

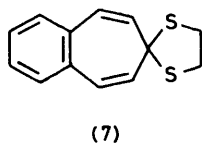
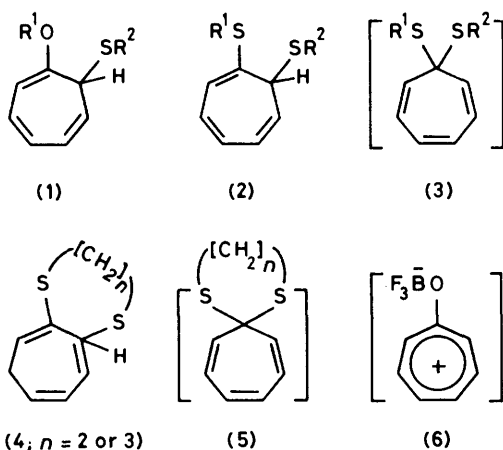
## Reaction of Tropone with 2-Mercaptoethanol: 1,2-Difunctionalization of Cycloheptatrienes with Oxygen and Sulphur in a Fused Ring

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Tropone reacts with excess of 2-mercaptoethanol in refluxing benzene in the presence of toluene-*p*-sulphonic acid to give a 95 : 5 mixture of 2,3-dihydro-9*H*-cyclohept[1,2-*b*]-1,4-oxathiin (8) and 2,3-dihydro-5*H*-cyclohept[1,2-*b*]-1,4-oxathiin (9), respectively, in 30% yield overall. Structures (8) and (9) are supported by (i) hydride abstraction by trityl cation to give 2,3-dihydrocyclohept[1,2-*b*]-1,4-oxathiinylium tetrafluoroborate (10); (ii) oxidation to 2-(2-hydroxyethylthio)tropone (11) by selenium dioxide; and (iii) by a detailed <sup>1</sup>H n.m.r. study with Eu(fod)<sub>3</sub> as a shift reagent.

DIFUNCTIONALIZED cycloheptatrienes bearing oxygen and sulphur in the place of hydrogen have been reported recently.<sup>1</sup> Thus, compounds (1) (R<sup>1</sup>, R<sup>2</sup> = alkyl) have been obtained by the reaction of alkoxytropenylium ion with thiolates at low temperatures.<sup>2</sup> Disulphur analogues (2) were obtained along a similar route starting from alkylthiotropenylium ions and mercaptides.<sup>3</sup>

It was interesting to observe that for compounds (2) with small alkylthio-groups there was a rapid interchange of the two alkylthio-groups.<sup>3</sup> This suggested the intermediacy of the elusive dithioacetals (3).<sup>3</sup> This is



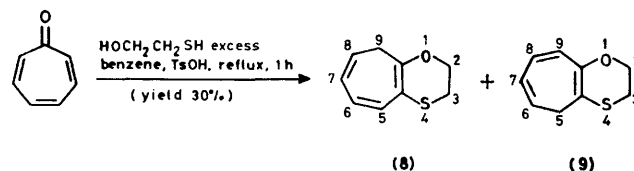
related to the failure to induce dithioacetalization of tropone by spiroannulation. Thus, tropone and either ethane-1,2-dithiol or propane-1,3-dithiol in methanol in the presence of BF<sub>3</sub> led to (4) instead of (5).<sup>4</sup> However, because of the above evidence for (3), it was attractive to envision formation of (4) *via* (5), although an ionic route, *via* dithiol attack on the tropenylium ion (6), is also able to rationalize our observations.

This state of affairs contrasts with the easy formation

and stability of (7), from 4,5-benzotropone and ethane-1,2-dithiol in the presence of BF<sub>3</sub>.<sup>4</sup> However, the fixed double bonds in this case inhibit both the ionic and the molecular routes above.

### RESULTS AND DISCUSSION

Functionalized cycloheptatrienes of the above type have found synthetic use (as yet unreported) in these laboratories. In this connection we became interested in analogues of (4) with an oxygen in the place of a sulphur atom. However, what seemed to be the obvious route to such compounds, from tropone and 2-mercaptoethanol, failed. We were surprised to obtain from this reaction a mixture of (8) and (9) (30% yield overall) in which (8) greatly predominated. Besides (8) and (9) only intractable tars were observed. Different reaction times led to similar results.



