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Synthesis and crystal structures of 2-substituted-2-phenylsulfonyloxiranes: evidence for a generalised anomeric effect in 2-phenylsulfonyloxiranes †

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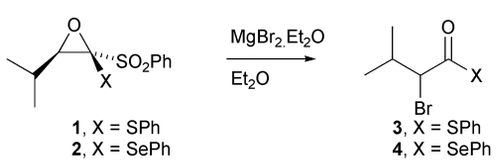
Crystal structures are reported for three new sulfonyloxiranes **5**, **6b** and **7**. Taken together with the structures previously reported for the two sulfonyloxiranes **1** and **2**, these structures provide evidence of the existence of a generalised anomeric effect in 2-phenylsulfonyloxiranes, accounting for the substantial bond asymmetry in the oxirane ring, and thus for the reactivity of these oxiranes towards nucleophiles.

Introduction

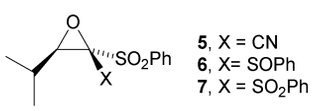
The anomeric effect is a well recognised and general phenomenon in organic chemistry, and occurs when a donor lone pair is antiperiplanar to an acceptor bond.[1–4] The consequences of this effect on conformational equilibria are what is most commonly observed. However, changes in bond lengths, in cases when they can be measured, and associated changes in reactivity, are the most graphic demonstration of the effect.[5]

Some time ago, we reported on the preparation of two 2-phenylsulfonyloxiranes (**1** and **2**), whose structures were determined by X-ray crystallography and each of which reacted, in good yield, with nucleophiles (specifically $MgBr_2$ acting as a source of bromide ions) to give the corresponding α-substituted carbonyl compounds **3** and **4**, respectively (Scheme 1).[6] The regiochemical outcome of this reaction was consistent with the observed lenthening of the C(3)–O bond of the oxirane, and a corresponding shortening of the C(2)–O bond, which ultimately becomes the carbonyl group. The origin of this effect was not, however, established.



Scheme 1

We have now prepared three new derivatives (**5**, **6** and **7**), each bearing a different substituent X, and have been able to determine the molecular structure of each of these compounds crystallographically. A comparison of the bond lengths (specifically C–O and C–SO_2Ph) allows an insight into the geometry of the oxirane ring, and has provided evidence of the origin of the bond asymmetry, namely a generalised anomeric effect involving a lone pair on the oxirane oxygen, and the antibonding orbital of the C–SO_2Ph bond.

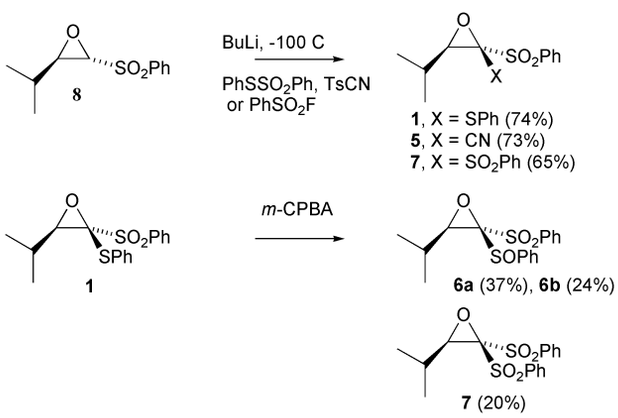


† Electronic supplementary information (ESI) available: PDB files of the crystal structures of compounds **5**, **6b** and **7**. See http://www.rsc.org/suppdata/ob/b3/b301409f/

‡ Deceased.

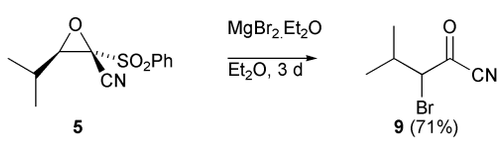
Results and discussion

The 2-cyanooxirane **5** and the 2,2-bis-phenylsulfonyloxirane **7** were prepared by lithiation[6] of the sulfonyloxirane **8**, followed by treatment with *p*-toluenesulfonyl cyanide or phenylsulfonyl fluoride,[7] respectively. Treatment of lithiated **8** with phenyl benzenethiosulfonate gave the oxirane **1**. Oxidation of the phenylsulfonylphenylthiooxirane **1** gave the 2-phenylsulfinyl-2-phenylsulfonyl oxirane **6**, as a mixture of diastereoisomers, together with the overoxidation product, bis-phenylsulfonyloxirane **7** (Scheme 2).



Scheme 2 Preparation of oxiranes.

