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Stereoselective synthesis of 3-hydroxy-2-sulfonyltetrahydrofurans from β-(triethylsilyloxy)aldehydes and *p*-tolylsulfonyldiazomethane

Steven R. Angle* and Stephanie Z. Shaw

Department of Chemistry, University of California at Riverside, Riverside, CA 92521, USA

Dedicated to Professor Barry M. Trost, an outstanding researcher, teacher, and mentor, on the occasion of his 60th birthday

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Abstract—A new method for the stereoselective syntheses of 2-sulfonyltetrahydrofurans from β-(triethylsilyloxy)aldehydes and *p*-tolylsulfonyldiazomethane in the presence of $BF_3{\cdot}OEt_2$ as Lewis acid is reported. The versatility of the sulfonyl functional group allows further functionalization alpha to the sulfonyl group. For example, treatment of 2-sulfonlytetrahydrofuran **2b** with $BF_3{\cdot}OEt_2$ and allyl silane afforded alkylative desulfonylation product in 85% yield.

1. Introduction

Many biologically active natural products contain highly substituted tetrahydrofuran (THF) subunits.[1–7] *C*-glycosides represent an important sub set of these five-membered oxygen heterocycles. The ready availability of highly substituted furanoses have made these carbohydrates logical starting materials for the preparation of *C*-glycosides. Indeed, the introduction of alkyl and aryl substituents at the anomeric position of cyclic acetals has been a strategically important synthetic route to *C*-glycosides.[8] In spite of the available methods, there is still a need to develop new general, versatile and selective routes to these compounds.

The sulfone is a versatile functional group that allows the formation of carbon–carbon bonds at the sulfonyl containing carbon by formation of either an anionic or a cationic intermediate depending upon the reaction conditions. Thus, an efficient synthesis of sulfonyl glycosides should provide versatile intermediates that could be used to prepare more complex THF containing natural products, including *C*-glycosides. For example, deprotonation of a 2-sulfonyltetrahydrofuran would afford an anion that could be alkylated[9–11] or acylated[12,13] to introduce a wide variety of substituents. Alternatively, alkylative desulfonylation[13–16] could be achieved by treatment of the 2-sulfonyltetrahydrofuran with a Lewis acid to afford an oxonium ion intermediate which can be trapped with an appropriate nucleophile, such as an allyl silane.

We have recently reported the stereoselective synthesis of THFs from β-(triethylsilyloxy)aldehydes with benzyldiazoacetate[17] and aryldiazomethanes.[18] The formation of THFs via our methodology is in direct competition with the well known[19] homologation of aldehydes to ketones with various diazo compounds. We have found that the formation of ketone byproducts can be suppressed and the yield of THFs enhanced by the careful choice of aldehyde, reaction temperature and Lewis acid. We report herein the extension of this methodology to the stereoselective synthesis of 2-(arylsulfonyl)tetrahydrofurans from acyclic precursors.

2. Results and discussion

Reaction of β-(triethylsilyloxy)aldehydes with *p*-tolylsulfonyldiazomethane[20] was studied under a variety of conditions to maximize the formation of 2-sulfonyltetrahydrofurans. The experimental conditions (temperature, reaction time, and Lewis acid) were optimized using aldehyde **1a** and *p*-tolylsulfonyldiazomethane (1.1 equiv.) as shown in Table 1. As seen in entry 1, $SnCl_4$ gave mainly β-ketosulfone. $ZrCl_4$ (entries 2 and 3) and $BF_3{\cdot}OEt_2$ (entries 4–7) afforded THF **2a** in comparable yields. Reactions mediated by $ZrCl_4$ afforded better THF/ketone ratios; however $BF_3{\cdot}OEt_2$ mediated reactions required shorter time, contained fewer byproducts, and were easier to purify. The optimized reaction conditions employed 1 equiv. of $BF_3{\cdot}OEt_2$ at −78°C for two hours and afforded THF **2a** in 35% yield (entry 5).

In an effort to investigate the scope and limitations of this methodology, various α-substituted β-(triethylsilyloxy)-

Keywords: stereoselection; tetrahydrofurans; diazo compounds; sulfone.

* Corresponding author. Tel.: +1-909-787-3548; fax: +1-909-787-4713; e-mail: steven.angle@ucr.edu

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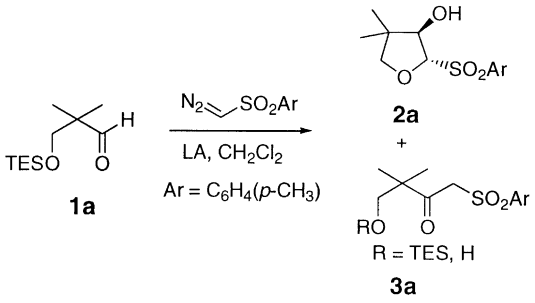
Table 1. Survey of Lewis acids and conditions



Entry	Lewis acid (equiv.)	Time (h)	Temperature (°C)	**2a** (%)	**3a** (%)
1	$SnCl_4$ (0.2)	2	−78	2	85
2	$ZrCl_4$ (0.2)[a]	27	−78	34	16
3	$ZrCl_4$ (1.0)[a]	7	−78	30	12
4	$BF_3{\cdot}OEt_2$ (0.2)	2	−78	29	40
5	$BF_3{\cdot}OEt_2$ (1.0)	2	−78	35	54
6	$BF_3{\cdot}OEt_2$ (2.0)	0.5	−78	35	49
7	$BF_3{\cdot}OEt_2$ (1.0)	0.5	0	17	42

[a] Reaction was carried out in toluene, all other reactions were ran in dicholormethane.

