

β -Thioxoketones. Part 9.¹ A Dynamic ¹H Nuclear Magnetic Resonance Spectroscopic Study of Thioacetylacetone and Related β -Thioxoketones. Direct Observation of the Enol and Enethiol Tautomeric Constituents and their Interconversion

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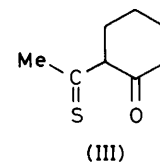
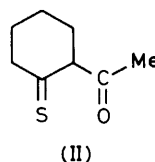
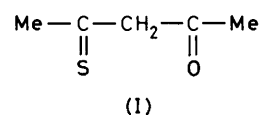
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Thioacetylacetone (I), 2-acetylcyclohexanethione (II), and 2-thioacetylcyclohexanone (III) have been studied by dynamic ¹H n.m.r. spectroscopy from ambient temperature down to *ca.* 130 K. The general co-existence of two tautomeric constituents has been established, and the constituents, in the cases of (I) and (III), directly observed. These were identified as the strongly chelated (*Z*)-enol form and the weakly chelated (*Z*)-enethiol form. Band-shape analysis provided ΔG^\ddagger (enol \rightarrow enethiol) 8.9 ± 0.1 kcal mol⁻¹ for (I) and 7.6 ± 0.1 kcal mol⁻¹ for (III).

As mono-sulphur analogues of β -diketones, the principal compounds connected with prototropic tautomerism and intramolecular enolic hydrogen chelation, β -thioxoketones † are of obvious interest as model compounds for studies of these phenomena, not least because of the molecular asymmetry generated by the incorporation of the sulphur atom. Recent ¹H n.m.r.,^{2,3} i.r.,^{2,3} and u.v.²⁻⁵ spectroscopic studies of thioacetylacetone (I)^{2,4,5} and of other simple β -thioxoketones such as 2-acetylcyclohexanethione (II)³ and 2-thioacetylcyclohexanone (III)³ have jointly indicated a common tautomeric arrangement for these compounds, namely equilibrated co-existence of the (*Z*)-enol and (*Z*)-enethiol forms (D) and (C), respectively (Scheme), between which interconversion takes place very rapidly at room temperature, probably by simple proton-transfer.

The actual site of the equilibrium depends primarily on the particular molecule,^{2,3} and otherwise on external conditions like temperature⁴ and the nature of the molecular surroundings.^{2,3,5} This picture of the state of existence of simple non-aromatic β -thioxoketones was based on the following general observations. (a) The ¹H n.m.r. spectra display a resonance pattern best interpreted in terms of the weighted average spectrum of two molecular species (C) and (D) in rapid interconversion.^{2,3} (b) The i.r. spectra show the co-existence of both enol and enethiol tautomeric forms in a concentration ratio conforming to that predicted by the ¹H n.m.r. spectrum.^{2,3} (c) The u.v. spectra display two characteristic bands at *ca.* 290 and *ca.* 360 nm, assignable to $\pi \rightarrow \pi^*$ transitions in the chromophore systems S=C=C-C=O and O=C=C-C=S, respectively; the intensities of the bands are inversely correlative, and vary with the temperature⁴ and the nature of the solvent^{2,3,5} consistent with the existence of a mobile enol \rightleftharpoons enethiol equilibrium system. Theoretical calculations⁵⁻⁷ and recent photoelectron spectroscopic investigations^{1,8} support this picture of tautomerism, which is also valid apparently for α -unsubstituted aromatic β -thioxoketones.⁹

Very recently Gebicki and Krantz¹⁰ have questioned the above findings. On the basis of i.r. spectroscopic monitoring at low temperature (12 K) of the equilibrium displacement



