Effect of a Phosphazene Base on the Diastereoselectivity of Addition of α-Sulfonyl Carbanions to Butyraldehyde and Isopropylideneglyceraldehyde

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Received October 25, 1995[⊗]

The effect of tBuP4, a strong and cation-free base, on the yield and diastereoselectivity of additions of thus formed "naked" α-sulfonyl carbanions to achiral butyraldehyde and chiral isopropylideneglyceraldehyde was studied. It has been found that with tBuP4 a reasonable yield (~55%) and a slightly better diastereoselectivity (72% of the *anti* diastreomer) are obtained with achiral and nonfunctionalized butyraldehyde while with isopropylideneglyceraldehyde the use of tBuP4 allowed us to greatly increase the yields (up to 95−100%) and the diastereoselectivities (83−89% of a single diastereomer over the four possible diastereomers). It was also shown that the extra oxygen atom in the α-position plays a determinant role in this effect.

Addition of α-sulfonyl carbanions to carbonyls is a well-studied reaction used for the synthesis of *trans* olefins.[1,2] The α-sulfonyl carbanions are usually generated with BuLi or EtMgBr, and the diastereoselectivity of the condensation with aldehydes ranges between 1:1 and 3:1.[2−4]

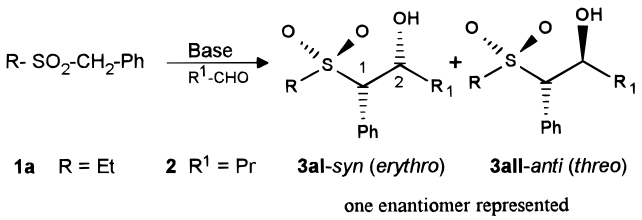
We report here the effect of tBuP4, a strong and cation-free base,[5] on the diastereoselectivity of additions of thus formed "naked"[6] α-sulfonyl carbanions to achiral butyraldehyde (**2**) and chiral isopropylideneglyceraldehyde (**4**).

Results

Addition to Achiral Butyraldehyde (2). Condensation of ethyl benzyl sulfone (**1a**) with butyraldehyde (**2**) gave a mixture of the two expected *syn* and *anti* diastereomers, Scheme 1.

The results are presented in Table 1. Noteworthy was the quantitative yield obtained upon condensation of the lithiosulfone anion **1a(Li)**[7] (generated from **1a** with Bu**Li** as base) with butyraldehyde **2** (Table 1, entry 1). Since these reactions are reversible[1] one must think in terms of stability of products and one may conclude that the Li-alcoholate formed, **3a(Li)**, is more stable than the starting reagents (**1a(Li)** and **2**), probably because of chelation, Figure 1.

Scheme 1



1a R = Et **2** R^1 = Pr **3aI**-*syn* (*erythro*) **3aII**-*anti* (*threo*)

one enantiomer represented

Table 1. Additions Ethyl Benzyl Sulfone (1a) to Achiral Butyraldehyde (2)

base		*syn* (R_f) **I**	*anti* (R_f) **II**	yield, %
BuLi	**3a**	41 (0.4)[a]	59 (0.24)	100
tBuP4	**3a**	28 (0.4)	72 (0.24)	56
tBuP4/Me_3SiCl[b]	**3a′**	18[c]	82[c]	72

[a] Et_2O/hex 6/4. [b] Me_3SiCl was added to the reaction mixture just before the workup. [c] Assigned using the J_{12} as compared with the unprotected compound.

When tBuP4 was used as base lower yield (56%) was obtained (Table 1, compare entries 1 and 2); this reflects the expected lower stability of the "naked" alcoholate **3a-(tBuP4H)** as compared with the chelated one, **3a(Li)**.

It must be noted that quenching with Me_3SiCl allowed us to increase the yield to 72% (Table 1, entry 3), thus making this reaction synthetically useful.[8]

It appeared that the *anti* (*threo*) isomer was favored (Table 1) in accord with literature results[4] and that the diastereoselectivity increased when tBuP4 was used as base (Table 1, compare entries 1 and 2). More interesting is the further increase of the diastereoselectivity upon quenching the alcoholate formed with Me_3SiCl (Table 1, compare entries 2 and 3).[8]

Addition to Chiral Isopropylideneglyceraldehyde (4) and Aldehydes 6 and 7. The results of the

[⊗] Abstract published in *Advance ACS Abstracts,* March 15, 1996.

(1) Julia, M.; Arnould, D. *Bull. Soc. Chim. Fr.* **1973**, 743. Julia, M.; Paris, J. M. *Tetrahedron Lett.* **1973**, 4833.

(2) Kocienski, P. J.; Lythgoe, B.; Ruston, S. *J. Chem. Soc., Perkin Trans. 1* **1978**, 829 and references therein.

(3) Truce,W. E.; Klinger, T. C. *J. Org. Chem.* **1970**, *35*, 1834 and references therein.

(4) Kingsbury, C. A. *J. Org. Chem.* **1972**, *37*, 102 and references therein.

(5) Schwesinger, R. *Nachr. Chem. Tech. Lab.* **1990**, *38*, 1214. Seebach, D.; Beck, A. K.; Studer, A. *Modern Synthetic Methods 1995*; Ernst, B., Leumann, C., Eds.; Verlag Helvetica Chimica Acta: Basel; VCH: Weinheim, 1995; Vol. 7.

(6) "Naked" means cation-free as the plus and minus species are very probably intimately associated in this solvent.

(7) For structure and conformation stability of lithiosulfones, cf.: Kaufman, M. J.; Gronert, S.; Bors, D. A.; Streitwieser, A. *J. Am. Chem. Soc.* **1987**, *109*, 602. Gais, H. J.; Hellmann, G.; Günther, H.; Lopez, F.; Lindner, H. J.; Braun, S. *Angew. Chem., Int. Ed. Engl.* **1989**, *28*, 1025.

