676. *2-Acyl Derivatives of Cyclic* 1 : 3-*Diones. Part III.* Ultraviolet and Infrared Absorption Spectra of 2-Acyl*cyclo*hexane*-1 : 3-*diones.*

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The ultraviolet and infrared absorption spectra of typical 2-acyl*cyclo*hexane-1 : 3-diones have been studied. The influences of the polarity of the solvent and variation in pH on the ultraviolet absorption spectra lead to the conclusion that these compounds are completely enolised. The infrared absorption spectra provide evidence of intramolecular conjugate chelation.

VARIOUS 2-acyl*cyclo*hexane-1 : 3-diones have been isolated from natural sources. They include calythrone,[1,2] humulone, and lupulone and related compounds,[3,4] usnic acid,[5,6] leptospermone,[7,8] angustione, and dehydroangustione,[2,9,10] and constituents of the resin of *Aspidium filix mas*.[2,11,12] Particular interest attaches to several members of the group which have activity as anthelmintics, insecticides, and antibiotics : in the last case it appears that the activity is dependent on the presence of the triketone structure in these compounds.[13]

We have studied the ultraviolet and infrared absorption spectra of 2-acyl*cyclo*hexane-1 : 3-diones to obtain knowledge of structure which may contribute to the correlation of biological activity with molecular constitution and to obtain information which may assist in the characterisation of this group of compounds.

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* Part II, *J.*, 1955, 2860.

[1] Penfold and Simonsen, *J.*, 1940, 412.
[2] Birch, *J.*, 1951, 3026.
[3] Wöllmer, *Ber.*, 1925, **58**, 672.
[4] Howard and Tatchell, *J.*, 1954, 2400; *Chem. and Ind.*, 1955, 1595.
[5] Curd and Robertson, *J.*, 1937, 894.
[6] Barton, Deflorin, and Edwards, *Chem. and Ind.*, 1955, 1039.
[7] Briggs, Hassall, and Short, *J.*, 1945, 706.
[8] Briggs, Hassall, and Taylor, *J.*, 1948, 383.
[9] Cahn, Gibson, Penfold, and Simonsen, *J.*, 1931. 286.
[10] Chan and Hassall, *J.*, 1955, 2860.
[11] Boehm, *Annalen*, 1901, **318**, 230 *et seq.*
[12] McGookin, Robertson, and Simpson, *J.*, 1953, 1828.
[13] Hassall, *Experientia*, 1950, **6**, 462.

The results in Table 1 indicate that the ultraviolet absorption spectra of 2-acyl*cyclo*hexane-1 : 3-diones in ethanol have two maxima, in the region of 235 and of 275 mμ. There is variation in the relative heights of the maxima. It will be shown that this may be related to the degree of dissociation of the enolic forms of the compounds. Substitution at the 4- or the 6-position in the *cyclo*hexane ring leads to minor variations in $\lambda_{max.}$ values. There are similar maxima (223—233 and 271—293 mμ) in the spectra of acyltetronic acids [17] and compounds containing an acylphloroglucinol nucleus.[18]

TABLE 1.*

	$\lambda_{max.}$ (mμ)	ε	Ref.
4 : 4 : 6 : 6-Tetramethyl-2-*iso*valeryl*cyclo*hexane-1 : 3 : 5-trione (I)	238, 279	7900, 11,600	
2-Acetyl-4 : 4 : 6 : 6-tetramethyl*cyclo*hexane-1 : 3 : 5-trione (II)	235, 277	8450, 10,500	
2-Acetyl-5 : 5-dimethyl*cyclo*hexane-1 : 3-dione (III)	231, 277	10,000, 10,000	2
2-Acetyl*cyclo*hexane-1 : 3-dione (IV)	235, 275	14,700, 11,600	14
2-Acetyl-4 : 4 : 6-trimethyl*cyclo*hexane-1 : 3-dione (VI)	233, 276	13,500, 13,500	10
2-Acetyl-4 : 4 : 6-trimethyl*cyclo*hex-5-ene-1 : 3-dione (VII)	233, 279	9000, 6200	
Usnic acid	233, 285	22,300, 22,800	
Flavaspidic acid	229, 292·5	26,350, 20,300	15
Albaspidin	223, 271	27,300, 13,400	15
Humulone	237, 282	13,760, 8330	16
Lupulone	228, 280	14,080, 6210	16

* Compounds dissolved in ethanol.

The molecular extinction values at the two maxima of the model compound 4 : 4 : 6 : 6-tetramethyl-2-*iso*valeryl*cyclo*hexane-1 : 3 : 5-trione (I) vary with concentration (Table 2).

TABLE 2.