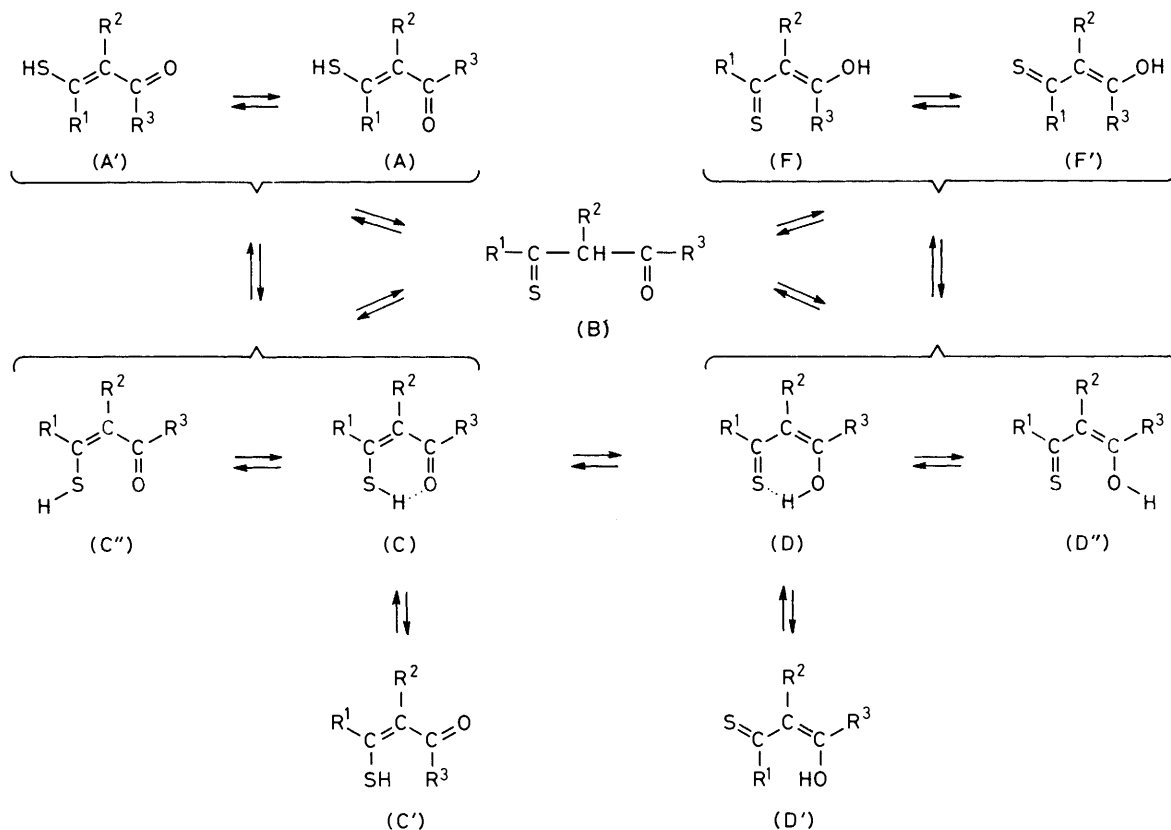
taking place between the constituents of thioacetylacetone (I) upon u.v. irradiation,⁴ they claim¹⁰ to have provided evidence for the existence of an equilibrium system composed exclusively of the enethiol from (C) and its rotamer (C') (Scheme).‡

It is evident from the ¹H n.m.r. spectrum of (I) (which constantly displays the resonance signal of a chelated proton) that neither the thioxoketone form (B), nor any of the (*E*)-enol or (*E*)-enethiol species (A), (A'), (F), and (F') can be constituents of (I). Interconversion processes involving these species (*i.e.* keto-enol tautomerization,^{11,12} thioxo-enethiol tautomerization,^{12,13} and *E-Z*-isomerisation^{13,14}) would proceed too slowly to effect spectrum averaging. In fact, (*E*)-enethiol and (*E*)-enol forms have been observed as distinct individual species in the ¹H n.m.r. spectra of 'less simple' β -thioxoketones.^{3,15} Thus, as regards (I) and related simple β -thioxoketones, a discussion of the tautomeric composition can comprise merely the structures (C) and (D), and their rotameric relatives (C'), (C''), (D'), and (D'') (Scheme).

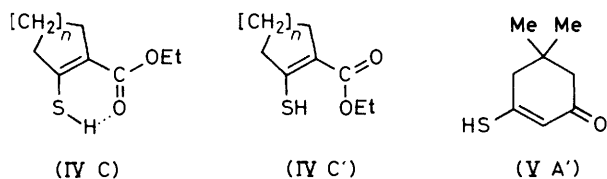
There are, however, several reasons to reject the finding of Gebicki and Krantz. (1) Unfortunately, and undoubtedly influenced by the thinking of Siiman *et al.*,¹⁶ Gebicki and Krantz in their discussion¹⁰ of the i.r. spectrum of thioacetylacetone (I) focus restrictively only on spectral details which confirm the hypothesis of rotamerism. For example, the very

† The β -thioxoketones are named as such for simplicity, regardless of which possible tautomer is actually predominant. The notation of the tautomeric forms as shown in the Scheme is consistent with that in previous parts.

