Pergamon

Tetrahedron Vol. 50, No. 23, pp. 6767-6782, 1994
Elsevier Science Ltd
Printed in Great Britain
0040-4020/94 $7.00+0.00

0040-4020(94)E0320-S

Synthetic and Kinetic Studies of Substituent Effects in the Furan Intramolecular Diels-Alder Reaction

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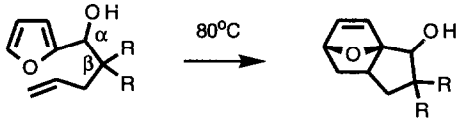
Abstract: The Intramolecular Diels-Alder reactions (IMDA) of a series of 2-sulfone substituted 1-furyl-4-penten-1-ols, **5a-c**, have been studied. As the steric demands of the alkyl group on the sulfone was increased the rate and product yields in the IMDA reaction have also been observed to increase. The kinetics of these systems have been studied in detail as well as solvent effects to quantify substituent group effects in the cyclization reactions. Activated dienophiles (CO_2Me) in these systems have been shown to be very reactive, cyclizing at ambient temperature.

INTRODUCTION

The substituent effects in the Intramolecular Diels-Alder Reaction (IMDA) with furan, utilizing a three-carbon tether, have been studied at great length in this laboratory[3] and others.[4-6] However, the synthetic potential of this reaction remains unrealized because of the substituent requirements for cyclization. Typically, disubstitution at the β-carbon (Scheme 1) has been necessary for cyclization, which requires a quaternary carbon to be formed in the construction of the Diels-Alder precursor. Work published[3a] from this laboratory used substituents such as R = dithiane, SEt, OEt (Scheme 1) in these systems to effect cyclization. These substituent limitations decreased the functionality options prior to and following the IMDA reaction and complicated precursor construction.

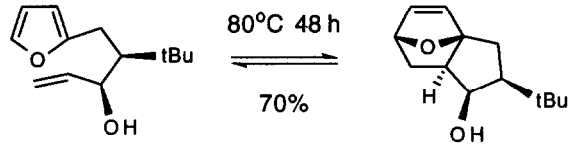


1 a-e **2 a-e**

Entry	R	Time (day)	Yield
a	$S(CH_2)_3S$	3	63
b	SEt	3	86
c	OEt	3	75
d	Me	14	0
e	Pr	3	58

Scheme 1

Recently, DeClerq[7] has reported that a single *t*-butyl in the β-position promoted cyclization in a similarly substituted furan IMDA precursor (Scheme 2). The *t*-butyl group was proposed to occupy the pseudoequatorial position on the tethering chain forcing the diene and dienophile anti to the large *t*-butyl. This would place the diene and the olefin in close proximity thereby improving the rate and yield of the reaction by promoting this reactive conformation. This was an important result since it demonstrated that only one bulky substituent is sufficient to induce a "reactive rotamer effect" and cyclization. For a variety of synthetic applications the product is somewhat limited, given the difficulty of refunctionalizing or removing a *t*-butyl group.



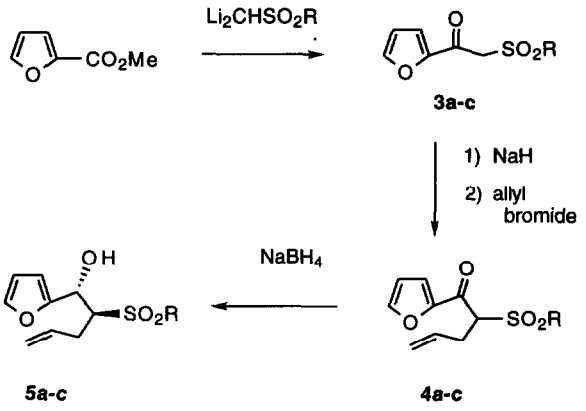
Scheme 2

To further develop the synthetic utility of the IMDA reaction with furan, we investigated systems in which a single group at the β-position is utilized that has the steric requirements to promote efficient cyclization. If possible a group should be chosen that might allow for further functionalization of the bridging chain, which is unavailable in the previous work cited. Although this is not the focus of this work, it would add some salient options for utilizing the results reported herein for future synthetic applications.

RESULTS AND DISCUSSION

Development of Sulfone Methodology

Initially, we thought that a methyl sulfone group would satisfy the requirements of a bulky group similar in steric demands to a *t*-butyl. Construction of the required system seemed feasible from furyl keto-sulfone **3a** (Scheme 3). In fact, producing **3a** from the condensation of the dimethyl sulfone anion and methyl furoate provided **3a** in reasonable yield (59%). Construction of the desired precursor was accomplished by deprotonation of **3a** with NaH followed by alkylation with allyl bromide to provide **4a**. Reduction of **4a** with $NaBH_4$ yielded IMDA precursor **5a** as a 6:1 ratio of diastereomers in 60% yield. High selectivity in the reduction of keto-sulfones has been observed with $NaBH_4$ in other systems to yield primarily anti-products.[8] X-ray crystallographic data provided unequivocal assignment of the relative configuration at C1 and C2 of the major isomer **5a** (Figure 1). Attempts were made to isolate the minor isomer to compare its reactivity to the major isomer in the IMDA reaction, but the compound seemed sensitive to purification procedures and no pure material could be obtained.



Scheme 3

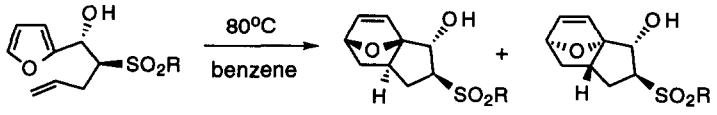
The IMDA reaction of **5a** under our standard conditions (80°C in C_6D_6, sealed tube) was monitored by ^1H NMR and was observed to have reached equilibrium after 9 days to yield 78% of products **6a** and **7a** in a ratio of 6.5:1. After purification by flash chromatography, 61% of pure **6a** was obtained. Assignment of the relative configuration in the cycloadducts was achieved by comparison with our earlier work which demonstrated that in the major isomer the OH is spatially close to the C8 olefin proton, deshielding that proton by ~0.3ppm.[3a] The products arise from attack at the two possible faces of the furan, with the major product placing the methyl sulfone and the OH in pseudoequatorial positions. Conversely, the minor product arises from attack at the face that places the OH and the methyl sulfone in pseudoaxial positions.

These initial results demonstrated the viability of using a sulfone in the β-position of the tethering chain to effect these cyclizations. However, the long reaction time and modest yield suggested that the reaction should be optimized further for synthetic applications.

From results in our laboratory[9] it has been shown that remote steric influences have a dramatic effect on the IMDA reaction. In the cases that have been studied with two identical alkyl substituents at the β-carbon, the reaction rate and yield have been shown to increase with increasing chain length of the substituent. For the furan IMDA reaction where R=Me, **1d**, no reaction is observed after extended reaction times. However, when R=Pr, **1e**, 58% products have been observed.(Scheme 2) Okamura has recently determined the relative rates of IMDA cyclization of his allenylphosphine oxides in which the two substituents on the β-carbon were varied from R=H to Pr, yielding a rate increase of 27.8 fold with increasing chain length.[10]

The sulfone systems also allowed for variance in the size of alkyl portion of the sulfone without changing the general synthetic procedure of the IMDA precursor. Two other sulfone systems were chosen for investigation; R= *t*-Bu and Ph. Methyl phenyl sulfone is commercially available and methyl *t*-butyl sulfone is easily prepared by oxidation of methyl *t*-butyl sulfide with oxone[11]. Following the procedure for the synthesis of **5a** the desired sulfone IMDA precursors were obtained in good to excellent yields. By subjecting these

substrates to the standard cyclization conditions (80°C, C_6D_6), the phenyl sulfone and *t*-butyl sulfone cyclized much more efficiently (93 and 97%) and at an increased rate (3 and 1.7 days).



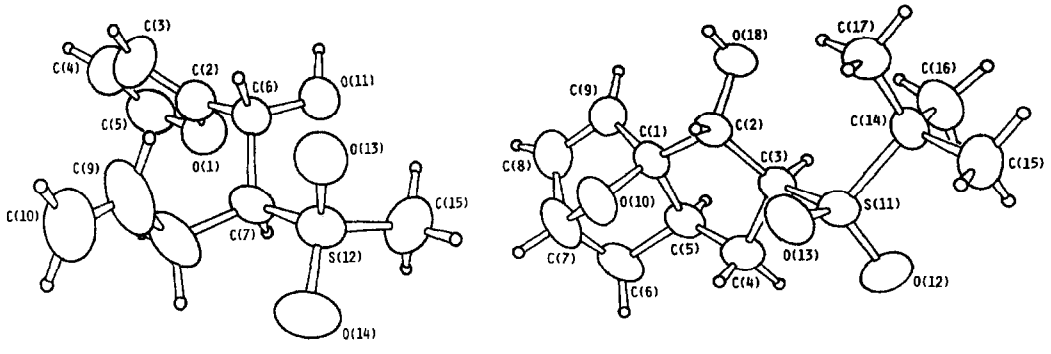
5a-c **6a-c** **7a-c**

Compound	R	time (days)	yield 6+7*
5a	Me	9	78%
5b	Ph	3	93%
5c	*t*-Bu	1.7	97%

*Yields determined by ^{1}H NMR.

