in reaction rate, yield and/or selectivity. In order to determine the regioisomeric ratio accurately via ^{1}H NMR, it was found beneficial to acylate the crude tetrahydrofuran-diol mixture, improved signal separation.

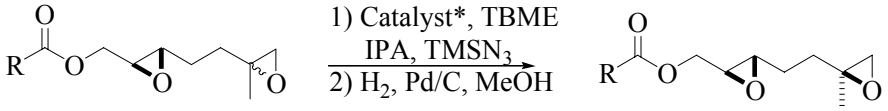
Table 3: Synthesis of diastereomeric diepoxides.

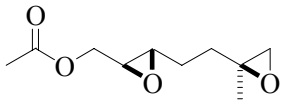
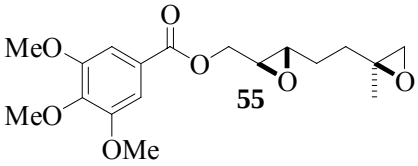
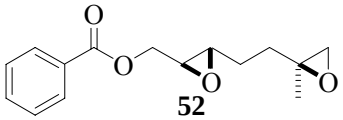
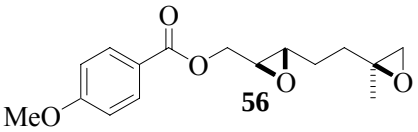
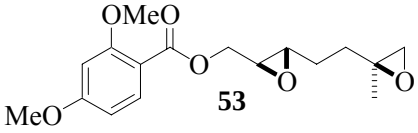
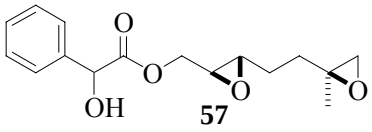
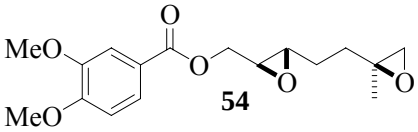
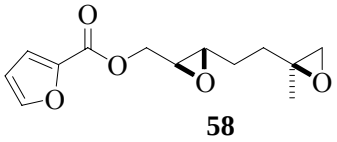
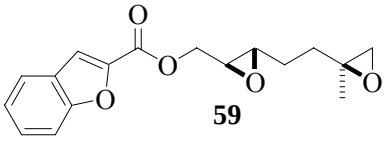


entry[a]	product	yield (%)	entry[a]	product	yield (%)
1	 **42**	77	5	 **46**	80
2	 **43**	78	6	 **47**	44
3	 **44**	46	7	 **48**	57
4	 **45**	52	8	 **49**	64
			9	 **50**	62

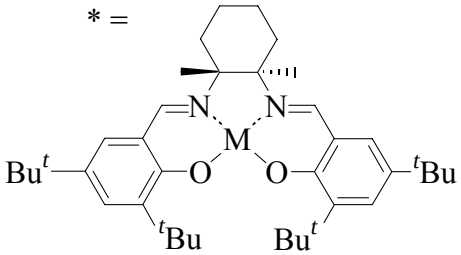
[a] A 1:1 diastereomeric ratio was determined for each substrate via ^{1}H NMR analysis.

Table 4: Kinetically resolved diepoxides.



entry	product	yield (%)	entry	product	yield (%)
1	 **51**	29	5	 **55**	26
2	 **52**	21	6	 **56**	23
3	 **53**	19	7	 **57**	30
4	 **54**	32	8	 **58**	44
			9	 **59**	41

* =



M = Co(OAc)

60

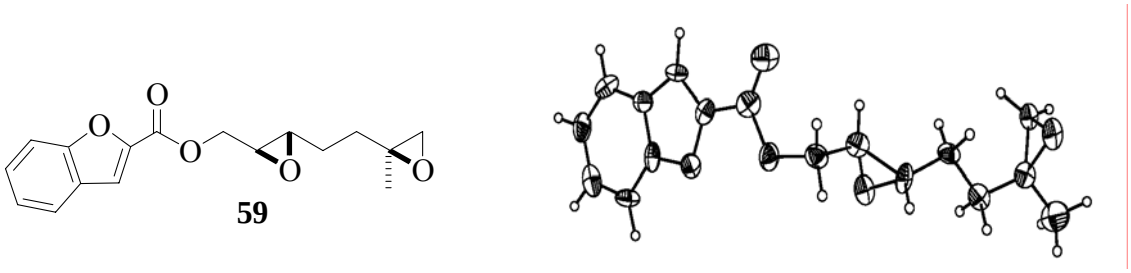


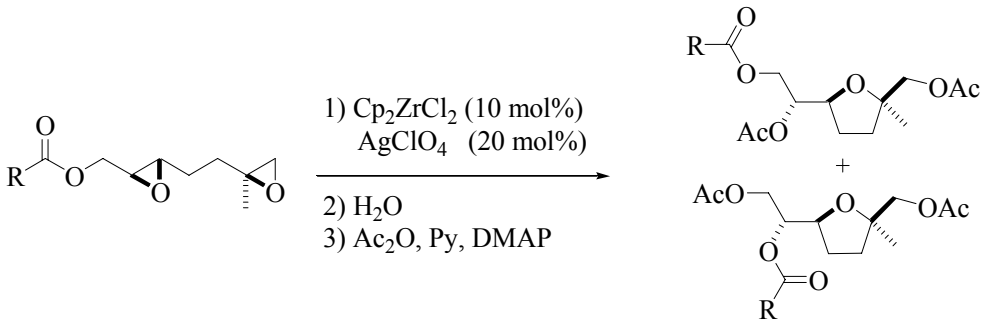
Figure 2: X-ray structure of 2-benzofuryl diepoxide **59.**

The enantiomerically pure diepoxide substrates listed in Table 4 were subjected to 10 mol% Cp_2ZrCl_2 and 20 mol% $AgClO_4$ in CH_2Cl_2 at room temperature, followed by acylation of the crude mixture. The results of these cyclizations are listed in Table 5.

Oxacyclization studies were first conducted using the electron deficient diepoxide acyl ester **51** which afforded the desired tetrahydrofuran **61** in low yield (35%). Similar results were obtained with the benzoic and mandelic acid derived diepoxides **52** and **57**, respectively. Interestingly, no reaction occurred for substrate **56** in which R = (4-OMe)C_6H_4. Based on the assumption that the tetrahydrofuran product formed via the carbocation intermediate **21** (Scheme 8), we believed that increasing the nucleophilicity of the terminal ester group would favor a cascade cyclization. To test this hypothesis, we explored a furoyl moiety as the terminal nucleophile. The 2-furyl derivative **58** afforded tetrahydrofurans **68** and **69** in 56% isolated yield and a 1.9:1 regioselectivity. Increasing the nucleophilicity of this group was accomplished by synthesizing the 2-benzofuryl derivative **59,** which upon cyclization afforded **70** and **71** in a 46% yield and as a 4.5:1 mixture of regioisomers.

Entries 5 and 6 of Table 5 gave the most promising results and it was decided that our efforts would be devoted towards optimizing the reaction conditions to try to obtain a synthetically viable yield and ratio regioisomeric ratio of the desired tetrahydrofuran.

Table 5: Scope of cyclizations using $Cp_2ZrCl_2/AgClO_4$.



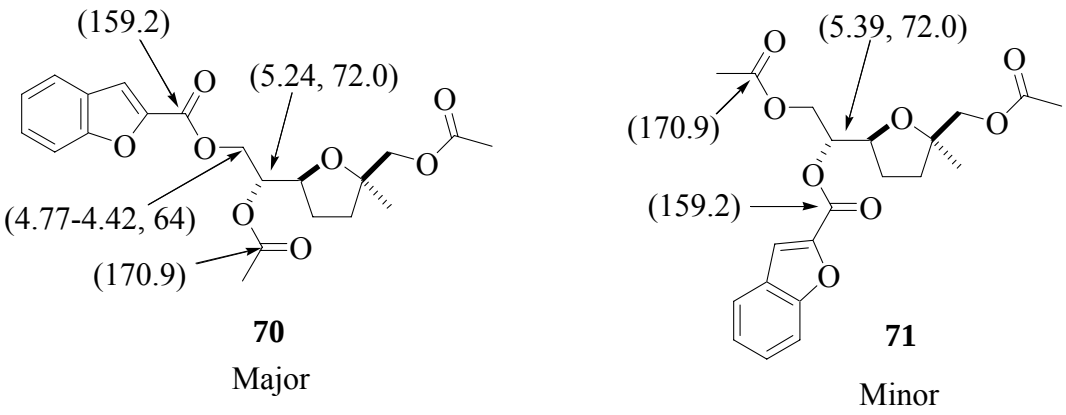
entry	diepoxide	products	yield (%)[a] (major/minor)	ratio of regioisomers
1	**51**	R = CH_3 (**61**)	35	n/a
2	**52**	R = C_6H_5 (**62/63**)	21	1.2:1[b]
3	**56**	R = 4-(OMe)C_6H_4 **(64/65**)	NR	---
4	**57**	R = CH(OH)C_6H_5 (**66/67**)	11	1:1[c]
5	**58**	R = 2-furyl (**68/69**)	56	1.9:1[d]
6	**59**	R = 2-benzofuryl (**70/71**)	46	4.5:1[e]

[a]Isolated yield. [b]Ratio based on the integration of peaks at 5.35 (minor), 5.26 (major) ppm, [c] 5.07 (minor) and 5.06 (major), [d] 5.33 (minor) and 5.20 (major), [e] 5.39 (minor) and 5.24 (major) ppm in the crude ^{1}H NMR after acylation.

Initially, it was believed that a mixture of diastereomers were obtained when the cascade cyclizations previously described took place. We believed that this was so due to the appearance of two doublet of triplets between 5.39-5.06 ppm in the ^{1}H NMR, depending on the diepoxide substrate used in the cyclization. Therefore, clearly two compounds were formed. After much

discussion, it was concluded that the hydrolysis of the dioxycarbenium ion (Scheme 8, Section 2) might be occurring in a non-regioselective manner resulting in a mixture of regioisomers not diastereomers. To test this hypothesis, a series of 2D-NMR (HMBC, HMQC and DEPT) experiments were performed.

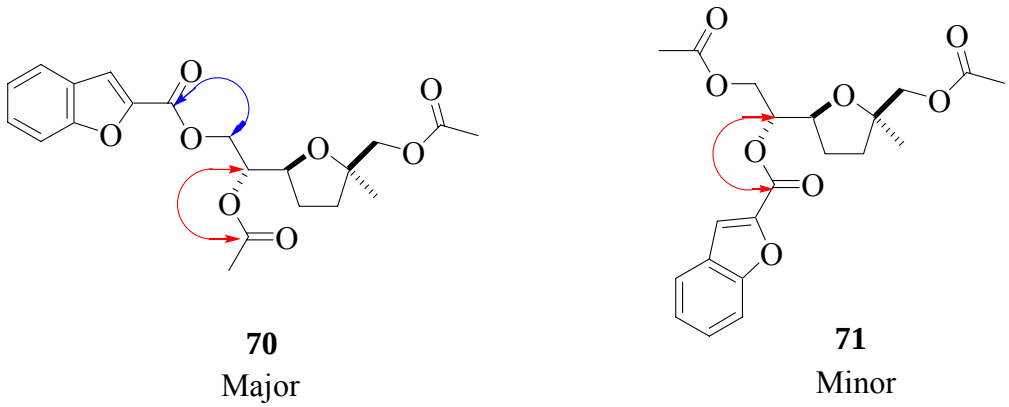
The DEPT and HMQC provided very little insight into the possible structure. The most conclusive pieces of evidence came from the HMBC. Figure 3 details the significant signals seen in ^{1}H and ^{13}C spectra of the major **70** and minor **71** regioisomers. When this data was combined and analyzed in the HMBC spectrum, crosspeaks were noticed between the proton signal at 5.24 ppm and the carbonyl carbon of the acyl group at 170.9 ppm. Also, the proton signals at 4.77-4.42 ppm had a crosspeak with the carbonyl carbon of the furan species. Based on these spectral correlations, it was concluded that the structure of the major isomer **70** consisted of the furoyl moiety attached to the 1^{o} hydroxy group while the acetyl groups were attached to the 2^{o} hydroxy. In support of this conclusion, the HMBC displayed a crosspeak between the minor proton signal at 5.39 ppm and the carbonyl carbon of the furoyl group at 159.2 ppm. From this, it was concluded that the structure of the minor isomer **71** had the furoyl species attached to the 2^{o} hydroxy group. The correlations between the proton and carbon signals for the major and minor isomers are shown in color in Figure 4.



70
Major

71
Minor

Figure 3: Important ^{1}H and ^{13}C chemical shifts of the major (**70**) and minor (**71**) isomers obtained in the cascade cyclization of diepoxide **59.**



70
Major

71
Minor

Figure 4: Important crosspeaks observed in the HMBC spectrum.

3.3. Optimization Using Group IV Lewis Acids for the Cyclization of 58

As discussed in Section 3.2, a 56% yield and 1.9:1 regioselectivity of **68** and **69** was obtained when **58** was exposed to 10 mol% Cp_2ZrCl_2 and 20 mol% $AgClO_4$ in CH_2Cl_2 at ambient temperature (Table 5). Attempts to optimize this reaction using solvents other than CH_2Cl_2 led to a decrease in yield when BTF (22 %, 1.5:1) or toluene (46%, 1.7:1) were used. We assumed that an improvement in the yield and regioselectivity could be achieved by subjecting **58** to the

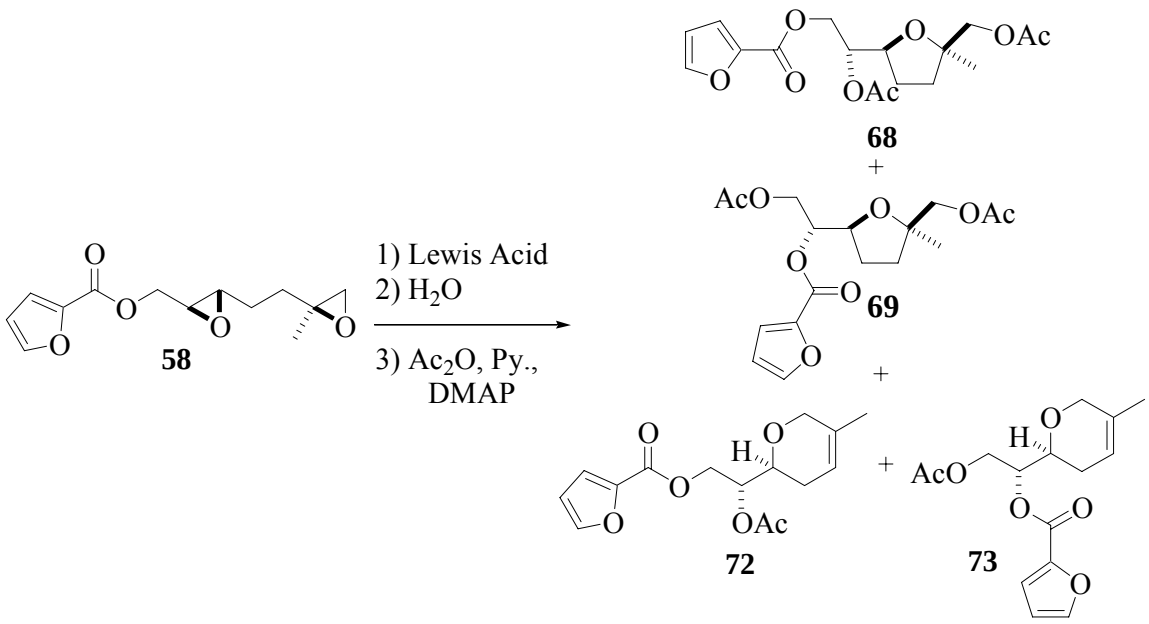
less reactive hafnocene dichloride. Unfortunately, when 10 mol% Cp_2HfCl_2 and 20 mol% $AgClO_4$ in CH_2Cl_2 at room temperature were used, a 20% yield of **68** and **69** was obtained as a 1:1 mixture of regioisomers (Table 6). Dihydropyrans **72** and **73** were isolated as the major byproduct in each cyclization with **72** being the major regioisomer and **73** the minor (*vide infra*).

3.3.1. Optimization of Lewis Acid

A variety of Lewis acids other than Cp_2ZrCl_2 or Cp_2HfCl_2 were explored to promote the cyclization of **58** to **68** and **69** in the hope of improving the yield and/or the regioselectivity. We observed that the reaction of **58** with BF_3•OEt_2 (entry 1, Table 7) at -78 ^oC in CH_2Cl_2 promoted rapid formation of a 1.3:1 ratio of regioisomers in 44% overall yield. We also explored $SnCl_2$ and $EtAlCl_2$ as catalysts (entries 2 and 3, Table 7) which converted substrate **58** to **68** and **69** in a 23% and 22% yield, respectively, with little or no improvement in the regioselectivity. An additional Lewis acid tested for this substrate was $ZnCl_2$, which afforded 15% of **68** and **69** as a 1.1:1 mixture of regioisomers.

Unfortunately, attempts to optimize the cascade cyclization using conditions discussed in Table 6 and Table 7 did not provide a better than 56% yield and a >1.9:1 regioisomeric mixture of the desired tetrahydrofurans.

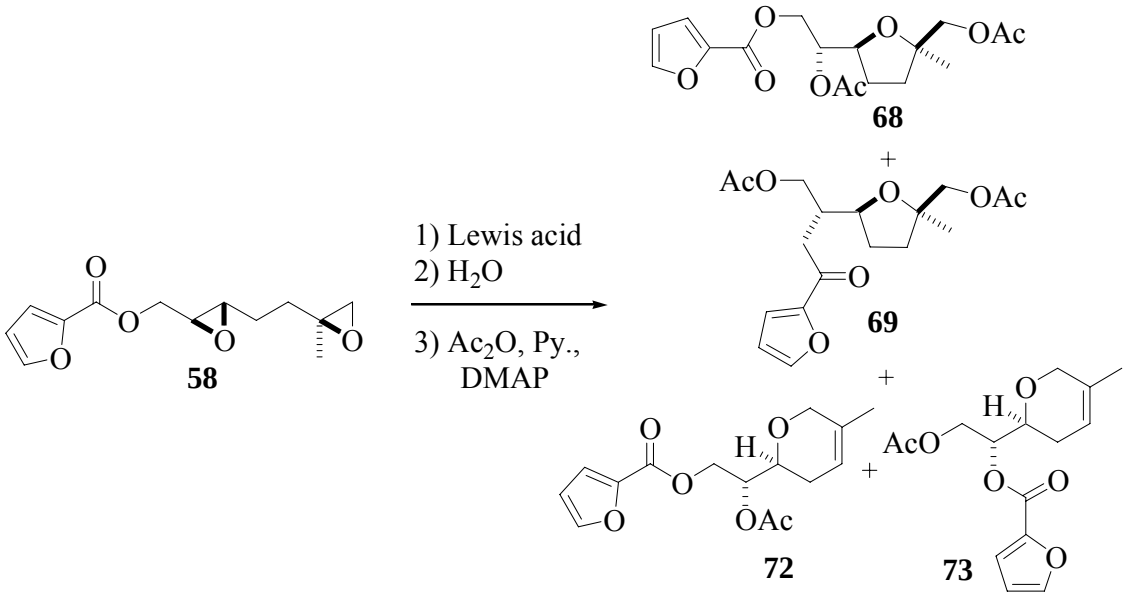
Table 6: Optimization using Cp_2ZrCl_2 of Cp_2HfCl_2.



entry	Lewis acid[a]	solvent	temp [^oC]	yield **68+69** (%)[b]	ratio of regioisomers[c]
1	Cp_2ZrCl_2/ $AgClO_4$	CH_2Cl_2	rt	56	1.9:1
2	Cp_2ZrCl_2/ $AgClO_4$	BTF	rt	22	1.5:1
3	Cp_2ZrCl_2/ $AgClO_4$	Toluene	rt	46	1.7:1
4	Cp_2HfCl_2/ $AgClO_4$	CH_2Cl_2	rt	20	1:1

[a]10 mol% Cp_2ZrCl_2 / 20 mol% $AgClO_4$.[b] Isolated yield. [c] Ratio based on the integration of peaks at 5.33 (minor) and 5.20 (major) ppm in the crude ^1H NMR after acylation.