aldehydes (**1a**–**1g**) were studied (Table 2). The yield of 4,4-disubstituted and 4-monosubstituted THFs seem to correlate to the steric bulk alpha to the aldehyde. As the size of the α-substituent increased, the yield of THF also increased relative to the β-ketosulfone. The reaction of nonsubstituted aldehyde **1c** with *p*-tolylsulfonyldiazomethane in the presence of $BF_3{\cdot}OEt_2$ afforded THF **2c** in 32% and β-ketosulfone **3c** in 29% yield. The more sterically hindered α,α-diethylaldehyde **1b** afforded THF **2b** in 65% yield and β-ketosulfone **3b** in 21% yield. In the case of α-monosubstituted aldehydes **1d**–**1g**, the yield of THFs **2d**–**2g** increased as the size of the α-substituent increased from methyl to *t*-butyl and the yield of β-ketosulfones **3d**–**3g** decreased (Table 2).

Our previous work with benzyldiazoacetate and aryldiazomethane showed an increase in diastereoselectivity of THF products as the steric bulk of α-substituents of the aldehydes increased from methyl to *t*-butyl.[17,18] It is remarkable that when the diazo compound was changed to an arylsulfonyldiazomethane, only one THF diastereomer was observed in every reaction. The stereochemistry of the THF products is consistent with that seen for the major THF diastereomers in the reaction of benzyldiazoacetate and aryldiazomethane with these same substrates.[17,18]

The stereochemical assignments of THFs **2a** and **2f** were determined by single crystal X-ray structures. All other THFs were assigned by comparison of the H–H coupling constants to these two compounds. In the case of the 2,3,4-trisubstituted THFs, the 4-alkyl substituent was in a *cis*-orientation relative to the hydroxy group and in a *trans*-orientation relative to the sulfone. The 4,4-disubstituted THFs also possess the same *trans* relationship between the alcohol and the sulfone substituents.

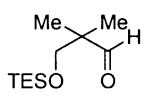
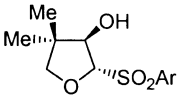
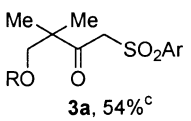
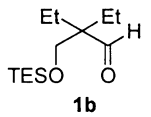
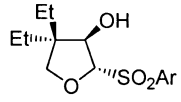
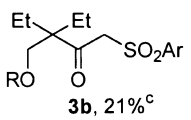
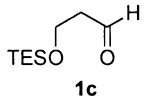
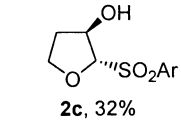
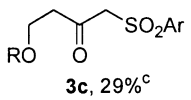
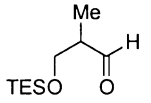
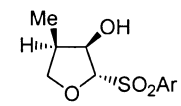
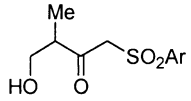
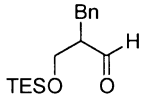
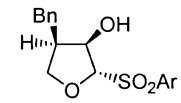
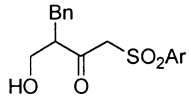
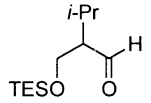
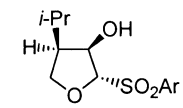
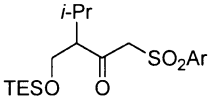
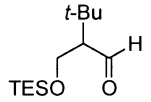
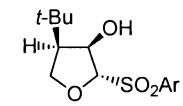
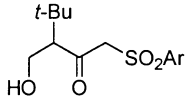
In an effort to further optimize the yield of THF, various para-substituted arylsulfonyldiazomethanes were studied (Table 3). Both *p*-chlorophenylsulfonyldiazomethane **4b** and *p*-methoxyphenylsulfonyldiazomethane **4c** were prepared under similar conditions to the preparation of *p*-tolylsulfonyldiazomethane.[20] Arylsulfonyldiazomethane **4b** afforded THF **2h** in 46% and β-ketosulfone **3h** in 35% while **4c** provided THF **2i** in 52% yield and β-ketosulfone **3i** in 28% yield (Table 3). To summarize the results, varying the para-substituents on arylsulfonyldiazomethane did not seem to have a significant effect on the yield of THFs.

To illustrate the synthetic utility of the 2-sulfonyltetrahydrofurans, 4,4-diethyl-3-hydroxy-2-sulfonyltetrahydrofuran **2b** was treated with trimethyl allylsilane (4 equiv.) and $BF_3{\cdot}OEt_2$ (2 equiv.) to afford 2-allyltetrahydrofuran **5** in 85% yield as a single diastereomer (Scheme 1).[21] To assign the stereochemistry of **5**, *p*-nitrobenzoate **6** (Scheme 2) was prepared and the relative stereochemistry was tentatively assigned to be *trans* between the ester and the allyl groups by the NOESY experiment summarized in Fig. 1. It is interesting to note that the addition of the allyl group at the 2-position of the THF retained the relative stereochemistry of the sulfonyl group.

3. Conclusion

In summary, we have shown a one-step method for the stereoselective synthesis of 4-alkyl-3-hydroxy-2-sulfonyltetrahydrofurans from β-(triethylsilyloxy)aldehydes and *p*-tolylsulfonyldiazomethane in the presence of $BF_3{\cdot}OEt_2$. The alkylative desulfonylation of 4,4-diethyl-3-hydroxy-2-sulfonyltetrahydrofuran with retention of configuration also demonstrates the versatility of the sulfone as a building block for formation of THF derivatives. Further functionalization of the THF products and application of this methodology natural product synthesis is currently under investigation.

