Chemistry of Sulphines. Part XVI. ¹ Aliphatic Sulphines from Non-
enethiolisable Thiketones and their Cycloaddition Reactions with
Diazalkanes

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Chemistry of Sulphines. Part XVI.\(^1\) Aliphatic Sulphines from Non-enethiolisable Thioketones and their Cycloaddition Reactions with Diazoalkanes

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Oxidation with peroxy-acid of the non-enethiolisable thioketones adamantanethione, 2,2,4,4-tetramethyl-3-thioxocyclobutanone and 2,2,4,4-tetramethylcyclobutane-1,3-dithione gives the corresponding sulphines in high yields. Cycloaddition reactions of these sulphines with 2-diazopropane lead to \(\Delta^2\)-1,3,4-thiadiazoline S-oxides; from diazomethane and 2,2,4,4-tetramethyl-3-thioxocyclobutanone S-oxide an episulphoxide was isolated.

Several types of sulphines (thione S-oxides) can conveniently be synthesised by peroxy-acid oxidation of the corresponding thiocarbonyl compounds.\(^2\) Aliphatic sulphines have not been prepared hitherto by this oxidation method, presumably because of the limited stability\(^3\) of the parent thiones. Thioacetone S-oxide has been reported\(^4\) as a transient intermediate during the dehydrohalogenation of propane-2-sulphinyl chloride.

With the aim of studying the chemical and spectroscopic properties of aliphatic sulphines, we selected three aliphatic thioketones, (I)—(III), which show no tendency towards enethiolisation or di-, tri-, or polymerisation at ordinary temperatures, and which therefore would probably be oxidisable to sulphines. Indeed, adamantanethione\(^5\) (I) smoothly reacted with \(m\)-chloroperbenzoic acid (MCPBA) in ether at 5° to give the stable aliphatic sulphine (IV) (75%). The product showed the characteristic \(\geq C=S=O\) i.r. absorption at 1070 cm\(^{-1}\), its u.v. spectrum (hexane) exhibited a maximum at 270 nm (\(\varepsilon\) 9555), and its n.m.r. spectrum (CCl\(_4\)) revealed, besides a broad absorption at \(\delta\) 2.00 (12H), broad one-proton singlets at \(\delta\) 2.87 and 4.02 p.p.m. The separation of 68 Hz between the latter two signals shows the difference between the deshielding properties of the two sides of the bent sulphine system unperturbed by other anisotropic effects.\(^6\)

\(\text{Tetramethyl-3-thioxocyclobutanone}\)\(^7\) (II) was readily

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\(^7\) E. U. Elam and H. E. Davis, \textit{J. Org. Chem.}, 1967, 32, 1562. This compound was supplied by Dr. J. A. Boerma (Groningen).
oxidised by MCPBA (1.0 equiv.) in ether at 0° to give the aliphatic sulphine (V) in 80% yield. The n.m.r. spectrum (CCl₄) showed the expected singlets for the two types of methyl protons at δ 1.48 and 1.63 p.p.m. The characteristic i.r. absorptions (CCl₄) were observed at 1785 (C=O) and 1065 cm⁻¹ (CSO).

On treatment of the dithione⁷ (III) with MCPBA in ether at 0° a rapid discharge of the red coloration was observed. A crystalline substance isolated in 86% yield consisted of a mixture of anti- and syn-bis-sulphines (VIIa and b). The n.m.r. spectrum (CDCl₃) showed the four methyl groups of the anti-isomer (VIIa) as one singlet at δ 1.84 and those of the syn-compound as two singlets at δ 1.71 and 1.98 p.p.m. According to the n.m.r. spectrum the anti-syn ratio varied from 9:1 to 4:1 depending on the conditions of the oxidation. Despite several attempts, separation of these isomers was not achieved. Isomerisation (syn to anti) took place readily on warming a solution of the mixture. The anti-isomer could then be obtained as a single compound.