Treatment of the cyano substituted oxirane **5** with magnesium bromide gave the α-bromo acyl cyanide **9** in good yield (71%) (Scheme 3). Analogous reactions on the oxiranes **6b** and **7** were complicated by the instability of the presumed intermediate acyl sulfoxides and acylsulfones.[8]



Scheme 3

Both derivatives **5** and **7** were crystalline, and amenable to X-ray diffraction analysis, as was one of the separable diastereoisomers of the sulfoxide, **6b**. The molecular structures of the three oxiranes are shown in Figs. 1–3, and the crystallographic data are presented in Table 1.

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Table 1 Crystallographic data

Compound	**5**	**6b**	**7**
Chemical formula	$C_{12}H_{13}NO_3S$	$C_{17}H_{18}O_4S_2$	$C_{17}H_{18}O_5S_2$
Formula weight M	251.3	350.4	366.4
Crystal system	Orthorhombic	Orthorhombic	Orthorhombic
Space group	$Pna2_1$	$Pbca$	$Pbca$
a/Å	12.419(1)	9.117(1)	9.399(1)
b/Å	10.721(1)	14.592(2)	14.683(1)
c/Å	9.853(1)	25.690(4)	25.747(3)
V/Å^3	1311.9(2)	3417.7(8)	3553.2(6)
Z	4	8	8
T/K	295	200	295
μ/mm^{-1}	2.18	0.33	0.32
Reflections measured	3239	3195	3725
Independent reflections	2079	3004	3126
R_{int}	0.040	0.015	0.051
Refined parameters	155	209	217
R (F, $F^2>2\sigma$)	0.061	0.035	0.062
R_w (F^2, all data)	0.161	0.102	0.197

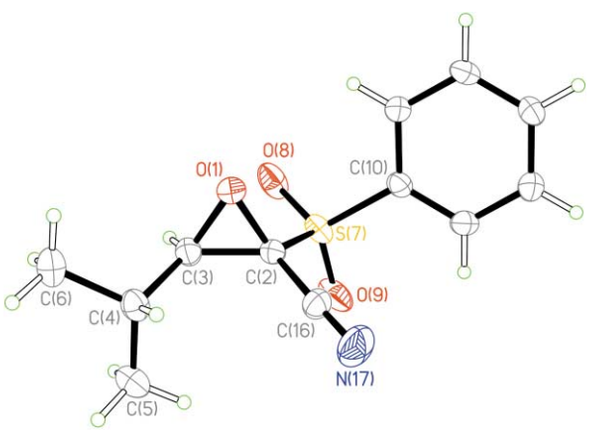

Fig. 1 The molecular structure of **5** with 20% probability ellipsoids and selected atom labels.

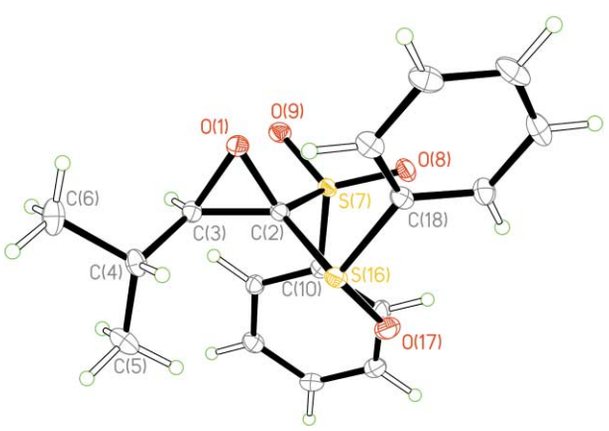

Fig. 2 The molecular structure of **6b**.

The bond lengths are shown in Table 2, which also includes data for compounds **1** and **2**, together with the mean values for these bond types, taken from the Cambridge Structural Database for comparison.[9] As can be seen from the data in Table 2, the carbon–oxygen bond lengths of the oxirane ring are markedly unequal in all of the compounds. In each of the oxiranes, the C(3) carbon–oxygen bond is slightly longer than the mean for all oxirane C–O bonds, which is entirely consistent with this bond being the one that is broken in nucleophilic attack. In the case of the structure of **7**, and in the structure of **6b**, where the C–SOPh bond is also lengthened, the C(3)–O bonds are each very long. This confirms that the nature of the group X does have an influence on the geometry of the oxirane, and suggests that it may also have an influence on the reactivity of the oxirane towards nucleophiles.

