Bis(chloromethyl) Sulfone and Sulfoxide as Precursors of the Corresponding α,α′-Dianionic Synthons by a Chlorine–Lithium Exchange

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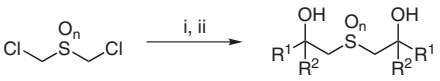
Dedicated to Professor Joaquín Plumet on the occasion of his 60th birthday

Abstract: The DTBB-catalyzed lithiation of bis(chloromethyl) sulfone (**1**) and sulfoxide (**3**) in the presence of different carbonyl compounds [*t*-BuCHO, *c*-C_6H_{11}CHO, PhCHO, Me_2CO, Et_2CO, *n*-Pr_2CO, $(CH_2)_4CO$, $(CH_2)_5CO$, $(c\text{-}C_3H_5)_2CO$, PhCOMe, norbonan-2-one] in THF at –90 ºC, followed by hydrolysis with water at the same temperature led to the formation of the corresponding dihydroxy sulfones (**2**) or sulfoxides (**4**). Representative compounds of both series have been analyzed by X-ray crystallography.

Key words: dimethyl sulfone dianion, dimethyl sulfoxide dianion, DTBB-catalyzed lithiation, chloro–lithium exchange

Generally speaking there are two types of organolithium compounds:[2] non-stabilized and stabilized derivatives. In the second case, the two most common compounds include: (a) organolithium compounds substituted by an electron withdrawing group (e.g. lithium enolates), or (b) organolithium compounds having a second-row element at the α-position, such as phosphorous or sulfur (e.g. ylides). In some cases these two characteristics are operating at the same time, for instance in the case of organolithium intermediates substituted by a sulfone or sulfoxide functionality. Thus, α-lithium sulfone[3,4] or sulfoxide[4] are frequently used in synthetic organic chemistry, especially in carbon–carbon bond forming reactions. However, whereas single metallated species are routinely used, the corresponding dimetallated intermediates are employed far less. In the case of dimethyl sulfone, its direct dilithiation by α,α′-deprotonation with *n*-butyllithium proceeds with low yield and gives a mixture of mono- and disubstituted products in the reaction with an electrophile, such as benzophenone.[5,6] For dimethyl sulfoxide the double deprotonation is even more difficult due to the expected less effective activation of the sulfoxide functionality compared to the sulfone.[4] For the above reasons, we decided to study the generation of the corresponding α,α′-dianion derived from dimethyl sulfone and dimethyl sulfoxide by chlorine–lithium exchange using arene-catalyzed lithiation.[7,8]

The reaction of bis(chloromethyl) sulfone (**1**) with an excess of lithium powder (1:7 molar ratio; theoretical 1:4) and a catalytic amount of 4,4′-di-*tert*-butylbiphenyl (DTBB, 1:0.1 molar ratio, 2.5 mol%) in the presence of a carbonyl compound as electrophile[9] (1:3 molar ratio) in THF at –90 °C gave, after hydrolysis with water at the same temperature, the corresponding dihydroxy sulfones **2**, in general with modest yields, (Scheme 1 and Table 1, entries 1–11).



1: n = 2
3: n = 1

2: n = 2
4: n = 1

Scheme 1 *Reagents and conditions*: (i) Li, DTBB (2.5% molar), E = *t*-BuCHO, *c*-C_6H_{11}CHO, PhCHO, Me_2CO, Et_2CO, *n*-Pr_2CO, $(CH_2)_4CO$, $(CH_2)_5CO$, $(c\text{-}C_3H_5)_2CO$, PhCOMe, norbornan-2-one, THF –90 °C; (ii) H_2O, –90 °C to r.t.

The reaction has to be carried out under the above-mentioned conditions[10] because (a) at higher temperature partial α-protonation occurred giving monosubstituted products **5** as by-products and (b) in the absence of the electrophile,[11] after lithiation, no reaction products were isolated. This behavior can be rationalized by considering that after the first chlorine–lithium exchange a lithiated intermediate **I** (n = 2) is generated. This functionalized organolithium compound[12] is very unstable and in the absence of the electrophile suffers γ-elimination giving the episulfone **V** (n = 2), which after SO_2 elimination affords ethylene.[6b] On the other hand, at higher temperatures hydrogen abstraction from the solvent (α-deprotonation of THF)[13] or from the α-proton of the carbonyl compound used as electrophile competes with the desired reaction. In the latter case, after a second chlorine–lithium exchange and reaction with the electrophile, the 'mono'-substituted product **5** is the main by-product isolated after hydrolysis (Figure 1).

The formation of products **2** is easily explained: after generation of the intermediate **I** (n = 2), rapid reaction with the carbonyl compound present in the reaction medium gave the alkoxide **II** (n = 2). A second lithiation afforded the new organolithium intermediate **III** (n = 2), condensation with a second molecule of the electrophile gave the dialkoxide **IV** (n = 2), which upon hydrolysis gave diols **2** (Figure 1).

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Table 1 Preparation of Compounds **2** and **4**

Entry	Starting material	Electrophile	Product[a]				
			Number	n	R^1	R^2	Yield[b] (%)
1	**1**	*t*-BuCHO	**2a**	2	H	*t*-Bu	54[c]
2	**1**	*c*-C_6H_{11}CHO	**2b**	2	H	*c*-C_6H_{11}	51[c]
3	**1**	PhCHO	**2c**	2	H	Ph	38[c]
4	**1**	Me_2CO	**2d**	2	Me	Me	44
5	**1**	Et_2CO	**2e**	2	Et	Et	51
6	**1**	*n*-Pr_2CO	**2f**	2	*n*-Pr	*n*-Pr	61
7	**1**	$(CH_2)_4CO$	**2g**	2	$(CH_2)_4$		27
8	**1**	$(CH_2)_5CO$	**2h**	2	$(CH_2)_5$		39
9	**1**	(*c*-$C_3H_5)_2CO$	**2i**	2	*c*-C_3H_5	*c*-C_3H_5	44
10	**1**	PhCOMe	**2j**	2	Me	Ph	20[c]
11	**1**	Norbornan-2-one	**2k**	2	–[d]		43
12	**3**	*t*-BuCHO	**4a**	1	H	*t*-Bu	24[e]
13	**3**	Et_2CO	**4e**	1	Et	Et	25 (32)[f]
14	**3**	*n*-Pr_2CO	**4f**	1	*n*-Pr	*n*-Pr	22 (31)[f]
15	**3**	$(CH_2)_5CO$	**4h**	1	$(CH_2)_5$		34
16	**3**	(*c*-$C_3H_5)_2CO$	**4i**	1	*c*-C_3H_5	*c*-C_3H_5	23
17	**3**	Norbornan-2-one	**4k**	1	–[d]		20

