HETEROCYCLES, Vol. 62, 2004, pp. 583 - 618
Received, 21st August, 2003, Accepted, 31st October, 2003, Published online, 14th November, 2003

INTRAMOLECULAR [4+3] CYCLOADDITIONS. TOWARDS A SYNTHESIS OF WIDDROL

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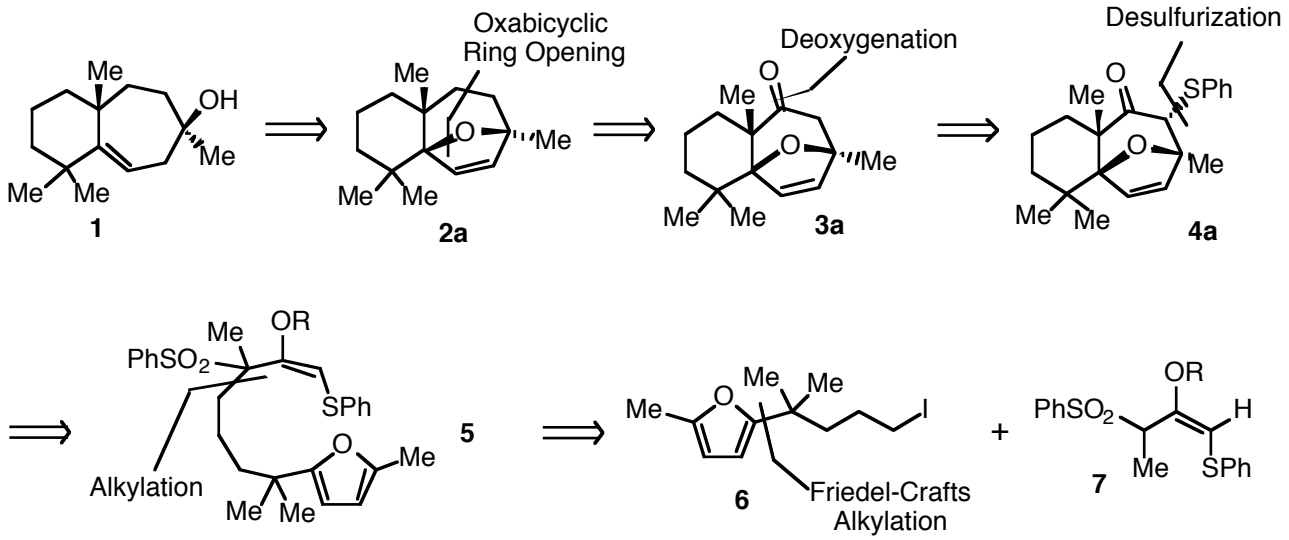
Abstract – Certain substituted alkoxyallylic sulfones were alkylated and treated with Lewis acids to produce vinylthionium ions that underwent intramolecular [4+3] cycloaddition reactions with a tethered furan. Manipulation of the cycloadduct led to the synthesis of widdrol. Other attempts to prepare the cycloadducts were made, but none were exceptionally better than the route using vinylthionium ions as intermediates. Interesting aspects of the alkylation chemistry of phenylthio-substituted alkoxyallylic sulfones are detailed as well.

INTRODUCTION

As part of a program of research involving synthetic and mechanistic aspects of intramolecular [4+3] cycloadditions of allylic cations,[1] we have begun to undertake studies of the application of such reactions to the synthesis of natural products.[2] Our first endeavor in the area resulted in the synthesis of the sesquiterpene aphanamol I and more importantly allowed us to identify uncertainties with respect to the regiochemistry of the cycloaddition process.[3] More recently, we published a synthesis of dactylol, which demonstrated methodology for the synthesis of cyclooctanoids using [4+3] cycloaddition chemistry.[4] In this paper we report the synthesis of another sesquiterpene, widdrol, using an approach that involves the use of a heteroatom-stabilized allylic cation, specifically a vinylthionium ion.[5]

RETROSYNTHETIC ANALYSIS AND STRATEGY

The general features of our approach to the synthesis of widdrol (**1**) are outlined retrosynthetically in Scheme 1. The natural product, widdrol (**1**), should be obtainable from oxabicyclic ether (**2a**) *via* a ring

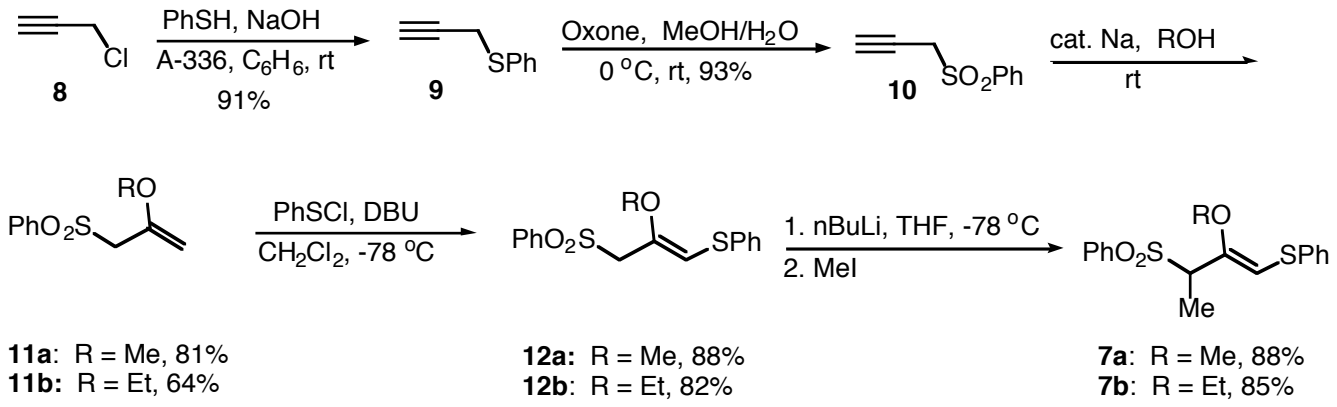


Scheme 1

opening reaction. One can envision the synthesis of this oxabicyclic ether (**2a**) from the tricyclic ketone (**3a**) using some kind of deoxygenation process. The ketone (**3a**) can be the retron for 4+3 cycloaddition from different precursors that will be mentioned later, but in this retrosynthetic scheme, it can be obtained from the ketosulfide (**4a**) *via* a desulfurization process. Compound (**4a**) can be regarded as a retron for the Lewis acid-mediated intramolecular 4+3 cycloaddition reaction. The synthesis of alkoxyallylic sulfone (**5**) can easily be achieved *via* an alkylation of sulfone (**7**) with the iodide (**6**). The alkoxyallylic sulfone (**7**) can be prepared from propargyl chloride in a few steps according to the method developed by our group.[6] The iodo compound (**6**) can be obtained *via* a Friedel-Crafts alkylation of 2-methylfuran followed by appropriate functional group manipulations.[7]

THE SYNTHESIS OF PRECURSORS

The synthesis of alkoxyallylic sulfone (**7**) was achieved according to the method reported by us earlier.[6] Treatment of propargyl chloride (**8**) with thiophenol in the presence of sodium hydroxide and a phase transfer catalyst (Aliquat 336, tricaprylylmethyl ammonium chloride) resulted in the propargylic sulfide (**9**) in 91% yield.[8] This sulfide was then oxidized to sulfone (**10**) with the method of Trost, using oxone in a 1:1 mixture of methanol and water.[9] Sulfone (**10**) was treated with a catalytic amount of sodium methoxide in methanol or sodium ethoxide in ethanol to give the enol ethers (**11a**) and (**11b**) in 81% and 64% yield, respectively.[10] Treatment of these sulfones with phenylsulfenyl chloride followed by DBU gave **12a** and **12b** in 88% and 82% yields after trituration with *tert*-butyl methyl ether or chromatography. Deprotonation with *n*-BuLi and the alkylation with iodomethane resulted in sulfones ((*E*)-**7a**) and ((*E*)-**7b**) in 88% and 85% yields with complete regio- and stereocontrol.

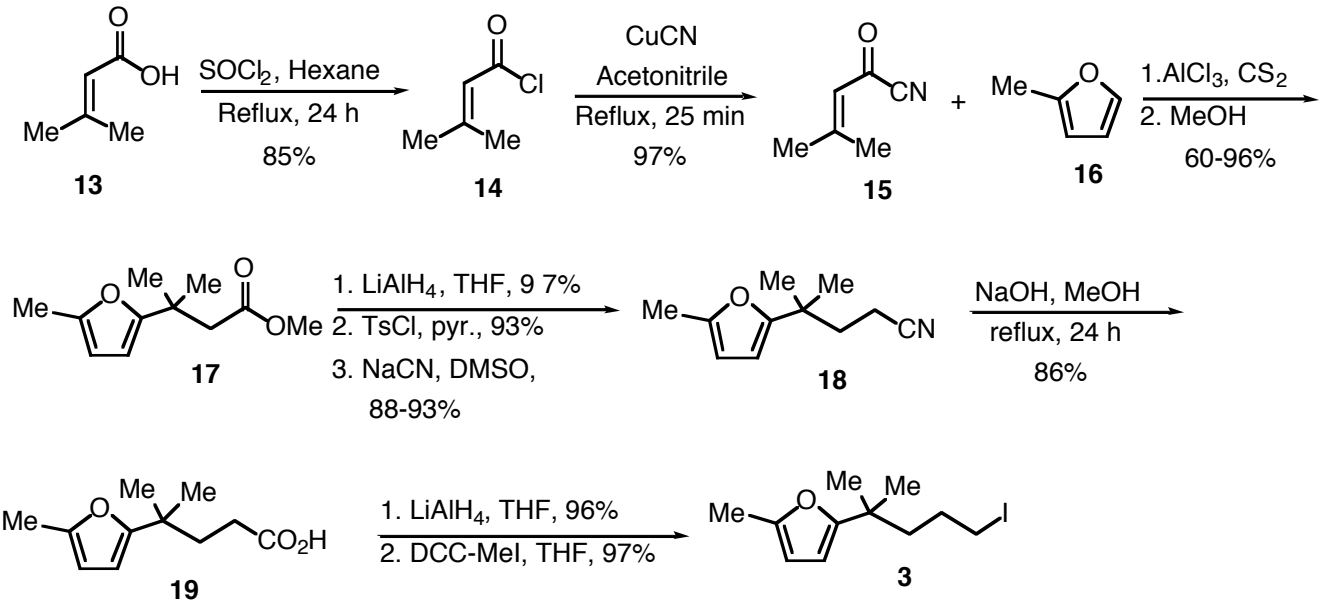


Scheme 2

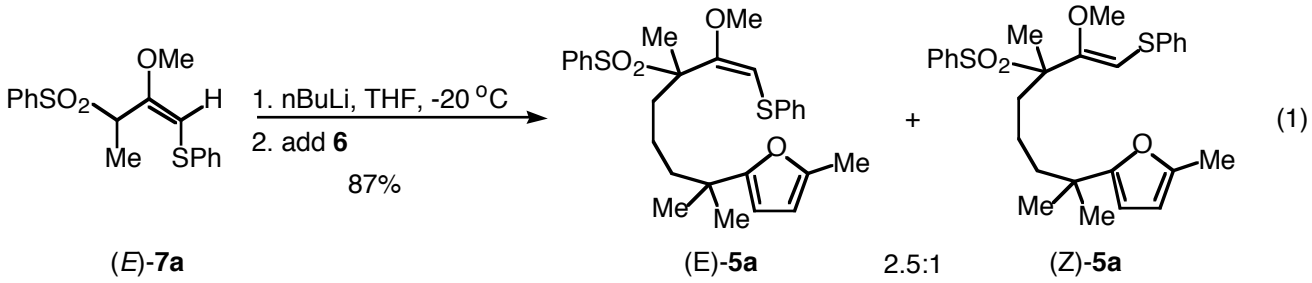
The iodide (**6**) needed for the synthesis of alkoxyallylic sulfone (**5**) was prepared by a method developed by Keay[7] for the synthesis of ester (**17**). The synthesis of the required iodide (**6**) was accomplished from **17** as shown in Scheme 3. First, 3,3-dimethylacrylic acid (**13**) was treated with thionyl chloride in refluxing hexane to afford the acid chloride (**14**) in 85% yield. This was then reacted with CuCN in acetonitrile to give acyl nitrile (**15**) in nearly quantitative yield. This acyl nitrile was subjected to Friedel-Crafts alkylation with 2-methylfuran in the presence of catalytic amount of aluminum trichloride in carbon disulfide as the solvent to yield the corresponding alkylated acyl nitrile, which was directly treated with methanol to give the ester (**17**) in 60-96% yield. Ester (**17**) was converted to the nitrile (**18**) in three steps as follows: First, the reduction with $LiAlH_4$ gave the corresponding primary alcohol in 97% yield. This alcohol was converted to sulfonate ester upon the treatment with *p*-toluenesulfonyl chloride in the presence of pyridine to afford the desired ester in 93% yield. Finally, the sulfonate ester was treated with sodium cyanide in dimethyl sulfoxide at 80-85 °C to give nitrile (**18**). The nitrile (**18**) was converted to the required iodide in three steps. Hydrolysis in methanolic sodium hydroxide afforded the carboxylic acid (**19**) in 84% yield. This acid was then reduced to an alcohol upon the treatment with $LiAlH_4$. Finally, the alcohol was converted to iodide (**6**) nearly quantitative yield by treatment of 1,3-dicyclohexylcarbodiimide-methyl iodide salt in tetrahydrofuran at 35 °C.[11]

The synthesis of the [4+3] cycloaddition precursor ((*E*)-**5a**) was accomplished as shown in equation 1. A THF solution of sulfone ((*E*)-**7a**) was cooled down to -78 °C in an isopropanol/dry ice bath and treated with *n*-butyllithium. The resulting anion was treated with the iodide (**6**) at -78 °C, but the alkylation did not take place. The bath temperature was warmed up to -20 °C and maintained at -20 °C for 24 h to give a mixture of (*E*)-**5a** and (*Z*)-**5a** in 87% yield in a ratio of 2.5:1, respectively. Initial attempts to optimize the reaction conditions in favor of *E* isomer failed. The rationale for the formation of both *E* and *Z* isomers is fairly simple. The metallation of alkoxyallylic sulfone ((*E*)-**7a**) with *n*-butyllithium gives the allyl anion which is in equilibrium at the reaction temperature with both its *E* and *Z* isomers. Presumably,

both isomers are alkylated at this temperature resulting in a mixture of (*E*)-**5a** and (*Z*)-**5a**. It thus appeared that the reaction was condition dependent. Further experiments were required for optimization.



Scheme 3



(*E*)-**7a**

The initial stereochemical assignment of (*E*)-**5a** and (*Z*)-**5a** was based on the comparison of the ^{1}H NMR spectra of the related compounds made by us.[6] Fortunately, this assignment process was carried out a step further and NOESY experiments were conducted on both isomers. It was found that the more polar isomer, which undergoes [4+3] cycloaddition (*vide infra*), had a strong nOe between the vinylic hydrogen and the methoxy group as well as a weak nOe between the allylic methyl group and the thiophenyl group, suggesting the *E* stereochemistry. On the other hand, for the less polar isomer, weak nOe signals were observed between the vinylic proton and the allylic methyl group as well as the methoxy group and the thiophenyl group, suggesting the *Z* stereochemistry. Further, the signals for olefinic hydrogens of the (*E*)-**5a** and (*Z*)-**5a** appeared at 5.49 and 5.64 ppm, respectively. Thus, the stereochemical assignments we had made originally[6] for compounds related to **5a** turned out to be incorrect and our rationale for the lack of cycloaddition reactivity for one of the isomers would have to be revised.

This discovery required a more careful investigation of the alkylation of sulfone ((*E*)-**7a**). Treatment of (*E*)-**7a** in THF with *n*-BuLi at -78 ºC followed by warming to room temperature for 5 min, recooling to -78 ºC for 5 min, quenching with water and slow warming to room temperature gave 2.5:1 mixture of starting material and a new compound assigned as (*Z*)-**7a**. Since the structure of (*E*)-**7a** had been established by X-Ray crystallography,[6] the new isomer had to be ((*Z*)-**7a**). This new isomer was slightly less polar than (*E*)-**7a**. Further, inspection of ^{1}H NMR spectrum of the mixture showed that the signal for the olefinic hydrogen appeared at 5.51 ppm, which is more downfield than that of (*E*)-**7a** (5.35 ppm). This is consistent with the assignment made for the stereoisomers of **5a**. However, further studies were required to understand the isomerization during the alkylation. Interestingly, when the anion from (*E*)-**7a** was stirred at room temperature for 5 min and cooled down to 0 ºC and quenched with water, the E:Z ratio of the product was 1:2.4 [(*E*)-**7a**:(*Z*)-**7a**].

