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INFRARED STUDIES WITH TERPENOID COMPOUNDS—VI[1]

INFRARED SPECTRA OF PENICILLIC ACID AND ITS DERIVATIVES

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Abstract—An abnormally persistent self-association of penicillic acid in solution has been observed. With all compounds studied an unusually high molar absorptivity of ($\nu_{C=C}$) is reported.

UNUSUALLY strong self-association has been observed with some substituted phenols and di and trihydroxy steroids. An explanation for this type of association based on the nature and stereochemistry of the interacting groups has been reported.[2, 3]

In the present work we report another example of an unusually strong self-association, observed with penicillic acid, and also abnormally strong absorptions ($\nu_{C=C}$) with penicillic acid (I), penicillic acid acetate (II) and methyl penicillate (III), respectively.

RESULTS AND DISCUSSION

From IR spectral data (Table 1) it follows that penicillic acid (I) strongly self-associates as the two concentration-dependent bands in the OH and CO regions, are observed at the relatively very low concentration in carbon tetrachloride (0·8 mM).

The stretching absorptions of OH (free) are shifted upwards with a change from carbon tetrachloride to chloroform as solvent (3590 → 3574 cm^{-1}) while the OH (bonded) shifts in the opposite direction (3300 → 3342 cm^{-1}) which is in accord with the spectral data of OH absorptions. If an approximation of the position of band centre of OH (bonded) is made, then it is found that it is less influenced by solvent than it would seem from a simple inspection.

Progressive dilution of I in carbon tetrachloride reveals a further band at 3548 cm^{-1} which almost certainly represents the first overtone of the fundamental ($\nu_{C=O}$).

In the carbonyl region (I) a small shift for ($\nu_{C=O}$) bonded to higher frequencies (1746 → 1752 cm^{-1}) upon dilution from 16 to 0·8 mM in carbon tetrachloride solution has been observed.

Examination of the Dreiding model (Fig. 1) of penicillic acid shows that there is no steric hindrance for the intermolecular H-bonding of the cyclic "dimer" type. Both interacting OH and CO groups in the two molecules of this compound can

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TABLE 1. HYDROXYL, CARBONYL AND C=C STRETCHING ABSORPTIONS OF PENICILLIC ACID IN CARBON TETRACHLORIDE AND CHLOROFORM

Solvent	Conc (mM)	Cell path (mm)	νOH						Cell paths (mm)	νCO						νC=C		
			Free			Bonded				Free			Bonded					
			ν	$\Delta\nu_{\frac{1}{2}a}$	ε_a	ν	$\Delta\nu_{\frac{1}{2}a}$	ε_a		ν	$\Delta\nu_{\frac{1}{2}a}$	ε_a	ν	$\Delta\nu_{\frac{1}{2}a}$	ε_a	ν	$\Delta\nu_{\frac{1}{2}a}$	ε_a
CCl_4	16	2·0	3,589[a]	26	35	3,288[b]	228	100	0·5	1,777	—	195	1,746[c]	24	530	1,641	17	850
	8	5·0	3,589[a]	26	50	3,302	226	80	0·5	1,778	(23)	250	1,746[c]	(28)	480	1,642	17	850
	3·2	20·0	3,590[a]	25	85	3,320	230	45	2·0	1,777	(23)	465	1,747	(28)	360	1,643	17	860
	1·6	20·0	3,591[a]	25	100	(3,345)	230	30	5·0	1,777	22	520	1,752	—	220	1,645	17	860
	0·8	20·0	3,592[a]	25	120	(3,345)	—	(15)	5·0	1,779	20	675	1,752	—	(75)	1,646	16	870
$CHCl_3$	80·0	0·51	3,574	42	75	3,342	260	40	0·11	1,768[d]	33	640				1,645	(13)	1,080
	50·0	1·0	3,574	41	85	3,342	255	30	0·11	1,767[d]	31	670				1,644	13	1,090
	25·0	2·0	3,574	40	95	3,342	—	20	0·11	1,767	27	725				1,644	13	1,090
	12·5	2·0	3,573	41	100	(3,342)	—	(15)	0·11	1,766	25	735				1,644	13	1,090
	6.25	5·0	3,574	41	110	(3,342)	—	(15)	0·51	1,767	26	735				1,645	13	1,080
	3·125	5·0	3,573	42	125	—	—		1·0	1,767	25	735				1,644	13	1,090

ν and $\Delta\nu_{\frac{1}{2}a}$ are in cm^{-1}; Values in parenthesis are approximate; [a] Band at 3,548 cm^{-1}; [b] A symmetrical band; [c] Shoulder at 1730 cm^{-1}; [d] Shoulder at 1,728 cm^{-1}.

approach within bonding distance ~3Å. The combined IR (Table 1) and osmometric data (Fig. 2) for apparent molecular weights in carbon tetrachloride solution suggest that the associated species is mainly "dimer".

