379. *The Dependence of Optical Rotatory Power on Chemical Constitution. Part XL.* (+)-*2-(2-Hydroxy-*n*-propyl)pyridine.*

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The rotatory powers of the carbinol named in the title are not especially sensitive to temperature changes. They vary very widely in different solvents, and are not related to the dipole moment or refractive index of the solvent. In non-hydroxylic solvents, the dispersions are anomalous. In hydroxylic solvents and in the homogeneous carbinol, they are comparatively simple. It is suggested that intermolecular association occurs in the homogeneous carbinol, that self-association of the carbinol is lessened in hydroxylic solvents, and that intramolecular association occurs in non-hydroxylic solvents; also that intramolecular association increases the contribution of the pyridine chromophore to the rotatory power, this stimulation of the longer wave-length term in the dispersion equation making the dispersion anomalous.

Table I summarises the absorption spectrum of 2-(2-hydroxy-*n*-propyl)pyridine (in ethyl-alcoholic solution) between 3000 and 2200 A. It shows a region of absorption, with $\lambda_{\text{max.}}$ at 2620 A. accompanied by some fine structure; ε falls to a minimum at 2260 A. ($\varepsilon_{\text{min.}} = 640$) and then rises as λ decreases below 2250 A., indicating the presence of a stronger band with $\lambda_{\text{max.}}$ below 2200 A. These two bands are related to the bands at 2500 and 1950 A. in the spectrum of pyridine (Braude, *Ann. Reports*, 1945, **42**, 128), shifted to longer wave-lengths by nuclear substitution.

Table II gives the rotatory powers of the (+)-carbinol. The rotatory power of the homogeneous carbinol is not especially sensitive to temperature changes. The rotatory powers at 20° give a linear $1/\alpha$–λ^2 plot, and the extrapolated λ_0 is 2500, which is not far removed from the long-wave absorption band and suggests that the pyridine chromophore may be optically active.

The rotatory powers in solution do not show any simple relation to the dipole moments of the solvents; they vary over a wider range than can be explained by variations in refractive index, as is shown by the values for rotivity (Ω in Table II). In each of the solvents chloroform, carbon tetrachloride, ethyl acetate, ethyl ether, acetone, dioxan, and benzene (2% solution), one or more of the characteristics of anomalous dispersion (inflexion, maximum, or reversal of sign in the α–λ plot) are apparent. In these cases a Drude equation with two terms of opposite sign would be required to fit the dispersion; in transparent regions, the term of shorter wave-length in such an equation dominates the rotatory power and must therefore be (+) in the present example. In nitromethane, curvature of the $1/\alpha$–λ^2 plot indicates complex dispersion. In carbon disulphide, water, ethyl alcohol, and acetic acid, $1/\alpha$–λ^2 plots are linear; in the first, $\lambda_0 = 0$, showing that a one-term equation is not valid. In the three hydroxylic solvents, the dispersion ratios are fairly constant and their high values may be ascribed to rotatory contributions arising from bands in the far ultra-violet, since the values of λ_0 are not sufficiently near the observed absorption band at 2620 A. Though the rotatory dispersion therefore cannot be simple, it does not show the marked anomalies observed in the non-hydroxylic solvents and, since the signs of rotatory power are the same in both kinds of solvents, the contribution of the term of longer wave-length must be lessened in the hydroxylic solvents.

TABLE I.

Ultra-violet absorption spectrum of 2-(2-*hydroxy*-n-*propyl*)*pyridine* (*in ethyl alcohol*).

$\lambda_{max.}$	2500 *	2570	2620	2685
$\varepsilon_{max.}$	2400	3190	3620	2690

* Inflexion.

TABLE II.