(8) As the reaction is reversible, the increase in diastereomer **II** upon quenching the reaction mixture with Me_3SiCl (72% **II** to 82% **II**) suggests that alcoholate **3aII(tBuP4H$^+$)** is more reactive toward Me_3SiCl than **3aI(tBuP4H$^+$)** and **1a(tBuP4H$^+$)**.

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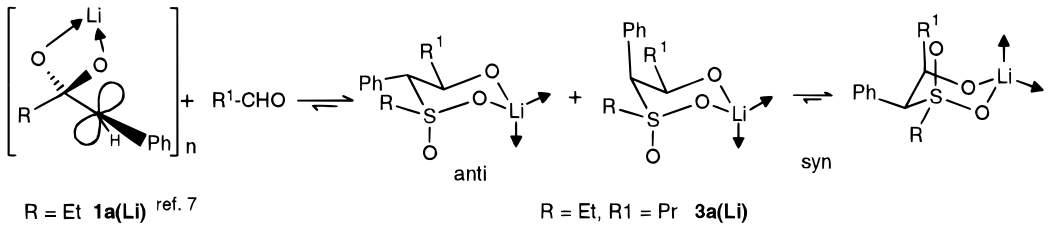


Figure 1.

Scheme 2

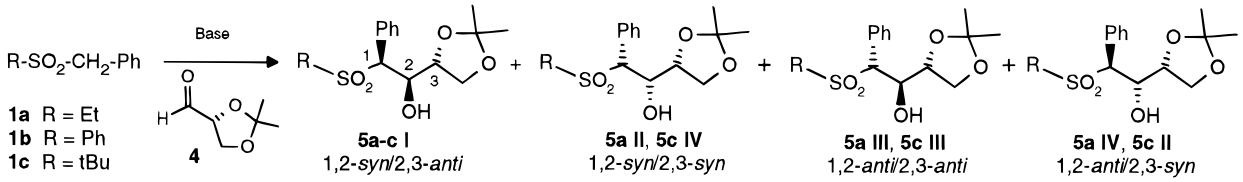
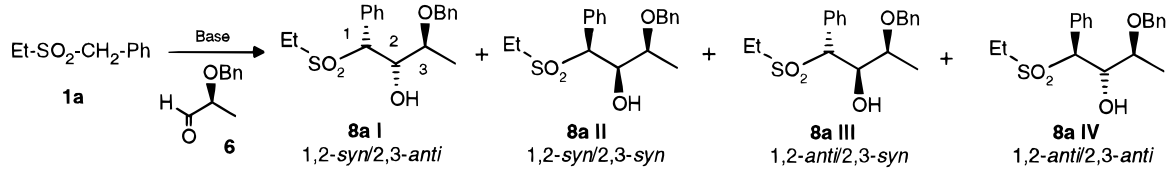


Table 2. Addition of Benzyl Sulfones 1a−c to Chiral Aldehyde 4

R	base	solvent, *T*, °C		**I** (R_f)	**II** (R_f)	**III** (R_f)	**IV** (R_f)	yield, %
Et	EtMgBr	THF, 0	**5a**	60 (0.35)[a]	7 (0.26)	17 (0.17)	16 (0.12)	61
	LDA	THF, −78	**5a**	43	2	40	15	62
	BuLi	THF, −78	**5a**	35	13	39	13	90
	BuLi	THF/TMEDA, −78	**5a**	34	14	14	38	45
	tBuP4	THF, −40	**5a**	75	0	25	0	90
	tBuP4	THF, −78	**5a**	83	0	17	0	95
Ph	tBuP4	THF, −78	**5b**	87 (0.31)[b]	13 (0.22)			100
tBu	BuLi	THF, −78	**5c**	31 (0.29)[c]	20 (0.26)	31 (0.19)	18 (0.12)	100
	tBuP4	THF, −78	**5c**	89	0	11	0	100

[a] Et_2O/hex 8/2. [b] Et_2O/hex 1/1. [c] Et_2O/hex 4/6.

Scheme 3



condensation of benzylsulfones **1a−c** with (*R*)-(+)-isopropylideneglyceraldehyde (**4**), Scheme 2, are given in Table 2.

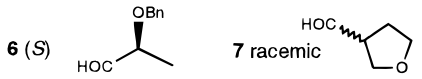
One must note the high yields (90−100%) obtained with tBuP4 in contrast with the previous result where the use of tBuP4 considerably lowered the yield (compare Table 2, entries 5, 6, 7, and 9 with Table 1, entry 2). It was reasonable to postulate that the extra oxygen atoms might play an important role by adding extra NC−$H^{\delta+}$···O interactions (which are known to contribute by *ca.* 4−6 kcal/mol[9]) between one or both oxygen atoms of the aldehydic part of the substrate and the conjugated acid of the phosphazene base ($tBuP4H^+$). Therefore, aldehydes **6** and **7** possessing only one oxygen atom either in the α-position or in the *β*-position have been examined, Scheme 3 and Table 3. One may note that the yields with aldehyde **6** were always higher than with aldehyde **7** (Table 3, compare entries 1−3 with 4 and 5) and that the use of tBuP4 as base again led to higher yields, but more so with **6** (100%) than with **7** (62%).

It thus appeared that an extra oxygen atom in the α-position is determinant for the obtention of high yields.

Most important is also the better diastereoselectivity obtained with tBuP4 as base where only two diastereomers over the four possible were observed with aldehyde **4** (Table 2, entries 5−7 and 9). However, the major diastereomers formed, **5a−cI**, are now 1,2-*syn* (*erythro*), Table 5, instead of 1,2-*anti* (*threo*) as in the case of condensation with butyraldehyde **2** having no extra oxygen (where **3aII** was the major compounds, Table 1).

