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Conformational Analysis of 1,4-Dithiane Derivatives

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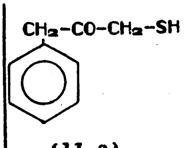
α-Mercapto ketones either exist as such (I-a; II-a; III-a) or dimerise to 2,5-dihydroxy-1,4-dithiane derivatives (I-b; II-b; III-b). The wide range of melting-points reported for these specific compounds provides a confusing dimension to the question of their structure. Infrared spectroscopy has given a qualitative evidence that these compounds exist in solution as a mixture of both forms. Cryoscopic molecular-weight measurements have also given values varying between those for one or two units. In addition to these, ¹H-nmr spectra have given good evidences that α-mercapto ketones are formed as a mixture of monomer and a dimer. No evidences are found to support the previously claimed isolation of two dimeric species. Generally, the dimer dissociates to the monomer on standing as a solution in chloroform, while the monomer is dimerised by the grinding effect.

INTRODUCTION

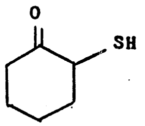
Preparation of some selected α-mercapto ketones such as α-mercapto acetone (I-a)[1-7]; 1-mercapto-3-phenyl-2-propanone (II-a)[8]; 2-mercapto cyclohexanone (III-a)[9,10] and its dimeric forms 2,5-dihydroxy-2,5-dimethyl-1,4-dithiane (I-b); 2,5-dihydroxy-2,5-dibenzyl-1,4-dithiane (II-b); 2,5-dihydroxy-2,3,5,6-bis-tetramethylene-1,4-dithiane (III-b) have been reported early. As an example of this class of compounds α-mercapto acetone (I-a) was first prepared by acid hydrolysis of the glycolic acid derviative[1]; but is more readily obtained by reacting α-haloacetone with sodium hydrogen sulphide[2].

CH_3-CO-CH_2-SH

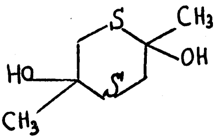
(I-a)



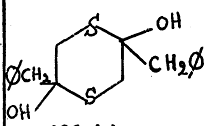
(II-a)



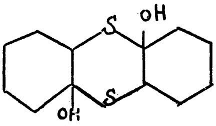
(III-a)



(I-b)



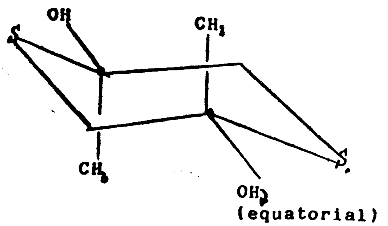
(II-b)



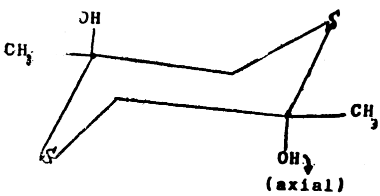
(III-b)

Varied melting points have been reported for products of these reactions[1–6], which contributed to the contention[4,5,7] that α-mercapto acetone exists as two distinct forms denoted hereafter as (A) and (B); where (A) refers to the form having m.pt. 81–83°C in Ref. (4) and 136–138 °C in Ref. (5); and (B) refers to that having m.pt. 107–108°C in Ref. (4) and 117–118°C in Ref. (5). The higher melting points reported in Ref. (5) were attributed to the method of measurement.

As a class, α-mercapto ketones are known to dimerise to the 2,5-dihydroxy-1,4-dithiane system[7] and both (A) and (B) have been postulated to be dimeric on the basis of cryoscopic[4] and i.r. spectral measurements[5]. Schotte[4] found that (A) and (B) gave the same X-ray powder diagrams and, after commenting upon the possibility of cis-trans isomerism, took the view that the forms were probably polymorphic. In another X-ray study, Haberl *et al.*[5] reported differences in the crystal structures; both forms had a centre of symmetry and trans structures (IV) and (V) were assigned to (A) and (B), respectively. However, the isolation of such structures, both recrystallizable from benzene, require a barrier to conformational inversion (IV) ⇌ (V) far in excess of that normally associated with such processes. Furthermore, the greater thermodynamic stability of (A) over (B), as judged by the reported conversion of (B) into (A) by steam distillation[4] and recrystallization from pyridine[5], is inconsistent with (A) having structure (IV) where steric and dipolar repulsions are at a maximum.



(IV)
(A) as reported by Haberl(5),
but it is not stable.



(V)
(A) as reported
by schotte(4) and
it is stable.

i.e., $(B) \rightleftharpoons (A)$

EXPERIMENTAL

According to the above-mentioned contradictions, we had the cause to prepare the three selected α-mercapto ketones mentioned above ourselves and subject all these compounds to ^{1}H-nmr and IR as well as to mass spectroscopic measurements. We ought to follow the same procedures of preparation reported in the literatures[2]. Then 60-MHz nmr spectra were obtained using a Perkin Elmer R-12 spectrometer. Chemical shifts are quoted as ppm downfield from TMS. Infrared spectra were measured using a Perkin Elmer 257-spectrometer, while mass spectra were measured using a Hitachi-Perkin Elmer RMU-6E-spectrometer. All the experimental data are tabulated in Table 1.

