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STRUCTURE AND ABSORPTION SPECTRA OF 2-PHENACYLPYRIDINES—1

SIMPLE DERIVATIVES

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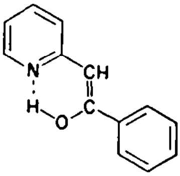
Abstract—Features of the I.R. and U.V. spectra of 2-phenacylpyridine and sixteen derivatives are reported. With four accountable exceptions, these compounds are shown to exist in the solid state in the enol form which is stabilized by a strong, intramolecular hydrogen bond. The spectra show that a keto–enol equilibrium exists in solution. The I.R. spectra of the solutions, and the spectra of some partially deuterated solid enols, have enabled frequency assignments for the ν(C=C) stretching, γ(=C—H) out-of-plane deformation, δ(=C—H) in-plane deformation and γ(OH) out-of-plane deformation vibrations to be made. The carbonyl frequencies of the keto forms show an approximately linear relation to the Hammett sigma values of the substituents in the benzene ring.

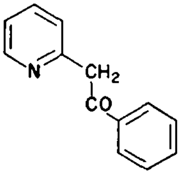
INTRODUCTION

The derivatives of 2-phenacylpyridine are chelating agents, and this property has led to their synthesis and testing for bacteriostatic activity.[1–3] During the course of this work, their I.R. and U.V. spectra were obtained, and measurements on seventeen compounds are now reported.

These compounds possess many features of interest which lend importance to their spectra. Thus, besides exhibiting chelating properties, they show keto–enol tautomerism, and stable enol forms can be isolated in the solid state. In a preliminary investigation,[4,5] it has been shown that the enol forms are stabilized by a powerful, intramolecular hydrogen bond. 2-Phenacylpyridine exists as the stable enol form (I) rather than as the keto form (II) under ordinary conditions.



I



II

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* Present address: Liverpool City College of Technology, Byrom St., Liverpool, 3.

[1] N. N. Goldberg, L. B. Barkley and R. Levine, *J. Amer. Chem. Soc.* **73**, 4301 (1951).

[2] A. H. Beckett and K. A. Kerridge, *J. Chem. Soc.* 2948 (1954).

[3] A. H. Beckett, K. A. Kerridge, P. Clark and W. G. Smith, *J. Pharm. Pharmacol.* **7**, 717 (1955).

[4] R. F. Branch, *Nature, Lond.* **177**, 671 (1956).

[5] R. F. Branch, *Nature, Lond.* **179**, 42 (1957).

These compounds are analogous, therefore, to the mono-enolic forms of the β-diketones which have been the subject of much study by spectroscopic methods.[6-9] Points of interest in the I.R. spectra of these mono-enols are the extremely low intensity of the ν(OH) absorption and the position of the deformation modes of the O—H and =C—H groups. To provide information on these points, a number of compounds in the present series have been partially deuterated, and the spectroscopic results suggest assignments for the ν(C=C), γ(OH), δ(=C—H) and γ(=C—H) vibrations. Both the I.R. and U.V. spectra of 2-phenacylpyridines in various solvents show clearly the existence of keto-enol tautomerism in solution.

Results and discussion of I.R. spectra

(a) *General.* Some details of the I.R. spectra of 2-phenacylpyridine and its derivatives in the 800–650 cm^{-1} region, and also the C=C and C=O frequencies are shown in Table 1. The most noteworthy feature of the spectra in the solid state is the absence, with four exceptions, of the expected conjugated carbonyl absorption in the range 1700–1680 cm^{-1}, and of the hydroxyl absorption. In solution in carbon tetrachloride or chloroform, however, a broad, weak absorption occurs with its peak at 2600 cm^{-1} (Fig. 1). This shows the presence of the enol OH group which is chelated through a strong, intramolecular hydrogen bond. These solutions also show a band in the 1700–1680 cm^{-1} region, indicating that the keto form is also present. This carbonyl band appears at the expense of a strong, sharp band at 1640 cm^{-1} in the