Scheme 4

The relative configuration of the *t*-butyl sulfone Diels-Alder product, **6c**, has been proven by X-ray crystallography (Figure 1). By spectroscopic comparison of **6c** to the other Diels-Alder products, **6a** and **6b**, the relative configuration of those products has been confirmed. The two X-ray crystal structures of **5a** and **6c** also demonstrate that there is no epimerization during the Diels-Alder reactions of these sulfone compounds.



5a **6c**

Figure 1: X-ray Crystal Structures of IMDA Precursor **5a** and IMDA Product **6c**

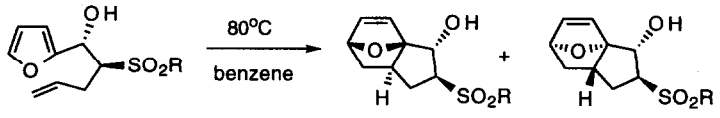
These results demonstrate that although the "mono tert-butyl effect" is playing a role in these systems, a remote steric effect is also involved and can have a dramatic affect on the IMDA outcome. There is no straightforward explanation for this effect, but given its observation in other systems, this remote steric effect

seems to have general application. These results fulfill the initial goals of producing reactive Diels-Alder systems which cyclize efficiently and use easily prepared precursors.

IMDA Reaction Kinetics

The relative reactivity of the substituted sulfone systems provided a good system for determining the effects of this increased substitution on the rates of the IMDA reactions. The kinetics of these reactions were monitored by observing the disappearance of the furan protons and the appearance of the vinyl protons of the products in the ^{1}H NMR. The kinetics of these reactions are complicated by the fact that two products are formed in the IMDA reactions. Given that these products are formed by attack at two different faces of the furan, there are two different rate expressions for the formation of the possible products. We chose to simplify the kinetics studies by treating this reaction as first order.[12] The rate constants obtained represent the macroscopic rate constants of starting material going to products collectively. These results are useful for quantifying the effects of substituent changes on the overall IMDA kinetics.

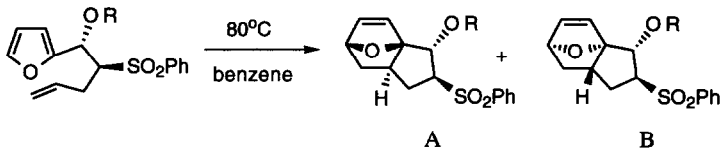
Rate studies on these cyclizations demonstrated that the phenyl sulfone exhibited a four-fold increase in the rate as compared to the methyl sulfone and the *t*-butyl sulfone increased the rate seven-fold. (Scheme 5) The increased rate and yield of the *t*-butyl sulfone as compared to the methyl sulfone is important for possible synthetic applications since the yield has been improved to nearly quantitative conversion to products in a reasonable time of reaction.



R	k_{rel}	$t_{1/2}$ x 10^4 s
Me	1.0	15.00
Ph	4.3	4.19
t-Bu	7.3	2.56

Scheme 5

We were interested in studying the effects of intramolecular hydrogen bonding on the IMDA reaction in these hydroxy sulfone systems. Two Diels-Alder experiments were run with the phenyl sulfone precursor, to determine the contribution of the hydrogen bonding to the success of the IMDA. One of the reactions was conducted in a hydrogen-bonding solvent, d_4-methanol, to determine its effect on the intramolecular hydrogen bond. A second experiment was run with the hydroxyl protected as the acetate (compound **5d**) in d_6-benzene. This substrate eliminates hydrogen bonding possibilities, although adds steric bulk to the bridging chain. The kinetic results from these experiments are shown in Scheme 6.



A B

Compound	R	solvent	k_{rel}	$t_{1/2}$ x 10^4 s	A:B
5b	H	C_6D_6	2.1	4.19	6.5:1
5b	H	CD_3OD	1.0	7.85	4.5:1
5d	Ac	C_6D_6	2.9	2.95	2.2:1

Scheme 6

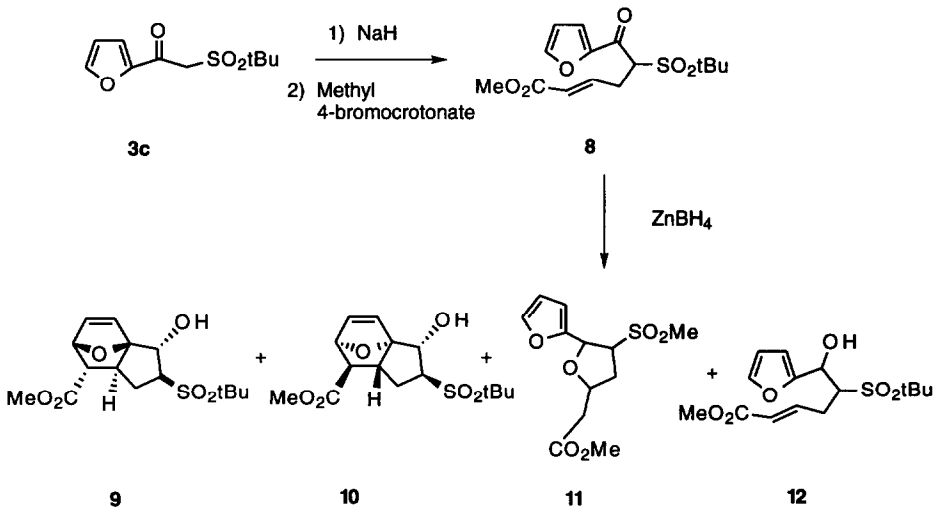
In the experiment using d_4-methanol as the solvent, the rate is halved as compared to the experiment in d_6-benzene and there is also a modest decrease in selectivity. This would suggest that intramolecular hydrogen bonding is playing a role in aiding the Diels-Alder reaction, possibly "holding" the chain in a reactive conformation. The acetate-protected precursor, **5d**, however cyclized slightly faster than the parent system. Although no hydrogen-bonding is possible, the steric influence of the acetate has an effect on the cyclization. As observed with the sulfone series, this steric effect increased the rate of the IMDA reaction. Interestingly, we also observed a loss in selectivity of the reaction, that decreased the ratio to 2:1. In the hydroxy sulfone series, the OH is close to the C8 proton causing a steric repulsion which destabilizes the major product. Protection of the hydroxyl increases this steric repulsion further destabilizing the major product and thereby decreasing the selectivity of the reaction.

Synthetic Studies

Earlier work in our group[13] and others[4b] as well as preliminary experiments with more highly substituted sulfone IMDA precursors had shown that added substitution on the 4-position of the furan and on the terminal position of the tethering chain decreased rates and product yields in these systems. We were interested in these additional substituents for synthetic applications which would allow for adding on a third ring to the IMDA bicyclic system. To minimize the effect of greater alkyl substitution on the IMDA reaction, an activated dienophile was studied to increase reactivity.

Using our previous alkylation procedure, deprotonation of keto-sulfone **3c** followed by alkylation with methyl 4-bromocrotonate as the electrophile provided **8** in 89% yield. The required reduction of the ketone was accomplished with $Zn(BH_4)_2$[14] which provided four products: two IMDA products **9** and **10** (19% yield), a tetrahydrofuran side product **11**, and a small amount of uncyclized hydroxy sulfone **12**. The reduction proved difficult with other reducing agents; $Zn(BH_4)_2$ was observed to be the best of the series for reducing the formation of side product **11** . These results were interesting in that upon reduction cyclization occurred,

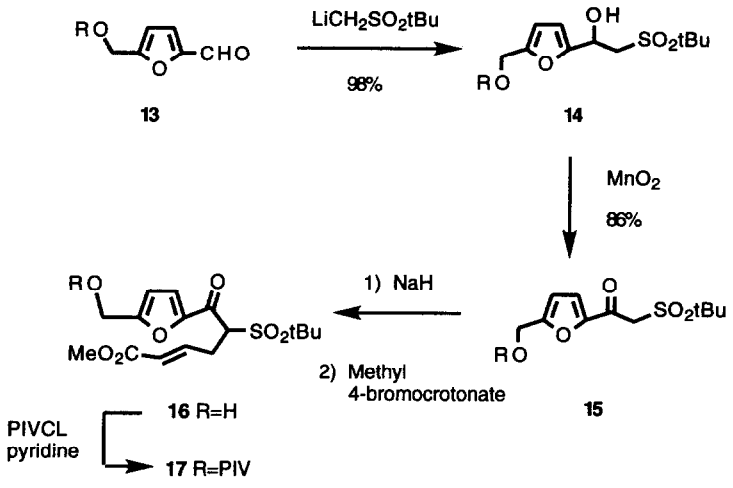
displaying the expected increased reactivity toward IMDA cyclization. Unfortunately, the competing side product from conjugate addition of the alkoxide to the α,β-unsaturated ester demonstrated that other cyclizations are also facile.



