

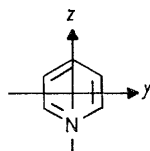
Circular Dichroism of Isomeric Pyridylethanols

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The room and low temperature absorption and c.d. spectra of the isomeric (-)-(S)-2-, 3-, and 4-pyridylethanols, (-)-(S)-(I)—(III) have been measured. The data obtained are satisfactorily interpreted by assuming the existence of a second $n \rightarrow \pi^*$ ($A_2 \leftarrow A_1$) electronic transition of the pyridine chromophore at *ca.* 240 nm.

THE absorption spectra of pyridine and the picolines have been investigated by several authors.¹ It is currently accepted that the low energy absorption between 300 and 230 nm is caused by two electronic transitions, $n \rightarrow \pi^*$ at lower energy and $\pi \rightarrow \pi^*$ at higher energy.²

These transitions are $B_1 \leftarrow A_1$ and $B_2 \leftarrow A_1$ respectively in group theory for the pyridine co-ordinate



(A)

system (A) (group C_{2v}). However it was observed³ that in passing from alcohol to iso-octane the fine structure of the band at *ca.* 260 nm was blurred and it

¹ K. K. Innes, J. P. Byrne, and I. G. Ross, *J. Mol. Spectroscopy*, 1967, **22**, 125.

² (a) H. H. Jaffé and M. Orchin, 'Theory and Applications of Ultraviolet Spectroscopy,' Wiley, New York, 1962, p. 361; (b) J. N. Murrell, 'The Theory of the Electronic Spectra of Organic Molecules,' Methuen, London, 1963.

was suggested that a second $n \rightarrow \pi^*$ transition might exist on the high energy side of $\pi \rightarrow \pi^*$. This transition undergoes a red shift when the solvent is changed from alcohol to iso-octane, and overlaps with $\pi \rightarrow \pi^*$, leading to a loss of fine structure.

More recently, a few studies on the c.d. spectra of pyridine derivatives have appeared.^{4,5} This type of spectroscopy, even with the resolution limit of the instruments now available, usually provides information which is not obtainable from isotropic absorption spectra. In particular, electronically forbidden but magnetically allowed transitions can be detected and studied.⁶

Smith *et al.*,⁵ from an analysis of the c.d. spectra of some pyridine derivatives, produced new evidence for the existence of the second $n \rightarrow \pi^*$ transition suggested by Kasha.³ They observed c.d. maxima at *ca.* 240 nm without corresponding maxima in the

³ H. P. Stephenson, *J. Chem. Phys.*, 1954, **22**, 1077.

⁴ G. Gottarelli and B. Samorì (a) *Tetrahedron Letters*, 1970, 2055; (b) *J.C.S. Perkin II*, 1972, 1998.

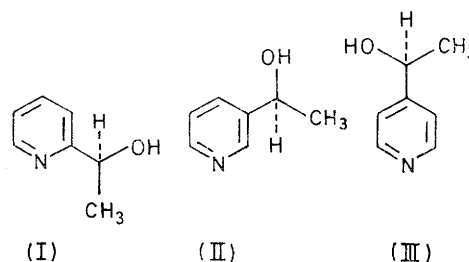
⁵ H. E. Smith, L. J. Schaad, R. B. Banks, C. J. Wiant, and C. F. Jordan, *J. Amer. Chem. Soc.*, 1973, **95**, 811.

⁶ S. F. Mason, *Quart. Rev.*, 1963, **17**, 20.

isotropic absorption, and assigned these dichroic absorptions to a magnetically allowed and electronically forbidden $n \rightarrow \pi^*$ ($A_2 \leftarrow A_1$) transition.

However, in all the c.d. spectra reported in refs. 4 and 5, the low energy $n \rightarrow \pi^*$ ($B_1 \leftarrow A_1$) transition was not evident, and this still left some uncertainty. Despite the arguments adduced in ref. 5, it was still possible, especially in the absence of a study on solvent effect, that the c.d. maximum at *ca.* 240 nm was caused by the $B_1 \leftarrow A_1$ ($n \rightarrow \pi^*$) transition, the strong blue shift observed being a result of concurrent effects from the solvent,⁷ cancellation of adjacent bands of opposite sign, and substituents. Furthermore, in a recent photoelectron spectral study⁸ it was shown that in 2-alkylpyridines and in variously disubstituted

with sodium borohydride. Compounds (I) and (III) were resolved with (–)-dibenzoyltartaric acid, (II) with (–)-tartaric acid.