[a] All products **2** and **4** were pure (>95% from 300 MHz ^{1}H NMR and/or GLC).
[b] Isolated yield after flash chromatography (silica gel, hexane–EtOAc) based on the starting materials **1** or **3**. Conversion in all cases was >95%.
[c] A ca. 1:1 diastereomeric mixture was obtained (300 MHz ^{1}H NMR or 75 MHz ^{13}C NMR).
[d] See structures **2k** and **4k** in text.
[e] A ca. 1:1 mixture of two of the three possible diastereomers (two meso-isomers and a pair of enantiomers) was obtained (300 MHz ^{1}H NMR or 75 MHz ^{13}C NMR).
[f] GLC yield before chromatographic purification.

In the case of norbornan-2-one as the electrophile the organolithium intermediate attacks the carbonyl group at the *exo*-face, as expected,[14] so the di-*endo* diol **2k** was isolated as a ca. 1:1 diastereomeric mixture (Table 1, entry 11). In addition, and as expected, other prochiral carbonyl compounds (*t*-BuCHO, *c*-C_6H_{11}CHO, PhCHO, PhCOMe) resulted in a ca. 1:1 diastereomeric mixture; it was not possible to separate the components by flash chromatography (Table 1, entries 1–3 and 10).

The X-ray structure of two representative dihydroxy sulfones, **2e** and **2h**, shows that both OH groups are directed to the oxygen atoms of the sulfone of a different molecule, through intermolecular hydrogen bonds (Figure 2, Table 2). The existence of this structural feature would explain the outstanding resistance of compounds **2** to undergo dehydration, to give either the cyclic ether or the corresponding olefinic products, under acidic or basic conditions as well as under Mitsunobu conditions.

In the second part of this paper, we studied the same chemistry using bis(chloromethyl) sulfoxide (**3**). Applying the same methodology, the corresponding dihydroxy sulfoxides **4** were obtained, in general, with lower yields than for the corresponding sulfones (Scheme 1 and Table 1, entries 12–17). In this case, the same type of intermediates **I**–**IV** (n = 1) were presumably formed in the process, the low yields being due to the problems resulting from decomposition of the first intermediate **I** (n = 1) under the reaction conditions (see above). Also the expected di-*endo* diol **4k** was isolated, arising from an expected *exo*-attack of the organolithium intermediate with the electrophile. In addition, the use of pivalaldehyde as electrophile gave a 1:1 mixture of two of the three possible diastereomers **4a** (Table 1, entry 12); currently we can not assign their stereochemistry.

The X-ray analyses of compounds **4e** and **4h** (Figure 3, Table 2) deserves special comment. In the first case, the asymmetric part of the unit cell is composed of two molecules of sulfoxide **4e** with differing orientation of the sulfur–oxygen bond. On the contrary, for **4h** we found disorder between the two possible positions of the oxygen