‡ Thioacetylacetone displays similar u.v. spectra as a solute at room temperature^{2,4} and as a matrix-isolated species at 12 K.¹⁰ This strongly indicates that the equilibrium system studied by Gebicki and Krantz is identical to that studied by us.



Scheme.



weak bands in the region of S-H stretching vibrations are carefully recognized, but no attention is paid to the O-H stretching mode.* A thorough examination of the i.r. spectrum of (I) leaves no doubt concerning the existence of the (C) \rightleftharpoons (D) equilibrium system.¹⁷ (2) Different rotameric forms of the same enethiol molecule do not exhibit so very different u.v. absorptions.^{2-5,10} According to ¹H n.m.r. and i.r. spectroscopic evidence,¹⁸ the practically completely enethiolized five- to nine-membered 2-ethoxycarbonylcycloalkanethiones (IV) populate two rotameric forms (IVC) and (IVC'), but they nevertheless display only a single u.v. absorption band above 220 nm.† Thiodimedone, known to exist entirely in the enethiol form (VA') in hexane solution, displays its $\pi \rightarrow \pi^*$ absorption band at 268 nm in that solvent.¹⁹ 4-(Methylthio)pent-3-

en-2-one, the *S*-methyl derivative of thioacetylacetone, also absorbs below 300 nm.^{2,20} In fact, enethiol forms of β -thioxo-carbonyl compounds are not at all expected to exhibit u.v. absorption at wavelengths as high as 350–370 nm, whereas this is likely to be the case for enolthioketones.^{5,9a,19} (3) 2-Thioacylcyclohexanone (III) cannot exist in the (C') rotameric form, but it nevertheless displays u.v. $\pi \rightarrow \pi^*$ absorption bands both at *ca.* 290 and *ca.* 370 nm.³

The obvious way of clarifying the constitution of thioacetylacetone (and of simple β -thioxo ketones in general) is to examine the constituents under conditions allowing for their characterization as individual species. Apparently the i.r. and u.v. spectroscopic methods are not sufficiently unambiguous. Individual characterization of the constituents of (I) by n.m.r. requires, owing to the rapid interconversion, a sufficiently low investigation temperature. Although limited successful attempts in this respect have been reported²¹⁻²⁴ (for related studies, see also ref. 25), we considered a further attempt desirable. Thioacetylacetone (I) and the cyclic β -thioxo ketones (II) and (III) were selected for this study.

Experimental

Compounds (I)–(III) were prepared by literature methods.^{2,3} The ¹H n.m.r. spectra were recorded on a JEOL model MH-100 spectrometer using standard variable-temperature equipment. The samples, with tetramethylsilane as internal standard, were degassed by repeated freeze-thaw cycles under high vacuum before being sealed off. The *T*₂ values and temperatures were determined as previously described.^{26,27} The rate constants for interconversion were determined by visual comparison of the experimental bandshapes with spectra calculated by the McConnell equation.²⁸ The free

* The O-H stretching vibration absorption is recognizable as a very broad band centred at *ca.* 2 350 cm⁻¹ in consequence of strong chelation. The assignment has been confirmed by deuterium labelling experiments.¹⁷

† The u.v. spectra of the compounds in question display (in cyclohexane solution) an absorption at above 220 nm due to $\pi \rightarrow \pi^*$ transition(s) as follows: (IV; *n* = 1), λ_{max} 272 nm (ϵ_{max} 10 400); (IV; *n* = 2), λ_{max} 272 nm (ϵ_{max} 8 550); (IV; *n* = 3), λ_{max} 281 nm (ϵ_{max} 8 740); (IV; *n* = 4), λ_{max} 279 nm (ϵ_{max} 8 650); (IV; *n* = 5), λ_{max} 277 nm (ϵ_{max} 8 525) (F. Duus, unpublished results).