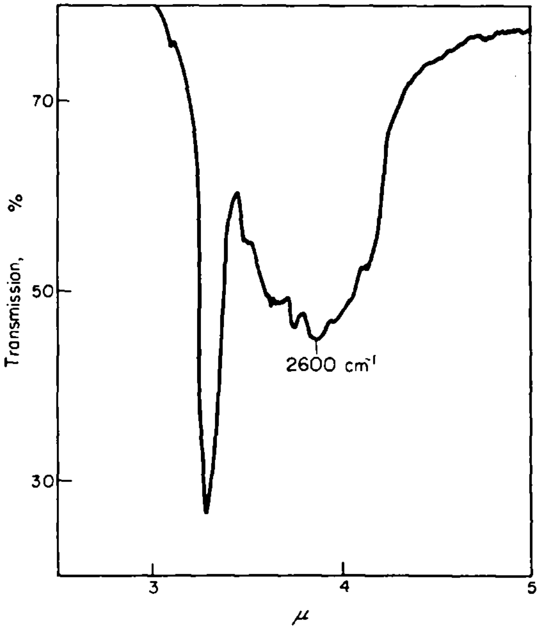

Fig. 1. I.R. spectrum of 2-phenacylpyridine (0·2% w/v CCl$_4$ soln. 0·4 mm compensated)

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[6] R. S. Rasmussen, D. D. Tunicliff, and R. R. Brattain, *J. Amer. Chem. Soc.* **71**, 1068 (1949).
[7] R. A. Morton, A. Hassan, and T. C. Calloway, *J. Chem. Soc.* 883 (1934).
[8] S. Bratoz, D. Hadzi, and G. Rossmy, *Trans. Farad. Soc.* **52**, 464 (1956).
[9] R. Mecke and E. Funck, *Z. fur Elektrochem.* **60**, 1124 (1956).

solid (Fig. 2), thus establishing that the latter band arises from the enol form. The band at 1640 cm^{-1} can only arise from the C=C linkage. The strength of this band is remarkable since although the presence of an oxygen atom adjacent to the double bond will cause intensity enhancement, the large degree of symmetry about the double bond acts against this. The intensity enhancement may be partly due to the participance of the bond in a resonance-stabilized ring. These results therefore confirm that the 2-phenacylpyridines show behaviour analogous to that of the mono-enols of the *β*-diketones, and suggest that the "conjugate chelation" of Rasmussen[6] occurs in these compounds.

This phenomenon is not observed with *p*-aminophenacylpyridine (cpd. 1) nor with *p*-hydroxyphenacylpyridine (cpd. 2), nor with those compounds in which the methylene group is substituted with an alkyl group [cpds. 3 and 4 (Table 1)]. The amino and hydroxy groups, with their powerful electron-releasing properties, cause sufficient stabilization of the keto form by contributions from structures III and IV to overcome the stabilizing hydrogen-bonding effect in the enol.

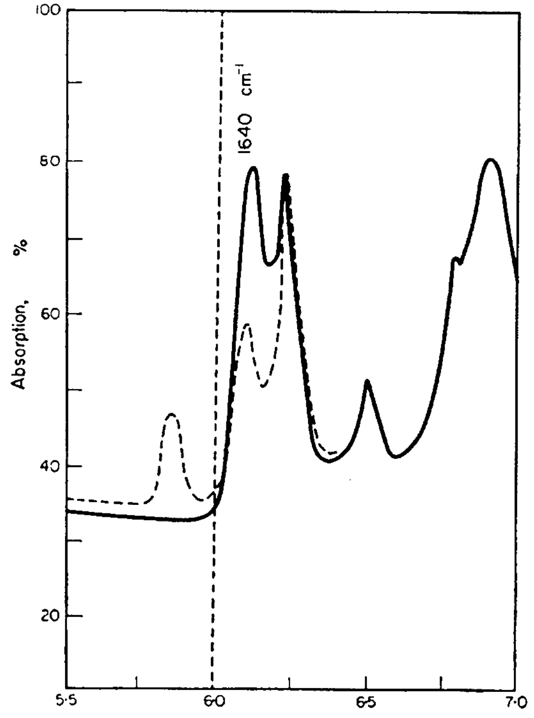
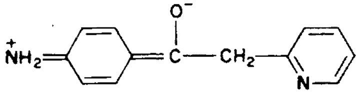
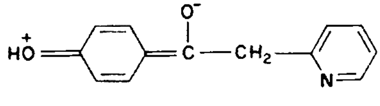


FIG. 2. I.R. spectrum of 2-phenacylpyridine ——— solid - - - - CCl_4 soln.