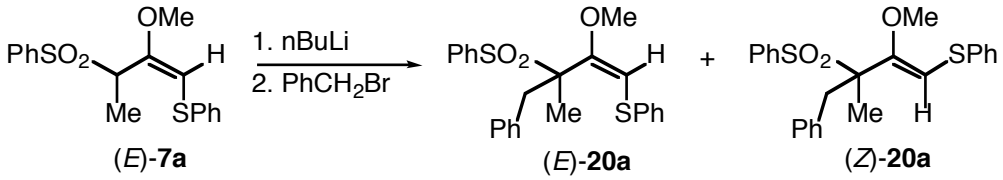


Table 1. Reaction of (*E*)-**7a** with benzyl bromide under various conditions.[a]

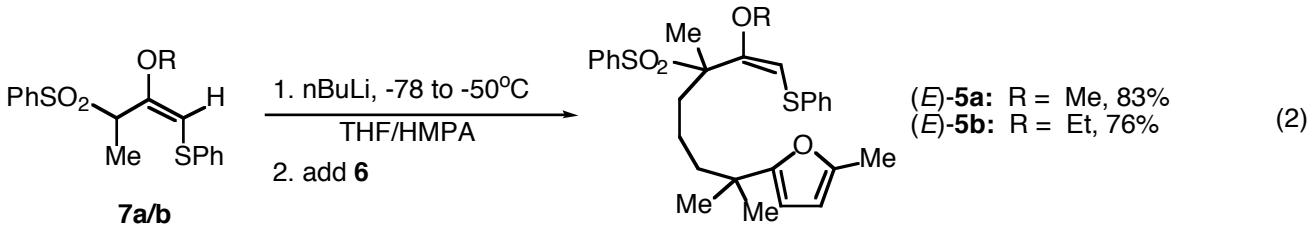
Entry	Product	E/Z Ratio[b]	Yield (%)[c,d]
1	**20a**	only E	84
2	**20a**	19:1	64
3	**20a**	1:7.5	52(57)
4	**20a**	1:8.3	30(44)
5	**20a**	only E	81

[a]See text for reaction conditions. [b]Ratios were determined by analysis of crude reaction mixture. [c]Isolated yield. [d]Yield in parentheses based on recovered starting material.

We conducted a study of the alkylation of (*E*)-**7a** using benzyl bromide. The results are summarized in Table 1. When the anion of ((*E*)-**7a**) was quenched at -78 ºC with benzyl bromide followed by slow warming only (*E*)-**20a** was formed in 84% yield (Table 1, Entry 1). The stereochemistry of this compound was established by X-Ray crystallography.[12] The signal for the olefinic hydrogen appeared at 5.47 ppm. When the anion was allowed to warm up to room temperature for 5 min and recooled to -78 ºC for 5 min and quenched with benzyl bromide followed by slow warming resulted in 19:1 mixture of *E*/*Z*-**20a** isomers in 64% yield (Table 1, Entry 2). When the anion was warmed to room temperature and cooled down to 0 ºC, quenching with benzyl bromide gave a 52% yield of (*E*)/(*Z*)-**20a** isomers in a 1:7.5 ratio, respectively (Table 1, Entry 3). As expected, when the anion was quenched at room temperature with the same halide, a 1:8.3 ratio of (*E*)-**20a** and (*Z*)-**20a** formed in 30% yield (Table 1, Entry 4).

The chemical shift of the olefinic hydrogen for the less polar ((*Z*)-**20a**) appeared at 5.62 ppm, downfield to the corresponding signal for (*E*)-**20a** (5.47 ppm). Finally, when the alkylation was carried out at -78 ºC in the presence of a small amount of HMPA, only ((*E*)-**20a**) was obtained as a single isomer in 81% yield (Table 1, Entry 5).

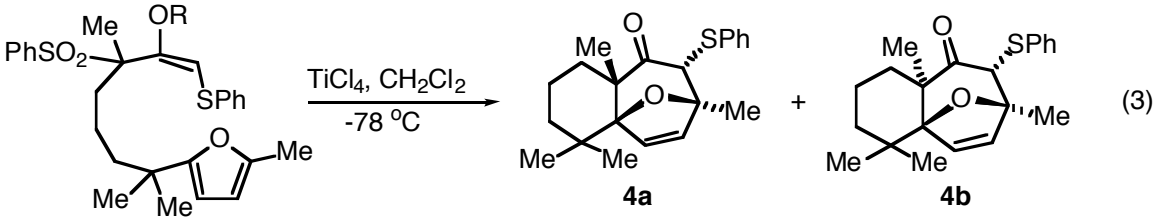
These data suggested the formation of exclusively *E* isomer in the alkylation of (*E*)-**7a**, if the alkylation was carried out at low temperatures. Therefore, we carried out the alkylations in the presence of small amounts of HMPA to obtain the precursors for 4+3 cycloaddition studies. Treatment of a 0.2 M solution of (*E*)-**7a** or (*E*)-**7b** in the presence of 20 % HMPA in freshly distilled THF at -78 ºC with *n*-BuLi (1.1 eq., 2.4 M in hexanes) gave a solution of the anion. Addition of iodide (**6**) followed by warming to approximately -50 ºC (bath temperature) resulted in alkylation and the formation of only *E* isomers of the corresponding alkylation products ((*E*)-**5a**) and ((*E*)-**5b**) with complete regiocontrol in excellent yields. The position of the chemical shift of olefinic protons in (*E*)-**5a** (5.49 ppm) and (*E*)-**5b** (5.46 ppm) indicated that the products formed with only *E* stereochemistry.[13]



7a/b

[4+3] CYCLOADDITION REACTIONS

Having the [4+3] cycloaddition precursors in hand, we used these alkoxyallylic sulfones in $TiCl_4$-mediated cycloadditions as shown in equation 3. To a cooled solution of $TiCl_4$ in methylene chloride at -78 ºC, a solution of sulfone ((*E*)-**5a**) or ((*E*)-**5b**) was added via a syringe over 10 min. Upon stirring at -78 ºC until the consumption of all starting material (*ca.* 20-30 min), the reaction afforded the cycloadducts (**4a**) and (**4b**) in 72-86% yield as a mixture of isomers in a ratio of approximately 1:1.



(*E*)-**5a**, R = Me
(*E*)-**5b**, R = Et

from (*E*)-**5a**, 86%, 1:1
from (*E*)-**5b**, 72%, 1.1:1

Cycloadducts (9**4a**) and (9**4b**) were separated using flash chromatography. Initial analyses of both cycloadducts at this stage by an ^{1}H NMR spectrum showed that the loss of the phenylsulfonyl, methoxy

or ethoxy groups and the complete disappearance of the furan ring. In addition to this, the ^{1}H NMR spectrum showed two new doublet signals at 6.28 ppm and 5.90 ppm for **4a** and 6.28 ppm and 5.91 ppm for **4b**. These are characteristic signals for [4+3] cycloadducts.

The relative stereochemistry of cycloadducts (**4a**) and (**4b**) was established by X-Ray crystallographic analysis of the corresponding sulfones, produced by oxidation of the sulfides with oxone.[9] Both of the sulfones turned out to be crystalline solids that were recrystallized from hexane and ethyl acetate to obtain X-ray quality crystals.[14]

The exact mechanism of the [4+3] cycloaddition reaction is still open to speculation. We have obtained theoretical evidence that the reaction may be concerted or stepwise, depending on the nature of the allylic cation involved in the reaction.[15] The lack of simple diastereoselection observed in the conversion of **5** to **4a** and **4b** is typical of the intramolecular [4+3] cycloaddition of furans that are tethered *via* a four carbon atom chain to the allylic cation dienophile.[16] It is to be noted, however, that in both **4a** and **4b**, the phenylsulfenyl group is *trans* to the oxygen bridge. This may be a kinetic effect, but the center at which the sulfur atom resides is highly epimerizable. It thus is quite likely that the configuration of the stereocenters bearing sulfur are the result of thermodynamic control. Further studies of the cycloaddition chemistry of vinylthionium ions will be necessary to determine the origins of stereocontrol arising in these systems.

ALTERNATIVE APPROACHES TO [4+3] CYCLOADDUCTS

Before we learned how to produce (*E*)-**5a** selectively, we accumulated quantities of (*Z*)-**5a**, which did not give cycloadducts under the reaction conditions used for (*E*)-**5a**. In fact, it stayed intact at low temperatures in the presence of Lewis acids. However, the reaction gave a complex reaction mixture at elevated temperatures along with very small amount of cycloadducts as determined by TLC and GC analyses. Further studies still remain to be conducted to effect the cyclization of (*Z*)-**5a** to form cycloadducts. One possible reason for the difficulty in cyclizing (*Z*)-**5a** may be due to its proclivity to serve as a bidentate ligand as illustrated in Figure 1 for the bidentate Lewis acid titanium tetrachloride. However, this does not explain problems encountered with Lewis acids that are nominally monodentate Lewis acids. In any case, we sought a different solution to the lack of reactivity associated with (*Z*)-**5a**.

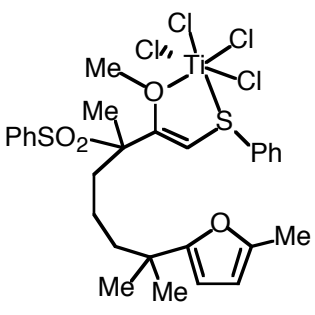
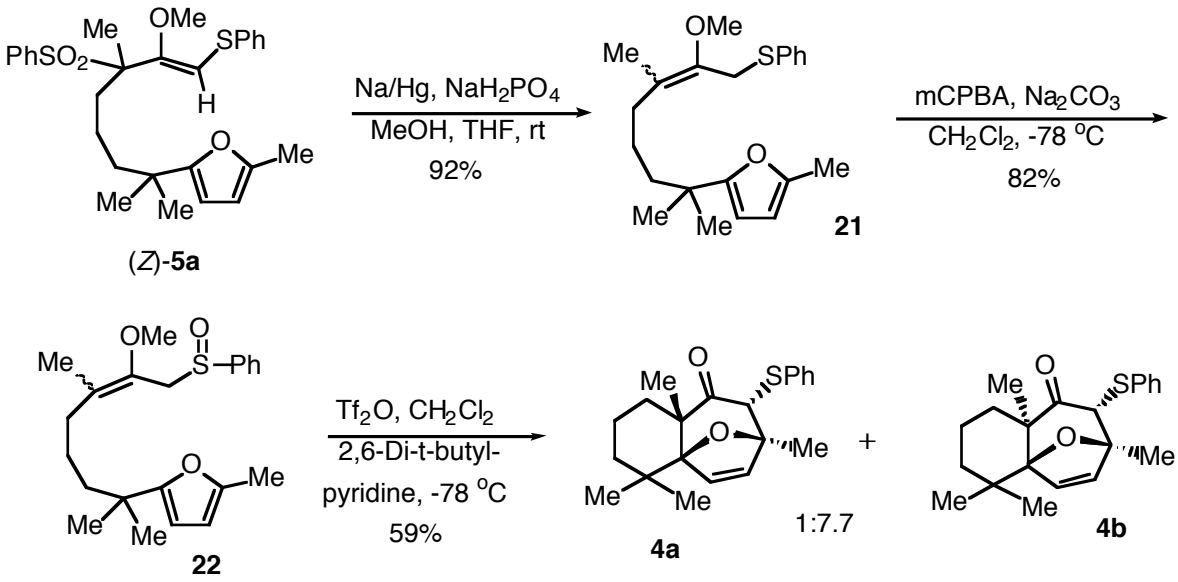


Figure 1

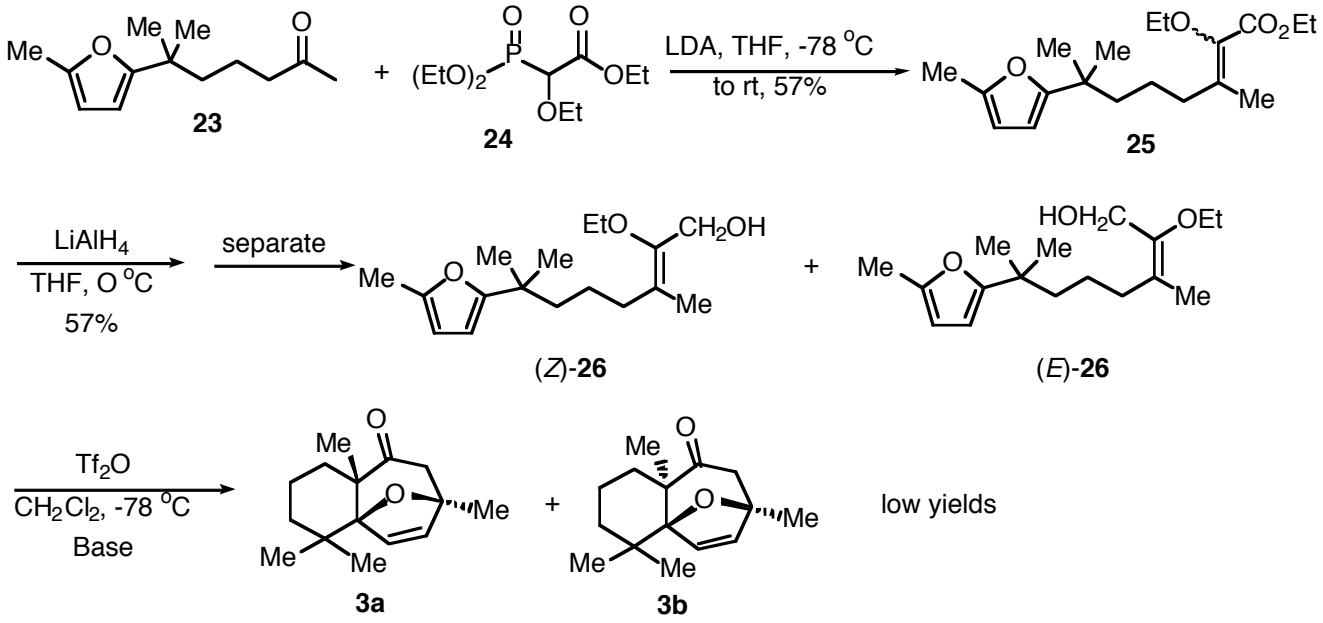


Scheme 4

Thus, (*Z*)-**5a** was treated with buffered sodium amalgam in methanol and THF at room temperature (Scheme 4). During this process, the sulfone moiety was cleaved and the double bond was isomerized to the most substituted position, but phenylthio functionality stayed intact. The allylic sulfide (**21**) was obtained from the sodium amalgam reaction as an approximately 1:1 mixture of *E* and *Z* isomers. It was treated with *m*-chloroperbenzoic acid in the presence of sodium carbonate to give an inseparable mixture of allylic sulfoxides (**22**) in a 1:1 ratio and in 82% yield. Treatment of the mixture of allylic sulfoxides with triflic anhydride in the presence of 2,6-di-*tert*-butylpyridine in methylene chloride at -78 °C resulted in a domino Pummerer-[4+3] cycloaddition[6] and yielded 59% of cycloadducts (**4a**) and (**4b**) as a 1:7.7 mixture, along with very small amount of an elimination product.

The stereochemical outcome of this reaction is clearly different from that involving (*E*)-**5a**. It is not clear whether the intermediates generated under Pummerer conditions have a structural bias towards a particular vinylthionium ion. For our purposes, this result was interesting, but the major product was not on the path to widdrol, but *epi*-widdrol, which was not a primary target. We thus did not pursue this reaction further, though the high diastereoselection observed definitely demands further study.

We also attempted to shorten the overall route to the cycloadduct. To that end, we wanted to demonstrate the feasibility of the [4+3] cycloaddition *via* a different precursor using a different method to generate the required allylic cation. We especially wanted to be rid of the phenylthio group, whose presence in the reaction was in principle not necessary. In order to accomplish this goal, we used the ketone (**23**) as a starting point. This compound is available in three steps from β-ionone.[17] Horner-Emmons homologation of the ketone (**23**) with triethyl 2-ethoxyphosphonoacetate[18] (**24**) using LDA as the base in THF at -78 °C



Scheme 5

to room temperature gave an inseparable mixture of □,□-unsaturated esters (**25**) in an unoptimized yield of 57% (Scheme 5). The mixture of was carried directly to the next step and reduced with $LiAlH_4$ in THF at 0 °C to give a separable mixture of allylic alcohols (**26**) in 57% yield. The ratio of the isomers was determined by ^1H NMR spectrometry of the crude reaction mixture to be 1:1.

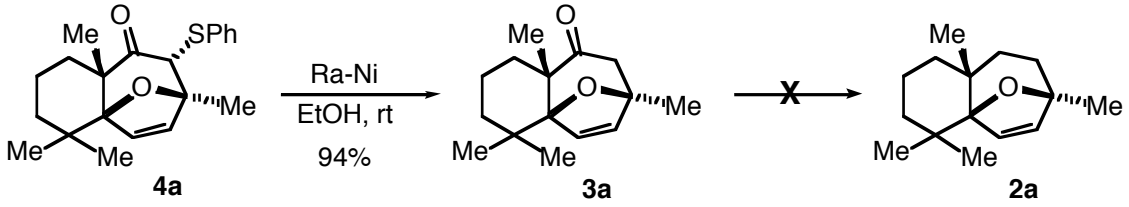
This mixture was separated by a flash chromatography and the double bond configuration was determined by NOESY experiments on the individual isomers. The isomers were separately taken for [4+3] cycloaddition studies. The first experiment conducted with (*Z*)-**26** used triflic anhydride as the Lewis acid in the presence of 2,6-lutidine as the base in methylene chloride at -78 °C.[19] The reaction gave a complex mixture of many unidentified products along with about 10% of the cycloadducts (**3a**) and (**3b**) as a 1:1.1 mixture, respectively.

Our attention turned to (*E*)-**26** in the hope of obtaining better results. Unfortunately, treatment of this allylic alcohol under the same reaction conditions resulted in a complex reaction mixture. In case of 2,6-lutidine as the base, GC analysis showed very small amounts of cyloadducts formed. Ionization of this allylic alcohol under different conditions was not pursued with vigor. The reason behind the poor results obtained is not clear.