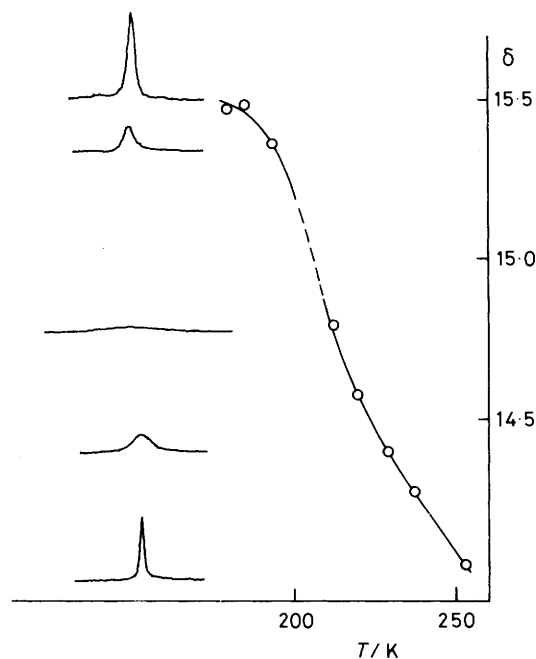


Figure 1. Temperature dependence of the low-field resonance of thioacetylacetone (I) in CS_2

energy barriers were obtained by the Eyring equation in the form (1).²⁹

$$\Delta G_{A \rightarrow B}^\ddagger = 0.004575T (10.319 + \log T/k_{A \rightarrow B}) \quad (1)$$

Results

The ^1H n.m.r. spectrum of thioacetylacetone (I) in CS_2 at -20°C appeared as four singlets in the intensity ratio 1 : 1 : 3 : 3 with chemical shifts δ 14.05, 6.27, 2.38, and 2.06. They are assigned in this order to the acidic and the vinylic protons, and to the thioacetyl and acetyl methyl protons. When the temperature was lowered, the low-field resonance broadened and appeared as a singlet with a halfwidth of 50 Hz at -60°C . At still lower temperatures the signal sharpened again. Due to solubility problems, spectra could not be recorded below -96°C , and at this temperature no new signals nor any selective broadening of the vinyl or methyl proton signals could be observed (Figure 1). The δ value of the acidic proton resonance increased from 14.05 at -20°C to 15.48 at -96°C .

In the same solvent 2-acetylcylohexanethione (II) shows one signal for the acidic proton with δ decreasing from 5.65 at -8°C to 4.55 at -60°C , below which temperature insufficient solubility precluded further measurements. In 3 : 1 (v/v) CS_2 - $[\text{H}_8]$ toluene the δ - T curve ran nearly parallel to the one in CS_2 solution, with some high-field displacement, and the measurements could be pursued down to -80°C (Figure 2). Above this temperature, no selective broadening could be observed. The CH_3CO signal in (II) appeared at δ 1.91.

In CS_2 solution 2-thioacetylcylohexanone (III) showed a methyl resonance at δ 2.44, and a sharp singlet with δ changing from 16.11 at -18°C to 16.51 at -80°C (Figure 2). No selective broadening could be observed in this temperature region.

Using the chemical shifts of the acidic protons in (II) and (III) as representative for the enethiol and enol sites in (I), the exchange-broadened bandshape of this resonance in (I) can be simulated. It corresponds to a 95 : 5 equilibrium with ΔG^\ddagger (major \rightarrow minor) $9.5 \pm 0.4 \text{ kcal mol}^{-1}$.

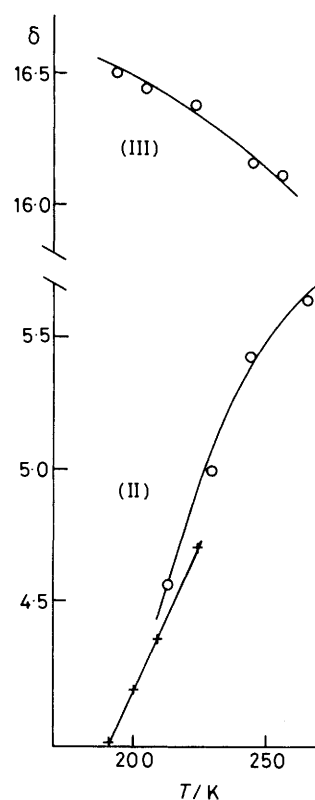


Figure 2. Temperature dependence of the chemical shift of the acidic proton in 2-acetylcylohexanethione (II) and 2-thioacetylcylohexanone (III): \circ , solvent CS_2 ; $+$, solvent CS_2 - $[\text{H}_8]$ toluene (3 : 1)

