3-Mercaptodihydrocarvone (True Carvone Hydrosulphide) and (1S, 4S, 5S)-4,7,7-Trimethyl-6-thia-1,5-bicyclo-[3,2,1]-octan-3-one

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(—)-(1S, 4S, 5S)-4-7-7-Trimethyl-6-thia-1,5-bicyclo-[3,2,1]-octan-3-one

True carvone hydrosulphide has been prepared and its CD and ORD spectra examined. The spectra of another product from the reaction of carvone and hydrogen sulphide, which is probably a bi-cyclic thiane, have also been recorded.

Whereas the compound formerly known as carvone hydrosulphide is, in fact, dicarvone sulphide [1], the genuine hydrosulphide, (—)-3-mercaptodihydrocarvone, has now been prepared by the addition of hydrogen sulphide to (—)-carvone in the presence of a base following a procedure analogous to that of van Tamelen and Grant [2]. It had boiling point 150–151°/0.5 mm, n_D^{20} , 1.5221 [α_D^{20} —6.3° ($c = 4$ in chloroform, $l = 1$). Altogether, three products were obtained and part of the ketone was recovered. One of the products was identified by melting point and infrared spectrum as that previously styled carvone hydrosulphide, here called dicarvone sulphide **1**.

The remaining liquid, on distillation, gave two new isomeric compounds, one liquid and one solid, having the molecular formula $C_{10}H_{16}OS$. The liquid product was assigned the structure **2** on the basis of its infrared and NMR spectra. It showed a positive Cotton effect, corresponding to the $n \rightarrow \pi^*$ transition of the carbonyl group at 290 nm ($\theta = +5,250$), a further positive Cotton effect at 235 nm ($\theta = +1,520$), and a negative Cotton effect below 220 nm. The NMR spectra (220 MHz) showed a signal (assigned to C-3H) at δ 3.70 ppm (J 7, 3.8, 3.5, 3.5 Hz) and to the SH proton at δ 1.22 (J 7 Hz). None of the coupling constants of C-3H is large

enough to allow for axial-axial coupling [3], thus an axial position is indicated for the mercapto group at C-3. Changing the solvent from deuteriochloroform to deuteriopyridine resulted in a downfield shift of the methyl doublet by 0.1 ppm. This indicates an equatorial position for the methyl group at C-2 [4]. Whilst the configuration of the carvone from which these compounds are derived has been established [5], the configuration of carvone hydrosulphide is only established by virtue of the argument above and, by the fact that the thiane **3**, which is likely to be derived from the hydrosulphide, must have the thiol and isopropenyl groups on the same side of the ring; given that the most likely preferred conformation is the chair form, formula **2** gives the most probable conformation. When **2** was treated with (—)-carvone **1** was obtained, which suggests that **2** is an intermediate stage in the formation of **1**. When **2** was treated with (+)-carvone a white solid with the same elemental composition as **1** was obtained. It was inactive and, presumably, the meso form of **1**. The ORD, CD and UV spectra of **2** are given in the Figures 1 and 2; the curves are different from those of the thiane but are rather similar in shape to those obtained from dicarvone sulphide.

The solid isomer from the preparation, **3**, m.p. 89–90° [α_D^{20} —39.5° ($c = 2.5$ in chloroform, $l = 1$) showed neither bands in the infrared spectrum at 2500–2600 cm^{-1} , thus indicating the absence of an SH group [6], nor bands present at 3100–3010 and 1650 and 900 cm^{-1} , where cycloalkenes may be expected to absorb [7, 8]. There was a strong band at 1705 cm^{-1} , indicative of the carbonyl group, and a doublet at 1365 and 1375 cm^{-1} , indicating a gem dimethyl group [9]. The NMR spectrum (100 MHz) in deuteriochloroform showed a methyl doublet at δ 1.16 ppm (C-3H J 7 Hz) and a methyl singlet at δ 1.42 ppm (6H) and is thus consistent with the

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Fig. 1.

— ORD ketothiane,
 ---- ORD carvone hydrosulphide,
 - · - · - ORD dicarvone sulphide,
 CD ketothiane,
 - - - - - CD carvone hydrosulphide,
 · · · · · CD dicarvone sulphide.

presence of a gem dimethyl group. There were maxima in the UV absorption at 206 and 239 nm (ϵ 2200 and 920) with a shoulder indicative of a peak at 290–295 nm, corresponding to the trough at 292 nm in the CD; the first two transitions correspond to a dialkyl sulphide [10], whilst the shoulder corresponds to the carbonyl group [11]. These various observations and the analysis suggest that

compound **3** is a bicyclic thiane. Since compound **3** is almost certainly derived from **2** by isomerisation (cyclisation) it is likely to have a structure such as **3a** or **3b**.