TOWARDS WIDDROL

Having the aforementioned cycloadducts (**4a**) and (**4b**) in hand, we pursued the chemistry of 4+3 adducts for the synthesis of widdrol (**1**) as well as *epi*-widdrol. First, the cycloadduct (**4a**) was desulfurized by

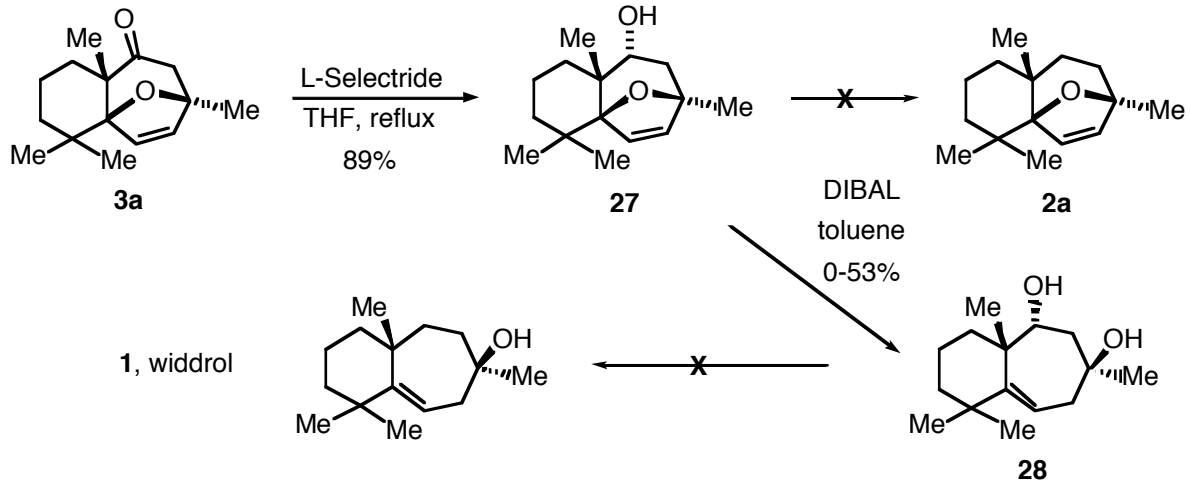
treatment with activated Raney nickel[20] in ethanol at room temperature to give the tricyclic ketone (**3a**) in 94% yield as shown in Scheme 6.



Scheme 6

Having tricyclic ketone (**3a**), we attempted to effect the deoxygenation at this stage using the Wolff-Kishner reaction,[21] but obtained a complex mixture. We then tried alternative ways of achieving this process. Attempts were made to functionalize **3a** with Lawesson's reagent,[22] ethanedithiol[23] and tosylhydrazine[24] in the hope of having a precursor for deoxygenation process. However, all attempts to produce **2a** were unsuccessful.

The tricyclic ketone (**3a**) was reduced by treatment with L-Selectride®,[25] which cleanly gave the alcohol (**27**) in 89% yield after chromatographic purification (Scheme 7). Other reducing agents resulted in a mixture of isomers. Examination of the ^{1}H NMR spectrum of **27** showed a doublet of doublets at 3.35 ppm that was assigned to the proton α to the hydroxy group. The stereochemistry of the hydroxy group was tentatively established to be at the β face of the ring. The bulky L-Selectride® can only approach from the exo (equatorial) face of the oxabicyclic ring system to give the (axial) alcohol.



Scheme 7

At this stage of the synthesis, we attempted the deoxygenation of the secondary alcohol to obtain **2a**. Attempts were made to derivatize this highly sterically hindered alcohol with 1,1-thiocarbonyldiimidazole,[26] pentafluorophenyl chlorothionoformate[27] and N,N,N,N-tetramethyldiamido-phosphorochloridate.[28] However, all attempts were unsuccessful. This alcohol was then derivatized as the acetate or the benzoate upon the treatment with corresponding acid chloride in the presence of

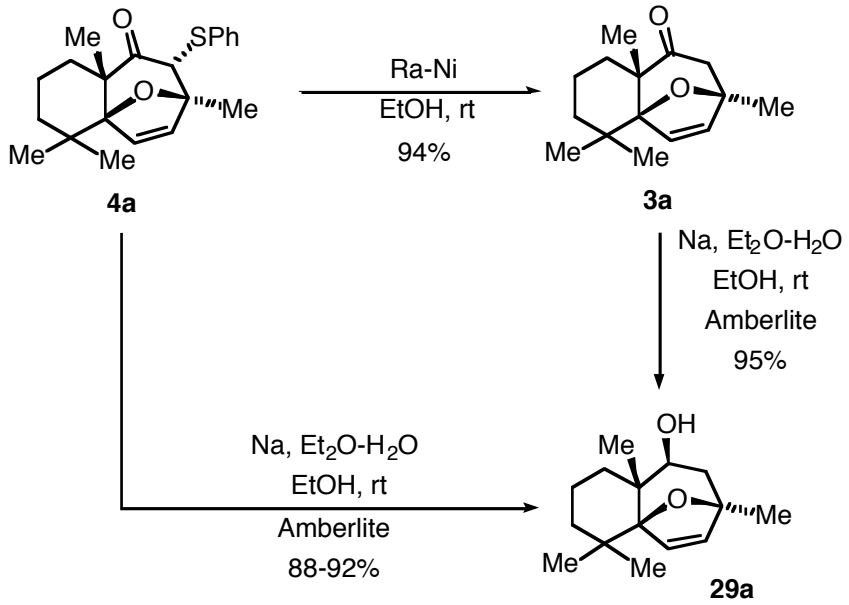
pyridine and DMAP. However, attempted deoxygenation failed to give the desired product upon photolysis in HMPA/water.[29]

Among the methods used to attempt the oxabicyclic ring opening of **27**,[30] DIBAL was the only reagent to effect this process. It is worth mentioning that this process was DIBAL dependent and rather capricious in our hands. The ring cleavage was sometimes not effected as desired due to unpredictable complications. Because of this, we were not able to bring up enough material to thoroughly examine reactions for the deoxygenation of the secondary alcohol in **28**.

With the limited supply of diol (**28**) in hand, several reactions were attempted to effect the removal of the secondary hydroxy group. The secondary alcohol was only functionalized in the presence of tertiary alcohol with highly reactive electrophiles such as acid chlorides and mesyl chloride. However the attempted deoxygenation failed to effect the removal of hydroxyl group. For example, treatment of diol (**28**) with methyl oxalyl chloride gave the corresponding ester in 52% yield. However, attempts to deoxygenate with various radical initiators failed, but resulted in the formation of **28**.[31] The deoxygenation attempt using the benzoate ester under photolytic conditions with *N*-methylcarbazole as a sensitizer resulted in a clean reaction, but the analysis showed that the product was not the desired one by ^{1}H NMR spectroscopic analysis.[32] At that time, there was no attempt to identify the product. One other approach to achieve deoxygenation was made through a sulfonate ester of **28**. The attempted deoxygenation of mesylate gave the diol back.[33] However, when the diol was fuctionalized as the isopropyl sulfonate under the reaction conditions reported, the reaction gave a clean, but unidentified product, which appeared to have changes in the carbon backbone.[34]

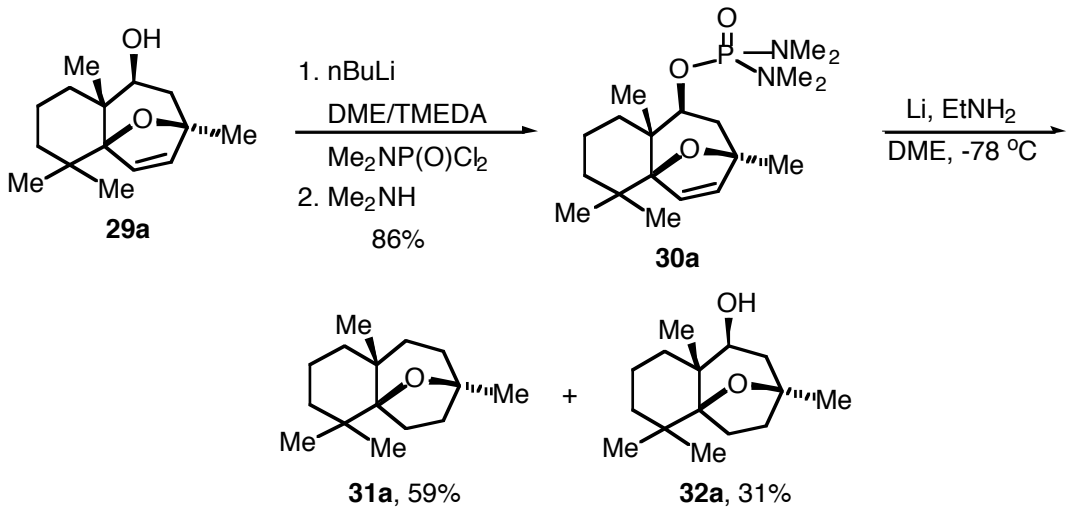
After our unsuccessful attempts to synthesize the natural product widdrol (**1**) at this stage, we decided to pursue an alternative approach in which the less sterically hindered alcohol (**29a**) would be prepared in the hope that functionalization and consequently deoxygenation processes would be facilitated, since the secondary hydroxy group in this compound is less hindered. In order to accomplish this, the cycloadduct (**4a**) was treated with Raney nickel as described above to give the ketone (**3a**) in 94% yield. Upon the treatment of the ketone **(3a**) with finely cut excess sodium in ether saturated with water in the presence of ethanol and amberlite resin, the alcohol (**29a**) was obtained as a single isomer in 95% yield (Scheme 8).[35] The structural assignment was made as for the alcohol (**27**), with which **29a** was clearly isomeric. The most thermodynamically stable alcohol was produced, as expected for a reduction of this type.

We reasoned that a dissolving metal reduction should allow us to prepare **29a** directly from **4a**. Indeed,



Scheme 8

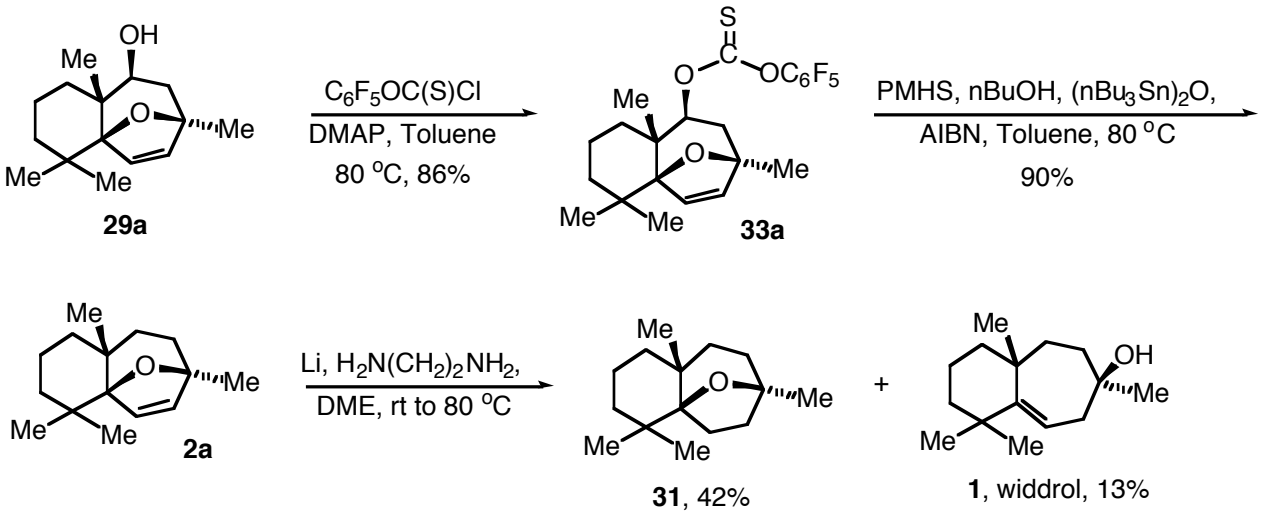
upon the treatment of keto sulfide (**4a**) with sodium metal, the alcohol (**29a**) was obtained directly in 88-92% yield. Presumably, the compound was initially desulfurized and the resulting enolate protonated to produce **3a** *in situ*. Subsequent reduction gave **29a**.



Scheme 9

Having the less sterically hindered alcohol (**29a**), we attempted to simultaneously effect the deoxygenation and ring cleavage. The substrate needed for this was prepared as shown in Scheme 9. Treatment of the alcohol (**29a**) with *n*-butyllithium in dimethoxyethane and tetramethylethylenediamine followed by quenching with *N*,*N*-dimethylphosphoramidic dichloride[36] and then aqueous dimethylamine gave phosphorodiamidate (**30a**) in 86% yield.

After the successful preparation of phosphorodiamidate (**30a**), we attempted a tandem deoxygenation and ring cleavage reaction. Thus, treatment of **30a** with freshly cut lithium shavings in ethylamine at -78 °C gave a mixture of two products (**31a**) and (**32a**) in 59% and 31% yields, respectively. The former was characterized by spectroscopic analysis as well as high resolution exact MS data. The ^{1}H NMR spectrum showed no olefinic or oxygen-associated signals, but only aliphatic signals between 1.91-0.93 ppm. However, the ^{13}C NMR spectrum showed signals at 87.7 and 81.3 ppm, suggesting the oxabicyclic ring stayed intact. Compound (**32a**) was also characterized by a combination of ^{1}H NMR, ^{13}C NMR, IR spectra as well as elemental analysis. Examination of the ^{1}H NMR and ^{13}C NMR spectra showed the complete loss of olefinic signals for **32a**. The hydroxy group absorption was evident from the IR spectrum. In addition, signals at 88.3, 79.9 and 72.6 ppm in the ^{13}C NMR spectrum suggested three carbons bound to an oxygen atom. Based on this result we decided to pursue a radical process for the dexoxygenation of **29a** in order to keep the olefinic double bond intact for the proposed ring opening reaction.



Scheme 10

Alcohol (**29a**) was treated with excess pentafluorophenyl chlorothionoformate in the presence of excess DMAP in toluene at 80 °C to yield 86% yield of thiocarbonate (**33a**) (Scheme 10). We then pursued deoxygenation. We first tried to initiate the radical process by use of triethylborane. A solution of **33a** in hexane was treated with triethylborane and tributyltin hydride at room temperature. The reaction was initiated with a stream of air. After a flash chromatographic purification, the desired product (**2a**) was obtained in as high as 67% yield. However, the yields were not consistent and the purity of the product was not high as might be expected for these reactions. A Barton-McCombie procedure was adopted using AIBN as the radical initiator. This reaction was better than preceding one, but for this reaction the required amount of tributyltin hydride is 2-3-fold in excess with respect to the substrate. This caused some problems for the purification and resulted in rather low yields. The deoxygenation procedure was

ultimately effected by the use of the catalytic Barton-McCombie reaction reported by Fu.[37] The mixture of the substrate, polymethylhydrosiloxane, *n*-butyl alcohol, bis(tribuytltin) oxide was heated to 80 ºC in toluene to give product (**2a**) in 90% yield.

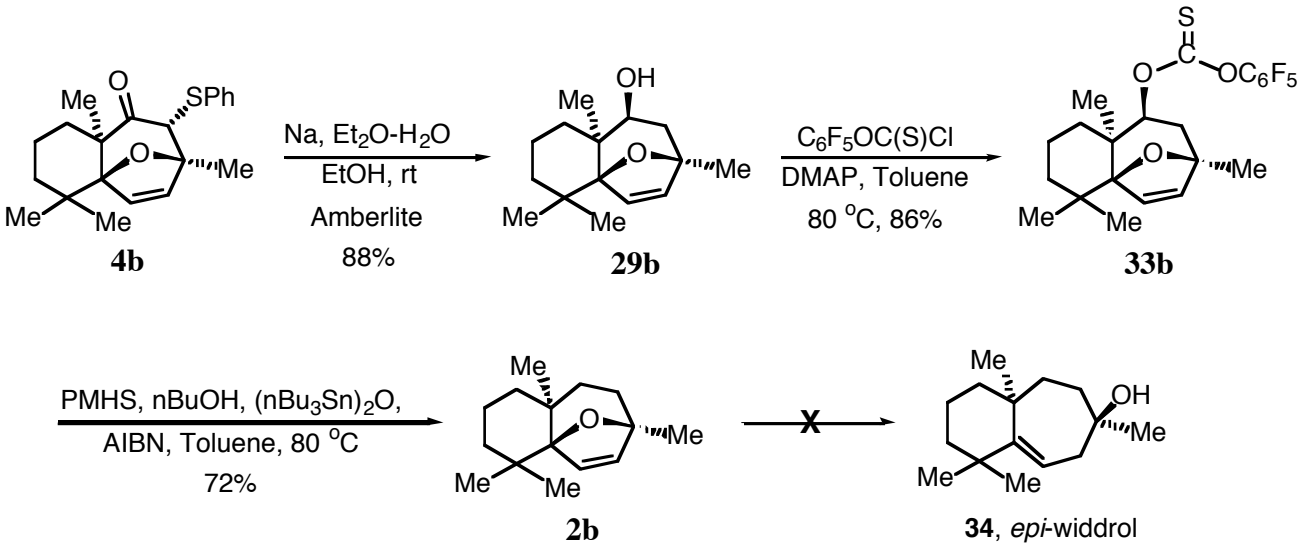
We then attempted to effect the ring cleavage of **2a** to obtain widdrol. Our first attempt to accomplish the ring cleavage involved the use of DIBAL. Treatment of the substrate with excess DIBAL (20 eq.) gave none of **1**, but a trace amount of a side product along with unreacted starting material. We did not investigate the structure of this side product, but it was assumed that treatment of oxabicyclic substrate with excess DIBAL resulted in hydroalumination, then the ring-opening with the wrong regiochemistry. After this unsuccessful attempt, our attention turned to the use of dissolving metal reductions. We first attempted the reaction using freshly cut excess lithium metal in ethylamine at -78 ºC. Into the deep-blue solution, a solution of substrate in DME was added and for 10-15 min, then quenched. The analysis of the crude reaction mixture with TLC and GC showed not even a trace of the desired product. However, the product (**31**) derived from a simple double bond reduction, was obtained in as high as 80% yield.