RESULTS AND DISCUSSION

We found that α-chloroacetone with H_2S in NaOH at 0°C afforded a product (I) which on recrystallization from benzene had m.pt. 102–106°C. A second recrystallization gave a crop of crystals, m.pt. 92°C and a second crop m.pt. 106°C. All samples showed m/e 180 corresponding to a dimeric structure. However the 60-MHz nmr spectrum of a crop of crystals of m.pt. 102–106°C in $CDCl_3$ showed that each material was a mixture, not of the previously supposed two dimers, but of one dimer and one monomer together. The nmr spectrum of the dimer showed two singlets, the first one at δ1.6 for the six methyl-protons (6H, S) and the other at δ4.3 for the two hydroxyl-protons (2H, S). In addition to that a significant doublet signal (i.e., AB pattern) was shown at δ(2.8–2.5) i.e. (2H, d, J = 14 Hz) and at δ(3.7–3,5) i.e., (2H, d, J = 14 Hz) assignable to the two methylene-protons of the ring. Moreover, the same nmr spectrum showed a sharp singlet at δ2.3 for the methyl-protons (3H, S); a doublet at δ(3.4–3.3) i.e.. (2H, d, J = 8 Hz) for the methylene protons and a triplet at δ(2.1–1.7) assignable to the SH proton (1H, t, J = 8 Hz) of the monomeric structure.

On the other hand, on scanning another crop of crystals of m.pt. 102–106°C in a mixture of $CDCl_3$ and two drops pyridine; pure pyridine alone or CH_2Cl_2, all showed n.m.r. spectra interpretable to the monomer only. Moreover, on using D_2O with $CDCl_3$ it showed n.m.r. spectrum having two sharp singlets of different intensity referring only to the methyl and methylene protons of the deuterated mercapto acetone.

We also found that 1-mercapto-3-phenyl-2-propanone (II-a), prepared from the corresponding chloroketone and NaSH[8] and previously reported[8] to exist as the dimer, behaves in an analogous manner. Freshly prepared material has m.pt. 85–89°C and 92–93°C after recrystallization from ethanol, with a 1 : 1 ratio of monomer to dimer by n.m.r. in $CDCl_3$.

The dimer showed a doublet-doublet i.e., (AB pattern) at δ(2.65–2.4) *i.e.* (2H, d, J = 14 Hz) and at δ(3.6–3.4) *i.e.* (2H, d, J = 14 Hz) for the methylene protons of the 1,4-dithiane ring. In addition to that another composed doublet was shown at δ(3.1–3) *i.e.*, (2H, d, J = 13.5 Hz) and at δ(3.25–3.1) *i.e.* (2H, d, J = 13.5 Hz) assignable to the methylene protons of the benzyl group (due to the geminal coupling). A sharp singlet resonating at δ4.0 was due to the OH protons (2H, S), whereas the