It is worth noting that the use of tBuP4 upon condensation of the benzyl sulfone **1a** with aldehyde **6** led also to an increase in diastereoselectivity, 70% of **8aI**, while with aldehyde **7** there was no change of the diastereoselectivity (Table 3, compare entries 1 and 2 with 3 and 4 with 5). *Obviously the extra oxygen atom in the α-position is also determinant for obtention of a better diastereoselectivity.*

Table 3. Addition of Benzyl Sulfone 1a to Aldehydes 6 and 7



alde-hyde	base		**I** (R_f)	**II** (R_f)	**III** (R_f)	**IV** (R_f)	yield, %
6	EtMgBr	**8a**	23 (0.33)[a]	35 (0.33)	23 (0.22)	19 (0.16)	77
6	BuLi	**8a**	16	32	29	23	80
6	tBuP4	**8a**	70	2	16	12	100
7	BuLi	**9a**	34 (0.13)[b]	34 (0.13)	17 (0.11)	15 (0.11)	48
7	tBuP4	**9a**	30	34	17	19	62

[a] Et_2O/hexane 7/3. [b] Et_2O/hexane 9/1.

(9) Taylor, R. ; Kennard, O. *J. Am. Chem. Soc.* **1982**, *104*, 5063. Mautner, M. *J. Am. Chem. Soc.* **1983**, *105*, 4912. Mautner, M.; Deakyne, C. A. *J. Am. Chem. Soc.* **1985**, *107*, 469.

Table 4. NMR Parameters of 3a and A: $PhSO_2CH(Ph)CH(OH)Ph$[a]

	δ H_1[b]	δ H_2[b]	J_{12}[b]	
3aI	3.98	4.82	2	*syn*
3aII	4.12	4.67	9	*anti*
AI	4.19	6.03	2.5	*syn*
AII	4.46	5.70	10	*anti*

[a] Compounds **AI** and **AII** have been resynthesized following ref 4. [b] δ in ppm and J in Hz.

Table 5. Characteristics of 5a−c and 8

	R_f	δ H_1	δ H_2	δ H_3	J_{12}	J_{23}	1,2	2,3
5aI[a]	0.35	4.47	4.70	3.52	1.5	9	*syn*	*anti*
5aII	0.26	4.05	4.65	4.20	3.5	5	*syn*	*syn*
5aIII	0.17	4.05	4.67	~3.90[b]	9	3.5	*anti*	*anti*
5aIV	0.12	4.25	4.35	~3.53[b]	10	1.5	*anti*	*syn*
5bI	0.31	4.43	4.56	3.54	1.5	9	*syn*	*anti*
5bII[c]	0.22		~4.70					
5cI	0.29	4.65	4.74	3.39	1.5	9.5	*syn*	*anti*
5cII	0.26	4.70	4.52	3.55	10	1.5	*anti*	*syn*
5cIII	0.19	4.48[d]	4.52[d]	~4[b]	6.5	5	*anti*	*anti*
5cIV	0.12	4.25	4.74	4.08	4	6	*syn*	*syn*
8aI	0.33	4.57	4.62	3.12	2	8.5	*syn*	*anti*
8aII	0.33	4.13	~4.6[e]	3.62	3.5	6	*syn*	*syn*
8aIII	0.22	4.05	4.80	3.20[b]	10	2.5	*anti*	*syn*
8aIV	0.16	4.45[f]	4.45[f]	3.25[b]			*anti*	*anti*

[a] Structure determined by X-ray, [b] Overlapped with a CH_2. [c] Not isolated. [d] AB part of an ABX system. [e] Overlapped with a signal of **8aI**. [f] Degenerated AB part of an ABXY system, with a small nonequivalence.

It must also be noted that *tert*-butyl benzyl sulfone (**1c**) gave a better diastereoselectivity than ethyl benzyl sulfone (**1a**) (Table 2, entries 6 and 9). A similar trend had already been observed but in the case of sulfoxides by Casey and coll.[10]

However, attempts to quench alcoholates **5aI−III-(tBuP4H)** with R_3SiCl failed, due to the low reactivity of these alcoholates. As a matter of fact, an attempt to protect the hydroxyl group of isolated **5aI** failed even with $tBuMe_2SiOTf$ after 3 days, and only 57% of protection was obtained after 1 day in the case of **5aII**.

Structures of Compounds 5aI−IV, 5bI, 5cI−IV, and 8aI−IV. All diastereomers have been numbered (**I**, **II**, ...) according to decreasing TLC frontal retentions (R_f), Tables 4 and 5.

After separation and recrystallization from EtOAc, diastereomer **5aI** was obtained as a single crystal suitable for an X-ray diffraction analysis. The structure, Figure 2, shows that the configuration of the two new asymmetric carbons created is 3*S*,4*R* (according to ORTEP numbering), that is, 1*S*,2*R* (according to the usual numbering given in Scheme 2), on the basis of the known *R* configuration of carbon C5 (ORTEP numbering), that is C3 (usual numbering, Scheme 2). *Diastereomer **5aI** is thus 1,2-syn/2,3-anti.*

It also appears that (1) the phenyl ring is almost eclipsed with the CH bond, S−C3−C10−C15 = 60°, (2) the α-oxygen atom of the acetal ring is almost *trans* to the hydroxyl group, O4−C5−C4−O3 = 173.5°, and one of the sulfone oxygens is pushed away from the hydroxyl groups, O1−S−C3−C4 = 160° (O2−S−C3−C4 = 40°).

