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Generation and Trapping of α,α'-Dioxosulfines from 1,4-Oxathiine-S-Oxides

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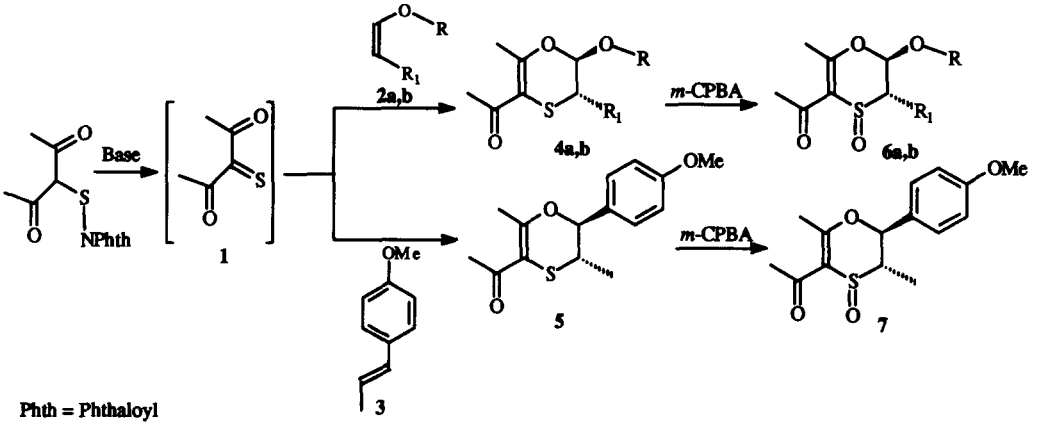
Abstract: *The 1,4-oxathiine-S-oxides 6 when heated at 60 °C in $CHCl_3$ undergo a retro Diels-Alder reaction with generation of α,α'-dioxosulfine 8. This reactive intermediate can be trapped by electron rich dienophiles as well as by dienes. In both cases the cycloaddition reactions show interesting stereoselective features.*

Despite the large number of publications dealing with the synthesis and the reactivity of sulfines[1] there are very few describing α-oxo or α,α'-dioxosulfines.[2-4] These have been obtained by reacting silyl enol ethers with thionyl chloride[2,3] or thermally generated from 1,4,3-oxathiazin-S-oxides[4] and are usually trapped with dienes. We recently published a new method for the preparation of 1,4-oxathiine heterocycles based on the regio and chemospecific inverse electron demanding Diels-Alder reaction of α,α'-dioxothione **1** with the electron-rich dienophilic enol ethers **2a,b** and the activated styrene **3**[5] (Scheme 1).

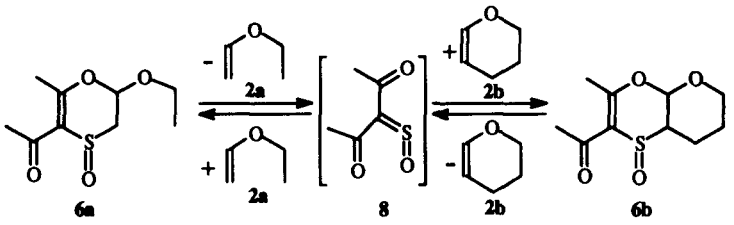


Scheme 1

Oxathiine derivatives have application as antifungal agents[6], but little regarding their reactivity has been published[7], it was decided therefore to undertake the study of the chemical behaviour of heterocycles of type **4a,b** and **5**, prepared as outlined in Scheme 1. In this communication we report the generation of α,α'-dioxosulfines from 1,4-oxathiine-S-oxides with trapping of the sulfines by Diels-Alder type reactions.

Oxidation of sulfides **4a,b** with an equivalent of *m*-CPBA gives the corresponding sulfoxides **6a,b** in 75% and 72% yields, respectively, as single diastereoisomers[8] (Scheme 1). When a solution of sulfoxide **6a** in $CDCl_3$ was heated at 60 °C for 45 hours in the presence of two equivalents of 2,3-dihydro-5H-pyrane **2b** gave the sulfoxide **6b**, which was isolated in 55% yield after flash chromatography (Scheme 2).