Table 2. Synthesis of THFs from aldehydes and *p*-tolylsulfonyldiazomethane[a]

Entry	Aldehyde	THF[b]	β-Ketosulfone
1	 **1a**	 **2a**, 35%	 **3a**, 54%[c] R = TES, H
2	 **1b**	 **2b**, 65%	 **3b**, 21%[c] R = TES, H
3	 **1c**	 **2c**, 32%	 **3c**, 29%[c] R = TES, H
4	 **1d**	 **2d**, 34%	 **3d**, 17%
5	 **1e**	 **2e**, 48%	 **3e**, 18%
6	 **1f**	 **2f**, 70%	 **3f**, <2%[d]
7	 **1g**	 **2g**, 74%	 **3g**, --

[a] *Reaction conditions:* 1 equiv. of aldehyde and $BF_3{\cdot}OEt_2$ and 1.1 equiv. of arylsulfonyldiazomethane for 2 h at −78°C.
[b] Ar=C_5H_4(*p*-CH_3).
[c] Combined yields of both silated and desilated ketones.
[d] Characterized by ^{1}H NMR only.

4. Experimental

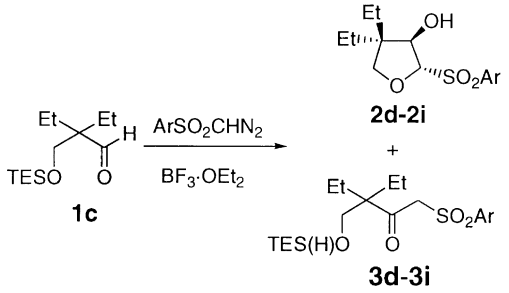
4.1. General procedure for the reaction of arylsulfonyldiazomethane with aldehydes 1

Freshly distilled $BF_3{\cdot}OEt_2$ (1.0 equiv.) was added dropwise over 30 min to a solution of aldehyde (1.0 equiv.) and arylsulfonyldiazomethane (1.1 equiv.) and CH_2Cl_2 (0.2 M) at −78°C. After stirring for 2 h, the reaction mixture was poured into a stirred solution of saturated aqueous $NaHCO_3$. The aqueous layer was extracted with CH_2Cl_2 (3×20 mL) and the combined organic extracts were dried ($MgSO_4$) and concentrated to afford crude product. Flash chromatography (hexanes/ethyl acetate) afforded THFs and the ketones in the yields indicated in Table 2.

4.1.1. (2*R**,3*S**)-4,4-Dimethyl-3-hydroxy-2-[(4-methylphenyl)-sulfonyl]tetrahydrofuran (2a) and 3,3-dimethyl-4-hydroxy-1-[(4-methylphenyl)sulfonyl]-2-butanone (3a).

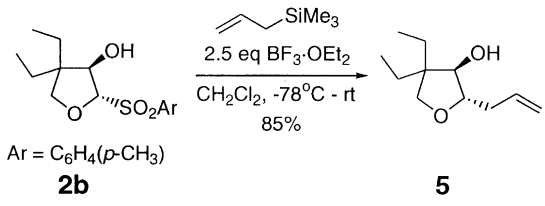
Aldehyde **1a** (111 mg, 0.51 mmol) afforded THF **2a** (48.3 mg, 35%) as a white solid (mp 120–121°C) and β-ketosulfone **3a** (triethylsilyl ether=87.9 mg, alcohol=10.8 mg, combined yield of 54%) as a white solid (mp 73.0–74.0°C). THF **2a**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.83 (d, *J*=8.2 Hz, 2H), 7.37 (d, *J*=8.1 Hz, 2H), 4.63 (d, *J*=6.6 Hz, 1H), 4.59 (br dd, *J*=2.9, 6.5 Hz, 1H),

Table 3. Reaction of aldehyde **1c** with arylsulfonyldiazomethanes

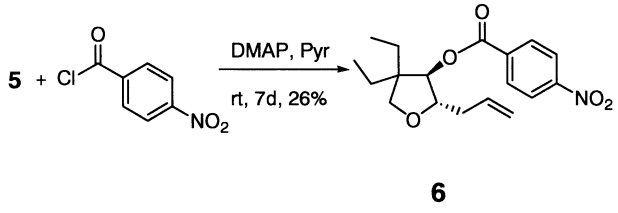


Entry	Ar	THF	β-Ketosulfone
1	**4a** C_6H_4(p-CH_3)	**2c** (65%)	**3c** (21%)[a]
2	**4b** C_6H_4(p-Cl)	**2h** (46%)	**3h** (35%)
3	**4c** C_6H_4(p-OCH_3)	**2i** (52%)	**3i** (28%)

[a] Combined yields of both silated and desilated ketones.



Scheme 1.



Scheme 2.

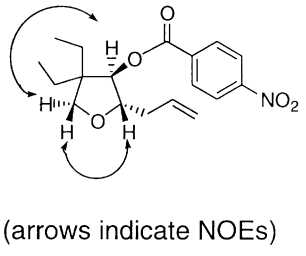


Figure. 1. NOE enhancements in NOESY experiments.

