# 3,3-Disubstituted 2-Sulphonyloxaziridines: Synthesis and Observation of Isomeric Nitrogen Invertomers

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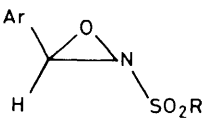
The synthesis of the title compounds from oximes is described; some of these compounds provide the first reported examples of *cis–trans* isomerism in *N*-sulphonyloxaziridines.



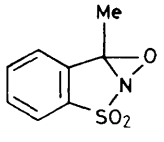
In recent years, 2-sulphonyloxaziridines have been the subject of extensive investigations, primarily by F. A. Davis and his co-workers,[1] and these compounds are now being recognised as synthetically useful neutral oxidants.[2] Despite the extensive study, virtually all the examples reported to date are of type (**1**), prepared from aromatic aldehydes. Until recently, compounds (**2**)[3] and (**3**)[4] appear to have been the only reported examples of 3,3-disubstituted 2-sulphonyloxaziridines bearing an alkyl substitutuent. Recently some 2-sulphonyl-1-oxa-2-azaspiro[2.5]octanes (**4**) have been obtained in this laboratory[5] in low yields by *N*-sulphonylation of 1-oxa-2-azaspiro[2.5]octane,† however more general preparation of 3,3-disubstituted 2-sulphonyloxaziridines from oximes is now described (Scheme 1). Some of the compounds prepared exhibit the phenomenon, previously unreported in 2-sulphonyloxaziridines, of *cis–trans* isomerism at pyramidal nitrogen.

The *N*-sulphonyl imines (**6a—f**) were obtained by rearrangement of the *O*-sulphinyl oximes (**5**), prepared by the reaction of equimolar quantities of oxime, 4-methylbenzenesulphinyl chloride, and triethylamine.[6] Biphasic oxidation of the crude sulphonyl imines (**6**) with 3-chloroperoxybenzoic acid (in $CH_2Cl_2/H_2O$ containing $NaHCO_3$) gave, after flash column chromatography on silica gel, the 2-sulphonyloxaziridines (**7a—f**) in overall yields of 25—50% from the oxime. With the exception of (**6f**), which contains a stabilizing 3-aryl group, the imines (**6**) are highly water-sensitive and are rapidly hydrolysed to give the sulphonamide and the parent ketone. Consequently compounds (**6a—f**) were not purified, but oxidised immediately. Clearly under the biphasic conditions employed, hydrolysis of (**6**) will accompany its oxidation. This is evident from the occurrence of sulphonamide and parent ketone in significant proportions in the crude oxidation product, and accounts for the somewhat lower yield of the oxaziridines (**7**) than of 3-aryl-2-sulphonyloxaziridines (**1**), derived from more hydrolytically stable imines.[3]

Compounds (**7a—f**) gave satisfactory results in elemental analysis and spectral data were in accord with the oxaziridine structure, quaternary $^{13}C$ resonances in the region δ 86—97 being particularly characteristic. The $^{13}C$ n.m.r. spectra of the symmetrically 3-substituted compounds (**7a—c**) show well separated resonances due to α-carbon *cis* and *trans* to the sulphonyl moiety (Table 1), reflecting the fact that nitrogen inversion in 2-sulphonyloxaziridines is slow on the n.m.r.




(**1**)