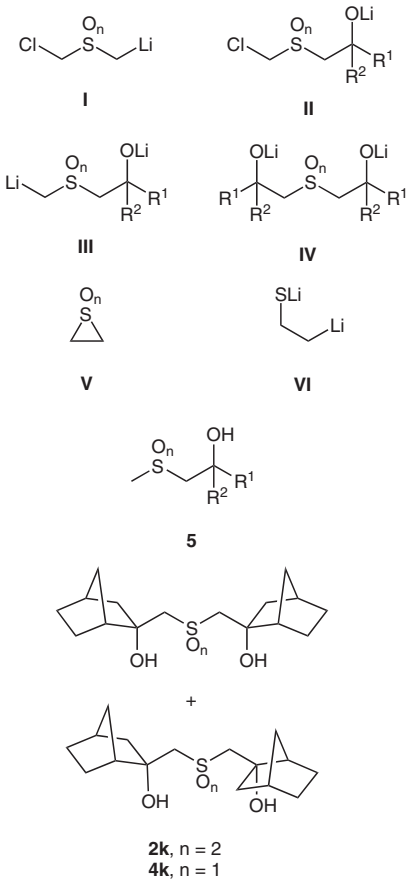

Figure 1

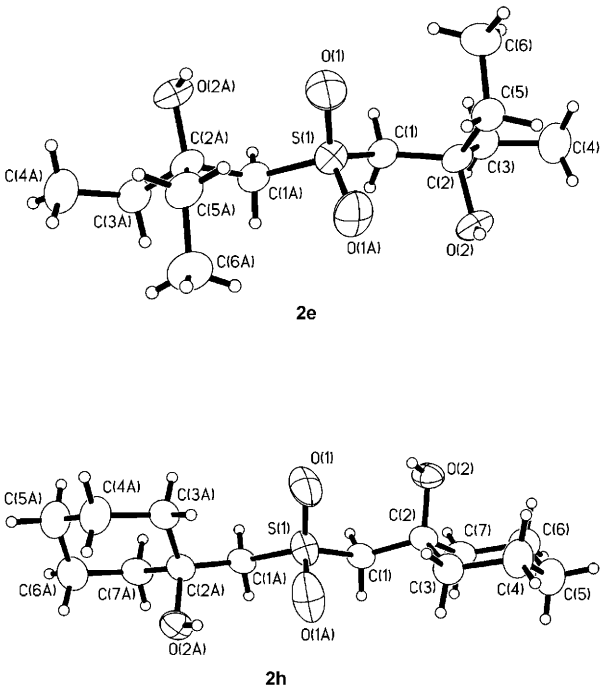

Figure 2

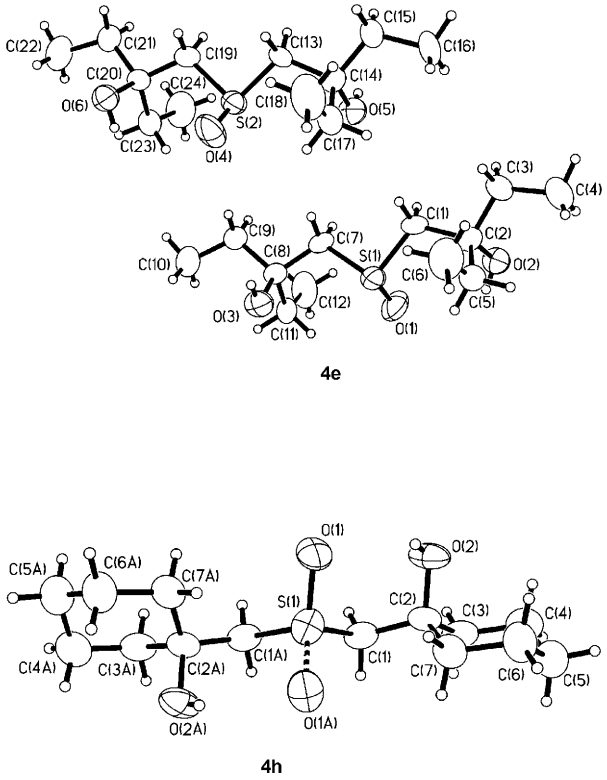

Figure 3

of the sulfoxide [O(1) and O(1A), 50%] in the unit cell. The existence of hydrogen bonds (both inter and intramolecular) makes compounds **4** also very resistant to dehydration under different acidic or basic conditions.

Starting materials **1**[15] and **3**[15,16] were prepared according to the corresponding procedures described in the literature.

Finally, we also studied the lithiation of bis(chloromethyl) sulfide. In all the conditions assayed (various temperatures and Barbier or non-Barbier reaction conditions) we never isolated the expected dihydroxy sulfides, due to the outstanding instability of the initially generated intermediate **I** (n = 0) resulting in episulfide **V** (n = 0). In this case, the thiirane can undergo ring-opening[17] under the reductive lithiation conditions giving a β-thioxide organolithium of type **VI**. This new intermediate is unknown because it is extremely unstable and undergoes β-elimination of lithium sulfide giving, at the end, ethylene.[18]

In conclusion, we have reported here a methodology to generate dianionic α,α′-syntons derived from dimethyl sulfone or dimethyl sulfoxide by a DTBB-catalyzed chlorine–lithium exchange starting from the corresponding dichlorinated materials. This methodology, which is not applicable to the corresponding bis(chloromethyl) sulfide, represents an advantageous alternative to the direct deprotonation of dimethyl sulfone or sulfoxide. In fact, even though only modest yields result (especially for sulfoxide

derivatives **4**), these yields are better than those obtained by direct deprotonation in the case of sulfone derivatives (see above). One merit of this methodology, which only works under Barbier conditions, is that decomposition of intermediate of type **I** by γ-elimination is partially avoided. This side reaction is the cause of the moderate yields obtained. Finally, products **2** and **4** are produced as if the corresponding α,α′-dianions were involved in the process, despite the fact that a step-by-step mechanism is probably involved in the whole process.

For experimental general information see previous publication.[19] X-ray analyses were performed at the University of Alicante. Lithium powder[20] and starting materials **1**[15] and **3**[15,16] were prepared according to the corresponding literature procedures. The diastereomeric ratio was determined by ^{1}H NMR spectroscopy for **2** and by ^{13}C NMR spectroscopy for **4**.

DTBB-Catalyzed Lithiation of Bis(chloromethyl) Sulfone (1) and Sulfoxide (3) and in situ Reaction with Carbonyl Compounds; General Procedure

To a cooled green suspension of Li (49 mg, 7 mmol) and DTBB (26 mg, 0.1 mmol) in THF (2 mL) at –90 °C was slowly added a solution of the corresponding electrophile (3 mmol) and bis(chloromethyl) sulfone (163 mg, 1 mmol) or bis(chloromethyl) sulfoxide (147 mg, 1 mmol) in THF (3 mL). The resulting mixture was stirred for 2 h at the same temperature, then it was hydrolyzed with H_2O (5 mL), and the temperature was allowed to rise to 20 °C. The resulting mixture was extracted with EtOAc (3 × 10 mL). The organic layer was dried over anhyd $MgSO_4$ and concentrated (15 Torr). The resulting residue was then purified by flash chromatography (neutral silica gel, hexane–EtOAc) to give the desired compounds **2** and **4**, which were recrystallized from hexane–Et_2O. Yields are given in Table 1.

1-(2-Hydroxy-3,3-dimethylbutylsulfonyl)-3,3-dimethyl-2-butanol (2a)

Diastereomeric mixture (ca. 1:1).

White crystals; mp 56 °C; t_R 13.24, 13.26 min; R_f 0.39 (hexane–EtOAc, 7:3).

IR (KBr): 3426 (OH), 1289, 1117 (SO_2) cm^{-1}.

^{1}H NMR: δ = 0.95 [s, 36 H, 4 × $(CH_3)_3$], 2.72 (2 br s, 4 H, 4 × OH), 3.17 (br d, J = 14.5 Hz, 4 H, 2 × CH_2), 3.40 (dd, J = 10.4, 14.5 Hz, 4 H, 2 × CH_2), 3.91 (dd, J = 1.2, 10.4 Hz, 4 H, 4 × C*H*OH).