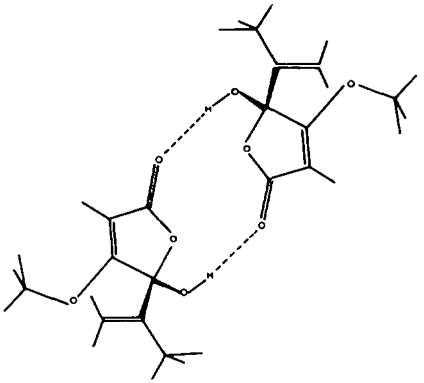

FIG. 1 Planar projection of the Dreiding molecular model of the "dimer" of penicillic acid. The dotted lines indicate the hydrogen bonds.

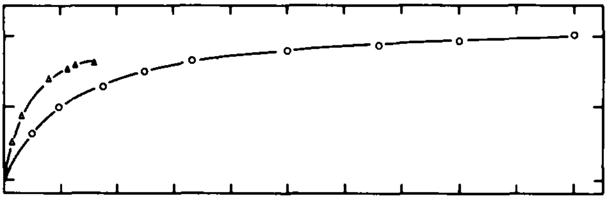

FIG. 2 Plot of the ratio M*/M of the apparent (M*) to true (M) molecular weight against molar concentrations in carbon tetrachloride: Δ-penicillic acid and o-stearic acid.

The abnormally strong self-association of penicillic acid (I) in solution may be due to the presence of the bulky substituents of (CH_3) $C{=}CH_2$, bonded to the same C atom as the OH groups, which hinder the H-bonds against the molecules of the solvent.

Osmometric studies (Fig. 1) also indicate that penicillic acid ($pK^{25}_{aH_2O}$ 5·90)[4] self-associates more strongly than does ethyl coumarate,[3] which is roughly equivalent to stearic acid ($pK^{25}_{aH_2O}$ 5·90).[5] The self-association of penicillic acid in chloroform is weaker than in carbon tetrachloride solution (Table 1). The stretching absorptions of $\nu_{C=C}$ (I) are also concentration-dependent, being shifted by 5 cm^{-1} upwards upon dilution in carbon tetrachloride. This could be attributed to $OH \cdots \pi$ bonding.

The UV spectrum of penicillic acid displays only one concetration-dependent band. In cyclohexane (Table 3), the band decreases in wave-lengths as the concentration is increased (λ_{max}, 226–221 mμ) while the intensity is increased (ε^a, 8370 → 10,830 l. $mole^{-1}$ cm^{-1}) over the range of concentrations from 0·394 to 0·785 mM. In ethanol solution, there is a significant decrease in intensity of the band (ε^a, 6800 l. $mole^{-1}$ cm^{-1}) at concentrations approx equal to those used in cyclohexane (Table 2).

α,β-Unsaturated-γ-lactones bearing and α-hydrogen almost invariably exhibit CO absorptions of complex shape and Fermi resonance involving the CO stretching

TABLE 2. CARBONYL AND C=C STRETCHING ABSORPTIONS OF PENICILLIC ACID ACETATE (II) AND METHYLPENICILLATE (III)

Compound	Solvent	Conc	ν_{CO} (—OAc)			ν_{CO} (—CO_2Me)			ν_{CO} (>CO)			ν C=C		
		(mM)	ν	$\Delta\nu_{\frac{1}{2}a}$	ε_a	ν	$\Delta\nu_{\frac{1}{2}a}$		ν	$\Delta\nu_{\frac{1}{2}a}$	ε_a	ν	$\Delta\nu_{\frac{1}{2}a}$	ε_a
II	Cyclohexane	11·97	1,806	13	1,080				1,777	(15)	670	1,652	13	925
	CCl_4	23·0	1,803[a]	–	(650)				1,776[a]	—	810	1,651	14	1,015
III	CCl_4	26·1				1,718	13	710	1,687	15	500	1,618	13	720

Cell paths 0·5 mm; Values in parenthesis are approximate; ν and $\Delta\nu_{\frac{1}{2}a}$ are in cm^{-1}; – not measured; [a] Very broad band $\Delta\nu_{\frac{1}{2}a} \sim 43\ cm^{-1}$ and the third maximum is at $\sim 1{,}785\ cm^{-1}$.