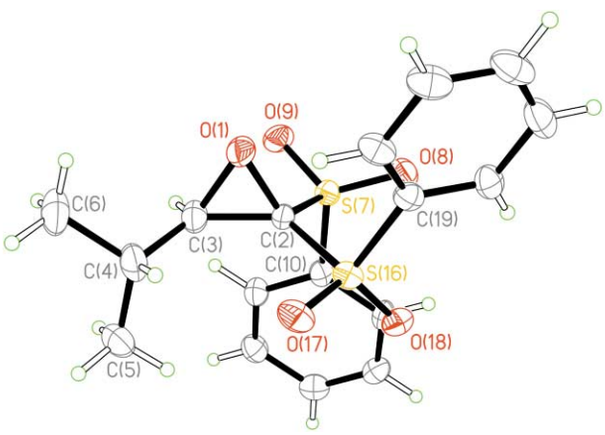

Fig. 3 The molecular structure of **7**.

However, it is most striking that, in every case, the C(2) carbon–oxygen bond is very much shorter than the mean for all oxirane C–O bonds. Moreover, the oxirane C–SO_2Ph bonds are found to be very long in all the oxirane structures. These latter two observations are evidence for an interaction between the oxirane oxygen lone pair and the σ* orbital of the *anti*-carbon–heteroatom bond, which leads to a shortening of the C(2) carbon–oxygen bond and a lengthening of the carbon–phenylsulfonyl bond, as illustrated in Fig. 4. In the case of the 2,2-bisphenylsulfonyloxirane **7**, the longer of the two C(2)–SO_2Ph bonds is that *cis* to the isopropyl substituent. It is possible to speculate that the *cis* phenylsulfonyl group therefore acts as the leaving group, but this has not been tested experimentally.

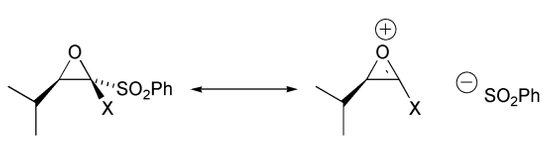

Fig. 4 Generalised anomeric effect in 2-phenylsulfonyloxiranes.

In conclusion, we have presented evidence in this paper that a generalised anomeric effect can be observed in the structures of 2-phenylsulfonyloxiranes. This effect appears to be important in controlling the regiochemical outcome of the reactions of such oxiranes with nucleophiles.

Experimental

General experimental procedures have been previously described.[11] All NMR spectra were recorded in $CDCl_3$ as solvent. J values are given in Hz. In the listing of the mass

Table 2 Bond lengths for 2-phenylsulfonyloxiranes

Oxirane[a,b]	**1**, X = PhS	**2**, X = PhSe	**5**, X = CN	**6b**, X = PhSO	**7**, X = $PhSO_2$	Mean values[9]
Bond	Length	Length	Length	Length	Length	Length
C(2)–O	1.425(4)	1.429(4)	1.405(4)[c]	1.412(3)[c]	1.410(7)[c]	1.446
C(3)–O	1.450(3)	1.457(3)	1.455(4)	1.464(3)	1.468(7)	1.446
C(2)–SO_2 (*trans*)	1.814(2)	1.812(3)	1.804(3)	1.827(2)	1.812(6)	1.786
C(2)–X (*cis*)	1.770(2)	1.918(3)	1.457(4)	1.832(2)	1.829(6)	1.470 (C–CN)
						1.789 (C–S)
						1.818 (C–SO)
						1.786 (C–SO_2)
						1.970 (C–Se)

[a] C(2), C(3) refer to the positions within the oxirane ring, numbering the oxygen as position (1), so C(2) bears the sulfonyl group, whilst C(3) bears the isopropyl group. [b] The label *trans* or *cis* indicates whether the substituent is *trans* or *cis* to the isopropyl group. [c] These extreme values lie below the 5th percentile for all relevant data in the November 2002 release of the Cambridge Structural Database.[10]

spectrum, peaks due to ^{79}Br only are recorded. The phenylsulfonyloxirane **8** was prepared by the literature method,[6] a minor modification of existing methods.[12,13]

