Intermolecular Pinacol Coupling of Sulfur-Substituted Aldehydes by $[V_2Cl_3(THF)_6]_2(Zn_2Cl_6)$. The Effect of the Substitution at Sulfur on the Stereochemical Outcome of the Coupling Reaction

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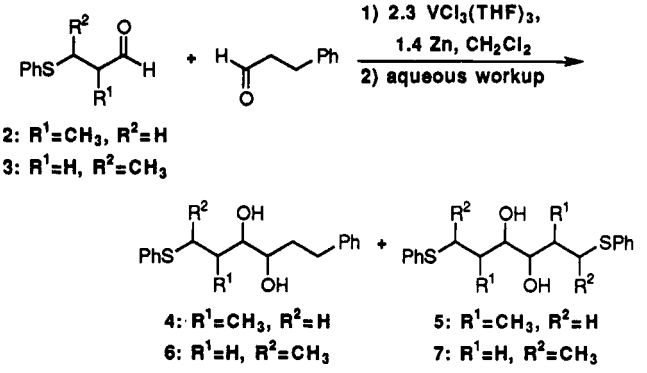
Previously, we have reported several stereoselective pinacol cross-coupling reactions between aldehydes using the readily available vanadium(II) reducing agent $[V_2Cl_3(THF)_6]_2(Zn_2Cl_6)$ (1).[1] These cross-coupling reactions require that one aldehyde be capable of forming a bidentate chelate with vanadium (a chelating aldehyde). Various sulfur-containing functional groups are also capable of acting as Lewis bases (for binding to vanadium) and can be removed under reductive conditions.[2-4] Herein we describe the pinacol coupling reactions of aldehydes bearing sulfide and sulfone groups.

Results and Discussion

At the outset of this project we felt that thioethers should bind well to vanadium(II), and thus we prepared two 3-(phenylthio) aldehydes. 2-Methyl-3-(phenylthio)propanal (2)and 3-(phenylthio)butanal (3) were prepared by Michael addition of thiophenol to crotonaldehyde or methacrolein, respectively.[5,6,18] These chelating aldehydes were cross-coupled with 3-phenylpropanal in the presence of 1 (Scheme I). Workup of the reactions with 10% sodium tartrate solution provided oils that were shown to consist of several compounds by TLC. Thiophenol and α,β-unsaturated aldehyde were present in the mixtures, presumably the result of Lewis acid-catalyzed elimination from 2 and 3. Unreacted 2 and 3 were also recovered and could not be separated from the diol products by flash column chromatography. These crude mixtures also contained self-coupled and cross-coupled products (diols) and unidentified olefinic compounds as determined by $^{13}C\{^1H\}$ NMR. Determination of the approximate diastereomeric ratios was accomplished by measuring signal intensities in the carbinol region of the $^{13}C\{^1H\}$ NMR spectra. Three cross-coupling diastereomers (4) in a ratio of 7:7:2 were found for the reaction of aldehyde 2. Two self-coupling isomers (5) were also observed.[7] Four cross-coupling diastereomers (6) in a ratio of 16:4:3:1 were observed in the cross-coupling reaction of 3. Again, self-coupling products (7) were formed. Separation of the cross-coupled isomers from each other was not possible.

Scheme I



Presumably the phenylthio group was not giving rise to a stable chelate with the vanadium(II) ion. However, it is worth mentioning that vanadium(II) complexes of the type $VX_2(THT)_4$ (THT = tetrahydrothiophene) have been prepared.[8] We expect that if we were to employ cyclic 5- or 6-membered ring thioethers in our chelating aldehydes, more stable chelates would result. Given the lack of selectivity of the reactions mentioned above, we turned our attention to sulfonyl-substituted aldehydes. Although the sulfoxide unit is the next most logical group to try, it suffers from two drawbacks. First, it can serve as an ambidentate ligand, and second, the presence of the asymmetric center at sulfur will complicate initial analyses.