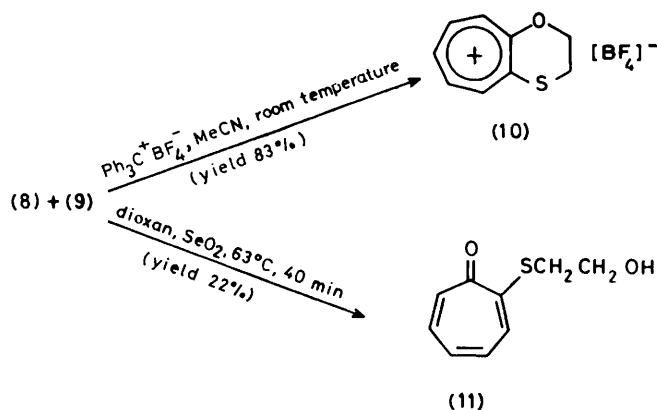
The two oily isomers (8) and (9), which could be separated by preparative HPLC, analysed correctly for C, H, and S. The basis for the structural assignment is as follows.

(i) The mixture of (8) and (9) on treatment with trityl tetrafluoroborate gave the crystalline tropenylium salt (10) in high yield. The structure for (10) which analysed correctly for C and H, is supported by the <sup>1</sup>H n.m.r. spectrum (see Experimental section).

(ii) Oxidation of (8) + (9) with SeO<sub>2</sub> gave (11) in moderate yield, besides much tar; no other product could be isolated from the mixture. The structure (11) was proved by unambiguous synthesis from 2-chlorotropone and the sodium salt of 2-mercaptoethanol.

(iii) The position of the cycloheptatriene methylene in the major isomer (8) and minor isomer (9) is suggested to be as shown here in the respective formulae by a detailed <sup>1</sup>H n.m.r. study with added Eu(fod)<sub>3</sub>. In fact, the <sup>1</sup>H n.m.r. spectra of (8) recorded after gradual additions of

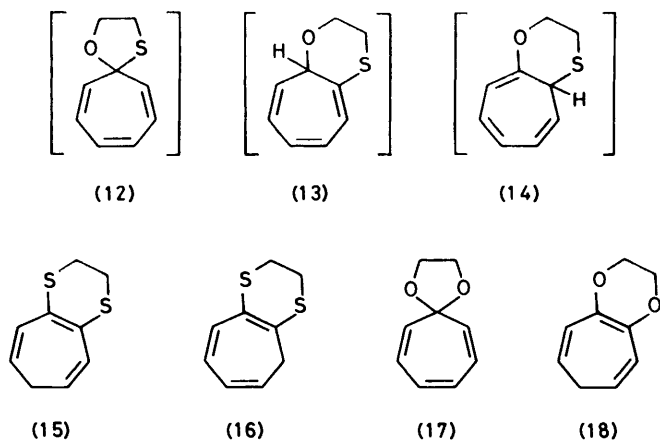
$\text{Eu}(\text{fod})_3$  show a greater lanthanide-induced shift (LIS) for the methylene H-2 and H-9 protons than for the H-3 and H-5 protons (see Experimental section). Since the sulphide sulphur is known to become less strongly bound to  $\text{Eu}(\text{fod})_3$  than to the ethereal oxygen,<sup>5</sup> the LIS observed here clearly support our proposed structure (8). As regards the other isomer, the  $^1\text{H}$  n.m.r. spectra of (9),



recorded after gradual additions of  $\text{Eu}(\text{fod})_3$  also show a smaller LIS for the methylene protons at H-5 and H-3 than for the H-9 and H-2 (see Experimental section) in accordance with expectations from structure (9). The observed LIS are unusually small because the heteroatoms are conjugated with a  $\pi$ -system, and they are thus less basic than typical ethers or thioethers.<sup>5</sup>

The sharp contrast between formation of (4) or (8) + (9) from tropone when dithiols or a mercaptoalcohol are used, respectively, needs some comment. The different course of the reaction cannot be due to the different conditions used ( $\text{BF}_3$ -MeOH-room temperature in the dithiol case and TsOH-benzene-reflux in the mercaptoalcohol case). We have shown that on refluxing tropone with ethane-1,2-dithiol in benzene-TsOH for 40 min, only (4;  $n = 2$ ) can be isolated, although in small yield (10%).