Scheme 7

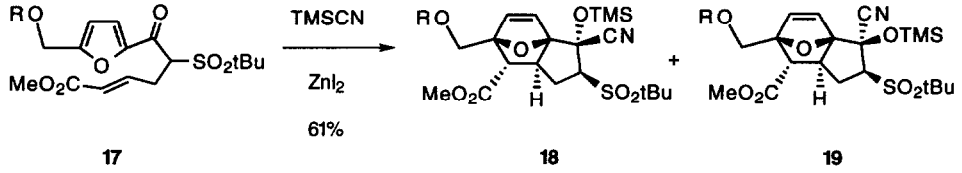
Because of the complications with this reduction, compound **8** required a different method of reducing or protection of the ketone. It should be noted that ketone **8** does not undergo IMDA reaction. Since we were interested in substitution on the 4-position of the furan, further investigations into functionalizing the ketone were postponed until a fully substituted system was obtained.

Construction of the desired keto-sulfone **15** with a protected hydroxy methyl group in the 4-position of the furan was produced in straightforward fashion from 5-*t*-butyldimethylsilyloxymethyl-2-furfuraldehyde, **13**, as shown in Scheme 8. The addition of lithio-methyl *t*-butyl sulfone to the furfuraldehyde **13** yielded the hydroxy compound **14** in excellent yield (98%). Oxidation of **14** was accomplished with MnO_2[15] in 86% yield. Manganese dioxide is not often used in the oxidation of furylic alcohols, but works well where other oxidation procedures failed (PCC, PDC) and allows for easy scale up. Alkylation of **15** with methyl 4-bromocrotonate provided **16** in good yield (86%, R=H). The silyl protecting group was lost in the dilute acid work-up of the alkylation reaction. Attempts to avoid this problem were unsuccessful therefore the alcohol was reprotected as the pivolate ester, **17** (R=PIV).



Scheme 8

Reduction of **17** with $Zn(BH_4)_2$ and other reducing agents yielded a product distribution similar to the reduction compound **8**, which produced a large amount of the tetrahydrofuran side product. Formation of the acetal would be ideal for protection of the ketone in the bridging chain; however **17** was resistant to all such attempts. Treatment of ketone **17** with trimethylsilyl cyanide and zinc iodide as the catalyst[16] provided the TMS-protected cyanohydrin IMDA products **18** and **19** in 61% overall yield.



Scheme 9

The yields for the two steps, cyanohydrin formation and the Diels-Alder reaction, averages to 80% per reaction which are acceptable yields for advanced synthetic applications. It is possible that the ZnI_2 may be catalyzing the IMDA reaction as well as cyanohydrin formation. To date, we have been unable to form the cyanohydrin in the absence of zinc to determine its catalytic effect on the IMDA reaction.[17]

This result completes our goal of a highly substituted IMDA precursor that cyclizes readily. In this case, cyclization is spontaneous at room temperature once the sp^2 center of the ketone is removed from the tethering chain. Compounds **18** and **19** allow for a wide range of synthetic transformations from these highly substituted advanced intermediates with all the functionality differentiated for easy manipulation.

SUMMARY

Substituent studies in the sulfone systems have shown that by increasing the steric demands of the group on sulfur, improved yields and rates of the furan IMDA reactions can be obtained. The reaction kinetics have been studied in detail to quantify the effects of the sulfone substituents and the remote steric influences in the IMDA reactions. Examination of more reactive, activated dienophiles has shown these initial results to be quite useful in synthetic efforts by producing highly functionalized IMDA products in good overall yield. The result of this work has shown that the remote steric effect is an important factor to consider in cyclization reactions and when utilized can greatly improve reaction results. The choice of the sulfone may prove to be important for future synthetic work, in that further funtionalization of the tethering chain should be possible utilizing the present knowledge of sulfone chemistry in the literature.[18,19,20]

EXPERIMENTAL

General. All reactions were carried out under an atmosphere of dry N_2 or Ar unless otherwise noted. Flash chromatography was performed using 230-400 Mesh silica. Tetrahydrofuran was distilled from sodium-benzophenone. NMR spectra were obtained on a Varian XL-300 spectrometer and were taken in $CDCl_3$ unless otherwise noted. IR spectra were obtained as $CDCl_3$ solutions. GC-MS analyses were obtained on a Hewlett-Packard 5988A, using NH_3 and CH_4 reagent gases for chemical ionization (CI). High resolution MS were performed on a Vacuum Generators, Limited Model VG-70S. Elemental analyses were performed by M-H-W Laboratories, P.O. Box 15853, Phoenix, Arizona, 85018. X-ray crystallography was conducted by Dr. A. T. McPhail of the Duke University Chemistry Department. All Diels-Alder reactions were carried out under vacuum in degassed deuterated solvents. These reactions were heated in a constant temperature bath and were conducted in sealed NMR tubes. In the kinetics studies, yields are reported from the integration in the ^1H NMR.

2-Methylsulfonyl-1-(2-furyl)ethanone (3a)

To a solution of dimethyl sulfone (2.0 g, 0.021 mol) in 50 mL of THF cooled to -78°C was added BuLi (18.3 mL of 2.5M solution, 0.0458 mol) dropwise. After addition, the solution was stirred for 45 min at -78°C. Methyl furoate (2.12 g, 0.021 mol) was added dropwise, and the reaction mixture was warmed slowly to room temperature. The mixture was stirred overnight, and the reaction was quenched by addition of 50 mL of water and acidified with 10% HCl solution. The mixture was extracted with ethyl acetate and the combined organic extracts washed with water and dried (Na_2SO_4). Filtration and evaporation yielded a crude mixture, which precipitated **3a** upon treatment with *t*-butyl methyl ether and after filtration yielded 2.30 g (59%) of **3a**. ^1H NMR ($CDCl_3$, δ) 3.14 (s, 3H, $-CH_3$), 4.47 (s, 2H, H1), 6.64 (dd, J=1.71, 3.67 Hz, 4 furyl), 7.41 (dd, 0.73, 3.71 Hz, 3 furyl), 7.71 (dd, 0.79, 1.76 Hz, 5 furyl). ^{13}C NMR ($CDCl_3$, δ) 41.90, 61.23, 113.54, 121.03, 148.66, 151.72, 178.6.. IR ($CDCl_3$, cm^{-1}) 1665 (C=O), 1580, 1467, 1320 (S=O), 1158, 1130. Anal. Calcd for $C_7H_8O_4S$ C, 44.67; H, 4.28. Found: C, 44.76; H, 4.48.

2-Phenylsulfonyl-1-(2-furyl)ethanone (3b)

Methyl phenyl sulfone (2.0 g, 0.013 mol) was treated using the same procedure for the formation of methyl keto-sulfone **3a** to yield 1.65 g (60%) of **3b**. ^1H NMR ($CDCl_3$, δ) 4.59 (s, 2H, H1), 6.58 (dd, 1H, J=1.68, 3.66 Hz, 4 furyl), 7.33 (dd, 1H, J=0.74, 3.67 Hz, 3 furyl), 7.58 (m, 4H, Ar, 5 furyl), 7.91 (m, 2H, Ar). ^{13}C NMR ($CDCl_3$, δ) 63.49, 113.28, 120.43, 128.57, 129.26, 134.29, 148.15, 151.86, 175.74. IR ($CDCl_3$, cm^{-1}) 3100 (Ar), 1675 (C=O), 1570, 1460, 1395, 1325 (S=O), 1225, 1095, 1025, 885. Anal. Calcd for $C_{12}H_{10}O_4S$ C, 57.59; H, 4.02. Found: C, 57.46; H, 4.16.