TABLE 3. UV ABSORPTION SPECTRAL DATA FOR PENICILLIC ACID (I), PENICILLIC ACID ACETATE (II) AND METHYLPENICILLATE (III)

Compound No.	Solvent	Conc mM		λ_{max} (mμ)				
				229	226	224	223	221
I	cyclohexane	0·394^{a}	ε		8,370			
		0·157^{b}					9,230	
		0·0785^{b}						10,830
	ethanol	0·294^{a}				6,800		
II	ethanol	0·236^{a}		10,600				
III	ethanol	0·271^{c}				19,200		
		0·0271^{a}				20,600		

cell paths (in mm): ^{a} 5·0; ^{b} 10·0; ^{c} 1·0.

frequency. The first overtone of the γ(CH) of the α-hydrogen has been postulated by Jones *et al.*[6] The relative intensities of the observed pairs of bands of the γ-lactones reported previously[7,8] are strongly solvent-dependent and the frequencies show much smaller and more irregular shifts than normal CO groups which is in accord with the literature findings.

Penicillic acid (I) as a α,β-unsaturated γ-lactone is an exception as this compound exhibits only one band in the CO region at extremely low concentration in carbon tetrachloride solution (Table 1). However, some splitting (shoulder at 1730 cm^{-1}) and a small increase in intensity of the $\nu_{(CO)}$ band in chloroform solution is observed (Table 1). This spectral anomaly, may be explained by isotopic substitution or by the investigation of more α,β-unsaturated γ-lactones.

All compounds studied exhibit very strong bands assigned to the absorptions of the C=C bond (I), ε^{a} 860; II, ε^{a} 1015 and (III), ε^{a}, 720 l. mole^{-1} cm^{-1} in carbon tetrachloride (Table 1 and 2).

In a large number of non-conjugated compounds the C=C stretching vibration gives rise only to weak bands in the IR. In many cases the main factors influencing both the frequency and the intensity are symmetry considerations, conjugation and the nature of substituents on the two C atoms bonded by a double bond.[9] Especially, the alkoxy substituents greatly intensify C=C bands as reported for vinyl ethers,[10] cyclopent-2-enones and cyclohex-2-enones,[11] and phorone derivatives.[12] Electron-release (+M) by the OMe group could be the main factor in determining the C=C intensity in the compounds studied, but the problem requires further study on systems similar to those of penicillic acid and related compounds.

EXPERIMENTAL

IR spectra were recorded with a Unicam S.P. 100 double beam spectrophotometer equiped with an S.P. 130 NaCl prism-grating double monochromator operated the general procedure described previously[1]. The apparent half-band widths, $\Delta\nu_{\frac{1}{2}}^{a}$, are quoted to the nearest integer; where necessary they were determined by reflection of the undisturbed wings of the unsymmetrical bands. Intensities are given as apparent molar absorptivities, ε^{a}, (l. mole^{-1} cm^{-1}) rounded to the nearest 5 units.

UV spectra were recorded with a Unicam S.P. 800 double beam spectrophotometer over a range of concentrations of 0·8 to 17 mM in cyclohexane. The mol wt measurements were carried out with a Mechrolab, model 301 A vapour pressure osmometer over a wide range of concentrations in CCl_4.

Materials. Analar $CHCl_3$ and cyclohexane (spectroscopic grade) were used without further purification. Analar $CHCl_3$ was dried several times by passage through a column of blue silica gel before use. The purity of compounds examined was checked by IR spectroscopy and gas chromatography.

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REFERENCES

[1] Part V: S. Kovac and G. Eglington, *Tetrahedron* **25**, 3259 (1969).
[2] W. S. Bennet, G. Eglinton and S. Kovac, *Nature* **214**, 776 (1967).
[3] S. Kovac and G. Eglinton, *Tetrahedron*, **25**, 3259 (1969).
[4] J. E. Page and F. A. Robertson, *J. Chem. Soc.* 133 (1943).
[5] N. P. Fatta, *J. Ind. Chem. Soc.* **16**, 573 (1939).
[6] R. N. Jones, C. L. Angell, T. Ito and R. J. D. Smith, *Canad. J. Chem.* **37**, 2007 (1959).
[7] R. P. M. Bond, T. Cairns, J. D. Connoly, G. Eglinton and K. H. Overton, *J. Chem. Soc.* 3958 (1965).
[8] T. Cairns, G. Eglinton, A. I. Scott and D. W. Young, *Ibid.* 654 (1966).
[9] L. J. Bellamy, *The Infrared Spectra of Complex Molecules* (4th Edition) p. 62. Methuen, London (1964).
[10] R. H. Hall, A. R. Philpotts, E. S. Stern and W. Thain; *J. Chem. Soc.* 3341 (1951).
[11] H. N. A. Al-Jallow and E. S. Waight, *Ibid.* (B) 73 (1966).
[12] H. N. A. Al-Jallow and E. S. Waight, *Ibid.* (B) 75 (1966).