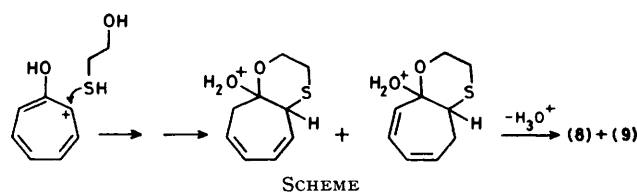
We dislike any route to (8) + (9) involving (12) as an intermediate because with (1) there is no evidence of interchange between the alkoxy and the thioalkyl group.



In line with this, 4,5-benzotropone failed to react with 2-mercaptoethanol and boron trifluoride.

An ionic route analogous to that proposed for the formation of (4) from tropone and dithiols<sup>4</sup> is also not able to rationalize the present results. In fact, with 2-mercaptoethanol such a route would lead to either (13) or (14), or a mixture of them. Sigmatropic shifts of hydrogen from (13) or (14) to give (8) + (9) are expected to require higher temperatures than those employed here to produce (8) + (9). Thus, the rearrangement of (4;  $n = 2$ ) into (15) and (16)<sup>4</sup> or of tropone acetal (17) into (18)<sup>6</sup> only occur at relatively high temperatures (115–150 °C).

We tentatively propose the alternative ionic route to (8) + (9) shown in the Scheme. The outstanding



feature of this route is  $\beta$ -elimination of both the tropone oxygen and a  $\beta$ -hydrogen. This contrasts with our previous proposal for nucleophilic replacement of the tropone oxygen in the ionic route to (4).<sup>4</sup>

#### EXPERIMENTAL

$^1\text{H}$  N.m.r. spectra (80 MHz) were recorded on a Varian CFT-20 spectrometer in  $\text{CDCl}_3$  and  $\text{CD}_3\text{CN}$  solutions. Chemical shifts are given in  $\delta$  (p.p.m.) from  $\text{SiMe}_4$  as internal reference. U.v. spectra were recorded on a Unicam SP 800 spectrometer and i.r. spectra on a Perkin-Elmer 337 spectrometer. Preparative HPLC was carried out on a Jobin-Yvon Miniprep LC equipped with  $20 \times 300$  mm columns packed with 15–25  $\mu\text{m}$  silica gel Merck 'Lichroprep Si 60', monitoring the elution with a Jasco Uvidec 100 II at 255 nm. T.l.c. was carried out on silica gel 60 F<sub>254</sub> Merck plates.

*Synthesis of (8) and (9).*—To tropone (0.557 g, 5.16 mmol) in dry benzene (10 ml) was added under nitrogen 2-mercaptoethanol (0.850 ml, 12.1 mmol) and toluene-*p*-sulphonic acid (0.132 mg, 0.76 mmol). The mixture was refluxed for 1 h, and red tars separated out. The benzene phase was separated, and washed first with 5% aqueous  $\text{K}_2\text{CO}_3$  and then twice with water. The organic layer was dried over  $\text{Na}_2\text{SO}_4$ , evaporated at reduced pressure, and the residue subjected to t.l.c. (2-mm plates) [eluant light petroleum-diethyl ether (95:5)]. The  $R_F$  0.5 band gave an oil (0.208 g) which proved to be a 95:5 mixture of (8) and (9) (1.25 mmol, 30%); unreacted tropone (0.1 g) was also recovered. The oily mixture above was fractionated by preparative HPLC [eluant light petroleum (b.p. 40–60 °C), flow rate 20 ml  $\text{min}^{-1}$ ]. First eluted was (8):  $\delta_{\text{H}}$  ( $\text{CDCl}_3$ ) 2.55 (d, 2 H,  $J$  7.0 Hz, H-9), 2.95 (m, 2 H, S- $\text{CH}_2$ ), 4.25 (m, 2 H, O- $\text{CH}_2$ ), 5.23–5.58 (m, 1 H, H-8), and 6.02–6.41 (m, 3 H, H-5, -6, and -7). Addition of  $\text{Eu}(\text{fod})_3$  such that  $[\text{Eu}(\text{fod})_3]/[(8)] = 1.7$ , induced the following shifts to lower field of the cycloheptatriene signals:  $\Delta\delta = 0.05$  (H-2); 0.03 (H-3); 0.03 (H-5); and 0.05 (H-9). The second eluted product was (9):  $\delta_{\text{H}}$  ( $\text{CDCl}_3$ ) 2.47 (d, 2 H,  $J$  6.8 Hz, H-5), 3.02 (m, 2 H, S- $\text{CH}_2$ ), 4.21 (m, 2 H, O- $\text{CH}_2$ ), 5.33–5.68 (m, 1 H, H-6), 5.94–6.38 (m, 3 H, H-7, -8, and -9).