In order to make possible studies at lower temperatures, samples of compounds (I)—(III) were prepared in a mixture of chlorodifluoromethane and dichlorodifluoromethane, though these solvents, being both weak donors and weak acceptors of hydrogen bonds, can be expected to perturb the position of the tautomeric equilibrium as well as the rate by which it is attained.

In this solvent at ambient temperature, (I) showed a spectrum rather similar to that in CS_2 solution at -20°C . The acid proton resonance appeared as a somewhat broad singlet ($\delta v_{\frac{1}{2}}$ 1.8 Hz) at δ 11.19, the vinylic resonance as a quartet (J ca 0.8 Hz) at δ 6.31, the thioacetyl resonance as a badly resolved doublet of doublets at δ 2.31, and the acetyl resonance as a singlet at δ 2.09. With decreasing temperature the acidic proton resonance broadened strongly and moved to higher field (Figure 3). At ca. -50°C it could not be distinguished from the baseline, and at still lower temperatures two new resonances appeared, one at δ 13.93 and the other at δ 3.33 (-102°C). These signals had similar intensities, and their positions changed insignificantly on further decrease in temperature. In the temperature region -50 to -110°C the acetyl and thioacetyl resonances also underwent broadening and decoalescence into nearly symmetrical doublets. Bandshape analysis of exchange-broadened signals at -100°C gave ΔG^\ddagger $8.9 \pm 0.1 \text{ kcal mol}^{-1}$ for the exchange process.

Under the same conditions, (II) showed only one set of signals, and no effects of exchange were observed. The acidic proton resonance appeared at δ 3.20 (-95°C), and its position showed only a small temperature dependence. Compound (III), on the other hand, showed decoalescence below -118°C of the acidic proton resonance into one singlet at δ 17.09 and one at δ 3.58 in the ratio 83 : 17 (Figure

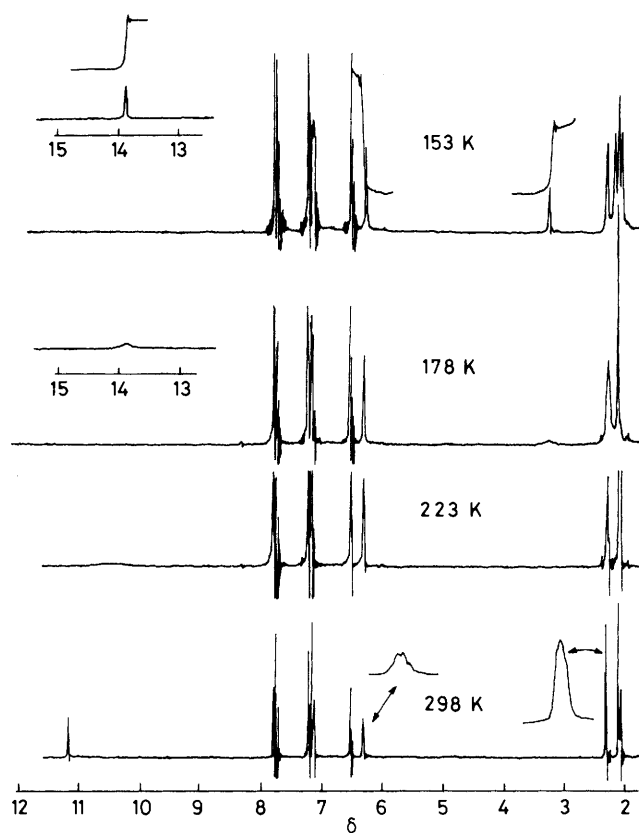


Figure 3. 100 MHz ^1H N.m.r. spectra of thioacetylacetone (I) in $\text{CHClF}_2\text{-CHCl}_2\text{F}$ at various temperatures

4). Bandshape simulation gave ΔG^\ddagger (major \rightarrow minor) $7.06 \pm 0.1 \text{ kcal mol}^{-1}$ at both -64 and -118°C .