^{13}C NMR: δ = 25.2, 25.3 (CH_3), 35.0, 35.1 (*C*Me_3), 56.7, 57.1 (CH_2SO_2), 73.8, 74.2 (CHOH).

MS: *m*/*z* (%) = 233 ($M^+ - H_2O$ – 15, 1), 191 (18), 84 (21), 83 (100), 57 (32).

MS: *m*/*z* (%) = 233 ($M^+ - H_2O$ – 15, 1), 191 (17), 84 (21), 83 (100), 57 (33).

HRMS: *m*/*z* calcd for $C_{11}H_{23}O_4S$ [M^+ – 15]: 251.1317; found: 251.1319.

HRMS: *m*/*z* calcd for $C_{11}H_{23}O_4S$ [M^+ – 15]: 251.1317; found: 251.1321.

Anal. Calcd for $C_{12}H_{26}O_4S·0.5H_2O$: C, 52.33; H, 9.88; S, 11.64. Found: C, 52.61; H, 9.96; S, 11.57.

1-Cyclohexyl-2-(2-cyclohexyl-2-hydroxyethylsulfonyl)-1-ethanol (2b)

Diastereomeric mixture (ca. 1:1).

White crystals; mp 94 °C; t_R 18.7, 18.9 min; R_f 0.48, 0.36 (hexane–EtOAc, 7:3).

IR (KBr): 3459 (OH), 1288, 1119 (SO_2) cm^{-1}.

^{1}H NMR: δ = 1.03–1.30, 1.38–1.49, 1.60–1.79 (3 m, 44 H, 20 × *c*-CH_2, 4 × *c*-CH), 2.75, 2.76 (2 br s, 4 H, 4 × OH), 3.09–3.48 (m, 8 H, 4 × CH_2SO_2), 3.99–4.05, 4.11–4.21 (2 m, 4 H, 4 × C*H*OH).

^{13}C NMR: δ = 25.7, 25.8, 25.9, 26.1, 27.5, 27.6, 28.5 (*c*-CH_2), 43.3, 43.5 (CH), 58.4, 58.7 (CH_2SO_2), 70.2, 70.5 (COH).

MS: *m*/*z* (%) = 282 ($M^+ - 2 \times H_2O$, 1), 217 (15), 110 (11), 109 (100), 83 (11), 67 (23), 55 (26).

MS: *m*/*z* (%) = 282 ($M^+ - 2 \times H_2O$, 0.31), 217 (18), 110 (17), 109 (100), 83 (12), 67 (19), 55 (18).

HRMS: *m*/*z* calcd for $C_{10}H_{17}O_3S$ [$M^+ - H_2O$ – 83]: 217.0898; found 217.0891.

HRMS: *m*/*z* calcd for $C_{10}H_{17}O_3S$ [$M^+ - H_2O$ – 83]: 217.0898; found 217.0888.

2-(2-Hydroxy-2-phenylethylsulfonyl)-1-phenyl-1-ethanol (2c)[5]

Diastereomeric mixture (ca. 1:1).

White crystals; mp 135 °C; t_R 19.9, 20.0 min; R_f 0.26, 0.21 (hexane–EtOAc, 7:3).

IR (KBr): 3372 (OH), 1280, 1115 (SO_2) cm^{-1}.

Diastereomer 1

^{1}H NMR: δ = 3.09 (br s, 2 H, 2 × OH), 3.28 (dd, J = 1.4, 14.2 Hz, 2 H, CH_2), 3.77 (dd, J = 10.3, 14.2 Hz, 2 H, CH_2), 5.40 (br d, J = 10.3 Hz, 2 H, 2 × CHOH), 7.31–7.39 (m, 10 H, ArH).

^{13}C NMR: δ = 62.6 (CH_2SO_2), 69.4 (COH), 125.7, 128.6, 129.0 (ArCH), 140.9 (ArC).

MS: *m*/*z* (%) = 270 ($M^+ - 2 \times H_2O$, 24), 206 (46), 205 (100), 204 (13), 191 (19), 151 (12), 128 (16), 123 (14), 120 (32), 107 (12), 105 (13), 104 (27), 103 (59), 102 (47), 91 (63), 78 (13), 77 (78), 76 (11), 51 (23).

HRMS: *m*/*z* calcd for $C_{16}H_{14}O_2S$ [$M^+ - 2 \times H_2O$]: 270.0715; found: 270.0695.

Diastereomer 2

^{1}H NMR: δ = 3.05 (br s, 2 H, 2 × OH), 3.39 (dd, J = 1.4, 14.2 Hz, 2 H, CH_2), 3.59 (dd, J = 10.3, 14.2 Hz, 2 H, CH_2), 5.40 (d, J = 10.3 Hz, 2 H, 2 × C*H*OH), 7.31–7.39 (m, 10 H, 10 × ArH).

^{13}C NMR: δ = 62.0 (CH_2SO_2), 69.0 (COH), 125.7, 128.6, 129.0 (ArCH), 140.7 (ArC).

MS: *m*/*z* (%) = 270 ($M^+ - 2 \times H_2O$, 3), 151 (11), 121 (12), 120 (100), 117 (19), 107 (26), 105 (25), 104 (32), 103 (40), 102 (22), 91 (24), 79 (16), 78 (14), 77 (45), 51 (12).

HRMS: *m*/*z* calcd for $C_{16}H_{14}O_2S$ [$M^+ - H_2O$]: 270.0715; found: 270.0718.

Anal. Calcd for $C_{16}H_{18}O_4S$: C, 62.72; H, 5.92; S, 10.47. Found: C, 63.71; H, 6.03; S, 10.23.

1-(2-Hydroxy-2-methylpropylsulfonyl)-2-methyl-2-propanol (2d)

White crystals; mp 65 °C; t_R 11.4 min; R_f 0.03 (hexane–EtOAc, 7:3).