3.74 (ABq, J=8.5 Hz, $\Delta\nu$=27.8 Hz, 2H), 2.98 (br d, J=3.3 Hz, 1H), 2.44 (s, 3H), 1.10 (s, 3H), 1.05 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 145.2, 133.9, 129.8, 129.0, 97.4, 80.7, 77.4, 42.6, 21.7, 19.2; IR ($CDCl_3$) 3593, 3585, 3057, 1598,, 1313, 1107 cm^{-1}; MS (CI, NH_3) m/z 288 (58, MNH_4^+), 253 (85), 139 (42), 115 (100), 97 (32); HRMS calcd for $C_{13}H_{22}NO_4S$ (MNH_4^+) 288.1270, found 288.1276. β-ketosulfone **3a** (alcohol): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.79 (d, J=8.3 Hz, 2H), 7.35 (d, J=8.1 Hz, 2H), 4.36 (s, 2H), 3.59 (s, 2H), 2.44 (s, 3H), 1.10 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 203.4, 145.2, 136.3, 129.7, 128.5, 68.8, 61.7, 50.8, 21.7, 20.6; IR ($CDCl_3$) 3615, 3585, 3058, 2974, 1715, 1598, 1471, 1324, 1031 cm^{-1}; MS (CI, NH_3) m/z 288 (29, MNH_4^+), 189 (20), 134 (61), 124 (18), 117 (100), 91 (32); HRMS calcd for $C_{13}H_{22}NO_4S$ (MNH_4^+) 288.1270, found 288.1264.

4.1.2. (2*R,3*S**)-4,4-Diethyl-3-hydroxy-2-[(4-methylphenyl)sulfonyl]tetrahydrofuran (2b) and 3,3-diethyl-4-triethylsilyloxy-1-[(4-methylphenyl)sulfonyl]-2-butanone (3b).** Aldehyde **1b** (137 mg, 0.56 mmol) afforded THF **2b** (109 mg, 65%) as a white solid (mp 89–91°C) and β-ketosulfone **3b** (triethylsilyl ether=31.6 mg, alcohol=13.0 mg, combined yield of 21%) as a white solid (mp 28.5–30.5°C). THF **2b**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.82 (d, J=8.2 Hz, 2H), 7.36 (d, J=8.2 Hz, 2H), 4.76 (d, J=6.2 Hz, 1H), 4.63 (d, J=6.2 Hz, 1H), 3.77 (ABq, J=9.2 Hz, $\Delta\nu$=50.1 Hz, 2H), 2.58 (br s, 1H), 2.45 (s, 3H), 1.67 (m, 1H), 1.46 (m, 3H), 0.95 (t, J=7.7 Hz, 3H), 0.88 (t, J=7.7 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 145.1, 133.8, 129.7, 129.0, 98.6, 48.6, 26.3, 21.8, 20.9, 8.8, 8.3; IR ($CDCl_3$) 2970, 1652, 1302, 1148, 1071 cm^{-1}; MS (CI, NH_3) m/z 316 (31, MNH_4^+), 281 (18), 160 (35), 143 (100), 139 (75), 128 (38); HRMS calcd for $C_{15}H_{26}NO_4S$ (MNH_4^+) 316.1583, found 316.1585. β-ketosulfone **3b** (triethylsilyl ether): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.82 (d, J=8.2 Hz, 2H), 7.32 (d, J=8.2 Hz, 2H), 4.34 (s, 2H), 3.52 (s, 2H), 2.40 (s, 3H), 1.61(dt, J=7.7, 14.9 Hz, 2H), 1.44 (dt, J=7.7, 14.9 Hz, 2H), 0.86 (t, J=8.2 Hz, 9H), 0.67 (t, J=7.2 Hz, 6H), 0.50 (q, J=7.7 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 202.7, 144.5, 136.7, 129.3, 128.5, 63.6, 62.3, 57.2, 22.7, 21.6, 7.70, 6.70, 4.10; IR ($CDCl_3$) 2959, 2877, 1713, 1597, 1414, 1321, 1091, 909 cm^{-1}; MS (EI) m/z 413 (5, MH^+), 383 (94), 241 (100), 227 (83), 177 (46), 91 (25); HRMS calcd for $C_{21}H_{37}O_4SiS$ (MH^+) 413.2182, found 413.2194.

4.1.3. (2*R,3*S**)-3-Hydroxy-2-[(4-methylphenyl)-sulfonyl]-tetrahydrofuran (2c) and 4-hydroxy-1-[(4-methylphenyl)-sulfonyl]-2-butanone (3c).** Aldehyde **1c** (121 mg, 0.64 mmol) afforded THF **2c** (49.8 mg, 32%) as a white solid (mp 97–98°C) and β-ketosulfone **3c** (triethylsilyl ether=56.8 mg, alcohol=6.6 mg, combined yield of 29%) as a white solid (mp 45.0–48.5°C). THF **2c**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.78 (d, J=8.2 Hz, 2H), 7.36 (d, J=8.2 Hz, 2H), 5.13–5.01 (m, 1H), 4.75 (d, J=2.1 Hz, 1H), 4.22–4.11 (m, 2H), 3.02 (d, J=4.6 Hz, 1H), 2.45 (s, 3H), 2.41–2.32 (m, 1H), 2.08–1.99 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 141.1, 133.4, 129.7, 129.0, 99.9, 72.1, 70.3, 34.5, 21.7; IR ($CDCl_3$) 3607, 2901, 2256, 1314, 1149 cm^{-1}; MS (CI, NH_3) m/z 260 (53, MNH_4^+), 225 (23), 139 (37), 104 (28), 87 (100); HRMS calcd for $C_{11}H_{18}NO_4S$ (MNH_4^+) 260.0957, found 260.0949. β-ketosulfone **3c** (alcohol): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.76 (d, J=8.2 Hz, 2H), 7.37 (d, J=8.2 Hz, 2H), 4.19 (s, 2H), 3.86 (t, J=5.6 Hz, 2H), 2.96 (t, J=5.6 Hz, 2H), 2.46 (s, 3H), 2.21 (br s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.5, 145.5, 135.5, 129.9, 128.2, 67.5, 57.4, 46.5, 21.8; IR ($CDCl_3$) 3608, 3019, 2931, 1716, 1597, 1396, 1216, 1063, 709 cm^{-1}; MS (EI) m/z 242 (3, M^+), 170 (68), 155 (85), 105 (45), 91 (100), 87 (51); HRMS calcd for $C_{11}H_{14}O_4S$ (M^+) 242.0613, found 242.0621.