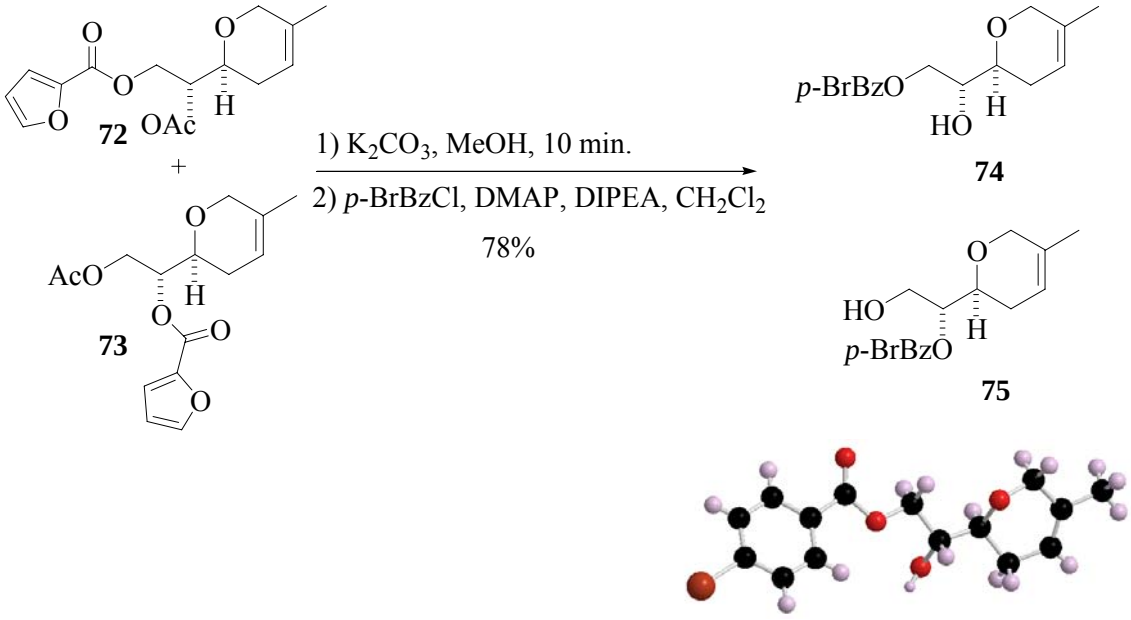
Table 7: Optimization attempts using non-group IV Lewis acids.



entry	Lewis acid	solvent	temp [^{o}C]	yield **68**+ **69** (%)[a]	ratio of regioisomers[b]
1	BF_3•OEt_2	CH_2Cl_2	-78	44	1.3:1
2	$SnCl_2$	CH_2Cl_2	-78 → rt	23	1.3:1
3	$EtAlCl_2$	CH_2Cl_2	-78 → -20	22	1.5:1
4	$ZnCl_2$	CH_2Cl_2	rt	15	1.1:1

[a]Isolated yield. [b]Ratio based on the integration of peaks at 5.30 (minor) and 5.17 (major) ppm in the crude ^{1}H NMR after acylation.

In all cases, the reaction mixtures contained dihydropyran byproducts **72**and **73**which could be isolated in 7-19% combined yield. These dihydropyrans were derivatized at the secondary alcohol position as the *p*-bromobenzoate ester **74** and **75**. The atom connectivity and relative configuration of **74**, the major regioisomer, was determined by X-ray diffraction analysis (Scheme 10).



Scheme 10: Preparation of dihydropyrans (**74**) and (**75**) and X-ray structure of the major regioisomer **74**.

3.4. Optimization Using Cp_2ZrCl_2 /$AgClO_4$ for the Cyclization of 59

As discussed in Section 3.2, a modest 46% yield and a 4.5:1 regioisomeric ratio was achieved when **59** was exposed to 10 mol% Cp_2ZrCl_2 and 20 mol% $AgClO_4$ in CH_2Cl_2 at ambient temperature (Table 5). We explored the temperature dependence of the regioselectivity by subjecting substrate **59** to cyclizations conditions ranging from -78 ^oC to 40 ^oC (Table 8). When

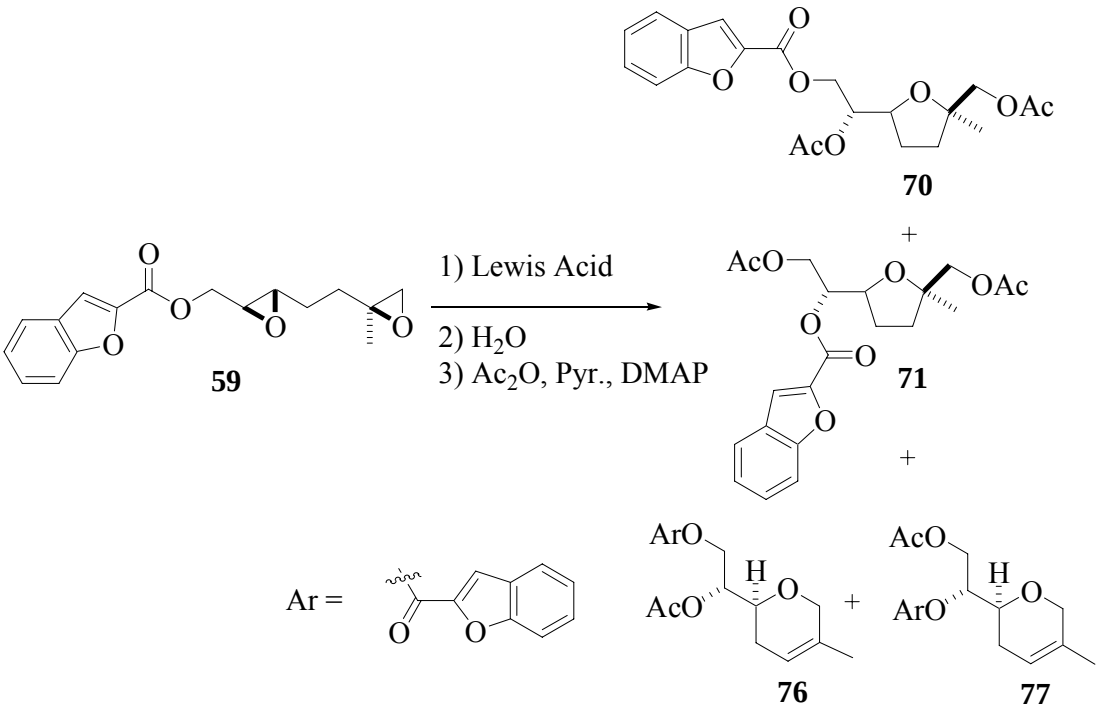
the cyclization reaction was carried out at -78 ^{o}C, no reaction was observed. It is noted in unpublished results from the Wipf group that Cp_2ZrCl_2 is relatively unreactive at temperatures below about -40 ^{o}C. At -20 ^{o}C, a 35% yield and 1.4:1 regioisomeric ratio was observed, while reaction at 0 ^{o}C produced the cyclized product in 51% yield as a 1.7:1 mixture of regioisomers. Improved regioselectivity (5.1:1) was observed when the reaction was carried out at 40 ^{o}C; however a drop in the isolated yield was noted (34%).

3.4.1 Optimization Using Other Lewis Acids

A variety of Lewis acids other than Cp_2ZrCl_2 were explored to promote the cyclization of **59** into **71** in the hope of improving the yield and/or regioselectivity. Exposure of **59** to BF_3•OEt_2 in CH_2Cl_2 at -78 ^{o}C afforded a 68% yield of **70** and **71** in a 1.4:1 ratio of regioisomers. In addition, 11% of the undesired dihydropyran was formed. Et_2AlCl and $EtAlCl_2$ both resulted in poor isolated yield and regioisomeric ratio with substantial dihyropyran formation (Table 9).

As in the case of the 2-furyl-derived diepoxide, attempts to optimize the cyclization of **59** to **70** and **71** by changing temperatures from -78 to 40 ^{o}C and using the Lewis acids detailed in Table 9 provided at best a 46% yield and a 4.5:1 mixture of regioisomers

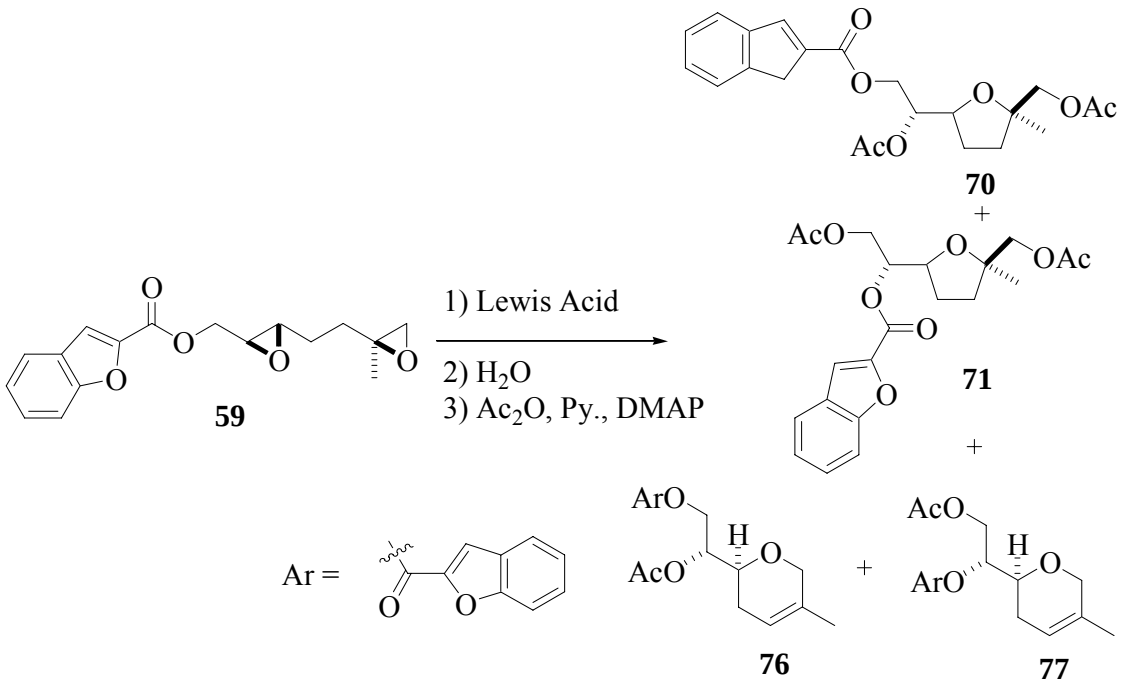
Table 8: Optimization of tetrhydrofuran formation using $Cp_2ZrCl_2/AgClO_4$.



entry	Lewis acid[a]	solvent	temp (^oC)	yield (%) **70** + **71**[b]	ratio of regioisomers[c]	yield (%) of **76** + **77**[b]
1	Cp_2ZrCl_2/ $AgClO_4$	CH_2Cl_2	-20	35	1.4:1	12
2	Cp_2ZrCl_2/ $AgClO_4$	CH_2Cl_2	0	51	1.7:1	8
3	Cp_2ZrCl_2/ $AgClO_4$	CH_2Cl_2	rt	46	4.5:1	7
4	Cp_2ZrCl_2/ $AgClO_4$	CH_2Cl_2	40	34	5.1:1	19

[a] 10 mol% Cp_2ZrCl_2 / 20 mol% $AgClO_4$. [b] Combined isolated yield. [c] Ratio based on the integration of peaks at 5.39 (minor) and 5.24 (major) ppm in the crude ^1H NMR after acylation

Table 9: Optimization using other Lewis acids.



entry	Lewis acid	solvent	temp (^{o}C)	yield (%) **70** + **71**[a]	ratio of regioisomers[b]	yield (%) of **76** + **77**[a]
1	BF_3•OEt_2	CH_2Cl_2	-78	68	1.4:1	11
2	Et_2AlCl	CH_2Cl_2	-78→-20	16	1.4:1	24
3	$EtAlCl_2$	CH_2Cl_2	-78	23	1.3:1	25

[a] Combined isolated yield. [b] Ratio based on the integration of peaks at 5.39 (minor) and 5.24 (major) ppm in the crude ^{1}H NMR after acylation.

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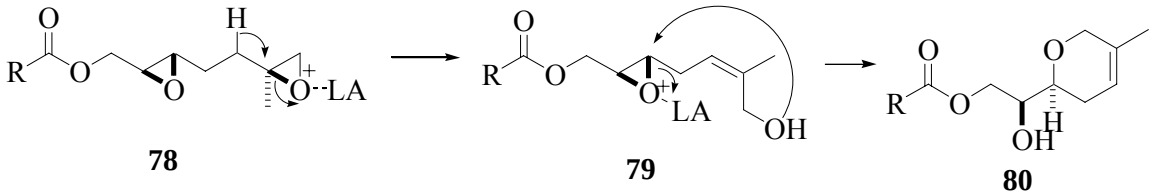
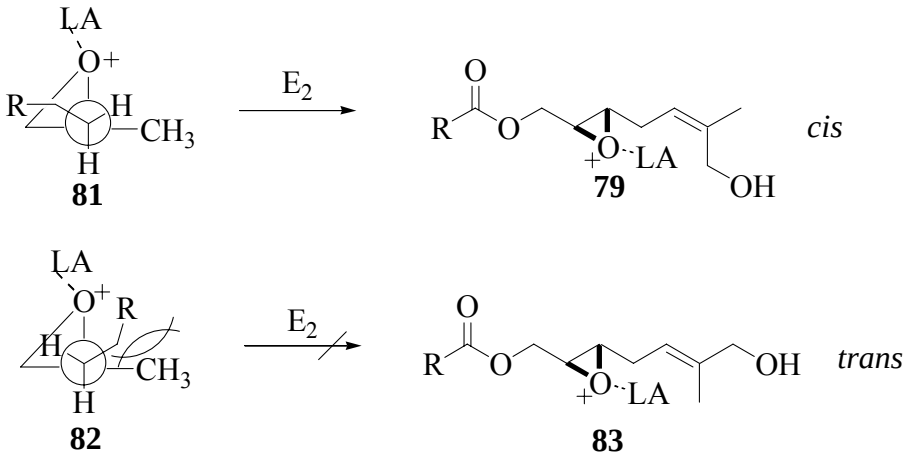


Scheme 11: Proposed mechanism of dihydropyran formation.

To account for the dihydropyan observed in each cyclization, an alternate mechanism was proposed (Scheme 11). E_2 elimination of the hydrogen shown in Scheme 11 can occur affording allylic alcohol **79**. Based on the Newman projection shown in Scheme 12, we propose that the elimination favors the *cis*-product due to the steric interactions in the conformation that generates the *trans*-product. At this point, attack onto the activated internal epoxide by the primary alcohol generates dihydropyran **80**.



Scheme 12: Newman projections can account for observed *cis*-product.

4. SYNTHESIS OF TRIEPOXIDES

As discussed in the introductory section, it is believed that nature utilizes triepoxids to synthesize complex polyether natural products via a cascade cyclization pathway. Therefore, the next step in our methodology was to attempt to synthesize enantiomerically pure triepoxides and determine whether cationic zirconocene is a suitable Lewis acid to promote a polyepoxide cascade cyclization. We were interested in the possibility of testing our cationic zirconium methodology on triepoxides **84** and **85** (Figure 5).

84 **85**

Figure 5: Target enentiomerically pure triepoxides **84** and **85**.

It should be noted that the only structural difference that exists between these substrates is the position of the methyl group. In compound **84**, the methyl substituent is positioned at C6 and in compound **85** it is at C7. This small difference should result in two different modes of cyclization when exposed to $Cp_2ZrCl_2/AgClO_4$. It is expected that substrate **84** will undergo an *exo,exo*-cyclization resulting in tethered tetrahydrofuran **86** while substrate **85** should undergo an *endo,endo*-cyclization to give **87**, a fused tetrahydropyran (Figure 6).

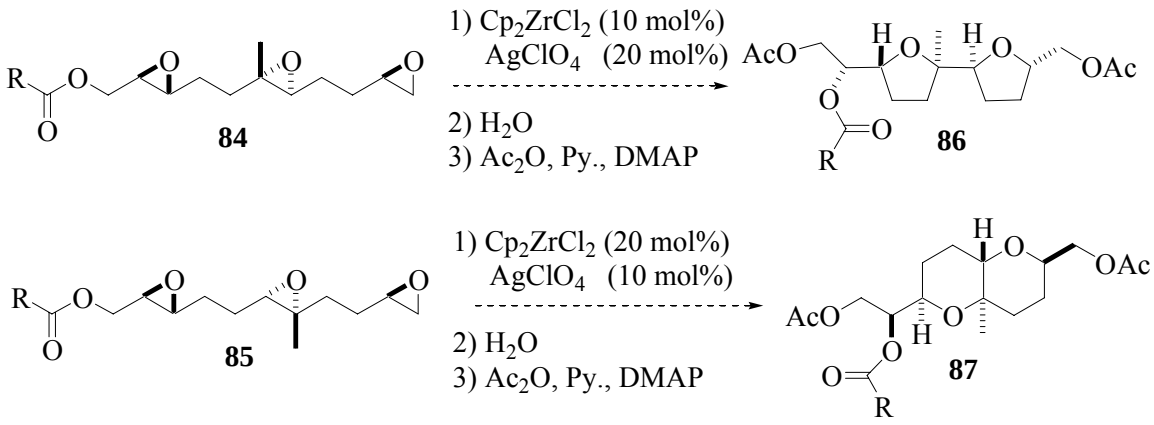
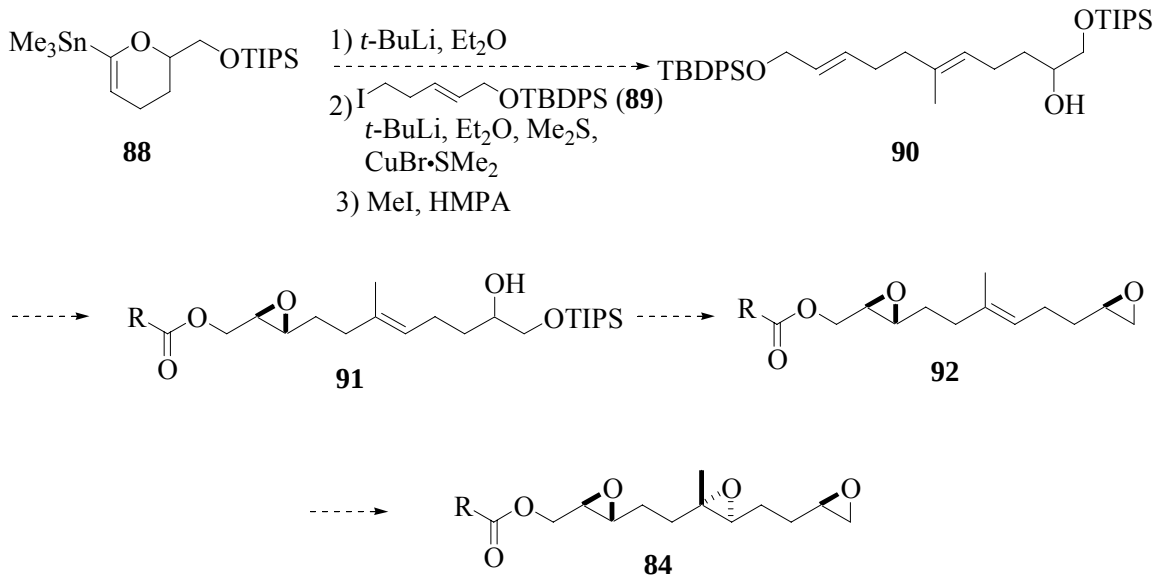


Figure 6: Expected mode of cyclization for triepoxides **84** and **85**.

