Generation of a Thioaldehyde S-Oxide (Sulphine) by Retro-Diels–Alder Reactions

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Cycloadducts of the thioaldehyde S-oxide (sulphine), ethyl thioxoacetate oxide, with anthracene, cyclopentadiene, and the alkaloid thebaine (7), dissociate when heated (60–111 °C), releasing the sulphine, which is trapped *in situ* by cycloaddition to various conjugated dienes.

Sulphines, the S-oxides of thiocarbonyl compounds, have recently been the subject of intensive study.[1–4] We report here a new method for generating the most reactive, and labile, class of sulphines, the thioaldehyde S-oxides. Thioaldehydes, for example ethyl thioxoacetate,[5] $EtO_2C \cdot CHS$, form Diels–Alder adducts with anthracene,[5,6] cyclopentadiene,[7] and the alkaloid thebaine[5] (7). All three types of adduct dissociate readily, at 80—111 °C; it seemed likely therefore that the corresponding sulphoxides would behave similarly, releasing thioaldehyde S-oxides. This has proved so for the cycloadducts (1a), (1b), (4), (5), and (6) of (E)-ethyl thioxoacetate oxide (2) and its (Z)-isomer.

The cycloadduct[5] of anthracene and ethyl thioxoacetate (1; SO = S) reacted at room temperature in dichloromethane with 3-chloroperbenzoic acid (1 equiv.) to give a crystalline mixture of the trans-(1a) and cis-(1b) sulphoxides (ca. 2.5 : 1).† Treatment of the mixture with hydrochloric acid in

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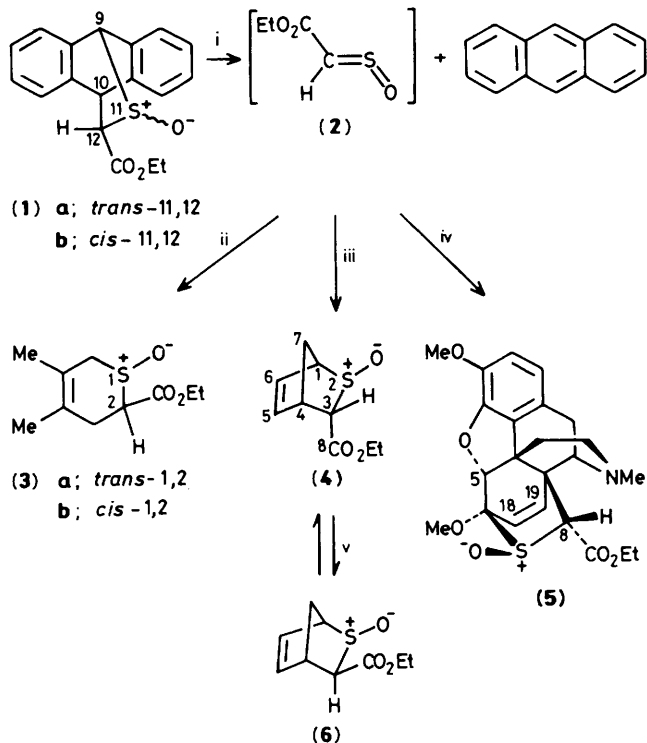
Scheme 1. *Reagents:* i, (1a) at 60 °C in C₆H₆ with ii, 2,3-dimethylbuta-1,3-diene, iii, cyclopentadiene, and iv, thebaine (7); v, Et₃N, C₆H₆, 60 °C.

dioxane[8] or, more conveniently, triethylamine in benzene at room temperature gave, predominantly (90—95%), the *trans*-sulphoxide (**1a**). Heating the oxide (**1a**) with 2,3-dimethylbuta-1,3-diene (1.1 mol. equiv.) in benzene at 60 °C for 5 h afforded anthracene and the *trans*-sulphoxide (**3a**), in high yield (Scheme 1). When the foregoing mixture of oxides (**1a**) and (**1b**) was heated at 60 °C with dimethylbutadiene, only the *trans*-oxide (**1a**) decomposed and the *cis*-oxide (**1b**) was obtained from the reaction mixture. However, the *cis*-oxide (**1b**) decomposed slowly at 80 °C in benzene in the presence of dimethylbutadiene to give the *cis*-sulphoxide (**3b**) cleanly. Similarly, the *trans*-oxide (**1a**), when heated in turn with cyclopentadiene and thebaine (**7**), gave the *trans*-sulphoxides (**4**) and (**5**), respectively, in high yield. The mixture of oxides (**1a**) and (**1b**) reacted completely with thebaine in benzene at 60 °C, giving the *trans*-sulphoxide (**5**) as the sole detectable product, presumably because the unreactive *cis*-anthracene oxide (**1b**) was converted into the reactive *trans*-isomer (**1a**) by the tertiary amine, thebaine.