IR (KBr): 3442 (OH), 1304, 1131 (SO_2) cm^{-1}.

^{1}H NMR: δ = 1.47 (s, 12 H, 4 × CH_3), 3.33 (s, 4 H, 2 × CH_2), 3.57 (br s, 2 H, 2 × OH).

^{13}C NMR: δ = 29.8 (CH_3), 65.6 (CH_2), 69.7 (COH).

MS: *m*/*z* (%) = 195 (M^+ – 15, 5), 177 (78), 134 (10), 95 (22), 73 (17), 69 (27), 59 (37), 58 (12), 56 (27), 55 (100).

Table 2 Crystallographic Data of Compounds **2e**, **2h**, **4e**, and **4h**

	2e	**2h**	**4e**	**4h**
Crystallized from	Et_2O	Et_2O	Et_2O	Et_2O
Empirical formula	$C_{12}H_{26}O_4S$	$C_{14}H_{26}O_4S$	$C_{12}H_{26}O_3S$	$C_{14}H_{26}O_3S$
Formula weight ($g \cdot mol^{-1}$)	266.39	290.41	250.39	274.41
Crystal color, habit	colorless, block	colorless, plate	colorless, block	colorless, block
Crystal dimensions (mm)	$0.28 \times 0.19 \times 0.12$	$0.21 \times 0.13 \times 0.04$	$0.15 \times 0.10 \times 0.05$	$0.19 \times 0.17 \times 0.17$
Temperature (K)	296(1)	294(1)	296(1)	296(1)
Crystal system	Orthorhombic	Monoclinic	Triclinic	Monoclinic
Space group	Pbcn	*C*2/*c*	*P*–1	*C*2/*c*
Z	4	4	4	4
Reflections for cell determination	3457	523	483	981
2θ Range for cell determination (°)	6.6–48.8	6.30–46.22	5.0–42.90	6.30–39.4
Unit cell parameters				
a (Å)	21.779(2)	26.148(6)	9.548(2)	26.150(3)
b (Å)	6.4421(6)	6.1670(15)	10.411(2)	6.2016(7)
c (Å)	10.2123(9)	9.432(2)	14.787(3)	9.2772(11)
α, β, γ (°)	90, 90, 90	90, 99.665(4), 90	84.768(5), 89.813(6), 78.687(5)	90, 99.437(2), 90
V ($Å^3$)	1432.8(2)	1499.4(6)	1435.2(5)	1484.1(3)
ρ_{calcd} (gcm^{-3})	1.235	1.287	1.159	1.228
μ (MoK_α) (mm^{-1})	0.228	0.224	0.218	0.217
Transmission factors (min; max)	0.8854; 0.9732	0.866; 0.991	–	0.891; 0.9638
$2\theta_{max}$ (°)	50.18	50.08	50.10	50.08
Total reflexions measured	10916	5751	12083	5851
Symmetry-independent reflections	1277	1325	5074	1312
Reflections with $I>2\sigma(I)$	1085	769	1908	1024
Reflections used in refinement	1277	1325	5074	1312
Parameters refined	81	88	293	91
R(F) [I > 2σ (I) reflections]	0.0372	0.0562	0.0675	0.0447
$wR(F^2)$ (all data)	0.1060	0.1315	0.1087	0.1091
Weighting parameters [a;b][a]	0.0595; 0.3986	0.0503; 0.000	0.009; 0.0	0.0465; 0.8479
Goodness-of-fit	1.053	1.010	0.929	1.042
Secondary extinction coefficients	–	–	–	–
Final Δ_{max}/σ	0.000	0.029	0.000	0.000
Δρ (max; min) ($eÅ^{-3}$)	0.292; –0.213	0.197; –0.233	0.268; –0.297	0.202; –0.171

HRMS: *m/z* calcd for $C_7H_{15}O_4S$ [M^+ – 15]: 195.0691; found: 195.0674.

Anal. Calcd for $C_8H_{18}O_4S{\cdot}0.4H_2O$: C, 44.18; H, 8.71; S, 14.74. Found: C, 44.21; H, 8.14; S, 12.96.

3-(2-Ethyl-2-hydroxybutylsulfonylmethyl)-3-pentanol (2e)[5]
White crystals; mp 65 °C; t_R 13.6 min; R_f 0.24 (hexane–EtOAc, 7:3).

IR (KBr): 3515 (OH), 1288, 1100 (SO_2) cm^{-1}.

^1H NMR: δ = 0.92 (t, *J* = 7.5 Hz, 12 H, 4 × CH_3), 1.29, 1.28 (2 q, *J* = 7.5 Hz, 8 H, 4 × C$H_2$$CH_3$), 3.31 (s, 4 H, 2 × CH_2SO_2), 3.36 (br s, 2 H, 2 × OH).

^{13}C NMR: δ = 7.6 (CH_3), 30.9 (*C*$H_2$$CH_3$), 62.1 ($CH_2SO_2$), 74.4 (COH).

MS: *m/z* (%) = 237 (M^+ – 29, 1), 219 (10), 137 (79), 83 (100), 73 (25), 57 (35), 55 (62).

HRMS: *m/z* calcd for $C_{10}H_{21}O_4S$ [M^+ – 29]: 237.1161; found: 237.1160.

Anal. Calcd for $C_{12}H_{26}O_4S$: C, 54.10; H, 9.84; S, 12.04. Found: C, 54.34; H, 9.85; S, 12.01.

4-(2-Hydroxy-2-propylpentylsulfonylmethyl)-4-heptanol (2f)
Yellow oil; t_R 16.3 min; R_f 0.52 (hexane–EtOAc, 7:3).

IR (film): 3482 (OH), 1307, 1109 (SO_2) cm^{-1}.

