

SYNTHESIS AND TRANSFORMATIONS OF MERCAPTOBICYCLO[2.2.2]OCTANES

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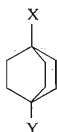
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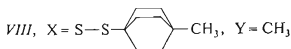
The paper describes preparation of 1-mercaptobicyclo[2.2.2]octanes by the isothiuronium method and transformations of 1-mercapto-4-methyl derivative into the corresponding methyl sulphide, methyl sulphoxide, methyl sulphone and disulphide.

1-Mercaptobicyclo[2.2.2]octanes and their functional derivatives represent a group of compounds which have not been studied yet. Within the framework of broader studies¹⁻⁵ of application of 1-hydroxybicyclo[2.2.2]octanes as starting substances for preparation of bicyclo[2.2.2]octane derivatives substituted at their bridgehead carbon atoms we were also interested in synthesis of several 1-mercaptobicyclo[2.2.2]octanes by substitution of hydroxy by thiol group.

It was found^{1,2} that in the bicyclo[2.2.2]octane series it is possible to substitute the bridgehead hydroxyl group by a halogen atom (except for fluorine) by heating bicyclo[2.2.2]octan-1-ols with inorganic halides in polyphosphoric acid (or in some cases more easily in 100% phosphoric acid⁵). With respect to this fact it seemed most advantageous to use (out of all the known mercaptane syntheses) a modification of the isothiuronium method⁶. Heating of the bicyclo[2.2.2]octan-1-ols *I* and *II* with thiourea in 100% phosphoric acid medium at 100 to 120°C for 1.5 h and subsequent alkaline hydrolysis gave the thiols *III* and *IV* in satisfactory yields. Methylation of the thiol *III* with dimethyl sulphate gave the methyl sulphide *V* the oxidation of which by usual methods⁷ gave either the methyl sulphoxide *VI* or methyl sulphone



- I*, X = OH, Y = CH₃
II, X = Y = OH
III, X = SH, Y = CH₃
IV, X = SH, Y = OH
V, X = SCH₃, Y = CH₃
VI, X = SOCH₃, Y = CH₃
VII, X = SO₂CH₃, Y = CH₃



VII. Direct oxidation of the thiol *III* with slight excess of permanganate gave the disulphide *VIII* in high yield.

EXPERIMENTAL

The melting points were determined with a Kofler apparatus and were not corrected. The IR spectra were measured with a UR-10 apparatus (Zeiss, Jena). The mass spectra were measured with a MCH-1303 apparatus.

1-Mercapto-4-methylbicyclo[2.2.2]octane (*III*)

The mixture of *I* (14.3 mmol) and thiourea (29 mmol) in 100% phosphoric acid (10 m) 85% H_3PO_4 and 6.7 g P_2O_5) was heated at 110 to 120°C with stirring for 1.5 h. Then the solution of 28.4 g NaOH in 200 ml water was added and the mixture was refluxed under nitrogen for 2 h. The hydrolysate was acidified with conc. HCl while cooling and extracted with 3×50 ml ether. The combined extracts were washed with water and dried with MgSO_4 . Evaporation of ether gave 2.2 g liquid which was distilled in vacuum to give 1.3 g (58.5%) thiol *III* (b.p. 74–76°C at $1.5 \cdot 10^3$ Pa) which solidified on standing (m.p. 40–41°C in a sealed capillary). For $\text{C}_9\text{H}_{16}\text{S}$ (156.3) calculated: 69.16% C, 10.32% H, 20.52% S; found: 69.21% C, 10.28% H, 19.54% S. IR spectrum (CCl_4): $\nu(\text{SH})$ 2567 cm^{-1} . Mass spectrum m/e (% relative intensity): 156 (100) (M^+), 123 (94.8), 86 (86.0), 81 (72.9), 67 (30.8).

