Generation of Ethyl Thioxoacetate, a Dienophilic Thioaldehyde

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Ethoxycarbonylmethanesulphenyl chloride reacts with triethylamine to give the transient thioaldehyde, ethyl thioxoacetate, which has been trapped, *in situ,* by cycloaddition to various conjugated dienes.

Until recently,[1,2] cycloaddition reactions of thioaldehydes with conjugated dienes had not been reported, although the synthetic utility of the Diels–Alder adducts of other thiocarbonyl compounds is well appreciated.[3] The neglect of simple[4] thio-

$$\underset{(1)}{EtO_2C.CH_2SH \xrightarrow{\text{i}} EtO_2C.CH_2SCl} \xrightarrow{\text{ii}} \underset{(2)}{[EtO_2C.CHS]}$$

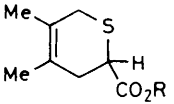
Scheme 1. i, *N*-Chlorosuccinimide; ii, Et_3N.

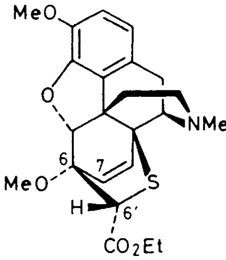
aldehydes stems largely from their known tendency to polymerise,[5] but it appeared to us that generation of thioaldehydes and trapping, *in situ*, with conjugated dienes should be feasible. In connection with other work,[6] we found that thioaldehydes could be generated by 1,2-elimination, with base, of hydrogen chloride from sulphenyl chlorides. We report here experiments with ethyl thioxoacetate (**2**) formed from ethyl mercaptoacetate according to Scheme 1.

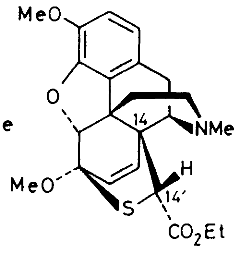
Ethyl mercaptoacetate (5.5 mmol) was treated with freshly purified *N*-chlorosuccinimide (6.5 mmol) in dry benzene (10 ml) with stirring at room temperature for 2 h. The resulting mixture, containing the corresponding sulphenyl chloride (**1**) and succinimide, was added dropwise to 2,3-dimethylbuta-1,3-diene (5.0 mmol) in benzene (10 ml) and methanol (10 ml) containing triethylamine (6.5 mmol) at room temperature. After 0.5 h the reaction mixture, freed from triethylamine hydrochloride and succinimide, was shown by ^1H n.m.r. spectroscopy to consist largely (>90%) of the cycloadduct (**3**; R = Et). Distillation (Kugelrohr, 110—120 °C, 0.03 mbar) (1 bar = 10^5 N m^{-2}) gave (**3**; R = Et) as a mobile oil (65%). Hydrolysis of this ester with aqueous sodium hydroxide in ethanol yielded the acid (**3**; R = H), m.p. 97—98 °C; $\delta(CDCl_3$, 90 MHz) 1.70 (br. s, 2 × Me), 2.47 (m, CH_2), 3.09 (m, CH_2S), 3.66 (t, *J* 6.4 Hz, CH), and 8.0 (br. s, CO_2H, exchangeable with D_2O). Formation of the dihydrothian (**3**; R = Et) is consistent with the view that triethylamine induced rapid elimination of hydrogen chloride from ethoxycarbonylmethanesulphenyl chloride (**1**) to give ethyl thioxoacetate (**2**). However, it is conceivable that the sulphenyl chloride first added (1,2 or 1,4) to the diene and that triethylamine then effected cycloelimination of hydrogen chloride. The latter possibility was discounted on the basis of the following experiment. Thus, 2,3-dimethylbuta-1,3-diene was treated with the sulphenyl chloride (**1**) under the usual conditions but in the absence of triethylamine. Addition of triethylamine then gave a mixture shown by ^1H n.m.r. spectroscopy to contain no significant amounts of the cycloadduct (**3**; R = Et).