4.1. Triepoxide Formation via a Key 1,2-Metallate Rearrangement

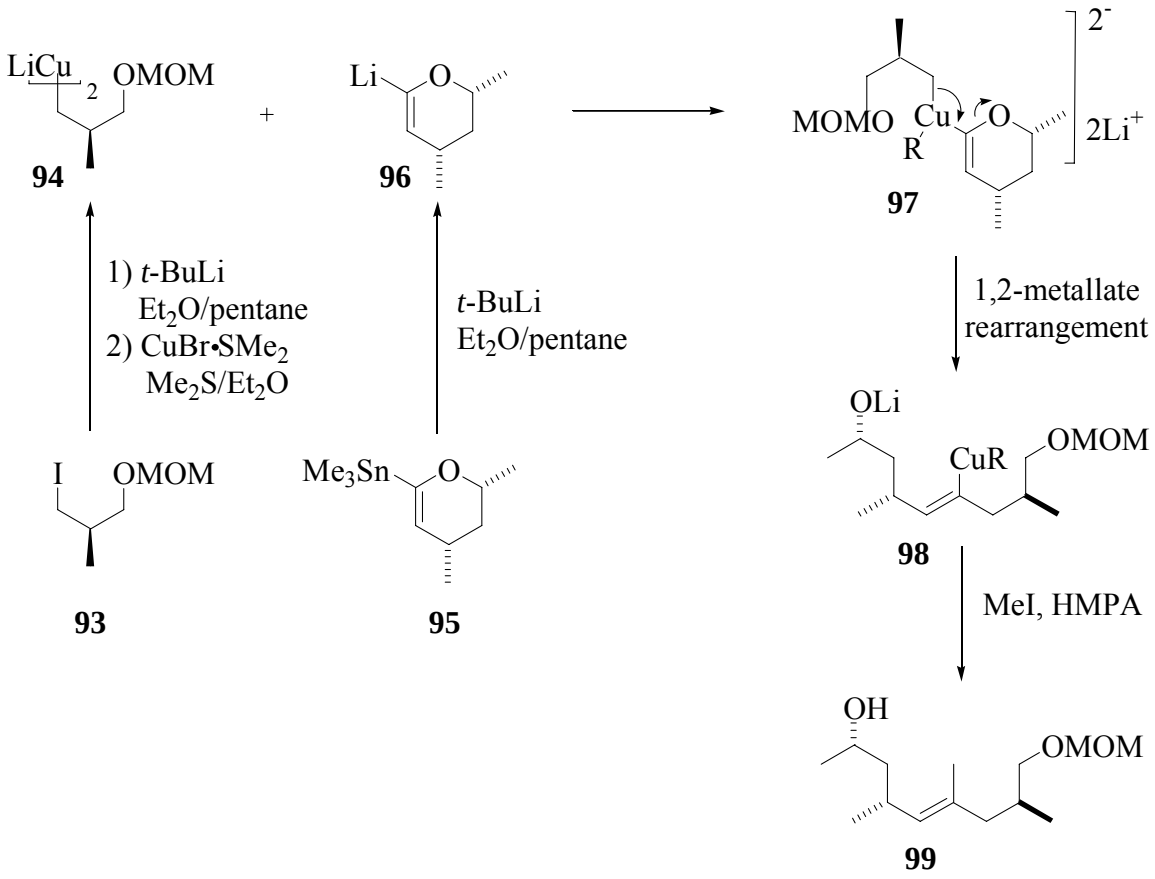
We devoted our initial efforts to the synthesis of triepoxide **84**. Instead of synthesizing **84** in a lengthy linear fashion, our goal was a convergent approach between enol stannane **88** and homoallylic iodide **89** via a key 1,2-metallate rearrangement (*vide infra*). With **90** in hand, one could envision arriving at our desired enantiomerically pure triepoxide by Sharpless asymmetric epoxidation of the C3-4 alkene followed by dihydroxylation of the terminal alkene, mesylation and subsequent ring closure to give **92**. The internal epoxide could plausibly also be set by a Sharpless asymmetric dihydroxylation followed by mesylation and base induced ring closure (Scheme 13).



Scheme 13: Proposed route to triepoxide **84**.

A 1,2-metallate rearrangement was selected as the key step in our efforts towards the synthesis of triepoxide **84** because it would generate the main scaffold of our desired triepoxide, including the methyl substituent at C6. Precedence for this transformation was found in the synthesis of manolide by Kocienski and coworkers.[25] In this synthesis, a 1,2-metallate rearrangement was employed between enol stannane **95** and alkyl iodide **93**. The proposed mechanism of Kocienski's 1,2-metallate rearrangement is shown in Scheme 14.

Specifically, this sequence involved the addition of lithiated enol ether **96** to homocuprate **94**. The resulting higher order cuprate **97** underwent a 1,2-metallate rearrangement with inversion of stereochemistry to give alkenylcuprate **98** which upon quenching with MeI gave **99** in 48% overall yield.

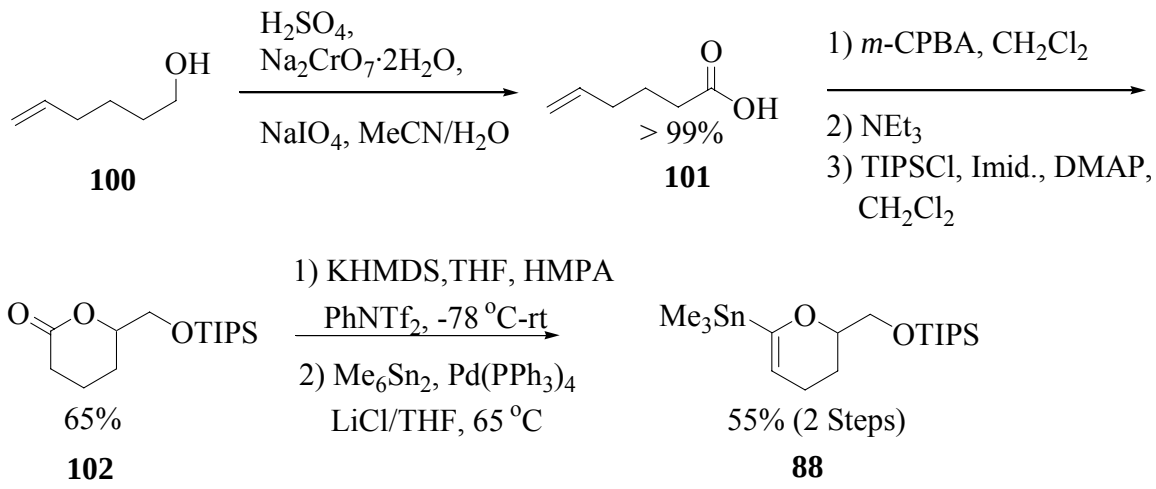


Scheme 14: Kocienski's 1,2-metallate rearrangement.

4.2. Synthesis of Enol Stannane and Homoallylic Iodide Compounds

4.2.1. Synthesis of Enol Stannane

For the preparation of enol stannane **88**, commercially available 5-hexen-1-ol was oxidized to **101** in quantitative yield. *m*-CPBA oxidation followed by NEt_3 quench and TIPS-protection yielded lactone **102** in 65% yield over 3 steps. To complete the sequence, lactone **102** was converted to its labile triflate. Unfortunately, triflate formation was not trivial and required much optimization to produce a ratio of triflate to starting material that was suitable to undergo stannation (Scheme 15).

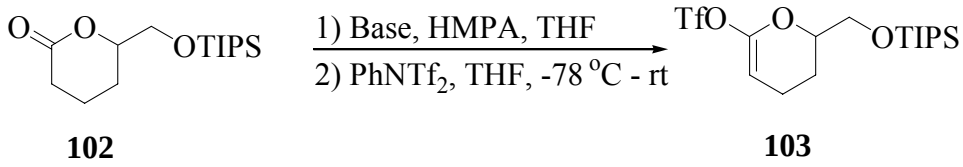


100 **101** **102** **88**

Scheme 15: Route to enol stannane **88**.

As Table 10 shows, it was found that subjecting **102** to 2.5 eq. KHMDS followed by warming to 0 °C for 30 min yieled a 8:1 ratio of triflate **103** to **102** With this triflate in hand, Pd(0)-catalyzed stannation yielded **88** in 55% yield over 2 steps.

Table 10: Optimization of triflate formation.

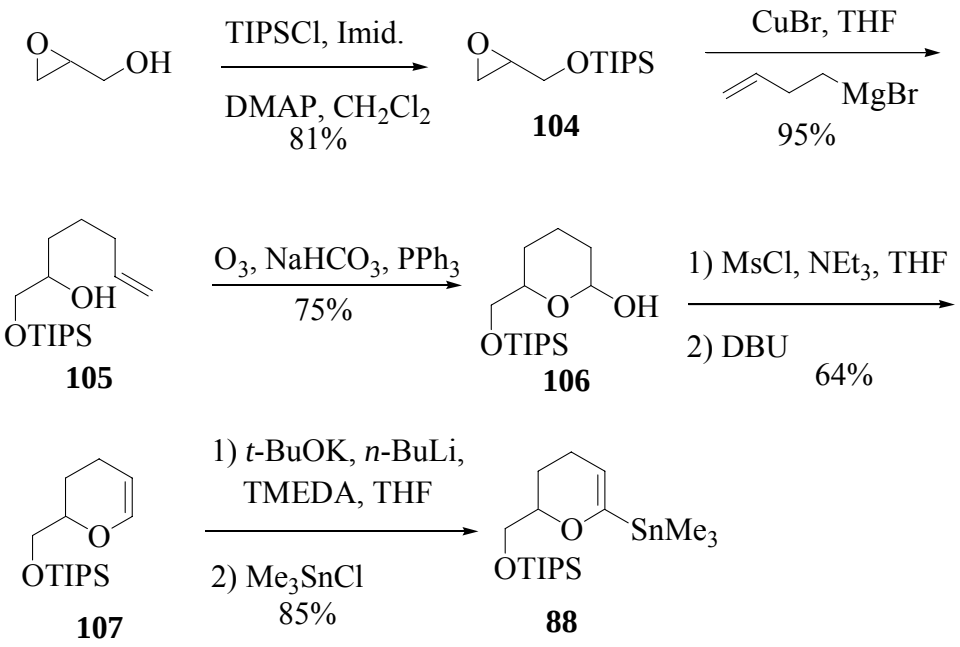


102 **103**

entry	Base	equiv.	temp. (°C)	ratio of **102:103**
1	LiHMDS	1.8	-78	5:1
2	NaHMDS	1.8	-78	3:1
3	KHMDS	1.8	-78	1:1.6
4	KHMDS	2.5	-78→-50	1:2
5	KHMDS	2.5	-78→-20	1:2.3
6	KHMDS	2.5	-78→ 0	1:8

4.2.2. Alternate Synthesis of Enol Stannane

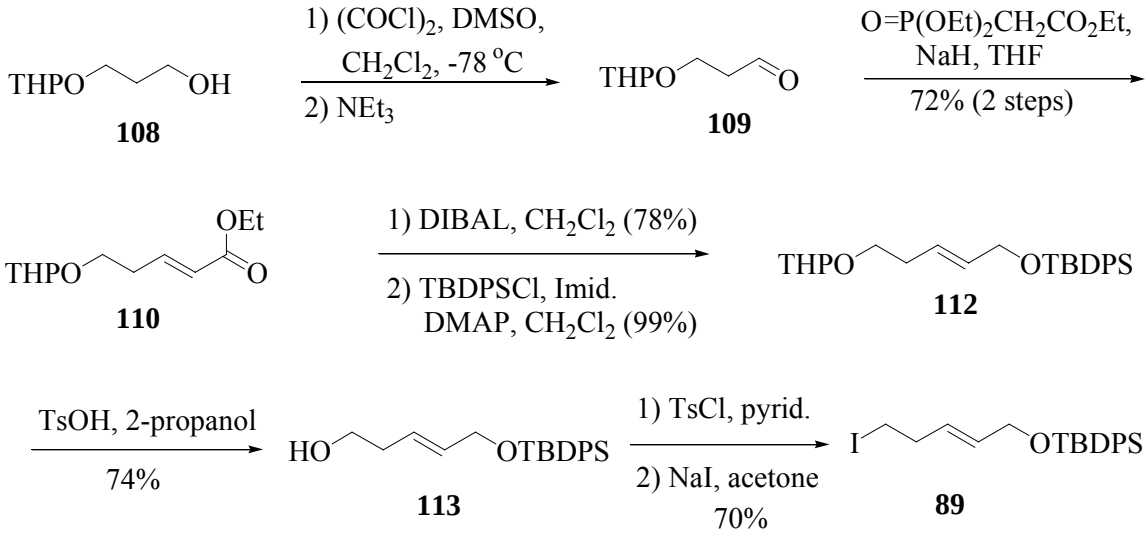
To circumvent the problems arising from triflate formation discussed in Section 4.2.1, an alternate route to **88** was explored. Following a procedure from Ley and coworkers,[26] **88** was easily synthesized from commercially available glycidol. TIPS protection gave **104**, and epoxide ring opening with but-3-enylmagnesium bromide and catalytic CuBr gave alkene **105** in high yield. Subsequent ozonolysis of **105** provided lactol **106** which was dehydrated via its corresponding mesylate to afford **107** in 70% yield over the two steps. Subjecting **107** to superbase conditions (*n*-BuLi-KOBut-TMEDA), followed by a Me_3SnCl quench afforded **88** in 85% yield (Scheme 16).



Scheme 16: Alternate route to enol stannane **88**.

4.2.3. Synthesis of Homoallylic Iodide

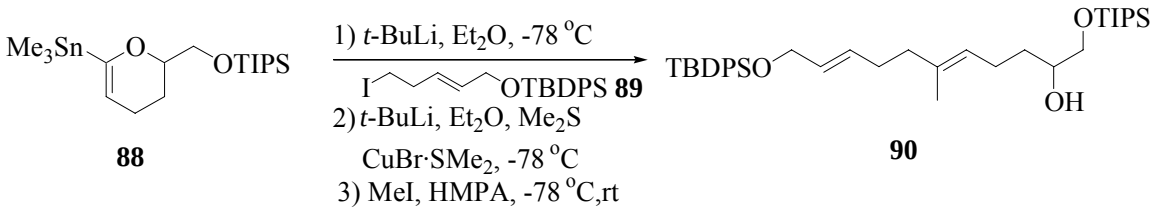
The synthesis of homoallylic iodide **89** started from commercially available 1,3-propanediol. Monoprotection with the THP group followed by Swern oxidation gave aldehyde **109** which underwent a Horner-Wadsworth-Emmons reaction to give ester **110**.[27] DIBAL-H reduction followed by TBDPS protection gave bis-protected **112**. Selective THP deprotection gave **113** according to a known procedure. Quantitative conversion of **113** to the corresponding *p*-toluenesulfonate ester, followed by a Finkelstein exchange provided the iodide **89** in 70% overall yield (Scheme 17).



Scheme 17: Synthesis of **89.**

4.3. Initial 1,2-Metallate Rearrangement

With compounds **88** and **89** in hand, a 1,2-metallate arrangement was attempted following Kocienski's published protocol (Scheme 18). Unfortunately, when this reaction was performed no desired diene **90** was isolated. The only observable product was hydrolyzed **89**.



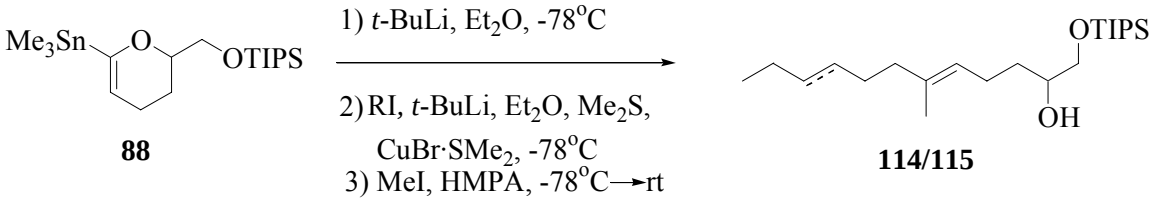
Scheme 18: Initial 1,2-metallate rearrangement.

Kocienski used a similar enol stannane in his rearrangement; therefore, the failure of our reaction was believed to lie in our alkyl iodide species. Kocienski used a simple MOM-proteced alkyl iodide, while we were using a more complex homoallylic iodide with a bulky TBDPS-protecting group. To test this hypothesis, 1,2-metallate rearrangement model studies were performed using simpler iodide compounds and/or less bulky protecting groups.

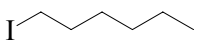
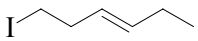
4.4. 1,2-Metallate Rearrangment Using Iodohexene and Iodo-3-hexene

Under similar 1,2-metallate rearrangement reaction conditions as discussed in Section 4.3, a 65% yield of **114** was obtained with iodohexane and a 34% yield of **115** was obtained with iodo-3-hexene (Table 11).

Table 11: 1,2-metallate rearrangement using iodohexene and iodo-3-hexene.

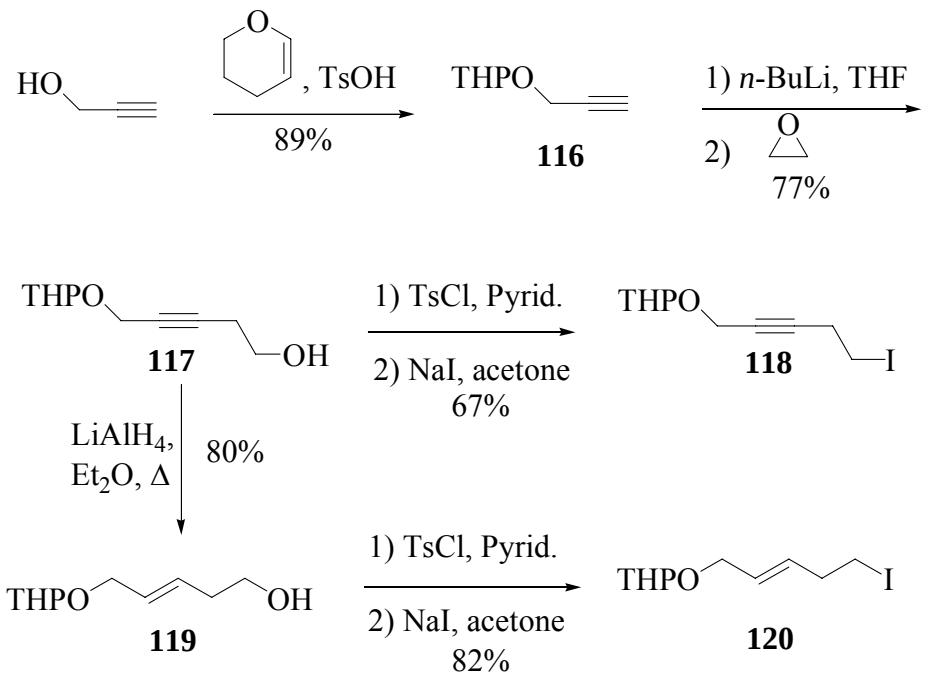


88 **114/115**

entry	RI	yield (%)	product
1		65	**114**
2		34	**115**

4.5. Synthesis of THP-Protected Iodo Alkene/Alkyne

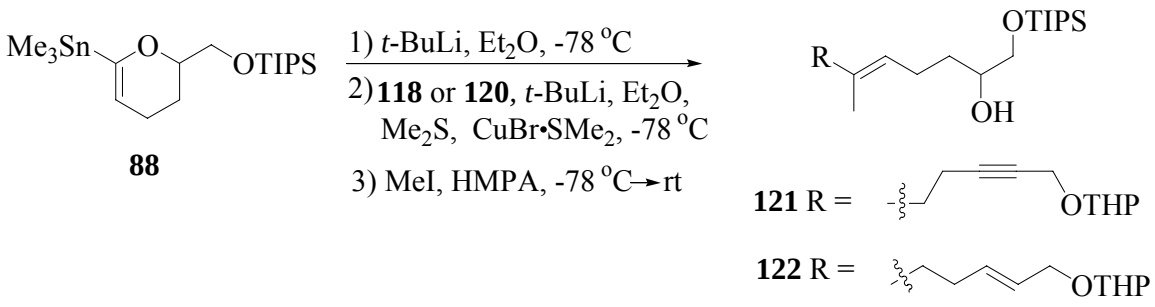
After performing the 1,2-metallate rearrangement on simpler iodides, we next tested the reaction using the less sterically encumbered THP protecting group. The synthesis of **118** and **120** started from commercially available propargyl aclohol which was protected with a THP group to give **116**. Deprotonation and subsequent reaction with oxirane gave **117**. Tosylation followed by nucleophilic displacement gave **118** in good yield.[28] Alternatively, **117** was reduced with $LiAlH_4$ to **119** which was converted to **120** via an S_N2-displacement (Scheme 19).[29]



Scheme 19: Synthesis of **118** and **120.**

4.5.1. 1,2-Metallate Rearrangement Using THP-Protected Iodo Alkene/Alkyne

Unfortunately, a 1,2-metallate rearrangement between enol stanne **88** and the THP-protected iodide species **118** and **120** synthesized in Section 4.5 resulted in no observable conversion (Scheme 20).