Discussion

Previous u.v. spectroscopic investigations of thioacetylacetone (I) in inert solvents have demonstrated⁴ that the equilibrium between the tautomeric constituents on temperature-lowering is shifted continuously in favour of one of the constituents, so that only this constituent, considered to be the (Z)-enol form (ID),⁴ exists at sufficiently low temperature. It is therefore no surprise that, even though the temperature-dependent ^1H n.m.r. spectra of (I) in CS_2 clearly display decoalescence at 213 K as regards the acidic proton resonance signal (Figure 1), no second constituent is directly observable below that temperature, evidently due to its lack of abundance. The temperature-dependent ^1H n.m.r. spectra of (II) and (III) in CS_2 show no distinct decoalescence, but the displacements of the resonance signals of the acidic protons towards δ 4.55 and 16.51, respectively, effected upon temperature-lowering down to 193 K (Figure 2), indicate in both these cases induced equilibrium displacements, favouring continuously the tautomeric constituent which appears as the thermodynamically more stable at ambient temperature.

It has been demonstrated^{2,3} that the equilibrium between the constituents of simple β -thioxoketones in solution is affected by the solvent, depending on the ability of the species to gain or lose stability by the interaction with the solvent molecules. Dissolved in the mixture of chlorodifluoromethane and dichlorofluoromethane (Freon) thioacetylacetone (I) displays a ^1H n.m.r. spectrum at 153 K in which the average acidic proton resonance signal appears at δ 11.19 (Figure 3),

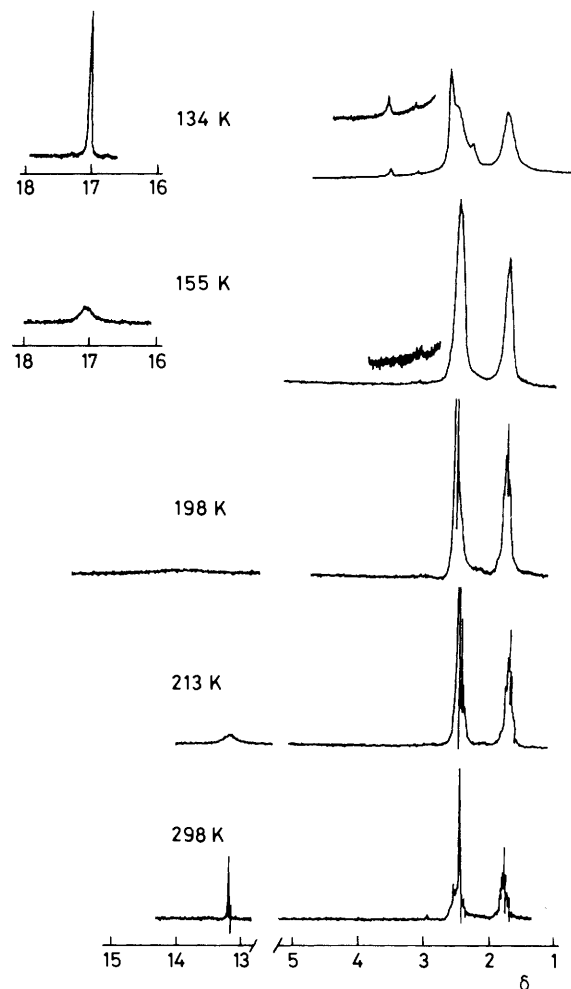
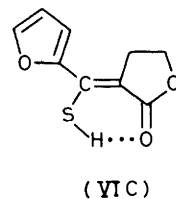


Figure 4. 100 MHz ^1H N.m.r. spectra of 2-thioacetylacetylhexanone (III) in $\text{CHClF}_2\text{-CHCl}_2\text{F}$ at various temperatures



thus indicating an increased equilibrium concentration of the minor constituent of (I) due to solvent effects. Consequently, at appropriately low temperature (153 K) complete resolution of the average spectrum of (I) into the spectra of two apparent constituents is achieved (Figure 3). A similar resolution could not be obtained for 2-acetylacetylhexanone (II), but in the case of 2-thioacetylacetylhexanone (III) the minor constituent became directly recognizable by its acidic proton resonance signal at δ 3.58 (Figure 4).