Structures of diastereomers **5aII**, **5aIII**, and **5aIV** have then been determined using vicinal H−H coupling constants (Table 5, columns 6 and 7) and comparison with

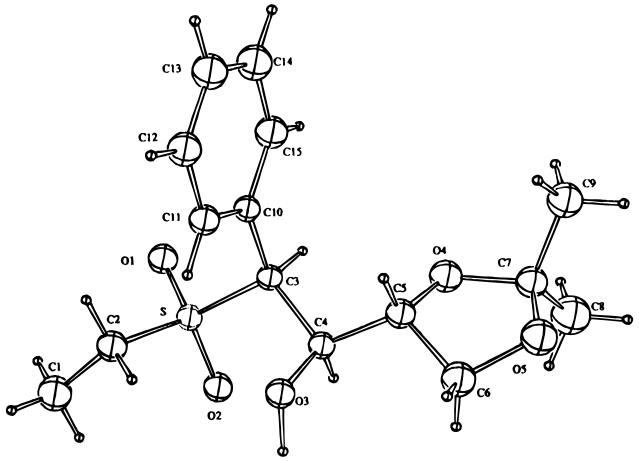
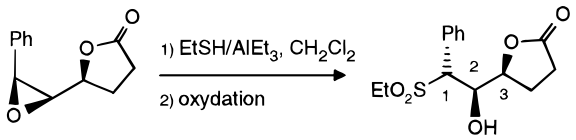


Figure 2. ORTEP plot of one molecule of **5aI**. Elipsoids are scaled to enclose 50% of the electronic density.

Scheme 4



10 (1*S*,2*R*,3*S*) [11]

11 (1*R*,2*R*,3*S*), 1,2-*anti*/2,3-*syn*
J_{12} = 10 Hz, J_{23} = 1.5 Hz
δ H1 = 4.50, δ H2 = 4.65
δ H3 = 4.07

those of **5aI**, **3aI**, **3aII**, **AI,** and **AII**[4] as well as **11** (whose 1,2-*anti*/2,3-*syn* structure was unambiguously assigned, *cf.* below).

The 1.5 Hz value of the J_{12} coupling constant observed in 1,2-*syn* **5aI** is consistent with the values observed for **3aI**-*syn* and **AI**-*syn*, probably because the O−H···O_2S H-bond is stronger than the O−H···OC(C) H-bond. It is thus reasonable to postulate, on the basis of J_{12} coupling constants, that **5aII**, **-III** and **-IV** are, respectively, 1,2-*syn* (J_{12} = 3.5 Hz), 1,2-*anti* (J_{12} = 9 Hz), and 1,2-*anti* (J_{12} = 10 Hz), Table 5.

Therefore, **5aI** being 1,2-*syn*/2,3-*anti*, **5aII** is 1,2-*syn*/2,3-*syn*, Table 5.

The 1,2-*anti*/2,3-*syn* structure was assigned to **5aIV** because the coupling constants (10 and 1.5 Hz) are similar to those (10 and 1.5 Hz) of compound **11** of known configuration (*cf.* below). Therefore, **5aIII** can only be 1,2-*anti*/2,3-*anti*.

The 1,2-*syn*/2,3-*anti* configurations of **5bI**, **5cI**, and **8aI** have then been assigned by direct comparison with **5aI**, and the 1,2-*anti*/2,3-*syn* configurations of **5cII** and **8aIII** have been assigned by comparison with **11** and **5aIV**. Finally **5cIV** and **8aII**, having coupling constants similar to those of **5aII**, were assigned the 1,2-*syn*/2,3-*syn* structure, and as a consequence, **5cIII** and **8aIV** must have the 1,2-*anti*/2,3-*anti* structure.

Structure of Compound 11. Since the (1*S*,2*R*,3*S*) structure of the lactoepoxide **10** was determined through X-ray diffraction analysis,[10] opening of the epoxide ring with $EtSH/AlEt_3$ (SN2 mecanism) followed by an oxidation step to the sulfone led to (1*R*,2*R*,3*S*)-**11**, Scheme 4, of known 1,2-*anti*/2,3-*syn* configuration. Because compound **11** (which also possesses an oxygen atom in the α-position) has a structure close to that of compounds **5a−c**, the vicinal coupling constants (J_{12} = 10 Hz and

(10) Casey, M.; Mukherjee, I.; Trabsa, H. *Tetrahedron Lett.* **1992**, *33*, 127.

(11) Solladié-Cavallo, A.; Roche, D.; Bold, G.; Acemoglu, F.; Tintel-not-Blomley, M., in press.

J_{23} = 1.5 Hz) measured on compound **11** can be used for the determination of the structures of compounds **5a**−**c**.

Conclusion

Although additions of α-sulfonyl carbanions to aldehydes are reversible reactions, the use of tBuP4, known to generate "naked" anions, led to a satisfying yield with butyraldehyde (56%) which can be increased to 72% upon quenching the reaction mixture with Me_3SiCl. However, the diastereoselectivity, although significantly higher with tBuP4, remained low (44%−64%).

Upon addition of α-sulfonyl carbanions to chiral aldehyde **4** having two extra oxygen atoms in the α- and β-positions, the use of tBuP4 increased the yield and the diastereoselectivity in favor of the *syn*/*anti* isomer (only two isomers, over the four possible, were observed). It also appeared that the extra oxygen atom in the α-position was determinant for obtention of high yields (90−100%) and better diastereoselectivities (de 66−78%).

It must be noted that such diastereoselectivities are the highest ever obtained for this kind of condensation and might well be further improved using more hindered Schwessinger bases.

