Phenylsulphonyl Oxirane: a Versatile Reagent for Organic Synthesis

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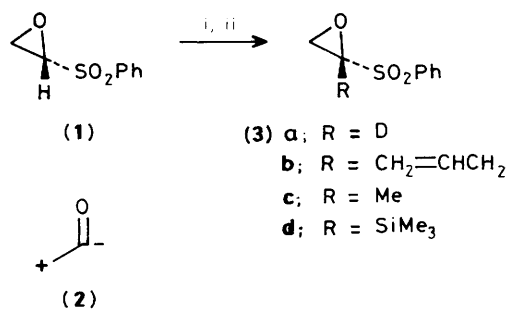Phenylsulphonyl oxirane (1) reacts as the synthetic equivalent of the acetaldehyde dipolar synthon (2).

The preparation of phenylsulphonyl oxirane (1) has recently been described.[1] Due to the well-known anion stabilising properties of the phenylsulphonyl group,[2,3] and to the reactivity of the phenylsulphonyl oxirane group towards nucleophiles,[4] we considered that phenylsulphonyl oxirane (1), a stable crystalline compound, would be a versatile reagent for organic synthesis, functioning as the synthetic equivalent of the acetaldehyde dipolar synthon (2). We now report our preliminary observations which demonstrate that phenylsulphonyl oxirane (1) is a valuable reagent which can function firstly as a nucleophile and then an electrophile.

Treatment of phenylsulphonyl oxirane (1) in tetrahydro-furan (THF) at $-102\,^{\circ}$C with n-butyl-lithium (1.8 mol equiv.) gave a stable pale yellow solution of the corresponding lithio anion. If the solution was allowed to warm above $-100\,^{\circ}$C and then quenched with water, recovery of phenylsulphonyl oxirane (1) was poor and substantial amounts of polymeric material were formed. However, quenching with D_2O (5 equiv. in THF) at $-102\,^{\circ}$C led to good recovery of 1-deuterio-1-phenylsulphonyl oxirane (3a, 83%) (Scheme 1). Due to the instability of the lithio anion, even very reactive electrophiles gave poor yields. For example, addition of allyl bromide, followed by warming to $-90\,^{\circ}$C and quenching gave the corresponding phenylsulphonyl oxirane (3b) in only 33%

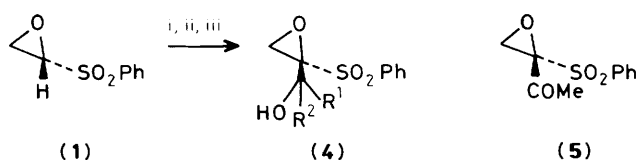**Table 1.** Reactions of lithiated phenylsulphonyl oxirane (1).†

Procedure	Temp./°C	Electrophile	Mol. equiv.	Product	% Yield
A	−102	D_2O	5	(3a)	83
A	−102 to −90	$CH_2=CHCH_2Br$	4	(3b)	33
B	−102	MeI	4	(3c)	82
B	−102	$ClSiMe_3$	2.5	(3d)	100[a]

[a] Yield after Kugelrohr distillation.

(1)   (3) a; R = D
       b; R = $CH_2=CHCH_2$
       c; R = Me
       d; R = $SiMe_3$

(2)

Scheme 1. *Reagents and conditions:* Procedure A: i, Bu^{n}Li (1.8 equiv.); ii, electrophile. Procedure B: i, electrophile; ii, Bu^{n}Li (1.8 equiv.).