4.1.4. (2*R,3*S**,4*S**)-3-Hydroxy-4-methyl-2-[(4-methylphenyl)sulfonyl]-tetrahydrofuran (2d) and 4-hydroxy-3-methyl-1-[(4-methylphenyl)sulfonyl]-2-butanone (3d).** Aldehyde **1d** (161 mg, 0.80 mmol) afforded THF **2d** (71.0 mg, 34%) as a white solid (mp 95–96°C) and β-ketosulfone **3d** (triethylsilyl ether, 50.8 mg, 17%) as a clear oil; THF **2d**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.79 (d, J=8.7 Hz, 2H), 7.36 (d, J=7.7 Hz, 2H), 4.89 (br s, 1H), 4.76 (d, J=2.6 Hz, 1H), 4.20 (dd, J=7.2, 8.2 Hz, 1H), 3.71 (apparent t, J=7.7 Hz, 1H), 2.80 (br d, J=4.1 Hz, 1H), 2.61–2.52 (m,1H), 2.44 (s, 3H), 1.07 (d, J=7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 145.1, 133.6, 129.7, 129.0, 99.8, 75.9, 73.4, 38.1, 21.8, 9.8; IR ($CDCl_3$) 3615, 2929, 2254, 1303, 1140, 1057 cm^{-1}; MS (CI, NH_3) m/z 274 (95, MNH_4^+), 239 (69), 174 (25), 139 (55), 118 (48), 101 (100); HRMS calcd for $C_{12}H_{20}NO_4S$ (MNH_4^+) 274.1113, found 274.1101. β-ketosulfone **3d** (alcohol): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.77 (d, J=8.7 Hz, 2H), 7.36 (d, J=8.2 Hz, 2H), 4.31 (s, 2H), 3.8–3.66 (m, 2H), 3.16–3.05 (m, 1H), 2.45 (s, 3H), 1.09 (d, J=7.2 Hz 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 201.8, 145.3, 135.8, 129.8, 128.2, 66.1, 64.3, 49.4, 21.8, 12.4; IR ($CDCl_3$) 3626, 2937, 2881, 2257, 1715, 1597, 1397, 1324, 1032 cm^{-1}; MS (EI) m/z 257 (24, MH^+), 239 (63), 155 (85), 105 (43), 91 (100), 65 (61); HRMS calcd for $C_{12}H_{17}O_4S$ (M^+) 257.0848, found 257.0844.

4.1.5. (2*R,3*S**,4*S**)-3-Hydroxy-4-(phenylmethyl)-2-[(4-methylphenyl)-sulfonyl]tetrahydrofuran (2e) and 4-hydroxy-3-(phenylmethyl)-1-[(4-methylphenyl)sulfonyl]-2-butanone (3e).** Aldehyde **1e** (167 mg, 0.60 mmol) afforded THF **2e** (95.7 mg, 48%) as a clear oil and β-ketosulfone **3e** (alcohol, 47.7 mg, 18%) as a clear oil. THF **2e**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.78 (d, J=8.2 Hz, 2H), 7.35 (d, J=8.2 Hz, 2H), 7.32–7.18 (m, 5H), 4.93 (br t, J=3.6 Hz,1H), 4.85 (d, J=2.1 Hz, 1H), 4.13 (apparent t, J=8.2 Hz, 1H), 3.86 (apparent t, J=8.2 Hz, 1H), 3.23 (br d, J=5.1 Hz, 1H), 3.00 (dd, J=6.7, 13.3 Hz, 1H), 2.84–2.70 (m,1H), 2.65 (dd, J=8.7, 13.3 Hz, 1H), 2.45 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 145.1, 139.5, 133.4, 129.7, 129.0, 128.51, 128.46, 126.2, 100.3, 74.1, 72.5, 45.3, 31.1, 21.7; IR ($CDCl_3$) 3609, 2360, 2255, 1314, 1149 cm^{-1}; MS (CI, NH_3) m/z 350 (81, MNH_4^+), 194 (43), 182 (100), 174 (46), 159 (40), 139 (68); HRMS calcd for $C_{18}H_{24}NO_4S$ (MNH_4^+) 350.1426, found 350.1426. β-ketosulfone **3e** (alcohol): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.65 (d, J=8.2 Hz, 2H), 7.32 (d, J=8.2 Hz, 2H), 7.28–7.13 (m, 5H), 4.10 (ABq, J=13.9 Hz, $\Delta\nu$=27.5 Hz, 2H), 3.85–3.70 (m, 2H), 3.42–3.34 (m, 1H), 2.83 (ddd, J=7.7, 13.9, 21.5 Hz, 3H), 2.45 (s, 3H), 2.25 (br t, J=5.6 Hz 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 201.4, 145.3, 137.9, 135.6, 129.8, 128.9, 128.6, 128.2, 126.6, 67.1, 62.5, 56.6, 33.9, 21.8; IR ($CDCl_3$) 3621, 2928, 2257, 1715, 1598, 1323, 1085 cm^{-1}; MS (CI, NH_3) m/z 350 (100, MNH_4^+), 332 (22), 320 (55),

159 (13), 146 (27), 91 (13); HRMS calcd for $C_{18}H_{24}NO_4S$ (MNH_4^+) 350.1426, found 350.1421.