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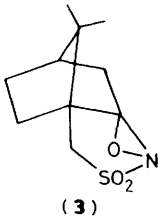
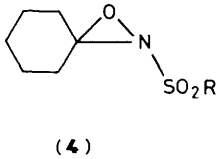
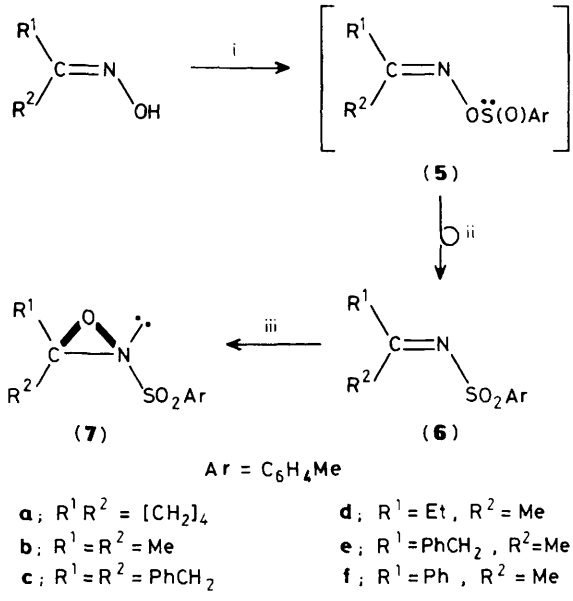



(**3**)




(**4**)




**Scheme 1.** *Reagents and conditions*: i, 4-$MeC_6H_4SOCl$, $Et_3N$, $Et_2O$, −15 °C, 10 min; ii, stir at ambient temperature for 1 h; iii, *N*-sulphonyl imine (10 mmol), 3-$ClC_6H_4CO_3H$ (22 mmol), $NaHCO_3$ (25 mmol), $CH_2Cl_2/H_2O$, 0 °C, 4 h.

**Table 1.** $^{13}C$ N.m.r. chemical shifts (δ) of symmetrically 3-substituted oxaziridines in deuteriochloroform.[a]

| Compound | Ring C | α-$C_c$ | α-$C_t$ |
|---|---|---|---|
| (**7a**) | 96.8 | 29.0 | 34.8 |
| (**7b**) | 87.3 | 19.0 | 26.0 |
| (**7c**) | 91.8 | 35.1 | 41.6 |

[a] α-$C_c$ and α-$C_t$ denote the alkyl α-carbon atoms *cis* and *trans*, respectively, to the *N*-sulphonyl group, assigned on the basis that carbon nuclei *trans* to the nitrogen lone pair are relatively shielded.[7]

† Further work has shown that this method does not appear to be suitable for the preparation of *N*-sulphonyloxaziridines from other dialkyl ketones owing to the instability of the corresponding NH-oxaziridines. Compounds of type (**4**) can be prepared in higher yield by the method described in this communication.

**Table 2.** $^{13}C$ N.m.r. chemical shifts (δ) and isomer ratios for unsymmetrically 3-substituted oxaziridines in deuteriochloroform.

| Compound | Isomer | Ring C | 3-Me | 3-$CH_2$ |
|---|---|---|---|---|
| (**7d**) | Major (77%) | 89.8 | 16.8 | 32.0 |
| | Minor (23%) | 91.7 | 22.6 | 25.7 |
| (**7e**) | Major (79%) | 89.1 | 16.4 | 45.6 |
| | Minor (21%) | 90.2 | 23.0 | 38.4 |
| (**7f**) | Major (73%) | 86.1 | 17.4 | |
| | Minor (27%) | 88.8 | 27.0 | |

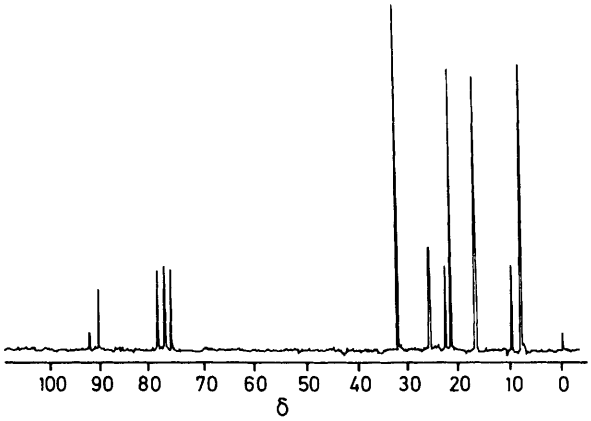
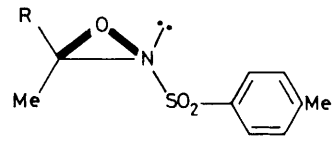



**Figure 1.** 22.5 MHz $^{13}C$ n.m.r. spectrum of (**7d**) in deuteriochloroform showing *cis* (minor) and *trans* (major) isomers.