The aliphatic sulphines (IV)—(VI) are reasonably stable at room temperature, in spite of the lack of conjugative stabilisation (cf. ref. 2a). Their cycloaddition reactions offer a unique possibility for the preparation of heterocyclic compounds.¹⁸ We have studied reactions with diazomethane and 2-diazopropane, particularly to compare the results with those obtained recently for the parent thiones.⁸⁻¹⁰

Adamantanethione S-oxide (IV) reacted with 2-diazopropane at -10° to give a 1:1 adduct to which structure (VII) was assigned on the basis of elemental analysis and the following spectral data: νₘᵦₓ (KBr) 1040s (S=O) and 1570m (N=N) cm⁻¹; δ (CDCl₃; -30°) 1.50 (s, Me), 1.88 (s, Me), 2.70—3.20 (1H, m), and 1.80—2.70 p.p.m. (13H, m). The alternative mode of addition which would lead to a 1,2,3-thiadiazoline S-oxide is ruled out, because then the N=N i.r. absorption would be expected¹¹ at a lower wavenumber. Moreover, the position of the methyl n.m.r. signals agrees well with those of 2,2,5,5-tetramethyl-1,3,4-thiadiazoline S-oxide [δ (CCl₄) 1.47 and 1.70 p.p.m.] prepared via an independent route.⁶

As observed previously,¹ diazomethane reacts much more slowly with sulphines than 2-diazopropane. With compound (IV) and diazomethane no reaction took place. However, adamantanethione (I) does react with diazomethane: Krapcho et al.⁹ report two different modes of addition, viz., via a trans-sulphoxide, and an adamantanethio-sulphoxide [δ (CCl₄) 1.47 and 1.70 p.p.m.].

The sulphine (V) reacted smoothly with 2-diazopropane to give the spiro-adduct (VIII) in 87% yield, νₘᵦₓ (CCl₄) 1785 (C=O), 1570 (N=N), and 1060 (S=O) cm⁻¹; νₘᵦₓ (CDCl₃) 0.98, 1.28, 1.47, 1.58, 1.88, and 1.99 p.p.m. (each s, Me). Oxidation of compound (VIII) with MCPBA gave the corresponding sulphone (26%) which showed, as expected, only three methyl signals in the n.m.r. spectrum [δ (CDCl₃) 1.30, 1.68, and 1.69 p.p.m.].

To our surprise the reaction of compound (V) with diazomethane did not lead to a thiaadiazoline S-oxide; instead a tetramethylcyclobutanone-spiro-thiiran S-oxide (IX) was isolated (29%). The structure became evident from elemental analysis and spectra. The i.r. spectrum (Nujol) showed absorption at 3060 cm⁻¹ (C-H) indicative of the three-membered ring system,¹⁸ strong bands in the S=O region at 1015, 1060, and 1085 cm⁻¹, and no absorption in the N=N region (1500—1600 cm⁻¹). N.m.r. signals were observed at δ 0.94, 1.30, 1.44, and 1.68 (each s, Me) and 2.44 and 2.48 p.p.m. (AB pattern, J 8.0 Hz, CH₃). Apparently, the initially formed five-membered ring loses nitrogen easily to give the episulphoxide. This behaviour of the primary cycloadduct is similar to that of the thiaadiazoline¹⁰ derived from the parent thione (II) and diazomethane, which also readily loses nitrogen, to give an episulphide.¹⁰

The bis-sulphine (VI), as a mixture of isomers, reacted with 2-diazopropane in an analogous way to (V), to give a mixture of isomeric dispiro-compounds (Xa and b, with one form predominating) containing two 1,3,4-thiadiazoline S-oxide units (yield 66%). The product composition changed according to the anti-syn ratio of the starting material. When pure anti-sulphine (VIIa) was used, a mixture of compounds was still obtained, in which the same main product dominated. If we assume a stereospecific cycloaddition reaction the anti-sulphine (VIIa) would give a mixture of trans- (Xa) and trans- (Xb) bis-sulphoxide. If we also consider that the approach of diazopropane to the two sulphine functions occurs from opposite sides of the

* From acetone azine, chlorine, and hydrogen sulphide, with subsequent oxidation. We thank Dr. R. M. Kellogg and Mr. J. Buter for providing this information prior to publication.

