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OPTICALLY ACTIVE AMINES—VIII[1]

OPTICAL ROTATORY DISPERSION OBSERVATIONS ON α- AND β-ARYLALKYLAMINES[2]

H. E. SMITH and M. E. WARREN, JR.[3]
Department of Chemistry, Vanderbilt University, Nashville, Tennessee
and
L. I. KATZIN
Chemistry Division, Argonne National Laboratory, Argonne, Illinois

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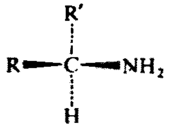
Abstract—In the ORD curves of (*R*)-α-phenylethylamine, (*R*)-α-phenyl-n-propylamine, (*R*)-α-phenylneopentylamine and (*S*)-α-benzylethylamine and their hydrochlorides, a correlation is shown between their configuration and the sign of the weak, first Cotton effect at about 268 mμ in the region of the phenyl absorption. A second, stronger component of the rotatory dispersion originates in an electronic transition or transitions lying below 220mμ and in general gives the sign to the rotation in the visible part of the spectrum. In some compounds, two contributions of opposite sign are recognizable in the far UV component of the ORD.

THERE exists a continuing interest in the correlation of ORD phenomena with the details of molecular configuration, and in particular, in the Ph ring as an optically active chromophore.[4–12] In this connection, we have measured the ORD curves for (*R*)-α-phenylethylamine (Ia),[13] (*R*)-α-phenyl-*n*-propylamine (IIa),[13] (*R*)-α-phenylneopentylamine (IIIa)[13] and (*S*)-α-benzylethylamine (IVa)[13] and their respective hydrochlorides (Ib–IVb) in various solvents from 295 to about 225 mμ, the region within which the long wavelength UV absorption band of the Ph group is found.[14]



Ia. R = Ph; R' = Me
IIa: R = Ph; R' = Et
IIIa: R = Ph; R' = CMe$_3$
IVa: R = Me; R' = PhCH$_2$

RESULTS AND DISCUSSION

As has been noted with similar compounds,[5,6,8,10,11,15,16] and in particular with Ia,[8,11] Ib[11] and IVa,[8] at least two distinct contributions to the ORD curves are found (Tables 1 and 2 and Figs 1 and 2) and in three cases (IIb, IIIa and IIIb), there is evidence of three contributions.

One contribution is that of the long wavelength absorption of the phenyl chromophore.[14] This shows multiple Cotton effects at about 245–270 mμ whether it is

TABLE 1. ROTATIONAL DATA FOR SOME α- and β-PHENYLALKYLAMINES

				ORD[a]							
		Visually measured[b]			Longest wavelength Cotton effect					Cut-off	
					First extremum		Second extremum				
Solvent	Compound[c]	$[\phi]_D$[d]	c[e]	$[\phi]_{295}$[d]	λ[f]	$[\phi]$[d]	λ[f]	$[\phi]$[d]	[A][g]	λ[f]	$[\phi]$[d]
None	Ia	+48·4									
MeOH		+34	2·8	+210	269	+50	267	+430	−380	226	+1400
Abs-EtOH		+36	2·0								
Iso-PrOH		+38	2·6	+260	270	+70	267	+490	−420	226	+1700
None	IIa	+28·7									
MeOH				+10	269	−290	266	+120	−410	227	+960
Abs-EtOH		+11	7·9								
Iso-PrOH				+40	270	−270	268	+170	−440	224	+1700
None	IIIa	+9·0									
MeOH				−140	269	−830	266	−140	−690	230	−1100
Abs-EtOH		+4·1	4·0	−170	269	−900	266	−170	−730	233	−910
Iso-PrOH				−180	270	−980	266	−220	−760	224	−2800
None	IVa	+46·1									
MeOH		+37	2·0	+310	270	+610	267	+460	+150	233	+1400
Abs-EtOH		+39	2·0								
Iso-PrOH		+42	2·0	+400	270	+720	268	+620	+100	242	+1300

[a] Room temp.

[b] Temp 21–27°.

[c] See text for structure and configuration.

[d] Molecular rotation in degrees.

[e] Concentration in g/100 ml.

[f] Wavelength in mμ.

[g] Apparent amplitude, $[\phi]_{\text{peak}} - [\phi]_{\text{trough}}$, in degrees of molecular rotation.

