Long range activation of a sulfonyl dienophile *via* its oxosulfoxonium ion

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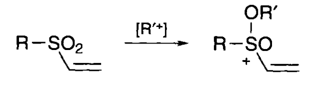
Complexation of BF_3 etherate to the epoxide oxygen of sulfone 1 triggers a reaction cascade that transforms the unreactive dienophile 1 into a diastereoisomeric pair of reactive oxosulfoxonium salts (γ-sultinium ions 6 and 7), corresponding to an activation occurring at five-bond distance from the reactive site.

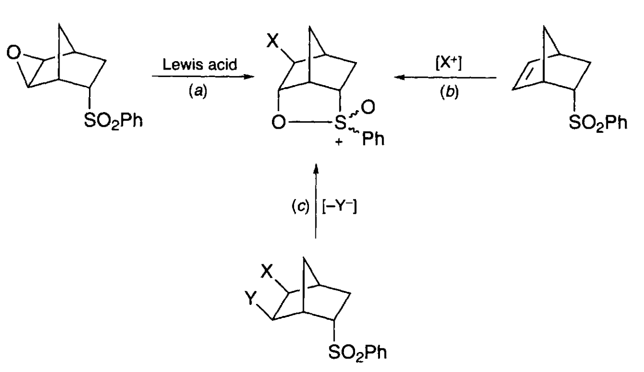
The sulfonyl group is among one of the most useful functionalities in organic synthesis.[1] The generation of its oxosulfoxonium ion, *via* protonation, alkylation, or metal complexation of one of the oxygen atoms is, in principle, a very useful method to improve its efficiency in those reactions where an increase in its electron-withdrawing ability is required. For example, such an activation would be highly welcome in a vinylsulfone used in a Diels–Alder cycloaddition reaction (Scheme 1). The poor nucleophilicity of the oxygen atoms of the sulfonyl group[2] usually prevents formation of the oxosulfonium ion from the sulfone.† This is why Lewis acid catalysed reactions of sulfonyl derivatives are so rarely reported.[1b]

Cadogan[5] and others,[6] as well as ourselves,[7] reported that, at variance with the intermolecular reaction of Scheme 1, the generation of oxosulfoxonium ions can occur intramolecularly, as in the Lewis acid catalysed opening of sulfonyl epoxides [Scheme 2, path (*a*)], in the addition of electrophiles to norbornenyl sulfonyl derivatives [Scheme 2, path (*b*)] and in the solvolysis of suitable norbornanyl halides [Scheme 2, path (*c*)]. Here we report the first practical application of oxosulfoxonium ions as generated *via* route (*a*) of Scheme 2.

On adding a catalytic quantity of BF_3 etherate to a chloroform solution of dienophile **1**‡ and cyclopentadiene (10% excess), conversion of the reagents into a mixture of two out of the possible four adducts **2–5** was observed.§ The reaction carried out without the addition of BF_3 etherate did not afford any adduct, even after a much longer time or at higher temperatures. The activation by the Lewis acid is ascribed to formation of the oxosulfoxonium ions **6** and **7**, generated by complexation to the epoxide oxygen and nucleophilic attack of either one of the two sulfonyl oxygens onto the juxtaposed carbon atom of the oxiranium ring *via* a 5-*exo*-tet cyclization.[8] Each of the so formed oxosulfoxonium ions **6** and **7** is now highly activated towards cycloaddition reactions, thus reacting with cyclopentadiene to form the Diels–Alder adducts. The direct activation of the sulfonyl group by the Lewis acid can be ruled out because, neither reagent **8** bearing no epoxide rings, nor the *exo*-isomer **9**, led to any adduct in the reaction with BF_3 etherate under the reactions conditions where sulfone **1** did react.



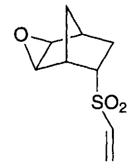
Scheme 1



Scheme 2

Each ion **6** or **7** can give rise to two *endo*- and two *exo*-isomers, derived by the cycloaddition to the *si* or *re* faces of the double bond. The number of possible products was reduced to four because the *si* face of **6** gives the same adduct of the *re* face of **7** and *vice versa*. To distinguish between these four possibilities, several attempts to isolate the sultinium ions **6** and **7** and react them individually with cyclopentadiene were unsuccessful because of the lability of the intermediates. The two oxosulfoxonium ions **6** and **7** could only be detected by NMR spectroscopy carrying out the reaction directly in the NMR tube with sulfur dioxide solvent. The two isomeric cycloadducts could not be separated, but careful NOE experiments allowed the assignment of the two products to one *endo* (either **2** or **3**) and to one *exo* (either **4** or **5**) isomers, while the exact definition of either one of the two *endo*- or *exo*-isomers remains to be defined.