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molecule, the main product most likely would be trans-
(Xa). Attempts to separate the mixture of products or to gain more definite information about the geometry of the constituents, failed.

Diazomethane reacted very sluggishly with the bis-sulphine (VI), yielding a small amount of a mixture of products to which bis-spiro-thiiran S-oxide structures were tentatively assigned. This behaviour of the sulphine (VI) is in line with that observed for the parent dithione (III) and the respective diazo-compounds.

EXPERIMENTAL

M.p.s were determined with a Kofer hot-stage apparatus. Combustion analyses were performed in the Micro-Analytical Department of the University at Groningen under the supervision of Mr. W. M. Hazenberg. I.r. spectra were recorded on a Perkin-Elmer 125 or 257 grating spectrometer; n.m.r. spectra were recorded with a Varian A60 spectrometer (tetramethylsilane as internal standard).

Adamantanethione S-Oxide (IV).—MCPBA (600 mg, 3 mmol) in ether (10 ml) was added gradually to a stirred ice-cooled solution of adamantanethione (500 mg, 3 mmol) in ether (15 ml). Rapid discharge of the pink colour took place. The mixture was washed with aqueous sodium hydrogen sulphite, saturated sodium hydrogen carbonate solution, and water, dried (Na₂SO₄), and evaporated to leave a white solid (530 mg). Crystallisation from light petroleum (b.p. 60—80°) at —20° gave the white crystalline sulphine (IV) (534 mg), m.p. 130° (sublimes) (Found: C, 65-8, 65-6; H, 7-6, 7-6; S, 17-35. C₁₄H₁₈N₂O₃S requires C, 65-8; H, 7-6; S, 17-3%) for spectra see Discussion section.

2,2,4,4-Tetramethyl-3-thioxocyclobutane S-oxide (V).—MCPBA (1-0 g, 5 mmol) in dry ether (25 ml) was added dropwise to a stirred solution of 2,2,4,4-tetramethyl-3-thioxocyclobutane (2) (in ether (50 ml) at 0°. The orange-red colour disappeared. m-Chlorobenzoic acid was removed as described for (IV). The residual oil was dissolved in pentane (5 ml); cooling overnight at —20° gave the white crystalline sulphine (V) (534 mg), m.p. 52—53°. Work-up of the mother liquor afforded another 285 mg (total yield 29%), m.p. 115° (decomp.) (Found: C, 61-7, 61-6; H, 7-95, 7-9; N, 16-8; S, 12-7%); for spectra see Discussion section.

2,2,4,4-Tetramethylcyclobutane-1,3-dithione SS-Dioxide (Vla and b).—MCPBA (2 g, 10 mmol) in ether (25 ml) was added gradually to a chilled (0°) solution of 2,2,4,4-tetramethylcyclobutane-1,3-dithione (3) (860 mg, 5 mmol) in ether (50 ml). Rapid decolourisation took place. The m-chlorobenzoic acid was removed as described for (IV). After removal of the solvent in vacuo the remaining white solid was dissolved immediately in dichloromethane-pentane (1 : 1; 10 ml) and cooled. The crystalline product (474 mg), m.p. 140—146° (decomp.), consisted of the anti-sulphine (Vla) and the syn-sulphine (Vlb) (ratio 3 : 1).

Another sample (410 mg) that crystallised from the mother liquor consisted of (Vla) and (Vlb) in the ratio of 25 : 65 (total yield 86%) (Found: C, 47-0, 46-9; H, 6-1, 6-0; S, 31-2, 31-0. C₁₄H₁₂O₂S₂ requires C, 47-0; H, 5-9; S, 31-4%). When a mixture of (Vla) and (Vlb) (any ratio) dissolved in carbon tetrachloride was heated at 70—75° for 2—5 h, isomerisation (according to the n.m.r. spectrum) to almost exclusively the anti-isomer took place. Upon cooling the anti-isomer crystallised: m.p. 145—147° (decomp.). δ max. (hexane) 271 nm (ε 17,180), δ max. (KBr) 1040 and 1120 cm⁻¹.