Sulfone aldehydes 8-10 were prepared in a manner analogous to that for the thioaldehydes, using commercially available sodium sulfinate and acrolein, methacrolein, or crotonaldehyde.[9] The cross-coupling reactions were performed in a similar manner as well, except a 4 h addition of the chelating aldehyde was implemented. A 1 h addition resulted in incomplete reaction, while a 9 h addition failed to decrease the percentage of sulfone aldehyde self-coupling products. The diastereomeric ratios of the crude diol products were assessed by $^{13}C\{^1H\}$ NMR and are reported in Table I. Crystalline cross-coupled diols were obtained in 61-67% yields after chromatography.

Attempts to reductively cleave the sulfone group from 12 with dissolving metals in amines[10] or Raney nickel[11] were unsuccessful. However, the use of sodium-mercury amalgam[12] provided desulfurized material in good yields. Using this method, we were able to demonstrate that the major diastereomer of 12 has the expected *threo* diol stereochemistry[1] by its conversion to 18 (Scheme II). The relative stereochemistry of the methyl groups in 13 and 15 is inferred from our previous cross-coupling results,[1] as well as with aldehydes 40-44 as described below.

It is worthy of mention here that successful desulfurization of these products allows one to think of using these pinacol coupling reactions as a method for cross-coupling

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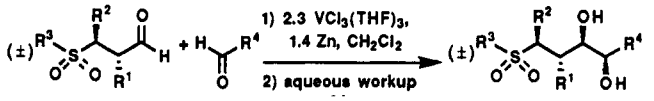
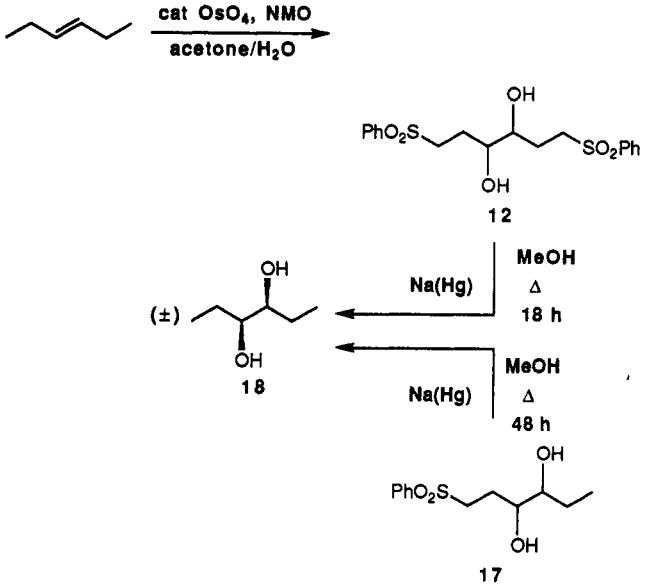
Table I