Experimental Section

Infrared spectra were obtained using $CHCl_3$ as solvent, and peaks are reported in cm^{-1}. ^1H (200 MHz) and ^{13}C (50 MHz) NMR spectra were obtained using $CDCl_3$ as solvent unless otherwise specified (δ in ppm refered to TMS, $\Delta\nu$ and J in Hz, sign of J not given). Melting points were determined on a microscope and are uncorrected. Flash chromatography was performed using Merck silica gel 70−230 mesh, and Kieselgel 60 F_{254} were used for TLC. All the solvents were distilled before use: THF over Na/benzophenone, Et_2O over $LiAlH_4$, CH_2Cl_2 over calcium hydride. Sulfones **1a** (mp 80−82 °C (lit.[12] mp 84 °C), **1b** (mp 141−143 °C (lit.[13] mp 144 °C), and **1c** (mp 122−123 °C (lit.[14] mp 126−127 °C) were prepared according to known procedures. The X-ray diffraction experiments are available as supporting information.

Preparation of Chiral Aldehydes 4, 6, and 7. (*R*)-2,3-Isopropylideneglyceraldehyde (**4**) was prepared from D-mannitol as described in refs 15 and 16. (*S*)-2-(Benzyloxy)propanal (**6**) was prepared from commercialy available (*S*)-ethyl lactate as described in ref 17.

(±)-3-Carbomethoxytetrahydrofuran. A solution of commercially available tetrahydrofuroic acid (0.54 g, 4.65 mmol) and *p*-toluenesulfonic acid (catalytic) in MeOH (10 mL) was stirred under reflux for 3 h. After evaporation of MeOH, the resulting colorless liquid was dissolved in Et_2O (50 mL), washed with water (2 × 40 mL), dried over $MgSO_4$, and concentrated to give a colorless liquid (0.537 g, 89%): ^1H NMR δ 4.02−3.71 (m, 4H), 3.70 (s, 3H), 3.08 (m, 1H), 2.17 (m, 2H); ^{13}C NMR δ 174.0, 70.0, 68.0, 51.7, 43.5, 29.4.

(±)-3-Formyltetrahydrofuran, 7. A 1 M solution of DIBAL in toluene (2.82 mL, 2.82 mmol) was added to a solution of 3-carbomethoxytetrahydrofuran (0.367 g, 2.82 mmol) in a mixture of Et_2O/pentane (1/9, 10 mL) at −78 °C. After the mixture was stirred for 1 h, a saturated solution of diethyl tartrate (6 mL) was added carefully. The stirring was maintained for 1 h, and the resulting two-phase solution was diluted with Et_2O (30 mL). After separation, the aqueous phase was extracted with Et_2O (30 mL), and the combined organic layers were washed with brine (40 mL), dried over $MgSO_4$, and concentrated under reduced pressure at 0 °C. The pure aldehyde was purified by flash chromatography to give a colorless liquid (100 mg, 35%): R_f = 0.16 (Et_2O/hexane 50/50); ^1H NMR δ 9.60 (d, J = 2.5, 1H), 3.92 (AB part of ABX, J_{AB} = 8.5, $J_{AX} \approx$ 4.5, $J_{BX} \approx$ 7.5, $\Delta\nu$ = 79, 2H), 3.87 (m, 2H), 3.05 (m, 1H), 2.16 (m, 2H).

General Procedure for the Synthesis of β-Hydroxy Sulfones 5a−c, 8a, and 9a. β-Hydroxy sulfones were prepared using EtMgBr, nBuLi, or tBuP4 as base according to the procedures described below. Ratio and yields in crude products are given in Tables 1−3. The ^1H NMR data used for analysis of the ratio and assignment of structure are collected in Tables 4 and 5.

Use of EtMgBr as Base. A 1 M solution of ethylmagnesium bromide (1.1 equiv, 0.67 mmol) in Et_2O was added to a solution of sulfone (1.1 equiv, 0.67 mmol) in THF (4 mL) at 0 °C. After formation of a white precipitate (30 min), the mixture was cooled to −78 °C and the desired aldehyde (1 equiv, 0.61 mmol) was added. The reaction was allowed to warm to rt (2 h) and was monitored by TLC. The mixture was then quenched with a saturated solution of NH_4Cl (20 mL). The aqueous phase was extracted with Et_2O (2 × 20 mL), and the combined organic layers were dried over $MgSO_4$ and concentrated. The crude mixture was analyzed by NMR before and after purification by flash chromatography.

Use of nBuLi as Base. A 1.6 M solution of nBuLi in hexane (1 equiv, 1.08 mmol) was added to a solution of sulfone (1 equiv, 1.08 mmol) in THF (5 mL) at −78 °C. The stirring was maintained for 30 min before addition of the desired aldehyde (1 equiv, 1.08 mmol). The reaction was allowed to warm to −50 °C (3 h) and was followed by TLC. The mixture was then quenched with water (20 mL). The aqueous phase was extracted with Et_2O (2 × 50 mL), and the combined organic layers were dried over $MgSO_4$ and concentrated. The crude mixture was analyzed by NMR before and after purification by flash chromatography.

Use of tBuP4 as Base. A 1 M solution of tBuP4 in hexane (1 equiv, 0.1 mmol) was added to a suspension of sulfone (1 equiv, 0.1 mmol) in THF (1 mL) at −78 °C. The resulting yellow solution was further stirred for 15 min before addition of the desired aldehyde (1.2 equiv, 0.12 mmol). After 15−30 min, the mixture was quenched with a 10% HCl solution (5 mL). The aqueous phase was extracted with CH_2Cl_2 (2 × 10 mL), and the combined organic layers were washed with a 10% HCl solution (2 × 10 mL) and with brine (10 mL), dried over $MgSO_4$, and concentrated. The crude mixture was analyzed by NMR before and after purification by flash chromatography.