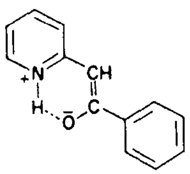
III



IV

The alkyl groups in compounds 3 and 4 can cause loss of planarity of the enol form with consequent loss of stability.[5] In compounds 1, 2, 3 and 4, a normal, conjugated carbonyl absorption is present in the solid state spectra.

The possibility that the chelated enol forms exist in the purely Zwitter ion form (V) can be ruled out, since although the —$\overset{+}{\text{N}}\text{H}=$ group would be expected to absorb near 2600 cm^{-1}, the band would be strong in the solid state, and this is not observed. Furthermore, the shape of the absorption at 2600 cm^{-1}, with its appearance of containing ill-resolved fine structure, is characteristic of the resonance-stabilized, intramolecular hydrogen bond.[10]

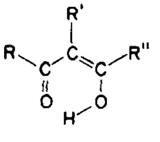


V

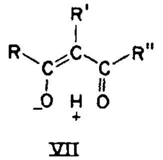
According to the relation between observed frequency shift ($\Delta\nu_{\text{free-associated}}$) and the X · · · Y distance in the structure X—H · · · Y noted by Lord and Merrifield[11], this shift of approximately 1000 cm^{-1} in the OH frequency would result if the N · · · O distance were 2·67 Å which agrees well with the N · · · O distance to be expected in these compounds assuming conventional bond lengths and angles,[12] especially since these will be modified by resonance effects.

(b) *The carbonyl frequencies.* It has been shown[13,14] that for a series of *meta or para* substituted compounds X—C_6H_4—CO—R, the carbonyl frequencies vary approximately linearly with the Hammett sigma value of X. This general trend is borne out by the present series of closely related compounds whose carbonyl frequencies were measured in chloroform solution (Table 1 and Fig. 3).

(c) *Enol* C═C *absorption.* The present compounds are analogous to the monoenolic forms of the β-diketones in which a large shift of the C═O absorption from its normal position is accompanied by a large intensity increase.[6] This effect is due to resonance stabilization of the intramolecular hydrogen bond, and Mecke[9] suggests that the mesomeric extremes VI and VII are important. Rasmussen[6] and Hadzi[8] found no band ascribable to the C═C vibration in simple β-diketones, but believed it to lie under the strong C═O absorption near 1610 cm^{-1}. Mecke[9] pointed out that although this would account for much of the intensity of the band near 1610 cm^{-1}, it is surprising that the C═C band is not drastically lowered in frequency in a manner



VI



VII

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[10] N. Sheppard, *Hydrogen Bonding* p. 85. Pergamon Press (1959).

[11] R. C. Lord and R. E. Merrifield, *J. Chem. Phys.* **21**, 166 (1953).

[12] E. W. Gill and E. D. Morgan, *Nature, Lond.* **183**, 248 (1959).

[13] A. H. Soloway and S. L. Friess, *J. Amer. Chem. Soc.* **73**, 5000 (1951).

[14] R. D. Campbell and H. M. Gilow, *J. Amer. Chem. Soc.* **82**, 5426 (1960).

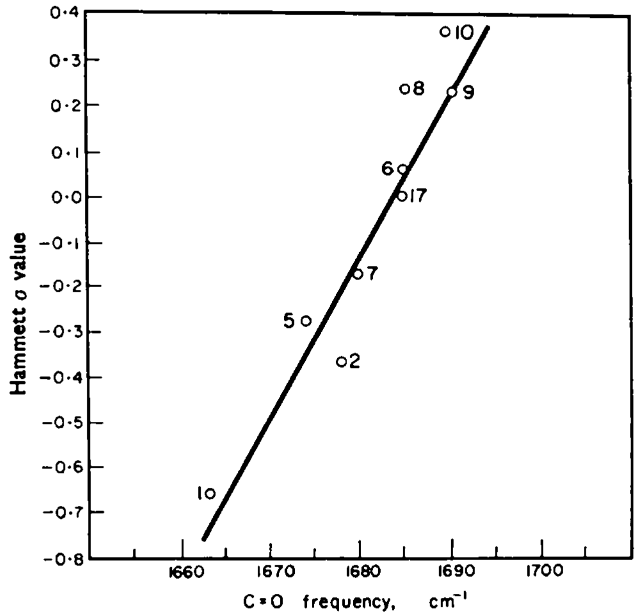

FIG. 3. Hammett σ value of benzene ring substituent plotted against C=O frequency. Numerals refer to cpd. nos in Table 1)