Solvent	Concn. (10^{-5} M)	$\lambda_{max.}$ (mμ)	ε
	*4 : 4 : 6 : 6-Tetramethyl-2-*iso*valeryl*cyclo*hexane-1 : 3 : 5-trione*		
95% EtOH	10	238, 279	7520, 11,530
,,	5	238, 279	7300, 11,800
,,	4	238, 279	6920, 12,400
,,	3	238, 279	6500, 13,000
,,	2	238, 279	5750, 14,000
,,	1	238, 279	4700, 14,500
EtOH–HCl	10	238, 279	8300, 10,800
*cyclo*Hexane	10	234, 281	8900, 10,720
	*2-Acetyl-5 : 5-dimethyl*cyclo*hexane-1 : 3-dione*		
95% EtOH	10	231, 277	10,000, 10,000
EtOH–HCl	10	232, 276	10,000, 9700
*cyclo*Hexane	10	230, 276	10,160, 9800

With increasing dilution the height of the maximum at 238 mμ decreases while that at 279 mμ increases. Also, the compounds (I) and (II) in *cyclo*hexane absorb more strongly in the 230 mμ region but less in the 279 mμ region than when solutions in ethanol are involved.

The ultraviolet absorption spectra of 2-acyl*cyclo*hexane-1 : 3-diones are sensitive to changes in pH. The results for the ketone (I), which are typical, are shown in the Figure. The single sharp isosbestic point (λ 256 mμ, log ε 3·84) indicates that only two molecular species are involved in the change in pH. It is evident that these are the enol and the corresponding ion, the latter being responsible for the maximum at 279 mμ. The results in Table 2 are in agreement with this. The increase in the proportion of ion with increasing dilution in an ionising solvent is the expected behaviour of a relatively weak acid.

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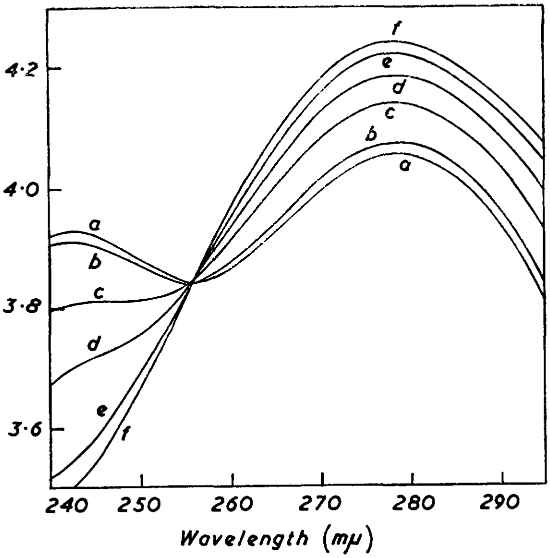
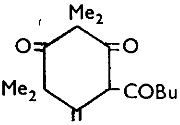
[14] Smith, *J.*, 1953, 803.
[15] Mulholland, Thesis, Manchester, 1947.
[16] Cook and Harris, *J.*, 1950, 1873.
[17] Lacey, *J.*, 1954, 832.
[18] Birch and Todd, *J.*, 1952, 3102.

Keto-enol equilibria are very sensitive to change in the polarity of solvent. In non-polar solvents, compounds such as Meldrum's acid, *cyclo*hexane-1 : 3-dione, and *cyclo*hexane-*spiro*-5-*cyclo*hexane-1 : 3-dione are largely in the keto-form, but the typical 2-acyl*cyclo*hexanone, benzoylcamphor, is 95% enolised. In polar solvents the *cyclo*hexane-1 : 3-diones are largely enolic and benzoylcamphor mainly (58%) in the keto-form.[19] The close similarity of the molecular extinction values of the 2-acyl*cyclo*-1 : 3-diones (I) and (III) in ethanol–hydrochloric acid and in *cyclo*hexane indicates that enolisation is essentially complete in both solvents.

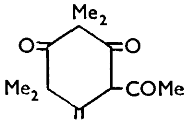
There are two ways of interpreting the variation in the form of the absorption spectrum with change in pH. Either the maxima at 238 and 279 mμ are separately due to the undissociated enol and the corresponding ion respectively, or the absorption at pH 1·2 (and in *cyclo*hexane) is due to the enol alone, *i.e.*, the enol has maxima at both 238 and 279 mμ while the ion has a maximum at 279 mμ alone. We favour the second alternative.



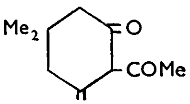
Ultraviolet-light absorption of 4 : 4 : 6 : 6-*tetramethyl*-2-isovaleryl*cyclo*hexane-1 : 3 : 5-*trione at* pH (*a*) 1·22, (*b*) 3·38, (*c*) 4·31, (*d*) 4·73, (*e*) 5·41, (*f*) 13.