The absolute configurations were assigned by means of the Horeau method using racemic phenylbutyric

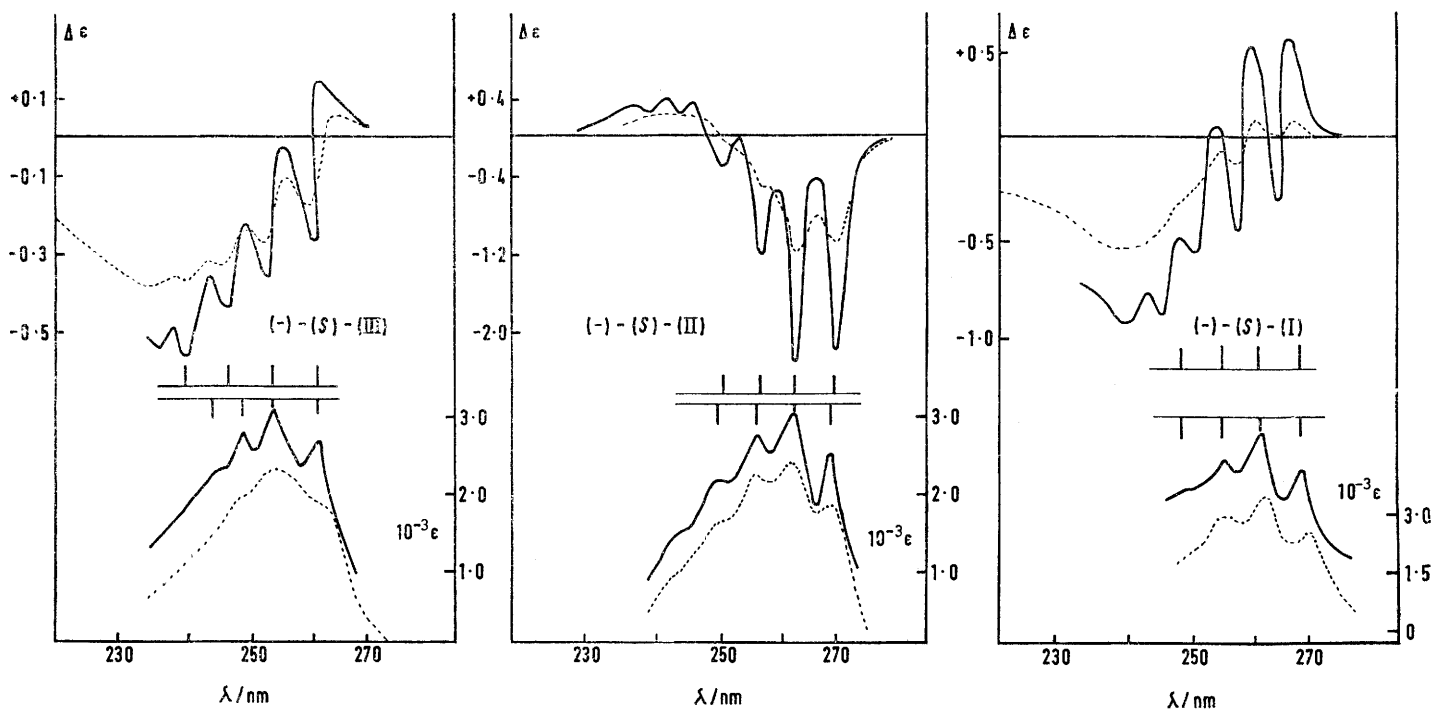


FIGURE 1 The room (----) and low temperature (-150°) (—) c.d. spectra of (–)-(S)-(I)–(III) (upper part). The room temperature u.v. spectra (----) and instrument trace (—) of the low temperature absorption (-150°) (lower part). Solvent methanol-glycerol 9 : 1 (v/v)

pyridines the highest occupied π orbital is at a higher energy than the lone pair on the nitrogen. This does not necessarily imply that in substituted pyridines the $n \rightarrow \pi^*$ transition must be of higher energy^{2b} than the $\pi \rightarrow \pi^*$, but indicates that this could be possible.

In this work we give further evidence in favour of the assignment of the transition at *ca.* 240 nm.⁵ This evidence comes chiefly from the c.d. spectrum of (–)-(S)-1-(4-pyridyl)ethanol where three distinct transitions are clearly observed in the region above 235 nm.

RESULTS AND DISCUSSION

2- (I), 3- (II),^{4a} and 4-pyridylethanol (III) were prepared by reduction of the corresponding acetylpyridines

⁷ R. M. Hochstrasser, *Accounts Chem. Res.*, 1968, **9**, 266.