Scheme 20: 1,2-metallate rearrangement using compounds **118** and **120**.

5. CONCLUSIONS

After screening numerous electronically different enantiomerically pure diepoxides, the 2-furyl **58** and 2-benzofuryl **59** derived esters afforded the most promising results when exposed to 10 mol% Cp_2ZrCl_2 and 20 mol% $AgClO_4$. After optimization attempts, species **58** yielded 56% of tetrahydrofuran **68** and **69** in a 1.9:1 ratio of regioisomers while compound **59** resulted in a 46% yield of **70** and **71** as a 4.5:1 mixture of regioisomers.

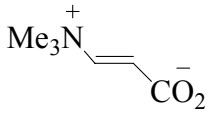
In spite of considerable efforts, the key 1,2-metallate rearrangement has yet to be performed successfully for the preparation of enantiomerically pure triepoxides. In model studies, this reaction progressed well between simple iodides and enol stannane **88**, but was unsuccessful when applied to slightly more complex alkyl iodides.

6. EXPERIMENTAL

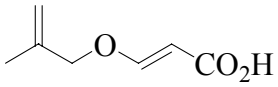
6.1. General

All moisture sensitive reactions were performed under an atmosphere of N_2 and all glassware was dried in an oven at 140 ^oC or flame dried under N_2 prior to use. THF and Et_2O were dried by distillation over Na/benzophenone under a nitrogen atmosphere. Dry CH_2Cl_2 was purified by filtration through activated alumina. Unless otherwise stated, solvents or reagents were used without further purification. Analytical thin layer chromatography (TLC) was performed on pre-coated silica gel 60 F-254 plates (particle size 0.040-0.055 mm, 230-400 mesh) and staining was accomplished with anisaldehyde or with a 254 nm UV lamp. NMR spectra were recorded at 300 MHz/75 MHz ($^1H/^{13}C$ NMR) in $CDCl_3$ using a BRUKER AVANCE 300 MHz spectrometer at 21 ^oC. Chemical shifts (δ) are reported in parts per million and the residual $CHCl_3$ peak was used as an internal standard. Data are reported as follows: chemical shift, multiplicity, integration and coupling constant. IR spectra were obtained on a Nicolet AVATAR 360 FT-IR E.S.P. spectrometer. Mass spectra were obtained on a VG-70-70 HF in the electron ionization mode.

6.2. Experimental Procedures

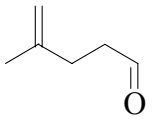


(*E*)–(Carboxyvinyl)trimethylammonium betaine (26). [22] This compound was prepared by a known procedure and its ^{1}H NMR was identical with the reported data: ^{1}H NMR (D_2O, DSS ref) 6.94 (d, 1 H, J = 13.9 Hz), 6.44 (d, 1 H, J = 13.9 Hz), 3.36 (s, 9 H).

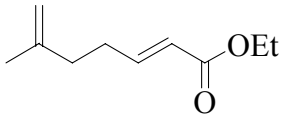


3-(2-Methylallyloxy)-acrylic acid (27). To a suspension of 6.84 g (0.171 mol) of 60% NaH in mineral oil in 90 mL of anhydrous THF was added a solution of 12.1 mL (0.143 mol) of β-methallyl alcohol in 180 mL of anhydrous THF via a dropping funnel over a period of 30 min. The reaction mixture was stirred for an additional 30 min at which point 25.0 g (0.194 mol) of **26** was added. The reaction mixture was heated to a gentle reflux for 15 h, cooled and slowly quenched with 600 mL of water and 220 mL of brine. The aqueous layer was washed with ether (x 3), and then acidified to pH 1.0 with approximately 21 mL of 6 N HCl. The aqueous layer was extracted with ether (x 3), dried ($MgSO_4$) and concentrated to afford 18.0 g (0.127 mol, 62%) of **27** a colorless solid which was used without further purification in the next step: ^{1}H NMR δ 9.53 (bs, 1 H), 7.67 (d, 1 H, J = 12.5 Hz), 5.25 (d, 1 H, J = 12.5 Hz), 5.03 (d, 2 H, J = 6.0 Hz), 4.33 (s, 2 H), 1.77 (s, 3 H) ; ^{13}C NMR δ 173.4, 163.9, 139.1, 113.9, 96.3, 74.8, 18.8; MS

(EI) *m/z* 142 (M^+, 9), 124 (30), 96 (58), 56 (100); HRMS (EI) *m/z* calcd for $C_7H_{10}O_3$ 142.0616, found 142.0622.

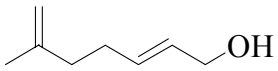


4-Methylpent-4-enal (28). To 18.0 g (0.127 mol) of crude **27** was added 2.0 mg (0.018 mmol) of neat hydroxyquinone, and the mixture was distilled under vacuum (120-122 ^oC /0.5 mmHg). The bath temperature was slowly increased to 200 ^oC and kept at 200 ^oC for 1 h. The product was collected in a receiver flask cooled with a dry ice-acetone bath to give 10.4 g (0.106 mol, 85%) of **28** as a colorless liquid which was used without further purification.

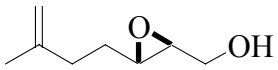


6-Methylhepta-2,6-dienoic acid ethyl ester (29). To a 0 ^oC solution of 2.81 g (0.177 mol) of 95% NaH in 137 mL of anhydrous THF was added 23.3 mL (0.177 mol) of triethylphosphonoacetate. The reaction mixture was stirred at 0 ^oC for 30 min and treated dropwise with 10.4 g (0.106 mol) of **28** over a period of 20 min. Stirring was continued at 0 ^oC for 1.5 h, before the mixture was quenched with H_2O. The aqueous phase was extracted with ether (x 3), dried ($MgSO_4$), concentrated and purified by chromatography on SiO_2 (40:1 hexanes/EtOAc) to give 11.3 g (0.0673 mol, 63%) of **29** as a light yellow liquid: IR (neat) 2980, 2936, 1722, 1654, 1314, 1267, 1153, 1043 cm^{-1}; ^1H NMR δ 6.96 (dt, 1 H, *J* = 15.6, 6.7 Hz), 5.84 (d, 1 H, *J* = 15.6 Hz), 4.73 (d, 2 H, *J* = 15.9 Hz), 4.19 (q, 2 H, *J* = 7.1 Hz), 2.39-2.31 (m, 2 H), 2.19-2.14 (m, 2 H), 1.73 (s, 3 H), 1.28 (t, 3 H, *J* = 7.1 Hz); ^{13}C NMR δ 166.1, 148.0, 143.7,

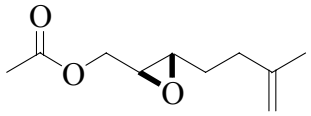
121.2, 110.4, 59.7, 35.6, 29.9, 22.0, 13.9; MS (EI) *m/z* 168 (M^+, 32), 122 (21), 95 (100), 94(74), 55 (83); HRMS (EI) *m/z* calcd for $C_{10}H_{16}O_2$ 168.1150, found 168.1148.



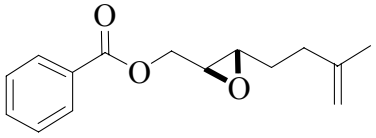
6-Methylhepta-2,6-dien-1-ol (30). To a solution of 150 mL of DIBAL (1.0 M in hexanes, 150.0 mmol) at -78 °C was added a solution of 11.3 g (67.4 mmol) of **29** in 87.0 mL of CH_2Cl_2. The reaction mixture was warmed to -55 °C for 30 min, then quenched at -78 °C using a 1 M aqueous solution of sodium potassium tartrate. The aqueous layer was extracted with CH_2Cl_2 (x 3), dried ($MgSO_4$), concentrated and purified by chromatography on SiO_2 (8:1 hexanes/EtOAc) to give 6.65 g (52.8 mmol, 78%) of **30** as a light yellow oil: IR (neat) 3324, 3075, 2932, 2853, 1649, 1446, 1374, 1007, 887 cm^{-1}; ^1H NMR δ 5.77-5.60 (m, 2 H), 4.73 (bs, 1 H), 4.69 (bs, 1 H), 4.10 (d, 2 H, *J* = 3.8 Hz), 2.25-2.05 (m, 4 H), 1.73 (s, 3 H), 1.37 (s, 1 H); ^{13}C NMR δ 144.9, 131.9, 129.1, 109.9, 63.0, 37.0, 30.1, 22.2; MS (EI) *m/z* 108 ($[M-H_2O]^+$, 45), 95 (75), 93 (100), 55 (95); HRMS (EI) *m/z* calcd for $C_8H_{14}O$ (M-H_2O) 108.0939, found 108.0936.



(2*R*,3*R*)-2,3-Epoxy-6-methylhept-6-en-1-ol (31).[24] This compound was prepared in 65% yield by a known procedure and its IR and ^1H NMR spectra were identical to the reported data: $[\alpha]_D$ +22.4 (*c* 1.00, $CHCl_3$); IR (neat) 3419, 2979, 2935, 2863, 1650, 1450, 1376, 1092, 1028, 886 cm^{-1}; ^1H NMR δ 4.76 (bs, 1 H), 4.72 (bs, 1 H), 3.90 (ddd, 1 H, *J* = 12.6, 5.6, 2.3 Hz), 3.61 (ddd, 1 H, *J* = 12.6, 6.6, 4.5 Hz), 2.99-2.94 (m, 2 H), 2.25-2.05 (m, 2 H), 1.82-1.68 (m, 2 H), 1.72 (s, 3 H).

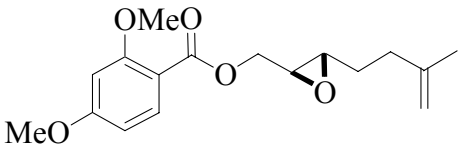


((2*S*,3*S*)-3-(3-Methylbut-3-enyl)ethyl)oxiran-2-yl)methyl acetate (33). A 0 ^{o}C solution of 200 mg (1.41 mmol) of **31** in 20 mL of anhydrous pyridine was treated dropwise with 1.64 mL (14.1 mmol) of acetic anhydride. The reaction mixture was stirred at ambient temperature for 3 h, quenched with saturated aqueous NH_4Cl, and the aqueous layer was extracted with CH_2Cl_2 (x 3). The combined organic extracts were washed with saturated aqueous $CuSO_4$ (x 3), dried ($MgSO_4$), concentrated and purified on SiO_2 (4:1 hexanes/EtOAc) to afford 236 mg (1.28 mmol, 92%) of **33** as a colorless oil: $[\alpha]_D$ +34.9 (*c* 1.05, $CHCl_3$); IR (neat) 3075, 2940, 1744, 1650, 1448, 1368, 1232, 1035, 973, 889 cm^{-1}; ^{1}H NMR δ 4.76 (bs, 1 H), 4.72 (bs, 1 H), 4.36 (dd, 1 H, *J* = 12.2, 3.2 Hz), 3.91 (dd, 1 H, *J* = 12.2, 6.3 Hz), 3.01-2.98 (m, 1 H), 2.88 (dt, 1 H, *J* = 5.6, 2.1 Hz), 2.19-2.10 (m, 2 H), 2.10 (s, 3 H), 1.76-1.69 (m, 2 H), 1.74 (bs, 3 H); ^{13}C NMR δ 170.0, 143.9, 110.1, 64.3, 55.6, 54.8, 33.3, 29.1, 21.8, 20.1; MS (EI) *m/z* 184 (M^+, 9), 166 (33), 115 (100), 81 (64), 67 (81), 55 (60); HRMS (EI) *m/z* calcd for $C_{10}H_{16}O_3$ 185.1177, found 185.1169.

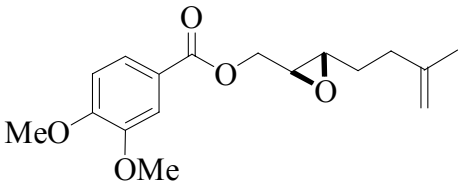


((2*S*,3*S*)-3-(3-Methylbut-3-enyl)ethyl)oxiran-2-yl)methyl benzoate (34). According to the procedure used for **33**, 205 mg (0.833 mmol, 60%) of **34** was obtained as a colorless oil: $[\alpha]_D$ +26.5 (*c* 1.26, $CHCl_3$); IR (neat) 2939, 1723, 1649, 1601, 1451, 1375, 1109, 1070, 1026, 889, 712 cm^{-1}; ^{1}H NMR δ 8.07 (d, 2 H, *J* = 7.1 Hz), 7.58 (t, 1 H, *J* = 7.2 Hz), 7.46 (t, 2 H, *J* = 7.2 Hz), 4.75 (s, 1 H), 4.73 (s, 1 H), 4.66 (dd, 1 H, *J* = 12.1, 3.2 Hz), 4.24 (dd, 1 H, *J* = 12.1, 6.4 Hz), 3.16-3.14 (m, 1 H), 3.00-2.96 (dt, 1 H, *J* = 5.6, 2.1 Hz), 2.19 (bt, 2 H, *J* = 7.4 Hz), 1.80-1.72 (m,

2 H), 1.75 (bs, 3 H); ^{13}C NMR δ 166.0, 144.2, 132.9, 129.5, 128.2, 110.5, 65.0, 56.5, 55.3, 33.7, 29.4, 22.2; MS (EI) *m/z* 246 (M^+, 6), 178 (58), 147 (66), 111 (83), 96 (91), 56 (100); HRMS (EI) *m/z* calcd for $C_{15}H_{18}O_3$ 246.1253, found 246.1251.

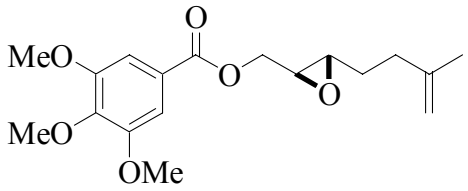


((2*S*,3*S*)-3-(3-Methylbut-3-enyl)ethyl)oxiran-2-yl)methyl 2,4-dimethoxybenzoate (35). According to the procedure used for **33**, 118 mg (0.386 mmol, 84%) of **35** was obtained as a light yellow oil: $[\alpha]_D$ +28.8 (*c* 1.3, $CHCl_3$); IR (neat) 3511, 2940, 1724, 1649, 1609, 1505, 1463, 1376, 1250, 1212, 1164, 1078, 1031, 889, 836, 769, 698 cm^{-1}; ^{1}H NMR δ 7.89 (d, 1 H, *J* = 7.8 Hz), 6.52-6.48 (m, 2 H), 4.75 (s, 1 H), 4.72 (s, 1 H), 4.56 (dd, 1 H, *J* = 12.3, 3.3 Hz), 4.13 (dd, 1 H, *J* = 12.3, 6.0 Hz), 3.89 (s, 3 H), 3.86 (s, 3 H), 3.13-3.09 (m, 1 H), 2.97 (dt, 1 H, *J* = 5.7, 2.1 Hz), 2.20-2.15 (m, 2 H) 1.76-1.71 (m, 2 H), 1.74 (bs, 3H); ^{13}C NMR δ 164.7, 164.2, 161.3, 144.1, 133.7, 111.3, 110.3, 104.3, 98.6, 64.1, 55.9, 55.6, 55.3, 55.1, 33.5, 29.3, 22.0; MS (EI) *m/z* 329 ($[M+Na]^+$, 100), 307 (27), 165 (25); HRMS (EI) *m/z* calcd for $C_{17}H_{22}O_5$ 329.1365, found 329.1364.

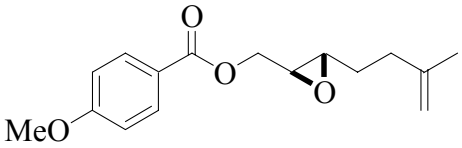


((2*S*,3*S*)-3-(3-methylbut-3-enyl)ethyl)oxiran-2-yl)methyl 3,4-dimethoxybenzoate (36). According to the procedure used for **33**, 90.0 mg (0.294 mmol, 42%) of **36** was obtained as a light yellow oil: $[\alpha]_D$ +24.3 (*c* 0.90, $CHCl_3$); IR (neat) 2938, 1712, 1649, 1600, 1514, 1417,

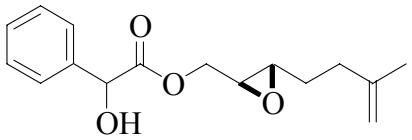
1270, 1176, 1134, 1025, 887, 823, 764, 729 cm^{-1}; ^1H NMR δ 7.72 (dd, 1 H, *J* = 8.5, 1.9 Hz), 7.56 (d, 1 H, *J* = 1.8 Hz), 6.90 (d, 1 H, *J* = 8.4 Hz), 4.76 (bs, 1 H), 4.73 (bs, 1 H), 4.61 (dd, 1 H, *J* = 12.2, 3.2 Hz), 4.14 (dd, 1 H, *J* = 12.2, 6.3 Hz), 3.95 (s, 3 H), 3.94 (s, 3 H), 3.15-3.11 (m, 1 H), 2.96 (dt, 1 H, *J* = 5.7, 2.1 Hz), 2.20-2.16 (m, 2 H), 1.79-1.70 (m, 2 H), 1.75 (bs, 3 H),^{13}C NMR δ 165.8, 152.9, 148.4, 144.1, 123.6, 121.9, 111.7, 110.4, 109.9, 64.9, 55.9, 55.7, 55.3, 33.6, 29.3, 22.1; MS (EI) *m/z* 329 ($[M+Na]^+$, 100), 307 (32), 165 (30); HRMS (EI) *m/z* calcd for $C_{17}H_{22}O_5$ 329.1365, found 329.1361.



((2*S*,3*S*)-3-(3-Methylbut-3-enyl)ethyl)oxiran-2-yl)methyl 3,4,5-trimethoxybenzoate (37). According to the procedure used for **33**, 540 mg (1.61 mmol, 70%) of **37** was obtained as a colorless oil: $[\alpha]_D$ +21.3 (*c* 1.0, $CHCl_3$); IR (neat) 2941, 1716, 1649, 1589, 1462, 1415, 1336, 1221, 1176, 1004, 888, 763, 732 cm^{-1}; ^1H NMR δ 7.32 (s, 2 H), 4.76 (s, 1 H), 4.73 (s, 1 H), 4.63 (dd, 1 H, *J* = 12.2, 2.9 Hz), 4.13 (dd, 1 H, *J* = 12.1, 6.3 Hz), 3.91 (s, 9 H), 3.14-3.11 (m, 1 H), 2.96-2.93 (m, 1 H), 2.21-2.16 (m, 2 H), 1.79-1.74 (m, 2 H), 1.74 (bs, 3 H); ^{13}C NMR δ 165.5, 152.6, 144.0, 142.1, 124.4, 110.4, 106.7, 65.1, 60.5, 55.9, 55.8, 55.2, 33.5, 29.3, 22.0; MS (EI) *m/z* 336 (M^+, 14), 267 (24), 212 (25), 195 (100), 109 (12); HRMS (EI) *m/z* calcd for $C_{18}H_{24}O_6$ 336.1572, found 336.1580.