Methyl *t*-butyl sulfone (3d)

To 150 mL of an aqueous solution of oxone [a source of $KHSO_5$ contains 3 moles of $KHSO_5$ per mol oxone] (88.6 g, 0.144 mol) was added methyl *t*-butyl sulfide (10.1 g, 0.096 mol) in 150 mL of methanol with the temperature of the solution maintained at 0°C. The solution was slowly warmed to room temperature and stirring continued for 4 h. The methanol was removed *in vacuo* and the aqueous solution extracted with ethyl

acetate. The combined organic layers were dried (Na_2SO_4) and evaporation of the solvent yielded 10.29 g (79%) of methyl *t*-butyl sulfone. ^1H NMR ($CDCl_3$, δ) 1.41 (s, 9H, -$C(CH_3)_3$), 2.79 (s, 3H, Me). ^{13}C NMR ($CDCl_3$, δ) 23.25, 32.05, 50.51. MS (CI, CH_4/NH_3) 154 (100, MNH_4^+), 137 (8.8, MH^+), 127 (2.0), 109 (9.2), 98 (0.6). IR ($CDCl_3$, cm^{-1}) 1308 (S=O), 1150, 1085, 958, 883.

2-*t*-Butylsulfonyl-1-(2-furyl)ethanone (3c)

Methyl *t*-butyl sulfone (2.0 g, 0.015 mol) was treated using the same procedure for the formation of methyl keto-sulfone **3a** to yield 2.22 g (66%) of **3c**. ^1H NMR ($CDCl_3$, δ) 1.48 (s, 9H, *t*-Bu), 4.43 (s, 2H, H1), 6.17 (dd, 1H, J=1.71, 3.67 Hz, 4 furyl), 7.42 (d, 1H, J=3.67 Hz, 3 furyl), 7.69 (d, 1H, J=0.87 Hz, 5 furyl). ^{13}C NMR ($CDCl_3$, δ) 23.501, 55.667, 62.295, 113.201, 120.886, 148.150, 152.215, 176.115. IR ($CDCl_3$, cm^{-1}) 2975, 1667 (C=O), 1575, 1430, 1305 (S=O), 1120, 1005 Anal. Calcd for $C_{10}H_{14}O_4S$: C, 52.15; H, 6.12. Found: C, 52.07; H, 6.08.

(±)-2-Methylsulfonyl-1-(2-furyl)-4-penten-1-one (4a)

To a solution of **3a** (0.20 g, 1.06 mmol) in 50 mL of THF cooled to 0°C was added sodium hydride (0.055 g, 2.3 mmol) and the resultant mixture was allowed to react for 45 min. To the mixture was added allyl bromide (0.138 mL, 1.59 mmol) and potassium iodide (0.876 g, 5.3 mmol) and the solution was brought to reflux. The mixture was stirred overnight, and the reaction was quenched by addition of 50 mL water and acidified with 10% HCl solution. The mixture was extracted with ethyl acetate and the combined organic extracts washed with water and dried (Na_2SO_4). Filtration and evaporationyielded a crude mixture, which precipitated **4a** upon treatment with *t*-butyl methyl ether and after filtration gave 0.164 g (68%) of **4a**. ^1H NMR ($CDCl_3$, δ) 2.93 (m, 5H, -CH_3, H1, H3), 4.70 (dd, 1H, J=4.64, 10.01 Hz, H1), 5.05 (dd, 1H, J=1.09, 10.12 Hz, H5), 5.11 (ddd, 1H, J=1.28, 2.63, 17.03 Hz, H6), 5.63 (m, 1H, H4), 6.59 (dd, 1H, J=1.65, 3.66 Hz, 4 furyl), 7.34 (dd, 1H, J=0.68, 3.64 Hz, 3 furyl), 7.66 (dd, 1H, J=0.65, 1.62 Hz, 5 furyl). ^{13}C NMR ($CDCl_3$, δ) 29.69, 32.16, 37.76, 68.80, 113.37, 119.39, 120.66, 131.36, 148.54, 180.58. MS (CI,CH_4/NH_3) 308 (100, MNH_4^+), 291 (35.8, MH^+), 240 (1.1), 223 (1.2), 168 (2.2), 151 (6.9), 149 (3.2). IR ($CDCl_3$, cm^{-1}) 2850-2950 (C-H), 1669 (C=O), 1566, 1463, 1317 (S=O), 1262, 1132, 1118, 922.

(±)-2-Phenylsulfonyl-1-(2-furyl)-4-penten-1-one (4b)

Phenyl keto-sulfone **3b** (1.30 g, 5.20 mmol) was treated using the same procedure for the formation of **4a** to yield 1.06 g (70%) of **4b**. ^1H NMR ($CDCl_3$, δ) 2.80 (m, 2H, H2, H3), 4.93 (dd, 1H, J=4.58, 10.25 Hz, H1), 4.99 (dd, 1H, J=1.16, 10.14 Hz, H5), 5.05 (ddd, 1H, J=1.28, 2.69, 18.37 Hz, H6), 5.60 (m, 1H, H4), 6.54 (dd, 1H, J=1.66, 3.66 Hz, 4 furyl), 7.27 (d, 1H, J=3.67 Hz, 3 furyl) 7.56 (m, 6H, Ar, 5 furyl). ^{13}C NMR ($CDCl_3$, δ) 31.57, 70.18, 113.53, 119.44, 120.15, 129.35, 130.03, 132.13, 134.69, 136.83, 148.32, 153.05, 179.90. MS (CI, CH_4/NH_3) 290 (6.6), 289 (15.8), 288 (100, MNH_4^+), 272 (5.2), 271 (30.2) 215 (12.9), 168 (2.2) 151 (39.5) 133 (3.6). IR ($CDCl_3$, cm^{-1}) 30.74 (Ar-H), 2984 (C-H), 1672 (C=O), 1566, 1463, 1323 (S=O), 1310, 1152, 1140, 1084, 1018.

(±)-2-*t*-Butylsulfonyl-1-(2-furyl)-4-penten-1-one (4c)

t-Butyl keto-sulfone **3c** (1.50 g, 6.52 mmol) was treated using the same procedure for the formation of methyl keto-sulfone **4a** to yield 1.72 g (98%) of **4c**. ^1H NMR ($CDCl_3$, δ) 1.41 (s, 9H, $(CH_3)_3C$-), 2.81 (m, 1H, H2), 3.16 (m, 1H, H3), 4.91 (dd, 1H, J=3.3, 11.7 Hz, H1), 4.97 (d, 1H, J=10.2 Hz, H5), 5.05 (dd, 1H, J=1.2, 17.1 Hz, H6), 5.59 (m, 1H, H4), 6.59 (dd, 1H, J=1.71, 3.69 Hz, 4 furyl), 7.35 (d, 1H, J=3.69 Hz, 3 furyl), 7.61 (d, 1H, J=0.97 Hz, 5 furyl). ^{13}C NMR ($CDCl_3$, δ) 23.82, 29.66, 32.44, 63.25, 113.36, 118.96, 119.20, 132.14, 145.06, 147.157, 180.01. MS (CI, CH_4/NH_3) 247 (12.7), 246 (100, MNH_4^+), 229 (50, MH^+), 151 (12.9), 150 (8.2) 149 (8.5) 95 (2.3). IR ($CDCl_3$, cm^{-1}) 2933 (C-H), 1677 (C=O), 1568, 1464, 1301 (S=O), 1120, 1016. Anal. Calcd for $C_{13}H_{18}O_4S$. C, 57.75; H, 6.71. Found: C, 57.57; H, 6.79.

(±)-(R*,S*)-α-(1-Methylsulfonyl-3-butenyl)-2-furanmethanol (5a)

To a solution of **4a** (0.019 g, 0.084 mmol) in 30 mL methanol cooled to 0°C, sodium borohydride was added (0.016 g, 0.42 mmol) and the reaction was monitored by TLC. After 2 h, a second portion of sodium borohydride was added (0.016 g). After the reaction was shown to be complete, the solvent was removed *in vacuo* and the resultant residue was dissolved in water. The reaction was quenched with 10% HCl and the

water layer was extracted with EtOAc. The combined organic layers were washed with saturated $NaHCO_3$ brine and dried (Na_2SO_4). Filtration and evaporation yielded 0.017 g (86%) of **5a** as a 6:1 mixture of diastereomers which was purified by flash chromatography (1:1 EtOAc: pentane) to yield pure **5a**. ^{1}H NMR ($CDCl_3$, δ) 2.51 (m, 2H, H3, H4), 2.85 (s,3H, CH_3SO_2-), 3.47 (m,1H,H2), 4.97 (dd, 1H, J=1.46, 2.98 Hz,H1), 5.04 (m, 2H, H6, H7), 5.67 (m,1H, H5), 6.35 (dd,1H, J=1.85,3,31 Hz, 4 furyl), 6.39 (d, 1H, J=3.23 Hz, 3 furyl), 7.39 (dd,1H, J=0.82, 1.77 Hz, 5 furyl). ^{13}C NMR ($CDCl_3$, δ) 29.51, 43.87, 66.62, 66.94, 109.31, 111.09, 119.13, 133.06, 143.02, 152.70. MS (Cl, CH_4/NH_3) 248 (100, MNH_4^+), 230 (6.3,MNH_4^+-H_2O), 213 (23.1, MH^+-H_2O), 151 (4.3), 134 (13.3), 133 (15.1), 108 (5.2), 97 (1.2), 95 (2.1). IR ($CDCl_3$, cm^{-1}) 3454 (OH), 2983 (C-H), 2940, 2806, 2256, 1726, 1445, 1376 (S=O), 1263, 1064. X-ray data provided in supplemental materials (see Figure 1, X-ray structure).