1-Mercapto-4-hydroxybicyclo[2.2.2]octane (*IV*)

The preparation was analogous to that of *III*, yield 42%. The raw product was purified by column chromatography (Al_2O_3) under nitrogen (CHCl_3 as eluent). The sample for analysis was sublimed in vacuum ($1.3 \cdot 10^3$ Pa; the bath temperature 100°C), m.p. 96–98°C (sealed capillary). For $\text{C}_8\text{H}_{14}\text{OS}$ (158.3) calculated: 60.71% C, 8.92% H, 20.26% S; found: 60.64% C, 8.97% H, 20.06% S. IR spectrum (CCl_4): $\nu(\text{SH})$ 2568 cm^{-1} , $\nu(\text{OH})$ 3610 cm^{-1} . Mass spectrum m/e 158 (M^+).

1-Methylmercapto-4-methylbicyclo[2.2.2]octane (*V*)

Solution of *III* (6.4 mmol) in aqueous sodium hydroxide (0.26 g NaOH in 10 ml water) was stirred under nitrogen, and equimolar amount of dimethyl sulphate was added thereto drop by drop. After 4 h stirring the mixture was extracted with 3.10 ml ether and the combined ether extracts were washed with water until neutral and dried with MgSO_4 . The residue obtained on evaporation of ether was purified by column chromatography (Al_2O_3 ; cyclohexane). After evaporation of cyclohexane the residue was distilled to give the methyl sulphide *V* in 65% yield. B.p. 90–92°C at $1.7 \cdot 10^3$ Pa; n_D^{22} 1.5070. For $\text{C}_{10}\text{H}_{18}\text{S}$ (170.3) calculated: 70.52% C, 10.65% H, 18.83% S; found: 70.18% C, 10.40% H, 18.88% S. Mass spectrum m/e (% relative intensity): 170 (72.3) (M^+), 155 (23.3), 123 (23.0), 100 (100), 81 (50.6), 67 (27.5), 41 (26.8).

Methyl 4-Methylbicyclo[2.2.2]oct-1-yl Sulphoxide (*VI*)

The methyl sulphide *V* (4.1 mmol) was dissolved in 8 ml aqueous methanol (1 : 1 v/v) and, with stirring and cooling, oxidized with 0.5M sodium metaperiodate (8.4 ml, i.e. 4.2 mmol). After 4 h stirring the separated salt was collected by suction, and the filtrate was extracted with

3. 15 ml ether. The extracts were dried, ether was evaporated, and the residue was sublimed in vacuum (67 Pa, the bath temperature 80°C). Yield of the sulphoxide *VI* was 65.5%; m.p. 81.5–83°C. For $C_{10}H_{18}OS$ (186.3) calculated: 64.46% C, 9.74% H, 17.21% S; found: 64.32% C, 9.72% H, 17.11% S. IR spectrum (CCl_4) $\nu(SO)$ 1059 cm^{-1} . Mass spectrum m/e (% relative intensity): 186 (8.83) (M^+), 170 (24.1), 123 (99.6), 100 (32.7), 81 (100), 67 (31.3).

Methyl 4-Methylbicyclo[2.2.2]oct-1-yl Sulphone (*VII*)

The dioxide *VII* was obtained by shaking solution of *V* (1 mmol) in 2 ml glacial acetic acid with 3% aqueous potassium permanganate (50% excess) for 20 min. The excess of permanganate was removed by sulphur dioxide. The separated sulphone *VII* was recrystallized from ethanol. Yield 76%; m.p. 139.5–140°C. For $C_{10}H_{18}O_2S$ (202.3) calculated: 59.37% C, 8.97% H, 15.85% S; found: 59.89% C, 8.99% H, 15.93% S. IR spectrum (CCl_4): $\nu(SO_2)$ 1155, 1315 cm^{-1} . Mass spectrum m/e (% relative intensity): 202 (0.14) (M^+), 123 (100), 81 (72.3), 67 (23.1), 55 (13.9), 41 (14.4), 39 (13.2).

Bis(4-methylbicyclo[2.2.2]oct-1-yl) Disulphide (*VIII*)

This compound was prepared from the thiol *III* in analogy to *VII* by oxidation with a 20% excess potassium permanganate. The separated precipitate was crystallized from ethanol. Yield 89%; m.p. 108–108.5°C. For $C_{18}H_{30}S_2$ (310.6) calculated: 69.61% C, 9.74% H, 20.65% S; found: 69.75% C, 9.89% H, 20.55% S. Mass spectrum m/e 310 (M^+).

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