TABLE 1. I. R. SPECTRA OF 2-PHENACYLPYRIDINE DERIVATIVES

Compound no.	Compound	Keto C=O cm^{-1}*	Enol C=C cm^{-1}‡	Range 800–650 cm^{-1}‡
1	2-*p*-aminophenacylpyridine	1663	—	833 763
2	2-*p*-hydroxyphenacylpyridine	1677	—	821 756
3	α-benzoyl-2-n-propylpyridine	(1690)	—	781 769 752 731 702 683
4	α-benzoyl-2-ethylpyridine	(1680)	—	— —
5	2-*p*-methoxyphenacylpyridine	1674	1640	834 803 738 [—]
6	2-*p*-fluorophenacylpyridine	1685	1640	803 738
7	2-*p*-methylphenacylpyridine	1680	1640	801 742 [800,810]
8	2-*p*-bromophenacylpyridine	1685	1640	800 740
9	2-*p*-chlorophenacylpyridine	1691	1640	802 741
10	2-*m*-chlorophenacylpyridine	1688	1640	801 736 781 687
11	6-methyl-2-phenacylpyridine	1685	1640	810 734 781 686 734
12	4-methyl-2-phenacylpyridine	1682	1640	826 769 746 693
13	2-*m*-chlorophenacyl-6-methylpyridine	1688	1640	805 793 771 760 732 692
14	2-*m*-chlorophenacyl-4-methylpyridine	1685	1640	808 793 769 732 721
15	α-1-naphthoyl-2-methylpyridine	1685	1628	801 795 780 739
16	α-(2′-furoyl)-2-methylpyridine	1677	1654	810 735
17	2-phenacylpyridine	1685	1640	807 775 738 689

*—Chloroform solution except figures in parentheses which refer to solid state.

‡—Solid state in paraffin.

[ ]—Bromoform solution.

analogous to the C=O absorption. Mecke therefore suggests that the ν(C=C) vibration couples markedly with the δ(OH) vibration to produce a band at, or near, that of the carbonyl absorption. When this coupling is removed by deuteration or chelation with a metal, a vibration which is largely C=C in character is found near 1536 cm^{-1}. This interpretation accords with his postulated mesomeric extremes VI and VII where considerable bond equalization has occurred.

The enol form of 2-phenacylpyridine (I) contains a double bond in a resonance-stabilized, hydrogen-bonded ring. If the phenomenon suggested by Mecke is taking place, deuteration should cause a considerable shift of the C=C band which is not, as in Mecke's case, obscured by a C=O absorption. In addition, the cupric and sodium derivatives should not contain the band at 1640 cm^{-1}. That this is indeed the case is evident from Figs. 4, 5 and 6. This supports Mecke's view that the ν(C=C) interacts with a motion of the OH group (probably δ(OH)) provided we disregard, with Hadzi,[8] the view of Shigorin,[15] that the band shift is due to differing absorptions of C=C—H and C=C—D. (The methine (=C—H) group becomes deuterated as well as the OH group. Shigorin's view was disregarded by Hadzi on the grounds that the shift is observed with acetylchloroacetone, in which no methine hydrogen is present.) The only new band to appear in this region upon deuteration is the weak one near 1570 cm^{-1}. This seems to correspond to the weak band at 1575 cm^{-1} in the cupric chelate and the stronger band at 1570 cm^{-1} in the sodium derivative. It is tempting to ascribe this band to the displaced C=C absorption, but this is difficult to accept in view of the fact that the cupric and sodium derivatives also show strong bands in the region 1520–1530 cm^{-1} (1531 cm^{-1} and 1525 cm^{-1} respectively) which is the region generally assigned to the C=C absorption in metal chelates of the mono-enolic β-diketones. These results conclusively show, however, that the C=C vibration is greatly affected by deuteration.