It seems, from models, that the cyclisation would

be easier in the boat rather than the chair form, thus giving **3a** rather than **3b**, although the parent compound **2** is almost certainly in the chair form. Changing the solvent from deuteriochloroform to deuteriopyridine only causes an upfield shift of 0.11 ppm in the methyl resonance, whereas had the methyl group been axial, as in **3b**, the shift might be expected to be greater than 0.2 ppm, so that on this basis **3a** is the preferred conformation [12].

A further consideration is the energy of the 1,3 interaction of the methyl group with the protons of the ring. In a chair form there are two actual interactions whereas in the boat form, the methyl group being equatorial, there are no such interactions and the enthalpy difference is of the order of 6.7 to 7.5 kJ/mol [13], which has to be set against the difference in the enthalpy of the boat and chair forms of cyclohexanone, *i.e.* 11.3 kJ/mol [14].

Fig. 2.

CD and ORD Spectra

Figures 1 and 2 show the ORD, CD and UV spectra of the thiane, carvone hydrosulphide and dicarvone sulphide. When the CD spectrum of the thiane is compared with that of the hydrosulphide it is seen that both the 290 and 235 nm bands have shifted to longer wavelengths, *i.e.* to 295 and 250 nm respectively and have changed in sign in the process, whereas a third band just below 220 nm appears to have the same negative sign in the thiane as in the sulphide. The ORD spectrum of the thiane suggests a positive sign for the bands below 200 nm whilst that of the hydrosulphide and dicarvone sulphide is probably only indicative of the negative CD absorption at around 210 nm.

The carbonyl $n-\pi^*$ transition in the thiane appears negative in the CD at 296 nm ($\theta = -9340$), as is a second band at 250 nm ($\theta = -6560$), which is probably ascribable to a sulphur transition [11], and that at *ca.* 205 nm is also negative (the maximum was not reached). It is, however, interesting to note that, from the general shape of the ORD curve, the absorption below 200 nm is strongly positive.

One of the interesting features of this series of spectra is that the molar ellipticity of dicarvone sulphide is roughly twice (1.77) that of the carvone hydrosulphide. This means that the actual observed ellipticity for solutions of similar concentration of the sulphide is roughly similar to that of the hydrosulphide. It is also interesting to note that the band

at about 290 nm is partially resolved in the hydro-sulphide into two peaks, whereas in the dicarvone sulphide only a single peak appears. In the band at 235 nm, θ has a value of 85 in the sulphide and 15 in the hydrosulphide; that is, a ratio of between 5 and 6. This might suggest that there is a conjugation in the dicarvone sulphide, both of the keto group at 290 nm and of the sulphide group at 235 nm. Conjugation, however, implies co-planarity and at least some bond relationship other than a single bond, but conjugation with the keto group is unlikely to be effective without affecting the stability of the hydrogen on C2 and, thus, causing the compound to racemise. Another possibility, which seems to be more likely, is that in the dicarvone sulphide there is conformational restriction which gives preference to a conformation with a high activity. It is noteworthy that CD λ_{max} 290 nm for the hydrosulphide increases in the dicarvone sulphide by about 5 nm. This bathochromic effect is a good deal smaller than might be expected if the compound were really conjugated. A further possibility is that the two halves of the sulphide molecule lie on top of one another in such a way that there is an interchange between the binding of the keto group and the methylene group in the side chain, which binding could apply to both keto and methylene groups at the same time, thus providing for further restriction of rotation and an interchange of electrons between the methylene and keto groups.