1-(Ethylsulfonyl)-1-phenylpentan-2-ol, 3a. 3aI: white powder; R_f = 0.40 (Et_2O/hexane 60/40); mp 94−96 °C; IR 3550; ^1H NMR δ 7.57 (m, 2H), 7.45 (m, 3H), 4.82 (dq, J = 2, 3, 3, 3, 1H), 3.98 (d, J = 2, 1H), 3.07 (d, J = 3, OH), 2.75 (q, 2H), 1.40 (m, 4H), 1.22 (t, 3H), 0.87 (t, 3H); ^{13}C NMR δ 130.9, 130.1, 129.3, 128.9, 71.4, 68.4, 46.3, 36.9, 18.9, 13.8, 6.2. Anal. Calcd for $C_{13}H_{20}O_3S$: C, 60.90; H, 7.86. Found: C, 60.65; H, 7.82.

3aII: white powder; R_f = 0.24 (Et_2O/hexane 60/40); mp 76−78 °C; ^1H NMR δ 7.36 (m, 5H), 4.67 (tdd, J = 2.5, 2.5, 6.5, 9, 1H), 4.12 (d, J = 9, 1H), 3.66 (d, J = 2.5, OH), 2.87 (AB part of ABX_3, 2H), 1.59−1.10 (m, 4H), 1.24 (t, CH_3), 0.78 (t, 3H).

1-(Ethylsulfonyl)-1-phenyl-2-[(trimethylsilyl)oxy]pentane, 3a′. Obtained as a mixture (*cf*. Table 1). Deprotection occurred upon chromatography: ^1H NMR δ **3aI′ (minor)** 7.6 (m, 2H), 7.38 (m, 3H), 4.78 (td, J = 3.5, 7, 7, 1H), 3.96 (d, J = 3.5, 1H), 2.73 (AB of an ABX_3, 2H), 1.6−1.15 (m, 4H), 1.22 (t, 3H), 0.88 (t, 3H), 0.15 (s, 9H); **3aII′ (major)** 7.30 (m, 5H), 4.5 (td, J = 2.5, 2.5, 9, 1H), 4.25 (d, J = 9, 1H), 2.6 (AB of an ABX_3, 2H), 1.6−1.1 (m, 7H), 0.7 (t, 3H), 0.0 (s, 9H).

1-(Ethylsulfonyl)-3,4-(isopropylidenedioxy)-1-phenylbutan-2-ol, 5a. 5aI (1*S*,2*R*,3*R*): white powder; R_f = 0.35 (Et_2O/hexane 80/20); mp 108−111 °C; $[\alpha]_D$ = +2 (c = 1.02 , CH_2Cl_2); IR 3550; ^1H NMR δ 7.60 (m, 2H), 7.40 (m, 3H), 4.70 (ddd, J = 1.5, 3, 9, 1H), 4.47 (d, J = 1.5, 1H), 4.00 (AB part of ABX, J_{AB} = 9, $J_{AX} \approx$ 5, $J_{BX} \approx$ 6, $\Delta\nu$ = 25, 2H), 3.52 (ddd, J = 9, 6, 5, 1H), 3.26 (d, J = 3, OH), 2.80 (AB part of ABX_3, 2H), 1.49 (s, 3H), 1.27 (t, 3H), 1.25 (s, 3H); ^{13}C NMR δ 131.2, 130.6, 129.3, 129.1, 128.9, 129.2, 109.8, 74.8, 69.7, 67.6, 67.1, 46.3,

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27.2, 25.4, 6.1. Anal. Calcd for $C_{15}H_{22}O_5S$: C, 57.30; H, 7.05. Found: C, 57.89; H, 6.90.

5aII (1*R*,2*S*,3*R*): white powder; $R_f = 0.26$ (Et_2O/hexane 80/20); ^1H NMR δ 7.60 (m, 2H), 7.40 (m, 3H), 4.65 (dt, $J = 3.5$, 3.5, 5, 1H), 4.20 (q, $J = 5$, 1H), 4.05 (d, $J = 3.5$, 1H), 3.87 (AB part of ABX, $J_{AB} = 8.5$, $J_{AX} \approx 6$, $J_{BX} \approx 6$, $\Delta\nu = 42$, 2H), 2.82 (AB part of ABX_3, 2H), 2.80 (d, $J = 3.5$, OH), 1.44 (s, 3H), 1.33 (s, 3H), 1.21 (t, 3H); ^{13}C NMR δ 130.9, 130.4, 129.5, 129.1, 110.1, 76.9, 70.4, 70.1, 65.8, 46.2, 26.6, 25.2, 5.6.

5aIII: white powder, 90/10 mixture of **5aIII** and **5aIV**; $R_f = 0.17$ (Et_2O/hexane 80/20); ^1H NMR δ 7.41 (s, 5H), 4.67 (dt, $J = 3.5$, 3.5, 9, 1H), 4.05 (d, $J = 9$, 1H), 3.90 (m, 3H), 3.20 (d, $J = 3.5$, OH), 3.14 (q, 2H), 1.40 (s, 3H), 1.36 (t, 3H), 1.26 (s, 3H).

5aIV: white powder, 88/12 mixture of **5aIV** and **5aIII**; $R_f = 0.12$ (Et_2O/hexane 80/20); ^1H NMR δ 7.30 (b s, 5H), 4.35 (ddd, $J = 1.5$, 6, 10, 1H), 4.25 (d, $J = 10$, 1H), 3.53 (m, 3H), 3.17 (d, $J = 6$, OH), 3.00 (q, 2H), 1.39 (s, 3H), 1.28 (t, 3H), 1.15 (s, 3H).