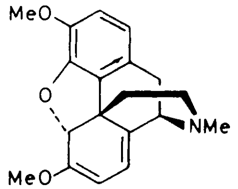
Similarly, thebaine (**4**) reacted with ethyl thioxoacetate (**2**), generated as before, to give the cycloadduct (**5**) (67%), m.p. 116—118 °C. Significantly, the crude reaction mixture was shown by ^1H n.m.r. spectroscopy to contain no appreciable amounts of any isomeric adduct. However, when adduct (**5**) was heated in refluxing toluene for 8 h clean conversion into the isomer (**6**), m.p. 125—128 °C, was observed. Thus, addition of the thioaldehyde to thebaine to give (**5**) had occurred under kinetic control. The structures (**5**) and (**6**) were elucidated by detailed analysis of their ^1H n.m.r. spectra ($CDCl_3$, 250 MHz).[7] In particular, the spectrum of isomer (**5**) showed long-range, 'W' coupling between 7-H and 6′-H [δ 4.01 (d, 0.7 Hz, 6′-H)], and that of isomer (**6**) showed deshielding of 14′-H by the lone-pair electrons of the adjacent nitrogen [δ 5.23 (s, 14′-H)].

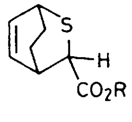
Addition of ethyl thioxoacetate to cyclohexa-1,3-diene under the foregoing conditions gave the expected adduct (**7**; R = Et)† in only 37% isolated yield. The by-products appeared (n.m.r. control) to be derived by attack of the sulphenyl chloride on the diene in competition with elimination to give the thioaldehyde. In accord with this interpretation, increasing the amount of triethylamine (to 3 mol. equiv.) caused an increase (*ca.* 2-fold) in the yield of adduct (**7**; R = Et). The cycloadduct (**7**; R = Et) was obtained as an oil [b.p. 120 °C, 0.05 mbar (Kugelrohr)]. The corresponding acid (**7**; R = H) had m.p. 113—114 °C; $\delta(CDCl_3$, 90 MHz) 1.1—2.3 (m, CH_2CH_2), 3.46 (m, 2 × CH), 4.05 (d, *J* 3.2 Hz, $SCHCO_2H$), 6.20 and 6.64 (2 × br. t, *J* 7.5 Hz, 2 × vinyl-H), and 8.60 (br. s, CO_2H, exchangeable with D_2O).

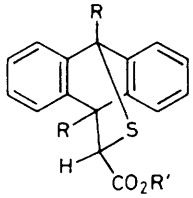

(**3**)


(**5**)


(**6**)


(**4**)


(**7**)


(**8**)

We had earlier shown[8] that nitrosocarbonyl compounds, a class of unstable dienophiles, can be trapped as their adducts with 9,10-dimethylanthracene. These adducts dissociated thermally allowing transfer of the labile dienophile to a variety of conjugated dienes. We have employed the same device with ethyl thioxoacetate. Thus, the sulphenyl chloride (**1**), formed from ethyl mercaptoacetate (11 mmol) and *N*-chlorosuccinimide (13 mmol) in chloroform (20 ml), was added slowly to anthracene (11 mmol) in chloroform (40 ml) containing triethylamine (13 mmol) with heating under reflux. The resulting adduct (**8**; R = H, R′ = Et) (37% yield isolated, *ca.* 50% by n.m.r. control) had m.p. 135—137 °C; $\delta(CDCl_3$, 90 MHz) 1.15 (t, *J* 7 Hz, Me), 4.12 (d, *J* 3.0 Hz, $SCHCO_2Et$), 4.09 (q, *J* 7 Hz, CH_2), 5.07 (d, *J* 3.0 Hz, CH), 5.12 (s, CH), and 7.1—7.5 (m, aryl-H). The corresponding adduct (**8**; R = Me, R′ = Et) of 9,10-dimethylanthracene was obtained (46%) similarly using dichloromethane in place of chloroform as solvent. This oily adduct was converted into the corresponding acid (**8**; R = Me, R′ = H), m.p. 173—175 °C; $\delta(CDCl_3$, 90 MHz) 2.20 (s, Me), 2.31 (s, Me), 3.87 (s, CH), 7.15—7.0 (m, aryl-H), and 7.9 (br. s, CO_2H exchangeable with D_2O). When the anthracene adduct (**8**; R = H, R′ = Et) was heated in toluene at 100 °C for 10 h with an equimolar amount of thebaine (**4**) the thebaine adduct (**6**) was obtained (78%). Similarly, the 9,10-dimethylanthracene adduct (**8**; R = Me, R′ = Et) and thebaine at 110 °C for 5 h gave (**6**) (86%). Finally, transfer of ethyl thioxoacetate from (**8**; R = H, R′ = Et) to cyclohexa-1,3-diene was effected at 110 °C during 3 h to give (**7**; R = Et) (79%).