⁸ E. Heilbronner, V. Hornung, F. H. Pinkerton, and S. F. Thames, *Helv. Chim. Acta*, 1972, **55**, 289.

anhydride.^{9a,b} In all three cases the (–)-isomers had the S-configuration. Such assignments are further supported by comparison of the c.d. spectra of (I)–(III) with those of the isomeric 1-(2-, 3-, and 4-pyridyl)-ethylamines⁵ whose absolute configurations were deduced from chemical evidence.¹⁰ The c.d. spectrum of compound (–)-(I) corresponds in sign and band position to that of (–)-(S)-1-(2-pyridyl)ethylamine. The c.d. spectrum of (–)-(II) is similar to the mirror image of that of (+)-(R)-1-(3-pyridyl)ethylamine. For (–)-(III), our c.d. spectrum shows more bands, but the dominant negative band at *ca.* 240 nm

⁹ (a) A. Horeau, *Tetrahedron Letters*, 1961, 506; 1962, 965; (b) A. Horeau and B. Kagan, *Tetrahedron*, 1964, **20**, 2431; (c) A. Horeau and R. Weidmann, *Bull. Soc. chim. France*, 1967, 117.

¹⁰ O. Cervinka, O. Belovsky, and P. Rejmanova, *Z. Chem.*, 1970, **10**, 69.

corresponds to the negative band observed at the same wavelength in (—)-(S)-I-(4-pyridyl)ethylamine.

The room and low temperature c.d. and u.v. spectra of the isomeric pyridylethanol are shown in Figures 1 and 2. Several common characteristics may be noted in the spectra of the three derivatives. A structured band with distinct maxima between 244 and 264 nm is present in both the absorption and the c.d. spectra of the three isomers; there is good correspondence between absorption and c.d. maxima, at least for the low energy part of the structure. The signs of these multiple Cotton effects are positive for (—)-(S)-I, and negative for (—)-(S)-II and -(III). The spacings between the maxima are roughly those expected from the average frequency separation of strong bands observed by Rush and Spomer in the $\pi \rightarrow \pi^*$ transition of the isomeric picolines.¹¹

In compound (III) this system is slightly shifted to the blue with respect to the other isomers as in the $\pi \rightarrow \pi^*$ transition of γ -picoline.¹¹ We assign this structured band to the $\pi \rightarrow \pi^*$ transition of the pyridine chromophore.

On the high energy side of the $\pi \rightarrow \pi^*$ transition, there are bands with maxima at ca. 240 nm in the c.d. spectra; these bands do not have corresponding maxima in the absorption spectra. The signs of these bands are negative for (—)-(S)-I and -(III), and positive for (—)-(S)-II.†

On changing the solvent from methanol to cyclohexane these band maxima are considerably shifted to the red (ca. 1000 cm^{-1}) for compounds (II) and (III) and overlap to a greater extent with the $\pi \rightarrow \pi^*$ transition whose fine structure is consequently lost (Figure 2). The hypothesis suggested by Kasha³ is sustained by this observation from the c.d. spectra. In compound (—)-(S)-I this solvent effect is not observed; this compound is capable of intramolecular hydrogen bond formation.¹² The i.r. spectrum has ν_{max} (CCl_4) 3450 cm^{-1} for OH stretching and this is independent of the concentration, in agreement with the presence of intramolecular hydrogen bonding.¹²

In the c.d. spectrum of (—)-(S)-III only a band (positive; 265 nm) on the low energy side of the $\pi \rightarrow \pi^*$ transition is evident; this band does not have a corresponding maximum in the isotropic absorption spectrum. As its intensity increases at -150° , it is unlikely to be a hot band. It is known from the work of Rush and Spomer¹¹ that in the spectrum of 4-picoline the energy separation between the $n \rightarrow \pi^*$ ($B_1 \leftarrow A_1$) and the $\pi \rightarrow \pi^*$ transitions is higher than in the spectra of the other isomers; therefore it is not completely fortuitous that in the c.d. spectrum

† In compound (—)-(S)-III the band at ca. 240 nm has the same sign as the $\pi \rightarrow \pi^*$ transition. However, even if, on account of overlap of the two bands, we cannot exactly say where one band ends and the other begins, it seems clear that the peaks at 261 and 254.5 nm, which correspond to absorption maxima, belong to the $\pi \rightarrow \pi^*$ transition, while the maximum at 237.5 nm, which is noticeably distant from the absorption maximum, belongs to another transition. The spectra recorded in cyclohexane and in 10% sulphuric acid confirm this interpretation.

of (—)-(S)-III one observes the well separated band at ca. 265 nm. We assign it to an intense $n \rightarrow \pi^*$ ($B_1 \leftarrow A_1$) transition. Furthermore the spectrum recorded in cyclohexane shows fine structure at >270 nm typical of this pyridine transition⁷ (Figure 2).