3,4-(Isopropylidenedioxy)-1-phenyl-1-(phenylsulfonyl)-butan-2-ol, 5b. 5bI (1*S*,2*R*,3*R*): white powder; $R_f = 0.31$ (Et_2O/hexane 50/50); mp 118−120 °C; $[\alpha]_D = +54$ ($c = 1.0$, $CHCl_3$); IR 3540; ^1H NMR δ 7.72 (m, 2H), 7.55 (m, 1H), 7.45 (m, 4H), 7.35 (m, 3H), 4.56 (ddd, $J = 1.5$, 2, 9, 1H), 4.43 (d, $J = 1.5$, 1H), 3.96 (AB part of ABX, $J_{AB} = 9$, $J_{AX} \approx 3.5$, $J_{BX} \approx 6$, $\Delta\nu = 31$, 2H), 3.54 (ddd, $J = 3.5$, 6, 9, 1H), 3.42 (d, $J = 2$, OH), 1.26 (s, 3H), 1.21 (s, 3H); ^{13}C NMR δ 137.8, 133.9, 131.6, 129.0, 128.7, 128.6, 128.4, 109.7, 75.1, 71.1, 70.2, 66.9, 27.0, 25.3. Anal. Calcd for $C_{19}H_{22}O_5S$: C, 62.96; H, 6.11. Found: C, 62.78; H, 6.18.

5bII not isolated, the ratio was determined on H2 signals before isolation of **5bI**.

1-(*tert*-Butylsulfonyl)-3,4-(isopropylidenedioxy)-1-phenylbutan-2-ol, 5c. 5cI was isolated pure from the mixture **5cI/5cIII** obtained using tBu-P4 as base, **5cII** and **5cIV** were obtained as mixtures.

5cI (1*S*,2*R*,3*R*): white powder; $R_f = 0.29$ (Et_2O/hexane 50/50); mp 86−88 °C; $[\alpha]_D = +2$ ($c = 0.33$, $CHCl_3$); IR 3550; ^1H NMR δ 7.62 (b s, 2H), 7.40 (m, 3H), 4.74 (ddd, $J = 1.5$, 2, 9.5, 1H), 4.65 (d, $J = 1.5$, 1H), 4.97 (AB part of ABX, $J_{AB} = 8.5$, $J_{AX} \approx 4.5$, $J_{BX} \approx 6$, $\Delta\nu = 24$, 2H), 3.39 (ddd, $J = 4$, 5.5, 9.5, 1H), 3.23 (d, $J = 2$, OH), 1.62 (s, 3H), 1.47 (s, 3H), 1.26 (s, 9H); ^{13}C NMR δ 131.6, 129.9, 129.0, 128.7, 128.4, 109.6, 74.5, 71.3, 67.61, 64.3, 62.9, 27.0, 25.3, 24.0. Anal. Calcd for $C_{17}H_{26}O_5S$: C, 59.53; H, 7.65. Found: C, 59.71 ; H, 7.64.

5cII: $R_f = 0.26$ (Et_2O/hexane 50/50); ^1H NMR δ 7.38 (b s, 5H), 4.70 (d, $J = 10$, 1H), 4.52 (dt, $J = 1.5$, 1.5, 10, 1H), 4.42 (t, $J = 1.5$, OH), 3.95 (t, $J = 6.5$, 1H), 3.74 (t, $J = 6.5$, 1H), 3.55 (tt, $J = 1.5$, 1.5, 6.5, 6.5, 1H), 1.46 (s, 3H), 1.25 (s, 9H), 1.15 (s, 3H).

5cIII: $R_f = 0.19$ (Et_2O/hexane 50/50); ^1H NMR δ 7.47 (m, 2H), 7.37 (m, 3H), 4.52 (dd, $J = 5$, 6.5, 1H), 4.48 (d, $J = 6.5$, 1H), 4.00 (m, 3H), 1.45 (s, 3H), 1.25 (s, 9H), 1.20 (s, 3H).

5cIV: $R_f = 0.12$ (Et_2O/hexane 50/50); ^1H NMR δ 7.58 (b s, 2H), 7.39 (m, 3H), 4.74 (dt, $J = 4$, 6, 6, 1H), 4.25 (d, $J = 4$, 1H), 4.08 (q, $J = 6$, 1H), 3.97 (t, $J = 6$, 1H), 3.72 (t, $J = 6$, 1H), 2.88 (d, $J = 6$, OH), 1.39 (s, 3H), 1.26 (s, 3H), 1.20 (s, 9H).

3-(Benzyloxy)-1-(ethylsulfonyl)-1-phenylbutan-2-ol, 8a. 8aI-(1*R*,2*S*,3*S*): isolated as a 97/3 mixture of **I** and **II** from the tBuP4 experiment; colorless oil; $R_f = 0.33$ (Et_2O/hexane 70/30); $[\alpha]_D = +37$ ($c = 1.74$, $CHCl_3$); IR 3550; ^1H NMR δ 7.52 (m, 2H), 7.32 (m, 8H), 4.62 (ddd, $J = 2$, 3, 8.5, 1H), 4.57 (d, $J = 2$, 1H), 4.50 (d, $J = 11$, 1H), 4.07 (d, $J = 11$, 1H), 3.32 (d, $J = 3$, OH), 3.12 (dq, $J = 6$, 6, 6, 8.5, 1H), 2.78 (q, 2H), 1.30 (d, $J = 6$, 3H), 1.22 (t, 3H); ^{13}C NMR δ 138.3, 131.4, 130.0, 129.1, 128.8, 128.5, 127.85, 127.8, 74.9, 72.2, 70.5, 68.0, 46.3, 16.0, 5.9. Anal. Calcd for $C_{19}H_{24}O_4S$: C, 65.39; H, 6.94. Found: C, 65.31; H, 6.95.

8aII: not isolated; $R_f = 0.33$ (Et_2O/hexane 70/30); ^1H NMR δ 7.6 (m, 2H), 7.45 (m, 3H), ~4.6 (2H, overlaped with **8aI**), 4.47 (d, $J = 11$, 1H), 4.13 (d, $J = 3.5$, 1H), 3.62 (quint, $J = 6$, 1H), ~2.9 (m, 3H, overlaped with **8aI**), 1.35−1.15 (6H, overlaped with **8aI**).