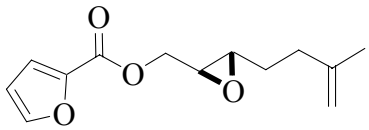


((2*S*,3*S*)-3-(3-Methylbut-3-enyl)ethyl)oxiran-2-yl)methyl 4-methoxybenzoate (38). According to the procedure used for **33**, 584 mg (2.11 mmol, 100%) of **38** was obtained as a light yellow oil: $[\alpha]_D$ +21.5 (*c* 1.2, $CHCl_3$); IR (neat) 3076, 2938, 1715, 1649, 1580, 1444, 1376, 1257, 1168, 1102, 1029, 889, 770, 728, 696, 614 cm^{-1}; ^1H NMR δ 8.02 (d, 2 H, *J* = 6.9 Hz), 6.92 (d, 2 H, *J* = 7.0 Hz), 4.76 (bs, 1 H), 4.73 (bs, 1 H), 4.58 (dd, 1 H, *J* = 12.1, 3.2 Hz), 4.14 (dd, 1 H, *J* = 12.4, 6.4 Hz), 3.97 (s, 3 H), 3.14-3.10 (m, 1 H), 2.96 (dt, 1 H, *J* = 5.6, 2.2 Hz) 2.21-2.16 (m, 2 H), 1.79-1.72 (m, 2 H), 1.74 (bs, 3 H); ^{13}C NMR δ 165.7, 163.3, 144.2, 131.6, 121.9, 113.4, 110.4, 64.7, 55.9, 55.4, 55.2, 33.6, 29.4, 22.1; MS (EI) *m/z* 276 (M^+, 19), 258 (25), 207 (45), 152 (24), 135 (100), 92 (24); HRMS (EI) *m/z* calcd for $C_{16}H_{20}O_4$ 276.1361, found 276.1348.

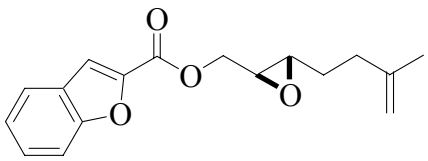


((2*S*,3*S*)-3-(3-Methylbut-3-enyl)ethyl)oxiran-2-yl)methyl 2-hydroxy-2-phenylacetate (39). According to the procedure used for **33**, 470 mg (1.70 mmol, 55%) of **39** was obtained as a light yellow oil: $[\alpha]_D$ +24.7 (*c* 1.0, $CHCl_3$); IR (neat) 3466, 3070, 2938, 1743, 1649, 1602, 1494, 1375, 1182, 1067, 1028, 969, 888, 732, 698 cm^{-1}; ^1H NMR δ 7.45-7.31 (m, 5 H), 5.24-5.20 (m, 1 H), 4.74 (bs, 1 H), 4.67 (bs, 1 H), 4.45-4.38 (m, 1 H), 4.07 (dd, 1 H, *J* = 12.1, 5.9 Hz), 3.40 (bs, 1 H), 2.96-2.87 (m, 1 H), 2.75-2.70 (m, 1 H), 2.11-2.05 (m, 2 H), 1.72 (s, 3 H), 1.68-1.61 (m, 2 H);

^{13}C NMR δ 173.1, 144.1, 137.9, 128.4, 126.4, 110.4, 72.7, 65.6, 65.3, 55.8, 55.7, 54.8, 54.7, 33.5, 29.2, 22.1; MS (EI) *m/z* 277 ([M+1]$^+$, 0.1), 142 (15), 107 (100), 79 (63); HRMS (EI) *m/z* calcd for $C_{16}H_{20}O_4$ 276.1362, found 276.1344.

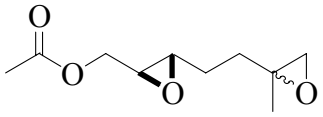


((2*S*,3*S*)-3-(3-methylbut-3-enyl)ethyl)oxiran-2-yl)methyl furan-2-carboxylate (40). According to the procedure used for **33**, 564 mg (2.39 mmol, 95%) of **40** was obtained as a colorless oil: $[\alpha]_D$ +13.0 (*c* 1.1, $CHCl_3$); IR (neat) 2940, 1728, 1650, 1580, 1474, 1397, 1294, 1231, 1180, 1120, 1015, 963, 885, 763 cm^{-1}; ^{1}H NMR δ 7.60 (d, 1 H, *J* = 1.6 Hz), 7.22 (d, 1 H, *J* = 2.9 Hz), 6.53-6.52 (m, 1 H), 4.75 (bs, 1 H), 4.71 (bs, 1 H), 4.57 (dd, 1 H, *J* = 12.2, 3.3 Hz), 4.15 (dd, 1 H, *J* = 18.3, 6.3 Hz), 3.12-3.08 (m, 1 H), 2.94 (dt, 1 H, *J* = 5.6, 1.9 Hz), 2.20-2.15 (m, 2 H), 1.79-1.71 (m, 2 H), 1.74 (s, 3 H); ^{13}C NMR δ 157.8, 146.2, 143.8, 118.0, 117.9, 111.6, 110.2, 64.6, 55.7, 54.8, 33.3, 29.1, 21.9; MS (EI) *m/z* 236 (M$^+$, 14), 218 (36), 180 (66), 95 (100); HRMS (EI) *m/z* calcd for $C_{13}H_{16}O_4$ 236.1095 found 236.2691.



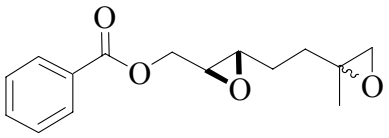
((2*S*,3*S*)-3-(3-Methylbut-3-enyl)ethyl)oxiran-2-yl)methyl benzofuran-2-carboxylate (41). To a solution of 1.00 g (7.04 mmol) of **31** in 23.5 mL of CH_2Cl_2 was added 3.42 g (21.1 mmol) of benzo[b]furan-2-carboxylic acid, 2.18 g (10.6 mmol) of DCC and 86.0 mg (0.704 mmol) of DMAP. The reaction mixture was stirred at rt for 3 h, quenched with a saturated solution of

NH_4Cl and filtered through a plug of celite. The aqueous phase was extracted with CH_2Cl_2 (x 3), dried ($MgSO_4$), concentrated and purified by chromotography on SiO_2 (10:1 hexanes/EtOAc) to give 1.90 g (6.64 mmol, 94%) of **41** as a colorless oil: $[\alpha]_D$ +26.5 (*c* 1.26, $CHCl_3$); IR (neat) 3071, 2938, 1793, 1731, 1650, 1614, 1593, 1446, 970, 885, 749 cm^{-1}; ^1H NMR δ 7.70 (d, 1 H, *J* = 8.0 Hz), 7.61-7.58 (m, 2 H), 7.47 (app. t, 1 H, *J* = 7.2 Hz), 7.35-7.26 (m, 1 H), 4.76 (s, 1H), 4.73 (s, 1 H), 4.66 (dd, 1 H, *J* = 12.1, 3.2 Hz), 4.24 (dd, 1 H, *J* = 12.1, 6.4 Hz), 3.16-3.14 (m, 1 H), 3.00-2.96 (m, 1 H), 2.19 (t, 2 H, *J* = 7.4 Hz), 1.80-1.75 (m, 2 H), 1.75 (s, 3 H); ^{13}C NMR δ 158.8, 155.4, 144.6, 144.0, 127.5, 126.5, 123.5, 122.6, 114.1, 111.9, 110.4, 65.2, 55.9, 54.8, 33.5, 29.2, 22.0; MS (EI) *m/z* 286 (M^+, 12), 217 (65), 162 (42), 145 (100), 89 (41); HRMS (EI) *m/z* calcd for $C_{17}H_{18}O_4$ 286.1205, found 286.1204.

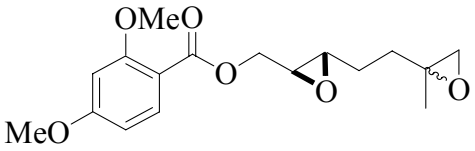


((2*S*,3*S*)-3-(2-(2-Methyloxirane-2-yl)ethyl)oxiran-2-yl)methyl acetate (42). To a solution of 1.00 g (5.41 mmol) of **33** in 20.0 mL of CH_2Cl_2 was added 1.96 g (7.97 mmol) of 70% *m*-CPBA at 0 ^oC. The reaction mixture was stirred at rt for 3 h, and quenched with an aqueous solution of 20% $Na_2S_2O_4$. The aqueous layer was extracted with CH_2Cl_2 (x 3), saturated aqueous $NaHCO_3$ (x 3), dried ($MgSO_4$), concentrated and purified by chromatography on SiO_2 (7:3 hexanes/EtOAc) to afford 837 mg (4,17 mmol, 77%) of **42** as a colorless oily mixture of diastereomers (1:1): IR (neat) 2950, 1450, 1389, 1232, 1147, 972, 804, 729 cm^{-1}; ^1H NMR δ 4.39-4.33 (m, 1 H), 3.93 (dd, 1 H, *J* = 12.2, 6.2 Hz), 3.00-2.97 (m, 1 H), 2.91-2.88 (m, 1 H), 2.64-2.59 (m, 2 H), 2.10 (s, 3 H), 1.79-1.59 (m, 4 H), 1.34, 1.33 (2s, 3 H); ^{13}C NMR δ 170.1,

64.1, 55.8, 55.7, 55.5, 54.9, 54.8, 53.2, 52.9, 32.5, 32.0, 26.9, 26.7, 20.6, 20.3; MS (EI) *m/z* 200 (M^+, 9), 152 (34), 83 (53), 69 (100), 56(89); HRMS (EI) *m/z* calcd for $C_{10}H_{16}O_4$ 200.1049, found 200.1058.

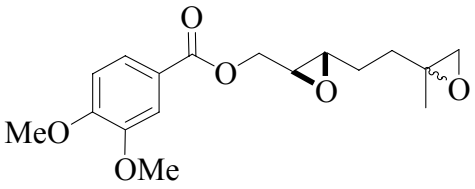


((2*S*,3*S*)-3-(2-(2-Methyloxirane-2-yl)ethyl)oxiran-2-yl)methyl benzoate (43). According to the procedure used for **42**, 170 mg (0.699 mmol, 78%) of **43** was obtained as a colorless oily mixture of diastereomers (1:1): IR (neat) 2950, 1720, 1601, 1584, 1390, 1274, 1070, 897, 805, 713 cm^{-1}; ^1H NMR δ 8.00 (d, 2 H, *J* = 7.5 Hz), 7.58 (t, 1 H, *J* = 7.3 Hz), 7.45 (t, 2 H, *J* = 7.8 Hz)4.65-4.58 (m, 1 H), 4.19 (dd, 1 H, *J* = 12.2, 6.1 Hz), 3.16-3.11 (m, 1 H), 2.98-2.96 (m, 1 H), 2.65-2.59 (m, 2 H), 1.81-1.64 (m, 4 H), 1.34, 1.33 (2s, 3 H); ^{13}C NMR δ 165.9, 132.9, 129.4, 128.2, 64.8, 56.0, 55.9, 55.8, 55.2, 55.1, 53.6, 53.2, 32.6, 32.2, 27.1, 26.9, 20.7, 20.5; MS (EI) *m/z* 262 (M^+, 12), 122 (25), 105 (75); HRMS (EI) *m/z* calcd for $C_{15}H_{18}O_4$ 262.1205, found 262.1206.

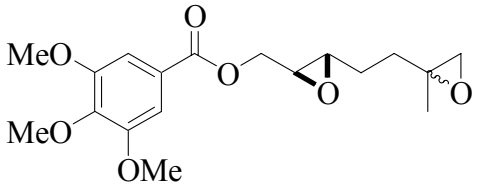


((2*S*,3*S*)-3-(2-(2-Methyloxirane-2-yl)ethyl)oxiran-2-yl)methyl 2,4-dimethoxybenzoate (44). According to the procedure used for **42**, 57.0 mg (0.177 mmol, 46%) of **44** was obtained as a colorless oily mixture of diastereomers (1:1): IR (neat) 2937, 1712, 1599, 1514, 1452, 1417, 1346, 1271, 1221, 1176, 1134, 1107, 1023, 877, 764, 727 cm^{-1}; ^1H NMR δ 7.89 (d, 1 H, *J* = 9.1

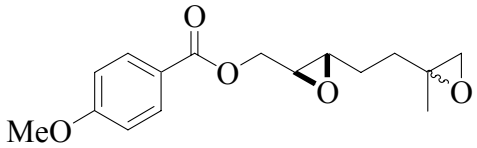
Hz), 6.52-6.48 (m, 2 H), 4.53 (dt, 1 H, *J* = 12.3, 3.7 Hz), 4.15 (dd, 1 H, *J* = 12.3, 5.8 Hz), 3.89 (s, 3 H), 3.86 (s, 3 H), 3.13-3.08 (m, 1 H), 2.98-2.95 (m, 1 H), 2.65-2.58 (m, 2 H) 1.80-1.62 (m, 4 H), 1.33, 1.32 (2s, 3H,); ^{13}C NMR δ 165.1, 164.6, 161.7, 134.1, 111.6, 104.7, 98.9, 64.3, 56.3, 56.2, 55.9, 55.7, 55.6, 55.0, 53.9, 53.6, 33.0, 32.6, 27.5, 27.3, 21.1, 20.8; MS (EI) *m/z* 322 (M^+, 10), 182 (14), 165 (100); HRMS (EI) *m/z* calcd for $C_{17}H_{22}O_6$ 322.1416, found 322.1426.



((2*S*,3*S*)-3-(2-(2-Methyloxirane-2-yl)ethyl)oxiran-2-yl)methyl 3,4-dimethoxybenzoate (45). According to the procedure used for **42**, 48.4 mg (0.150 mmol, 52%) of **45** was obtained as a colorless oily mixture of diastereomers (1:1): IR (neat) 2944, 1723, 1608, 1505, 1463, 1390, 1249, 1164, 1080, 1029, 896, 836, 770, 699 cm^{-1}; ^{1}H NMR δ 7.71 (dd, 1 H, *J* = 8.4, 1.9 Hz), 7.55 (d, 1 H, *J* = 1.8 Hz), 6.89 (d, 1 H, *J* = 8.5 Hz), 4.63-4.54 (m, 1 H), 4.14 (dd, 1 H, *J* = 12.2, 6.3 Hz), 3.94 (s, 3 H), 3.93 (s, 3 H), 3.15-3.09 (m, 1 H), 2.98-2.94 (m, 1 H), 2.64-2.57 (m, 2 H), 1.79-1.61 (m, 4 H), 1.33, 1.32 (2s, 3 H); ^{13}C NMR δ 165.9, 153.1, 148.5, 123.7, 122.0, 111.9, 110.1, 64.8, 56.1, 55.9, 55.6, 53.8, 53.4, 32.8, 32.4, 27.3, 27.0, 20.9, 20.6; HRMS (ESI) *m/z* calcd for $C_{17}H_{22}O_6Na$ (M+Na) 345.1314, found 345.1306.

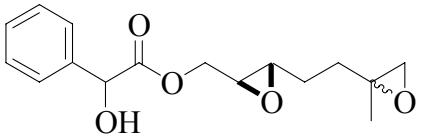


((2*S*,3*S*)-3-(2-(2-Methyloxirane-2-yl)ethyl)oxiran-2-yl)methyl 3,4,5 trimethoxybenzoate (46). According to the procedure used for **42**, 453 mg (1.29 mmol, 80%) of **46** was obtained as a colorless oily mixture of diastereomers (1:1): IR (neat) 2942, 1716, 1589, 1415, 1336, 1220, 1128, 1002, 864, 764, 732, 675 cm^{-1}; ^{1}H NMR δ 7.32 (s, 2 H), 4.63 (dt, 1 H, *J* = 12.2, 3.3 Hz), 4.15 (dd, 1 H, *J* = 12.3, 6.5 Hz), 3.91 (s, 9 H), 3.15-3.10 (m, 1 H), 2.96-2.93 (m, 1 H), 2.64-2.58 (m, 2 H), 1.80-1.62 (m, 4 H), 1.33, 1.32 (2s, 3 H); ^{13}C NMR δ 165.8, 152.8, 142.2, 124.5, 106.8, 65.2, 60.7, 56.1, 55.4, 53.7, 53.3, 32.7, 32.3, 27.2, 26.9, 20.9, 20.6; MS (EI) *m/z* 352 (M^{+}, 37), 212 (40), 195 (100), 109 (7); HRMS (EI) *m/z* calcd for $C_{18}H_{24}O_7$ 352.1522, found 352.1509.

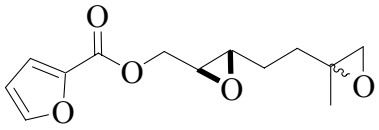


((2*S*,3*S*)-3-(2-(2-Methyloxirane-2-yl)ethyl)oxiran-2-yl)methyl 4-methoxybenzoate (47). According to the procedure used for **42**, 270 mg (0.921 mmol, 44%) of **47** was obtained as a light yellow oily mixture of diastereomers (1:1): IR (neat) 2936, 1716, 1606, 1580, 1455, 1389, 1316, 1258, 1169, 1028, 897, 849, 770, 735, 697, 614 cm^{-1}; ^{1}H NMR δ 8.02 (d, 2 H, *J* = 7.0 Hz), 6.92 (d, 2 H, *J* = 8.9 Hz), 4.61-4.54 (m, 1 H), 4.16 (ddd, 1 H, *J* = 11.4, 6.2, 0.8 Hz), 3.86 (s, 3 H), 3.14-3.08 (m, 1 H), 2.98-2.93 (m, 1 H), 2.94-2.58 (m, 2 H), 1.79-1.63 (m, 4 H), 1.33, 1.32 (2s, 3 H) ; ^{13}C NMR δ 165.3, 163.1, 131.2, 121.6, 113.2, 64.3, 55.7, 55.6, 55.6, 55.5, 55.1, 55.0, 54.9,

53.2, 52.9, 32.4, 32.0, 26.9, 26.7, 20.5, 20.3; MS (EI) *m/z* 292 (M^+, 6), 152 (37), 135 (100), 92 (17), 77 (23), HRMS (EI) *m/z* calcd for $C_{16}H_{20}O_5$ 292.1311, found 292.1318.

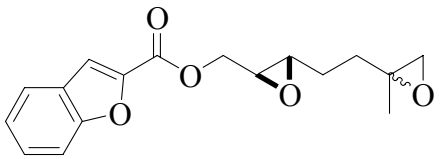


((2*S*,3*S*)-3-(2-(2-Methyloxirane-2-yl)ethyl)oxiran-2-yl)methyl 2-hydroxy-2-phenylacetate (48). According to the procedure used for **42**, 282 mg (0.966 mmol, 57%) of **48** was obtained as a colorless oily mixture of diastereomers (1:1): IR (neat) 3454, 3033, 2930, 1743, 1494, 1453, 1391, 1181, 1096, 1067, 1028, 984, 898, 787, 732, 699 cm^{-1}; ^1H NMR δ 7.45-7.32 (m, 5 H), 5.27 (d, 1 H, *J* =5.7 Hz), 4.44-4.38 (m, 1 H), 4.15- 4.02 (m, 1 H), 3.45-3.34 (m, 1 H), 2.98-2.86 (m, 1 H), 2.74-2.70 (m, 1 H), 2.60-2.56 (m, 2 H), 1.72-1.51 (m, 4 H), 1.31, 1.30, 1.29 (3s, 3 H); ^{13}C NMR δ 172.6, 137.9, 128.2, 126.2, 72.5, 64.9, 64.7, 56.0, 55.9, 55.5, 55.4, 54.6, 53.4, 53.0, 32.3, 31.9, 26.7, 26.5, 20.5, 20.2; MS (EI) *m/z* 292 (M^+, 33), 185 (19), 107 (100), 79 (78); HRMS (EI) *m/z* calcd for $C_{16}H_{20}O_5$ 292.1311, found 292.1312.