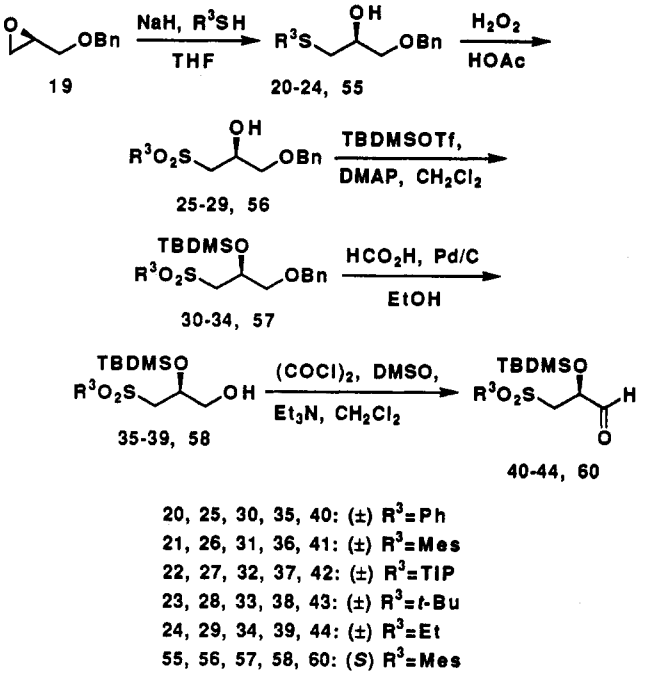
	β-sulfonyl aldehydes				diols			
entry	no.	R^1	R^2	R^3	no.	R^4	ds[a]	yield[b] (%)
1	8	H	H	Ph	11	CH_2CH_2Ph	3:1	65
2	9	CH_3	H	Ph	13	CH_2CH_2Ph	12:1	67
3	10	H	CH_3	Ph	15	CH_2CH_2Ph	10:1:1	61
4	40	OTBDMS	H	Ph	45	$CH_2CH(CH_3)_2$	3:1	55
5	41	OTBDMS	H	Mes	46	$CH_2CH(CH_3)_2$	9:1	97
6	42	OTBDMS	H	TIP[c]	47	$CH_2CH(CH_3)_2$	5:1	93
7	43	OTBDMS	H	*t*-Bu	48	$CH_2CH(CH_3)_2$	8:1	78
8	44	OTBDMS	H	Et	49	$CH_2CH(CH_3)_2$	6:3:1	not determined[d]

[a] These ratios are reported for crude products. [b] These yields are reported for pure products. [c] TIP = triisopropylphenyl. [d] The crude reaction mixture was contaminated with unreacted 44 and diol 49 could not be isolated.

Scheme II



Scheme III



20, 25, 30, 35, 40: (±) R^3=Ph
21, 26, 31, 36, 41: (±) R^3=Mes
22, 27, 32, 37, 42: (±) R^3=TIP
23, 28, 33, 38, 43: (±) R^3=*t*-Bu
24, 29, 34, 39, 44: (±) R^3=Et
55, 56, 57, 58, 60: (*S*) R^3=Mes

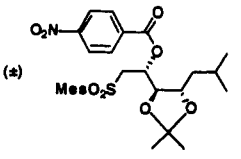
two nonchelating aldehydes (Scheme II). For example, aldehyde 8 was coupled with propionaldehyde to afford diol 17 as a mixture of two diastereomers. The major product was transformed to 18 by the sodium–mercury amalgam procedure. Certainly one can conceive of more complicated examples.

We also examined cross-coupling reactions of α-alkoxy β-sulfonyl aldehydes. Beginning with racemic 2-(benzyloxymethyl)oxirane (19) we prepared aldehydes 40–44 in 61–89% yields from 19 (Scheme III). This synthetic sequence required only two purification steps: after the epoxide opening and after the silylation step. Crude aldehydes 40–44 were judged to be sufficiently pure by ^1H and $^{13}C\{^1H\}$ NMR spectroscopy and were used directly in the coupling reactions. The aldehydes were coupled with isovaleraldehyde under the usual conditions, utilizing a 4 h slow addition of the chelating aldehyde. Diastereomeric ratios were again determined by $^{13}C\{^1H\}$ NMR spectroscopy for the crude reaction mixtures. The yields of pure cross-coupled diols 45–49 from aldehyde and the diastereomeric ratios are summarized in Table I. The relative stereochemistry of the major cross-coupled product was determined by X-ray analysis of a suitable derivative of 46.[13] The stereochemistry of the major isomer is the same as that observed for pinacol coupling reactions involving other chelating aldehydes.[1]

In the phenyl sulfone case (entry 4), the low selectivity coupled with low yield suggested we examine other variables. In particular, we decided to investigate the influence of the substituent at the sulfone center (R^3). As can be seen for entry 5, use of the more sterically demanding mesityl (Mes) group increases the diastereomeric ratio to 9:1 and the yield to 97% for the cross-coupled diols 46. No self-coupled diol 51 was formed. Increasing the size of the substituent on the aryl ring from methyl to isopropyl has a negative effect on the diastereoselectivity.[14]

We also examined two alkyl-substituted sulfones to determine if similar steric effects were observable. Entry

(13)



(14) At this time, we do not know the reason for this reversal in the trend.

