Useful New Acyl Anion Equivalents Using Oxiranyl Phenyl Sulphones

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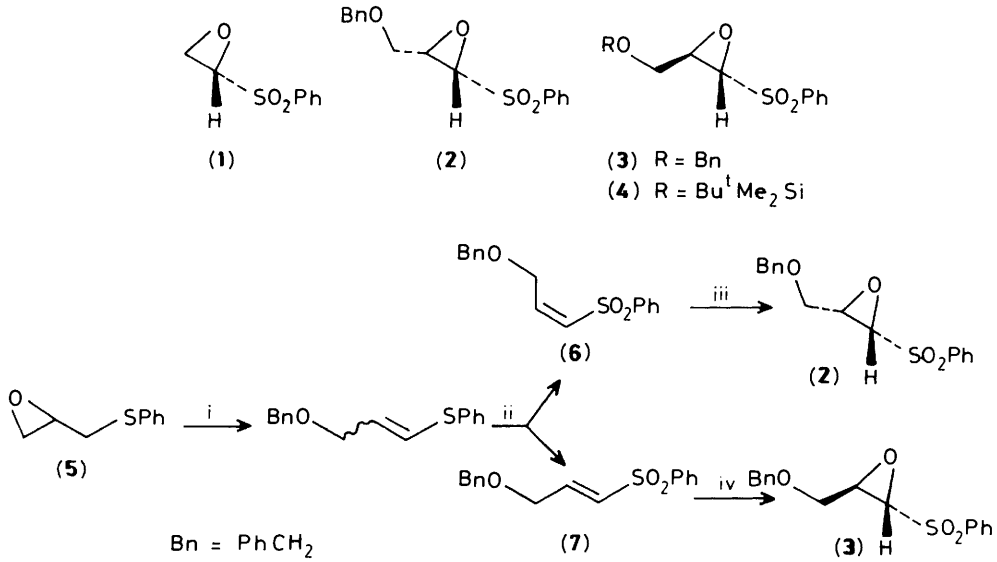
The functionalised oxiranyl phenyl sulphone (**4**) is an effective reagent for the preparation of multifunctional organic compounds.

We have recently reported on the synthetic utility of oxiranyl phenyl sulphone (**1**) as a functionalised acyl anion equivalent.[1] We now report that the functionalised oxiranes (**2**), (**3**), and (**4**) are even more effective acyl anion equivalents,[2] allowing the expeditious synthesis of a wide variety of compounds including 1,2,3-functionalised carbon chains, lactones, and spiroacetals.

cis- and *trans*-3-Benzyloxymethyloxiran-2-yl phenyl sulphones (**2**) and (**3**) were prepared by the route shown in Scheme 1, starting from oxiran-2-ylmethyl phenyl sulphide (**5**).[3] stable,[7] and reacted smoothly on addition of electrophiles at −95 °C, followed by warming to −75 °C over 2 min, to give the *trans* adducts (**9**) (Table 2).

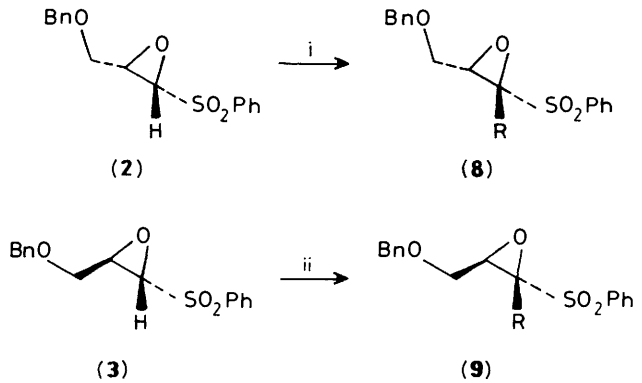
For synthetic purposes, where ease of removal of the hydroxy protecting group is a consideration, we chose to prepare the *trans*-oxirane (**4**) in three steps by the route outlined in Scheme 3; the overall yield was 68%.[8] The lithio anion derived from compound (**4**) was also configurationally stable, and reacted efficiently with a wide range of electrophiles to give the substituted products (**10**) in high yield (Table 3). This should be