(±)-(R*,S*)-α-(1-Phenylsulfonyl-3-butenyl)-2-furanmethanol (5b)

Compound **4b** (0.265 g, 0.914 mmol) was treated using the same procedure for the formation **5a** to yield 0.060 g (60%) of **5b** as a 6 : 1 mixture of diastereomers which was purified by flash chromatography (1:1 EtOAc: pentane) to yield pure **5b**. ^{1}H NMR ($CDCl_3$, δ) 2.40 (m, 2H, H3, H4), 3.67 (dt, 1H, 5 = 7.51, 4.83 Hz, H2), 4.85 (m,2H, H6, H7), 5.10 (dd, 1H, J = 4.83, 7.76 Hz, H1), 5.42 (m,1H, H5), 6.26 (dd, 1H, J = 1.79, 3.26 Hz, 4 furyl), 6.32 (d, 1H, J = 3.23 Hz, 3 furyl), 7.20 (dd, 1H, J = 0.79, 1.77 Hz, 5 furyl). ^{13}C NMR ($CDCl_3$, δ) 30.54, 66.74, 108.90, 110.45, 118.81,128.60, 129.16, 132.50, 133.84, 138.41, 142.38, 151.74. MS (CI, CH_4/NH_3) 312 (6), 310 (100, MNH_4^+), 292 (10, MNH_4+ - H_2O), 275 (36,MH^+-H_2O), 224 (2), 207 (4), 171 (4), 151 (5), 150 (5), 134 (9), 133 (55). IR ($CDCL_3$, cm^{-1}) 3489 (OH), 3201 (Ar, C-H), 3075 (C-H), 2257, 1730, 1447, 1296 (S=O), 1143, 1084.

(±)-(R*,S*)-α-(1-*t*-Butylsulfonyl-3-butenyl)-2-furanmethanol (5c)

Compound **4c** (0.37 g, 1.37 mmol) was treated using the same procedure for the formation **5a** to yield 0.271 g (73%) of **5c** as a 12 : 1 mixture of diastereomers which was purified by flash chromatography (1:1 EtOAc: pentane) to yield pure **5c**. ^{1}H NMR ($CDCl_3$, δ) 1.44 (s, 9H, $(CH_3)_3CSO_2$-), 2.45 (m, 2H, H3 and H4), 3.76 (ddd, 1H, J=7.92, 4.34, 5.42 Hz,H2), 4.27 (d, 1H, J=4.69, -OH), 4.87 (dd,1H, J=16.93,1.49 Hz,H6), 4.96 (d,1H,J=10.12,Hz), 5.09 (dd,1H, J=4.64, 8.11 Hz, H1), 5.49 (m,1H, H5), 5.95 (dd,1H, J= 1.76, 3.17 Hz, 4 furyl), 6.03 (d, 1H, J=3.17 Hz, 3 furyl), 6.97 (d,1H,J=1.71 Hz, 5 furyl). ^{13}C NMR ($CDCl_3$, δ) 23.29, 32.54, 61.22, 61.72, 66.97, 109.09, 110.58, 118.22, 113.03, 143.29, 151.73. MS (CI, CH_4/NH_3) 290 (100,MNH_4^+), 272 (8.4), 255 (32.9, MH^+ - H_2O), 216 (3.4), 199 (15.3), 191 (33.0), 151 (17.0), 135 (27.4), 134 (10.0), 133 (25.4). IR ($CDCl_3$,d) 3502 (OH), 2980 (C-H), 2256, 1462, 1282 (S=O), 1264, 1149, 1110, 1010.

(±)-(2β,3α,3aβ,6β,7aα) and (2β,3α,3aα,6α,7aβ)-1,6,7,7a-Tetrahydro-2-methylsulfonyl-[3a,6]-epoxy-[3a,H]-inden-3-ol (6a, 7a)

A solution of **5a** (0.077g, 0.334 mmol) in 0.5 mL of d_6-benzene was heated to 80°C under vacuum and the progress of the reaction monitored by ^{1}H NMR. After 8.5 days the reaction had reached equilibrium to yield 78% products and a product ratio, **6a**: **7a**, of 6.5:1. Evaporation followed by purification by flash chromatography (1:1 EtOAc: pentane) yielded 0.047 g (61%) of **6a**. ^{1}H NMR ($CDCl_3$, δ) 1.41 (dd, 1H, J=7.7, 19.5 Hz, H7a), 1.67(m, 1H, H7b), 1.69(m, 1H, H1a), 1.98(m, 1H, H7a), 2.41(m, 1H, H1b), 2.89(s, 3H,-SO_2Me), 3.58(m, 1H, H2), 4.59 (d, 1H, J=5.86 Hz, H3), 4.98 (dd, 1H, J=1.16, 4.44 Hz, H6), 6.28 (dd, 1H, J=1.28, 5.86 Hz, H5), 6.50 (d, 1H, J=5.86 Hz, H4). ^{13}C NMR ($CDCl_3$, δ) 31.18, 32.22, 39.43, 41.45, 60.37, 72.11, 73.75, 79.89, 133.91, 135.80. MS (CI, CH_4/NH_3) 2.48 (100, MNH_4^+), 230(12), 213(40), 53(14), 135(19), 134(20), 133(73), 109(11). IR ($CDCl_3$, cm^{-1}) 3482(OH), 2962, 2904, 1729, 1604, 1507, 1446, 1410, 1303, 1260 (S=O), 1063.

(±)-(2β,3α,3aβ,6β,7aα) and (2β,3α,3aα,6α,7aβ)-1,6,7,7a-Tetrahydro-2-phenylsulfonyl-[3a,6]-epoxy-[3a,H]-inden-3-ol (6b, 7b)

A solution of **5b** (0.042 g, 0.142 mmol) in 0.5 mL of d_6-benzene was heated to 80°C under vacuum and the progress of the reaction monitored by ^{1}H NMR. After 3 days the reaction had reached equilibrium to yield 93% products and a product ratio, **6b**: **7b**, 6.5:1. Evaporation followed by purification by flash chromatography (1:1 EtOAc: pentane) yielded 0.040g (76%) of **6b**. This reaction was also run at 80°C in

CD_3OD and the reaction monitored by ^1H NMR to yield 83% products after 4.5 days in a ratio of 4.5 : 1 of **6b** to **7b**. ^1H NMR ($CDCl_3$, δ) 1.35 (dd, 1H, J=7.57, 11.48 Hz, H7a), 1.60 (m, 1H, H7b), 1.66 (m, 1H, H1a), 1.89 (m, 1H, H7a), 2.13 (m, 1H, H1b), 3.68 (m, 1H, H2), 4.68 (d, 1H, J=6.11 Hz, H3), 4.95 (d, 1H, J=3.37 Hz, H6), 6.24 (dd, 1H, J=5.99, 0.77 Hz, H5), 6.49 (d, 1H, J=5.86 Hz, H4), 7.4 - 7.9 (m, 54, Ar). ^{13}C NMR ($CDCl_3$, δ) 31.89, 32.28, 41.30, 71.56, 75.28, 79.89, 98.85, 128.56, 129.27, 133.90, 134.061, 135.51, 138.05. MS (CI, CH_4/NH_3), 310(67, MNH_4^+), 275(49), 214(15), 160(10), 151(12), 143(12), 134(20), 133(100), 114(7). IR ($CDCl_3$, cm^{-1}) 3482(OH), 3068, 2979, 2947, 1729, 1447, 1291(S=O), 1146, 1083, 1046, 999, 951.