7 shows that the *tert*-butyl sulfone aldehyde **43** cross-couples to give **48** as an 8:1 mixture of diastereomers in 78% yield. The isomers were separable by flash column chromatography, and no self-coupling product **53** was observed in the crude $^{13}C\{^1H\}$ NMR spectrum. The less sterically demanding ethylsulfonyl group provided dramatically poorer results (entry 8). Clearly, steric effects are of considerable importance in this chemistry. Changing from *tert*-butyl to ethyl had an effect similar to that observed between mesityl (entry 5) and phenyl (entry 4), in that diastereoselectivity and yield of the cross-coupled products were decreased.

It is worth noting here that the self-coupling reaction of an enantiomerically pure sulfone aldehyde provides one major product. Starting with (*S*)-2-(benzyloxymethyl)-oxirane, (*S*)-α-(silyloxy)-β-sulfonyl aldehyde **60** was synthesized in a manner analogous to that for **41**. The enantiomeric purity of the precursor alcohol **58** was checked by ^{19}F NMR spectroscopy of the (*R*) Mosher esters. The $^{13}C\{^1H\}$ NMR spectrum of the crude self-coupled product indicated that two C_2-symmetric diols were present in a 13:1 ratio. The major isomer **61** was isolated by flash chromatography in 79% yield. The expected stereochemistry[1d] was confirmed by X-ray crystallographic analysis of derivative **63**.[15]

In summary, an easily prepared vanadium(II) reagent has been used to couple β-sulfonyl aldehydes with aliphatic aldehydes. In one case, diastereoselectivity has been examined as a function of the size of the sulfur substituent and has been found to increase with increasing size up to a certain limit.

Experimental Section

General. Silica gel for flash column chromatography (200–430 mesh) was purchased from EM Reagents. Column size was selected according to the guidelines of Still.[16] Melting points are uncorrected. ^1H NMR spectra were recorded at 250, 400, or 500 MHz. $^{13}C\{^1H\}$ NMR spectra were obtained at 100 or 125 MHz. Fast atom bombardment (FAB) mass spectra were recorded using a 3-nitrobenzyl alcohol matrix. In many cases, LiCl was added to enhance the molecular ion signal.[17] Please see ref 1a–d for additional details.

Chemical shifts for ^1H NMR spectra are reported in parts per million (ppm) and are referenced to $CDCl_3$, $\delta = 7.25$. In the case of compounds **8–10**, **21**, and **26** the chemical shifts are reported in ppm downfield from tetramethylsilane, $\delta = 0.00$. Chemical shifts for $^{13}C\{^1H\}$ NMR spectra are reported in ppm relative to the $CDCl_3$ solvent resonance, $\delta = 77.0$.

General procedures and data for key compounds are outlined here. Information pertaining to all other compounds is located in the supplementary material.

Synthesis of Cross-Coupled Diols. General Procedure. The following procedure was carried out under a nitrogen atmosphere. A 50-mL round-bottom flask was charged with 4.06 g (10.9 mmol) of $VCl_3(THF)_3$,[19] 384 mg (5.88 mmol) of Zn dust, and 10 mL of CH_2Cl_2. After the solution had turned bright green (*ca.* 15–60 min), 674 mg (5.00 mmol) of isovaleraldehyde or 3-phenylpropanal in 2 mL of CH_2Cl_2 was added. The mixture turned dark red immediately. The sulfur-substituted aldehyde (750 mg, 4.20 mmol) in 5 mL of CH_2Cl_2 was added to the flask *via* syringe pump over 4 h. The resulting mixture was stirred for an additional 30 min and then poured into 180 mL of a 10% sodium tartrate solution. Stirring was continued until the CH_2Cl_2 layer became transparent (*ca.* 3 h), at which time the layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 60 mL). The combined organic extracts were washed with 10% sodium tartrate solution (2 × 70 mL), dried over Na_2SO_4, filtered, and concentrated on a rotary evaporator and a vacuum line if necessary. A $^{13}C\{^1H\}$ NMR spectrum was taken of the crude product before purification by flash chromatography. Except where noted, crude products were contaminated with the corresponding self-coupling product. Spectral data are given for purified compounds. Cross-coupled diols were prepared by this general procedure on scales from 0.8 to 9 mmol.