Scheme 1. *Reagents and conditions:* i, NaH (60% dispersion in mineral oil) (1 equiv.), THF, reflux, 30 min; benzyl bromide (1.1 equiv.), room temp., 24 h; ii, 3-chloroperoxybenzoic acid (80—90%; 2.6 equiv.), CH_2Cl_2, 0 °C to 20 °C, 2 h, followed by flash chromatography, yielding (**6**), 43%, and (**7**), 40%, from (**5**); iii, Bu^{t}OOH (1.5 equiv.), BuLi (1.1 equiv.), 0.15M (**6**) in THF, −20 °C, 1 h, 93%; iv, Bu^{t}OOH (1.5 equiv.), BuLi (1.1 equiv.), 0.15M (**7**) in THF, −20 °C, 1 h, 88%

Separation of *cis*- and *trans*-3-benzyloxyprop-1-enyl phenyl sulphone (**6**) and (**7**) was effected by careful flash chromatography. Epoxidation of (**6**) and (**7**) using t-butyl hydroperoxide and butyl-lithium[4] was stereospecific, leading to the oxiranes (**2**) and (**3**), respectively, with none of the other isomer detectable by highfield ^{1}H n.m.r. spectroscopy.

Anions derived from (**2**) and (**3**) showed markedly different stability and reactivity (Scheme 2). Deprotonation of the *cis*-oxirane (**2**) with butyl-lithium at −102 °C in tetrahydrofuran was extremely rapid, occurring within 30 s. Immediate addition of electrophiles gave good yields of the corresponding *cis* adducts (**8**), together with traces (< 5%) of the *trans* adducts (**9**) (Table 1).[5] However, if addition of the electrophile was delayed (−102 °C, 3 min), yields were reduced and the proportion of the *trans* adducts (**9**) increased. By contrast, efficient anion formation from the *trans* oxirane (**3**) required addition of butyl-lithium at −95 °C, followed by stirring at the same temperature for 8 minutes.[6] The anion derived from (**3**) was configurationally



Scheme 2. *Reagents and conditions:* i, 0.1M (**2**) in THF, BuLi (1.1 equiv.), −102 °C, 30 s, then electrophile, Table 1; ii, 0.1M (**3**) in THF, BuLi (1.1 equiv.), −95 °C, 8 min, then electrophile, Table 2

Table 1. Reactions of the *cis* oxirane (**2**)

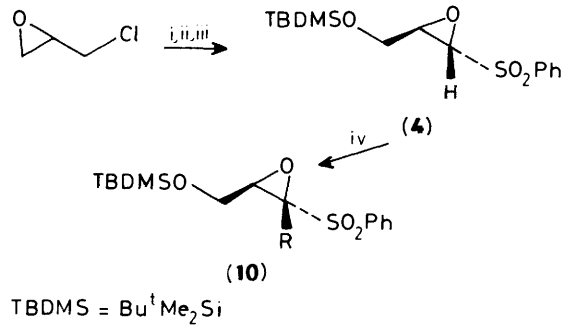
Electrophile	Product	R	Yield (%)[a]
D_2O	(**8a**)	D	85[b]
TMSCl	(**8b**)	TMS	63
MeI	(**8c**)	Me	71
MeCHO	(**8d**)	MeCH(OH)	63

[a] Yields refer to chromatographically purified samples, containing < 5% of the corresponding *trans* adducts (**9**), according to 300 MHz ^{1}H n.m.r. [b] Solvent was THF–pentane (2:1).

Table 2. Reactions of the *trans* oxirane (**3**)

Electrophile	Product	R	Yield (%)[a]
D_2O	(**9a**)	D	80
TMSCl	(**9b**)	TMS	80
MeI	(**9c**)	Me	87
MeCHO	(**9d**)	MeCH(OH)	87

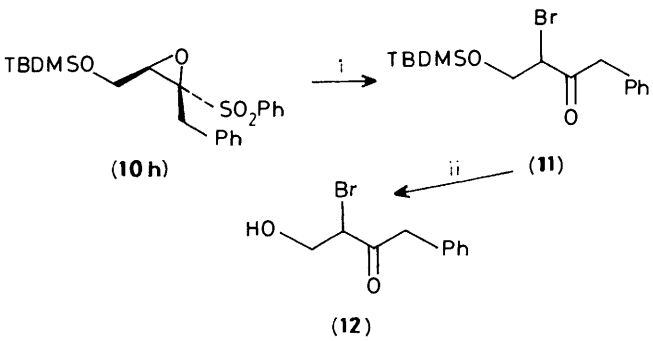
[a] Yields refer to chromatographically purified samples, homogeneous according to 300 MHz ^{1}H n.m.r. spectroscopy.