The highest δ value ever reported for a carbonyl-chelated thiolic proton is 8.44, found for the completely enethiolized α -thiofuroyl- γ -butyrolactone, *i.e.* (Z)-2-[α -mercaptofurfurylidene]- γ -butyrolactone (VIC).³⁰ Chelated enols, however, generally display their acidic proton resonance signal in the region δ 12–18.¹² It would be a coarse violation of the validity of empiricism to postulate an enethiol structure for that constituent of (I) and (III) which demonstrably displays its acidic proton resonance signal in this region. Hence the enol structure (D) must be assigned to this species.

The free energies of activation determined for the conversion of the thiocarbonyl-chelated enol (D) into 'the second constituent' [$\Delta G^\ddagger(\text{I}) 8.9 \pm 0.1$, $\Delta G^\ddagger(\text{II}) 7.6 \pm 0.1$ kcal mol⁻¹] rule out assignment of the rotameric enol forms (D') and (D'') to the latter, since the energies connected with hydroxy-group rotamerism [*i.e.* (D) \rightleftharpoons (D')] are normally considerably smaller.³¹ Furthermore, (D) \rightleftharpoons (D') rotamerism is not physically feasible for (II). Remembering that 'the second constituent' is the predominant species in the case of 2-acetylcyclohexanethione (II), it is also worth mentioning that this particular compound, the only one among the hitherto known simple β -thioxo ketones, displays in its i.r. spectrum a really strong absorption band in the region of carbonyl group stretching vibrations [$\nu(\text{C}=\text{O}) 1670$ cm⁻¹] and, in addition, an unambiguous, although weak band in the region of thiol stretching vibrations [$\nu(\text{S}-\text{H}) 2540$ cm⁻¹].³ Thus, an enethiol structure, most probably (C), is the only plausible structure for 'the second constituent'.

The chemical shifts of the acidic proton of the enethiol constituents in Freon [$\delta(\text{IC}) 3.33$ at 171 K, $\delta(\text{IIC}) 3.20$ at 178 K, $\delta(\text{IIIC}) 3.58$ at 155 K] as well as in CS₂-[²H₆]toluene solution [$\delta(\text{IIC}) 3.5$, upon extrapolation to 173 K, see Figure 2] are considerably smaller than those observed for the chelated enethiolic proton in enethiolized β -thioxoesters (normal range, $\delta 4.5$ — 7.5),^{14,18} although hardly as small as those found for enethiol protons not engaged in hydrogen bonding (normal range, $\delta 2.7$ — 3.2).^{14,18} With this background we conclude that the enethiol constituent most probably corresponds to structure (C), but that the intramolecular hydrogen-bonding connected with this structure is very weak, and probably weak enough to allow easy perturbation and consequently population of rotameric forms like (C'') and perhaps also (C') [in (I) and (II)] through low interconversion energy barriers.

In connection with the above discussion a study by Noe³² of the hindered rotation of the SH group in thiolacetic acid is of interest. Noe found barriers of 7.0 and 7.3 kcal mol⁻¹ (minor to major constituent, and the reverse) for this process in chlorodifluoromethane. Since the barriers to rotation of the amino-group in simple aliphatic *NN*-dimethylamides are 4.5 kcal mol⁻¹ higher than those in the corresponding vinylogous amides,³³⁻³⁵ the barrier found by Noe certainly represents an upper limit for the barrier to rotation of the SH group in (IC). Hence we conclude that the barriers we have measured are not between the forms (C) and (C'') (*cf.* ref. 10).

With this work the first direct proof for the co-existence of two tautomeric forms as the constituents of simple β -thioxo ketones has been provided. It is consistent with theoretical predictions^{7,36} that one of these constituents, the (*Z*)-enol form (D), exhibits very strong acidic proton chelation, and the other, the (*Z*)-enethiol form (C), in consequence of considerably weaker intramolecular hydrogen bonding, can apparently exist in rotameric forms.

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Received 1st November 1982; Paper 2/1835