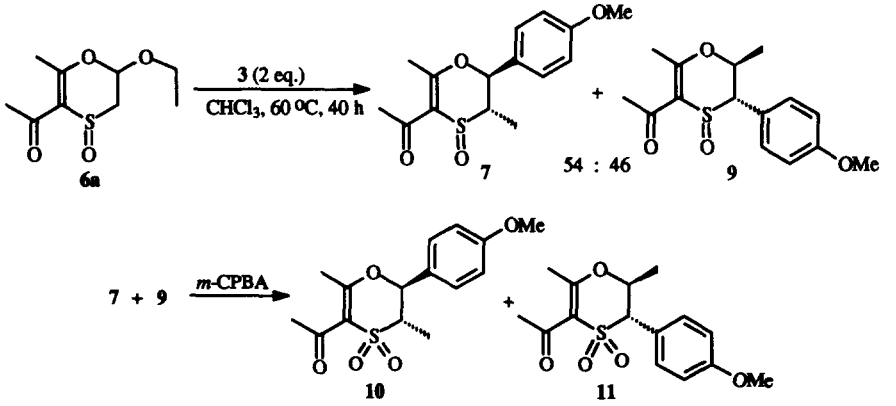
A reasonable hypothesis for the formation of **6b** implies a retro Diels-Alder process of **6a** to give ethyl vinyl ether **2a** and α,α'-dioxosulfine **8**. The latter is trapped as an electron poor diene by the dienophile **2b**. Similarly, by heating oxathiine-S-oxide **6b** in the presence of a four fold excess of ethyl vinyl ether (**2a**) it was possible to isolate the sulfoxide **6a** quantitatively, clearly *via* the formation of the acylsulfine **8** as intermediate (Scheme 2).



Scheme 2

Interestingly the sulfoxides **6a** and **6b** which were obtained as single stereoisomers in the cycloaddition reactions of **8** with enol ethers **2a** and **2b** are identical to those obtained by oxidation of the corresponding oxathiines **4a** and **4b**, thus, in this case, the oxidation of oxathiines and the cycloaddition of sulfine **8** give the same products.

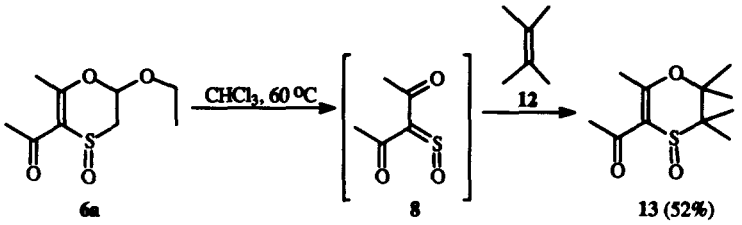
When oxathiine-S-oxide **6a** was heated for 40 hours in the presence of two equivalents of anethole (**3**) resulted in the formation of the two sulfoxides **7** and **9** in a 54:46 ratio and isolated in 62% overall yield. Analysis of their ^1H nmr spectra indicates that the two possible regioisomers have been actually obtained (Scheme 3).[9] This hypothesis was confirmed by the oxidation of a mixture of **7** and **9** with 1.2 equivalents of *m*-CPBA which afforded the isomeric sulfones **10** and **11**. If the reaction of **8** with anethole had produced a mixture of (*E,Z*) and (*E,E*) **7** (or **9**), a single sulfone should have been obtained (Scheme 3).



Scheme 3

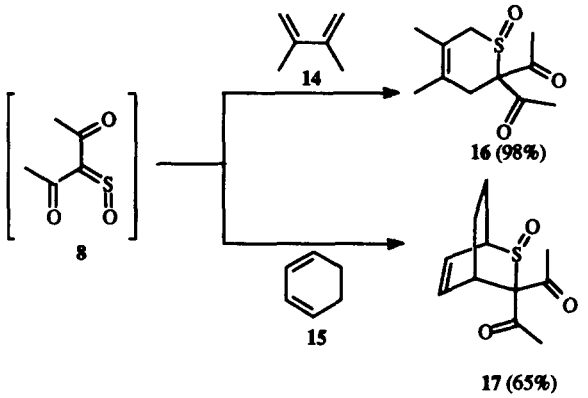
The generation of α,α'-dioxosulfine **8** in the presence of two equivalents of 2,3-dimethyl-2-butene **12** resulted in the isolation of the oxathiine-S-oxide **13** in 52% yield (Scheme 4). No trace of possible thiophilic or

carbophilic "ene" adducts were detected. This represents a further differentiation between the chemical behaviour of acylsulfine **8** and α,α'-dioxothione **1** which, in turn, gave only a thiophilic "ene" adduct when reacted with **12**[5].