After this disappointment, it was thought that reaction might benefit from the use of elevated temperatures. In order to achieve that, we replaced ethylamine with ethylenediamine and carried out the reaction at room temperature. The initial results were encouraging and we were able to obtain very low yield of widdrol **1**, but the reaction gave 64% of **31**. Then, we elevated the temperature to about 80 ºC and carried out the reaction. We were able to obtain a 13% yield of widdrol (**1**) along with a 42% yield of **31**. Inspection of molecular models indicated that distortion of the ring system does not favor a suitable alignment of the olefinic □-system and C-O bond to effect the ring cleavage. This probably explains the reluctance of the allylic ether to open efficiently. Further attempts were made to improve the yield of this process, but none were successful.

Finally, we have attempted to convert the cycloadduct (**4b**) to *epi*-widdol (**34**) using the same methodology developed for widdrol. The chemistry described for the transformations of **4a** essentially all worked for **4b**. One example is given in Scheme 11. Treatment of **4b** with freshly cut excess sodium metal in ether saturated with water in the presence of ethanol as proton donor and amberlite gave the alcohol (**29b**) in 88% yield. Alcohol (**29b**) was treated with excess pentafluorophenyl chlorothionoformate in the presence of excess DMAP in toluene at 80 ºC to give an 86% yield of thiocarbonate (**33b**). Deoxygenation as previously described afforded **2b** in good yield. However, all attempts to convert (**2b**) to *epi*-widdrol (**34**) were unsuccessful, dissolving metal procedures giving only reduction of the double bond or recovered starting material.

Summary

The use of alkoxyallylic sulfones for the preparation and generation of vinylthionium ions has been demonstrated. It was also shown that the outcome of the alkylation of the anion derived from alkoxyallylic sulfones is dependent on the reaction conditions. With the development of a new alkylation procedure, we found that the alkylation can produce *E*-alkoxyallylic sulfones, which are the precursors for [4+3] cycloaddition reactions. However, such cycloadditions produce 6,7-fused ring systems with almost no stereocontrol.



Scheme 11

We have applied this methodology to build the ring system of widdrol and *epi*-widdrol. We were able to synthesize widdrol, with only the final step being problematic. Recent advances in the opening of oxabicyclic ring systems suggest that it should be possible to improve the yields of the final step in the widdrol sequence.[38] More generally, the conversion of [4+3] cycloadducts derived from furans to unbridged systems could provide access to many other natural products.

EXPERIMENTAL

All air and moisture sensitive reactions were carried out in flame-dried or oven-dried (at 120 °C) glassware under an inert atmosphere of nitrogen. All reactive liquid reagents were transferred by syringe or cannula and were added into the flask through a rubber septa. Methylene chloride was freshly distilled from CaH_2 prior to use. Tetrahydrofuran and ether were freshly distilled from sodium and benzophenone ketyl immediately prior to use. Methanol was distilled over magnesium methoxide prior to use. All other reagent grade solvents, hexanes, ethyl acetate etc., were distilled prior to use. Melting points were obtained on a Fisher-Johns Hot Stage melting point apparatus and are not corrected. X-Ray data were obtained on an Enraf-Nonius CAD-4 diffractometer. All analytical samples were either distilled or

recrystallized using HPLC grade solvents before submitting them for elemental analysis.

Both ^{1}H and ^{13}C NMR spectra were obtained on either a Bruker AMX-500 or AMX-250 at 500 MHz and 250 MHz for ^{1}H NMR and 125 MHz and 62 MHz for ^{13}C NMR, respectively. All NMR spectra were obtained as a solution in $CDCl_3$ with TMS as the internal standard unless otherwise stated.

Gas chromatographic analyses were done on Shimadzu GC-9A instrument equipped with an SPB-5 fused silica capillary column (length 15 m, i.d. 0.25 mm) using a flame ionization detector and helium as the carrier gas. A Hewlett-Packard HP 3390 integrator was used to record chromatograms.

Phenylsulfenyl chloride[39] was prepared as reported. All other reagents were obtained from commercial sources and used directly unless otherwise stated.

(*E*)-2-Methoxy-1-phenylsulfenyl-3-phenylsulfonyl-1-propene (12a). To a 1L flame-dried flask equipped with a magnetic stir bar, a septum and a nitrogen balloon, sulfone (**11a**) (35.99 g, 0.16 mol) and freshly distilled 564 mL of dichloromethane were added to give ca. 0.3 M solution and the flask was cooled down to -78 ºC in an isopropanol/dry ice bath. Meanwhile, a 100 mL flame-dried, pear-shaped flask was charged with phenylsulfenyl chloride (25.7 g, 0.178 mol) dissolved in 50 mL dry dichloromethane and cooled down to -78 ºC. The sulfenyl chloride solution was transfered into the 1L flask *via* a cannula over 20-25 min. The mixture was allowed to stir at -78 ºC for about 10-15 min and warmed up to rt and stirred at room temperature for 1 hour and followed by recooling to -78 ºC. DBU (27.09 g, 26.61 mL, 0.178 mol) was added *via* a syringe slowly over 15-20 min. The cold bath was removed and the mixture was allowed to stir at rt for 1 h. TLC showed the completion of the reaction. The mixture was quenched with 1N HCl and transfered into a separatory funnel. It was washed with water (3x100 mL), 1N HCl (1x100 mL), brine (1x100 mL) and dried over Na_2SO_4. Removal of the solvent on a rotary evaporator gave an oily crude product which was purified by flash chromatography (20% ethyl acetate in hexanes) (47.76 g, 88%).

(±)-(*E*)-2-Methoxy-3-methyl-1-phenylsulfenyl-3-phenylsulfonyl-1-propene (7a). To a flame-dried, 500 mL round bottomed flask equipped with a magnetic stir bar, a nitrogen balloon and a septum, sulfone (**12a**) (20.0 g, 0.062 mol) was aded and dissolved in freshly distilled THF (312 mL) to give *ca*. 0.2 M solution. This solution was cooled down to -78 ºC in an isopropanol/dry ice bath. To this cooled solution was added *n*BuLi (30.83 mL, 2.4 M solution in hexanes, 0.074 mol) slowly *via* a syringe over 10-15 min. After the addition was complete, the mixture was allowed to stir at this temperature for about 15 min, resulting in a yellow solution. To this solution iodomethane (13.20 g, 0.093 mol) was added *via* a syringe

over a few min at -78 ºC and the mixture was allowed to stir at -78 ºC for 1 h. TLC showed the completion of the reaction. The mixture was quenched by addition of sat. NH_4Cl and rinsed into a separatory funnel with ether. The mixture was extracted with ether (4x50 mL), and the combined organic layers were washed with water (2x50 mL), brine (1x50 mL) and dried over Na_2SO_4. Removal of the solvent on a rotary evaporator gave the crude product which was recrystallized from hexanes and ethyl acetate to give white crystals (18.36 g, 88%).

(*E*)-2-Ethoxy-1-phenylsulfenyl-3-phenylsulfonyl-1-propene (12b). This sulfone was prepared in the same fashion as **12a**. The crude product was purified by flash chromatography to afford a clear oil. Yield: 82%. An analytical sample was obtained by taking a middle fraction from flash chromatography (4:1 hexane:ethyl acetate). ^{1}H NMR (250 MHz, $CDCl_3$) □ 7.92-7.89 (m, 2H), 7.67-7.48 (m, 3H), 7.28-7.11 (m, 5H), 5.42 (s, 1H), 4.35 (s, 2H), 3.75 (q, 2H, J=7.0 Hz), 1.13 (t, 3H, J=7.0 Hz); ^{13}C NMR (62.9 MHz, $CHCl_3$) □ 152.9, 139.3, 137.2, 133.6, 128.9, 128.8, 128.5, 126.9, 125.7, 96.4, 64.0, 58.9, 14.0; IR (NaCl, neat) 1603m, 1584m, 1332s, 1309m, 1217s, 1131m, 1086m, 1070m cm^{-1}. Anal. Calcd for $C_{17}H_{18}O_3S_2$ C: 61.05; H, 5.39. Found: C, 61.26; H, 5.39.

(±)-(*E*)-2-Ethoxy-3-methyl-1-phenylsulfenyl-3-phenylsulfonyl-1-propene (7b). This sulfone was prepared in the same fashion as **7a**. The crude product was purified by flash chromatography to afford a clear oil. Yield: 85%. An analytical sample was obtained by taking a middle fraction from flash chromatography (4:1 hexane:ethyl acetate). ^{1}H NMR (250 MHz, $CDCl_3$) □ 7.87 (dd, 2H, J=1.5. 7.4 Hz), 7.65-7.59 (m, 1H), 7.52-7.46 (m, 2H), 7.27-7.10 (m, 5H), 5.33 (s, 1H), 4.93 (q, 1H, J=7.1 Hz), 3.89-3.69 (m, 2H), 1.54 (d, 3H, J=7.1 Hz), 1.23 (t, 3H, J=7.0 Hz); ^{13}C NMR (62.9 MHz, $CHCl_3$) □ 157.1, 138.0, 137.42, 133.53, 129.10, 128.82, 128.69, 125.58, 94.96, 63.96, 61.46, 14.04, 12.09; IR (NaCl, neat) 1601s, 1582m, 1483s, 1447s, 1320s, 1307s, 1204s, 1149s, 1140s, 1073s, cm^{-1}. Anal. Calcd for $C_{18}H_{20}O_3S_2$ C: 62.04; H, 5.78. Found: C, 62.27; H, 5.56.

3-[2-(5-Methyl)furyl]-3-methylbutanol. To a 500 mL round-bottomed, 3-necked flask equipped with magnetic stir bar, an addition funnel, septa and a nitrogen balloon, $LiAlH_4$ (3.92 g, 0.1 mol) and freshly distilled THF (172 mL) were added. This suspension was then cooled down to 0 ºC in an ice bath, followed by the addition of the ester (**17**)[6] (17.0 g, 0.086 mol) as a solution in 100 mL of dry THF through the addition funnel over 30-40 min. After the addition was complete, the ice bath was removed and the mixture was allowed to stir at rt for 1 h. To the reaction mixture was slowly added $Na_2SO_4.10{\cdot}H_2O$ until a white precipitate formed which was filtered and washed with some ether. The solvent was removed on a rotary evaporator to give the crude product. The crude product was distilled on Kugelrohr to give a clear liquid.(13.92 g, 97%) bp 120-130 ºC/1.5 mmHg. An analytical sample was obtained by taking a middle fraction from flash chromatography (5:1 hexane:ethyl acetate). ^{1}H NMR (250 MHz, $CDCl_3$) □ 5.82 (m, 2H), 3.51 (t, 2H, J=7.4 Hz), 2.28 (s, 1H, br), 2.22 (d, 3H, J=0.8 Hz), 1.84

(t, 2H, J=7.1 Hz), 1.25 (s, 6H); ^{13}C NMR (125 MHz, $CHCl_3$) 160.3, 150.1, 105.4, 103.7, 59.6, 44.2, 34.2, 27.1, 13.3; IR (NaCl, neat) 3347w, 1562s, 1472m, 1450 m, 1221s, 1194m, 1023s, 781s, cm $^{-1}$. Anal. Calcd for $C_{10}H_{16}O_2$: C, 71.38; H, 9.59. Found: C, 71.31; H, 9.44.

3-[2-(5-Methyl)furyl]-3-methylbutyl-*p*-toluenesulfonate. To a flame-dried 500 mL round-bottomed flask equipped with a magnetic stir bar, a nitrogen balloon and a septum, the above alcohol (13.92 g, 0.083 mol) and 166 mL of anhydrous chloroform were added. The flask was cooled down to 0 ºC in an ice bath and pyridine (12.96 g, 13.22 mL, 0.166 mol) was added via a syringe. After 20 min, tosyl chloride (23.82 g, 0.125 mol) was added as solid in one portion, resulting in yellow solution. The bath was removed and the mixture was allowed to stir at room temperature for 24 h. The reaction was monitored by TLC. The reaction mixture was then rinsed into a separatory funnel and was washed with 1N HCl (2x100 mL), water (2x100 mL), brine (1x100 mL) and dried over Na_2SO_4. Removal of the solvent on a rotary evaporator gave the crude product which was purified by flash chromatography (10% ethyl acetate in hexanes) affording the product in (24.81 g, 92%). mp 37-38 ºC. ^{1}H NMR (250 MHz, $CDCl_3$) 7.75 (d, 2H, J=8.3 Hz), 7.33 (d, 2H, J= 8.3 Hz), 5.77-5.75 (m, 2H), 3.95 (t, 2H, J=7.2 Hz), 2.45 (s, 3H), 2.20 (d, 3H, J= 0.6 Hz), 1.94 (t, 2H, J= 7.3 Hz), 1.22 (s, 6H); ^{13}C NMR (62.9 MHz, $CDCl_3$) 159.0, 150.5, 144.5, 133.2, 129.7, 127.8, 105.5, 104.4, 68.2, 40.2, 34.4, 27.1, 21.6, 13.5.

4-[2-(5-Methyl)furyl]-4-methylpentanenitrile (18). To a flame-dried 300 mL round-bottomed flask equipped with a magnetic stir bar, a reflux condenser, a nitrogen balloon and a septum, the tosylate (24.0 g, 0.075 mol) and anhydrous DMSO (149 mL) were added. Sodium cyanide (5.49 g, 0.112 mol) was added as solid in one portion and the reaction mixture was placed in an oil bath, and heated gently to 90 ºC for 2 h. TLC showed the completion of the reaction. The flask was then cooled down to rt and poured into 200 mL sat. NH_4Cl, rinsed into a separatory funnel and extracted with methylene chloride (4x100 mL). The combined organic layers were washed with water (2x100 mL), brine (1x100 mL) and dried over Na_2SO_4. Removal of the solvent on a rotary evaporator gave a yellow oil which was purified by flash chromatography (10% ethyl acetate in hexanes) to afford the product (11.90 g, 90%). An analytical sample was obtained by taking a middle fraction from the flash chromatography. ^{1}H NMR (500 MHz, $CDCl_3$) 5.87 (d, 1H, J= 3.0 Hz), 5.83 (d, 1H, J=1.0 Hz), 2.25 (s, 3H), 2.13 (t, 2H, J=7.6 Hz), 1.94 (t, 2H, J=7.5 Hz), 1.26 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) 158.0, 150.9, 120.0, 105.6, 105.2, 37.4, 35.3, 26.3, 13.4, 12.9; IR (NaCl, neat) 2246s, 1611m, 1561s, 1474s, 1452s, 1390 (s), 1369s, 1220s, 1197m, 1179m, 1121s, 1022s, 958s, 939s, 784s, cm^{-1}. Anal. Calcd for $C_{11}H_{15}NO$: C, 74.53; H, 8.54. Found: C, 74.57: H, 8.40.

4-[2-(5-Methyl)furyl]-4-methylpentanoic acid (19). To a 3L round-bottomed flask equipped with a reflux condenser and a magnetic stir bar, nitrile (**18**) (18.0 g, 0.1 mol) and methanol (1,016 mL) were added. To this solution was added 850 mL of aqueous 5N NaOH (42 eq.) and the mixture was allowed to

reflux for 24 h. The flask was cooled down to rt and conc. HCl was added until the pH was about 5. The mixture was extracted with ether (4x100 mL), and the combined organic layers were washed with 10% $NaHCO_3$ (1x100 mL), water (2x100 mL), brine (1x100 mL) and dried over Na_2SO_4. Removal of the solvent on a rotary evaporator gave the crude product which was purified by flash chromatography (25% ethyl acetate in hexanes) affording the product (17.22 g, 86%). An analytical sample was obtained by taking a middle fraction from flash chromatography, then recrystallization from hexane and ethyl acetate). mp 49-50 ºC. ^{1}H NMR (500 MHz, $CDCl_3$) □ 10.78 (s, 1H, br), 5.83-5.79 (m, 2H), 2.22 (s, 3H), 2.19 (t, 2H, J=7.9 Hz), 1.89 (t, 2H, J=7.9 Hz), 1.23 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) □ 180.4, 159.5, 105.5, 104.5, 36.4, 35.1, 30.0, 26.6, 13.5; IR (CCl_4) 1711s, 1415 (m), 1387 (w), 1303m, 1221s, 1119m, 1022m, 960m, 939m cm $^{-1}$. Anal. Calcd for $C_{11}H_{16}O_3$: C, 72.49; H, 9.95. Found: C, 72.60; H, 9.77.

4-[2-(5-Methyl)furyl]-4-methylpentanol. To a 500 mL round-bottomed, 3-necked flask equipped with magnetic stir bar, an addition funnel, septum and a nitrogen balloon, $LiAlH_4$ (3.94 g, 0.104 mol) and freshly distilled THF (173 mL) were added. This suspension was then cooled down to 0 ºC in an ice bath, followed by the addition of the acid (**19**) (17.0 g, 0.086 mol) as a solution in 100 mL of dry THF through the addition funnel over 30-40 min. After the addition was complete, the ice bath was removed and the mixture was allowed to stir at rt for 1 h. The reaction mixture was quenched by addition of $Na_2SO_4.10{\cdot}H_2O$ until a white precipitate formed. This was filtered and washed with some ether and the solvent was removed on a rotary evaporator to give the crude product. The crude product was distilled (Kugelrohr) to give a clear liquid (15.94 g, 96%). bp 130-135 ºC/0.5 mm Hg. An analytical sample was obtained by taking a middle fraction from flash chromatography (5:1 hexane:ethyl acetate). ^{1}H NMR (500 MHz, $CDCl_3$) □ 5.82-5.80 (m, 2H), 3.55 (t, 2H, J= 6.6 Hz), 2.24 (s, 3H), 1.62-1.58 (m, 2H), 1.45-1.39 (m, 2H) 1.37 (s, 1H, br), 1.23 (s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) □ 160.9, 150.0, 105.4, 103.8, 63.4, 37.9, 35.3, 28.2, 26.2, 13.5. IR (NaCl, neat) 3436m, 1563m, 1452m, 1348w, 1221s, 1118m, 1081m, 1022s, 981w, 999m, cm^{-1}. Anal. Calcd for $C_{11}H_{18}O_2$: C, 72.49; H, 9.95. Found: C, 72.60; H, 9.77.