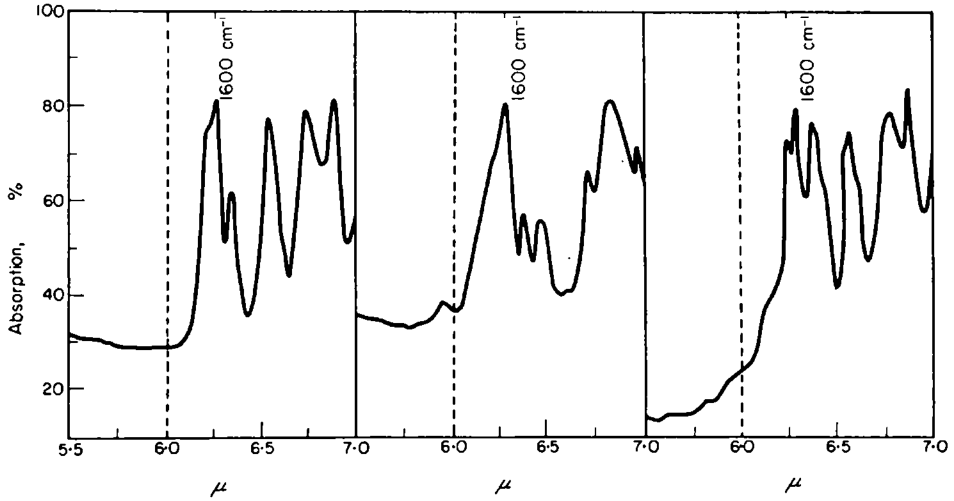

FIG. 4. I.R. spectrum of cupric chelate of 2-phenacylpyridine (nujol).
FIG. 5. I.R. spectrum of partially deuterated 2-phenacylpyridine (nujol).
FIG. 6. I.R. spectrum of sodium derivative of 2-phenacylpyridine (nujol).

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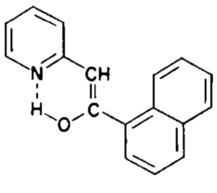
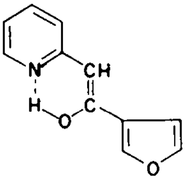
[15] D. N. Shigorin, *Zh. fiz. Khim.* **28**, 584 (1954).

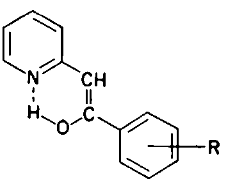
All compounds of the type VIII in Table 1 show the strong band at 1640 cm^{-1} regardless of the nature of R. Compounds 15 (IX) and 16 (X) show this band at 1628 cm^{-1} and 1654 cm^{-1} respectively. Compounds of type VIII are partially analogous to the substituted stilbenes. Little data is available on the C=C absorption in these latter molecules, no doubt due to the high degree of symmetry about this bond. However, the band at 1640 cm^{-1} is in the general range quoted by Katritsky[16] for stilbene derivatives. It is of interest that these workers find the C=C band in XI to be at 1632 cm^{-1}. This compound is unlikely to form a strong, resonance-stabilized hydrogen bond. Thus, apparently, as with the mono-enolic β-diketones, in a resonance stabilized, hydrogen bonded ring the C=C absorption occurs in the normal position for a conjugated double bond.



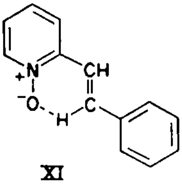
IX



X



VIII



XI

(d) *The range* 800–650 cm^{-1}. In *para* substituted compounds of the type VIII, it has been noted that only two medium or strong bands appear in the solid state spectra in this region.[4] These were assigned to the benzene and pyridine ring C—H out-of-plane deformation vibrations. In bromoform solution, however, the band ascribed to the benzene ring near 800 cm^{-1} appears as a doublet, and there is a progressive weakening of one component with time. This change corresponds to the slow attainment of keto-enol equilibrium in bromoform solution where the keto form is preferred, and this change can be followed by the gradual increase in intensity of the carbonyl absorption and reduction of C=C band intensity. Figure 7 shows this change for 2-*p*-methylphenacylpyridine in bromoform solution. The disappearing component is therefore due to the enol form and might be ascribed to the =C—H (methine) vibration or to the γ(OH) vibration. Mecke,[9] in a study of acetylacetone, assigns a band at 778 cm^{-1} to the =C—H vibration and another at 955 cm^{-1} to the γ(OH) vibration. If an analogous assignment holds in the present work, the disappearing band near 800 cm^{-1} is due to =C—H, and it occurs close to the out-of-plane C—H vibration of the benzene ring (*para* substitution). In the solid state these two bands are not resolved from one another.