5',6'-Dimethyladamantane-2-spiro-2'-Δ⁴'-1',3',4'-thiadiazoline-5-S-Oxide (VII).—The sulphine (IV) (182 mg, 1 mmol) dissolved in pentane (5 ml) and ether (1 ml) was treated with 2-diazopropane (1 equiv.) at −10°. The mixture was left overnight at −20°; crystals of the product (70 mg) had then appeared. Work-up of the mother liquor gave a further 128 mg (total yield 78-5%), m.p. 115° (decomp.) (Found: C, 61-7, 61-6; H, 8-05, 7-9; N, 11-3, 11-3; S, 12-9, 12-8. C₁₃H₁₇N₂O₃S requires C, 61-85; H, 8-0; N, 11-1; S, 12-7%); for spectra see Discussion section.

2',3',4',5,5'-Hexamethyl-Δ²-A1,3,4-thiadiazolino-2-spiro-cyclobutan-3'-one S-Oxide (VIII).—In the same manner as described for (VII), the sulphine (V) (344 mg) was treated with 2-diazopropane. After 2 weeks at −20° the crystalline product was collected (300 mg, 87%), m.p. 107° (decomp.) (Found: C, 54-45, 54-6; H, 7-45, 7-6; N, 11-5, 11-5; S, 13-1, 13-15. C₁₃H₁₇N₂O₃S requires C, 54-5; H, 7-6; N, 11-5; S, 13-9%); for spectra, see Discussion section.

This mono-oxide was converted into the SS-dioxide by treatment with MCPBA (1-05 equiv.) in dichloromethane-ether (2 : 5) at 20°. After 1 week the mixture was worked up by thick-layer chromatography on silica (development with dichloromethane-ether, 2 : 1). The sulphine crystallised from light petroleum (b.p. 60—80°) at −20° (yield 26%); m.p. 60—61° (correct CHNS analysis for C₆H₁₄N₂O₃S, δ max (KBr) 1785 (CO), 1512 (N=N), and 1120 and 1315 (SO₂) cm⁻¹; for n.m.r. see Discussion section. This material was recovered (68%) from the chromatogram.

When diazomethane was used instead of 2-diazopropane, a further 157 mg (total yield 80%) (Found: C, 57-75; 57-8; H, 7-6, 7-6; S, 17-35. C₁₃H₁₇N₂O₃S requires C, 57-7; H, 7-6; S, 17-3%); for spectra, see Discussion section.

Reactions of the SS-Dioxide (VI) with 2-Diazopropane and Diazomethane.—A solution of compound (VI) (mixture of anti- and syn-isomers) (155 mg, 0-75 mmol) in dichloromethane (1 ml) and ether (3 ml) was treated with 2-diazopropane (2-2 equiv.) at −10°. The mixture was left for 2 weeks at −20°. The crystalline product was collected (170 mg, 86%); m.p. 107° (decomp.) (Found: C, 48-9, 49-5; H, 6-95, 7-1; N, 16-0, 18-9; S, 18-75, 18-6. Calc. for C₁₃H₁₇N₂O₃S: C, 48-8; H, 7-0; N, 16-3; S, 18-6%). δ max. (KBr) 1565 (N=N) and 1035 and 1045 (SO₂) cm⁻¹. It consisted of a mixture of isomers (Xa, cis and trans; Xb, cis and trans) of which one predominated according to the n.m.r. spectrum [methyl signals at 8 1-38 and 1-17 (C-2 and C-4) and at 2-06 and 1-98 p.p.m. (C-2')].

When diazomethane was used instead of 2-diazopropane, after 2 weeks only a small amount of material had crystallised. The i.r. spectrum showed absorptions at 3060 (C-H) and 1045 and 1060 cm⁻¹ (S=O), compatible with an episulphoxide structure. The n.m.r. spectrum exhibited, besides several methyl signals, an AB pattern at 8 2-66 and 2-80 p.p.m. (J 8 Hz).