Table 2. Reactions of phenylsulphonyl oxirane (1) with carbonyl compounds.‡

| Electrophile (R^1COR^2)			Final		
R^1	R^2	Equiv.	temp./°C	Product	% Yield
Bu^n	H	2.0	−90	(4a)	75
Ph	H	1.5	−70	(4b)	80
Me	H	3.5	−70	(4c)	75
Me	Me	3.0	−65	(4d)	67
$(CH_2)_5$		1.5	−60	(4e)	79
$(CH_2)_4$		3.0	−55	(4f)	77
Me	Et	2.0	−58	(4g)	78
Me	OMe	3.0	−50	(5)	55
Me	NMe_2	3.0	−50	(5)	48

(1)   (4)   (5)

Scheme 2. *Reagents and conditions:* i, Bu^{n}Li (1.25 equiv.), −102 °C; ii, MgBr$_2$ (1.35 equiv., Et$_2$O/toluene solvent), −102 to −90 °C; iii, R^{1}COR^2, −90 °C to temperature indicated in Table 2, then aq. NH$_4$Cl.

yield, with poor recovery of starting material. Use of longer reaction times at −102 °C resulted in poor conversion to (3b). However, we have found that the reactions with iodomethane and chlorotrimethylsilane, leading to the substituted oxiranes (3c) and (3d), respectively, are most efficiently carried out by addition of n-butyl-lithium to a solution of the electrophile and phenylsulphonyl oxirane in THF at −102 °C. This *in situ* anion quenching technique has previously been used with amide bases to generate kinetic silyl enol ethers,[5] although the possibility of using n-butyl-lithium as base, particularly in the

† See scheme 1.

‡ See scheme 2.

Table 3. Reactions of substituted phenylsulphonyl oxiranes with MgBr$_2$.§

Substrate	R	% Yield
(3d)	$SiMe_3$	66
(4c)	CH(OH)Me	68
(4f)	COH(CH$_2$)$_4$	80
(4g)	CMe(OH)Et	62
(5g)	COMe	64

(6)
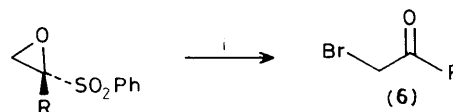
Scheme 3. *Reagents and conditions:* i, MgBr$_2$ (1 M in Et$_2$O/toluene, 1.05 equiv.), 2 h, 20 °C.

presence of iodomethane, has not been recognised before, Table 1.

Our initial results using carbonyl compounds as electrophiles were not promising. Although benzaldehyde did react (in low yield), other carbonyl compounds failed to give the corresponding substituted oxiranes. This problem could be overcome, however, by the addition of a solution of magnesium bromide (1.35 mol. equiv.) in ether/toluene[6] to the lithio anion, generated at −102 °C using n-butyl-lithium (1.25 mol. equiv.), followed by warming to −90 °C and addition of the carbonyl compound (1.5 to 3 mol. equiv.). Subsequent warming to the temperatures indicated in Table 2 by removal of the cooling bath, followed by quenching, afforded the 1-substituted-1-phenylsulphonyl oxiranes (4a)—(4g) and (5) (Scheme 2). Both possible diastereoisomers are produced from aldehydes and unsymmetrical ketones, with one diastereoisomer predominant.¶

It has been known for some time that 2-substituted-1-phenylsulphonyl oxiranes react with magnesium bromide in diethyl ether at room temperature to give α-bromo carbonyl compounds.[7] Clearly, reaction of the 2-unsubstituted oxiranes (1), (3a)—(3d), (4a)—(4g), and (5) with magnesium bromide could constitute a straightforward synthesis of a wide variety of bromomethyl ketones (6) (Scheme 3). We have examined a representative selection of oxiranes, which all react smoothly to give the corresponding bromomethyl ketones (6). The work-up involves addition of pH 7 phosphate buffer and extraction, Table 3.

The present method allows the synthesis of a wide variety of useful intermediates, which are not easily available in such high states of purity by other means.[8] The preparation of 2-bromoacetyl trimethylsilane[9] from 1-phenylsulphonyl-1-

§ See scheme 3.

¶ Although this does not affect subsequent ring-opening reactions, we are now attempting to separate the diastereoisomers in order to assign their stereochemistry.

trimethylsilyl oxirane (**3d**), is particularly noteworthy. Extension of the present chemistry to more substituted phenylsulphonyl oxiranes should provide a valuable addition to present methods for the synthesis of α-substituted carbonyl compounds.

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