Specific rotatory powers of (+)-2-(2-*hydroxy*-n-*propyl*)*pyridine.*

Solvent and μ.		*t.*	λ, A. 6708.	6438.	6104.	5893.	5780.	5461.	5086.	4800.	4358.	$[\alpha]_{4358}/[\alpha]_{5461}$.	λ_0.	Ω 5893.
None	*d*, 1·049	20°	—	46·3°	—	55·5°	59·6°	68·6°	82·3°	95·4°	124°	1·81	2500	38·7
	d, 1·045	25	—	43·9	—	—	57·2	65·9	77·4	—	118	1·79	—	—
	d, 1·030	43	—	40·1	—	—	50·1	57·6	68·2	—	—	—	—	—
	d, 1·016	59	—	35·9	—	—	45·1	51·9	61·7	—	—	—	—	—
	d, 0·983	98	—	—	—	—	36·5	41·7	—	—	—	—	—	—
Ethyl ether, 1·22	*c*, 2·103	18	—	9·5	—	10·2	—	11·7 *	12·1	—	6·7	0·57	—	7·98
Benzene, 0	*c*, 1·887	21·5	22·0°	22·0	23·6°	26·1	27·3	29·7	31·1	31·6	31·6	1·06	—	18·42
	c, 20·96	18	26·2	29·4	31·7	34·4	35·4	39·4	45·1	50·3	58·5	1·48	—	24·24
Carbon tetrachloride, 0	*c* 2·135	19·5	13·6	14·1	15·5	16·6	16·9	17·6	17·1	16·0	9·8	0·56	—	12·03
Chloroform, 1·18	*c*, 2·392	21	—	1·9	—	5·8 *	6·1	—	4·6	—	−9·2	—	—	4·26
Ethyl acetate, 1·81	*c*, 2·103	17·5	—	—	—	—	10·4	11·0 *	11·6	—	8·3	0·75	—	—
Acetone, 2·74	*c*, 2·011	21	9·5	10·2	—	11·5	12·0	13·7	14·7	—	12·0	0·88	—	8·97
Carbon disulphide, 0	*c*, 2·122	16	—	51·8	—	61·0	65·0	71·6	83·7	95·1	114	1·60	0	39·3
Water, 1·9	*c*, 2·236	21·5	—	50·3	—	61·5	64·4	74·3	87·7	102	135	1·81	2365	48·6
Ethyl alcohol, 1·74	*c*, 2·074	16·5	29·2	33·5	36·6	39·5 *	41·4	48·2	57·4	66·2	86·1	1·79	2360	30·6
Acetic acid, 1·04	*c*, 2·139	17	—	75·2	—	90·0 *	94·0	109	131	154	195	1·79	2160	69·3
Nitromethane, 3·13	*c*, 2·169	20	—	28·1	—	33·0 *	33·9	37·8	44·9	49·3	58·7	1·55	—	25·29
Dioxan, 0	*c*, 2·167	18	23·0	23·7	25·8	27·7	29·3	32·7	38·4	43·3	49·8	1·52	—	20·64
	c, 2·119	25	—	27·4	—	—	28·3	33·1	38·2	—	50·0	1·51	—	—
	—	63	—	18·9	—	—	21·2	25·5	34·0	—	42·0	1·65	—	—

* Interpolated.

The effects of solvents on the rotatory power may be explained by the following assumptions :

(i) In the homogeneous carbinol, the association is intermolecular and the dispersion term associated with the 2620-A. band is significant.

(ii) When the carbinol is diluted with non-hydroxylic solvents, its molecules, being more separated from one another, associate intramolecularly. The contribution to the rotatory power from the pyridine chromophore, which is the longer wave-length term in the rotatory power expression, is thereby stimulated, and the rotatory dispersion becomes complex. Such an association (hydrogen bonding) between the hydroxyl group and the nitrogen atom, is stereochemically possible and would introduce the possibility of molecular dissymmetry as well as affecting the pyridine chromophore. The two observations on benzene solutions show that at high concentration (*c*, 20) the dispersion is less complex ($1/\alpha$–λ^2 is linear though the dispersion ratio is 1·48, and λ_0 is imaginary), than in more dilute solution (*c*, 2·0), where the dispersion becomes anomalous : continued reduction of the molecular association by dilution would explain this.

(iii) In hydroxylic solvents, intra- and inter-molecular associations are prevented by association with the solvent : the rotatory power is dominated by a short-wave length (far ultra-violet) term and is comparatively simple.