The structures of the sulphine cycloadducts (**3**), (**4**), and (**5**) were verified by their synthesis from the corresponding sulphides[5,7] using 3-chloroperbenzoic acid in dichloromethane at room temperature. The *trans*-sulphoxide (**3a**) was accompanied by the *cis*-isomer (**3b**) (*trans* : *cis* ratio *ca.* 4 : 1, changing to *ca.* 2 : 1 after epimerisation with triethylamine). The major oxidation product (**4**) of the sulphide (**4**; SO = S) was epimerised with triethylamine to afford a mixture of isomers (**4**) and (**6**) (*ca.* 7 : 3), and the latter was obtained directly by oxidation of the corresponding sulphide. The thebaine derivative (**5**), the sole detectable oxidation product of the sulphide (**5**; SO = S), was reduced[9] to this sulphide with phosphorus pentasulphide.

The cyclopentadiene adduct (**4**) dissociated more slowly than the anthracene adduct (**1a**) but was, nevertheless, an efficient precursor of the (*E*)-sulphine (**2**). Thus, heating the sulphoxide (**4**) with dimethylbutadiene (2 mol equiv.) in benzene under reflux for 10 h gave (*ca.* 90%) the *trans*-adduct (**3a**). In contrast, the *cis*-sulphoxide (**6**) was stable in benzene at 80 °C, but, when heated in toluene under reflux for 10 h in the presence of dimethylbutadiene, gave a mixture of the adducts (**3a**) and (**3b**) (ratio *ca.* 2 : 1 and *ca.* 1 : 1 in separate experiments). This loss of stereochemical control must arise from isomerisation of either the precursor (**6**) or the (*Z*)-sulphine,[10] because the *trans*-sulphoxide (**3a**) was unaffected by heating in toluene under reflux for 10 h. Finally, heating the thebaine adduct (**5**) with dimethylbutadiene in benzene gave the *trans*-sulphoxide (**3a**) cleanly.

The stereochemistry of the cyclopentadiene adduct (**4**), and consequently that of its C-2 epimer (**6**), was determined unambiguously by X-ray crystallography.‡ The signal for H(3) in the n.m.r. spectrum of the *trans*-oxide (**4**), δ 3.32, appeared upfield (Δδ −1.10) of that for H(3) in the *endo*-sulphide (**4**; SO = S),[7] δ 4.42. A much smaller shift (Δδ +0.26) was observed for H(3) in the *cis*-oxide (**6**), δ 3.56, and *exo*-sulphide (**6**; SO = S),[7] δ 3.30. A similar, large shielding effect

(**7**)

(**8**)
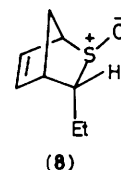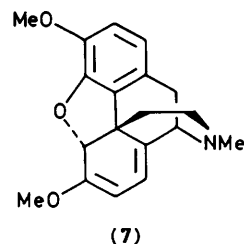
(Δδ −1.01) by a sulphoxide oxygen *cis*, and synperiplanar, to a vicinal proton was observed for H(12) in the anthracene sulphoxide (**1a**), δ 3.11, and the sulphide (**1**; SO = S),[5] δ 4.12. Again, the effect was smaller (Δδ −0.19) for the epimer (**1b**), δ 3.93, having oxygen *trans* to H(12). The assignment of stereochemistry of the anthracene derivatives (**1**) is further supported by their equilibration with base (see above) to give mainly the *trans*-oxide (**1a**), since similar behaviour is shown by the cyclopentadiene derivatives (**4**) and (**6**). Thus, the *trans*-oxide (**4**) is more stable than the *cis*-oxide (**6**) (equilibrium ratio *ca.* 7 : 3), although the *endo*-sulphide (**4**; SO = S) is less stable than the *exo*-sulphide (**6**; SO = S) (equilibrium ratio *ca.* 3 : 7).[7]

Diels–Alder reactions[1,11] of thioaldehyde oxides with conjugated dienes, including 2,3-dimethylbuta-1,3-diene[3,4] and cyclopentadiene,[2] have been reported before. However, to our knowledge, the corresponding retro-Diels–Alder reactions have not previously been described. Recently, Elsässer and Sundermeyer[12] reported the preparation of the thioketone oxide, $(CF_3)_2C=SO$, by thermolysis of its anthracene adduct at 180 °C. Block *et al.*[2] found the *trans*-sulphoxide (**8**) to be stable for 20 h in refluxing toluene, conditions that lead to the complete dissociation of the similar ester (**4**). Clearly, the rate of dissociation of sulphine adducts is markedly dependent upon their stereochemistry and the electronic effects of substituents. This dependence will be explored further with the *S*-oxides of the readily accessible[7] cyclopentadiene adducts of thioaldehydes.

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