4.1.6. (2*R,3*S**,4*S**)-3-Hydroxy-4-(methyl)ethyl-2-[(4-methylphenyl)-sulfonyl]tetrahydrofuran (2f).** Aldehyde **1f** (114 mg, 0.50 mmol) afforded THF **2f** (98.9 mg, 70%) as a white solid (mp 112–113°C). THF **2f**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.75 (d, J=8.2 Hz, 2H), 7.33 (d, J=7.7 Hz, 2H), 4.90 (t, J=5.1 Hz, 1H), 4.84 (s, 1H), 4.24 (t, J=7.7 Hz, 1H), 3.81 (dd, J=7.7, 11.3 Hz, 1H), 3.11 (br d, J=4.6 Hz, 1H), 2.43 (s, 3H), 2.24–2.10 (m, 1H), 1.92–1.80 (m, 1H), 1.03 (d, J=6.7 Hz, 3H), 0.86 (d, J=6.7 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 145.6, 134.0, 129.6, 129.0, 102.0, 74.9, 72.7, 51.9, 25.9, 22.3, 22.2; IR ($CDCl_3$) 3615, 2964, 2882, 2263, 1315, 1148 cm^{-1}; MS (CI, NH_3) m/z 302 (96, MNH_4^+), 174 (57), 156 (24), 146 (100), 139 (56), 129 (30); HRMS calcd for $C_{14}H_{24}NO_4S$ (MNH_4^+) 302.1426, found 302.1413.

4.1.7. (2*R,3*S**,4*S**)-3-Hydroxy-4-(dimethyl)ethyl-2-[(4-methylphenyl)-sulfonyl]tetrahydrofuran (2g).** Aldehyde **1g** (161 mg, 0.66 mmol) afforded THF **2g** (144 mg, 74%) as a white solid (mp 103–104°C). THF **2g**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.78 (d, J=8.2 Hz, 2H), 7.35 (d, J=7.7 Hz, 2H), 4.97 (t, J=5.1 Hz, 1H), 4.80 (s, 1H), 4.19 (t, J=7.7 Hz, 1H), 4.05 (dd, J=7.7, 11.8 Hz, 1H), 2.94 (d, J=5.1 Hz, 1H), 2.43 (s, 3H), 2.20 (ddd, J=5.1, 8.2, 11.8 Hz 1H), 1.04 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 145.0, 133.5, 129.7, 129.6, 129.0, 128.9, 101.8, 73.4, 71.4, 53.0, 31.0, 29.4, 21.7; IR ($CDCl_3$) 3608, 2960, 2906, 2257, 1367, 1312, 1148, 1098 cm^{-1}; MS (CI, NH_3) m/z 316 (21, MNH_4^+), 174 (44), 143 (54), 139 (100), 85 (68), 57 (55); HRMS calcd for $C_{15}H_{26}NO_4S$ (MNH_4^+) 316.1583, found 316.1569.

4.1.8. (2*R,3*S**)-4,4-Diethyl-3-hydroxy-2-[(4-chlorophenyl)-sulfonyl]tetrahydrofuran (2h) and 3,3-diethyl-4-triethylsilyloxy-1-[(4-chlorophenyl)-sulfonyl]-2-butanone (3h).** Aldehyde **1b** (165 mg, 0.68 mmol) afforded THF**2h** (98.9 mg, 46%) as a white solid (mp 102.5–103.5°C) and β-ketosulfone **3h** (triethylsilyl ether=75 mg, alcohol=21 mg, combined yield of 35%) as a white solid (mp 28.5–30.5°C). THF **2h**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.88 (d, J=8.2 Hz, 2H), 7.54 (d, J=8.7 Hz, 2H), 4.78 (d, J=5.6 Hz, 1H), 4.64 (d, J=5.6 Hz, 1H), 3.80 (ABq, J=9.2 Hz, $\Delta\nu$=45.7 Hz, 2H), 2.73 (br s, 1H), 1.74–1.35 (m, 4H), 0.95 (t, J=7.7 Hz 3H), 0.88 (t, J=7.7 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 140.9, 135.4, 130.4, 129.4, 98.7, 77.3, 77.1, 48.7, 26.3, 21.0, 8.8, 8.3; IR ($CDCl_3$) 3599, 2970, 2882, 2260, 1582, 1476, 1314, 1080 cm^{-1}; MS (CI) m/z 319 (9, MH^+), 301 (43), 177 (48), 143 (99), 125 (80), 97 (58), 55 (100); HRMS calcd for $C_{14}H_{20}O_4SCl$ (MH^+) 319.0771, found 319.0762. β-ketosulfone **3h** (triethylsilyl ether): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.91 (d, J=8.7 Hz, 2H), 7.52 (d, J=8.7 Hz, 2H), 4.39 (s, 2H), 3.54 (s, 2H), 1.69–1.54 (m, 2H), 1.53–1.41 (m, 2H), 0.89 (t, J=8.2 Hz, 9H), 0.72 (t, J=7.2 Hz, 6H), 0.54 (q, J=7.7 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 202.8, 140.4, 138.1, 130.3, 129.1, 63.9, 62.6, 57.4, 22.7, 7.80, 6.70, 4.20; IR ($CDCl_3$) 2959, 2877, 1711, 1583, 1395, 1326, 1092, 1014 cm^{-1}; MS (EI) m/z 433 (28, MH^+), 403 (92), 261 (100), 227 (98), 111 (64); HRMS calcd for $C_{20}H_{34}O_4SiSCl$ (MH^+) 433.1636, found 433.1648.