TABLE 2. ROTATIONAL DATA FOR SOME α- AND β-PHENYLALKYLAMINE HYDROCHLORIDES

				ORD[b]							
		Visually measured[c]			Longest wavelength Cotton effect					Cut-off	
					First extremum		Second extremum				
Solvent	Compound[c]	$[\phi]_D$[d]	c[e]	$[\phi]_{295}$[d]	λ[f]	$[\phi]$[d]	λ[f]	$[\phi]$[d]	[A][g]	λ[f]	$[\phi]$[d]
H_2O	Ib	+8	2·1								
MeOH		+9·8	2·0	+60	268	−50	265	+200	−250	219	+1000
Abs-EtOH		+11	2·0								
Iso-PrOH		+12	2·1	+120		+20	266	+310	−290	236	+690
H_2O	IIb	+13	2·2								
MeOH		+11	2·1	−100	268	−430	264	−210	−220	230	−860
Abs-EtOH		+10	1·9								
Iso-PrOH				−90	268	−360	265	−190	−170	230	−880
MeOH	IIIb			−60	268	−340	264	−160	−180	228	−950
Abs-EtOH		+11	2·0								
Iso-PrOH				−30	268	−230	264	−90	−140	222	−1500
H_2O	IVb	+37·1	9·0	+320	268	+490	266	+440	+50	223	+1700
MeOH		+12	3·4	+150	269	+380	268	+130	+250	223	+440
Abs-EtOH		−4·6	7·9								
Iso-PrOH		−19	3·4	−100	269	+90	267	−300	+390	223	−860

[a] Room temp.
[b] Temp 21–27°.
[c] See text for structure and configuration.
[d] Molecular rotation in degrees.
[e] Concentration in g/100 ml.
[f] Wavelength in mμ.
[g] Apparent amplitude, $[\phi]_{\text{peak}} - [\phi]_{\text{trough}}$, in degrees of molecular rotation.

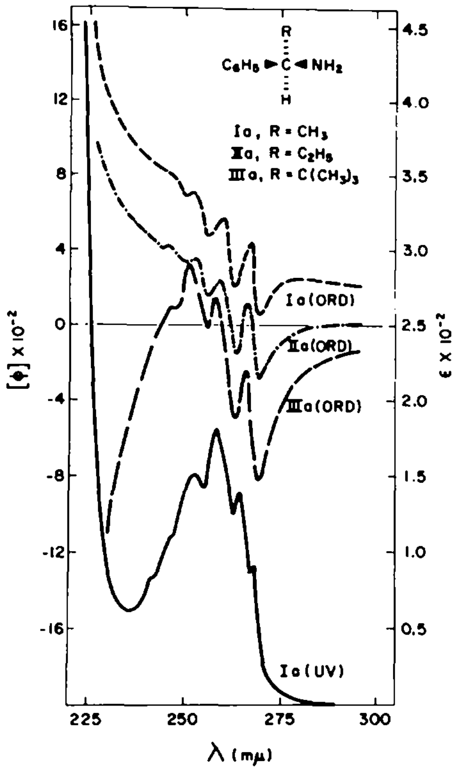


FIG. 1. The UV absorption spectrum of (*R*)-α-phenylethylamine (Ia) in absolute ethanol and the ORD curves of (*R*)-α-phenylethylamine (Ia), (*R*)-α-phenyl-n-propylamine (IIa) and (*R*)-α-phenylneopentylamine (IIIa) in methanol.

attached directly to the asymmetric center, as in Ia–IIIa (Fig. 1) and Ib–IIIb (Fig. 2), or is separated from it by a methylene group, as in IVa and IVb. The individual Cotton effects correspond to the fine structure of the absorption band[14] (Table 3). In qualitative agreement with earlier measurements using Ia[8,11] and Ib,[11] but with greater resolution, for the amines Ia–IIIa and their hydrochlorides there were observed from 5 to 9 extrema with the magnitudes of the change in rotatory power from peaks to troughs decreasing as the wavelength becomes shorter. Below 242–250 mμ to cut-off (Tables 1 and 2) extrema were not observed, and in this region only plain dispersion curves were found. As observed earlier with IVa,[8] in the 245–270 mμ region the magnitude of the change in rotatory powers from peaks to troughs are much smaller with IVa and IVb than with the others, and in these two cases only two or three extrema were distinctly observed. Since the magnitude of these Cotton effects has been shown to be conformationally dependent,[10–12] this difference may be explained on the basis of the greater range of conformational possibilities of IVa and IVb.

Although the difference in solvents generally was not great, as has been noted previously,[10,12] the general trend is that, with the exception of IIb, IIIb and IVa, the magnitude of the Cotton effects is largest in the solvent of least polarity. In addition, although there are not great differences between the UV absorption characteristics of the α-phenylalkylamines and the amine hydrochlorides (Table 3), the Cotton