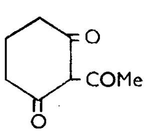
(I)



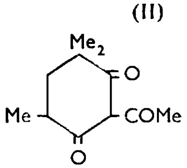
(II)



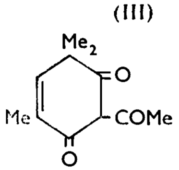
(III)



(IV)



(VI)



(VII)

To accept the first would imply that in *cyclo*hexane or in 0·1N-hydrochloric acid the compound (I) is substantially ionised. This is unreasonable as it is a relatively weak acid, having pK_a estimated by potentiometric titration * as 5·0.

In considering the ultraviolet absorption spectrum of 2-acetyl*cyclo*hexane-1 : 3-dione,

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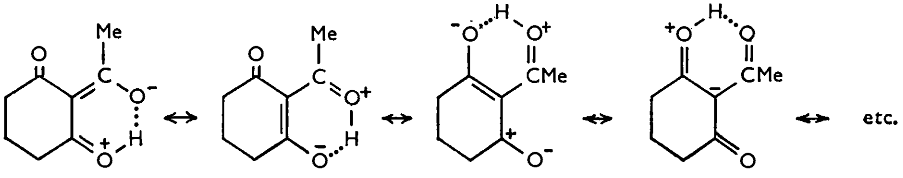
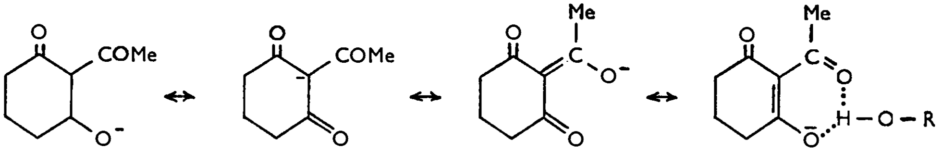
* The potentiometric titration was carried out in 20% ethanol. The pK_a value deduced from the absorption spectra by plotting pH against ε (at $\lambda_{max.}$), separately for the enol and the enol ion, is 4·5. The difference between the two values is doubtless due, at least in part, to the use of different solvents.

[19] Eistert and Reiss, *Chem. Ber.*, 1954, **87**, 92.

Smith [14] suggested that the maximum at 235 mμ (ε 14,700) arises from the $\alpha\beta$-unsaturated carbonyl system in the enol formulated as (IVa) while the maximum at 275 mμ (ε 11,600) may be attributed to the conjugated diene chromophore in the ring involving hydrogen bonding. There is no evidence that such a compact, cross-conjugated system may be dissected into two chromophoric groups in this way. In fact it seems preferable to regard the enol as being a resonance hybrid of such forms as (IVa—d). The corresponding forms for the ion would be (Va—d). There are good indications from the studies on 2-acetyl*cyclo*hexanone that " solvent chelate " complexes such as (Vd) may exist in hydroxylic solvents.[19]



(IVa) (IVb) (IVc) (IVd)



(Va) (Vb) (Vc) (Vd)

The infrared absorption spectra of several 2-acyl*cyclo*hexane-1 : 3-diones have been determined. The maxima in the regions 1900—1400 and 4000—2700 cm.$^{-1}$ are recorded in Table 3. There is no absorption in the region 3520—3100 cm.$^{-1}$, where simple hydrogen-bonded hydroxyl bands normally appear, but there is an indication of a very broad band of low intensity and without a definite maximum overlapping the C–H stretching frequencies near 2800 cm.$^{-1}$ and extending to approximately 2500 cm.$^{-1}$. In all cases there are strong bands in the region 1678—1650 cm.$^{-1}$. These fall close to the range 1685—1665 cm.$^{-1}$ assigned to $\alpha\beta$-unsaturated ketones and may reasonably be attributed to conjugated carbonyl groups. The absence of carbonyl absorption in the region 1725—1705 cm.$^{-1}$, except in the case of the ketone (I) which has an isolated carbonyl group, indicates that the 2-acyl*cyclo*hexane-1 : 3-diones are completely enolised.

TABLE 3.

