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Trifluoromethyl substituted *N*-phosphinoyloxaziridines: organic oxidants with enhanced reactivity

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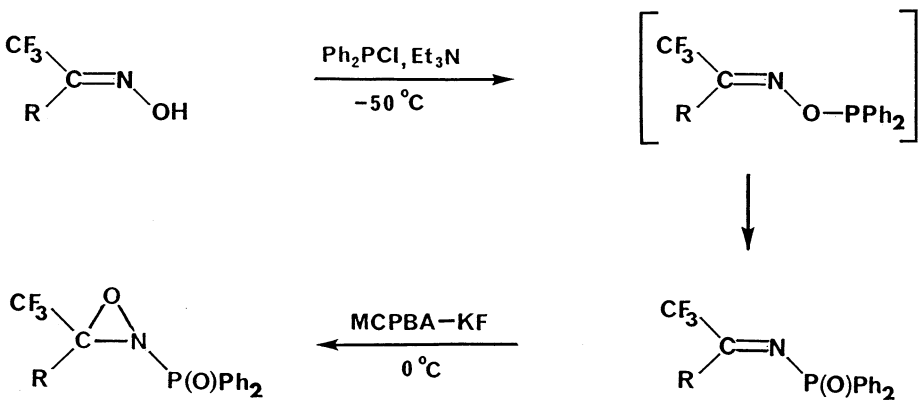
Abstract—New *N*-phosphinoyloxaziridines containing a trifluoromethyl group at the 3-position are reported. Comparative studies of the rate of oxidation of methyl phenyl sulphoxide to methyl phenyl sulphone indicate that the presence of the CF_3 group greatly enhances the oxidising power of *N*-phosphinoyl (and *N*-sulphonyl) oxaziridines.



1a R = CH_3
1b R = 4-FC_6H_4
1c R = C_6H_5

Scheme 1.

We have previously reported methodology for the preparation of *N*-phosphinoyloxaziridines derived from simple alkyl ketones.[1] These compounds are moderately active oxidising agents capable inter alia of converting sulphides to sulphoxides. We now report that the incorporation of a trifluoromethyl group on the ring carbon provides compounds with considerably enhanced oxidising power.

These fluorine-containing *N*-phosphinoyloxaziridines **1a–c** were obtained in a tandem reaction from the oxime of the trifluoromethyl ketone (Scheme 1).[2] Due to the sensitivity of the intermediate *N*-phosphinoyl imines to hydrolysis, it is important that the reagents used are thoroughly dried and that the non-aqueous KF/MCPBA oxidation procedure is used to convert the imines to the oxaziridines **1**. Crude oxaziridines were purified by flash column chromatography on silica gel using hexane–ether as eluant to give crystalline compounds which if necessary can be recrystallised from hexane–ether (avoiding prolonged heating). The structure of compounds **1a–c** was confirmed by their ^1H and ^{13}C NMR spectra and their satisfactory CHN microanalyses. A particular characteristic of these com-

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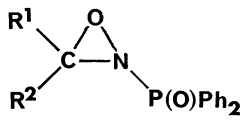
pounds is a quaternary ^{13}C signal in the region δ 82–83 typical of an oxaziridine ring carbon but split into a doublet of quartets by coupling to both phosphorus and fluorine ($^3J_{CP}$ 5.0±0.5 Hz; $^2J_{CF}$ 38.0±0.5 Hz).

Table 1. Second order rate constants (k) for the oxidation of methyl phenyl sulphoxide by oxaziridines at 35.3°C[a]

Compd	R^1	R^2	k (l mol^{-1} s^{-1})	Relative rate
1a	CF_3	CH_3	3.1×10^{-3}	816
1b	CF_3	4-FC_6H_4	9.0×10^{-4}	237
1c	CF_3	C_6H_5	6.7×10^{-4}	176
2a	CH_3	CH_3	3.8×10^{-6}	1
2b	CH_3	1-Naphthyl	2.2×10^{-6}	0.58
3	CH_3	CH_3	2.6×10^{-5}	6.9

[a] Reactions were monitored by ^1H NMR using 0.143 M solutions of methyl phenyl sulphoxide in $CDCl_3$.

The oxidising power of these new fluorine-containing *N*-phosphinoyloxaziridines relative to the 3,3-dimethyl and 3-methyl-3-naphthyl oxaziridines **2a** and **2b** was assessed by kinetic studies of the representative oxidation of methyl phenyl sulphoxide to the sulphone (Table 1). The results in Table 1 show that the trifluoromethyl substituted oxaziridines **1a**–**c** are much more active oxidants than the standard *N*-phosphinoyloxaziridines **2a** and **2b**. The most reactive compound **1a** derived from trifluoroacetone shows a remarkable rate enhancement of about three orders of magnitude over the non-fluorinated analogues **2a** and **2b**. A comparison of oxaziridine **2a** with **2b**, and **1a** with **1b** or **1c**, indicates that the replacement of a 3-methyl group by a 3-aryl group causes a modest reduction in the rate of oxygen transfer.