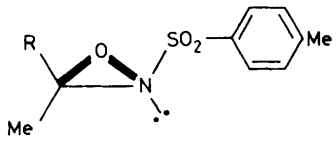
time-scale at ambient temperature. The $^1H$ n.m.r. spectrum of (**7a**) is complex, but (**7b**) shows diastereotopic 3-methyl groups at δ 2.07 and 1.55, and (**7c**) shows two equally intense AB quartets centred at δ 3.65 ($\Delta\delta_{AB}$ 0.45 p.p.m., $J_{AB}$ 14.7 Hz) and 2.84 ($\Delta\delta_{AB}$ 0.38 p.p.m., $J_{AB}$ 14.3 Hz).

The n.m.r. spectra of the unsymmetrically substituted compounds (**7d—f**) shows the presence of two stereoisomers. Thus the $^1H$ n.m.r. spectrum of (**7d**) shows 3-methyl singlets at δ 2.05 and 1.53 in the ratio 1:0.27. Similarly, (**7e**) shows 3-methyl singlets at δ 1.95 and 1.40 in the ratio 1:0.25, and (**7f**) 3-methyl singlets at δ 2.60 and 1.85 in the ratio 1:0.36.

The configurations of the major and minor isomers can be assigned from the $^{13}C$ n.m.r. spectra (Table 2; Figure 1) since it is known from studies of *N*-alkyloxaziridines that the $^{13}C$ resonances of 3-Me or 3-$CH_2$ *trans* to the nitrogen lone pair experience a considerable upfield shift relative to *cis* substituents.[7] These assignments (Table 2) lead to the conclusion that in (**7d—f**) the *seqtrans* configuration (**8**) is favoured over the *seqcis* (**9**). This conclusion is consistent with expectations based on steric considerations, the 2-sulphonyl moiety preferring to reside *cis* to the less bulky 3-substituent (methyl in these cases). The observed equilibrium preference of (**7f**) provides further support for the view that 3-phenyl-2-sulphonyloxaziridines of type (**1**) exist exclusively in the *seqtrans*




(**8**)




(**9**)

configuration in solution,[3] since replacement of the 3-methyl group in (**8**) by hydrogen will further stabilize this isomer by reducing the steric interactions.

The *cis–trans* isomer distribution in these oxaziridines is under thermodynamic (equilibrium) control. Thus dissolution of crystals of recrystallised (**7d—f**) in deuteriochloroform at −50 °C in the n.m.r. probe affords spectra of the major (*trans*) isomer alone. On warming the sample to 0 °C, signals of the minor (*cis*) isomer rapidly develop. Preliminary kinetic measurements on the equilibration of (**7d**) in the n.m.r. probe at −20 °C gave $k = 4.5 \times 10^{-5}$ s$^{-1}$, $\Delta G^{\ddagger} = 19.8$ kcal mol$^{-1}$ (*trans* → *cis*) and $k = 1.7 \times 10^{-4}$ s$^{-1}$, $\Delta G^{\ddagger} = 19.2$ kcal mol$^{-1}$ (*cis* → *trans*). These results compare well with the nitrogen inversion barriers of 19.9—20.6 kcal mol$^{-1}$ determined for *N*-sulphonyloxaziridines of type (**4**) by inversion transfer experiments.[5]

These observations also confirm the view[5] that the nitrogen atom in *N*-sulphonyloxaziridines is not configurationally stable on the chemical time-scale at ambient temperature.

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## References

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