Experimental

(—)-3-Mercaptodihydrocarvone

(—)-Carvone (28 g) was added dropwise over a period of 1.5 h to a stirred, saturated solution of hydrogen sulphide in chloroform (200 ml) containing triethylamine (10 ml); hydrogen sulphide gas was passed through the solution for a further 20 h. The temperature of the solution was maintained at 8–10 °C for the first 5 h and was then allowed to reach room temperature. The solution was washed with dilute acetic acid (5%, 200 ml) and then ten times with water. Evaporation of the solvent after drying (MgSO_4) left a viscous oil (30 g) from which (—)-carvone sulphide was precipitated by shaking with petroleum ether (40–60 °C); the oil remaining after evaporation of the petroleum ether was distilled through a 6' Vigreux column at reduced pressure under nitrogen to yield unreacted (—)-carvone (6.7 g, b.p. 65–110 °C/1 mm) and crude (—)-3-mercaptodihydrocarvone (16.8 g, b.p. 148 to 151 °C/0.6 mm). Redistilled, it had b.p. 150–151 °C/0.5 mm. Yield 15.8 g (46%) n_D^{20} 1.5221; $[\alpha]_D^{20}$ –6.3° (c, 4 in chloroform).

$C_{10}H_{16}OS$

Calcd C 65.2 H 8.7 S 17.4,
Found C 65.3 H 8.7 S 17.3.

ν cm^{-1} 3100 ($=\text{CH}_2$), 1650 ($\text{C}=\text{C}$), 2575 ($-\text{SH}$), 1710 (satd. $>\text{C}=\text{O}$), 890 ($=\text{CH}_2$); δ ppm. (220 MHz, CDCl_3) 1.11 (d, 3H, J 6.5 Hz, $-\text{CH}-\text{CH}_3$), 1.22 (d, 1H, J 7 Hz, $-\text{SH}$), 1.76 (s, 3H, $-\text{CH}_3$), 3.70 (m, J 7, 3.8, 3.5, 3.5 Hz, H3), 4.76 and 4.81 (s, each 1H, $=\text{CH}_2$).

(1S, 4S, 5S)-(—)-4,7,7-Trimethyl-6-thiabicyclo-(3,2,1)octan-3-one

Repetition of the preparation above at room temperature using a small excess of triethylamine (15 ml/25 g of (—)-carvone) gave, in addition to 3-mercaptodihydrocarvone, a small amount of product which, distilled at 124 °C/0.2 mm, slowly solidified. The solid (0.5 g) recrystallised from aqueous methanol had m.p. 89–90 °C, $[\alpha]_D^{20}$ –39.5° (c 2.5 in chloroform, l = 1).

$C_{10}H_{16}OS$

Calcd C 65.2 H 8.7 M (mass spec) 184.0922,
Found C 65.2 H 8.8 M (mass spec) 184.0920.

ν cm^{-1} 1705 (satd. $>\text{C}=\text{O}$), 1365, 1375 ($-\text{CMe}_2$); δ ppm. (100 MHz, CDCl_3) 1.16 (d, 3H, J 7 Hz, $-\text{CH}-\text{CH}_3$), 1.42 (s, 6H, $-\text{CMe}_2$), 3.42 (m, 1H, probably H5); δ ppm. (100 MHz, $\text{C}_5\text{D}_5\text{N}$) 1.05 (d, 3H, J 7 Hz, $-\text{CH}-\text{CH}_3$), 1.32 and 1.36 (s, each 3H, $-\text{CMe}_2$), 3.36 (m, 1H, probably H5).

Reaction of (—)-3-mercaptodihydrocarvone with (—)-carvone and (+)-carvone

(—)-3-Mercaptodihydrocarvone (2.0 g) was added to an ice-cooled, stirred solution of (—)-carvone (2.0 g) in ethanol (1 ml) saturated with ammonia; the white solid, m.p. 221–222 °C, which precipitated after a few minutes, was identified as (—)-dicarvone sulphide by mixed m.p., $[\alpha]_D^{20}$, and IR spectrum.

When the mercapto-compound (1.0 g) was allowed to react with (+)-carvone (1 g) (n_D^{15} 1.5018, $[\alpha]_D^{20}$ +58.0° in chloroform) in ethanol (0.5 ml) as above, a white solid (0.97 g) was obtained which crystallised from ethyl acetate, had m.p. 197–199 °C.

$C_{20}H_{30}O_2S$

Calcd C 71.9 H 9.0 S 9.45,
Found C 71.6 H 9.0 S 9.5.

The compound did not show any rotation at the sodium D line. ν cm^{-1} 3100 ($=\text{CH}_2$), 1710 sh, 1705 (satd. $\text{C}=\text{O}$), 1650 ($\text{C}=\text{C}$), 904, 892 ($=\text{CH}_2$), 1710 sh, 1705 (satd. $\text{C}=\text{O}$), 1650 ($\text{C}=\text{C}$), 904, 892 ($=\text{CH}_2$).

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