It is also worth noting that other methods aimed at generating oxosulfoxonium ions, such as the addition of electrophiles to **8**, or the solvolysis of properly substituted bromo-derivatives of **8** [Scheme 2, paths (*b*) and (*c*)], failed to give Diels–Alder adducts or gave complex reaction mixtures.



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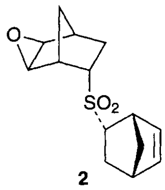

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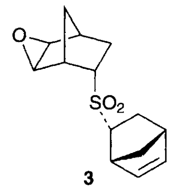

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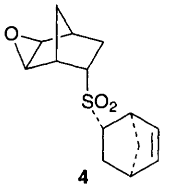

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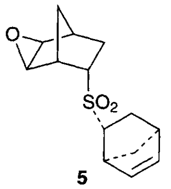

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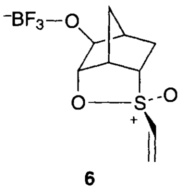

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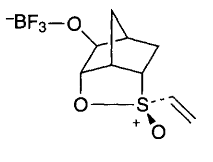

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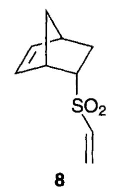

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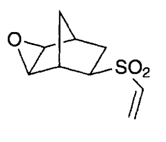

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The reaction of epoxide **1**, appears to be general as a very similar trend of reactivity was also observed with cyclohexa-1,3-diene. The scope of such a reaction is, however, still to be defined.

This work was supported by C.N.R. (Rome).

Footnotes

† Indicative of the poor nucleophilicity of the sulfonyl oxygen is the formation of oxosulfoxonium ions only with diazonium salts[3] and strongly methylating agents.[4]

‡ Cycloaddition of cyclopentadiene to divinyl sulfone in water (0–> 100 °C, 3 h, 85% yield) followed by oxidation with MCPBA in CH_2Cl_2 (reflux, 12 h) gave **1** as an oil (35%). *Spectroscopic data* for **1**: δ_H (400 MHz, $CDCl_3$) 6.63 (1 H, dd, *J* 16.8, 10.0 Hz), 6.41 (1 H, d, *J* 16.8 Hz), 6.16 (1 H, d, *J* 10.0 Hz), 3.62 (1 H, dd, *J* 3.7, 1.7 Hz), 3.32 (1 H, ddd, *J* 10.4, 5.6, 3.6 Hz), 3.28 (1 H, dd, *J* 3.6, 1.6 Hz), 3.00 (1 H, m), 2.67 (1 H, dq, *J* 4.0, 1.6 Hz), 1.92 (1 H, ddd, *J* 12.9, 10.4, 4.0 Hz), 1.70 (1 H, ddd, *J* 12.9, 5.6, 2.7 Hz), 1.60 (1 H, dq, *J* 10.3, 2.7 Hz) and 0.80 (1 H, dm, *J* 10.3 Hz). δ_C (100 MHz, $CDCl_3$) 136.59, 130.25, 64.36, 50.33, 48.09, 40.16, 37.10, 27.13 and 26.40.

§ Isolated as an oily mixture of isomers by silica gel column chromatography (eluent hexane–AcOEt gradient) in 70% yield: δ_H (400 MHz, $CDCl_3$) 6.27 (2 H, dt, *J* 5.7, 3.2 Hz), 6.11 (2 H, td, *J* 5.7, 2.8 Hz), 3.66 (1 H, dq, *J* 3.6, 0.6 Hz), 3.62 (1 H, *J* 3.6, 0.5 Hz), 3.48 (2 H, tdd, *J* 9.0, 4.9, 3.2 Hz), 3.35 (2 H, dm, *J* 9.6 Hz), 3.30 (2 H, dd, *J* 5.7, 3.6 Hz), 3.28 (2 H, tdd, *J* 10.1, 5.5, 3.6 Hz), 3.06 (2 H, m), 3.03 (2 H, m), 2.68 (2 H, m), 2.11 (2 H, m), 1.96 (1 H, dt, *J* 10.2, 4.3 Hz), 1.93 (1 H, dt, *J* 10.2, 4.3 Hz), 1.77 (2 H, m), 1.61 (2 H, m), 1.55 (2 H, m), 1.52 (2 H, m), 1.31 (2 H, dm, *J* 8.7 Hz) and 0.80 (2 H, dm, *J* 10.1 Hz). δ_C (100 MHz, $CDCl_3$) 137.44, 137.35, 131.29, 131.26, 64.03, 63.98, 62.42, 50.41, 49.80, 49.76, 48.29, 48.23, 44.99, 44.71, 42.70, 40.48, 37.21, 28.86, 28.81, 27.19, 27.11, 27.07 and 26.81.

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Received, 30th November 1995; Com. 5/07799K