The c.d. spectrum of (—)-(S)-III seems particularly significant as, for the first time, three different transitions can be clearly seen in the region between 235 and 280 nm. The c.d. maximum at ca. 240 nm does not correspond to an $n \rightarrow \pi^*$ ($B_1 \leftarrow A_1$) transition shifted to lower wavelengths than the $\pi \rightarrow \pi^*$ transitions because of several factors, such as substituent, solvent, and cancellation effects. This band must correspond to a very weak, magnetically allowed

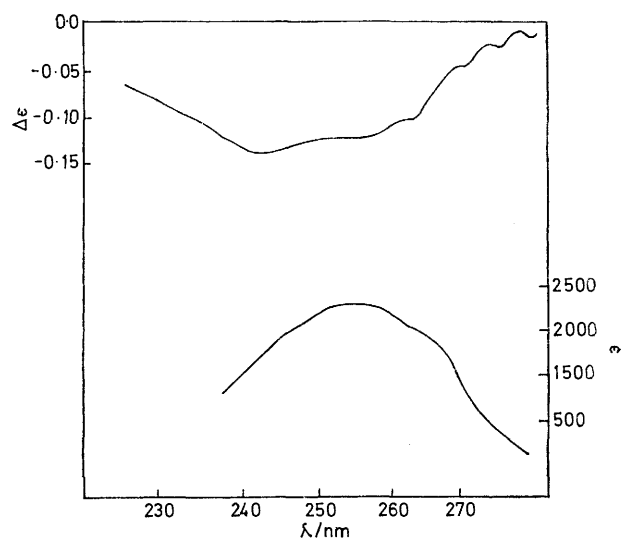


FIGURE 2 The room temperature c.d. and absorption spectra of (—)-(S)-III in cyclohexane

transition; our data support the assignment to the $n \rightarrow \pi^*$ ($A_2 \leftarrow A_1$) transition proposed in ref. 5 and recently confirmed by MO calculations.¹³

In the spectra of (I) and (II) the first $n \rightarrow \pi^*$ ($B_2 \leftarrow A_1$) transition is not detectable; however, once the assignment of the 240 nm band of (III) is made, it is easy to assign to the same transition the 240 nm bands of (I) and (II) which are very similar in shape and intensity to that of (III).

U.v. and c.d. spectra of (I)—(III) recorded in 10% sulphuric acid

Compound	U.v.		C.d.	
	$\lambda_{\text{max.}}/\text{nm}$	$\epsilon_{\text{max.}}$	$\lambda_{\text{max.}}/\text{nm}$	$\Delta\epsilon_{\text{max.}}$
(I)	263	7110	261.5	+1.58
(II)	261	5550	261	-0.25
(III)	254	5180	255	-0.35

Characteristics of the spectra of (—)-(S)-I—(III) recorded in 10% sulphuric acid are reported in the Table. The u.v. spectra on changing from the free

¹¹ J. H. Rush and H. Spomer, *J. Chem. Phys.*, 1952, **20**, 1847.

¹² L. P. Kuhn, R. A. Wires, W. Ruoff, and H. Kwart, *J. Amer. Chem. Soc.*, 1969, **91**, 4790.

¹³ R. L. Ellis, G. Kuehnlenz, and H. H. Jaffé, *Theor. Chim. Acta*, 1972, **26**, 131.

base to the protonated species, show the usual modifications,^{2a} *i.e.* increase of ϵ_{max} and loss of fine structure. (The pK_a of pyridine and several substituted pyridines was measured by Brown and Mihm.¹⁴ The values range between 5.17 for pyridine and 6.02 for 4-picoline. This ensures complete protonation in our experimental conditions.)

The c.d. spectra show in the three cases one band having the same sign as the $\pi \rightarrow \pi^*$ c.d. band observed for the free base. The maxima of these c.d. bands correspond to the isotropic absorption maxima. While the c.d. bands of compounds (I) and (III) are easily detected, some care was needed in identifying that of compound (II) which was not previously reported. In all cases the c.d. band at *ca.* 240 nm was no longer detectable. Also the c.d. absorption corresponding to the $n \rightarrow \pi^*$ ($B_1 \leftarrow A_1$) transition of compound (III) is no longer evident. These results are in agreement with the assignments proposed above.