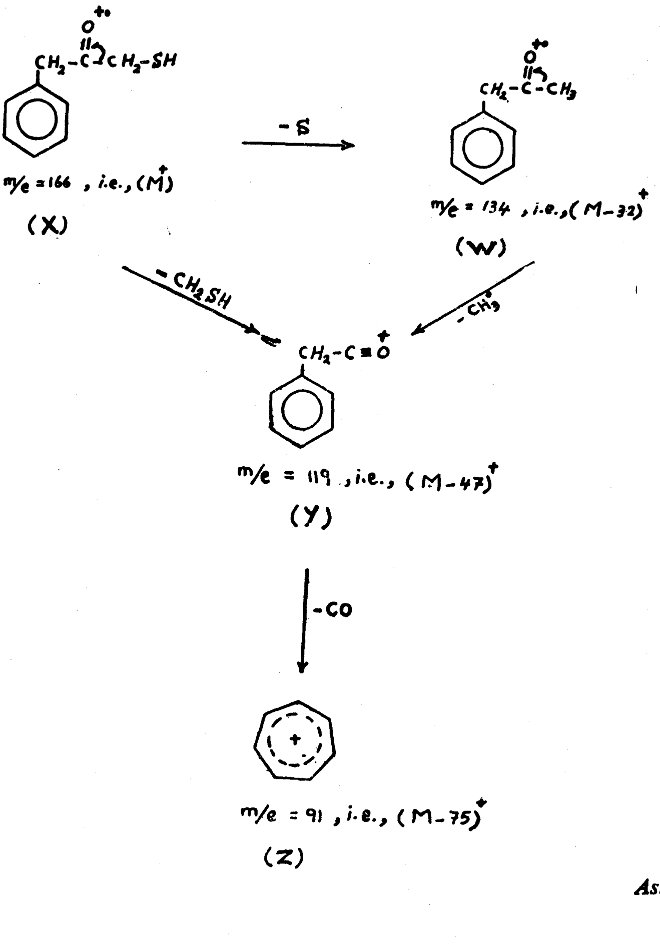
TABLE 1

EXPERIMENTAL RESULTS OF α-MERCAPTO KETONES AND ITS DIMERIC FORMS

Structure	Elemental Analysis (%)				Yield %	M. pt. (°C)	M. Wt.		IR–Assignments; (cm^{-1})		
		C	H	S			Calc.	Found	νCO	νOH	Media
(I) $C_6H_{12}O_2S_2$ as dimer & C_3H_6OS as monomer.	CALC	39.90	6.71	35.50	45	(102–106) at once	180 as dimer	180	— 1720	3460 3600	in $CHCl_3$ in CH_2Cl_2
						(75) after 4 months		—	1720	3470	in $CHCl_3$ in CH_2Cl_2
	FOUND	39.72	6.61	35.49		(92) after further recryst. from benzene or by grinding		180	—	3370	in nujol
(II) $C_{18}H_{20}O_2S_2$ as dimer and $C_9H_{10}OS$ as monomer.	CALC	65.06	6.02	19.29	84	(85–89); (92–93) at once	332 as dimer	314	— 1720 1720	3360 3450 —	in nujol in $CHCl_3$ in CH_2Cl_2
	FOUND	64.80	6.13	18.79		(92–93) after 25 days		166	1720	—	in CH_2Cl_2
						(85) for solid after grinding		330	—	3540	in nujol
(III) $C_{12}H_{20}O_2S_2$ as dimer and $C_6H_{10}OS$ as monomer	CALC	55.34	7.74	24.63	42	(156) at once	260 as dimer	130	— 1700 1720	3340 3450 3670	in nujol in $CHCl_3$ in CH_2Cl_2
						(140–143) after 22 days		—	1720 1720	3450 3660	in $CHCl_3$ only in ($CHCl_3$+Py)
	FOUND	54.88	7.51	25.59		(152) after grinding		260	— — 1720	3330 3450 3660	in nujol in $CHCl_3$ in CH_2Cl_2

broad singlet appeared at δ7.25 was assignable to the phenyl protons (10 H, S). On the other hand, the monomer showed a triplet at δ(2–1.7) for the SH-proton (1H, d, J = 8 Hz), whereas the methylene protons of —CO—CH_2—SH group showed a doublet at δ(3.3–3.2) *i.e.* (2H, d, J = 8 Hz). The CH_2 protons of the benzyl group appeared at δ3.8 as a singlet (2H, S). The five phenyl protons showed a broad singlet at δ7.25 (5H, S). On leaving the material for four days in $CDCl_3$, or as the solid for 25 days, it showed characteristic peaks for only the monomeric species (m.pt. 92–93°C). Grinding the solid again caused dimerization, lowering the m. pt. to 85°C. The schematic diagram of the mass spectrum data for the material left for 25 days (m.pt. 92–93°C) showed M+ at m/e=166, (X), which decomposed to (W) (m/e=134; 12%) due to the loss of S-atom. On further decomposition of (X) and (W) to the cation (Y), the m/e values decreased to 119 (30%) due to the loss of CH_2SH or CH_3 radicals, respectively.

The cation (Y) lost CO giving the resonance stabilized tropylium ion (Z) where m/e=91 (100%). In general, we found that the behaviour of



2-mercapto cyclohexanone (III–a) and its dimeric form (III–b) was in agreement with that discussed above. Now we can generalize that the reaction between H_2S and α-haloketones usually gives α-mercapto ketones which are found to be easily dimerized to the corresponding 1,4-dithianes. We can make the following observations about the composition of the mixtures obtained in the case of α-mercapto acetone:

I — Sample of m.pt. 92°C was (0·8 : 1) monomer to dimer.

II — Sample of m.pt. 106°C was (1.1 :1) monomer to dimer.

III — Sample left for 3 weeks in $CDCl_3$ contained only monomer. This conversion was rapid (< 15 min) on addition of two drops of pyridine tothe solution.

IV — In contrast, grinding of a monomer-dimer mixture increased the amount of dimer present. Indeed the i.r. spectrum of a well ground Nujol mull showed no C=O band but a strong OH absorption.

The structure of the dimer cannot be assigned unambiguously but simple conformational considerations predict that the trans-isomer is more stable than the cis-form. We do not wish to speculate about previous reports claiming the isolation of two dimeric species other than to note the following points :

I — Evidence in favor of dimeric structures obtained from i.r. spectra as Nujol mulls[5] is equivocal in view of the dimerization of monomer during mulling.

II — The reported conversion of (B) into (A) on recrystailization from pyridine[5], and our observations on the effect of pyridine on our dimer, raise doubts about the exclusively dimeric nature of (A).

III — The (9.5–4) μ-region of the i.r. spectra of (A) and (B) in CCl_4 illustrated in Ref. (5) indeed show strong O–H absorption. However, inspection shows that both (A) and (B) exhibit a weak band at 3.9μ where S–H bonds absorb, implying that neither (A) nor (B) is exclusively dimeric.

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