The strong band at 803 cm^{-1} in solid 2-*p*-methoxyphenacylpyridine is not split into a doublet in bromoform solution, but virtually disappears with the change to

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[16] A. R. Katritsky, A. J. Boulton, and D. J. Short, *J. Chem. Soc.* 1519 (1960).

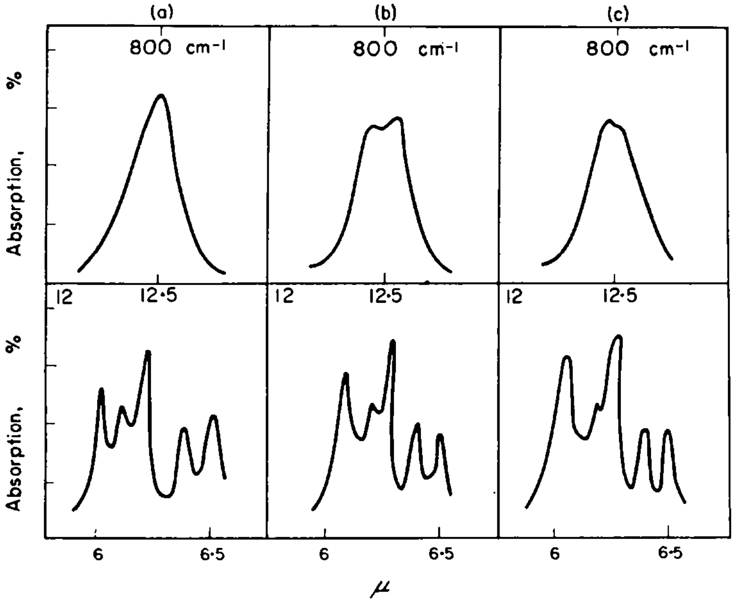
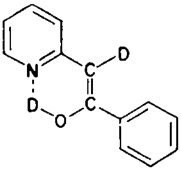


Fig. 7. I.R. spectrum of 2-*p*-methyl-phenacylpyridine in bromoform.
(a) on dissolving solid
(b) after one hour
(c) after two hours.

the keto form. This band, therefore, is solely due to =C—H in the solid state, and we now ascribe a band at 834 cm^{-1} to the *para* di-substituted benzene ring (cf. the band at 833 cm^{-1}/ in *p*-methoxy acetophenone[17]).

Hadzi[8] places the γ(OH) frequency in dibenzoylmethane and benzoylacetone at 960 cm^{-1} which is in agreement with Mecke. To establish the position of this band in the present compounds, some deuteration studies were made.

(e) *Deuteration studies.* Owing to the presence of two mobile hydrogen atoms in 2-phenacylpyridine, deuterium exchange will lead to the structure XII. Bands



XII

due to both O—H and =C—H will therefore undergo a marked change upon deuteration. The spectra of deuterated alcohols often show features which are as yet unexplained,[18] and it is common for more new bands to appear in the spectra of deuterated compounds than disappear from the spectra of the hydrogen compounds. This phenomenon is noted with the present compounds, four of which have been partially deuterated. Changes in the solid state spectra produced on deuteration are recorded

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[17] L. J. Bellamy, *J. Chem. Soc.* 2818 (1955).

[18] C. A. Coulson, *Hydrogen Bonding* p. 339 Pergamon Press (1959).

in Table 2. The most marked changes which assist in band assignments are:

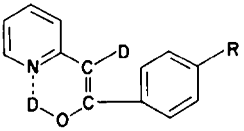
(i) the almost complete disappearance of the C=C absorption at 1640 cm^{-1} and the appearance of a new, weak band at 1570–1580 cm^{-1} (see section c)

(ii) the marked reduction of intensity of the band near 805 cm^{-1}, which from solution studies is believed to be partly due to γ(=C—H).