4.1.9. (2*R,3*S**)-4,4-Diethyl-3-hydroxy-2-[(4-methoxyphenyl)sulfonyl]tetrahydrofuran (2i) and 3,3-diethyl-4-hydroxy-1-[(4-methoxyphenyl)sulfonyl]-2-butanone (3i).** Aldehyde **1b** (150 mg, 0.61 mmol) afforded THF**2i** (99.4 mg, 52%) as a white solid (mp 95–96.5°C) and β-ketosulfone **3i** (triethylsilyl ether=40 mg, alcohol=52 mg, combined yield of 28%) as a white solid (mp 45.0–47.0°C). THF 2i: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.86 (d, J=8.7 Hz, 2H), 7.01 (d, J=8.7 Hz, 2H), 4.73 (d, J=6.2 Hz, 1H), 4.63 (d, J=6.2 Hz, 1H), 3.86 (s, 3H), 3.75 (ABq, J=8.7 Hz, $\Delta\nu$=30.66 Hz, 2H), 3.05 (bs, 1H), 1.72–1.32 (m, 4H), 0.92 (t, J=7.7 Hz 3H), 0.86 (t, J=7.7 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 145.1, 133.8, 129.8, 129.7, 129.0, 128.9, 98.6, 48.6, 26.3, 21.8, 20.9, 8.8, 8.3; IR ($CDCl_3$) 3597, 2970, 2882, 2256, 1595, 1497, 1297, 1073 cm^{-1}; MS (EI) m/z 314 (4, M^+), 172 (68), 143 (100), 125 (42), 71 (65), 55 (81); HRMS calcd for $C_{15}H_{22}O_5S$ (M^+) 316.1583, found 316.1585. β-ketosulfone 3I (alcohol): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.85 (d, J=8.7 Hz, 2H), 7.00 (d, J=9.2 Hz, 2H), 4.34 (s, 2H), 3.86 (s, 3H), 3.68 (s, 2H), 3.05 (bs, 1H), 1.56(q, J=7.7 Hz, 4H), 0.73 (t, J=7.7 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 203.3, 163.8, 130.8, 130.7, 114.2, 63.4, 61.9, 57.9, 55.7, 22.8, 7.90; IR ($CDCl_3$) 3524, 2971, 2842, 2257, 1708, 1596, 1323, 1262, 1028, 921 cm^{-1}; MS (CI, NH_3) m/z 332 (57, MNH_4^+), 315 (4, MH^+), 302 (74), 285 (100), 266 (57), 171 (46), 155 (84), 95 (20); HRMS calcd for $C_{15}H_{26}NO_5S$ (MNH_4^+) 332.1532, found 332.1523.

4.1.10. (2*R,3*S**)-2-Allyl-4,4-diethyl-3-hydroxytetrahydrofuran (5).** Freshly distilled $BF_3{\cdot}OEt_2$ (0.31 mL, 2.46 mmol) was added to a solution of **2b** (29.4 mg, 0.99 mmol), trimethyl allylsilane (0.63 mL, 3.94 mmol) and CH_2Cl_2 (0.2 M) at −78°C. The solution was allowed to warm to room temperature and stirred for 2 d. The reaction mixture was then poured into a stirred solution of saturated aqueous $NaHCO_3$. The aqueous layer was extracted with CH_2Cl_2 (3×20 mL) and the combined organic extracts were dried ($MgSO_4$) and concentrated to afford crude product. Flash chromatography (hexanes/ethyl acetate) afforded **5** (155 mg, 85%) as a clear oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.93–5.79 (m, 1H), 3.64–3.53 (m, 3H), 3.64–3.53 (m, 3H), 2.44–2.35 (m, 2H), 1.73 (d, J=4.1 Hz, 1H), 1.60–1.27 (m, 4H), 0.86 (t, J=7.2 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 134.5, 117.2, 84.8, 81.6, 76.2, 47.9, 38.5, 27.2, 21.4, 8.5, 8.4; IR ($CDCl_3$) 3620, 3457, 2969, 2880, 2248, 1641, 1458 cm^{-1}; MS (EI) m/z 185 (5, MH^+), 183 (5, $(M-H)^+$), 167 (17), 143 (100), 125 (22), 85 (25); HRMS calcd for $C_{11}H_{21}NO_2$ (MH^+) 185.1542, found 185.1540.

4.1.11. (2*R,3*S**)-2-Allyl-4,4-diethyl-3-[4-nitrobenzoate]-tetrahydrofuran (6).** A solution of **5** (10.3 mg, 0.56 mmol), *p*-nitrobenzoyl chloride (12.4 mg, 0.67 mmol), DMAP (14.0 mg, 0.11 mmol), pyridine (0.10 mL, 1.23 mmol) in CH_2Cl_2 (0.1 M) was stirred at room temperature for 7 d. The reaction mixture was diluted with ether and washed with saturated aqueous $NaHCO_3$, 1N HCl and water. The organic extract was dried over $MgSO_4$ and concentrated. Flash chromatography (hexanes/ethyl acetate) afforded **6** (47.7 mg, 26%) as a white solid; mp 62–63°C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.31 (d, J=8.7 Hz, 2H), 8.20 (d, J=9.2 Hz, 2H), 5.92–5.78 (m, 1H), 5.16 (bdd, J=27.7, 1.02 Hz, 1H), 5.11 (bdd, J=21.0, 1.03 Hz 1H), 3.93–3.87 (m, 1H), 3.73 (ABq, J=9.2 Hz, $\Delta\nu$=42.4 Hz, 2H), 2.64–

2.42 (m, 2H), 1.64–1.47 (m, 4H), 0.93 (t, J=7.2 Hz, 3H), 0.84 (t, J=7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.8, 150.6, 135.3, 133.8, 130.6, 123.6, 117.6, 84.2, 82.9, 49.2, 38.3, 26.5, 22.0, 8.6, 8.2; IR ($CDCl_3$) 2971, 1723, 1530, 1349, 1275 cm^{-1}; MS (CI, NH_3) *m/z* 334 (11, MH^+), 304 (100), 292 (33), 174 (22), 167 (13), 52 (31); HRMS calcd for $C_{18}H_{24}NO_5$ (MH^+) 334.1654 found 334.1651.