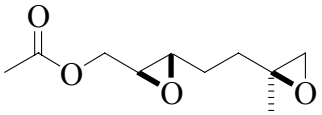


((2*S*,3*S*)-3-(2-(2-Methyloxirane-2-yl)ethyl)oxiran-2-yl)methyl furan-2-carboxylate (49). According to the procedure used for **42**, 385 mg (1.53 mmol, 64%) of **49** was obtained as a yellow oily mixture of diastereomers (1:1): IR (neat) 3138, 2930, 1723, 1580, 1474, 1396, 1328, 1294, 1231, 1179, 1119, 1015, 963, 884, 762 cm^{-1}; ^1H NMR δ 7.60 (d, 1 H, *J* = 1.6 Hz), 7.22 (d, 1 H, *J* = 3.5 Hz), 6.52 (dd, 1 H, *J* = 3.5, 1.7 Hz), 4.57 (ddd, 1 H, *J* = 12.2, 6.0, 3.4 Hz), 4.18 (ddd, 1 H, *J* = 12.2, 6.0, 1.6 Hz), 3.11-3.05 (m, 1 H), 3.00-2.92 (m, 1 H), 2.64-2.56 (m, 2 H), 1.79-1.61

(m, 4 H), 1.33, 1.32 (2s, 3 H); ^{13}C NMR δ 158.3, 146.7, 144.2, 118.6, 112.0, 64.9, 56.4, 56.3, 56.2, 55.4, 55.3, 53.9, 53.6, 32.9, 32.5, 27.4, 27.1, 21.0, 20.8; MS (EI) *m/z* 252 (M^+, 15), 180 (45), 164 (93), 95 (100); HRMS (EI) *m/z* calcd for $C_{13}H_{16}O_5$ 252.0998, found 252.1000.

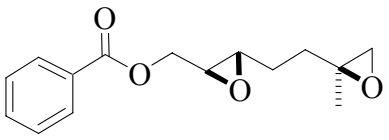


((2*S*,3*S*)-3-(2-(2-Methyloxirane-2-yl)ethyl)oxiran-2-yl)methyl benzofuran-2-carboxylate (50). According to the procedure used for **42**, 1.24 g (4.11 mmol, 62%) of **50** was obtained as a colorless oily mixture of diastereomers (1:1): IR (neat) 2951, 1731, 1613, 1564, 1476, 1447, 1390, 1259, 1096, 970, 839, 751 cm^{-1}; ^{1}H NMR δ 7.73 (d, 1 H, *J* = 12.2 Hz), 7.62-7.59 (m, 2 H), 7.50-7.45 (m, 1 H), 7.36-7.30 (m, 1 H), 4.67 (ddd, 1 H, *J* = 9.6, 6.1, 3.5 Hz), 4.26 (ddd, 1 H, *J* = 12.1, 6.0, 1.4 Hz), 3.18-3.13 (m, 1 H), 3.00-2.97 (m, 1 H), 2.66-2.60 (m, 2 H), 1.81-1.62 (m, 4 H), 1.35, 1.34 (2s, 3 H); ^{13}C NMR δ 158.8, 155.4, 144.6, 144.0, 127.5, 126.5, 123.6, 122.6, 114.2, 112.0, 112.0, 65.1, 55.9, 55.8, 54.9, 54.8, 53.5, 53.2, 32.5, 32.1, 27.0, 26.7, 20.7, 20.4 29.2, 22.0; MS (EI) *m/z* 302 (M^+, 9), 162 (49), 145 (100), 89 (50); HRMS (EI) *m/z* calcd for $C_{17}H_{18}O_5$ 302.1154, found 302.1147.



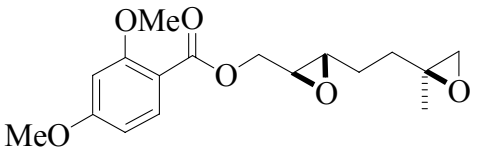
((2*S*,3*S*)-3-(2-((*S*)-2-Methyloxirane-2-yl)ethyl)oxiran-2-yl)methyl acetate (51). To a solution of 1.00 g (5.41 mmol) of **42** in 2.05 mL of TBME was added 52.0 mg (0.0820 mmol) of (1*R*,2*R*)-(-)-[1,2-cyclohexanediamino-N,N'-bis(3,5-di-*t*-butylsalicylidene)]chromium(III) chloride (**60**). The resulting brown mixture was stirred for 5 min at rt, cooled to 0 °C and treated with 0.180 mL

(2.97 mmol) of 2-propanol and 0.325 mL (2.97 mmol) of $TMSN_3$. The reaction mixture was stirred at rt for 6 h, concentrated and purified by chromatography on SiO_2 (4:1 hexanes/EtOAc) to give 310 mg (1.68 mmol) of **51** and azide as a orange oil (2.60:1). To the crude mixture was added 24 mg (0.0947 mmol) of Pd/C followed by 4.7 mL of MeOH. The reaction mixture was stirred under an atmosphere of H_2 at rt for 2 h, before being filtered through a pad of celite. The filtrate was concentrated and purified by chromatography on SiO_2 (4:1 hexanes/EtOAc) to afford 290 mg (1.57 mmol, 29%) of **51** as a colorless oil and single diastereomer: $[\alpha]_D$ +25.6 (*c* 2.3, $CHCl_3$); IR (neat) 2933, 1743, 1450, 1369, 1232, 1036, 973, 885, 729, 699, 606 cm^{-1}; ^1H NMR δ 4.34 (dd, 1 H, *J* = 12.2, 3.3 Hz), 3.92 (dd, 1 H, *J* = 12.2, 6.2 Hz), 3.01-2.95 (m, 1 H), 2.90-2.87 (m, 1 H), 2.63-2.58 (m, 2 H), 2.09 (s, 3 H), 1.74-1.63 (m, 4 H), 1.32 (s, 3 H); ^{13}C NMR δ 170.1, 64.4, 56.2, 56.0, 55.9, 55.2, 53.4, 32.3, 26.9, 20.6; MS (EI) *m/z* 201 ($[M+1]^+$, 5), 187 (25), 97 (62), 83 (63), 69 (100), 56 (92); HRMS (EI) *m/z* calcd for $C_{10}H_{16}O_4$ 200.1049, found 200.1055.

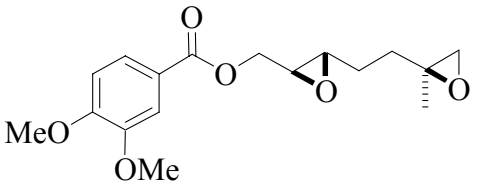


((2*S*,3*S*)-3-(2-((*S*)-2-Methyloxirane-2-yl)ethyl)oxiran-2-yl)methyl benzoate (52). According to the procedure used for **51**, 23.2 mg (0.089 mmol, 21%) of **52** was obtained as a colorless oil and single diastereomer: $[\alpha]_D$ +11.1 (*c* 1.0, $CHCl_3$); IR (neat) 2933, 1743, 1450, 1369, 1232, 973, 885, 729, 699, 642, 606 cm^{-1}; ^1H NMR δ 8.07 (d, 2 H, *J* = 7.1 Hz), 7.58 (t, 1 H, *J* = 7.7 Hz), 7.45 (t, 2 H, *J* = 7.7 Hz), 4.61 (dd, 1 H, *J* = 12.2, 3.3 Hz), 4.20 (dd, 1 H, *J* = 12.2, 6.1 Hz), 3.14-3.11 (m, 1 H), 3.00-2.97 (m, 1 H), 2.64, 2.60 (AB, 2 H, *J* = 4.7 Hz), 1.78-1.61 (m, 4 H), 1.34 (s, 3 H); ^{13}C NMR δ 166.3, 133.2, 129.7, 128.4, 64.9, 56.2, 56.1, 55.5, 53.6, 32.5, 27.1, 21.0; MS

(EI) *m/z* 262 (M^+, 21), 139 (19), 105 (55), 77 (100), 69 (37); HRMS (EI) *m/z* calcd for $C_{15}H_{18}O_4$ 262.1205, found 262.1210.

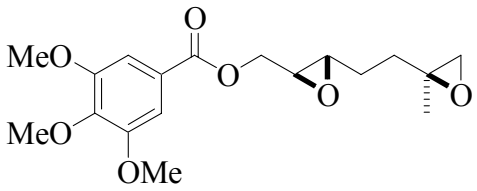


((2*S*,3*S*)-3-(2-((*S*)-2-Methyloxirane-2-yl)ethyl)oxiran-2-yl)methyl 2,4-dimethoxybenzoate (53). According to the procedure used for **51**, 95.0 mg (0.296 mmol, 19%) of **53** was obtained as a colorless oil and single diastereomer: $[\alpha]_D$ +9.7 (*c* 0.37, $CHCl_3$); ^{1}H NMR δ 7.90 (d, 1 H, *J* = 9.1 Hz), 6.55-6.48 (m, 2 H), 4.53 (dd, 1 H, *J* = 12.2, 3.4 Hz), 4.16 (dd, 1 H, *J* = 12.2, 6.2 Hz), 3.90 (s, 3 H), 3.87 (s, 3 H), 3.13-3.11 (m, 1 H), 2.98-2.95 (m, 1 H), 2.64, 2.60 (AB, 2 H, *J* = 4.7 Hz), 1.81-1.61 (m, 4 H), 1.34 (s, 3 H); MS (EI) *m/z* 322 (M^+, 38), 182 (52), 165 (100), 97 (32), 69 (39); HRMS (EI) *m/z* calcd for $C_{17}H_{22}O_6$ 322.1411, found 322.1416.

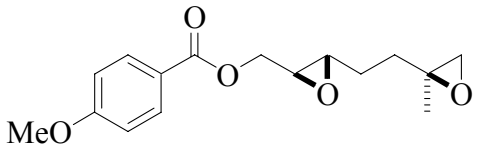


((2*S*,3*S*)-3-(2-((*S*)-2-Methyloxirane-2-yl)ethyl)oxiran-2-yl)methyl 3,4-dimethoxybenzoate (54). According to the procedure used for **51**, 160 mg (0.496 mmol, 32%) of **54** was obtained as a colorless oil and single diastereomer: $[\alpha]_D$ +14.7 (*c* 0.17, $CHCl_3$); ^{1}H NMR δ 7.71 (dd, 1 H, *J* = 8.4, 1.9 Hz), 7.55 (d, 1 H, *J* = 1.9 Hz), 6.90 (d, 1 H, *J* = 8.5 Hz), 4.60 (dd, 1 H, *J* = 12.1, 3.3 Hz), 4.16 (dd, 1 H, *J* = 12.2, 6.2 Hz), 3.95 (s, 3 H), 3.94 (s, 3 H), 3.13-3.11 (m, 1 H), 2.98-2.95 (m, 1 H), 2.64, 2.60 (AB, 2 H, *J* =, 4.7 Hz), 1.81-1.61 (m, 4 H), 1.34 (s, 3 H); MS (EI) *m/z* 322

(M^+,16), 182 (19), 165 (100), 69 (15); HRMS (EI) *m/z* calcd for $C_{17}H_{22}O_6$ 322.1414, found 322.1416.

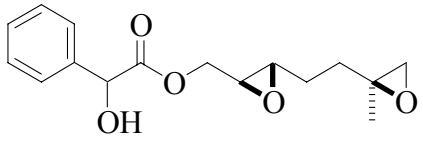


((2*S*,3*S*)-3-(2-((*S*)-2-Methyloxirane-2-yl)ethyl)oxiran-2-yl)methyl 3,4,5-trimethoxybenzoate (55). According to the procedure used for **51**, 116 mg (0.329 mmol, 26%) of **55** was obtained as a light yellow oil and single diastereomer: $[\alpha]_D$ +20.0 (*c* 0.98, $CHCl_3$); IR (neat) 2942, 2641, 2252, 1956, 1716, 1589, 1336, 1127, 1001, 916, 731, 675, 647 cm^{-1}; ^1H NMR δ 7.31 (s, 2 H), 4.63 (dd, 1 H, *J* = 12.2, 3.2 Hz), 4.14 (dd, 1 H, *J* = 12.2, 6.4 Hz), 3.91 (s, 9 H), 3.15-3.11 (m, 1 H), 2.98-2.95 (m, 1 H), 2.64, 2.60 (AB, 2 H, *J* = 4.7 Hz)), 1.74-1.59 (m, 4 H), 1.34 (s, 3 H); ^{13}C NMR δ 165.6, 152.6, 142.1, 124.3, 106.6, 65.0, 60.6, 55.9, 55.8, 55.7, 55.2, 53.2, 32.2, 26.8, 20.7; MS (EI) *m/z* 352 (M^+, 81), 212 (43), 195 (100); HRMS (EI) *m/z* calcd for $C_{18}H_{24}O_7$ 352.1522, found 352.1527.

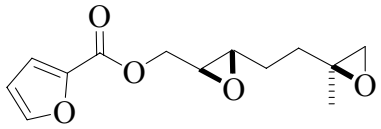


((2*S*,3*S*)-3-(2-((*S*)-2-Methyloxirane-2-yl)ethyl)oxiran-2-yl)methyl 4-methoxybenzoate (56). According to the procedure used for **51**, 56.0 mg (0.191 mmol, 23%) of **56** was obtained as a light yellow oil and single diastereomer: $[\alpha]_D$ +20.0 (*c* 1.0, $CHCl_3$); IR (neat) 3502, 2934, 1713, 1606, 1511, 1455, 1257, 1168, 848, 770, 734, 697, 613 cm^{-1}; ^1H NMR δ 8.01 (d, 2 H, *J* = 7.0 Hz), 6.92 (d, 2 H, *J* = 7.0 Hz), 4.57 (dd, 1 H, *J* = 12.2, 3.2 Hz), 4.16 (dd, 1 H, *J* = 12.2, 6.0 Hz),

3.87 (s, 3 H), 3.13-3.09 (m, 1 H), 2.98-2.95 (m, 1 H), 2.64, 2.60 (AB, 2 H, J = 4.7 Hz), 1.78-1.58 (m, 4 H), 1.34 (s, 3 H); ^{13}C NMR δ 165.9, 163.4, 131.7, 121.9, 113.6, 64.6, 56.1, 55.9, 55.5, 55.5, 53.4, 32.4, 27.0, 20.9; MS (EI) *m/z* 292 (M^+, 32), 152 (63), 135 (100), 92 (51), 77 (61), HRMS (EI) *m/z* calcd for $C_{16}H_{20}O_5$ 292.1311, found 292.1319.

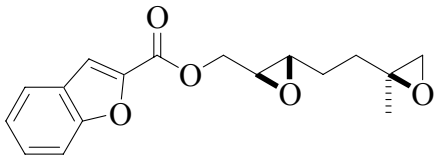


((2*S*,3*S*)-3-(2-((*S*)-2-Methyloxirane-2-yl)ethyl)oxiran-2-yl)methyl 2-hydroxy-2-phenylacetate (57). According to the procedure used for **51**, 43.0 mg (0.147 mmol, 30%) of **57** was obtained as a colorless oil: $[\alpha]_D$ +9.6 (*c* 1.0, $CHCl_3$); IR (neat) 3446, 3032, 2929, 1743, 1494, 1453, 1391, 1181, 1097, 1067, 1028, 984, 897, 786, 733, 699 cm^{-1}; ^{1}H NMR δ 7.45-7.33 (m, 5 H), 5.22 (d, 1 H, J = 5.7 Hz), 4.44-4.39 (m, 1 H), 4.13-4.04 (m, 1 H), 3.48-3.39 (m, 1 H), 2.96-2.86 (m, 1 H), 2.74-2.71 (m, 1 H), 2.60-2.56 (m, 2 H), 1.69-1.53 (m, 4 H), 1.31 (s, 3 H); ^{13}C NMR (major isomer) δ 173.2, 138.0, 128.6, 126.5, 72.8, 65.6, 65.3, 56.1, 55.9, 55.7, 54.9, 53.8, 53.4, 32.3, 26.9, 20.9; MS (EI) *m/z* 292 (M^+, 5), 155 (13), 111 (74), 107 (57), 77 (100); HRMS (EI) *m/z* calcd for $C_{16}H_{20}O_5$ 292.1311, found 292.1308.

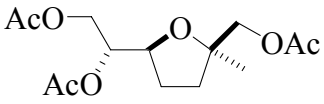


((2*S*,3*S*)-3-(2-((*S*)-2-Methyloxirane-2-yl)ethyl)oxiran-2-yl)methyl furan-2-carboxylate (58). According to the procedure used for **51**, 85.0 mg (0.337 mmol, 44%) of **58** was obtained as a colorless oil and single diastereomer: $[\alpha]_D$ +24.0 (*c* 0.88, $CHCl_3$); IR (neat) 2985, 2306, 1724,

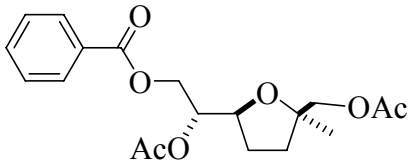
1581, 1474, 1397, 1296, 1181, 1076, 1015, 966, 885, 742 cm^{-1}; ^1H NMR δ 7.60 (d, 1 H, *J* = 1.6 Hz), 7.22 (d, 1 H, *J* = 3.4 Hz), 6.54-6.52 (m, 1 H), 4.57 (dd, 1 H, *J* = 12.2, 6.0 Hz), 4.18 (dd, 1 H, *J* = 12.1, 6.0 Hz), 3.11-3.09 (m, 1 H), 3.04-2.90 (m, 1 H), 2.64, 2.60 (AB, 2 H, *J* = 4.7 Hz), 1.80-1.60 (m, 4 H), 1.33 (s, 3 H,); ^{13}C NMR δ 158.0, 146.5, 143.8, 118.3, 111.7, 64.6, 55.9, 55.8, 54.9, 53.2, 32.2, 26.8, 20.8; MS (EI) *m/z* 252 (M^+, 15), 180 (45), 164 (93), 95 (100); HRMS (EI) *m/z* calcd for $C_{13}H_{16}O_5$ 252.0998, found 252.1003.



((2*S*,3*S*)-3-(2-((*S*)-2-Methyloxirane-2-yl)ethyl)oxiran-2-yl)methyl benzofuran-2-carboxylate (59). According to the procedure used for **51**, 174 mg (0.576 mmol, 41%) of **59** was obtained as a colorless solid and single diastereomer: mp 70-74 °C; $[\alpha]_D$ +10.9 (*c* 1.0, $CHCl_3$); IR (KBr) 2966, 1712, 1571, 1443, 1293, 970, 918, 802, 751 cm^{-1}; ^1H NMR δ 7.70 (d, 1 H, *J* = 7.9 Hz), 7.61-7.58 (m, 2 H), 7.47 (app. t, 1 H, *J* = 7.3 Hz), 7.31 (app. t, 1 H, *J* = 7.3 Hz)), 4.65 (dd, 1 H, *J* = 12.2, 3.4 Hz), 4.26 (dd, 1 H, *J* = 12.1, 6.1 Hz), 3.16-3.10 (m, 1 H), 3.04-2.99 (m, 1 H), 2.64, 2.60 (AB, 2 H, *J* = 4.7 Hz), 1.79-1.61 (m, 4 H), 1.34 (s, 3 H); ^{13}C NMR δ 159.0, 155.6, 144.8, 127.6, 126.7, 123.7, 122.7, 114.3, 114.1, 112.2, 65.4, 65.2, 56.0,55.0, 53.6, 53.5, 53.3, 32.7, 32.3, 27.1, 26.9, 20.8, 20.5; MS (EI) *m/z* 142 (M^+, 36), 162 (45), 145 (100), 89 (50); HRMS (EI) *m/z* calcd for $C_{17}H_{18}O_5$ 302.1154, found 302.1166.