^1H NMR: δ = 0.94 (t, *J* = 7.3 Hz, 12 H, 4 × CH_3), 1.23–1.41 (m, 8 H, 4 × C$H_2$$CH_3$), 1.65, 1.67 (2 t, *J* = 9.8 Hz, 8 H, 4 × C$H_2$$CH_2CH_3$), 3.31 (s, 4 H, 2 × CH_2SO_2), 3.50 (br s, 2 H, 2 × OH).

^{13}C NMR: δ = 13.9 (CH_3), 16.6 (*C*$H_2$$CH_3$), 41.2 (*C*$H_2$$CH_2CH_3$), 62.6 ($CH_2SO_2$), 73.8 (COH).

MS: *m/z* (%) = 279 (M^+ – 43, 2), 261 (10), 111 (100), 71 (16), 69 (41), 55 (15).

HRMS: *m/z* calcd for $C_{16}H_{32}O_3S$ [M^+ – H_2O]: 304.2072; found: 304.2049.

1-(1-Hydroxycyclopentylmethylsulfonylmethyl)-1-cyclopentanol (2g)
White crystals; mp 129 °C; t_R 16.1 min; R_f 0.21 (hexane–EtOAc, 7:3).

IR (KBr): 3510 (OH), 1295, 1123 (SO_2) cm^{-1}.

^1H NMR: δ = 1.71 – 1.99 (m, 16 H, 8 × cCH_2), 3.27 (br s, 2 H, 2 × OH), 3.47 (s, 4 H, 2 × CH_2SO_2).

^{13}C NMR: δ = 23.1 (3-*c*-CH_2), 40.1 (2-*c*-CH_2), 64.5 (CH_2SO_2), 79.4 (COH).

MS: *m/z* (%) = 226 (M^+ – 2 × H_2O, 2), 82 (10), 81 (100), 80 (33), 79 (18), 55 (17).

HRMS: *m/z* calcd for $C_{12}H_{18}O_2S$ [M^+ – 2 × H_2O]: 226.1028; found: 226.1033.

1-(1-Hydroxycyclohexylmethylsulfonylmethyl)-1-cyclohexanol (2h)
White crystals; mp 170 °C; t_R 17.5 min; R_f 0.19 (hexane–EtOAc, 7:3).

IR (KBr): 3514 (OH), 1250, 1167 (SO_2) cm^{-1}.

^1H NMR: δ = 1.23–1.85 (m, 20 H, *c*-CH_2), 3.31 (s, 4 H, 2 × CH_2SO_2).

^{13}C NMR: δ = 21.7, 25.1 (3,4-*c*-CH_2), 37.7 (2-*c*-CH_2), 65.2 (CH_2SO_2), 71.1 (COH).

MS: *m/z* (%) = 272 (M^+ – H_2O, 1), 165 (11), 112 (11), 99 (13), 96 (10), 95 (100), 94 (28), 67 (13), 55 (21).

HRMS: *m/z* calcd for $C_{14}H_{26}O_4S$ [M^+]: 290.1552; found: 290.1552.

Anal. Calcd for $C_{14}H_{26}O_4S$: C, 57.90; H, 9.02; S, 11.04. Found: C, 57.87; H, 8.85; S, 12.14.

1,1-Dicyclopropyl-2-(2,2-dicyclopropyl-2-hydroxyethylsulfonyl)-1-ethanol (2i)
White crystals; mp 98 °C; t_R 16.6 min; R_f 0.5 (hexane–EtOAc, 7:3).

IR (KBr): 3414 (OH), 1309, 1123 (SO_2) cm^{-1}.

^1H NMR: δ = 0.38–0.61 (m, 16 H, 8 × *c*-CH_2), 1.00–1.09 (m, 4 H, 4 × CH), 3.05 (br s, 2 H, 2 × OH), 3.54 (s, 4 H, 2 × CH_2SO_2).

^{13}C NMR: δ = 1.3 (*c*-CH_2), 19.3 (CH), 65.2 (CH_2SO_2), 70.2 (COH).

MS: *m/z* (%) = 314 (M^+, 3), 173 (12), 111 (56), 108 (37), 107 (48), 97 (27), 96 (18), 95 (10), 93 (23), 91 (27), 83 (13), 80 (12), 79 (76), 77 (15), 69 (100), 67 (22), 55 (34), 53 (10).

HRMS: *m/z* calcd for $C_{13}H_{21}O_4S$ [M^+ – 41]: 273.1161; found: 273.1174.

Anal. Calcd for $C_{16}H_{26}O_4S{\cdot}0.4H_2O$: C, 59.75; H, 8.40; S, 9.97. Found: C, 59.74; H, 8.64; S, 9.41.

1-(2-Hydroxy-2-phenylpropylsulfonyl)-2-phenyl-2-propanol (2j)
Diastereomeric mixture (ca. 1:1).

White crystals; mp 109 °C; t_R 19.0, 19.2 min; R_f 0.36, 0.34 (hexane–EtOAc, 7:3).

IR (KBr): 3450 (OH), 1306, 1123 (SO_2) cm^{-1}.

Diastereomer 1

^1H NMR: δ = 1.65 (s, 6 H, 2 × CH_3), 2.99 (d, *J* = 14.6 Hz, 2 H, CH_2), 3.21 (d, *J* = 14.6 Hz, 2 H, CH_2), 4.12 (br s, 2 H, 2 × OH), 7.25–7.34 (m, 10 H, 10 × ArH).

^{13}C NMR: δ = 30.0 (CH_3), 65.6 (CH_2SO_2), 72.8 (COH), 124.7, 127.6, 128.5, (ArCH), 144.7 (ArC).

MS: *m/z* (%) = 334 (M^+, 2), 301 (37), 199 (13), 132 (11), 131 (17), 121 (100), 120 (31), 118 (34), 117 (38), 115 (14), 105 (80), 91 (22), 79 (11), 78 (16), 77 (67), 51 (19).

HRMS: *m/z* calcd for $C_{17}H_{19}O_4S$ [M^+ – 15]: 319.1004; found: 319.0989.