(*trans*)-3-(1′-Methylethyl)-2-phenylsulfonyl-2-phenylthiooxirane 1

A solution of (*trans*)-3-(1′-methylethyl)-2-phenylsulfonyloxirane **8** (0.23 g, 1.00 mmol) in THF (10 cm^3) was cooled to −100 °C, *n*-butyllithium (0.82 cm^3, 1.8 mmol, 2.2 M solution in hexanes) was added at below −100 °C, and the mixture was stirred at −100 °C for 13 min. A solution of phenyl benzenethiosulfonate (0.50 g, 2.00 mmol) in THF (0.5 cm^3) was added at −100 °C and the mixture was stirred at −80 °C for 30 min, quenched with aqueous ammonium chloride (5 cm^3, 10%), and allowed to warm to room temperature. The mixture was extracted into ethyl acetate (3 × 10 cm^3) and the combined organic washings were dried and concentrated. The residue was purified by chromatography using 50 : 1 toluene–ethyl acetate as the eluent, yielding (*trans*)-3-(1′-methylethyl)-2-phenylsulfonyl-2-phenylthiooxirane **1** as a white solid (0.25 g, 74%, mp. 86–87 °C; lit.[6] mp. 93–94.5 °C). This compound has previously been synthesised by a similar route using diphenyl disulfide as the electrophile,[6] and also by nucleophilic epoxidation of the corresponding alkene.[6]

(*trans*)-2-Cyano-3-(1′-methylethyl)-2-phenylsulfonyloxirane 5

A solution of (*E*)-3-(1′-methylethyl)-2-phenylsulfonyloxirane **8** (0.23 g, 1.01 mmol) in THF (10 cm^3) was cooled to −100 °C. *n*-Butyllithium (0.83 cm^3, 1.83 mmol, 2.2 M solution in hexanes) was added at below −100 °C, and the solution was then stirred at −100 °C for 12 min. A suspension of tosyl cyanide (0.385 g, 95%, 2.02 mmol) in THF (1 cm^3) was added, and the mixture was stirred for 10 min at −75 °C, quenched with aqueous ammonium chloride solution (10%, 5 cm^3) and allowed to warm to room temperature. The mixture was extracted into ethyl acetate (3 × 10 cm^3) and the combined extracts were dried and concentrated. The residue was purified by chromatography, using 10 : 1 40–60 petrol–ethyl acetate as the eluent, to yield (*trans*)-2-cyano-3-(1′-methylethyl)-2-phenylsulfonyloxirane **5** as a pale yellow solid (mp. 44–46 °C, 0.18 g, 73%). Found: C, 57.8; H, 5.1; N, 5.6; $C_{12}H_{13}NO_3S$ requires C, 57.35; H, 5.2; N, 5.6%; δ_H(200 MHz) 1.16 (3H, d, *J* 7), 1.20 (3H, d, *J* 7), 1.65–1.83 (1H, m), 3.74 (1H, d, *J* 9), 7.63–7.86 (3H, m), 7.97–8.03 (2H, m); ν_{max}(film)/cm^{-1} 3069, 2971, 2936, 2882, 2248, 1350, 1163; *m*/*z* (EI) 141 ($PhSO_2$, 70%), 125 (62), 110 ($M^+ - PhSO_2$, 32), 77 (99), 55 (100).

Oxidation of (*trans*)-3-(1′-methylethyl)-2-phenylsulfonyl-2-phenylthiooxirane 1 with *m*-chloroperoxybenzoic acid (MCPBA)

m-Chloroperoxybenzoic acid (MCPBA) (0.22 g, 85%, 1.1 mmol) was added to a solution of (*trans*)-3-(1′-methylethyl)-2-phenylsulfonyl-2-phenylthiooxirane **1** (0.32 g, 0.95 mmol) in dichloromethane (10 cm^3). After stirring at room temperature for 2 days, the reaction mixture was diluted with dichloromethane (20 cm^3), washed with saturated sodium sulfite solution (2 × 10 cm^3) and brine (10 cm^3), dried and concentrated. The residue was purified by chromatography, using 20 : 1 toluene–ethyl acetate as the eluent, to yield the two diastereoisomeric sulfoxides **6a** and **6b** and (*trans*)-3-(1′-methylethyl)-2,2-bisphenylsulfonyloxirane **7**.

The sulfoxide **6a** (S*R*′, 2*R*′, 3*R*′) with the higher R_f value was obtained as a yellow oil (0.12 g, 37%). Found: MH^+ 351.0834; $C_{17}H_{19}O_4S_2$ requires 351.0944; ν_{max}(film)/cm^{-1} 3059, 2928, 1331, 1159; δ_H (200 MHz) 1.03 (3H, d, *J* 6.5), 1.08 (3H, d, *J* 6.5), 2.33–2.51 (1H, m), 3.68 (1H, d, *J* 10), 7.33–7.53 (7H, m), 7.63–7.77 (3H, m); *m*/*z* (EI) 351 (MH^+, 5%), 209 (2), 141 (66), 125 (81), 77 (79), 43 (100).