(±)-(2β,3α,3aβ,6β,7aα) and (2β,3α,3aα,6α,7aβ)-1,6,7,7a-Tetrahydro-2-*t*-butylsulfonyl-[3a,6]-epoxy-[3a,H]-inden-3-ol (6c, 7c)

A solution of **5c** (0.045 g, 0.163 mmol) in 0.5 mL of d_6-benzene was heated to 80°C under vacuum and the progress of the reaction monitored by ^1H NMR. After 1.7 days (40 h) the reaction had reached equilibrium to yield 97% products (**6c**,**7c**) and a product ratio, **6c**: **7c**, of 6.5:1. Evaporation followed by purification by flash chromatography (1:1 EtOAc: pentane) yielded 0.038 g (85%) of **6c**. ^1H NMR ($CDCl_3$, δ) 1.47 (s, 9H,$(CH_3)_3SO_2$-), 1.48 (m, 1H, H7a), 1.76 (ddd, 1H, J=2.93, 4.34, 11.48 Hz, H7b), 1.88 (t, 1H, J=11.77 Hz, H1a), 2.03 (m, 1H, H7a), 2.35 (m, 1H, H1b), 3.77 (m, 1H, H2), 4.81 (d, 1H, J=5.81 Hz, H3), 5.06 (dd, 1H, J=1.32, 4.39 Hz, H6), 6.34 (dd, 1H, J=1.41, 5.86 Hz, H5), 6.57 (d, 1H, J=5.86 Hz, H4). ^{13}C NMR ($CDCl_3$, δ) 23.68, 31.91, 33.40, 39.02, 42.05, 60.06, 68.16, 72.22, 7 9.93,134.09,135.71. IR ($CDCl_3$,cm^{-1}) 3595 (OH,free) 3461(OH, bonded) 2979, 2948, 2874, 1477, 1282(S=O), 1130, 1045. X-ray data provided in supplemental materials (see Figure 1 for X-ray structure).

(±)-(R*,S*)-α-(1-Phenylsulfonyl-3-butenyl)-2-furanmethanol, acetate (5d)

To a sample of **5b** (0.023 g, 0.078 mmol) was added 2 mL of pyridine and 2 mL of acetic anhydride and the mixture was stirred overnight. Evaporation of the excess reagents followed by flash chromatography (1:1 EtOAc: pentane) yielded 0.006 g (23%) of **5d** and 0.008 g of **6d** and **7d** (85% combined yield). ^1H NMR ($CDCl_3$, δ) 1.67 (s, 3H, CH_3CO_2-), 2.49 (t, 2H, J=6.6 Hz, H3, H4), 3.88 (dt, 1H, J=5.4, 9.0 Hz, H2), 4.82 (dd, 1H, J=1.2, 17.1 Hz, H7), 4.94 (d, 1H, J=10.2 Hz, H6), 5.66 (m, 1H, H5), 6.16 (d, 1H, J=9.3 Hz, H1), 6.27 (dd, 1H, J=1.8, 3.0 Hz, 4 furyl), 6.35 (d, 1H, J=3.3 Hz, 3 furyl), 7.29 (d, 1H, J=1.8 Hz, 5 furyl), 7.5-7.9 (m, 5H, $PhSO_2$-). ^{13}C NMR ($CDCl_3$, δ) 30.16, 65.40, 66.90, 110.59, 111.38, 118.29, 128.28, 129.11, 132.62, 133.53, 140.25, 142.92, 145.08, 148.55, 168.66. MS (CI, CH_4/NH_3) 352 (12, MNH_4^+), 303 (8), 275 (62), 207 (9), 193 (18), 133(100), 111 (32).

(±)-(2β,3α,3aβ,6β,7aα) and (2β,3α,3aα,6α,7aβ)-1,6,7,7a-Tetrahydro-2-phenylsulfonyl-[3a,6]-epoxy-[3a,H]-inden-3-ol, acetate (6d, 7d)

A solution of **5d** (3.7 mg, 0.011 mmol) in 0.5 mL of d_6-benzene was heated to 80°C under vacuum and the progress of the reaction monitored by ^1H NMR. After 2.5 days the reaction had reached equilibrium to yield 89% products and a product ratio, **6d**: **7d**, of 2.2: 1. ^1H NMR ($CDCl_3$, δ) 1.42 (dd, 1H, J=7.5, 11.7 Hz, H7a), 1.72 (m,1H, H7b), 1.87 (t, 1H, J=11.7 Hz, H1a), 1.94 (m, 1H, H7a), 2.47 (m, 1H, H1b), 3.89 (m,1H, Hz, H2), 5.02 (dd, 1H, J=1.5, 4.5 Hz, H6), 5.56 (d, 1H, J=6.9 Hz, H4), 6.10 (d, 1H, J=6.0 Hz, H3), 6.26 (dd, 1H, J=1.8, 6.0 Hz, H5), 7.5 - 7.9 (m, 5H, Ar). ^{13}C NMR ($CDCl_3$, δ), 20.21, 31.03, 31.85, 41.91, 71.83, 72.74, 80.16, 97.57, 118.56, 128.88, 129.27, 132.98, 133.89, 135.89, 166.84. MS (CI, CH_4/NH_3) .352(15, MNH_3^+), 275(55), 193(12), 135(64), 133(100), 111(22).

(±)-(E)-6-Oxo-5-*t*-butylsulfonyl-2-furanhex-2-enoic acid, methyl ester (8)

To a sample of **3c** (1.21 g, 5.26 mmol) in 50 mL of THF was added NaH (0.329 g, 13.71 mmol) and the mixture was stirred at room temperature for 30 min. Methyl 4-bromocrotonate (1.139 g, 6.36 mmol) was added and the resultant mixture was refluxed overnight. The reaction was quenched with water followed by acidification with 10% HCl and extraction with EtOAc. The combined organic extracts were dried (Na_2SO_4) and evaporation yielded 1.56 g (89%) of reasonably pure **8**. ^1H NMR ($CDCl_3$, δ), 1.41 (s, 9H, $(CH_3)_3CSO_2$-), 2.91 (m, 1H, H4), 3.34 (m, 1H, H3), 3.64 (s, 3H, -OCH_3), 4.98 (dd, 1H, J=2.99, 11.48 Hz, H5), 5.83 (d, 1H, J=15.57 Hz, H1), 6.58 (dd, 1H, J=1.60, 3.61 Hz, 4 furyl), 6.70 (dt, 1H, J=6.95, 15.57 Hz, H2),

7.35 (d, 1H, J=3.47 Hz, 3 furyl), 7.60 (s, 1H,5 furyl). ^{13}C NMR ($CDCl_3$, δ) 23.78, 30.68, 51.63, 63.61, 113.61, 119.59, 124.43, 142.02, 145.04, 147.36, 152.25, 166.0, 178.99. MS (CI,CH_4/NH_3) 386 (2.2), 348 (6.8), 347 (15.9), 346 (100), 329 (5.4), 297 (2.4), 249 (2.5), 226 (54.1), 209 (70.1), 177 (41.4), 136 (11.5), 111 (3.4). IR ($CDCl_3$, cm^{-1}) 2963, 1723 (CO_2CH_3), 1678 (C=O), 1567, 1464, 1301 (S=O), 1213, 1120, 1017.

(±)-(2α,3β,3aβ,6β,7α,7aα) and (2α,3β,3aα,6α,7β,7aβ)-1,6,7,7a-Tetrahydro-7-carbomethoxy-2-*t*-butylsulfonyl-[3a,6]-epoxy-[3a,H]-inden-3-ol (9, 10)

To an ethereal solution (15mL) of **8** (0.185 g, 0.567 mmol) cooled to 0°C was added zinc borohydride (1.70 mL of a 0.4 M solution in ether, 0.681 mmol) and the mixture was stirred for 1h at 0°C. After warming to room temperature, the reaction was quenched with water and 10% HCl. The water was washed with EtOAc and the combined organic extracts were washed with saturated $NaHCO_3$ and brine. Drying (Na_2SO_4) and evaporation yielded a crude mixture which was purified by flash chromatography (SiO_2, 1:1 EtOAc; pentane). Four products were isolated, **9** and **10** as a 1:1 mixture of products; **11** and **12** in a ratio of 1.5 : 1: 1 respectively in an overall yield of 45% (0.0843 g isolated).

Spectral data for **9, 10**: ^1H NMR ($CDCl_3$, δ) 1.47 (s, 9H, $(CH_3)_3SO_2$-), 1.93 (m, 1H, H1a), 2.41 (m, 1H, H7a), 2.63 (m, 1H, H1b), 2.99 (dd, 1H, J=3.22, 4.64 Hz, H7), 3.61 (s, 3H, -OCH_3), 3.81(m, 1H, H2), 4.97 (d, 1H, J=8.54 Hz, H3), 5.23 (dd, 1H, J=1.41, 4.63 Hz, H6), 6.33(d, 1H, J=1.65 Hz, H5), 6.85(s, 1H, H4). **10** (selected H's): 4.74 (d, 1H, J=6.64 Hz, H3), 5.20 (dd, 1H, J=1.60, 4.63 Hz, H6), 6.26 (dd, 1H, J=1.6, 5.83 Hz, H5), 6.69 (d, 1H, J=5.86 Hz, H4). ^{13}C NMR ($CDCl_3$, δ) 22.93, 30.61, 32.45, 42.86, 51.55, 54.36, 59.75, 62.06, 70.18, 80.05, 97.27, 134.49, 135.26, 170.93. MS (CI,CH_4/NH_3) 348 (100, MNH_4^+), 313 (16), 252 (10), 193 (86), 161 (9), 97 (13).