8aIII: isolated; $R_f = 0.22$ (Et_2O/hexane 70/30); ^1H NMR δ 7.32 (m, 10H), 4.80 (dt, $J = 2.5$, 2.5, 10, 1H), 4.47 (s, 2H), 4.05 (d, $J = 10$, 1H), 3.20 (m + q, 3H), 3.07 (d, $J = 2.5$, OH), 1.37 (t, 3H), 1.06 (d, $J = 6$, 3H); ^{13}C NMR δ 137.9, 130.1, 129.6, 129.4, 129.2, 128.5, 127.9, 127.8, 74.7, 71.7, 70.8, 69.3, 49.6, 12.5, 6.7.

8aIV: isolated; $R_f = 0.16$ (Et_2O/hexane 70/30); ^1H NMR δ 7.28 (m, 10H), 4.45 (d, $J = 11$, 1H + AB part of ABXY, 2H), 3.93 (d, $J = 11$, 1H), 3.25 (m, 3H), 3.01 (q, 2H), 1.31 (t, 3H), 1.25 (d, $J = 6$, 3H); ^{13}C NMR δ 137.8, 130.9, 129.9, 129.1, 128.4, 127.9, 127.8, 74.5 , 73.4, 70.8, 70.6, 48.5, 15.5, 6.3.

(±)-3-[2′-(Ethylsulfonyl)-2′-phenyl-1′-ethanol]tetrahydrofuran, 9a. Anal. Calcd for $C_{14}H_{20}O_4S$: C, 59.13; H, 7.08. Found: C, 59.41; H, 7.33. The diastereomers have not been isolated in pure forms but as enriched mixtures of two isomers, **I** + **II** and **III** + **IV**.

9aI: $R_f = 0.13$ (Et_2O/hexane 90/10); ^1H NMR δ 7.60 (m, 2H), 7.35 (m, 3H), 4.71 (ddd, $J = 2$, 2.5, 8, 1H), 4.06 (d, $J = 2$, 1H), 3.78 (m, 4H), 3.41 (d, $J = 2.5$, OH), 2.75 (q, 2H), 2.05 (quint, $J = 8$, 1H), 1.8 (m, 1H), 1.6 (qd, $J = 7$, 7, 7, 10, 1H), 1.21 (t, 3H).

9aII: $R_f = 0.13$ (Et_2O/hexane 90/10); ^1H NMR δ 7.60 (m, 2H), 7.35 (m, 3H), 4.71 (ddd, $J = 2.5$, 3, 8, 1H), 3.87 (d, $J = 2.5$, 1H), 3.70 (m, 4H), 3.44 (d, $J = 3$, OH), 2.75 (q, 2H), 2.1 (quint, $J = 8$, 1H), 1.8 (m, 2H), 1.25 (t, 3H).

9aIII: $R_f = 0.11$ (Et_2O/hexane 90/10); ^1H NMR δ 7.39 (m, 5H), 4.76 (dt, $J = 3$, 3, 9, 1H), 4.13 (d, $J = 9$, 1H), 3.54 (m, 5H), 2.82 (m, 2H) 2.20−1.52 (m, 3H), 1.27 (t, 3H).

9aIV: $R_f = 0.11$ (Et_2O/hexane 90/10); ^1H NMR δ 7.39 (m, 5H), 4.70 (dt, $J = 3$, 3, 9, 1H), 4.07 (d, $J = 9$, 1H), 3.54 (m, 5H), 2.85 (q, 2H) 2.20−1.52 (m, 3H), 1.20 (t, 3H).

(4*S*,5*R*,6*R*)-6-(Ethylsulfonyl)-5-hydroxy-6-phenyl-4-hexanolide, 11. A 1 M solution of $AlMe_3$ in hexane (0.51 mL, 0.51 mmol) was added dropwise to a solution of ethanethiol (0.02 mL, 0.27 mmol) in CH_2Cl_2 (1 mL) at rt. After being stirred for 30 min, this mixture was added to a solution of lactoepoxide **10**[13] (50 mg, 0.24 mmol) in CH_2Cl_2. The reaction was quenched after 2 h with a saturated Na_2SO_4 solution (1 mL). The stirring was maintained for 1 h. The mixture was then diluted in CH_2Cl_2, dried over $MgSO_4$, filtered, and concentrated. The resulting oil (20 mg, 0.075 mmol) was taken up in MeOH (1 mL) and cooled to 0 °C. A buffered (KH_2PO_4, pH = 5) solution of Oxone (50 mg, 0.16 mmol) in H_2O (1 mL) was then added. The reaction was stirred for 1 h, quenched with water, and extracted with Et_2O (2 × 20 mL). The combined organic layers were washed with brine (30 mL), dried over $MgSO_4$, and concentrated. Pure **11** (11 mg, 15%) was recovered after flash chromatography: $R_f = 0.11$ (Et_2O/CH_2Cl_2 20/80); ^1H NMR δ 7.52−7.38 (m, 5H), 4.65 (ddd, $J = 1.5$, 2.5, 10, 1H), 4.50 (d, $J = 10$, 1H), 4.13 (t, $J = 1.5$, 1H), 4.07 (tdd, $J = 1.5$, 1.5, 4, 8, 1H), 2.98−2.65 (m, 4H) 2.44−1.13 (m, 2H), 1.30 (t, 3H). Anal. Calcd for $C_{14}H_{18}O_5S$: C, 56.36; H, 6.08. Found: C, 56.09; H, 6.28.

The author has deposited atomic coordinates for the structure of **5aI** 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.

Acknowledgment. We would like to thank CIBA-GEIGY (Basel) for financial support as well as Dr. M. Lang and Dr. G. Bold from CIBA-GEIGY for their interest and for constructive discussions.

Supporting Information Available: Copies of NMR spectra (11 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.

JO9518967