Compound	Liquid film (cm.$^{-1}$)	$CHCl_3$–1% EtOH (cm.$^{-1}$)	Assignment
4 : 4 : 6 : 6-Tetramethyl-2-*iso*valeryl*cyclo*hexane-1 : 3 : 5-trione (I)	2650—2450	—	OH (H-bonded)
		1715	C=O (unconjugated)
		1660	C=O (conjugated)
		1550	C=O (conjugate chelate)
2-Acetyl-5 : 5-dimethyl*cyclo*hexane-1 : 3-dione (III)	2700—2500	—	OH (H-bonded)
		1656	C=O (conjugated)
		1555	C=O (conjugate chelate)
2-Acetyl-4 : 4 : 6-trimethyl*cyclo*hex-5-ene-1 : 3-dione	2700—2440	—	OH (H-bonded)
		1660	C=O (conjugated)
		1630	C=C (conjugated)
		1540	C=O (conjugate chelate)
2-Acetyl-4 : 4 : 6-trimethyl*cyclo*hexane-1 : 3-dione	2630—2410	—	OH (H-bonded)
		1650	C=O (conjugated)
		1543	C=O (conjugated chelate)
2-Acetyl*cyclo*hexane-1 : 3-dione [14]	2630 (diffuse)	—	OH (H-bonded)
		1680	C=O (conjugated)
		1565	C=O (conjugated chelate)

All the spectra have a very intense band at 1565—1540 cm.$^{-1}$. There are several recorded examples of carbonyl absorption in this region. Enolised acetylacetone and dibenzoylmethane do not absorb in the usual αβ-unsaturated ketone region but have very strong bands [20] between 1639 and 1538 cm.$^{-1}$. 2-Hydroxyacetophenone and salicylaldehyde have bands at 1639—1613 cm.$^{-1}$ and the examination of a series of aromatic ketones has shown that the *o*-hydroxyl group is necessary for the shift of the carbonyl band from its normal position.[21, 22] Cyclic β-keto-esters,[23] tetronic acids,[24] *cyclo*hexane-1 : 3-diones,[20, 25] and chelated hydroxy-quinones [26, 27] have bands between 1656 and 1538 cm.$^{-1}$. In all these cases the position of this absorption maximum has been attributed to conjugate chelation [20]—the formation of unusually strong hydrogen bonds through the stabilisation arising from ionic resonance forms. The strong bands at 1565—1540 cm.$^{-1}$ in the spectra of 1-acyl*cyclo*hexane-1 : 3-diones may be explained in terms of conjugate-chelation effects. Ionic resonance forms such as (IVb) will make an important contribution to the stabilisation of hydrogen bonds. The effect is enhanced by the symmetry of the β-triketone system. The bands are not dependent on concentration. It follows that no significant proportion of an intermolecular hydrogen-bonded form is present. The broad hydroxyl band (2700—2410 cm.$^{-1}$) of low intensity is a consequence of the conjugate chelation.[20]

Bellamy [25] has correlated the frequency of the conjugated chelate carbonyl band in aliphatic β-diketones such as acetylacetone and aromatic aldehydes, or in ketones such as 2 : 4-dihydroxybenzaldehyde and 1 : 5-dihydroxyanthraquinone, with the double-bond character of the enol or ring double bond. He has shown that there is a linear relation such that for complete double-bond character the carbonyl frequency for this class of compound is 1600 cm.$^{-1}$. The carbonyl shift due to conjugate chelation in 2-acyl*cyclo*hexane-1 : 3-diones is greater than this. No doubt this is due to the effect of conjugation with the second carbonyl group in the *cyclo*hexane ring. It is significant that the band (1678—1650 cm.$^{-1}$) due to this carbonyl group is at a somewhat lower frequency than that normally found for αβ-unsaturated ketones.

The information obtained from the ultraviolet and infrared absorption spectra is in agreement. It leads to the conclusion that 2-acyl*cyclo*hexane-1 : 3-diones should be regarded as completely enolised, with unusually strong intramolecular hydrogen bonds.

EXPERIMENTAL

2-Acyl*cyclo*hexanediones were freshly purified and distilled. Stock solutions for spectroscopic measurements were made up in 95% ethanol which had been purified by distillation from sodium hydroxide and silver oxide. Ultraviolet-absorption measurements were made with a Beckman spectrophotometer, model DU, with the same matched pair of 1 cm. quartz cells throughout. Measurements summarised in the Figure were carried out in approx. 0·1N-sodium hydroxide, 0·1N-sulphuric acid, and phosphate–citric acid buffer solutions. Aliquot parts of the stock solution were diluted with appropriate volumes of the buffer solutions. Measurements of pH were made with a Cambridge meter.

The pK_a values were determined by potentiometric titration of the compound (approx. 10^{-3}M in 20% ethanol–water) against 0·1N-barium hydroxide. The pK_a value was read in the usual way from the graph of pH against volume of alkali used.

Infrared absorption spectra were determined on Perkin–Elmer double-beam spectrometers (model 21B), for each compound at several concentrations in chloroform and as a liquid film. We are indebted to Dr. L. J. Bellamy and Dr. Seymour Bernstein for these determinations.

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[24] Duncanson, *J.*, 1953, 1207.
[25] Bellamy, *J.*, 1954, 4487.
[26] Flett, *J.*, 1948, 1441.
[27] Hadži and Sheppard, *Trans. Faraday Soc.*, 1954, **50**, 911.