The fact that in acid media the c.d. absorption corresponding to the $\pi \rightarrow \pi^*$ transition is still present for the compounds studied here as well as for (–)-(S)-5,6,7,8-tetrahydroquinolin-5-ol,^{4a} raises doubts about the one-electron interpretation of the optical activity previously proposed by us^{4a} and recently elaborated by Smith *et al.*⁵ In fact, once the lone pair of the pyridine nitrogen atom is engaged in σ bonding with the acid proton, no more occupied orbitals of A_1 symmetry are available (obviously if one does not consider σ orbitals). It is therefore impossible to obtain excited states of B_1 symmetry which are required in the one-electron theory in order to obtain magnetic moments along the y axis, parallel to the electric dipole moment of the $\pi \rightarrow \pi^*$ ($B_2 \leftarrow A_1$) transition. The optical activity, at least in acid media, must be entirely caused by dynamic couplings¹⁵ between the chromophore and asymmetric surrounding. Smith *et al.*⁵ surprisingly did not detect any c.d. absorption in acid media between 230 and 300 nm for the three isomeric 1-pyridylethylamines. However, the fact of having observed optical activity in the three alcohols excludes one-electron optical activity, while the fact that the corresponding amines do not show optical activity does not necessarily prevent dynamic coupling which in certain conformations can easily give small values.

We are presently studying the conformation of a few isomeric 5,6,7,8-tetrahydroquinolines in order to evaluate

¹⁴ H. C. Brown and X. R. Mihm, *J. Amer. Chem. Soc.*, 1955, **77**, 1723.

the importance of dynamic couplings in their optical activity.

EXPERIMENTAL

Optical rotations were measured with a Bendix NPL automatic polarimeter. U.v. absorption spectra were recorded with an Unicam SP 700 spectrophotometer. C.d. spectra were recorded with a Jouan C.D. II dichrograph, fitted with a 150 W xenon lamp. In order to check the correspondence between u.v. and c.d. maxima a trace of the photomultiplier tension was recorded, by connecting a Leeds and Northrup Speedomax recorder to the photomultiplier supply.

Synthesis and Resolution of the Pyridylethanol.—The alcohols were obtained by refluxing the corresponding acetylpyridines (Merck-Schuchart) with sodium borohydride in ethanol (2 h). The solutions were then cooled and acidified with dilute hydrochloric acid, the ethanol was evaporated under reduced pressure, and the residual aqueous solutions, basified with 20% aqueous sodium hydroxide, were carefully extracted with ether, dried, and evaporated under vacuum. The residual oils were distilled under reduced pressure; (I), b.p. 108–110° at 25 mmHg (lit.,¹⁶ 95° at 10 mmHg); (II), b.p. 140–143° at 15 mmHg (lit.,¹⁶ 128–129° at 10 mmHg); (III), b.p. 155–157° at 23 mmHg, m.p. 57–59° (from light petroleum) (lit.,¹⁴ b.p. 130–132° at 14 mmHg, m.p. 56–57°). Compound (I) was resolved by crystallisation of its acid (–)-dibenzoyltartrate derivative from ethanol. The salt had m.p. 144–145° (lit.,¹⁶ 145–147°), free base $[\alpha]_D -56.1^\circ$ (*c* 0.5, EtOH) (lit.,¹⁶ –56.6°). Compound (II) was resolved as reported in ref. 4a. Compound (III) was resolved by crystallisation of its (–)-dibenzoyltartrate derivative from ethanol; the salt had m.p. 146–148° (Found: C, 62.45; H, 4.8; N, 2.85. Calc. for $C_{25}H_{23}NO_9$: C, 62.35; H, 4.8; N, 2.9%) free base $[\alpha]_D -43.4^\circ$ (*c* 0.5, EtOH); on recrystallisation from light petroleum the free base had $[\alpha]_D -49.8^\circ$, m.p. 63–65° (lit.,¹⁶ $[\alpha]_D +4.27^\circ$).

Absolute Configurations of the Alcohols determined by the Horeau Method.—The method which employs racemic phenylbutyric anhydride and optically active alcohols was followed. Phenylbutyric anhydride was prepared following ref. 9c; the operations performed are described in detail in ref. 9b. The recovered phenylbutyric acid had in all three cases a negative optical rotation, hence the S-configuration was assigned to the alcohols.

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¹⁵ I. Tinoco, jun., *Adv. Chem. Phys.*, 1962, **4**, 113.

¹⁶ O. Cervinka, O. Belovsky, and P. Rejmanova, *Coll. Czech. Chem. Comm.*, 1973, **38**, 1358.