Diastereomer 2

^1H NMR: δ = 1.66 (s, 6 H, 2 × CH_3), 3.14 (d, *J* = 14.6 Hz, 2 H, CH_2), 3.29 (d, *J* = 14.6 Hz, 2 H, CH_2), 3.86 (br s, 2 H, 2 × OH), 7.25–7.34 (m, 10 H, 10 × ArH).

^{13}C NMR: δ = 29.3 (CH_3), 65.3 (CH_2), 72.5 (COH), 124.7, 127.6, 128.5 (ArCH), 144.7 (ArC).

MS: *m/z* (%) = 334 (M^+, 1), 302 (10), 301 (33), 199 (14), 132 (11), 131 (15), 121 (100), 120 (31), 118 (31), 117 (34), 115 (12), 106 (98), 91 (19), 79 (11), 78 (15), 77 (67), 51 (19).

HRMS: *m/z* calcd for $C_{17}H_{19}O_4S$ [M^+ – 15]: 319.1004; found: 319.0991.

Anal. Calcd for $C_{18}H_{22}O_4S$: C, 64.64; H, 6.63; S, 9.59. Found: C, 64.71; H, 6.04; S, 10.01.

2-(2-Hydroxybicyclo[2.2.1]hept-2-ylmethylsulfonylmethyl)bicyclo[2.2.1]heptan-2-ol (2k)
Diastereomeric mixture (ca. 1:1).

White crystals; mp 136 °C; t_R 19.1 min; R_f 0.21, 0.06 (hexane–EtOAc, 7:3).

IR (KBr): 3482 (OH), 1301, 1116 (SO_2) cm^{-1}.

^{1}H NMR: δ = 1.29–1.49, 1.54–1.61, 1.92–2.05, 2.26, 2.49 (3 m, 2 br s, 40 H, 16 × *c*-CH_2, 8 × *c*-CH), 3.36 (s, 4 H, 2 × CH_2SO_2), 3.40 (s, 4 H, 2 × CH_2SO_2).

^{13}C NMR: δ = 21.7, 28.2 (*c*-CH_2), 37.2 (*c*-CH), 38.4, 46.1, 46.2 (*c*-CH_2), 46.6, 46.7 (*c*-CH), 65.6 (CH_2SO_2), 77.9 (COH).

MS: *m*/*z* (%) = 296 (M^+ – H_2O, 1), 229 (11), 173 (13), 164 (11), 125 (14), 124 (48), 111 (15), 110 (10), 109 (10), 108 (17), 106 (12), 96 (10), 91 (16), 83 (11), 81 (22), 80 (18), 79 (83), 67 (55), 66 (37), 55 (16).

HRMS: *m*/*z* [M^+ – H_2O] calcd for $C_{16}H_{24}O_3S$: 296.1446; found: 296.1442.

1-(2-Hydroxy-3,3-dimethylbutylsulfinyl)-3,3-dimethyl-2-butanol (4a)

Diastereomeric mixture (ca. 1:1).

White crystals; mp 140 °C; t_R 13.29, 13.51 min; R_f 0.2, 0.3 (EtOAc).

IR (KBr): 3349 (OH), 980 (SO) cm^{-1}.

^{1}H NMR: δ = 0.97 (s, 36 H, 12 × CH_3), 2.82–2.91 (m, 8 H, 4 × CH_2), 3.08 (2 br s, 4 H, 4 × OH), 3.91–3.98 (m, 4 H, C*H*OH).

^{13}C NMR: δ = 25.4, 25.5 (CH_3), 35.0, 35.1, 35.3 (*C*Me_3), 52.2, 54.2, 55.3 (CH_2SO), 73.0, 73.5, 76.1, 77.2 (CHOH).

MS: *m*/*z* (%) = 250 (M^+, 1), 193 (18), 175 (27), 101 (16), 84 (10), 83 (100), 57 (42), 55 (12).

MS: *m*/*z* (%) = 235 (M^+ – 15, 1), 193 (16), 175 (35), 101 (17), 84 (10), 83 (100), 57 (43), 55 (12).

HRMS: *m*/*z* calcd for $C_{12}H_{25}O_2S$ [M^+ – OH]: 233.1575; found: 233.1552.

HRMS: *m*/*z* calcd for $C_{12}H_{25}O_2S$ [M^+ – OH]: 233.1575; found: 233.1581.

3-(2-Ethyl-2-hydroxybutylsulfinylmethyl)-3-pentanol (4e)

White crystals; mp 87 °C; t_R 13.8 min; R_f 0.27 (EtOAc).

IR (KBr): 3317 (OH), 979 (SO) cm^{-1}.

^{1}H NMR: δ = 0.93, 0.94 (2 t, *J* = 7.5 Hz, 12 H, 4 × CH_3), 1.65, 1.77, 1.80 (3 q, *J* = 7.5 Hz, 8 H, 4 × C*H*$_2$$CH_3$), 2.82, 3.03 (2 d, *J* = 13.3 Hz, 4 H, 2 × CH_2SO), 3.32 (br s, 2 H, 2 × OH).

^{13}C NMR: δ = 7.6, 8.1 (CH_3), 31.5, 31.7 (*C*H_2CH_3), 60.8 (CH_2SO), 74.8 (COH).

MS: *m*/*z* (%) = 250 (M^+, 1), 221 (10), 203 (10), 132 (19), 121 (18), 101 (14), 87 (14), 84 (10), 83 (100), 59 (17), 57 (17), 55 (30).

HRMS: *m*/*z* calcd for $C_{12}H_{26}O_3S$ [M^+]: 250.1603; found: 250.1598.

4-(2-Hydroxy-2-propylpentylsulfinylmethyl)-4-heptanol (4f)

White crystals; mp 68 °C; t_R 15.5 min; R_f 0.31 (hexane–EtOAc, 1:1).