4-[2-(5-Methyl)furyl]-4-methylpentyl iodide (6). A flame-dried, 250 mL round-bottomed flask equipped with a magnetic stir bar, a reflux condenser, a nitrogen balloon and a septum, was charged with the preceding alcohol (7.0 g, 0.0386 mol) and freshly distilled THF (193 mL). To this mixture was added *N*,*N*'-dicyclohexylcarbodiimidium iodide (26.92 g, 0.077 mol) as a solid in one portion. The flask was then placed in a pre-heated oil bath (35 ºC) and allowed to stir at this temperature for 24 h, resulting in a brown solution. The mixture was cooled down to rt and about 3/4 of the solvent was removed on a rotary evaporator. The residue was redissolved in 200 mL of hexane and rinsed into a separatory funnel, washed with 4:1 mixture of methanol/water (3x100 mL), water (1x100 mL) and brine (1x50 mL) and dried over Na_2SO_4. Removal of the solvent on a rotary evaporator gave the crude product which was purified by flash chromatography (100% hexane) to give the desired product (10.94 g, 97%). bp 110-112 ºC/ 0.5 mm

Hg. An analytical sample was obtained by taking a middle fraction from flash chromatography. ^{1}H NMR (500 MHz, $CDCl_3$) □5.83-5.81 (m, 2H), 3.09 (t, 2H, J=6.6 Hz), 2.25 (s, 2H), 1.70-1.62 (m, 4H), 1.24 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) □ 160.5, 150.3, 105.4, 104, 42.9, 35.2, 29.3, 26.9 (br), 13.6, 7.5; IR (NaCl, neat) 1385m, 1367m, 1220s, 1193m, 1180m, 1023s, 958m, 938m, cm $^{-1}$. Anal. Calcd for $C_{11}H_{17}OI$: C, 45.22; H, 5.82. Found: C, 45.12; H, 6.00.

(±)-(*E*)-3,7-Dimethyl-2-methoxy-7-[2-(5-methyl)furyl]-1-phenylsulfenyl-3-phenylsulfonyl-1-octene (5a) and (±)-(*Z*)-3,7-Dimethyl-2-methoxy-7-[2-(5-methyl)furyl]-1-phenylsulfenyl-3-phenylsulfonyl-1-octene (5a). To a flame-dried, 250 mL round-bottomed flask was equipped with a magnetic stir bar, a nitrogen balloon and a septum, sulfone ((*E*)-**7a**) (4.0 g, 0.012 mol) and freshly distilled THF (60 mL) were added. This solution was cooled down to -78 ºC in an isopropanol/dry ice bath. To this cooled solution was added *n*BuLi (5.48 mL, 2.4 M solution in hexanes, 0.013 mol) slowly *via* a syringe over 10-15 min. After the addition was complete, the mixture was allowed to stir at this temperature for about 15 min, resulting in a yellow solution. To this solution iodide **6** (3.80 g, 0.013 mol) was added *via* a syringe over a few min at -78 ºC and the flask was carefully transferred into a pre-cooled bath at -20 ºC and allowed to stir at this temperature for about 24 h. TLC showed the completion of the reaction. The mixture was quenched by addition of sat. NH_4Cl and rinsed into a separatory funnel with ether. Then the mixture was extracted with ether (4x50 mL), and the combined organic layers were washed with water (2x50 mL), brine (1x50 mL) and dried over Na_2SO_4. Removal of the solvent on a rotary evaporator gave the crude product which was purified by flash chromatography (5% ethyl acetate in hexanes) affording 5.18 g of the products ((*E*)-**5a**) and ((*Z*)-**5a**) in ratio of 2.5: 1. Yield: 87%.

An improved alkylation of sulfone ((*E*)-7a). To a flame-dried 10 mL round-bottomed flask equipped with a magnetic stir bar, a nitrogen balloon and a septum, sulfone ((E)-**7a**) (25 mg, 0.074 mmol) and freshly distilled THF (0.4 mL) were added. This solution was cooled down to -78 ºC in an isopropanol/dry ice bath. To this cooled solution was added 75 □L of freshly distilled HMPA. After stirring for 10 min, *n*BuLi (34 □L, 2.4 M solution in hexanes, 0.082 mmol) was added slowly via a syringe over 1-2 min. After the addition was complete, the mixture was allowed to stir at this temperature for about 15 min, resulting in a yellow solution. To this solution the iodide (**6**) (24 mg, 0.082 mmol) was added *via* a syringe over a few min at -78 ºC and the flask was slowly warmed up to -50 ºC (bath temperature) and allowed to stir at this temperature for about 30 min. TLC showed the completion of the reaction. The mixture was quenched by addition of sat. NH_4Cl and rinsed into a separatory funnel with ether. The mixture was extracted with ether (4x10 mL), and the combined organic layers were washed with water (2x10 mL), brine (1x10 mL) and dried over Na_2SO_4. Removal of the solvent on a rotary evaporator gave the crude product which was purified by flash chromatography (5% ethyl acetate in hexanes) affording (*E*)-**5a** as an oil (31 mg, 83%). An analytical sample of (*E*)-**5a** was obtained by

taking a middle fraction from flash chromatography (5% ethyl acetate in hexanes). ^{1}H NMR (250 MHz, $CDCl_3$) 7.83 (d, 2H, J=7.4 Hz), 7.62-7.45 (m, 3H), 7.30-7.12 (m, 5H), 5.75-5.72 (m, 2H), 5.49 (s, 1H), 3.27 (s, 3H), 2.92-2.80 (m, 1H), 2.17 (s, 3H), 1.71-1.51 (m, 6H), 1.26-1.09 (m, 2H), 1.11 (s, 3H), 1.09 (s, 3H); ^{13}C NMR (62.9 MHz, $CDCl_3$) 160.9, 152.4, 149.8, 138.0, 136.4, 133.4, 130.2, 128.9, 128.4, 127.4, 125.8, 105.3, 103.6, 100.5, 72.9, 55.3, 42.0, 35.5, 31.6, 27.1, 26.4, 19.4, 18.7, 13.4; IR (NaCl, neat) 1584s, 1446 s, 1302s, 1204s, 1146s, 1023m, 938m, 911m, 737s cm $^{-1}$. Anal. Calcd For $C_{28}H_{34}O_4S_2$: C, 67.44; H, 6.87. Found: C, 67.62; H, 6.80. An analytical sample of (*Z*)-**5a** was obtained by taking a middle fraction from flash chromatography (5% ethyl acetate in hexanes). ^{1}H NMR (250 MHz, $CDCl_3$) 7.83 (dd, 2H, J=1.6, 7.0 Hz), 7.61-7.47 (m, 3H), 7.31-7.18 (m, 5H), 5.77 (m, 2H), 5.63 (s, 1H), 3.72 (s, 3H), 2.19 (s, 3H), 2.19-2.00 (m, 1H), 1.81-1.60 (m, 1H), 1.60-1.53 (m, 2H), 1.40 (s, 3H), 1.19 (s, 6H), 1.16-1.12 (m, 2H); ^{13}C NMR (62.9 MHz, $CDCl_3$) 160.7, 152.1, 150.0, 136.2, 136.0, 133.4, 130.6, 129.1, 128.7, 128.5, 126.5, 110.7, 105.4, 103.8, 72.8, 60.0, 42.2, 35.6, 32.9, 26.9, 26.8, 19.5, 17.9, 13.5; IR (NaCl, neat) 1583s, 1562m, 1480s, 1471m, 1447s, 1384m, 1309s, 1148s, 1118s, 1097s, 1088s, 1070s, 1024s, 784s cm^{-1}. Anal. Calcd for $C_{28}H_{34}O_4S_2$: C, 67.44; H, 6.87. Found: C, 67.52; H, 6.86.

(±)-(*E*)-2-Methoxy-3-methyl-4-phenyl-1-phenylsulfenyl-3-phenylsulfonyl-1-butene ((*E*)-20a). To a flame-dried, 10 mL round-bottomed flask equipped with a magnetic stir bar, a nitrogen balloon and a septum, sulfone ((*E*)-**7a**) (0.2 g, 0.59 mmol) and freshly distilled THF (2.9 mL) were added. This solution was cooled down to -78 ºC in an isopropanol/dry ice bath. To this cooled solution was added *n*BuLi (0.27 mL, 2.4 M solution in hexanes, 0.64 mmol) slowly *via* a syringe over 5 min. After the addition was complete, the mixture was allowed to stir at this temperature for about 15 min, resulting in a yellow solution. To this solution benzyl bromide (0.1 mL, 0.88 mmol) was added via a syringe over a few min at -78 ºC and the flask was carefully allowed to warm up to rt. TLC showed the completion of the reaction. The mixture was quenched by addition of sat. NH_4Cl and rinsed in to a separatory funnel with ether. The mixture was extracted with ether (4x10 mL), and the combined organic layers were washed with water (2x10 mL), brine (1x10 mL) and dried over Na_2SO_4. Removal of the solvent on a rotary evaporator gave the crude which was purified by flash chromatography (10% ethyl acetate in hexanes) affording 0.21 g of the product. Yield: 84%. An analytical sample was obtained by recrystallization from hexane and ethyl acetate. mp 134-135 ºC. ^{1}H NMR (250 MHz, $CDCl_3$) 7.91 (d, 2H, J=7.41 Hz), 7.67-7.50 (m, 3H), 7.25-7.09 (m, 8H), 7.04 (d, 2H, J=7.1 Hz), 5.47 (s, 1H), 4.20 (d, 1H, J=13.1 Hz), 3.40 (s, 3H), 3.03 (d, 1H, J=13.1 Hz), 1.70 (s, 3H); ^{13}C NMR (62.9 MHz, $CDCl_3$) 152.6, 137.6, 136.7, 135.6, 133.6, 130.5, 130.3, 128.9, 128.5, 128.2, 127.6, 126.9, 125.9, 101.2, 73.8, 55.2, 36.9, 19.2; IR (NaCl, KBr) 1587s, 1566s, 1500s, 1479s, 1451s, 1436s, 1294s, 1204s, 1139s, 1068s, 907s, 796s, 780s, 749s cm^{-1}. Anal. Calcd for $C_{24}H_{24}O_3S_2$: C, 68.46; H, 5.98. Found: C, 68.51; H, 5.72.

(±)-(Z)-2-Methoxy-3-methyl-4-phenyl-1-phenylsulfenyl-3-phenylsulfonyl-1-butene ((*Z*)-20a). To a

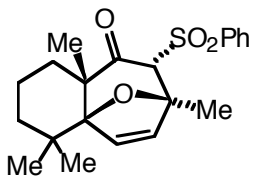
flame-dried 1 mL recovery flask equipped with a magnetic stir bar, a nitrogen balloon and a septum, sulfone ((E)-**7a**) (20 mg, 0.059 mmmol) and freshly distilled THF (0.3 mL) were added. This solution was cooled down to -78 ºC in an isopropanol/dry ice bath. To this cooled solution was added nBuLi (37 μL, 2.4 M solution in hexanes, 0.089 mmmol) slowly *via* a syringe over one min. After the addition was complete, the mixture was allowed to stir at this temperature for about 5 min, resulting in a yellow solution. This solution was warmed up to rt and stirred for 5 min. To this solution benzyl bromide (9 μL, 0.089 mmol) was added via a syringe over a few min and the flask was stirred at rt for 30 min. TLC showed the completion of the reaction. The mixture was quenched by addition of sat. NH_4Cl and rinsed in to a separatory funnel with ether. The mixture was extracted with ether (4x10 mL), and the combined organic layers were washed with water (2x10 mL), brine (1x10 mL) and dried over Na_2SO_4. Removal of the solvent on a rotary evaporator gave the crude product in a 1:8.3 ratio of *E* and *Z* isomers. The isomers were isolated upon flash chromatography (hexane/ethyl acetate, 10%) to afford overall 13.8 mg of products in 30% yield. An analytical sample was obtained by recrystallization from hexane and ethyl acetate. mp 118-120 ºC. ^{1}H NMR ($CDCl_3$, 250 MHz,) δ 7.94 (d, 2H, J=7.4 Hz), 7.69-7.53 (m, 3H), 7.31-7.10 (m, 10H), 5.62 (s, 1H), 3.83 (s, 3H), 3.78 (d, 1H, J=13.1 Hz), 3.54 (d, 1H, J=13.1 Hz). ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 151.8, 136.5, 136.0, 135.1, 133.6, 130.6, 130.6, 129.1, 128.7, 128.6, 128.2, 127.0, 126.5, 109.7, 73.3, 59.9, 38.0, 18.5. IR (NaCl, KBr) 1580s, 1561s, 1493s, 1475s, 1448s, 1430s, 1290s, 1200s, 1135s, 1065s, 907s, 796s, 788s, 745s cm^{-1}. Anal. Calcd for $C_{24}H_{24}O_3S_2$: C, 68.46; H, 5.98. Found: C, 68.22; H, 5.90.

(±)-(*E*)-3,7-Dimethyl-2-ethoxy-7-[2-(5-methyl)furyl]-1-phenylsulfenyl-3-phenylsulfonyl-1-octene ((*E*)-5b). To a flame-dried, 10 mL round-bottomed flask equipped with a magnetic stir bar, a nitrogen balloon and a septum, sulfone ((*E*)-**7b**) (19 mg, 0.054 mmol) and freshly distilled THF (0.27 mL) were added. Then this solution was cooled down to -78 ºC in an isopropanol/dry ice bath. To this cooled solution was added freshly distilled HMPA (40 μL) and stirred for 10 min, followed by addition of nBuLi (25 μL, 2.4 M solution in hexanes, 0.059 mmol) slowly *via* a syringe over a few min. After the addition was complete, the mixture was allowed to stir at this temperature for about 15 min, resulting in a yellow solution. To this solution iodide (**6**) (17 mg, 0.059 mmol) was added *via* a syringe over a few min at -78 ºC and the flask was slowly warmed up to -50 ºC (bath temperature) and allowed to stir at this temperature for about 30 min. TLC showed the completion of the reaction. The mixture was quenched by addition of sat. NH_4Cl and rinsed into a separatory funnel with ether. The mixture was extracted with ether (4x10 mL), and the combined organic layers were washed with water (2x10 mL), brine (1x10 mL) and dried over Na_2SO_4. Removal of the solvent on a rotary evaporator gave the crude product which was purified by flash chromatography (5% ethyl acetate in hexanes) affording (E-**5b**) as an oil (21.2 mg, 76%). An analytical sample was obtained by taking a middle fraction from flash chromatography. ^{1}H

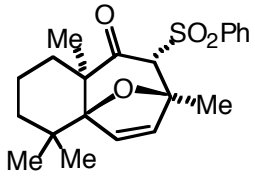
NMR (250 MHz, $CDCl_3$) □7.84 (d, 2H, J = 8.0 Hz), 7.63-7.45 (m, 3H), 7.30-7.13 (m, 5H), 5.74-5.72 (m, 2H), 5.46 (s, 1H), 3.45 (q, 1H, J=8.7 Hz), 3.32 (q, 1H, J=7.2 Hz), 2.91-2.80 (m, 1H), 2.18 (s, 3H), 1.65 (s, 3H), 1.69-1.42 (m, 3H), 1.26-1.08 (m, 2H), 1.11 (s, 3H), 1.08 (s, 3H), 0.83 (t, 3H, J=6.8 Hz); ^{13}C NMR (62.9 MHz, $CDCl_3$) □161.0, 151.9, 149.9, 138.3, 136.7, 133.3, 130.3, 128.9, 128.3, 127.4, 125.7, 105.3, 103.6, 100.5, 72.8, 63.6, 42.2, 35.5, 31.6, 27.1, 26.5, 19.4, 18.6, 13.9, 13.5. IR (NaCl, neat) 1311s, 1149s, 1071m, 1026m, 786m cm^{-1}. Exact MS Calcd for $C_{29}H_{36}O_4S_2$: 512.2055. Found: 512.2072.