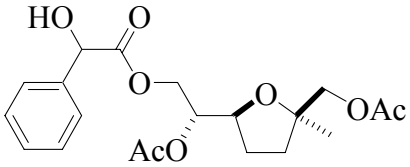


(*R*)-2-Acetoxy-1-((2*S*,5*R*)-5-(acetoxymethyl)-5-methyltetrahydrofuran-2-yl)ethyl acetate (61). To a solution of 25.0 mg (0.135 mmol) of **51** in 0.680 mL of CH_2Cl_2 was added 3.94 mg (0.0135 mmol) of Cp_2ZrCl_2 and 4.28 mg (0.0207 mmol) of $AgClO_4$. The reaction mixture was stirred at rt for 5 h, quenched with 0.20 mL of H_2O, filtered through a pad of celite, dried ($MgSO_4$) and concentrated to give a yellow oil. To the crude oil was added 0.50 mL of CH_2Cl_2, 94 μl (0.99 mmol) of acetic anhydride, and 1.2 mg (0.099 mmol) of DMAP. The reaction was cooled to 0 ^oC at which point 0.164 mL (0.990 mmol) of DIPEA was added. The mixture was stirred at rt for 12 h, and quenched with saturated aqueous NH_4Cl. The aqueous layer was extracted with CH_2Cl_2 (x 3), dried ($MgSO_4$), concentrated and purified by chromatography on SiO_2 (4:1 hexanes/EtOAc) to afford 13.4 mg (0.0443 mmol, 35%) of crude **61** as a yellow oil: $[\alpha]_D$ -0.89 (*c* 1.34, $CHCl_3$); IR (neat) 2971, 1743, 1455, 1373, 1232, 1119, 1047 cm^{-1}; ^1H NMR δ 5.11-5.04 (m, 1 H), 4.47-4.39 (m, 1 H), 4.18-4.07 (m, 2 H), 3.99, 3.96 (AB, 2 H, *J* = 11.4 Hz), 2.11 (s, 3 H), 2.09 (s, 3 H), 2.05 (s, 3 H), 1.99-1.57 (m, 4 H), 1.24 (s, 3 H); MS (EI) *m/z* 243 ([M-OAc]$^+$, 51), 229 (100), 127 (21), 97 (30), 71 (48); HRMS (EI) *m/z* calcd for $C_{14}H_{22}O_7$ (M-OAc) 243.1232, found 243.1239.

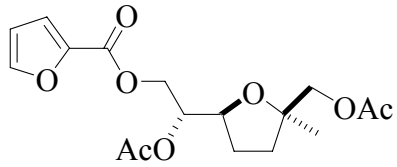


(*R*)-2-Acetoxy-1-((2*S*,5*R*)-5-(acetoxymethyl)-5-methyltetrahydrofuran-2-yl)ethyl benzoate (62). According to the procedure for **61**, 6.9 mg (0.0190 mmol, 21%) of **62** was obtained as a yellow oil in a 1.2:1 mixture of regioisomers (only major isomer shown): IR (neat) 2924, 2853,

1724, 1452, 1373, 1272, 1229, 1112, 1046, 712 cm^{-1}; Major isomer :^{1}H NMR δ 8.02 (d, 2 H, *J* = 7.5 Hz), 7.61-7.52 (m, 1 H), 7.48-7.40 (m, 2 H), 5.26 (dt, 1 H, *J* = 6.4 ,3.2 Hz), 4.35 (ABX, 2 H, *J* = 12.2, 6.8, 2.9 Hz), 4.31-4.21 (m, 1 H), 4.02, 3.98 (AB, 2 H, *J* = 11.3 Hz), 2.16-1.90 (m, 8 H), 1.74-1.66 (m, 2 H), 1.26 (s, 3 H); MS (EI) *m/z* 321 (20), 157 (93), 149 (68), 105 (100), 97 (91), 77 (66), 69 (48); HRMS (EI) *m/z* calcd for $C_{19}H_{24}O_7$ (M-C_2H_3O) 321.1328, found 321.1338.



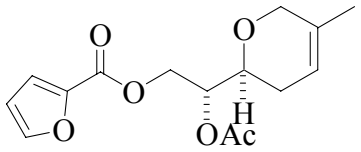
(*R*)-2-Acetoxy-1-((2*S*,5*R*)-5-(acetoxymethyl)-5-methyltetrahydrofuran-2-yl)ethyl 2-hydroxy-2-phenylacetate (66). According to the procedure used for **61**, 3.6 mg (0.00898 mmol, 11%) of crude **66** as a yellow oil in a 1.1:1 mixture of regioisomers (only major isomer shown): ^{1}H NMR δ 7.45-7.33 (m, 5 H), 5.07 (dt, 1 H, *J* = 6.8, 3.2 Hz), 5.00 (dt, 1 H, *J* = 7.0, 3.6 Hz), 4.50-3.85 (m, 8 H), 2.12-1.64 (m, 9 H), 1.23 (s, 3 H).



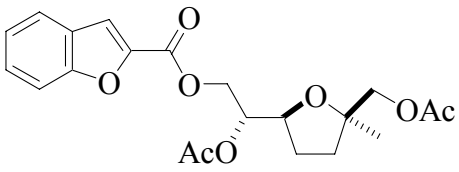
(*R*)-2-Acetoxy-1-((2*S*,5*R*)-5-(acetoxymethyl)-5-methyltetrahydrofuran-2-yl)ethyl furan-2-carboxylate (68). According to the procedure used for **61**, 19.6 mg (0.0477 mmol, 56%) of **68** was obtained as a yellow oil in a 1.9:1 ratio of regioisomers (only major isomer shown) in addition to 10.0 mg (0.0340 mmol, 35%) of crude **72** as a yellow oil.

(*R*)-2-Acetoxy-1-((2*S*,5*R*)-5-(acetoxymethyl)-5-methyltetrahydrofuran-2-yl)ethyl furan-2-carboxylate (68): $[\alpha]_D$ +8.5 (*c* 1.14, $CHCl_3$); IR (neat) 3140, 2971, 1720, 1580, 1474, 1374,

1225, 1047, 937, 884, 763, 736, 702, 597 cm^{-1}; ^1H NMR δ 7.58 (d, 1 H, *J* = 4.7 Hz), 7.25-7.20 (m, 1 H), 6.52-6.50 (m, 1 H), 5.33 (dt, 0.4 H, *J* = 6.4, 2.9 Hz), 5.20 (dt, 1 H, *J* = 6.4, 2.9 Hz), 4.65-3.90 (m, 5 H), 2.12-1.69 (m, 10 H), 1.25 (s, 3 H); MS (EI) *m/z* 252 (M^+, 15), 180 (45), 164 (93), 95 (100); HRMS (EI) *m/z* calcd for $C_{17}H_{22}O_8$ 354.1329, found 354.13404.

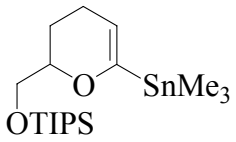


(*R*)-2-Acetoxy-1-((2*S*)-5-methyl-3,6-dihydro-2*H*-pyran-2-yl)ethyl furan-2-carboxylate (72): ^1H NMR δ 7.59 (bs, 1 H), 7.17 (d, 1 H, *J* = 3.3 Hz), 6.52 (dd, 1 H, *J* = 3.4, 1.7 Hz), 5.50-5.49 (m, 1 H), 5.16 (dt, 1 H, *J* = 6.3, 2.8 Hz), 4.65 (d of AB, 1 H, *J* = 12.0, 2.8 Hz), 4.46 (d of AB, 1 H, *J* = 12.1, 6.6 Hz), 4.05 (s, 3 H), 3.76-3.69 (m, 1 H), 2.10 (s, 3 H), 2.07-2.01 (m, 1 H), 1.61 (s, 3 H); ^{13}C NMR δ 170.4, 158.5, 146.7, 144.4, 133.0, 118.4, 117.6, 111.9, 73.2, 72.2, 69.3, 63.2, 26.9, 21.1, 18.6; MS (EI) *m/z* 294 (M^+, 15), 182 (22), 140 (44), 122 (69), 95 (100), 69 (64); HRMS (EI) *m/z* calcd for $C_{15}H_{18}O_6$ 294.1103, found 294.1111.



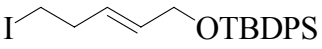
(*R*)-2-Acetoxy-1-((2*S*,5*R*)-5-(acetoxymethyl)-5-methyltetrahydrofuran-2-yl)ethyl benzofuran-2-carboxylate (70). According to the procedure used for **61**, 14.5 mg (0.0359 mmol, 46%) of **70** was obtained as a yellow oil in a 4.5:1 mixture of regioisomers (only major isomer shown): $[\alpha]_D$ +8.5 (*c* 1.14, $CHCl_3$); IR (neat) 2971, 1739, 1647, 1563, 1372, 1297, 1234, 886, 751, 702 cm^{-1}; Major isomer:^1H NMR δ 7.59 (d, 1 H, *J* = 7.7 Hz), 7.49 (d, 1 H, *J* = 8.3 Hz),

7.51 (s, 1 H), 7.46-7.43 (m, 1 H), 7.34-7.29 (m, 1 H), 5.24 (dt, 1 H, *J* = 6.5, 2.8 Hz), 4.72 (d of AB, 1 H, *J* = 12.0, 2.8 Hz), 4.45 (d of AB, 1 H, *J* = 12.0, 6.5 Hz), 4.31-4.23 (m, 1 H), 4.02, 3.98 (AB, 2 H, *J* = 11.3 Hz), 2.14 (s, 3 H), 2.11 (s, 3 H), 2.09-1.90 (m, 2 H), 1.76-1.70 (m, 1 H), 1.32-1.23 (m, 1 H), 1.26 (s, 3 H); ^{13}C NMR δ 170.9, 170.3, 159.2, 155.8, 145.0, 127.7, 126.9, 123.8, 122.9, 114.2, 112.4, 82.6, 72.4, 69.3, 63.9, 33.4, 31.9, 28.1, 23.9, 21.0, 20.9; MS (EI) *m/z* 404 (M^+, 29), 331 (89), 183 (37), 162 (100), 109 (85), 89 (94); HRMS (EI) *m/z* calcd for $C_{21}H_{24}O_8$ 404.1471, found 404.1472.

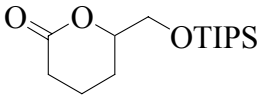


2-Triisopropylsiloxymethyl-3,4-dihydro-2*H*-pyran-6-yl-trimethylstannane (88).[26] To a -78 °C suspension of 250 mg (2.22 mmol) of freshly sublimed potassium *tert*-butoxide in 3.6 mL of hexanes was added 1.4 mL of *n*-BuLi (1.6 M in hexanes, 2.31 mmol) and 0.464 mL (3.07 mmol) of TMEDA. The reaction mixture warmed to -15 °C for 30 min. After re-cooling to -78 °C, a solution of 400 mg (1.48 mmol) of **107** in 0.30 mL of hexanes was added and the mixture was allowed to warm to -15 °C over a period of 2 h. The reaction mixture was cooled to -78 °C at which point a solution of 676 mg (3.30 mmol) of Me_3SnCl in 1.0 mL of hexanes was added in one portion. The reaction mixture warmed to rt for 1 h before it was quenched with water. The aqueous layer was extracted with ether (x 2), dried ($MgSO_4$), concentrated and purified by chromatography on SiO_2 (hexanes) to afford 562 mg (1.18 mmol, 85%) of **88** as a colorless oil: IR (neat) 2955, 2922, 2866, 1607, 1463, 1376, 1270, 1218, 1183, 1139, 1108, 1057 cm^{-1}; ^{1}H NMR δ 4.77-4.75 (m, 1 H), 3.82-3.66 (m, 4 H), 2.18-1.88 (m, 6 H), 1.73-1.60 (m, 3 H), 1.57 (s, 3 H), 1.08-1.05 (m, 47 H), 0.145 (s, 11 H); ^{13}C NMR

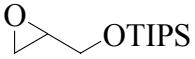
δ 162.0, 111.3, 75.9, 66.1, 24.6, 20.9, 18.0, 17.9 ,12.0, –9.8; MS (EI) *m/z* 434 (M^+, 14), 391 (49), 227 (97), 165 (100), 163 (74), 101 (33), 75 (34), 59 (38); HRMS (EI) *m/z* calcd for $C_{18}H_{38}O_2SiSn$ 434.1663, found 434.1664.



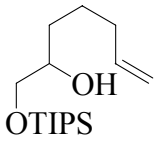
***tert*-Butyl-(5-iodopent-2-enyloxy)-diphenylsilane (89).**[29] This compound was prepared in 70% yield by a known procedure and its ^{1}H NMR spectrum was identical with the reported data.



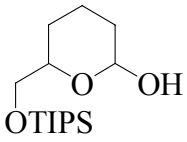
6-(*tert*-Butyldimethylsilanyloxymethyl)-tetrahydropyran-2-one (102).[29] This compound was prepared in 65% yield by a known procedure and its ^{1}H NMR spectrum was identical with the reported data: ^{1}H NMR δ 4.37 (m, 1 H), 3.77 (d, 2 H, *J* = 5.0 Hz), 2.70-2.32 (m, 2 H), 2.20-1.60 (m, 4 H), 1.90 (s, 9 H), 0.07, (s, 6 H).



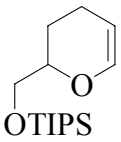
3-Triisopropylsiloxy-1,2-epoxypropane (104).[26] This compound was prepared by a known procedure in 81% yield and its ^{1}H NMR spectrum was identical with the reported data: ^{1}H NMR δ 3.91 (dd, 1 H, *J* = 11.6, 3.2 Hz), 3.75 (dd, 1 H, *J* = 11.6, 4.6 Hz), 3.11 (m, 1 H), 2.77 (dd, 1 H, *J* = 5.1, 4.3 Hz), 2.67 (dd, 1 H, *J* = 5.2, 2.6 Hz), 1.14-1.00 (m, 21 H).



6-Hydroxy-7-triisopropylsiloxyhept-1-ene (105).[26] This compound was prepared by a known procedure in 95% yield and its ^{1}H NMR spectrum was identical with the reported data: ^{1}H NMR δ 5.81 (m, 1 H), 5.01 (m, 1 H), 4.95 (dd, 1 H, *J* = 17.1, 1.6 Hz), 3.71 (dd, 1 H, *J* = 9.5, 3.3 Hz), 3.69-3.64 (m, 1 H), 3.48 (dd, 1 H, *J* = 9.5, 7.7 Hz), 2.53 (t, 1 H, *J* = 2.5 Hz), 2.10-2.06 (m, 2 H), 1.60-1.55 (m, 1 H), 1.48-1.39 (m, 3 H), 1.15-1.00 (m, 21 H).

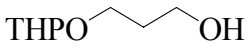


6-Hydroxy-2-triisopropylsiloxymethyl-3,4,5,6-tetrahydro-2*H*-pyran (**106**).[26] This compound was prepared by a known procedure in 75% yield and its ^{1}H NMR spectrum was identical with the reported data: ^{1}H NMR δ 9.78 (t, 0.06 H, *J* = 1.5 Hz), 5.26 (s, 0.41 H), 4.75-4.72 (m. 0.53 H), 4.05-4.00 (m, 0.41 H), 3.85-3.79 (m, 0.59 H), 3.71 (dd, 0.41 H, *J* = 10.0, 5.3 Hz), 3.61 (dd, 0.53 H, *J* = 9.7, 6.7 Hz), 3.58-3.53 (m. 0.94 H), 3.48 (dd, 0.06 H, *J* = 7.14, 8.6 Hz), 3.07 (d, 0.53 H, *J* = 6.2 Hz), 2.59 (dt, 0.12 H, *J* = 7.2, 1.4 Hz), 1.94-0.94 (m, 27 H).

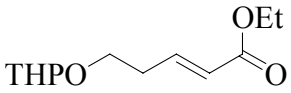


2-Triisopropylsilyloxymethyl-3,4-dihydro-2*H*-pyran (107).[26] This compound was prepared by a known procedure in 64% yield and its ^{1}H NMR spectrum was identical with the reported data: ^{1}H NMR δ 6.36 (d, 1 H, *J* = 6.2 Hz), 4.67-4.64 (m, 1 H), 3.90-3.85 (m, 1 H), 3.84 (dd, 1 H,

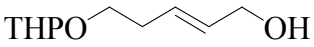
J = 9.9, 5.1 Hz), 3.69 (dd, 1 H, *J* = 9.9, 6.1 Hz), 2.12-2.05 (m, 1 H), 2.01-1.94 (m, 2 H), 1.70-1.64 (m,1 H), 1.15-1.02 (m, 21 H).



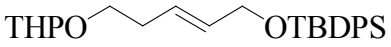
3-Tetrahydropyranyloxy-1-propanol (108).[27] This compound was prepared by a known procedure in quantitative yield and its ^{1}H NMR spectrum was identical with the reported data: ^{1}H NMR δ 4.52 (t, 1 H, *J* = 4.5 Hz), 4.95-3.65 (m, 2 H), 3.60-3.40 (m, 3 H), 2.85-2.65 (s, 1 H), 1.90-1.40 (m, 8 H).



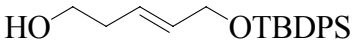
Ethyl (*E*)-5-tetrahydropyranyloxy-2-penteneoate (110).[27] This compound was prepared by a known procedure in 72% yield and its ^{1}H NMR spectrum was identical with the reported data: ^{1}H NMR δ 6.97 (dt, 1 H, *J* = 15.9, 7.0 Hz), 5.88 (dt, 1 H, *J* = 15.9, 1.5 Hz), 4.60 (t, 1 H, *J* = 3.1 Hz), 4.17 (q, 2 H, *J* = 7.0 Hz), 3.87-3.80 (m, 2 H), 3.53-3.47 (m, 2 H) 2.49 (dq, 2 H, *J* = 6.7, 1.8 Hz), 1.84-1.75 (m, 1 H), 1.74-1.65 (m, 1 H), 1.61-1.48 (m, 4 H), 1.27 (t, 3 H, *J* = 7.0 Hz).



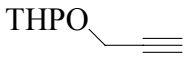
4-[(2-Tetrahydropyranyl)oxy]butyne (111).[28] This compound was prepared by a known procedure in 78% yield and its ^{1}H NMR spectrum was identical with the reported data: ^{1}H NMR δ 5.79-5.72 (m, 2 H), 4.60 (t, 1 H, *J* = 3.5 Hz), 3.94-3.77 (m, 1 H), 3.77-3.45 (m, 1 H), 2.45 (td, 2 H, *J* = 7.0, 2.5 Hz), 1.94 (t, 1 H, *J* = 2.5 Hz), 1.88-1.42 (m, 6 H).



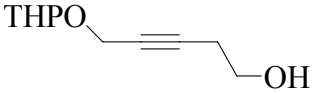
***tert*-Butyldiphenyl-[5-(tetrahydropyran-2-yloxy)-pent-2-enyloxy]-silane (112).**[28] This compound was prepared in 88% yield by a known procedure and its ^{1}H NMR spectrum was identical with the reported data: ^{1}H NMR δ 5.75-5.60 (m, 2 H), 4.62-4.60 (m, 1 H), 4.18-4.16 (m, 2 H), 3.92-3.73 (m, 2 H), 3.52-3.39 (m, 2 H), 2.35 (q, 2 H, *J* = 13.1, 6.8 Hz), 1.85-1.52 (m, 9 H), 1.09-1.05 (m, 12 H).



5-(*tert*-Butyldiphenylsilanyloxy)-pent-3-en-1-ol (113).[28] This compound was prepared by a known procedure in 74% yield and its ^{1}H NMR spectrum was identical with the reported data: ^{1}H NMR δ 7.70-7.67 (m, 4 H), 7.41-7.38 (m, 6 H), 5.71-5.63 (m, 2 H), 4.19 (d, 1 H, *J* = 1.3 Hz), 3.64-3.63 (m, 2 H), 2.30 (q, 2 H, *J* = 6.1 Hz), 1.60 (s, 1 H), 1.07 (s, 9 H).

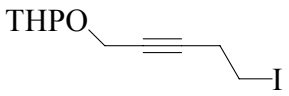


2-Prop-2-ynyloxytetrahydropyran (116).[28] This compound was prepared by a known procedure in 89% yield and its ^{1}H NMR spectrum was identical with the reported data: ^{1}H NMR δ 4.80 (m, 1 H), 4.22 (d, 2 H, *J* = 2.3 Hz), 4.00 (m, 2 H), 2.38 (t, 1 H, *J* = 2.4 Hz), 1.80-1.30 (m, 6 H).