Scheme 3. *Reagents and conditions:* i, $PhSO_2Na$ (0.5 equiv.), H_2O–DMF (20:1), reflux, 4 h, 90% (based on $PhSO_2Na$); ii, Bu^tMe_2SiCl (1.1 equiv.), imidazole (1.1 equiv.), DMF, room temp., 16 h, 95%; iii, Bu^tOOH (1.5 equiv.), BuLi (1.1 equiv.), THF, −20 °C, 2 h, 80%; iv, 0.1 M (**4**) in THF, BuLi (1.1 equiv.), −95 °C, 8 min, then electrophile, warm to −75 °C over 2 min, 10% aq. NH_4Cl, Table 3

contrasted with the behaviour of the lithio anion derived from the oxirane (**1**), which required addition of magnesium bromide for reaction with carbonyl compounds, and could only be efficiently alkylated with iodomethane.[1]

We have carried out a selection of transformations on the substituted oxiranes (**10**) to demonstrate their utility in synthesis. For example, treatment of compound (**10h**) with magnesium bromide in diethyl ether[9] gave the corresponding



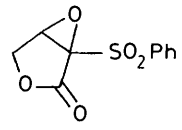
Scheme 4. *Reagents and conditions:* i, $MgBr_2$·Et_2O (1.3 equiv.), Et_2O, 4.5 h; ii, BF_3·Et_2O (1.5 equiv.), CH_2Cl_2, 2.5 h

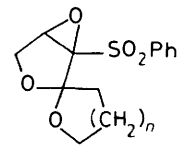
Table 3. Reactions of the *trans* oxirane (**4**)

Electrophile	Product	R	Yield %[a]
D_2O	(**10a**)	D	85
TMSCl	(**10b**)	TMS	84
MeI	(**10c**)	Me	79
MeCHO	(**10d**)	MeCH(OH)	85
PhSSPh	(**10e**)	PhS	76
EtI	(**10f**)	Et	68[b]
BuI	(**10g**)	Bu	75[b]
$PhCH_2Br$	(**10h**)	$PhCH_2$	60[b]
Pr^iCHO	(**10i**)	$Pr^iCH(OH)$	81
$[CH_2]_3CH{=}CHCO$	(**10j**)	$[CH_2]_3{-}CH{=}CH{-}C(OH)$	73
MeOCOCl	(**10k**)	MeO_2C	77
EtO_2CCOCl	(**10l**)	EtO_2CCO	50[c]
$O[CH_2]_3CO$	(**10m**)	$HO[CH_2]_3CO$	76
$O[CH_2]_4CO$	(**10n**)	$HO[CH_2]_4CO$	87

[a] Yields refer to chromatographically purified samples, homogeneous according to 300 MHz ^{1}H n.m.r, except where indicated otherwise. [b] Hexamethylphosphoramide (4 equiv.) was used as co-solvent. [c] Yield of crystallised material.

bromo ketone (**11**) (85%). Removal of the TBDMS protecting group could be efficiently achieved by treatment with boron trifluoride–diethyl ether in dichloromethane to give the bromohydrin (**12**) (70%), without affecting the α-bromo ketone functionality (Scheme 4). Reaction of the adduct (**10k**), derived from methyl chloroformate, with catalytic trifluoromethanesulphonic acid in dichloromethane gave the lactone (**13**) (90%). Treatment of the adduct (**10m**), derived from γ-butyrolactone, with a trace of perchloric acid in acetone led to the spiroacetal[10] (**14**) in 62% overall yield from (**4**).* Analogous treatment of the δ-valerolactone adduct (**10n**) gave the spiroacetal (**15**) in 58% overall yield from (**4**).†





* The spiroacetal (**14**) is a chromatographically separable 10:1 mixture of diastereoisomers.

† The spiroacetal (**15**) is a chromatographically inseparable 2.2:1 mixture of diastereoisomers, as judged by 300 MHz ^{1}H n.m.r. spectroscopy.

Acknowledgements

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