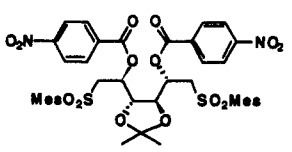
Synthesis of Self-Coupled Diols. General Procedure. The following procedure was carried out under a nitrogen atmosphere. A 50-mL round-bottom flask was charged with 3.14 g (8.40 mmol) of $VCl_3(THF)_3$, 293 mg (4.48 mmol) of Zn dust, and 20 mL of CH_2Cl_2 until a bright green color persisted. A 1.00 g portion (5.60 mmol) of the sulfur-substituted aldehyde in 5 mL of CH_2Cl_2 was added. The resulting dark red solution was stirred at ambient temperature for 6 h and then poured into 120 mL of 10% aqueous sodium tartrate solution with stirring. After the CH_2Cl_2 layer became transparent this mixture was extracted with CH_2Cl_2 (3 × 40 mL). The combined organic extracts were dried with Na_2SO_4 and concentrated on a rotary evaporator and a vacuum line if necessary. A $^{13}C\{^1H\}$ NMR spectrum was taken before the crude product was purified by flash chromatography. Self-coupled diols were synthesized according to this procedure on scales from 0.27 to 5 mmol.

Synthesis of 3-(Phenylsulfonyl) Aldehydes 8–10.[9] General Procedure. Sodium benzenesulfinate (14.6 g, 89.2 mmol) was suspended in 375 mL of CH_2Cl_2. Glacial acetic acid (5.1 mL, 89.2 mmol) was added, immediately followed by the addition of acrolein (6.0 mL, 89.2 mmol) in 200 mL of CH_2Cl_2 over a 1-h period. The reaction was monitored by GC and upon completion (*ca.* 3 h) the mixture was washed with 200 mL of saturated $NaHCO_3$, dried with Na_2SO_4, filtered, and concentrated on a rotary evaporator. The crude material was used without further purification.

Synthesis of Alcohols 20–24. General Procedure. NaH (1.78 g, 44.6 mmol) was washed with pentane and suspended in 100 mL of THF. The thiol[21] (6.22 g, 40.9 mmol) was added dropwise with the aid of a syringe, and the mixture was allowed to stir until all gas evolution had ceased (30 min). In the case of **21** and **22** transparent solutions instead of thick suspensions were formed. The racemic epoxide **19**[22] (6.10 g, 37.1 mmol) was dissolved in 100 mL of THF and transferred *via* cannula to the thiolate mixture. An additional 50 mL of THF was used to rinse the epoxide container and was added to the reaction flask. The reaction was monitored by GC and was complete after 12–18 h. The reaction mixture was diluted with 50 mL of water, the water layer was extracted with ethyl acetate (3 × 20 mL), and the combined extracts were washed with 100 mL of saturated NaCl solution. The extracts were dried with Na_2SO_4, filtered, and concentrated on a rotary evaporator and a vacuum line. The red or brown residue contained thiol and was purified by flash chromatography. Alcohols were prepared by this general procedure on scales from 3 to 67 mmol.