IR (KOH): 3365 (OH), 978 (SO) cm^{-1}.

^{1}H NMR: δ = 0.95, 0.96 (2 t, *J* = 7.2 Hz, 12 H, 4 × CH_3), 1.30–1.46, 1.58–1.74 (2 m, 16 H, 4 × C*H*$_2$C*H*$_2$$CH_3$), 2.78, 3.02 (2 d, *J* = 13.3 Hz, 4 H, 2 × CH_2SO), 3.29 (br s, 2 H, 2 × OH).

^{13}C NMR: δ = 14.4, 14.5 (CH_3), 16.6, 17.0 (*C*H_2CH_3), 41.8, 42.0 (*C*H_2CH_2CH_3), 61.7 (CH_2SO), 74.5 (COH).

MS: *m*/*z* (%) = 279 (M^+ – 43, 1), 261 (10), 111 (100), 71 (16), 69 (41), 55 (15).

HRMS: *m*/*z* calcd for $C_{16}H_{34}O_3S$ [M^+ – H_2O]: 306.2229; found: 306.2157.

1-(1-Hydroxycyclohexylmethylsulfinylmethyl)-1-cyclohexanol (4h)

White crystals; mp 136 °C; t_R 17.9 min; R_f 0.2 (EtOAc).

IR (KBr): 3440 (OH), 987 (SO) cm^{-1}.

1H NMR: δ = 1.31–1.91 (m, 20 H, 10 × *c*-CH_2), 2.84, 3.02 (2 d, *J* = 13.1 Hz, 4 H, 2 × CH_2SO), 3.40 (br s, 2 H, 2 × OH).

^{13}C NMR: δ = 21.7, 21.9, 25.3 (3,4-*c*-CH_2), 37.5, 38.4 (2-*c*-CH_2), 63.5 (CH_2SO), 71.5 (COH).

MS: *m*/*z* (%) = 256 (M^+ – H_2O, 1), 113 (26), 99 (10), 95 (100), 81 (11).

HRMS: *m*/*z* calcd for $C_{14}H_{26}O_3S$ [M^+]: 274.1603; found: 274.1654.

Anal. Calcd for $C_{14}H_{26}O_3S$: C, 61.27; H, 9.55; S, 11.68. Found: C, 61.46; H, 9.63; S, 11.68.

1,1-Dicyclopropyl-2-(2,2-dicyclopropyl-2-hydroxyethylsulfinyl)-1-ethanol (4i)

White crystals; mp 77 °C; t_R 16.6 min; R_f 0.4 (hexane–EtOAc, 1:1).

IR (KBr): 3402 (OH), 1025 (SO) cm^{-1}.

^{1}H RMN: δ = 0.34–0.74 (m, 16 H, 8 × *c*-CH_2), 0.91–1.00 (m, 4 H, 4 × CH), 2.95, 3.13 (2 d, *J* = 13.1 Hz, 4 H, 2 × CH_2SO), 3.34 (br s, 2 H, 2 × OH).

^{13}C NMR: δ = 0.0, 0.1, 0.4, 0.6 (*c*-CH_2), 18.7, 20.8 (CH), 63.9 (CH_2SO), 70.9 (COH).

MS: *m*/*z* (%) = 298 (M^+, 1), 239 (13), 197 (15), 173 (35), 155 (13), 139 (10), 111 (54), 108 (29), 107 (12), 93 (23), 91 (12), 79 (26), 69 (100), 67 (9), 55 (13).

HRMS: *m*/*z* calcd for $C_{13}H_{21}O_3S$ [M^+ – 41]: 257.1211; found: 257.1204.

2-(2-Hydroxybicyclo[2.2.1]hept-2-ylmethylsulfinylmethyl)bicyclo[2.2.1]heptan-2-ol (4k)

Diastereomeric mixture (ca. 1:1).

White crystals; mp 136 °C; t_R 19.1 min; R_f 0.27 (EtOAc).

IR (KBr): 3376 (OH), 994 (SO) cm^{-1}.

^{1}H NMR: δ = 1.27–1.49, 1.54–1.63, 1.73–1.80, 2.00–2.18, 2.25–2.31, 2.49–2.54 (6 m, 40 H, 16 × *c*-CH_2, 8 × *c*-CH), 2.82–2.91, (2 m, d at 2.89, *J* = 13.1 Hz, 4 H, 2 × CH_2SO), 3.11–3.19 (m, d at 3.15, *J* = 13.1 Hz, 4 H, 2 × CH_2SO).

^{13}C NMR: δ = 21.1, 21.8, 28.0, 28.4 (*c*-CH_2), 37.0, 37.5 (*c*-CH), 38.1, 38.8, 45.3, 46.2 (*c*-CH_2), 46.3, 47.3, 48.0 (*c*-CH), 61.7, 61.9 (CH_2SO), 78.6, 79.2 (COH).

MS: *m*/*z* (%) = 298 (M^+, 1), 281 (12), 221 (12), 170 (16), 156 (15), 154 (14), 139 (26), 125 (54), 124 (19), 111 (100), 108 (18), 107 (58), 95 (13), 93 (19), 91 (18), 83 (17), 81 (26), 79 (68), 77 (15), 67 (49), 66 (23), 62 (10), 55 (18).

HRMS: *m*/*z* calcd for $C_{16}H_{26}O_3S$ [M^+ – H_2O]: 298.1603; found: 298.1622.

Anal. Calcd for $C_{16}H_{26}O_3S$: C, 64.39; H, 8.78; S, 10.74. Found: C, 64.83; H, 8.88; S, 9.14.

X-ray Crystal Structure Analysis

Diffraction data were taken on a Bruker Smart CCD SMART APEX diffractometer at the University of Alicante. Crystal data are summarized in Table 2 and have been deposited at the Cambridge Crystallographic Data Centre: **2e** (CCDC 262934), **2h** (CCDC 262935), **4e** (CCDC 262936), **4h** (CCDC 262937).

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