Spectral data for **11**: ^1H NMR ($CDCl_3$, δ) 1.48 (s, 9H, $(CH_3)_3SO_2$-), 2.70 (m, 1H, H3), 2.90 (m, 1H, H4), 3.68 (s, 3H, -OCH_3), 3.75 (m, 1H, H2), 5,48 (s, 1H, H1), 5.72 (d, 1H, J=15.3 Hz, H6), 6.35 (m, 1H, 4 furyl), 6.43 (m, 1H, 3 furyl), 6.70 (m, 1H, H5), 7.36 (s, 1H, 5 furyl). MS (CI,CH_4/NH_3) 348 (100, MNH_4^+), 331 (20), 313 (22), 210 (30), 193 (78), 161 (28), 97 (26)

Spectral data for **12**: ^1H NMR ($CDCl_3$, δ) 1.40 (s, 9H, $(CH_3)_3SO_2$-), 1.51 (m, 2H, H3, H4), 2.12 (m, 2H, H6, H7), 3.58 (s, 3H, -OCH_3), 3.62 (m, 2H, H2, H5), 5.07 (d, 1H, J=8.41 Hz, H1), 6.32 (m, 2H, 3, 4 furyl), 7.38 (s, 1H, 5 furyl). MS (CI,CH_4/NH_3) 348 (50, MNH_4^+), 331 (8), 252 (20), 193 (100), 161 (34), 136 (19), 97 (42).

5-Hydroxymethyl-2-furfuraldehyde

A solution of 5-acetoxymethyl-2-furfuraldehyde (22.6 g, 0.134 mol) in 200 mL of methanol was treated with potassium carbonate (5.0g, 0.021 mol) and the progress of the reaction was monitored by TLC (SiO_2, 1:1 pentane : EtOAc). After 12 h, the solvent was evaporated and the residue dissolved in EtOAc. The organic layer was washed with water and dried (Na_2SO_4). Filtration and evaporation yielded 16.65 g (98%) of 5-hydroxymethyl-2-furfuraldehyde. ^1H NMR ($CDCl_3$, δ) 4.69 (s, 2H,-CH_2OH), 6.50 (d, 1H, J=3.55 Hz, 4 furyl), 7.20 (d, 1H, J=3.60 Hz, 3 furyl), 9.52 (s, 1H, -CHO). ^{13}C NMR ($CDCl_3$, δ) 57.36, 109.94, 123.22, 152.13, 160.85, 177.76. MS (CI, NH_3/CH_4) 155 (6.4), 144 (4.6), 128 (6.4), 127 (100,MH^+), 126 (7.7), 125 (3.1), 109 (37), 97 (3.3). IR ($CDCl_3$, cm^{-1}) 3605 (free OH), 3417 (bonded OH), 2931, 2836, 1683 (C=O), 1522, 1401, 1278, 1233, 1191, 1021.

5-*t*-Butyldimethylsiloxymethyl-2-furfuraldehyde (13)

To a solution of *t*-butyldimethylsilyl chloride (23.89 g, 0.159 mol) in 60 mL of *N,N*-dimethylformamide was added imidazole (16.1 g, 0.238 mol) and 5-hydroxymethyl-2-furfuraldehyde(16.65 g, 0.132 mol) and the mixture was stirred for 8 h. The reaction mixture was then diluted with pentane and washed with water. The organic layer was dried (Na_2SO_4) and filtered through a small plug of silica. Evaporation yielded 23.48 g (74%) of **13**. ^1H NMR ($CDCl_3$, δ) 0.09 (s, 6H, $(CH_3)_2CSi$), 0.90 (s, 9H, $(CH_3)_2Si$), 4.72 (s, 2H,-CH_2OTBS), 6.46 (d, 1H, J=3.5 Hz, 3 furyl), 7.20 (d, 1H, J=3.61 Hz, 4 furyl), 9.58 (s, 1H, -CHO). ^{13}C NMR ($CDCl_3$, δ) 18.29, 25.73, 58.56, 109.39, 145.05, 152.11, 161.42, 171.57, 177.52. MS (CI, CH_4/NH_3) 260 (5.3), 259 (18.2), 258 (100,MNH_4^+), 242 (6.6), 241 (31.1, MH^+), 200 (4.5), 128 (6.4), 111 (12.0). IR ($CDCl_3$, cm^{-1}) 2955, 2931, 2888, 2858, 1677, 1521, 1466, 1256, 1181, 1020. Anal. Calcd. for $C_{12}H_{20}O_3Si$: C, 59.96; H, 8.39 Found: C, 59.80; H, 8.13.

(±)-α-(*t*-Butylsulfonylmethyl)-5-(*t*-butyldimethylsiloxymethyl)-2-furanmethanol (14)

Methyl *t*-butyl sulfone (11.35 g, 0.083 mol) was treated with BuLi (36.6 mL of a 2.5M solution, 0.092 mol) in 100 mL of THF at -78°C. After 45 min, **13** (18.20 g, 0.076 mol) was added and the reaction mixture was stirred for 3h at -78°C and gradually warmed to room temperature. The reaction was quenched with saturated NH_4Cl and extracted with EtOAc. Drying (Na_2SO_4) and evaporation yielded 29.62 g (98%) of pure **14** as a crystalline white solid. ^1H NMR ($CDCl_3$, δ) 0.09 (s, 6H, $(CH_3)_2Si$), 0.90 (s,9H, $(CH_3)_3Si$), 1.43 (s, 9H, $(CH_3)_3SO_2$-), 3.29 (dd, 1H, J=1.84, 13.61 Hz, H2(a)), 3.48 (dd, 1H, J=9.95, 13.61 Hz, H3(b)), 4.62 (s, 2H, $TBSOCH_2$-), 5.50 (dd, 1H, J=1.33, 9.82 Hz, H1), 6.20 (d, 1H, J=3.18 Hz, 3 furyl), 6.30 (d, 1H, J=3.18 Hz, 4 furyl). ^{13}C NMR ($CDCl_3$, δ) 18.28, 23.13, 25.86, 50.88, 58.15, 59.91, 62.19, 108.07, 132.48, 145.07, 152.24, 154.52. MS (CI, CH_4/NH_3) 394 (10, $MNH4^+$), 376 (16, M^+), 359 (20, MH^+-H_20), 285 (25), 241 (100), 227 (20), 154 (49), 125 (30), 123 (88), 109 (29), 107 (94). IR ($CDCl_3$, cm^{-1}) 3517 (OH) 2958, 2932, 1466, 1384, 1290, 1260 (S=O), 1113, 1016. Anal. Calcd. for $C_{17}H_{32}O_4SSi$: C, 54.22; H, 8.57 Found C, 54.41; H, 8.41.

2-*t*-Butylsulfonyl-1-(5-*t*-butyldimethylsiloxymethyl-2-furyl)-ethanone (15)

To a solution of **14** (27.83 g, 0.074 mol) in CH_2Cl_2 was added freshly oven-dried MnO_2 (57.6 g, 0.66 mol) and 2 g of activated, crushed 4Å molecular sieves. After overnight stirring the mixture was filtered through Celite and the solids washed with CH_2Cl_2. Evaporation yielded 23.86 g (86%) of **15** a white solid. ^1H NMR ($CDCl_3$, δ) 0.06 (s, 6H, $(CH_3)_2Si$), 0.87 (s, 9H, $(CH_3)_3Si$), 1.43 (s, 9H, $(CH_3)_3SO_2$-), 4.35 (s, 2H, H1), 4.89 (s, 2H, $TBSOCH_2$-), 6.43 (d, 1H, J=3.6 Hz, 3 furyl), 7.34 (d, 1H, J=3.6 Hz, 4 furyl). ^{13}C NMR ($CDCl_3$, δ) 18.22, 23.46, 25.69, 55.57, 58.56, 62.19, 109.98, 122.49, 145.00, 151.28, 161.63. IR ($CDCl_3$, cm^{-1}) 2955, 2931, 2858, 1670 (C=O), 1516, 1307 (S=0), 1257, 1121, 1044. Anal. Calcd. for $C_{17}H_{30}O_4SSi$: C, 54.51; H, 8.07 Found C, 54.06; H, 8.02.