(*RS*)-1-*O*-Benzyl-3-(mesitylthio)-1,2-propanediol (21). The crude alcohol was obtained as a brown liquid. Flash column chromatography with an EtOAc–hexane eluant (10:90–20:80 v/v) gave 7.30 g of an orange liquid: ^1H NMR (400 MHz, $CDCl_3$) δ

(15)



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(21) (a) Oae, S.; Togo, H. *Bull. Chem. Soc. Jpn.* **1983**, *56*, 3802. This is the preferred procedure. (b) Blower, P. J.; Dilworth, J. R.; Hutchinson, J.; Nicholson, T.; Zubieta, J. A. *J. Chem. Soc., Dalton Trans.* **1985**, 2639.
(22) Racemic **19** was synthesized from allyl alcohol in two steps. First, the alcohol was alkylated with benzyl bromide. Second, the resulting ether was epoxidized with *m*-CPBA.

2.24 (s, 3H), 2.49 (s, 6H), 2.66 (br s, 1H), 2.73 (dd, 1H, J = 13.2, 7.1 Hz), 2.79 (dd, 1H, J = 13.2, 5.6 Hz), 3.46 (dd, 1H, J = 9.6, 6.1 Hz), 3.54 (dd, 1H, J = 9.6, 3.9 Hz), 3.77 (m, 1H), 4.49 (s 2H), 6.90 (s, 2H), 7.31 (m, 5H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 20.9, 21.9, 39.0, 69.6, 72.7, 73.4, 127.7, 128.2, 128.4, 129.1, 129.5, 137.8, 138.2, 142.6; TLC EtOAc–hexane (30:70 v/v) R_f 0.53.

Synthesis of Alcohols 25–29. General Procedure. Following a modified literature procedure,[23] 7.20 g (22.8 mmol) of **21** was dissolved in 93 mL of glacial acetic acid and treated with a 26-mL portion of 30% H_2O_2 solution (228 mmol). The reaction was monitored by TLC and was complete in 16–21 h. The contents were transferred to a larger Erlenmeyer flask, cooled in an ice bath, and cautiously neutralized with 60% KOH solution (150 mL), stirring vigorously. The mixture was extracted with ethyl acetate (3 × 50 mL), the combined extracts were washed with 50 mL of saturatedNaCl solution, and dried with Na_2SO_4. Concentration on a rotary evaporator and vacuum line provided a product which was used without further purification. Alcohols were prepared using this procedure on scales from 0.70 to 23 mmol.

(*RS*)-1-*O*-Benzyl-3-(mesitylsulfonyl)-1,2-propanediol (26). Two days were required for this reaction to go to completion. A yellow oil (7.70 g) was obtained: ^1H NMR (400 MHz, $CDCl_3$) δ 2.30 (s, 3H), 2.65 (s, 6H), 3.29 (dd, 1H, J = 14.3, 8.3 Hz), 3.36 (dd, 1H, J = 14.3, 3.2 Hz), 3.40 (br s, 1H), 3.54 (d, 2H, J = 5.1 Hz), 4.43 (m, 1H), 4.51 (d, 2H, J = 5.8 Hz), 6.96 (s, 2H), 7.30 (m, 5H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 20.9, 22.8, 59.2, 65.3, 72.3, 73.4, 127.7, 127.8, 128.4, 132.3, 133.1, 137.4, 139.8, 143.6; TLC EtOAc–hexane (30:70 v/v) R_f 0.29.

Preparation of Silyl Ethers 30–34. General Procedure. Under a nitrogen atmosphere 6.50 g (18.7 mmol) of **26** was dissolved in 125 mL of dry CH_2Cl_2 and was treated with 4.56 g (37.3 mmol) of DMAP (2,6-lutidine may be used instead) and 4.5 mL (19.6 mmol) of TBDMSOTf. The reaction was monitored by TLC and was complete in 2–5 h. The reaction was quenched with 44 mL of water, and the aqueous layer was extracted with CH_2Cl_2 (3 × 15 mL). The combined extracts were washed with 10% HCl solution (3 × 55 mL) and once with 55 mL of saturated NaCl solution, dried with Na_2SO_4, filtered, and concentrated on a rotary evaporator to afford a crude product that typically contained a very small amount of disiloxane. The crude product was usually carried on to the next step without purification, since any disiloxane was destroyed during that step. This procedure was used to prepare silyl ethers on scales from 2 to 22 mmol.