Esterification of the alcohol would prevent such forms of association. Results with the (+)-acetate (Table III) are consistent with this suggestion. It is pseudo-simple, whether the acetate is homogeneous or in solution in two non-hydroxylic solvents. In all three cases

$1/\alpha$–λ^2 plots are linear, extrapolated values of λ_0 are about 2250 A., and dispersion ratios are 1·75. The *p*-diphenylylurethane is probably too complex a molecule to give a satisfactory test of the suggestion (it contains an additional ultra-violet chromophore), but in two non-hydroxylic and one hydroxylic solvent it gives linear $1/\alpha$–λ^2 plots and dispersion ratios of about 1·6, though the λ_0's vary very widely.

TABLE III.

Specific rotatory powers of esters of (+)-2-(2-*hydroxy*-n-*propyl*)*pyridine*.

			λ, A.								
Solvent.		*t*.	5893.		5780.	5461.	5086.	4800.	4358.	Dispersion ratio.	λ_0.
Hydrogen phthalate.											
5N-HCl	*c*, 2·049	19·5°	58·5°		79·0°	92·2°	112°	132°	178°	1·93	2730
Water	*c*, 0·945	20	—		76·8	88·5	—	—	167	1·89	2600
N-NaOH	*c*, 1·957	20	—		—	96·0	—	—	—	—	—
Acetate.											
None	*d*, 1·048	23	8·4		10·8	12·3	14·4	16·4	21·4	1·74	2120
Benzene	*c*, 2·161	23	12·5		15·5	18·3	21·6	—	32·2	1·76	2280
Carbon tetrachloride	*c*, 1·992	23	9·3		11·3	13·3	15·1	—	23·3	1·75	2390
Diphenylylurethane.											
Benzene ...	*c*, 2·015	20	10·0	11·2°	—	13·7	15·9	—	22·0	1·60	0
Ethyl alcohol	*c*, 2·215	17·5	25·7	31·6	32·7	36·8	43·3	—	60·3	1·63	1565
Carbon tetrachloride	*c*, 1·337	19	7·9	8·6	10·1	11·6	12·4	—	18·4	1·59	1380

The hydrogen phthalate cannot be used to test the suggestion because it is soluble only in aqueous solutions (it probably exists in the zwitterion form); its dispersion ratios are high, probably on account of increased absorption in the ultra-violet, and it gives linear $1/\alpha$–λ^2 plots. The rotatory powers $[\alpha]_{5461}$ of the hydrogen phthalate are 88°, 92°, and 96° respectively in water (in which it probably contains positively and negatively charged groups), in hydrochloric acid (in which it contains a positively charged group only), and in sodium hydroxide (in which it contains a negatively charged group only); this comparative insensitivity to the polarity of the substituents is somewhat unusual.

The rotatory power of tetrahydrofurfuryl alcohol resembles that of 2-(2-hydroxy-*n*-propyl)-pyridine in that it is very sensitive to change in solvent, but not especially so to change of temperature. In Part XXXV (*J.*, 1941, 312) it was argued that the comparative insensitivity to temperature shows that labile structures do not occur in the alcohol. However, since the rotatory powers of tetrahydrofurfuryl alcohol in solution are not related to the dipole moments of the solvents, and the rotivities (calculated from data given in Part XXXV) vary as widely as the rotatory powers, the arguments now developed suggest that alterations in the molecular species do occur on change of solvent, as was suggested by Irwin, Thesis, London, 1947). Intramolecular association (hydrogen bonding) between the two oxygen atoms is stereochemically possible in tetrahydrofurfuryl alcohol.

EXPERIMENTAL.

(±)-2-(2-*Hydroxy*-n-*propyl*)*pyridine*.—This was prepared as described by Walter, Hunt, and Fosbinder (*J. Amer. Chem. Soc.*, 1941, **63**, 2771; *Org. Synth.*, 1943, **23**, 83) from the lithium derivative of α-picoline and acetaldehyde; the purified carbinol was obtained in 45% yield. It did not yield crystalline salts with optically active acids.