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References

1. Diflorio, R.; Rizzacasa, M. A. *J. Org. Chem.* **1998**, *63*, 8595–8598 and references cited therein.
2. Jiang, Z.; Chen, R.; Chen, Y.; Yu, D. *J. Nat. Prod.* **1998**, *61*, 86–88.
3. Bermejo, A.; Tormo, J. R.; Cabedo, N.; Estornell, E.; Figadere, B.; Cortes, D. *J. Med. Chem.* **1998**, *41*, 5158–5166.
4. Boivin, T. L. B. *Tetrahedron* **1987**, *43*, 3309–3362.
5. Yu, P.; Yang, Y.; Zhang, Z. Y.; Mak, T. C. W.; Wong, H. N. C. *J. Org. Chem.* **1997**, *62*, 6359–6366.
6. Evans, D. A.; Ratz, A. M.; Huft, B. E.; Sheppard, G. S. *J. Am. Chem. Soc.* **1995**, *117*, 3448–3467.
7. Holler, U.; Konig, G. M.; Wright, A. D. *J. Nat. Prod.* **1999**, *62*, 114–118.
8. For recent examples and leading references: (a) Brown, D. X.; Bruno, M.; Ley, S. V. *Heterocycles (Special Issue)* **1989**, *28* (2), 773 and references cited therein. (b) Postema, M. H. D. *C-Glycoside Synthesis*, CRC: Boca Raton, 1995. (c) Postema, M. H. D. *Tetrahedron* **1992**, *48*, 8545–8599. (d) Du, Y. G.; Linhardt, R. J.; Vlahov, I. R. *Tetrahedron* **1998**, *54*, 9913–9959. (e) Bichard, C. J. F.; Brandstetter, T. W.; Estevez, J. C.; Fleet, G. W. J.; Hughes, D. J.; Wheatley, J. R. *J. Chem. Soc., Perkin Trans. 1* **1996**, 2151–2156. (f) Tomooka, K.; Kikuchi, M.; Igawa, K.; Keong, P. H.; Nakai, T. *Tetrahedron Lett.* **1999**, *40*, 1917–1920. (g) Dotz, K. H.; Jakel, C.; Haase, W. C. *J. Organomet. Chem.* **2001**, *617–618*, 119–132. (h) Khan, N.; Cheng, X.; Mootoo, D. R. *J. Am. Chem. Soc.* **1999**, *121*, 4918–4919.
9. Julia, M.; Uguen, D.; Verpeaus, J.; Zhang, D. *Synth. Lett.* **1991**, 505–506.
10. Brown, D. S.; Bruno, M.; Davenport, R. J.; Ley, S. V. *Tetrahedron* **1989**, *45*, 4293–4295.
11. Rothberg, I.; Sundoro, B.; Balanikas, G.; Kirsch, S. *J. Org. Chem.* **1983**, *48*, 4345–4348.
12. Brown, D. S.; Ley, S. V. *Tetrahedron Lett.* **1988**, *29*, 4869–4872.
13. (a) Trost, B. M.; Ghadiri, M. R. *J. Am. Chem. Soc.* **1986**, *108*, 1098–1100. (b) Trost, B. M.; Ghadiri, M. R. *Bull. Soc. Chim. Fr.* **1993**, *130*, 442–443.
14. Simpkins, N. S. *Sulphones in Organic Synthesis*, Pergamon: Oxford, 1993.
15. Ley, S. V.; Lygo, B.; Wonnacott, A. *Tetrahedron Lett.* **1985**, *26*, 535–538.
16. Fotsch, C. H.; Chamberlin, A. R. *J. Org. Chem.* **1991**, *56*, 4141–4147.
17. (a) Angle, S. R.; Wei, G. P.; Ko, Y. K.; Kubo, K. *J. Am. Chem. Soc.* **1995**, *117*, 8041–8042. (b) Angle, S. R.; Bernier, D. S.; El-Said, N. A.; Jones, D. E.; Shaw, S. Z. *Tetrahedron Lett.* **1998**, *39*, 3919–3922. (c) Angle, S. R.; Bernier, D. S.; Chann, K.; Jones, D. E.; Kim, M. S.; Neitzel, M. L.; White, S. L. *Tetrahedron Lett.* **1998**, *39*, 8195–8198.
18. Angle, S. R.; Neitzel, M. L. *J. Org. Chem.* **1999**, *64*, 8754–8757.
19. For leading references and recent examples: (a)Holmquist, C. R.; Roskamp, E. J. *J. Org. Chem.* **1989**, *54*, 3258–3260. (b) Holmquist, C. R.; Roskamp, E. J. *Tetrahedron Lett.* **1992**, *33*, 1131–1134. (c) Angle, S. R.; Neitzel, M. L. *J. Org. Chem.* **2000**, *65*, 6458–6561 and references cited therein.
20. Van Leusen, A. M.; Strating, J. Organic Synthesis Collective Volume VI, Noland, W. E., Ed.; Wiley: New York, 1988; pp 981.
21. For stereoselective allylation of five-membered-ring oxocarbenium ions in a similar system see: Larsen, C. H.; Ridgway, B. R.; Shaw, J. T.; Woerpel, K. A. *J. Am. Chem. Soc.* **1999**, *121*, 12208–12209.