(*RS*)-1-*O*-Benzyl-2-*O*-(*tert*-butyldimethylsilyl)-3-(mesitylsulfonyl)-1,2-propanediol (31). This compound required 1.10 equiv of TBDMSOTf instead of 1.05 equiv and a 2 day reaction time. A yellow oil was obtained (8.63 g): ^1H NMR (500 MHz, $CDCl_3$) δ 0.057 (s, 3H), 0.064 (s, 3H), 0.85 (s, 9H), 2.29 (s, 3H), 2.64 (s, 6H), 3.20 (dd, 1H, J = 14.2, 4.5 Hz), 3.54 (m, 3H), 4.50 (m, 3H), 6.94 (s, 2H), 7.30 (m, 5H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ −5.0, −4.7, 17.9, 20.9, 22.8, 25.7, 59.8, 66.1, 73.2, 73.5, 127.5, 128.3, 132.2, 134.2, 138.0, 139.7, 143.1; TLC EtOAc–hexane (30:70 v/v) R_f 0.74.

Preparation of Primary Alcohols 35–39. General Procedure. Silyl ether **31** (9.70 g, 21.0 mmol) was dissolved in 106 mL of absolute EtOH and was treated with 4.90 g of 10% Pd/C and 7.9 mL (9.91 mmol) of formic acid. The reaction was monitored by TLC and was complete in 16–24 h. The reaction was filtered through Celite, and the filter cake was washed with ethyl acetate until the original volume was doubled. The filtrate was washed with 50% saturated $NaHCO_3$ solution (2 × 70 mL) and once with 70 mL of saturated NaCl solution, dried with Na_2SO_4, filtered, and concentrated on a rotary evaporator to afford a crude product that was carried on to the next step without purification. This procedure was used to prepare primary alcohols on scales from 0.13 to 21 mmol.

(*RS*)-2-*O*-(*tert*-Butyldimethylsilyl)-3-(mesitylsulfonyl)-1,2-propanediol (36). A colorless oil was obtained (7.80 g): ^1H NMR (400 MHz, $CDCl_3$) δ 0.07 (s, 3H), 0.08 (s, 3H), 0.85 (s, 9H), 2.18 (br s, 1H), 2.29 (s, 3H), 2.64 (s, 6H), 3.14 (dd, 1H, J = 14.1, 3.4 Hz), 3.53 (dd, 1H, J = 14.1, 7.9 Hz), 3.72 (m, 2H), 4.38 (m, 1H), 6.96 (s, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ −5.0, −4.9, 17.9, 20.9, 22.8, 25.6, 58.9, 66.0, 67.0, 132.3, 133.7, 139.7, 143.4; TLC EtOAc–hexane (30:70 v/v) R_f 0.57.

Preparation of Aldehydes 40–44. General Procedure. A procedure adapted from Luly *et al.*[24] was followed. An oven-dried 1-L flask was purged with nitrogen and charged with 260 mL of dry CH_2Cl_2. At −63 °C, oxalyl chloride (2.7 mL, 30.6 mmol) and DMSO (2.9 mL, 40.8 mmol) were added in succession. Alcohol **36** was dissolved in 125 mL of CH_2Cl_2 and added dropwise. After 30 min, Et_3N (11.4 ml, 81.6 mmol) was added. Progress was monitored by GC, with completion taking between 30 min and 2 h. The reaction was quenched at −63 °C by the addition of 270 mL of 20% saturated $KHSO_4$ solution. The aqueous layer was extracted with Et_2O (3 × 90 mL). The combined extracts were washed with 185-mL portions of saturated $NaHCO_3$ (1×), water (3×), and saturated NaCl (1×) and then were dried with Na_2SO_4, filtered, and concentrated on a rotary evaporator using a room-temperature bath. The crude product was carried on to the next step without purification. This procedure was used to prepare aldehydes on scales from 0.45 to 20 mmol.