Addition of  $\text{Eu}(\text{fod})_3$  such that  $[\text{Eu}(\text{fod})_3]/[(8)] = 2.9$ , induced the following shifts to lower field of the cycloheptatriene signals:  $\Delta\delta = 0.09$  (H-2); 0.03 (H-3); 0.04 (H-5); and 0.09 (H-9).

**Synthesis of (10).**—To triphenylmethyl tetrafluoroborate (0.440 g, 1.33 mmol) in dry acetonitrile (2 ml) was added under nitrogen the above 95 : 5 mixture of (8) and (9) (0.221 g, 1.32 mmol) dissolved in dry acetonitrile (1 ml). After 5 min dry benzene (60 ml) was added, whereupon pale yellow crystals of (10) separated out. These were filtered off, washed with dry benzene, and dried (0.250 g, 1.11 mmol, 83%) (Found: C, 42.8; H, 3.6; S, 12.9.  $\text{C}_9\text{H}_9\text{OS}$  requires C, 42.89; H, 3.57; S, 12.70%;  $\lambda_{\text{max}}$  400 nm;  $\delta_{\text{H}}$  ( $\text{CD}_3\text{CN}$ ) 3.55 (m, 2 H, S- $\text{CH}_2$ ), 4.82 (m, 2 H, O- $\text{CH}_2$ ), and 8.20 (m, 5 H, tropylium protons);  $\nu_{\text{max}}$  (Nujol) 2 900, 1 580, 1 370, 1 320, 1 280, 1 240, 1 120, 1 010, 950, 830, 770, 740, 620, and 550  $\text{cm}^{-1}$ .

**Oxidation of (8) + (9).**—To a 95 : 5 mixture of (8) + (9) (0.227 g, 1.37 mmol) in dioxan (5 ml) was added, under nitrogen,  $\text{SeO}_2$  (0.167 g, 1.5 mmol). The mixture was warmed at 63 °C for 40 min, whereupon it darkened while a dark-red solid separated out. The solution was separated and evaporated *in vacuo* to give a residue which was subjected to t.l.c. (2-mm plate) [eluant benzene-ethanol (80 : 20)]. The yellow band at  $R_F$  0.33 was extracted with chloroform to give (11) as yellow crystals, m.p. 54—55 °C (50 mg, 0.27 mmol, 22%) identical in all respects with those obtained below. The  $R_F$  0.85 band gave 0.023 g unreacted (8) + (9) (0.023 g).

**Synthesis of (11).**—To 2-chlorotropone (0.507 g, 3.6 mmol) in absolute ethanol (3 ml) was added a methanolic solution of  $\text{NaSCH}_2\text{CH}_2\text{OH}$  (3.9 mmol, 2.18 mm). The mixture immediately became yellow and NaCl separated out. The solution was evaporated at reduced pressure and the residue chromatographed as above to give (11), m.p. 54—55 °C (0.226 g, 1.24 mmol, 34%) (Found: C, 59.45; H, 5.4; S, 17.65.  $\text{C}_9\text{H}_{10}\text{O}_2\text{S}$  requires C, 59.32; H, 5.53; S, 17.59%);  $\lambda_{\text{max}}$  280, 342, and 367 nm;  $\delta_{\text{H}}$  ( $\text{CDCl}_3$ ) 3.20 (br s, 1 H, OH), 3.28 (t, 2 H, S- $\text{CH}_2$ ,  $J$  6 Hz), 4.18 (t, 2 H, O- $\text{CH}_2$ ,  $J$  6 Hz), and 7.35 (m, 5 H, tropone protons).

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