(±)-4a,7-Epoxy-1,2,3,4,7,8,9a-heptahydro-4,4,7□,9a□-tetramethyl,8□-phenylsulfenyl-4a*H*-benzocyclohepten-9(2*H*)-one (4a) and (±)-4a,7-Epoxy-1,2,3,4,7,8,9a-heptahydro-4,4,7□,9a□-tetramethyl,8-□-phenylsulfenyl-4aH-benzocyclohepten-9(2*H*)-one (4b). To a flame-dried, 250 mL round-bottomed flask equipped with a magnetic stir bar, a nitrogen balloon and a septum, freshly distilled CH_2Cl_2 (159 mL) was added. To this $TiCl_4$ (1.656 g, 0.95 mL, 8.74 mmol) was added *via* a syringe. This solution was cooled down to -78 °C in an isopropanol/dry ice bath. To this cooled solution was added *E*-alkoxyallylic sulfone (**5a**) or (**5b**) (3.94 g 7.95 mmol) as a solution in 10 mL dry CH_2Cl_2 slowly via a syringe over 5-10 min. After the addition was complete, the brown solution was allowed to stir at this temperature for about 30 min. TLC showed the completion of the reaction. The mixture was quenched by addition of the mixture of methanol, water, 1N HCl (1:1:1) and rinsed into a separatory funnel with ether. The mixture was extracted with ether (4x50 mL), and the combined organic layers were washed with 1N HCl (1x50 mL) water (2x50 mL), brine (1x50 mL) and dried over Na_2SO_4. Removal of the solvent on a rotary evaporator gave the crude product which was purified by flash chromatography (5% ethyl acetate in hexanes) affording products (**4a**) and (**4b**) in ratio of about 1:1 (2.38 g, 87%). An analytical sample of **4a** was obtained by taking a middle fraction from flash chromatography (5% ethyl acetate in hexanes). ^{1}H NMR (500 MHz, $CDCl_3$) □7.50-7.49 (m, 2H), 7.28 (m, 3H), 6.28 (d, 1H, J=5.9 Hz), 5.90 (d, 1H, J=5.9 Hz), 3.37 (s, 1H), 1.75 (m, 2H), 1.60 (s, 3H), 1.54 (s, 3H), 1.54-1.4 (m, 3H), 1.35-1.27 (m, 1H), 1.17 (s, 3H), 0.85 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) □209.4, 137.1, 136.4, 135.2, 131.4, 129.0, 127.1, 92.8, 86.3, 62.0, 54.9, 38.4, 36.0, 30.1, 28.2, 22.9, 22.7, 20.3, 17.3; IR (NaCl, neat) 1707s, 1583m, 1499s, 1480, 1462s, 1386s, 1377s, 1295s, 1145s, 1088s, 1062s, 1035s, 1025s, 973s, 899s, 793s cm^{-1}. Anal. Calcd for $C_{21}H_{26}O_2S$: C, 73.64; H, 7.65. Found: C, 73.46; H, 7.62. An analytical sample of **4b** was obtained by taking a middle fraction from flash chromatography (5% ethyl acetate in hexanes), followed by recrystallization from hexane and ethyl acetate. mp 75-78 °C. ^{1}H NMR (500 MHz, $CDCl_3$) □7.53-7.50 (m, 2H), 7.30-7.22 (m, 3H), 6.28 (d, 1H, J=5.9 Hz), 5.91 (d, 1H, J=5.9 Hz), 3.40 (s, 1H), 2.47-2.41 (m, 1H), 1.82-165 (m, 2H), 1.60 (s, 3H), 1.59-1.54 (m, 1H), 1.41-1.28 (m, 2H), 1.22 (s, 3H), 1.16 (s, 3H), 0.94 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) □209.9, 135.9, 135.9, 135.9, 131.9, 129.0, 127.3, 93.6, 85.2, 61.6, 56.5, 35.6, 35.1, 34.8, 28.2, 25.2, 21.1, 18.5, 18.3; IR (NaCl, thin Layer) 1741s, 1719m, 1481s, 1469s, 1439s, 1385s, 1377s, 1259s, 1131s, 1110s, 1067s, 1059s, 1005s, 882s, 737s cm^{-1}. Anal.

Calcd for $C_{21}H_{26}O_2S$: C, 73.64; H, 7.65. Found: C, 73.77; H, 7.53.



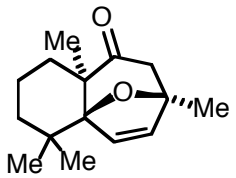
(±)-4a,7-Epoxy-1,2,3,4,7,8,9a-heptahydro-4,4,7,9a-tetramethyl-8-phenylsulfonyl-4a*H*-benzocyclohepten-9(2H)-one. To a 25 mL recovery flask equipped with a magnetic stir bar, sulfide (**4a**) (25 mg, 0.073 mmol) and methanol (0.150 mL) were added. The flask was cooled down to 0 ºC in an ice bath and oxone (66 mg) suspended in 0.150 mL of distilled water was added *via* a pasteur pipet, resulting a cloudy mixture. This was stirred at rt for 4-6 h. The mixture was transferred into a separatory funnel and extracted with chloroform (3x10 mL). The combined organic layers were washed with water and brine, and dried over Na_2SO_4. The evaporation of the solvent on a rotary evaporator gave the compound as solid. The crude product was purified by flash chromatography (50% ethyl acetate in hexanes) to give the product as solid (17.1 mg, 63%). An analytical sample was obtained by recrystallization from hexane and ethyl acetate. mp 179-181 ºC. ^{1}H NMR (250 MHz, $CDCl_3$) 7.97 (d, 2H, J=7.7 Hz), 7.62-7.48 (m, 3H), 6.24 (d, 1H, J=5.9 Hz), 6.20 (d, 1H, J=5.9 Hz), 4.52 (s, 1H), 1.93 (s, 3H), 1.72-1.23 (m, 6H), 1.19 (s, 3H), 1.09 (s, 3H), 0.84 (s, 3H); ^{13}C NMR (62.9 MHz, $CDCl_3$) 201.6, 141.2, 135.9, 134.3, 133.3, 128.7, 128.6, 92.8, 88.5, 53.8, 38.0, 36.1, 29.9, 27.9, 23.0, 22.5, 19.6, 17.3; IR (NaCl, thin layer) 1701s, 1378m, 1313s, 1288m, 1148s, 1080s, 1016m, 968m, cm^{-1}. Exact MS Calcd for $C_{21}H_{26}O_4S$: 374.1552. Found: 374.1548.



(±)-4a,7-Epoxy-1,2,3,4,7,8,9a-heptahydro-4,4,7,9a-tetramethyl-8-phenylsulfonyl-4a*H*-benzocyclohepten-9(2*H*)-one. This sulfone was prepared in the same fashion as above (18.8 mg, 70%). An analytical sample was obtained by recystallization from hexane and ethyl acetate. mp 169-171 ºC. ^{1}H NMR (250 MHz, $CDCl_3$) 7.94 (dd, 2H, J= 1.34, 6.9 Hz), 7.64-7.50 (m, 3H), 6.43 (d, 1H, J=6.0 Hz), 6.29 (d, 1H, J=6.0 Hz), 4.26 (s, 1H), 1.88 (s, 3H), 1.70-1.46 (m, 3H), 1.26-1.22 (m, 3H), 1.19 (s, 3H), 1.13 (s, 3H), 0.91 (s, 3H); ^{13}C NMR (62.9 MHz, $CDCl_3$) 205.8, 141.9, 135.1, 134.6, 133.4, 128.8, 128.7, 92.7, 86.1, 55.1, 35.5, 34.9, 33.7, 27.8, 25.0, 24.1, 19.2, 17.9; IR (NaCl, Thin Layer) 3062 (w), 2985 (s), 2952 (s), 2931 (s), 2869 (s), 1710 (s), 1481 (s), 1451 (m), 1396 (m), 1382 (m), 1324 (s), 1313 (s), 1291 (m), 1151 (s), 1101 (m), 1082 (m), 1018 (m), 972 (m), 911 (m), 751 (s) cm^{-1}. Exact MS Calcd For $C_{21}H_{26}O_4S$: 374.1552. Found: 374.1552.

(±)-4a,7-Epoxy-1,2,3,4,7,8,9a-heptahydro-4,4,7,9a-tetramethyl-4a*H*-benzocyclohepten-9(2*H*)-one (3a). To a flame-dried 25 mL recovery flask equipped with a magnetic stir bar, a septum and a nitrogen balloon, keto sulfide (**4a**) (0.41 g, 1.2 mmol) and absolute ethanol (11.9 mL) were added. To this well-stirred solution, freshly activated Raney nickel (0.27 g, 2.4 mmol) was added. This mixture was then allowed to stir at room temperature for about 3-4 h (**Caution**: Extended reaction time results in double bond reduction). The reaction mixture was filtered through celite and the filtrate was transferred into a

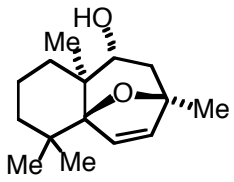
separatory funnel. The mixture was diluted with 50 mL of ether, washed with water (2x25 mL), brine (1x25 mL) and dried over Na_2SO_4. Removal of the solvent gave the crude product which was purified by flash chromatography (5% ethyl acetate in hexanes) affording the product as a solid (0.265 g, 94 %). An analytical sample was obtained by recrystallization from hexane and ether. mp 37-38 ºC. ^{1}H NMR (500 MHz, $CDCl_3$) 6.16 (d, 1H, J=5.9 Hz), 5.90 (d, 1H, J=5.9 Hz), 2.76 (d, 1H, J=14.4 Hz), 2.17 (d, 1H, J=14.4 Hz), 1.76-1.47 (m, 6H), 1.46 (s, 3H), 1.32 (s,3H), 1.14 (s,3H), 0.85 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) 211.2, 135.7, 135.2, 92.1, 84.7, 53.9, 49.3, 38.4, 36.0, 29.8, 28.3, 22.8, 20.0, 17.5; IR (CCl_4) 1716s, 1152m, 1089s, 799s, cm^{-1}. Anal. Calcd for $C_{15}H_{22}O_2$: C, 76.88; H, 9.46. Found: C, 77.00; H, 9.32.



(±)-4a,7-Epoxy-1,2,3,4,7,8,9a-heptahydro-4,4,7,9a-tetramethyl-4a*H*-benzocyclohepten-9(2*H*)-one. This ketone was prepared in the same fashion as **3a**. Yield: 93%. An analytical sample was obtained by recrystallization from hexane and ether. mp 59-60 ºC. ^{1}H NMR (500 MHz, $CDCl_3$) 6.18 (d, 1H, J=5.9 Hz), 5.94 (d, 1H, J=5.9 Hz), 2.66 (d, 1H, J=16.6 Hz), 2.28 (d, 1H, J=16.6 Hz), 1.95 (m, 1H), 1.72 (m, 2H), 1.52 (m, 1H), 1.41 (s, 3H), 1.27 (m, 1H), 1.20 (s, 3H), 1.21-1.16 (m, 1H), 1.16 (s, 3H), 0.95 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) 121.8, 136.9, 133.7, 92.5, 83.3, 55.2, 48.8, 35.5, 34.9, 32.3, 28.2, 25.1, 23.4, 18.1, 18.0. IR (CCl_4) 1705s, 1377m, cm^{-1}. Anal. Calcd. for $C_{15}H_{22}O_2$: C, 76.88; H, 9.46. Found: C, 76.77; H, 9.32.

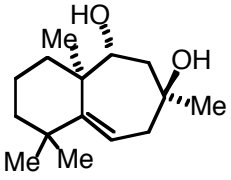
(±)-4a,7-Epoxy-1,2,3,4,7,8,9a-heptahydro-4,4,7,9a-tetramethyl-4a*H*-benzocyclohepten-9()-ol (27). To a flame-dried 25 mL recovery flask equipped with a magnetic stir bar, a reflux condenser, a septum and a nitrogen balloon, ketone (**3a**) (0.1 g, 0.42 mmol) and freshly distilled THF (4.2 mL) were added. To this well-stirred solution, L-Selectride (6.4 mmol, 6.4 mL, 1 M solution in hexanes) was added via a syringe in one portion. This mixture was then brought to a gentle reflux for 20-25 min. The reaction was monitored by TLC. The reaction mixture was cooled down to rt and 1N NaOH was added until the vigrous reaction subsided. Then 30% H_2O_2 was added dropwise until there was no vigrous reaction. The mixture was transferred into a separatory funnel and diluted with 50 mL of ether, washed with water (2x25 mL), brine (1x25 mL) and dried over Na_2SO_4. Removal of the solvent gave the crude product which was purified by flash chromatography (25% ethyl acetate in hexanes) affording the product as a white solid (87 mg, 87%). An analytical sample was obtained by recrystallization from hexane and ether. mp 40-42 ºC. ^{1}H NMR (250 MHz, $CDCl_3$) 6.39 (d, 1H, J=5.8 Hz), 6.09 (d, 1H, J=5.8 Hz), 3.35 (dd, 1H, J= 5.1, 11.6 Hz), 2.37 (d, 1H, J=11.8 Hz), 2.20 (dd, 1H, J=5.4, 14.5 Hz), 1.77-1.44 (m, 6H), 1.35 (s, 3H), 1.27-1.23 (m, 1H), 1.24 (s, 3H), 1.08 (s, 3H), 0.79 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) 138.7, 136.7, 92.4, 84.8, 78.0, 42.2, 41.1, 38.8, 36.0, 31.9, 28.4, 23.4, 23.3, 18.0; IR (CCl_4) 1376m, 1086s, 1018m, 788s, cm^{-1}. Anal. Calcd for $C_{15}C_{24}O_2$: C, 76.23; H, 10.24. Found: C, 76.10; H, 10.12.

(±)-4a,7-Epoxy-1,2,3,4,7,8,9a-heptahydro-4,4,7,9a-tetramethyl-4a*H*-benzocyclohepten-9()-ol.



The alcohol was prepared in the same fashion as **27**. (89 mg, 89%). An analytical sample was obtained by recrystallization from hexane and ether. mp 29-31 ºC. ^{1}H NMR (250 MHz, $CDCl_3$) δ 6.32 (d, 1H, J=5.9 Hz), 6.07 (d, 1H, J=5.9 Hz), 3.2 (s, 1H, br), 2.16 (dd, 1H, J=5.6 Hz, 14.1 Hz), 1.9 (dt, 1H, J=4.1 Hz, J=8.7 Hz), 1.88-1.44 (m, 5H), 1.30 (s, 3H), 1.14-1.09 (m, 2H), 1.10 (s, 3H), 1.09 (s, 3H), 0.9-0.8 (m, 2H), 0.82 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.9, 135.9, 93.6, 83.3, 77.5, 41.2, 35.8, 35.2, 33.4, 27.8, 24.7, 23.9, 21.1, 18.7; IR(CCl_4) 3605w, 1376m, 1161m, 1073m, 1024m, 1005m cm^{-1}. Anal. Calcd for $C_{15}H_{24}O_2$: C, 76.23; H, 10.24. Found: C, 76.20; H, 10.00.

(±)-1,1,4α,7α-Tetramethyl-2,3,4,4a,5,6,7,8-octahydro-1*H*-benzocycloheptene-5,7-diol (28). To a flame-dried 25 mL recovery flask equipped with a magnetic stir bar, a reflux condenser, a septum and a nitrogen balloon, alcohol (**27**) (0.1 g, 0.42 mmol) and 4.2 mL freshly distilled toluene were added. To this stirred solution, DIBAL-H (8.5 mmol, 8.5 mL, 1 M a solution in toluene, 20 eq.) was added *via* a syringe in one portion. This mixture was then brought to a gentle reflux for 24-36 h. (**Caution**: Extended reaction time may result in decomposition or further reduction of the double bond under these conditions). The reaction mixture was cooled down to rt and sat. NH_4Cl (10 mL) was added, resulting in a gelatinous precipitate. This was dissolved by addition of 1M H_2SO_4. The mixture was then transferred into a separatory funnel and diluted with 50 mL of ethyl acetate, washed with water (2x25 mL), brine (1x25 mL) and dried over Na_2SO_4. Removal of the solvent gave the crude product which was purified by flash chromatography (50% ethyl acetate in hexanes) affording the product as a white solid (53 mg, 53%). An analytical sample was obtained by taking a middle fraction from flash chromatography (50% ethyl acetate in hexanes). ^{1}H NMR (250 MHz, $CDCl_3$) δ 5.62 (dd, 1H, J=6.0, 8.6 Hz), 3.8 (s, 1H, br), 2.45 (dd, 1H, J=5.8, 14.2 Hz), 2.19-2.01 (m, 2H), 1.82-1.5 (m, 8H), 1.46-1.33 (m, 1H), 1.29 (s, 3H), 1.26 (s, 3H), 1.12 (s, 3H), 1.10 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 152.9, 118.7, 76.3, 72.7, 46.0, 45.2, 40.4, 39.7, 37.1, 33.0, 32.1, 30.0, 24.7, 17.7; IR (NaCl, Thin Layer) 3401m, 1466m, 1387m, 1123m cm^{-1}. Exact MS Calcd for $C_{15}H_{26}O_2$: 238.1933. Found: 238.1934.



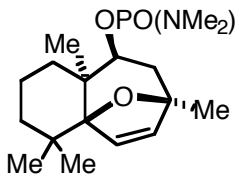
(±)-1,1,4aα,7α-Tetramethyl-2,3,4,4a,5,6,7,8-octahydro-1*H*-benzocycloheptene-5,7-diol. This alcohol was prepared in the same fashion as **28**. (50 mg, 50%). An analytical sample was obtained by taking a middle fraction from flash chromatography (50% ethyl acetate in hexanes). ^{1}H NMR (250 MHz, $CDCl_3$) δ 5.63 (dd, 1H, J=4.3, 9.5 Hz), 3.66 (dd, 1H, J= 6.4, 6.5 Hz), 2.38 (dd, 1H, J= 4.3, 15.1 Hz), 2.28-2.18 (m, 1H), 1.99-1.95 (m, 3H), 1.78-1.41 (m, 7H), 1.26 (s, 3H), 1.15 (s, 3H), 1.10 (s, 3H), 1.08 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 155.9, 119.2, 72.9, 70.3, 48.9, 43.3, 40.8, 38.1, 37.4, 35.5, 33.6, 32.7, 31.1, 17.0, 16.3; IR (NaCl, Thin Layer) 3405m, 1464s, 1377s, 1259 s, 1127m, 1054m, 1006s cm^{-1}. Exact MS Calcd for $C_{15}H_{26}O_2$: 238.1933. Found: 238.1928.