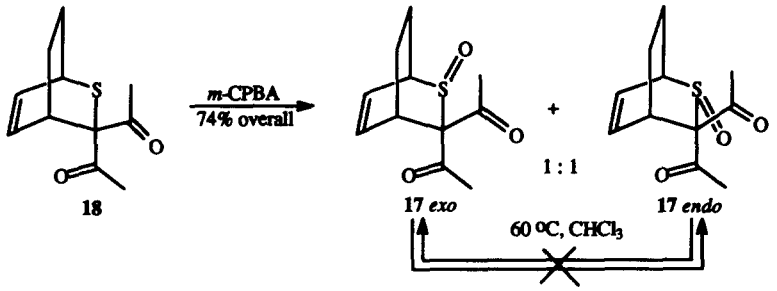
Scheme 4

The dualistic nature of α,α'-dioxosulfines is shown by the reaction of **8** with 2,3-dimethyl-1,3-butadiene **14** or cyclohexadiene **15**. In these cases the dienophilic character of the sulfine predominates and affords the dihydrothiopyran-S-oxides **16** and **17**, respectively (Scheme 5).



Scheme 5

Interestingly the reaction of **8** with **15** leads to the single sulfoxide **17**. The ^{1}H nmr spectrum of this compound seems to indicate an *exo* geometry. The formation of a single sulfoxide as the result of a thermodynamic equilibration between the *exo* and *endo* isomers can be ruled out since no isomerization products were observed after heating both the *exo* and *endo* sulfoxides **17**, which were prepared independently by oxidation of the bicyclic sulfide **18**[10] (Scheme 6).



Scheme 6

It is noteworthy that neither 1,4-oxathiines nor 1,4-oxathiine-S,S-dioxides yielded any trace of the corresponding α,α'-dioxothiones or α,α'-dioxosulfenes when heated at 60 °C. These results indicate that among the 1,4-oxathiine systems bearing a sulfur atom at various oxidation states, only the oxathiine-S-oxides can undergo a retro Diels-Alder reaction under such mild conditions.

The easy availability of the precursors coupled with the very mild conditions required to liberate the α,α'-dioxosulfines make the method described in this communication useful for the study of this interesting class of polyfunctionalised heterocumulenes.

Detailed studies regarding the generality of α,α'-dioxosulfines generation from oxathiine systems, as well as the stereoselectivity observed in their cycloaddition reactions, are currently in progress in our laboratories.

ACKNOWLEDGEMENTS.

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8. An high stereoselectivity was observed in all the oxidations carried out on 1,4-oxathiine systems. However the stereochemistry of the sulfoxides has not been yet determined.
9. All compounds were fully characterised and gave satisfactory elemental analysis. Selected data for sulfoxides **7** and **9** are as follows:
   7: I.R. : 3008 + 2934 (C-H stret.); 1668 (C=O stret.); 1611 + 1513 (C=C stret.); 1252 (C-O stret.); 1026 (S=O stret.) cm^{-1}. ^1H nmr ($CDCl_3$, 200 MHz): 1.36 (d, 3H, X_3 part of an AMX_3 system, $J_{AX}=J_{MX}=6.6$ Hz); 2.44 (s, 3H); 2.53 (s, 3H); 3.55 (d, 1H, A part of an AMX_3 system $J_{AM}=11.0$ Hz, $J_{AX}=6.6$ Hz); 3.81 (s, 3H); 5.10 (dq, 1H, M part of an AMX_3 system $J_{AM}=11.0$ Hz, $J_{MX}=6.6$ Hz); 6.90-7.00 (m, 2H arom.); 7.22-7.32 (m, 2H arom.) δ. ^{13}C nmr ($CDCl_3$, 75 MHz): 18.44; 23.08; 29.09; 55.31; 61.01; 67.83, 114.52; 117.82; 123.31; 130.88; 160.23; 171.61; 194.44 δ. Elemental analysis calcd. for $C_{15}H_{18}O_4S$: C, 61.20; H, 6.16. Found: C, 61.50; H, 6.20.
   9: I.R. : 3010 + 2934 (C-H stret); 1668 (C=O stret.); 1609 + 1513 (C=C stret.); 1246 (C-O stret.); 1028 (S=O stret.) cm^{-1}. ^1H nmr ($CDCl_3$, 200 MHz): 1.14 (d, 3H, X_3 part of an AMX_3 system, $J_{AX}=J_{MX}=7.0$ Hz); 2.43 (s, 3H); 2.61 (s, 3H); 2.83 (dq, 1H, M part of an AMX_3 system $J_{AM}=11.0$ Hz, $J_{MX}=7.0$ Hz); 3.83 (s, 3H); 5.18 (d, 1H, A part of an AMX_3 system $J_{AM}=11.0$ Hz); 6.90-7.00 (m, 2H arom.); 7.22-7.32 (m, 2H arom.) δ. ^{13}C nmr ($CDCl_3$, 75Mz): 11.75; 22.97; 29.20; 50.63; 55.31; 74.34; 114.36; 117.32; 127.24; 129.03; 160.40; 171.77; 194.43 δ.
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