(iii) the disappearance of a band of medium strength near 1060 cm^{-1} and the appearance of a new band near 790 cm^{-1}.

(iv) the disappearance of a weak band 1200 cm^{-1} and the appearance of a weak band near 850 cm^{-1}.

TABLE 2. I.R. SPECTRAL CHANGES CAUSED BY DEUTERATION OF 2-PHENACYLPYRIDINE DERIVATIVES TO PRODUCE



Remarks	R = OCH_3 (cm^{-1})	R = Cl (cm^{-1})	R = F (cm^{-1})	R = CH_3 (cm^{-1})
Disappears	1640	1640	1640	1640
New band	1587	1567	—	—
New band	1342	1333–42	1333–42	1338
Disappears	1212	1212	1196	—
Disappears	1063	1060	1058	1058
New band	789	788	784	787
Weakened	805	803	805	803
New band	858	851	858	—
New band	—	726	730	727
New band	1075	—	—	1075
New band	—	915	—	909
Weakened	890 881	—	—	826
New band	678	—	—	677

The following frequency assignments can be made from these results:

γ(=C—H) occurs near 805 cm^{-1}, and deuteration should result in a new band outside the rock salt region, but this has not been investigated.

γ(OH) occurs near 1060 cm^{-1}, and deuteration results in a new band near 790 cm^{-1} γ(OD). The frequency ratio of 1·34 supports the association of these two bands.

δ(=C—H) occurs near 1212 cm^{-1}, and deuteration results in a new band near 850 cm^{-1} δ(=C—D). The frequency ratio of 1·39–1·41 supports the association of these two bands.

The suggested position of the γ(OH) vibration at the high frequency of 1060 cm^{-1} implies that the hydrogen bond in 2-phenacylpyridines is stronger than in the mono-enols of the β-diketones.

Results and discussion of U.V. spectra

(a) *General.* The U.V. spectra of the 2-phenacylpyridines support the conclusions drawn from their I.R. spectra. They show that these compounds form the same stable enol in both ethanol and cyclohexane solution. The U.V. spectra are tabulated in Table 3, and a typical example is shown in Fig. 8. The spectrum of the keto form is established by that of α-benzoyl-2-ethylpyridine (XIII), where C-methyl substitution causes the keto form to be preferred in both ethanol and cyclohexane. It has a broad maximum near 245 mμ (Fig. 8). The other derivatives in Table 3 exist in equilibrium between the keto and enol forms in both ethanol and cyclohexane solution, although as expected the proportion of the keto form is increased in ethanol. However, the proportion of enol to keto is very high in both solvents. The enol band occurs close to 340 mμ. The enol–keto ratio, measured in cyclohexane solution after three days to ensure attainment of equilibrium, increases as the Hammett sigma value of the *para* substituent increases, with the exception of the halogens which show an approximately constant effect (Table 4).

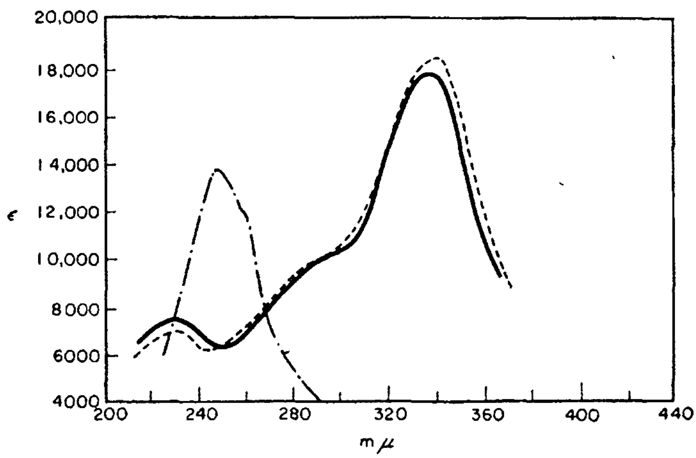
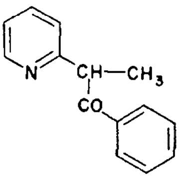


FIG. 8. U.V. spectra.
——— 2-phenacylpyridine in ethanol.
- - - - 2-phenacylpyridine in cyclohexane
— . — α-benzoyl-2-ethyl pyridine in ethanol.