(±)-4a,7-Epoxy-1,2,3,4,7,8,9a-heptahydro-4,4,7α,9aβ-tetramethyl-4a*H*-benzocyclohepten-9(β)-ol (29a). To a 50 mL recovery flask equipped with a magnetic stir bar and a yellow cap, ketone (**4a**) (50 mg, 0.21 mmol) and bulk ether (25 mL) were added. To this solution was then added 5-6 drops of distilled water and 1.25 mL absolute ethanol, followed by addition of 5 g of Amberlite (Ion exchange resin, CG-120, 100-200 mesh). To this well-stirred mixture freshly cut sodium metal (0.31 g, 13.8 mmol) was added and allowed to stir at rt for about 6 h. The reaction was monitored by TLC. Methanol (20 mL) was added to this mixture which was allowed to stir for 15 min at rt. The reaction mixture was filtered through a short column of Amberlite (5 g) with methanol. Removal of the solvent gave the crude product which was purified by flash chromatography (25% ethyl acetate in hexanes) affording the product as a white solid (47 mg, 95%). An analytical sample was obtained by recrystallization from hexane and ethyl acetate. mp 114-115 ºC. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.06 (d, 1H, J=5.9 Hz), 5.75 (d, 1H, J=6.0 Hz), 3.49 (ddd, 1H, J= 1.55, 6.0, 10.0 Hz), 1.77-1.67 (m, 2H), 1.61 (dd, 1H, 5.6, 12.7 Hz), 1.57-1.44 (m, 3H), 1.43 (d, 1H, J=2.6 Hz), 1.35 (s, 3H), 1.20 (d, 1H, J=6.6 Hz), 1.12 (s, 3H), 1.11 (s, 3H), 0.96 (dt, 1H, J=3.9. 13.4 Hz), 0.8 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 133.0, 132.8, 92.5, 84.0, 75.0, 40.1, 38.9, 38.5, 35.8, 34.4, 28.5, 23.6, 23.3, 18.3, 12.8; IR (NaCl, KBr) 3324 s, 1384m, 1359m, 1140m, 1090s, 1070s, 1038s, 1012m, 975s cm^{-1}. Anal. Calcd for: $C_{15}H_{24}O_2$: C, 76.23; H, 10.23. Found: C, 76.38; H, 10.49.

(±)-4a,7-Epoxy-1,2,3,4,7,8,9a-heptahydro-4,4,7α,9aβ-tetramethyl-4a*H*-benzocyclohepten-9(α)-ol (29b). This alcohol was prepared in the same fashion as **29a** (45 mg, 90%). An analytical sample was obtained by recrystallization from hexanes and ethyl acetate. mp 110-112 ºC. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.0 (d, 1H, J=5.9 Hz), 5.82 (d, 1H, J=5.9 Hz), 3.46-3.41 (m, 1H), 1.81 (dd, 1H, J=6.4, 12.4 Hz), 1.73-1.54 (m, 4H), 1.46 (dd, 1H, J=10.4, 12.5 Hz), 1.31 (s, 3H), 1.22-1.13 (m, 2H), 1.12 (s, 3H), 1.08 (d, 1H, J=8.7 Hz), 1.03 (s, 3H), 0.82 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 135.2, 129.9, 93.5, 83.2, 74.9, 39.6, 39.4, 35.5, 35.4, 28.2, 25.3, 24.7, 23.8, 21.1, 17.9; IR (NaCl, KBr) 3338s, 1444m, 1374m, 1322m, 1075m, 1006s, 960m cm^{-1}. Anal. Calcd for. $C_{15}H_{24}O_2$: C, 76.23; H, 10.23. Found: C, 76.40; H, 10.20.

(±)-4a,7-Epoxy-1,2,3,4,7,8,9a-heptahydro-4,4,7α,9aβ-tetramethyl-4a*H*-benzocyclohepten-9(α)-bis(*N*,*N*-dimethylamino)phosphate (30a). To a flame-dried, 10 mL recovery flask equipped with a magnetic stir bar, a nitrogen balloon and a septum, alcohol (**29a**) (20 mg, 0.085 mmol) and a 4:1 mixture of anhydrous DME/ freshly distilled TMEDA were added. To this solution was then added *n*BuLi (8 mg, 53 μL of 2.4 M solution in hexanes) *via* a syringe and stirred at room temperature for 15-20 min. To this reaction mixture was added N,N-dimethyl phosphoramidic dichloride (68 mg, 0.42 mmol) via a syringe and stirring was continued for about 6 h at rt. The reaction was monitored by TLC. The flask was cooled down to 0 ºC in an ice bath. To this cooled reaction mixture was added dimethylamine (2 mL, 40% aqueous solution) and stirring was continued for 30 min. The reaction mixture was quenched with water

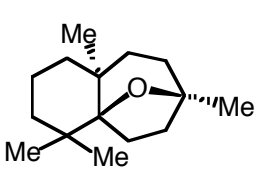
(10 mL). The mixture was then transfered into a separatory funnel and was extracted with ether (4x25 mL). The combined organic layers were washed with water (2x25 mL), brine (1x25 mL) and dried over Na_2SO_4. The removal of the solvent gave the crude product which was purified by flash chromatography (100% ethyl acetate) affording the product as white solid (24.3 mg, 77%). An analytical sample was obtained by recrystallization from ethyl acetate. mp 117-120 ºC. ^{1}H NMR (250 MHz, $CDCl_3$) δ 6.00 (d, 1H, J=5.9 Hz), 5.79 (d, 1H,J=5.0 Hz), 4.11 (ddd, 1H, J=5.8, 7.6, 13.4 Hz), 2.62 (s, 3H), 2.61 (s, 3H), 2.58 (s, 3H), 2.57 (s, 3H), 1.79 (dd, 1H, J=5.7, 12.6 Hz), 1.70-1.60 (m, 3H), 1.47-1.42 (m, 3H), 1.34 (s, 3H), 1.18 (s, 3H), 1.10 (s, 3H), 1.10-108 (m, 1H), 0.79 (s, 3H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 133.1, 132.9, 92.5, 83.9, 79.5 (d, J_{P-C}=4.6 Hz), 40.1 (d, J_{P-C}=5.6 Hz), 38.7, 36.9, 36.7, 36.6, 36.6, 36.5, 35.9, 34.6, 28.4, 23.5, 23.2, 18.1, 13.6; ^{31}P NMR ($CDCl_3$, 85% H_3PO_4, external standard at 0 ppm) δ 19.6; IR (NaCl, thin layer) 1383m, 1293m, 1222m, 1213s, 1184 m, 1068m, 1038s, 1012s, 989s, 974s cm^{-1}.

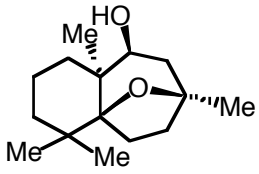


(±)-4a,7-Epoxy-1,2,3,4,7,8,9a-heptahydro-4,4,7δ,9aδ-tetramethyl-4a*H*-benzocyclohepten-9(δ)-bis(*N*,*N*-dimethylamino)phosphate. This was prepared in the same fashion as **30a** (27.2 mg, 86%). mp. 124-125 ºC. ^{1}H NMR (250 MHz, $CDCl_3$) δ 5.99 (d, 1H, J=5.9 Hz), 5.84 (d, 1H, J=5.9 Hz), 4.11 (ddd, 1H, J=4.5, 7.4, 14.5 Hz), 2.63 (s, 3H), 2.61 (s, 3H), 2.59 (s, 3H), 2.57 (s, 3H), 1.94 (dd, 1H, J=6.6, 12.3 Hz), 1.84-1.50 (m, 6H), 1.31 (s, 3H), 1.31-1.17 (m, 1H), 1.11 (s, 3H), 1.05 (s, 3H), 0.81 (s, 3H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 135.5, 130.2, 93.6, 83.0, 79.8 (d, J_{P-C}=4.3 Hz), 39.6 (d, J_{P-C}=6.3 Hz), 37.8, 36.7, 36.6, 36.6, 36.5, 35.6, 35.5, 28.3, 26.6, 24.8, 23.9, 21.2 18.1; ^{31}P NMR ($CDCl_3$, 85% H_3PO_4 external standard at 0 ppm) δ 19.7; IR (NaCl, thin layer) 1456m, 1381m, 1339m, 1305s, 1291m, 1228s, 1188s, 1004 s, 977s, 744s cm^{-1}.

(±)-4a,7-Epoxy-1,2,3,4,5,6,7,8,9,9a-decahydro-4,4,7δ,9aδ-tetramethyl-4a*H*-benzocycloheptene (31a) and (±)-4a,7-Epoxy-1,2,3,4,5,6,7,8,9,9a-decahydro-4,4,7δ,9aδ-tetramethyl-4a*H*-benzocyclohepten-9(δ)-ol (32a). To a 5 mL recovery flask equipped with a magnetic stir bar, a nitrogen balloon and a septum, **30a** (10 mg, 0.027 mmol) was added and the flask was cooled down to -78 ºC in an isopropanol/ dry ice bath. To this about 2.5-3.00 mL of $EtNH_2$ was condensed and 10 μL *t*-BuOH and 0.5 mL freshly distilled THF were added. To this mixture were added freshly cut shavings of lithium wire (4 mg, 0.54 mmol) and stirring was continued for a few min, resulting in a deep blue color. This reaction was quenched by addition of sat. NH_4Cl (2mL). The mixture was then transferred into a separatory funnel and extracted with ether (4x10 mL). The combined organic layers were washed with water (2x10 mL), brine (1x10 mL) and dried over Na_2SO_4. Removal of the solvent gave the crude product which was purified by flash chromatography (100% hexanes first, then 5% ethyl acetate in hexane) affording 3.5 mg of **31a** and 2 mg of **32a** in 59% and 31% yields, respectively. An analytical sample of (**31a**) was obtained by taking a middle fraction from flash chromatography. Yield: 59%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.91-1.87 (m, 2H), 1.75-1.55 (m, 4H), 1.46-1.42 (m, 2H), 1.37-1.22 (m, 4H), 1.26 (s, 3H), 1.21-

1.19 (m, 1H), 1.19 (s, 3H), 1.08 (s, 3H), 1.02 (ddd, 1H, J= 1.3, 5.0, 12.8 Hz), 0.93 (s, 3H), ^{13}C NMR (125 MHz, $CDCl_3$) 87.7, 81.3, 38.8, 38.0, 37.8, 37.1, 36.5, 36.4, 34.4, 29.7, 27.9, 26.4, 24.5, 23.3, 18.4; IR (NaCl, neat) 1457m, 1380m, 1043m cm^{-1}. Exact MS Calcd for $C_{15}H_{26}O$: 222.1983. Found: 222.2002. An analytical sample of **32a** was obtained by taking a middle fraction from flash chromatography, followed by recrystallization from hexane/ethyl acetate. Yield: 31%. mp 114-115 ºC. ^{1}H NMR (500 MHz, $CDCl_3$) 3.73 (dd, 1H, J=5.2, 11.2 Hz), 1.91 (dt, 1H, J=3.0, 12.6 Hz), 1.87-1.84 (m, 1H), 1.74-1.63 (m, 3H), 1.58 (dd, 1H, J=5.2, 12.3 Hz), 1.49-1.34 (m, 4H), 1.30-1.21 (m, 3H), 1.28 (s, 3H), 1.15 (s, 3H), 1.06 (s, 3H), 0.95 (s, 3H), ^{13}C NMR (125 MHz, $CDCl_3$) 88.3, 79.9, 72.6, 43.3, 43.0, 38.5, 37.3, 36.9, 32.42, 28.9, 27.93, 25.96, 24.7, 18.1, 13.9; IR (NaCl, neat) 1455m, 1374m, 1360s, 1330m, 1239m, 1141m, 1095s, 1073s, 1038s, 1016s, 977m cm^{-1}. Anal. Calcd for $C_{15}H_{26}O_2$: C, 75.58; H, 10.99. Found: C, 75.49; H, 10.77.





(±)-4a,7-Epoxy-1,2,3,4,5,6,7,8,9,9a-decahydro-4,4,7,9a-tetramethyl-4a*H*-benzocycloheptene and 4a,7-Epoxy-1,2,3,4,5,6,7,8,9,9a-decahydro-4,4,7,9a-tetramethyl-4a*H*-benzocyclohepten-9()-ol. The same procedure was followed as for **31a** and (**32a**). An analytical sample of (**31b**) was obtained by taking a middle fraction from flash chromatography (5% ethyl acetate in hexanes). Yield: 50%. ^{1}H NMR (500 MHz, $CDCl_3$) 2.06 (dt, 1H, J=4.0, 13.0 Hz), 1.77-1.61 (m, 6H), 1.55 (dd, 1H, J=5.5, 13.0 Hz), 1.51-1.41 (m, 2H), 1.25-1.20 (m, 2H), 1.23 (s, 3H), 1.16-1.15 (m, 1H), 1.14-1.12 (m, 1H), 0.95 (s, 3H), 0.92 (s, 3H), 0.88 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) 89.6, 79.6, 36.9, 36.8, 36.2, 36.0, 34.4, 32.1, 26.9, 26.8, 26.7, 25.9, 24.7, 18.8; IR (NaCl, neat) 1462m, 1382m, 1378s, 1043s cm^{-1}. Exact MS Calcd for $C_{15}H_{26}O$: 222.1983. Found: 222.1998. An analytical sample of **32b** was obtained by taking a middle fraction from flash chromatography (5% ethyl acetate in hexanes), followed by recrystallization from hexane and ethyl acetate. Yield: 31%. mp 110-112 ºC. ^{1}H NMR (500 MHz, $CDCl_3$) 3.6-3.50 (m, 1H), 1.76-1.71 (m, 6H), 1.54-1.48 (m, 2H), 1.26 (s, 3H), 1.26-1.25 (m, 3H), 1.19-1.15 (m, 1H), 1.13 (s, 3H), 1.04 (d, 1H, J=8.11 Hz), 0.95 (s, 3H), 0.89 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) 89.1, 78.9, 73.1, 43.3, 42.5, 36.9, 36.8, 29.7, 27.0, 26.7, 26.4, 25.1, 24.8, 20.8, 20.2,18.1; IR (NaCl, KBr) 3274s, 1469w, 1456s, 1444s, 1374s,1360m, 1340m, 1324s, 1008s cm^{-1}. Anal. Calcd for $C_{15}H_{26}O_2$: C, 75.58; H, 10.99. Found: C, 75.87; H, 10.87.

(±)-4a,7-Epoxy-1,2,3,4,7,8,9a-heptahydro-4,4,7,9a-tetramethyl-4a*H*-benzocyclohepten-9()-yl pentafluorophenyl thiocarbonte (33a). To a 5 mL recovery flask equipped with a magnetic stir bar, a reflux condenser, a septum and a nitrogen balloon, **29a** (20 mg, 0.085 mmol mmol) and freshly distilled toluene (0.8 mL) were added. To this stirred solution, DMAP (52 mg, 0.42 mmol) was added in one portion, followed by addition of pentafluorophenyl chlorothionoformate (0.11g 67 mL, 0.42 mmol) in one

portion *via* a syringe. This mixture was then heated to 80 ºC in an oil bath for 3 h. The reaction was monitored by TLC. The reaction mixture was cooled down to rt and diluted with about 0.5 mL of dichloromethane. It was directly placed on a flash column and eluted with hexane first, then 2% ethyl acetate in hexanes, affording 32.1 mg of the product. Yield: 82 %. mp 103-104 ºC. ^{1}H NMR (500 MHz, $CDCl_3$) 6.19 (d, 1H, J=5.8 Hz), 5.89 (d, 1H, J=5.8 Hz), 5.19 (dd, 1H, J=5.6, 10.1 Hz), 1.99 (dd, 1H, J=5.7, 12.4 Hz), 1.79-1.64 (m, 3H), 1.52-1.44 (m, 3H), 1.41 (s, 3H), 1.29 s, 3H), 1.17-1.13 (m, 1H), 1.13 (s, 3H), 0.83 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) 191.5, 142 (m), 140.8 (m), 140.13 (m), 138.9 (m), 136.92 (m), 133.3 , 130.0, 127,5, 92.4, 91.9, 84.1, 40.3, 38.6, 35.9, 34.3, 33.4, 28.4, 23.4, 23.1, 17.8; IR (NaCl, KBr) 1520s, 1385m, 1373s, 1354m, 1323s, 1160s, 1149s, 1033m, 997s cm^{-1}.

(±)-4a,7-Epoxy-1,2,3,4,7,8,9a-heptahydro-4,4,7,9a-tetramethyl-4a*H*-benzocyclohepten-9()-yl pentafluorophenyl thiocarbonate (33b). The same procedure was followed as for **33a**. Yield: 86 %, mp 114-115 ºC. ^{1}H NMR (500 MHz, $CDCl_3$) 6.11 (d, 1H, J=5.9 Hz), 5.94 (d, 1H, J=5.9 Hz), 5.11 (dd, 1H, J=6.6, 10.2 Hz), 2.18 (dd, 1H, J=6.7, 12.2 Hz), 2.06-1.83 (m, 1H), 1.73-1.60 (m, 3H), 1.57-1.50 (m, 1H), 1.38 (s, 3H), 1.38-1.33 (m, 1H), 1.23 (d, 1H, J=6.7 Hz), 1.14 (s, 3H), 1.05 (s, 3H), 0.85 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) 192.0, 142.2 (m), 140.9 (m), 140.2 (m), 138.9 (m), 137.0 (m), 135.5 , 130.5, 93.5, 92.0, 83.2, 39.8, 35.5, 35.3, 33.7, 28.2**,** 26.9, 24.7, 23.6, 21.2, 17.8; IR (NaCl, KBr) 1519s, 1392m, 1384s, 1338m, 1317s, 1152s, 998 (s), 949s cm^{-1}.