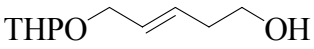


5-(Tetrahydropyran-2-yloxy)-pent-3-yn-1-ol (117).[28] This compound was prepared by a known procedure in 77% yield and its ^{1}H NMR spectrum was identical with the reported data:

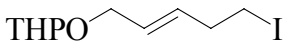
^{1}H NMR δ 4.77 (t, 1 H), 4.22 (m, 2 H), 4.00-3.40 (m, 4 H), 2.47 (m, 2 H), 2.07 (m, 1 H), 1.60 (m, 6 H), 1.90-1.40 (m, 8 H).



2-(5-Iodopent-2-ynyloxy)-tetrahydropyran (118). [29] This compound was prepared by a known procedure in 67% yield and its ^{1}H NMR spectrum was identical with the reported data: ^{1}H NMR δ 4.82 (t, 1 H, *J* = 3.4 Hz), 4.23 (qt, 2 H, *J* = 15.6, 2.0 Hz), 3.87-3.79 (m, 1 H), 3.57-3.48 (m, 1 H), 3.21 (t, 2 H, *J* = 7.3 Hz), 2.81 (tt, 2 H, *J* = 7.3, 2.0 Hz), 1.88-1.46 (m, 6 H).



5-(Tetrahydropyran-2-yloxy)-pent-3-en-1-ol (119).[29] This compound was prepared by a known procedure in 80% yield and its ^{1}H NMR spectrum was identical with the reported data: ^{1}H NMR δ 4.52 (t, 1 H, *J* = 4.5), 4.95-3.65 (m, 2 H), 3.60-3.40 (m, 3 H), 2.85-2.65 (s, 1 H), 1.90-1.40 (m, 8 H).



2-(5-Iodopent-2-enyloxy)-tetrahydropyran (120).[29] This compound was prepared in 82% yield by a known procedure and its ^{1}H NMR spectrum was identical with the reported data: ^{1}H NMR δ 5.69-5.66 (m, 2 H), 4.65 (t, 1 H, *J* = 2.9 Hz), 4.23-4.18 (m, 1 H), 3.98-3.84 (m, 2 H), 3.58-3.48 (m, 1 H), 3.18 (t, 2 H, *J* = 7.3 Hz), 2.66-2.60 (m, 2 H), 1.88-1.51 (m, 8 H).

Appendix A

X-ray crystal data for 59

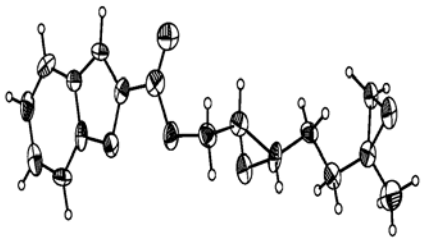


Table 12: Crystal data and structure refinment for **59**.

Identification code:	jm0326t (**59**)	
Empirical formula:	C_{17} H_{18} O_5	
Formula weight:	302.31	
Temperature:	273(2) K	
Wavelength:	0.71073 Å	
Crystal system:	Monoclinic	
Space group:	P2(1)	
Unit cell dimensions	a = 10.523(2) Å	□= 90°.
	b = 4.3519(9) Å	□= 102.411(4)°.
	c = 16.083(3) Å	□ = 90°.
Volume:	719.3(3) Å^3	
Z:	2	
Density (calculated):	1.396 Mg/m^3	
Absorption coefficient:	0.103 mm^{-1}	
F(000):	320	
Crystal size:	0.29 x 0.12 x 0.12 mm^3	
Theta range for data collection:	1.98 to 24.98°.	
Index ranges:	-12<=h<=12, -5<=k<=5, -19<=l<=19	
Reflections collected:	5579	
Independent reflections:	2500 [R(int) = 0.0784]	
Completeness to theta =	24.98°	99.9 %
Absorption correction:	Sadabs	
Max. and min. transmission:	0.9878 and 0.9708	
Refinement method:	Full-matrix least-squares on F^2	
Data / restraints / parameters:	2500 / 1 / 199	
Goodness-of-fit on F^2:	1.399	
Final R indices [I>2sigma(I)]	R1 = 0.0963, wR2 = 0.1996	

R indices (all data): R1 = 0.1170, wR2 = 0.2068
Absolute structure parameter: 2(3)
Largest diff. peak and hole: 0.336 and -0.332 e.Å^{-3}

Table 13: Atomic coordinates

	x	y	z	U(eq)
O(1)	7463(3)	6919(9)	3156(2)	36(1)
O(2)	5023(4)	8872(10)	1382(3)	46(1)
O(3)	7118(4)	10095(9)	1771(2)	40(1)
O(4)	8428(4)	8255(9)	389(2)	39(1)
O(5)	7638(4)	8989(9)	-2957(2)	39(1)
C(1)	7353(5)	5087(13)	3822(3)	34(1)
C(2)	8339(5)	4359(14)	4494(4)	40(2)
C(3)	8028(6)	2491(15)	5099(4)	44(2)
C(4)	6810(6)	1338(15)	5020(4)	43(2)
C(5)	5843(5)	2003(14)	4331(4)	41(2)
C(6)	6127(5)	3984(13)	3715(3)	31(1)
C(7)	5438(5)	5230(13)	2963(3)	32(1)
C(8)	6253(5)	6965(13)	2647(4)	32(1)
C(9)	6041(5)	8750(12)	1867(4)	34(1)
C(10)	7052(5)	11756(14)	999(3)	38(2)
C(11)	7190(5)	9668(12)	300(3)	34(1)
C(12)	8000(6)	10372(13)	-300(3)	35(1)
C(13)	7747(5)	9125(14)	-1161(3)	37(1)
C(14)	8942(5)	8490(13)	-1486(3)	37(1)
C(15)	8712(6)	7508(14)	-2391(4)	37(1)
C(16)	7544(6)	5780(12)	-2780(4)	37(2)
C(17)	9875(6)	7120(20)	-2743(4)	61(2)

Table 14: Bond lengths [Å] and angles [°] for jm0326t.

O(1)-C(1)	1.359(7)
O(1)-C(8)	1.358(6)
O(2)-C(9)	1.182(6)
O(3)-C(9)	1.313(6)
O(3)-C(10)	1.426(6)
O(4)-C(11)	1.419(6)
O(4)-C(12)	1.437(6)
O(5)-C(16)	1.433(6)
O(5)-C(15)	1.442(6)
C(1)-C(6)	1.352(8)
C(1)-C(2)	1.365(8)
C(2)-C(3)	1.361(8)
C(3)-C(4)	1.356(8)
C(4)-C(5)	1.365(8)
C(5)-C(6)	1.393(8)
C(6)-C(7)	1.381(8)
C(7)-C(8)	1.323(8)
C(8)-C(9)	1.452(8)
C(10)-C(11)	1.477(8)
C(11)-C(12)	1.450(7)
C(12)-C(13)	1.458(8)
C(13)-C(14)	1.488(7)
C(14)-C(15)	1.486(8)
C(15)-C(16)	1.462(8)
C(15)-C(17)	1.463(8)
C(1)-O(1)-C(8)	104.9(4)
C(9)-O(3)-C(10)	116.5(4)
C(11)-O(4)-C(12)	61.0(3)
C(16)-O(5)-C(15)	61.1(4)
C(6)-C(1)-O(1)	110.4(5)
C(6)-C(1)-C(2)	124.0(6)
O(1)-C(1)-C(2)	125.6(5)
C(3)-C(2)-C(1)	116.5(5)
C(4)-C(3)-C(2)	121.5(6)
C(3)-C(4)-C(5)	121.5(6)
C(4)-C(5)-C(6)	118.1(5)
C(1)-C(6)-C(7)	106.2(5)
C(1)-C(6)-C(5)	118.3(5)
C(7)-C(6)-C(5)	135.5(5)
C(8)-C(7)-C(6)	107.4(5)
C(7)-C(8)-O(1)	111.2(5)
C(7)-C(8)-C(9)	130.2(5)
O(1)-C(8)-C(9)	118.6(4)
O(2)-C(9)-O(3)	125.9(5)
O(2)-C(9)-C(8)	122.8(5)

O(3)-C(9)-C(8)	111.3(4)
O(3)-C(10)-C(11)	110.9(5)
O(4)-C(11)-C(12)	60.1(3)
O(4)-C(11)-C(10)	115.3(5)
C(12)-C(11)-C(10)	123.0(5)
O(4)-C(12)-C(11)	58.9(3)
O(4)-C(12)-C(13)	117.2(5)
C(11)-C(12)-C(13)	122.6(5)
C(12)-C(13)-C(14)	114.0(5)
C(15)-C(14)-C(13)	115.2(5)
O(5)-C(15)-C(16)	59.2(3)
O(5)-C(15)-C(17)	114.5(5)
C(16)-C(15)-C(17)	118.1(6)
O(5)-C(15)-C(14)	115.5(5)
C(16)-C(15)-C(14)	120.7(5)
C(17)-C(15)-C(14)	116.0(5)
O(5)-C(16)-C(15)	59.7(3)

Symmetry transformations used to generate equivalent atoms:

.

Table15: Anistropic displacement parameters ($Å^2 x\ 10^3$) for **59**

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O(1)	43(2)	26(2)	38(2)	0(2)	10(2)	-8(2)
O(2)	43(2)	35(2)	57(3)	11(2)	7(2)	-2(2)
O(3)	50(3)	32(2)	39(2)	5(2)	14(2)	-2(2)
O(4)	59(3)	23(2)	34(2)	7(2)	9(2)	7(2)
O(5)	60(3)	14(2)	41(2)	9(2)	7(2)	1(2)
C(1)	45(4)	23(3)	33(3)	-8(3)	9(3)	11(3)
C(2)	35(3)	33(3)	51(4)	1(3)	4(3)	-4(3)
C(3)	57(4)	42(4)	31(3)	0(3)	8(3)	18(4)
C(4)	58(4)	39(4)	35(3)	6(3)	14(3)	6(3)
C(5)	33(3)	28(3)	63(4)	-1(3)	16(3)	2(3)
C(6)	37(3)	22(3)	34(3)	-6(3)	11(2)	0(3)
C(7)	31(3)	24(3)	40(3)	2(3)	5(2)	4(2)
C(8)	32(3)	24(3)	41(3)	0(3)	10(3)	-1(3)
C(9)	36(3)	19(3)	45(3)	-8(3)	5(3)	-8(3)
C(10)	42(3)	37(4)	35(3)	3(3)	6(3)	-4(3)
C(11)	40(3)	16(3)	44(3)	8(3)	5(3)	-2(2)
C(12)	53(4)	22(3)	33(3)	19(3)	14(3)	-1(3)
C(13)	40(3)	29(3)	41(3)	6(3)	7(3)	4(3)
C(14)	49(3)	16(3)	42(3)	9(3)	3(3)	-1(3)
C(15)	46(3)	29(3)	37(3)	12(3)	11(3)	8(3)
C(16)	58(4)	13(3)	40(4)	1(2)	11(3)	2(3)
C(17)	60(4)	61(5)	66(5)	-20(4)	22(4)	-9(4)

Table 16: Hydrogen coordinates (x 10^4) for **59**.

	x	y	z	U(eq)
H(2A)	9180	5101	4537	48
H(3A)	8663	1993	5577	52
H(4A)	6631	66	5444	52
H(5A)	5017	1157	4274	49
H(7A)	4563	4909	2723	39
H(10A)	7740	13283	1081	46
H(10B)	6225	12821	848	46
H(11A)	6441	8338	82	41
H(12A)	8420	12394	-230	42
H(13A)	7209	10567	-1541	44
H(13B)	7258	7231	-1171	44
H(14A)	9473	10332	-1418	44
H(14B)	9436	6898	-1136	44
H(16A)	7607	4332	-3228	45
H(16B)	6961	5169	-2417	45
H(17A)	9623	6468	-3326	92
H(17B)	10430	5594	-2420	92
H(17C)	10333	9036	-2714	92

Appendix B

X-ray crystal data for 74

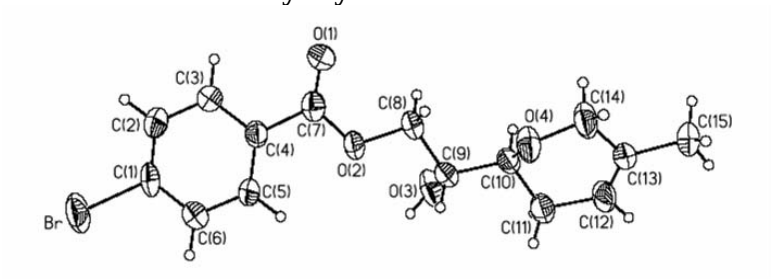


Table 17: Crystal data and refinement for **74.**

Identification code:	jm0301m (**74**)	
Empirical formula:	C_{15} H_{17} Br O_4	
Formula weight:	341.20	
Temperature:	295(2) K	
Wavelength:	0.71073 Å	
Crystal system:	Monoclinic	
Space group:	P2(1)	
Unit cell dimensions:	a = 9.1201(11) Å	a= 90°.
	b = 5.8260(7) Å	b= 98.308(2)°.
	c = 14.1916(17) Å	g = 90°.
Volume:	746.14(16) $Å^3$	
Z:	2	
Density (calculated):	1.519 Mg/m^3	
Absorption coefficient:	2.764 mm^{-1}	
F(000):	348	
Crystal size:	0.36 x 0.21 x 0.21 mm^3	
Theta range for data collection:	2.26 to 29.99°.	
Index ranges:	-12<=h<=12, -8<=k<=8, -19<=l<=19	
Reflections collected:	8639	
Independent reflections:	4258 [R(int) = 0.1123]	
Completeness to theta =	29.99°	99.6 %
Absorption correction:	None	
Max. and min. transmission:	0.5944 and 0.4361	
Refinement method:	Full-matrix least-squares on F^2	
Data / restraints / parameters:	4258 / 1 / 181	
Goodness-of-fit on F^2:	0.656	
Final R indices [I>2sigma(I)]:	R1 = 0.0457, wR2 = 0.0936	

R indices (all data):	R1 = 0.1118, wR2 = 0.1077
Absolute structure parameter:	-0.009(12)
Largest diff. peak and hole:	0.468 and -0.321 e.Å^{-3}

Table 18: Atomic coordinates

	x	y	z	U(eq)
Br	8942(1)	6548(1)	-907(1)	72(1)
O(1)	4726(3)	1738(7)	2198(2)	59(1)
C(1)	7726(5)	5645(8)	5(3)	46(1)
O(2)	4743(4)	5446(5)	2598(2)	55(1)
C(2)	7043(5)	3592(8)	-73(3)	50(1)
C(3)	6174(5)	2937(8)	615(3)	47(1)
O(3)	2695(4)	8687(6)	3029(2)	66(1)
O(4)	3340(4)	5686(4)	5241(2)	52(1)
C(4)	6026(4)	4415(7)	1365(3)	37(1)
C(5)	6722(4)	6512(12)	1414(3)	52(1)
C(6)	7623(5)	7097(8)	749(3)	58(2)
C(7)	5092(4)	3646(8)	2088(3)	41(1)
C(8)	3791(6)	5001(8)	3324(4)	52(1)
C(9)	3507(5)	7295(6)	3726(3)	43(1)
C(10)	2560(5)	7103(7)	4527(3)	40(1)
C(11)	2237(5)	9380(8)	4950(3)	53(1)
C(12)	1586(5)	9015(9)	5863(3)	52(1)
C(13)	1656(5)	7049(7)	6302(3)	42(1)
C(14)	2433(6)	5075(8)	5942(3)	59(1)
C(15)	922(5)	6573(13)	7175(3)	58(1)

Table 19: Bond lengths [Å] and angles [°] for **74**.

Br-C(1)	1.896(4)
O(1)-C(7)	1.177(6)
C(1)-C(2)	1.346(6)
C(1)-C(6)	1.367(6)
O(2)-C(7)	1.338(5)
O(2)-C(8)	1.463(5)
C(2)-C(3)	1.397(6)
C(3)-C(4)	1.391(6)
O(3)-C(9)	1.405(5)
O(4)-C(10)	1.416(5)
O(4)-C(14)	1.427(5)
C(4)-C(5)	1.374(7)
C(4)-C(7)	1.495(5)
C(5)-C(6)	1.381(5)
C(8)-C(9)	1.491(6)
C(9)-C(10)	1.527(5)
C(10)-C(11)	1.503(6)
C(11)-C(12)	1.516(6)
C(12)-C(13)	1.302(6)
C(13)-C(14)	1.481(6)
C(13)-C(15)	1.517(5)
C(2)-C(1)-C(6)	122.1(4)
C(2)-C(1)-Br	120.0(3)
C(6)-C(1)-Br 1	17.9(3)
C(7)-O(2)-C(8)	116.9(3)
C(1)-C(2)-C(3)	119.2(4)
C(4)-C(3)-C(2)	119.5(4)
C(10)-O(4)-C(14)	111.2(3)
C(5)-C(4)-C(3)	119.6(4)
C(5)-C(4)-C(7)	122.4(4)
C(3)-C(4)-C(7)	117.9(4)
C(4)-C(5)-C(6)	120.0(4)
C(1)-C(6)-C(5)	119.3(5)

Table 20: Anisotropic displacement parameters

	U^{11}		U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
Br	70(1)	103(1)	51(1)	0(1)	37(1)	-9(1)	
O(1)	86(2)	38(2)	62(2)	-1(2)	36(2)	-12(2)	
C(1)	46(3)	66(4)	31(2)	3(2)	21(2)	4(2)	
O(2)	76(2)	44(2)	53(2)	-2(1)	43(2)	-6(2)	
C(2)	57(3)	56(3)	42(3)	-12(2)	18(2)	-2(3)	
C(3)	53(3)	40(2)	50(3)	-6(2)	20(2)	-7(2)	
O(3)	73(2)	77(2)	56(2)	28(2)	34(2)	11(2)	
O(4)	62(2)	53(2)	47(2)	13(1)	27(2)	20(2)	
C(4)	39(2)	36(2)	39(2)	2(2)	15(2)	4(2)	
C(5)	64(3)	55(3)	45(2)	-18(3)	30(2)	-17(4)	
C(6)	67(3)	50(4)	65(3)	-7(2)	34(3)	-15(2)	
C(7)	38(2)	53(3)	32(2)	0(2)	7(2)	1(2)	
C(8)	66(3)	49(3)	47(3)	0(2)	33(3)	-9(3)	
C(9)	48(3)	38(3)	46(3)	3(2)	20(2)	-6(2)	
C(10)	45(2)	35(3)	45(2)	3(2)	21(2)	-2(2)	
C(11)	65(3)	48(3)	51(3)	4(2)	28(2)	0(3)	
C(12)	51(3)	53(3)	61(3)	-2(3)	34(2)	6(2)	
C(13)	48(2)	42(3)	40(2)	-3(2)	18(2)	-6(2)	
C(14)	84(4)	55(3)	46(3)	15(2)	34(3)	13(3)	
C(15)	72(3)	67(3)	41(2)	-4(4)	26(2)	-6(4)	

Table 21: Hydrogen coordinates (x 10^4) for **74**.

	x	y	zU(eq)	
H(2A)	7148	2621	-579	61
H(3A)	5697	1521	571	56
H(3B)	3263	9539	2797	99
H(5A)	6587	7539	1896	63
H(6A)	8154	8464	807	70
H(8A)	4285	3997	3816	62
H(8B)	2870	4289	3043	62
H(9A)	4452	8039	3966	51
H(10A)	1620	6359	4277	49
H(11A)	1543	10235	4499	63
H(11B)	3144	10266	5082	63
H(12A)	1120	10240	6117	63
H(14A)	3048	4346	6473	71
H(14C)	1703	3960	5669	71
H(15D)	466	7952	7363	87
H(15A)	1654	6059	7686	87
H(15B)	181	5406	7029	87

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