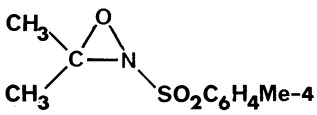


2

The marked effect of the 3-trifluoromethyl group parallels the enhanced oxidising ability of methyl(trifluoromethyl)dioxirane over dimethyldioxirane.[3] Compounds **1a**–**c** are still much weaker oxidants than dioxiranes, but they have the advantage of being reasonably stable off-the-shelf crystalline reagents which can be readily prepared from simple commercially available precursors. The initial by-product of oxidations using oxaziridines **1a** and **2a** is the *N*-diphenylphosphinoyl imine which can be hydrolysed to the highly volatile ketone and the relatively insoluble diphenylphosphinic amide, $Ph_2P(O)NH_2$.

The similar reactivity of comparable *N*-phosphinoyl- and *N*-sulphonyl-oxaziridines suggests a similar mechanism of oxygen transfer. Model ab initio MO calculations on the hypothetical oxidation of sulphoxide H_2SO by the unsubstituted oxaziridine $H_2C[O]NH$ indicate that the oxygen transfer process can be regarded as a nucleophilic attack by sulphur on the electrophilic oxaziridine oxygen, with synchronous cleavage of the N–O and C–O bonds.[4] The imine $H_2C{=}NH$ is effectively the leaving group. There is considerable lengthening of the N–O and C–O bonds in the calculated transition state. The present results appear to be consistent with this mechanism as a CF_3 group on the ring carbon could inductively enhance the electrophilicity of the adjacent oxygen and aid cleavage of the C–O bond.

N-Sulphonyloxaziridines, introduced by Davis,[5] are finding application in organic synthesis as mild aprotic electrophilic oxidants. Compounds **1**, especially **1a**, may offer a more reactive option, readily available from inexpensive starting materials. A comparison of the reactivity of *N*-phosphinoyloxaziridine **2a** with the corresponding *N*-sulphonyloxaziridine **3**[6] indicates that the latter is somewhat more reactive by a factor of about 7:1 (Table 1); however, the new trifluoromethyl substituted *N*-phosphinoyloxaziridines **1a**–**c** are much more reactive than **3**.[7]



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Investigations are underway to explore the synthetic applications of these new *N*-phosphinoyl-oxaziridines. Initial results using the most reactive oxaziridine **1a** indicate that in addition to converting sulphides to sulphoxides and sulphoxides to sulphones, alkenes can be epoxidised and some alcohols can even be oxidised to ketones.[8] These applications will be reported in due course.

Acknowledgements

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References

1. Cook, S. D.; Hamor, T. A.; Jennings, W. B.; Tebbutt, A. A.; Watson, S. P.; Boyd, D. R. *J. Chem. Soc., Perkin Trans. 2* **1991**, 1281.
2. The experimental procedure followed was similar to that reported in Ref. 1. Typically chlorodiphenylphosphine (2.21 g, 10.0 mmol) in dry dichloromethane (30 ml) was added to a solution of the oxime (10.0 mol) and triethylamine (10.1 mmol) in dry hexane (90 ml) cooled to ca. −50°C and under nitrogen. The temperature was then allowed to slowly rise to ca 5°C over 1–2 h. The solution containing the imine was then rapidly filtered to remove the precipitated triethylamine hydrochloride, and immediately added to a stirred suspension of the 2:1 KF/MCPBA complex, prepared from activated anhydrous KF (4.7 g) and a $MgSO_4$ dried solution of commercial 70% MCPBA (10.0 g), in 75 ml dichloromethane. (Camps, F.; Coll, J.;

Messeguer, A.; Pujol, F. *J. Org. Chem.* **1982**, *47*, 5402). The resulting mixture was stirred at 0°C for 3 h and then filtered to remove the KF/MCPBA complex. Rotary evaporation of the filtrate afforded the crude oxaziridine which was purified by flash column chromatography on silica gel eluting with hexane/diethyl ether. These oxaziridines should not be left in contact with silica gel for extended periods. Yields after chromatography were normally in the range 35–50%.

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4. Bach, R. D.; Coddens, B. A.; McDouall, J. W.; Schlegel, H. B.; Davis, F. A. *J. Org. Chem.* **1990**, *55*, 3325.
5. For a review of *N*-sulphonyloxaziridines see: Davis, F. A.; Sheppard, A. C. *Tetrahedron* **1989**, *45*, 5703.
6. Compound **3** has been reported previously, Jennings, W. B.; Watson, S. P.; Boyd, D. R. *J. Chem. Soc., Chem. Commun.* **1988**, 931. **CAUTION**: We have recently experienced sudden violent decomposition of aryl sulphinyl chlorides (the precursor of **3**) during vacuum distillation including disintegration of glassware in a Kugelrohr apparatus. Accordingly, it is recommended that these sulphinyl chlorides should be handled with care and not subjected to heating except possibly on a very small scale with explosion precautions.
7. We have also prepared for comparison purposes the *N*-sulphonyloxaziridine analogous to **1a** from trifluoroacetone oxime and *para*-toluenesulphinyl chloride (**CAUTION**: see note under Ref. 6 above). It is a slightly more reactive oxidant than **1a** (by a factor of ca. 2.5) but its preparation is potentially hazardous.
8. Perfluoroalkyloxaziridines have also been reported to be good oxidants but they appear to be less easily prepared, see: Petrov, V. A.; Resnati, G. *Chem. Rev.* **1996**, *96*, 1809.