5-*t*-Butylsulfonyl-6-(5-hydroxymethyl-2-furyl)-6-oxo-2-hexenoic acid, methyl ester (16)

A sample of **15** (23.86 g, 0.0637 mol) was treated with NaH (3.36 g, 0.140 mol) and was allowed to react at room temperature for 30 min. Methyl 4-bromocrotonate (13.68 g, 0.0764 mol) was added and the mixture was brought to reflux. The reaction was monitored by TLC, and was shown to be complete after 8 h. The reaction was quenched with water and 10% HCl, and the aqueous layer was extracted with EtOAc. Evaporation of the solvent yielded crude **16** which was dissolved in EtOAc and treated with decolorizing carbon. Filtration through a plug of silica gel and evaporation yielded 19.60 g (86%) of relatively pure **16**. ^1H NMR ($CDCl_3$, δ) 1.46 (s, 9H, $(CH_3)_3CSO_2$-), 2.94 (m, 1H, H4), 3.37 (m, 1H, H3), 3.67 (s, 3H, $-CO_2CH_3$), 4.69 (s, 2H, $-CH_2OH$), 4.99 (dd, 1H, J=2.99, 11.53 Hz, H1), 5.88 (d, 1H, J=15.62 Hz, H5), 6.20 (d, 1H, J=3.66 Hz, 3 furyl), 6.74 (dt, 1H, J=7.33, 15.62 Hz, H2), 7.34 (d, 1H, J=3.47 Hz, 4 furyl). ^{13}C NMR ($CDCl_3$, δ) 23.79, 30.68, 521.64, 57.54, 63.76, 110.98, 120.68, 124.39, 142.06, 145.01, 151.61, 159.90, 166.17. MS (CI, CH_3/NH_4), 376 (100, MNH_4^+), 358 (5.5), 300 (5.9), 256 (30.3), 239 (11.1), 140 (48.8), 110 (35.5), 108 (42.6). IR ($CDCl_3$, cm^{-1}) 3155 (OH), 2963, 1734 (CO_2CH_3), 1675 (C=O), 1388, 1465, 1435, 1382, 1300 (S=O), 1255, 1178, 1122, 1026.

5-*t*-Butylsulfonyl-6-oxo-6-(5-trimethylacetoxymethyl-2-furyl)-2-hexenoic acid, methyl ester (17)

To a solution of **16** (5.10 g, 0.0142 mol) in CH_2Cl_2 was added pyridine (2.25 g, 0.0285 mol), trimethylacetyl chloride (2.06 g, 0.0171 mol) and 4-dimethylaminopyridine (0.050 g, 0.409 mmol). The mixture was allowed to react until complete by TLC. The reaction was quenched with water and extracted with EtOAc. Drying (Na_2SO_4) and evaporation yielded 4.85 g (75%) of reasonably pure **17**. Purification of a sample of **17** (1.11g) by flash chromatography (SiO_2, 1:1 EtOAc: pentane) yielded 0.92g (83% purification yield, 63% overall) of pure **17** as a white solid. ^1H NMR ($CDCl_3$, δ) 1.16 (s, 9H, $(CH_3)_3CCO_2$-), 1.43 (s, 9H, $-SO_2C(CH_3)_3$), 2.88 (m, 1H, H3), 3.34 (m,1H, H4), 4.94 (dd, 1H, J=3.3, 11.4 Hz, H5), 5.05 (dd, 1H, J=13.8, 26.1 Hz, $-CH_2OTBS$), 5.82 (d, 1H, J=15.6 Hz, H1), 6.53 (d, 1H, J=3.9 Hz, 3 furyl), 6.66 (dt, 1H, J=7.2, 15.6 Hz, H2), 7.30 (d, 1H, J=3.6Hz, 4 furyl). ^{13}C NMR ($CDCl_3$, δ) 23.37, 26.61, 30.23, 38.37, 51.18, 57.33, 63.22, 112.78, 119.84, 124.03, 141.51, 151.57, 154.73, 160.01, 165.60, 177.29, 178.31. MS (CI, CH_4/NH_3) 460 (71, $MNH4^+$), 418 (3), 358 (36), 341 (87), 340 (16), 285 (23), 221 (100), 140 (42), 122 (40), 103 (30). IR ($CDCl_3$, cm^{-1}) 2973, 2909, 2874, 1725, 1679, 1519, 1437, 1343, 1304(S=O), 1282, 1209, 1143, 1122, 1021, 983. Anal. Calcd. for $C_{22}H_{30}O_8S$: C, 56.99; H, 6.83. Found: C, 56.90; H, 6.70.

(±)-(2β,3α,3aβ,6β,7α,7aα) and (2β,3β,3aβ,6β,7α,7aα)-1,6,7,7a-Tetrahydro-7-carbomethoxy-2-*t*-butylsulfonyl-6-trimethylacetoxymethyl-3-trimethylsiloxy-[3a,6]-epoxy-[3a,H]-inden-3-carbonitrile (18, 19)

To **17** (0.141 g, 0.319 mmol) was added trimethylsilyl cyanide (1.5 mL, 1.12 g, 11.3 mmol) and a catalytic amount of zinc iodide (0.022 g). The mixture was allowed to stir overnight during which the solution turned orange. The excess TMSCN was removed *in vacuo* and the product diluted with diethyl ether and filtered through silica. Evaporation yielded 0.164 g (95%) of crude **18** and **19** as a 1.9: 1 mixture of isomers. The mixture was purified by flash chromatography (2:1 pentane: EtOAc) and pure **18** and **19** were isolated (0.105 g, 61% combined yield).

Spectral data for **18**: ^{1}H NMR ($CDCl_3$, δ) 0.22 (s, 6H, TMS), 1.17 (s, 9H, $(CH_3)_3CCO_2$-), 1.37 (s, 9H, $-SO_2C(CH_3)_3$), 1.92 (ddd, 1H, J=13.9, 4.2, 9.8 Hz, H1a), 2.74 (ddd, 1H, J=9.8, 3.4, 4.2 Hz, H7a), 2.84 (d, 1H, J=3.36 Hz, H7), 2.88 (ddd, 1H, J=13.9, 9.8, 9.8 Hz, H1b), 3.62 (s, 3H, $-OCH_3$), 4.15 (dd, 1H, J=9.8 Hz, H2), 4.47 (d, 1H, J=12.7 Hz, $-CH_2$OPIV), 4.87 (d, 1H, J=12.8 Hz, $-CH_2$OPIV), 6.28 (d, 1H, J=5.81 Hz, H5), 6.67 (d, 1H, J=5.86 Hz, H4). ^{13}C NMR ($CDCl_3$, δ) 1.49, 23.20, 27.13, 28.89, 38.90, 45.82, 52.40, 56.37, 60.80, 62.29, 65.29, 73.70, 90.91, 98.99, 116.28, 134.15, 134.46, 162.10, 170.40. MS (CI, CH_4/NH_3) 559 (100, MNH_4^+), 460 (35), 401 (10), 340 (48), 238 (8), 195 (10), 117 (32). HRMS (CI, CH_4/NH_3) 541.2183 (M^+, 3.2 ppm), 559.2510 (MNH_4^+, 0.1 ppm). IR ($CDCl_3$, cm^{-1}) 2968, 2907, 2874, 2360, 2337, 1731 (CO_2CH_3), 1479, 1458, 1438, 1367, 1298 (S=O), 1164, 1121, 1011

Spectral data for **19**: ^{1}H NMR ($CDCl_3$, δ) 0.35 (s, 6H, TMS), 1.15 (s, 9H, $(CH_3)_3CCO_2$-), 1.36 (s, 9H, $-SO_2C(CH_3)_3$), 1.87 (ddd, 1H, 2.9, 10.3, 12.7 Hz, H1a), 2.83 (ddd, 1H, J=10.9, 3.3, 3.3 Hz, H7a), 2.87 (d, 1H, J=3.36 Hz, H7), 2.91 (m, 1H, H1b), 3.62 (s, 3H, $-OCH_3$), 4.10 (dd, 1H, J=9.6 Hz, H2), 4.56 (d, 1H, J=12.69 Hz, $-CH_2$OPIV), 4.80 (d, 1H, J=12.64 Hz, $-CH_2$OPIV), 6.29 (d, 1H, J=5.86 Hz, H5), 6.55 (d, 1H, J=5.86 Hz, H4). ^{13}C NMR ($CDCl_3$, δ) 1.72, 23.43, 27.13, 31.44, 38.93, 48.53, 52.36, 55.52, 60.96, 61.86, 64.39, 73.38, 90.72, 99.87, 116.40, 132.88, 135.74, 170.85, 177.80. MS (CI, CH_4/NH_3) 559 (100, MNH_4^+), 460 (20), 401 (15), 340 (52), 230 (8), 195 (12), 117 (82). HRMS (CI, CH_4/NH_3) 542.2229 (MH^+, 2.8 ppm). IR ($CDCl_3$, cm^{-1}) 2967, 2906, 2257, 1732 (CO_2CH_3), 1479, 1438, 1367, 1298 (S=O), 1251. 1228, 1207, 1156, 1030, 1005

ACKNOWLEDGEMENTS

We would like to thank Dr. Al Crumbliss and Dr. Ned Porter for helpful discussions and the American Cancer Society for funding of this project. We would also like to thank Dr. Robert and Pat Pfeiffer for assisting in the revisions of this manuscript.

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(*Received in USA* 29 *November* 1993; *accepted* 4 *April* 1994)