XIII

(b) *Effect of acid.* The effect of addition of acid to the ethanol solutions is to remove the enol band completely, thus showing that the nitrogen lone pair of electrons is essential for enol stability, since it is required to form the hydrogen bond.

EXPERIMENTAL

Spectra. I.R. spectra were determined on either a Perkin–Elmer Model 21 double-beam automatic recording spectrophotometer using a rock salt prism, or a Grubb-Parsons G.S.2A double-beam automatic recording spectrophotometer using a 1200 l.p.i. grating. The samples were examined as solids

TABLE 3. U.V. SPECTRA OF 2-PHENACYLPYRIDINE DERIVATIVES

Compound no.	Compound	Solvent	λ_{max} (mμ)	ε_{max}
17	2-phenacylpyridine	cyclohexane	233·5	6640
			313	11070
			341	18180
		ethanol*	229	7770
			300	
			337	17980
		aqueous	249	13930
5	2-p-methoxyphenacylpyridine	cyclohexane	271	11830
			277	11810
			282·5	11760
			305	8010
			348	13430
7	2-p-methyl-phenacylpyridine	cyclohexane	242	7790
			254	7540
			299·5	10170
			343·5	16930
6	2-p-fluorophenacylpyridine	cyclohexane	237	6930
			295	10390
			340·5	16700
9	2-p-chlorophenacylpyridine	cyclohexane	242	7470
			257	7210
			291	10030
			343	20220
		ethanol	255	12050
			338	12680
8	2-p-bromophenacylpyridine	cyclohexane	244·5	9690
			265·5	9100
			291·5	15160
			343·5	23000
4	α-benzoyl-2-ethyl-pyridine	cyclohexane	245	14690
			263	5082
			269·8	3680
		ethanol	245·5	13680
			263	6840
			269	4400
		aqueous	249	13160
			262	9805
			269	5760

* Measured after ½ hour at room temp.

TABLE 4. RATIO OF ε_{max} (ENOL) TO ε_{max} (KETO) FOR 2-PHENACYLPYRIDINES IN CYCLOHEXANE AFTER THREE DAYS AT ROOM TEMPERATURE

Para substituent	Ratio	Hammett σ of substituent
MeO	1·2	−0·268
Me	2·2	−0·170
H	2·7	0
F	2·7	+0·062
Cl	2·7	+0·226
Br	2·4	+0·232

ground in liquid paraffin, or in solution in chloroform, carbon tetrachloride or bromoform. U.V. Spectra were determined on a Beckman D.K.2 automatic recording spectrophotometer. The samples were examined in ethanol and cyclohexane solutions, and the results in Table 3 for cyclohexane solutions refer to measurements after 3 days at room temp. In general, the concentration of the solutions was 10–20 mg/l., and the path length 1 cm. The effect of acid was studied by the addition of 1–2 drops of dil hydrochloric acid to the ethanol solutions.

Deuteration was carried out by dissolving a few milligrams of the compound in dry ether, and shaking for 24 hours with excess heavy water. The solution was dried (Na_2SO_4 anhyd.), and the ether evaporated off to yield the partially deuterated compound.

Preparation of the compounds. The synthesis of compounds 1–17 has been described previously.[2,3] The sodium derivative of 2-phenacylpyridine was prepared by the action of sodium hydride on 2-phenacylpyridine in dry toluene. A slight excess of 2-phenacylpyridine was used, and the precipitated yellow sodium derivative thoroughly washed with dry toluene. The *cupric chelate of* 2-*phenacylpyridine* was prepared as follows: 2-Phenacylpyridine (2 g) was dissolved in a few ml ethanol and the solution diluted with water without precipitation occurring. Cupric sulphate (1·25 g) dissolved in water was added. The precipitated brown chelate was extracted with benzene and the solution was dried ($MgSO_4$). The solution yielded 2 g crude product which was recrystallized from equal parts of benzene and pet. ether as dark purple needles, m.p. 188–190°. (Found: C, 68·76; H 4·42; N, 6·15; $C_{26}H_{20}N_2O_2Cu$ requires: C, 68·5, H, 4·42; N, 6·15%).