(*RS*)-2-[*O*-(*tert*-Butyldimethylsilyl)oxy]-3-(mesitylsulfonyl)propanal (41). A colorless oil was obtained (7.55 g): ^1H NMR (500 MHz, $CDCl_3$) δ 0.10 (s, 3H), 0.12 (s, 3H), 0.85 (s, 9H), 2.28 (s, 3H), 2.63 (s, 6H), 3.37 (dd, 1H, J = 14.3, 5.4 Hz), 3.59 (dd, 1H, J = 14.4, 4.6 Hz), 4.61 (t, 1H, J = 5.0 Hz), 6.94 (s, 2H), 9.70 (s, 1H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ −5.2, −4.8, 18.1, 20.9, 22.8, 25.6, 58.8, 72.4, 132.3, 134.0, 139.7, 143.5, 200.2.

2-[(*tert*-Butyldimethylsilyl)oxy]-1-(mesitylsulfonyl)-6-methyl-3,4-heptanediol (46). The crude compound was obtained as 827 mg of a pale yellow oil, free of **51**: ^1H NMR (500 MHz, $CDCl_3$) δ 0.07 (s, 3H), 0.10 (s, 3H), 0.82 (s, 9H), 0.86 (t, 6H, J = 6.9 Hz), 1.19 (m, 1H), 1.53 (qd, 1H, J = 19.3, 9.2, 5.6 Hz), 1.72 (m, 1H), 2.23 (s, 3H), 2.59 (s, 6H), 3.16 (br s, 1H), 3.22 (dd, 1H, J = 14.5, 3.5 Hz), 3.46 (br s, 1H), 3.50 (dd, 1H, J = 14.5, 6.2 Hz), 3.83 (m, 1H), 4.44 (m, 1H), 6.90 (s, 2H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ −5.2, −4.9, 17.6, 20.7, 21.7, 22.7, 23.2, 24.1, 25.6, 42.7, 59.8, 67.5, 68.3, 75.6 (major isomer), −4.5, 21.67, 22.8, 23.6, 25.56, 42.4, 58.7, 67.8, 67.9, 69.5 (minor isomer), 132.2, 133.7, 139.6, 143.3; TLC EtOAc–hexane (30:70 v/v) R_f 0.49.

(2*S*,3*S*,4*S*,5*S*)-2,5-Bis[(*tert*-butyldimethylsilyl)oxy]-1,6-bis(mesitylsulfonyl)-3,4-hexanediol (61). A procedure similar to that used for **41** provided a yellow oil. The 13:1 mixture of isomers was separated by flash column chromatography with an EtOAc–hexane eluant (10:30–30:70 v/v) to afford the major isomer as 765 mg of white foam (79%): FAB-MS m/z 743 (MH^+, 54), 685 (43), 341 (82), 299 (52), 283 (45), 167 (42), 119 (100); $[\alpha]^{25}_D$ = +7.38° (c 0.0145, $CHCl_3$); high-resolution FAB-MS calcd for $C_{36}H_{61}O_8S_2Si_2$ 743.3486, found 743.3490; TLC EtOAc–hexane (30:70 v/v) R_f 0.80.

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Supplementary Material Available: ORTEP drawings for **62** and **63**, ^{13}C NMR spectra for **16**, **38**, **60**, and **61**, and experimental data for **3–7**, **11–18**, **20**, **22–25**, **27–30**, **32–35**, **37–40**, **42–45**, and **47–60** (27 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information. Tables of crystal data collection, solution and refinement parameters, and thermal factors for **62** and **63** have been deposited with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK.

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