(±)-*Hydrogen Phthalate*.—From a solution of the carbinol (51 g.) and phthalic anhydride (55 g.) in acetone (140 c.c.), warmed under reflux for 30 minutes, the hydrogen phthalate (91 g.; m. p. 138—141°) separated during 18 hours. It is insoluble in carbon disulphide, *cyclo*hexane, benzene, acetone, and ethyl acetate, sparingly soluble in chloroform or cold water, dissolves readily in hot water (from which it does not separate on cooling), ethyl alcohol, aqueous acids, or alkalis. These solubilities suggest that it exists as the zwitterion, and is only slowly soluble in cold water because it is not easily wetted.

(+)-2-(2-*Hydroxy*-n-*propyl*)*pyridine*.—Brucine (197 g.) and the (±)-(hydrogen phthalate) (142 g.) were dissolved in hot acetone (1250 c.c.); the crystalline brucine salt (m. p. 148—150°) which separated during 18 hours at room temperature was recrystallised from ethyl acetate (3950 c.c.), yielding 100 g. of brucine salt, m. p. 154—156°, with $[\alpha]_D^{19}$ −20·2° in chloroform (*c*, 2·147), which was not altered by further recrystallisation. A mixture of the salt (10 g.) and 5N-sodium hydroxide (10 c.c.) was heated on the steam-bath for 30 minutes, cooled, and extracted with ether. The ethereal solution was dried (K_2CO_3) and concentrated, and the residue distilled, yielding the (+)-carbinol (1·5 g.), b. p. 111°/10 mm., n_D^{18} 1·5142. Rotatory powers are in Table II. The usual procedure for conversion of alkaloid salt to carbinol *via* the hydrogen phthalate is not applicable in this case, because the phthalate is soluble in aqueous solutions and not in organic solvents. The filtrate from the first crystallisation yielded a *lævo*carbinol, $[\alpha]^{19}_{D}$ −42·0° in carbon disulphide (*c*, 2·2); this was converted into the hydrogen phthalate, from which a crystalline alkaloidal salt could not be obtained. Rotivities, Ω in Table II are calculated as $3[\alpha]_{5893}/(n^2 + 2)$, by using the weighted means of refractive indices of solvents and solute.

The (+)-(hydrogen phthalate) was prepared from the (+)-carbinol as described above. Rotatory powers are in Table II. The rotatory power in sodium hydroxide solution is an extrapolation to zero time from the following observations of $[\alpha]_{5461}$/mins. after dissolution: 79°/24, 70°/45, 61°/65, 53°/90, 36°/240, 33°/2670. The final observation is a little lower than would be derived from the equivalent concentration of (+)-carbinol in water, *viz.*, +37°.

(+)-2-(2-Hydroxy-*n*-propyl)pyridine acetate was prepared from equal volumes of the carbinol (2·2 g.) and acetic anhydride, heated at 60° for 3 hours, diluted with ether, washed with N-sodium hydroxide till neutral, dried (Na_2SO_4), and concentrated. The (+)-acetate (1·3 g.), obtained from the residual oil, had b. p. 124—125°/19 mm. n^{21}_{D} 1·4915, d^{25}_{4} 1·048. Rotatory powers are in Table III.

(+)-2-(2-*Hydroxy*-n-*propyl)pyridine* p-*diphenylylurethane*. A solution of the (+)-carbinol (0·5 g.) and *p*-diphenylylcarbimide (0·75 g.) in benzene (10 c.c.) was heated under reflux for 30 minutes. On cooling, the (+)-urethane crystallised and, recrystallised from benzene–light petroleum, had m. p. 134° (0·85 g.). Rotatory powers are in Table III.

The absorption spectrum was determined by Dr. G. H. Beaven, using a Beckman photoelectric quartz spectrophotometer. Thanks are expressed to the Government Grants Committee of the Royal Society and to Imperial Chemical Industries Limited for grants, and to the Department of Scientific and Industrial Research for a maintenance grant (to I. G. A.).

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