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† The stereochemistry of (**7**) has not yet been determined.

Vedejs *et al.*[1] generated, and trapped as Diels–Alder adducts, a variety of thioaldehydes, including methyl thioxoacetate, by photolysis of the *S*-phenacyl derivatives of thiols. More recently Baldwin and Lopez[2] have shown that alkyl thiosulphinates are cleaved thermally to form thioaldehydes in high yield. The latter authors also demonstrated the formation of thiobenzaldehyde by thermolysis of the corresponding anthracene adduct. Armitage and Clark[9] reported that methanesulphenyl chloride and dialkylamines react to give methanesulphenamides and, in lesser amounts, bis(dialkylamino)methanes. They suggested that the latter products might arise from thioformaldehyde, a view supported by our experiments with ethoxycarbonylmethanesulphenyl chloride (**1**). Professor J. K. Sutherland has kindly informed us[10] that butyl thioxoacetate is formed, and can be trapped by dienes, by the reaction of butyl glyoxalate and phosphorus pentasulphide.

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References

1 E. Vedejs, T. H. Eberkin, and D. L. Varie, *J. Am. Chem. Soc.*, 1982, **104**, 1445, and references cited therein.

2 J. E. Baldwin and R. C. G. Lopez, *J. Chem. Soc., Chem. Commun.*, 1982, 1029.

3 S. M. Weinreb and R. S. Staib, *Tetrahedron*, 1982, **38**, 3087.

4 The preparation of 2,4,6-tri-t-butylthiobenzaldehyde has been reported recently; R. Okazaki, A. Ishii, N. Fukuda, H. Oyama, and N. Inamoto, *J. Chem. Soc., Chem. Commun.*, 1982, 1187. Thials stabilised by extended conjugation have been known for some time: *e.g.* R. K. Mackie, S. McKenzie, D. H. Reid, and R. G. Webster, *J. Chem. Soc., Perkin Trans.* 1, 1973, 657.

5 *Cf.* H. G. Giles, R. A. Marty, and P. de Mayo, *Can. J. Chem.*, 1976, **54**, 537.

6 D. C. McDougall, Ph.D. Thesis, University of Glasgow, 1981.

7 Comparison was made with the spectrum of the known adduct (**5**; CH_2 in place of S): K. W. Bentley and D. G. Hardy, *J. Am. Chem. Soc.*, 1967, **89**, 3267; W. Fulmor, J. E. Lancaster, G. O. Morton, J. J. Brown, C. F. Howell, C. T. Nora, and R. A. Hardy, Jr., *J. Am. Chem. Soc.*, 1967, **89**, 3322.

8 G. W. Kirby and J. G. Sweeny, *J. Chem. Soc., Perkin Trans.* 1, 1981, 3250.

9 D. A. Armitage and M. J. Clark, *Chem. Commun.*, 1970, 104.

10 J. K. Sutherland, personal communication.