(±)-4a,7-Epoxy-1,2,3,4,7,8,9,9a-octahydro-4,4,7,9a-tetramethyl-4a*H*-benzocycloheptene (2a). To a flame-dried, 5 mL recovery flask equipped with a magnetic stir bar, a reflux condenser, a septum and a nitrogen balloon, thionocarbonate (**33a**) (10 mg, 0.020 mmol) and freshly distilled benzene (0.4 mL) were added. This well-stirred solution was heated to reflux, followed by addition of *n*Bu_3SnH (17 mg, 0.060 mmol) and 1 mg of AIBN as a solution in 0.5 mL of dry benzene via a syringe pump over 2 h. After the addition was complete, the mixture was allowed to reflux for an additional hour. The reaction was monitored by TLC. The flask was cooled down to rt and concentrated on a rotary evaporator, keeping the bath temperature below 10 ºC. Then it was directly placed on a flash column and eluted with 100% hexane first, then 1% ethyl acetate in hexanes, affording 4.1 mg of the product. Yield: 86 %. **An alternative deoxygenation procedure**: To a 5 mL, recovery flask equipped with a magnetic stir bar, a reflux condenser, a septum and a nitrogen balloon, thionocarbonate (**33a**) (50 mg, 0.1 mmol), 45 mg of PMHS (0.75 mmol based on 60 g/mol), freshly distilled n-BuOH (60 mg, 75 L, 0.8 mmol), $(Bu_3Sn)_2O$ (67 mg, 0.11 mmol), 2 mg of AIBN (0.022 mmol) and freshly distilled toluene (0.3 mL) were added. This mixture was freeze-thaw degassed two times and then the flask was placed in a pre-heated oil bath and the mixture was brought to gentle reflux for 1 h. TLC showed the completion of the reaction. After cooling to rt, the mixture was treated with 1 mL of 1N NaOH for 1 h and then rinsed into a separatory funnel and extracted with ether (3x10 mL), washed with water (1x10 mL) and brine (1x10 mL), and dried

over Na_2SO_4. Solvent was removed on a rotary evaporator to afford the crude product which was first flashed with 100% hexanes and then 2% ethyl acetate in hexanes to give 21.3 mg of the product. Yield: 89%. An analytical sample was obtained by taking a middle fraction from flash chromatography. ^{1}H NMR (250 MHz, $CDCl_3$) 6.15 (d, 1H, J=5.9 Hz), 5.64 (d, 1H, J=5.9 Hz), 1.79-1.62 (m, 2H), 1.59-1.42 (m, 3H), 1.39-1.30 (m, 1H), 1.34 (s, 3H), 1.26-1.07 (m, 4H), 1.21 (s, 3H), 1.03 (s, 3H), 0.79 (s, 3H); ^{13}C NMR (62.9 MHz, $CDCl_3$) 134.5, 131.4, 93.3, 85.8, 39.0, 38.7, 38.1, 35.7, 34.1, 30.0, 28.5, 23.7, 23.4, 21.5, 18.5; IR (NaCl, neat) 1519m, 1459m, 1385m, 1378m, 1089s, 1033 m, 999m, 895m cm^{-1}. Anal. Calcd for $C_{15}H_{24}O$: C, 81.76; H, 10.98. Found: C, 81.70; H, 10.82.

(±)-4a,7-Epoxy-1,2,3,4,7,8,9,9a-octahydro-4,4,7,9a-tetramethyl-4a*H*-benzocycloheptene (2b). The same procedure was followed as for **2a** Yield : 71%. An analytical sample was obtained by taking a middle fraction from flash chromatography. ^{1}H NMR (250 MHz, $CDCl_3$) 6.03 (d, 1H, J=5.96 Hz), 5.77 (d, 1H, J=6.0 Hz), 2.12-2.02 (m, 1H), 1.76-1.42 (m, 5H), 1.28 (s, 3H), 1.28-1.13 (m, 2H), 1.08 (s, 3H), 1.03-0.91 (m, 2H), 0.87 (s, 3H), 0.82 (s, 3H); ^{13}C NMR (62.9 MHz, $CDCl_3$) 134.71,130.9, 94.4, 84.2, 36.8, 35.77, 35.5, 33.5, 32.1, 30.2, 28.1, 25.9, 24.7, 24.1, 18.7; IR (NaCl, neat) 1452m, 1379m, 1244m, 1079m, 989m cm^{-1}. Exact MS Calcd for $C_{15}H_{24}O$: 220.1827. Found: 220.1825.

(±)-1,1,4,7-Tetramethyl-2,3,4,4a,5,6,7,8-octahydro-1*H*-benzocyclo heptene-7-ol (1), widdrol. To a 5 mL recovery flask equipped with a magnetic stir bar, a nitrogen balloon and a septum, freshly distilled ethylenediamine (0.2 mL) was added *via* a syringe. To this mixture was then added freshly cut shavings of lithium wire (1.5 mg, 0.22 mmol) and stirring was allowed for a few min, resulting in a deep blue color. The flask was placed in a pre-heated oil bath *ca*. 80-90 ºC. To this mixture starting material (5 mg, 0.022 mmol) was added as a solution in 0.1 mL of freshly distilled DME and allowed to stir for 10-15 min. This mixture was quenched by addition of sat. NH_4Cl (1.0 mL) then transferred into a separatory funnel and extracted with ether (4x10 mL). The combined organic layers were washed with water (2x10 mL), brine (1x10 mL) and dried over Na_2SO_4. Removal of the solvent gave the crude product which was purified by flash chromatography eluted with 100% hexanes first, then 20% ether in hexane affording 2.1 mg of **34** and 0.65 mg of **1** in 13% yield. The synthetic widdrol was found to be identical with an authentic widdrol by TLC, GC and ^{1}H NMR spectral analysis.

(*E* and *Z*)-3,7-Dimethyl-2-methoxy-7-[2-(5-methyl)furyl]-1-phenylsulfenyl-2-octene (21). To a 100 mL round-bottomed flask equipped with a magnetic stir bar, a septum and a nitrogen balloon, a 4:1 mixture of MeOH and THF (25 mL) was placed. Into this, 7.2 g of 6% sodium amalgam (10 fold excess) was dispersed, followed by addition of 2.82 g of Na_2HPO_4 (2.82 g, 20 mmol). To this well-stirred mixture, (*Z*)-**5a** (1.0 g, 2.0 mmol) was added as a solution in 5 mL of THF over several min. This mixture was then allowed to stir at rt for 24 h. The reaction mixture was filtered through some celite. The filtrate was first diluted with 50 mL of ether, then washed with water (2x50 mL), brine (1x25 mL)

and dried over Na_2SO_4. The solvent was removed on a rotary evaporator to afford the crude product. The product was isolated upon flash chromatography with 10% ethyl acetate in hexanes to give 1:1 mixture of *E* and *Z* isomers (0.68 g, 94%). An analytical sample was obtained by taking a middle fraction from flash chromatography. Data for (*E*) and ((*Z*)-**21**). ^{1}H NMR (250 MHz, $CDCl_3$) 7.40-7.35 (m,4H), 7.28-7.16 (m, 6H), 5.78-5.78 (m, 4H), 3.79-3.65 (m, 4H), 3.54 (s, 3H), 3.50 (s, 3H), 2.22 (s, 3H), 2.21 (s, 3H), 2.0 (t, 2H, J=7.6 Hz), 1.79 (t, 2H, J=7.5 Hz), 1.59 (m, 4H, br), 1.54-1.44 (m, 4H), 1.38 (m, 2H), 1.20 (s, 6H), 1.18 (s, 6H), 1.22-1.88 (m, 4H); ^{13}C NMR (62.9 MHz, $CDCl_3$) 161.3, 161.1, 149.8, 149.7, 145.0, 144.9, 136.8, 136.3, 131.1, 130.6, 130.3, 128.1, 128.6, 127.2, 126.5, 126.3, 122.7, 122.6, 105.3, 103.6, 103.5, 57.6, 57.5, 41.7, 41.4, 35.5, 35.5, 33.0, 32.6, 32.5, 31.2, 26.9, 23.2, 22.8, 16.1, 14.7, 13.5; IR (NaCl, neat) 1562m, 1480m, 1458m, 1438s, 1206s, 1115m, 1023s, 780s cm^{-1}. Anal. Calcd for $C_{22}H_{30}O_2S$: C, 73.77; H, 8.43. Found: C, 74.00; H, 8.17.

(±)- (*E* and *Z*)-3,7-Dimethyl-2-methoxy-7-[2-(5-methyl)furyl]-1-phenylsulfinyl-2-octene (22). To a 25 mL round-bottomed flask equipped with a magnetic stir bar, an addition funnel, a septum and a nitrogen balloon, a 1:1 mixture of sulfide (**21**) (0.5 g, 1.3 mmol) and freshly distilled CH_2Cl_2 (14 mL) were added. Na_2CO_3 (0.2g, 1.9 mmol) was added and stirred for 5-10 min and the flask was cooled down to -78 ºC in an IPA/dry ice bath, followed by addition of mCPBA (0.42 g, 1.4 mmol, 60%) as a solution in CH_2Cl_2 *via* the addition funnel slowly over 20 min. A white precipitate formed and the mixture was allowed to stir for an additional 5 min. TLC showed the completion of the reaction. The mixture was quenched with addition of water, rinsed into a separatory funnel with CH_2Cl_2 (50 mL) and washed with water (2x50 mL), brine (1x25 mL) and dried over Na_2SO_4. The solvent was removed on a rotary evaporator to afford the crude product. The product was isolated upon flash chromatography with 50% ethyl acetate in hexanes to give 1:1 mixture of *E* and *Z* isomers (0.43 g, 83%). An analytical sample was obtained by taking a middle fraction from flash chromatography. Data for (*E*)- and (*Z*)-**22**. ^{1}H NMR (250 MHz, $CDCl_3$) 7.63-7.59 (m,4H), 7.48-7.43 (m, 6H), 5.82-5.75 (m, 4H), 3.93-3.85 (m, 4H), 3.58-3.51 (m, 4H), 3.49 (s, 3H), 3.46 (s, 3H), 2.23 (s, 3H), 2.22 (d, 3H, J=0.6 Hz), 2.03-1.97 (m, 4H), 1.60-1.25 (m, 12H), 1.21-1.14 (m, 4H), 1.21 (s, 3H), 1.16 (s, 3H); ^{13}C NMR (62.9 MHz, $CDCl_3$) 161.2, 160.9, 149.9, 149.85, 143.8, 143.6, 140.6, 140.1, 131.1, 131.0, 128.8, 127.5, 127.39, 124.4, 124.2, 105.3, 103.6, 103.6, 58.2, 57.9, 57.5 (br), 41.9, 41.5, 35.5, 32.7, 31.3, 26.9, 26.8, 26.8, 22.9, 22.8, 16.1, 14.7, 13.5 (br); IR (NaCl, neat) 1736m, 1457m, 1443s, 1200m, 1128m, 1114m, 1086s, 1069s, 1048s, 1022s cm^{-1}. Anal. Calcd for $C_{22}H_{30}O_3S$: C, 70.55; H, 8.07. Found: C, 70.63; H, 8.41.

(*E* and *Z*)-Ethyl 3,7-Dimethyl-2-ethoxy-7-[2-(5-methyl)furyl]-2-octenote (25). To a 25 mL round-bottomed flask equipped with a magnetic stir bar, a septum and a nitrogen balloon, freshly distilled DIPA (0.41 mL, 3.1 mmol) and dry THF (14 mL) were added. The flask was cooled down to -78 ºC in an isopropyl alcohol/dry ice bath. To this cooled solution, 1.28 mL of nBuLi (3.1 mmol, 2.4M in hexanes)

was added *via* a syringe. This mixture was allowed to stir for 5-10 min. The triethyl 2-ethoxyphoshonoacetate (0.83 g, 3.1 mmol) was added into the flask as a solution in 5 mL dry THF over 5 min. The mixture was allowed to stir at -78 ºC for 30 min. Ketone **23** (0.63 g, 2.8 mmol) was added as a solution in dry THF (5 mL) over 10 min, followed by slow warming to rt and stirring overnight. TLC showed the completion of the reaction. It was quenched by addition of water, and rinsed into a separatory funnel with ether (50 mL), washed with water (3x25 mL), brine (1x25 mL), and dried over Na_2SO_4. The solvent was removed on a rotary evaporator to give the crude product which was purified by flash chromatography (5% ethyl acetate in hexanes) affording a 1:1 mixture of (*E*)- and (*Z*)-**25** (0.61g, 68%). An analytical sample was obtained by taking a middle fraction from a flash chromatography. Data for (*E*)- and (*Z*)-**25**. ^{1}H NMR (250 MHz, $CDCl_3$) 5.79 (m, 4H, br), 4.26-4.17 (m, 4H), 3.73-3.61 (m, 4H), 2.39-2.24 (m, 2H0, 2.22 (s, 6H), 2.23-2.14 (m, 2H), 1.94 (s, 3H), 1.76 (s, 3H), 1.59-1.52 (m, 4H), 1.34-1.22 (m, 16H), 1.21 (s, 6H), 1.20 (s, 6H); ^{13}C NMR (62.9 MHz, $CDCl_3$) 164.7, 164.3, 161.0, 160.9, 149.7, 149.6, 140.5, 138.6, 138.4, 127.5, 127.4, 105.3, 103.6, 67.5, 67.1, 60.1, 41.7, 41.4, 35.4, 35.4, 33.4, 33.3, 33.0, 26.7 (broad), 23.3, 22.6, 17.2, 15.1, 15.1, 14.1, 13.3; IR (NaCl, neat) 1714s 1446m, 1366m, 1283s, 1222s, 1178s, 1132m, 1107s, 1068m, 1022m cm^{-1}. Anal. Calcd for $C_{19}H_{30}O_4$: C, 70.77; H, 9.38. Found: C, 70.60; H, 9.52.

(*E*)-3,7-Dimethyl-2-ethoxy-7-[2-(5-methyl)furyl]-2-octen-1-ol (26) and (Z)-3,7-Dimethyl-2-ethoxy-7-[2-(5-methyl)furyl]-2-octen-1-ol (26). To a 25 mL recovery flask equipped with a magnetic stir bar, an addition funnel, a septum and a nitrogen balloon, $LiAlH_4$ (50 mg, 0.13 mmol) and freshly distilled THF (9 mL) were added. The flask was cooled down to 0 ºC in an ice bath, followed by addition of ester (**25**) (0.3 g, 0.92 mmol) as a solution in THF (5 mL) via the addition funnel over 20 min. The bath was removed and the mixture was allowed to stir at room temperature for 2 h. TLC showed completion of the reaction. The reaction quenched by careful addition of Na_2SO_4 $10H_2O$ until a white precipate formed. It was diluted with ether (20 mL) and filtered through celite and rinsed with ether (20 mL). The solvent was removed on a rotary evaporator to give the product as colorless oil. It was purified by flash chromatography (10% ethyl acetate in hexanes) to give 0.119 g of *E* and 0.141g of *Z* allylic alcohols. An analytical sample was obtained by taking a middle fraction from flash chromatography. Data for (E)-**26**: ^{1}H NMR (250 MHz, $CDCl_3$) 5.81-5.78 (m, 2H), 4.17 (d, 2H, J=5.1 Hz), 3.75 (q, 2H, J=7.0 Hz), 2.23 (s, 3H), 1.94 (t, 2H, J=7.4 Hz), 1.60 (s, 3H), 1.59-1.46 (m, 3H), 1.26 (dt, 3H, J= 0.6, 7.0 Hz), 1.19 (s, 6H, br), 1.19-1.14 (m, 2H); ^{13}C NMR (62.9 MHz, $CDCl_3$) 161.1, 149.9, 147.7, 122.4, 105.4, 103.7, 65.3, 57.5, 41.3, 35.5, 32.6, 26.9, 23.4, 15.5, 14.9, 13.5; IR (NaCl, neat) 1718m, 1675m, 1561m,1452m, 1384s, 1347m, 1263m, 1221m, 1179 s, 1043s, 1022s cm^{-1}. Anal. Calcd for $C_{17}H_{28}O_3$: C, 72.81; H, 10.06. Found: C, 72.93; H, 10.16. An analytical sample was obtained by taking a middle fraction from flash chromatography. Data for ((*Z*)-**26**): ^{1}H NMR (250 MHz, $CDCl_3$) 5.79-5.78 (m, 2H), 4.20 (s, 2H, br),

3.71 (q, 2H, J=7.0 Hz), 2.34-2.25 (m, 2H), 2.23 (s, 3H), 2.06 (t, 2H, J=7.1 Hz), 1.5 (s, 3H), 1.80-1.51 (m, 2H), 1.27-1.19 (m, 4H), 1.20 (s, 6H); ^{13}C NMR (62.9 MHz, $CDCl_3$) □ 161.3, 149.8, 147.21, 122.1, 105.3, 103.6, 65.4, 57.8, 41.8, 35.6, 31.2, 26.8, 22.8, 15.7, 15.4, 13.5; IR (NaCl, neat) 3413m, 1718m, 1672m, 1562m, 1459m, 1450s, 1384 s, 1347m, 1234m, 1221s, 1180s, 1088s, 1043s, 1021s, 980m, 938s cm^{-1}. Anal. Calcd for $C_{17}H_{28}O_3$: C, 72.81; H, 10.06. Found: C, 72.76; H, 10.20.

ACKNOWLEDGEMENTS

This paper is dedicated to Professor Leo A. Paquette on the occasion of his 70th birthday. This work was supported by the National Science Foundation, to whom we are grateful. We thank to Professor G. Majetich for providing us with authentic samples of widdrol and epi-widdrol. We are greatful to Professor B. A. Keay for a procedure for the preparation of **17** prior to publication. M.K. thanks to Turkish Ministry of Education for a fellowship.

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