The sulfoxide **6b** (S*S*′, 2*R*′, 3*R*′) with the lower R_f value was obtained as a colourless solid (mp 123–128 °C, 0.08 g, 24%). Found: C, 58.3, H, 5.2. $C_{17}H_{18}O_4S_2$ requires C, 58.3, H, 5.2%; ν_{max}(KBr disc)/cm^{-1} 3088, 3067, 3032, 2965, 2934, 2870, 1325, 1154; δ_H (200 MHz) 0.75 (3H, d, *J* 6.5), 1.36 (3H, d, *J* 6.5), 1.93–2.11 (1H, m), 3.76 (1H, d, *J* 3.5), 7.38–7.52 (5H, m), 7.60–7.83 (5H, m); *m*/*z* (EI) 141 ($PhSO_2$, 48%), 125 (91), 91 (95), 77 (100).

3-(1′-Methyl)ethyl-2-bis(phenylsulfonyl)oxirane **7** was obtained as a solid (0.06 g, 20%).

3-(1′-Methylethyl)-2,2-bis(phenylsulfonyl)oxirane 7

A solution of (*trans*)-3-(1′-methylethyl)-2-phenylsulfonyloxirane **8** (0.23 g, 1.00 mmol) in THF (10 cm^3) was cooled to −100 °C. *n*-Butyllithium (0.82 cm^3, 1.80 mmol, 2.2 M solution in hexanes) was added at −100 °C and the solution was then stirred at −100 °C for 13 min. A solution of benzenesulfonyl fluoride (0.24 cm^3, 1.99 mmol) and DMPU (0.24 cm^3, 2.00 mmol) in THF (1 cm^3) was added and the reaction mixture was stirred at −80 °C for 20 min. The mixture was quenched with aqueous ammonium chloride solution (10%, 8 cm^3) and allowed to warm to room temperature. The mixture was extracted with ethyl acetate (3 × 10 cm^3), and the combined organic extracts were dried and concentrated. The residue was purified by chromatography, using 10 : 1 40–60 petrol–ethyl acetate as the eluent, to yield 3-(1′-methylethyl)-2,2-bis(phenylsulfonyl)oxirane **7** as a white solid (mp 125–126 °C, 0.24 g, 65%). Found: C 55.7, H 5.2; $C_{17}H_{18}O_5S_2$ requires C 55.7, H 4.95; δ_H(200 MHz) 0.88 (3H, d, *J* 6.5), 1.18 (3H, d, *J* 6.5), 2.38–2.60 (1H, m), 3.77 (1H, d, *J* 10), 7.43–7.55 (4H, m), 7.62–7.72 (2H, m), 7.76–7.82 (2H, m), 7.91–7.97 (2H, m); δ_C (200 MHz) 18.5, 20.5, 26.0, 70.9, 86.4, 128.85, 129.0, 129.7, 129.85, 134.6, 134.85, 136.7, 138.0; ν_{max}(KBr disc)/cm^{-1} 3067, 3019, 2969, 2957, 1348, 1325, 1157; *m*/*z* (EI) 367 (MH^+, 0.7%), 183 (3), 141 (52), 125 (76), 77 (100).

2-Bromo-1-cyano-3-methylbutan-1-one 9

Magnesium bromide–diethyl ether (0.21 g, 0.81 mmol) was added to a solution of (*E*)-2-cyano-3-(1′-methylethyl)-2-phenylsulfonyloxirane **5** (0.21 g, 0.50 mmol) in diethyl ether (5 cm^3), and stirred at room temperature for 3 days. The reaction

mixture was diluted with 40–60 petrol (30 cm^3) and filtered through a Celite® pad. the residue was washed with further petrol (5 × 10 cm^3), and the washings were combined and concentrated to give 2-bromo-1-cyano-3-methylbutan-1-one **9** as a pale brown oil (0.07 g, 71%). Found: M^+ 188.9777; C_6H_8BrNO requires 188.9764; ν_{max}(film)/cm^{-1} 2975, 2938, 2878, 2224, 1167; δ_H (200 MHz) 1.07–1.23 (6H, m), 2.24–2.47 (1H, m), 4.16 (1H, d, *J* 8.5); *m*/*z* (EI) 190 (MH^+, 12%), 189 (15), 163 (42), 110 (64), 55 (90), 41 (100).

Crystal structure determinations §

Data were collected on a Stoe-Siemens four-circle diffractometer with CuKα (**5**; λ = 1.54184 Å) or MoKα (**6b**, **7**; λ = 0.71073 Å) radiation. No absorption corrections were applied. **6b** and **7** are isomorphous. All samples were colourless.

§ CCDC reference numbers 203327–203329. See http://www.rsc.org/suppdata/ob/b3/b301409f/ for crystallographic data in .cif or other electronic format.

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