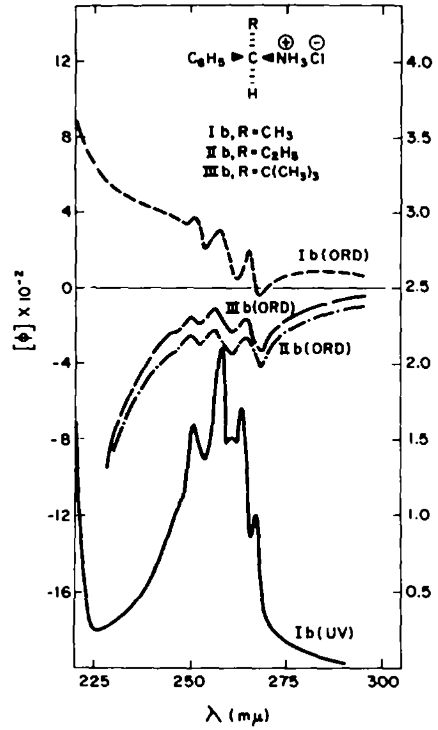
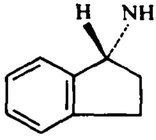
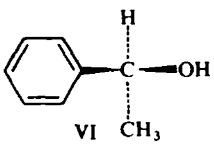


FIG. 2. The UV absorption spectrum of (*R*)-α-phenylethylamine hydrochloride (Ib) in absolute ethanol and the ORD curves of (*R*)-α-phenylethylamine hydrochloride (Ib), (*R*)-α-phenyl-n-propylamine hydrochloride (IIb) and (*R*)-α-phenylneopentylamine hydrochloride (IIIb) in methanol.

effects of the former are greater than those of the latter. This, however, is in sharp contrast to that found for (*R*)-1-aminoindane (V) and a series of N-substituted (*R*)-1-aminoindanes and their respective salts.[11] In each of these latter cases, the salt in methanol has a first long wavelength Cotton effect of greater amplitude than


V


VI

the free base in isooctane.[11] Although these changes in rotational strength and in fact the high rotational strength of the Cotton effects associated with the phenyl chromophore in α-phenylalkylamines and their salts and (*S*)-α-phenylethyl alcohol (VI)[5, 17] when compared with the Cotton effects displayed by optically active 2-phenylbutane[5] and long-chain alkylphenylcarbinols[10] are not completely explained, it has been shown that the presence of a group posessing a pair of nonbonding electrons such as a hydroxyl or amino group attached to the aromatic ring[6, 7] is

TABLE 3. UV SPECTRAL DATA FOR SOME α-PHENYLALKYLAMINES AND THEIR HYDROCHLORIDES IN ABSOLUTE ETHANOL

Compound[a]	Absorption maxima[b]						
Ia	268 (90)	264 (140)		258 (180)	252 (150)	248 (110)[c]	242 (82)[c]
IIa	268 (80)[c]	264 (130)		258 (180)	253 (150)	248 (110)[c]	244 (78)[c]
IIIa		264 (140)		258 (190)	252 (160)	248 (120)	242 (93)[c]
Ib	267 (100)	263 (170)	260 (150)	258 (210)	251 (160)	248 (110)[c]	
IIb	268 (120)	264 (190)	261 (170)	258 (230)	251 (170)	248 (120)[c]	
IIIb	268 (100)	265 (170)	263 (150)	256 (220)	252 (150)	248 (110)[c]	243 (71)[c]

[a] See text for structure.

[b] Wavelength in mμ. Numbers in parentheses are molecular absorptivities.

[c] Shoulder.

important. In addition, it has been suggested that similar groups α to the aromatic ring at the asymmetric center,[10,11] that a group at the α-position with a positive charge such as in quaternary ammonium salts,[11] that dissymmetric internal hydrogen bonding to the aromatic nucleus[11] and that conformational preference due to intramolecular hydrogen bonding[10] may all be important.

Most significantly, for the α- and β-phenylalkylamines Ia–IVa and their hydrochlorides, a negative sign for the longest wavelength Cotton effect at about 268 mμ correlates with the (*R*) configuration. In the case of the α-phenylalkyamines and their hydrochlorides, this correlation augments the argument used to explain the fact that for (*R*)-α-phenylethylamine (Ia) the Cotton effect is *negative* whereas for (*R*)-1-aminoindane (V) the Cotton effect is *positive*.[11] As expected, the effective size of the alkyl group attached at the asymmetric center in the series Ia–IIIa and Ib–IIIb has no great effect on the Cotton effect at 268 mμ.

The second component of the ORD curves originates in an UV absorption band or bands lying below 220 mμ.[14] It far overrides in intensity the Ph ring contribution at 245–270 mμ and in general gives the sign to the rotation in the visible part of the spectrum.[5,11] Two contributions to this far UV component are recognizable in the case of IIb, IIIa and IIIb. In each, the sign of the first phenyl Cotton effect is negative, the plain curve in the 225–245 mμ region is also negative, but the rotation in the visible region, which sums the rotatory contributions throughout the spectrum, is positive. This reveals that there is also a positive Cotton effect of greater intensity and at even shorter wavelength.

As has been suggested previously,[5,11] it is probable that these two strong contributions to the far UV component have their origin in the two strong absorption bands which usually appear in mono-substituted benzene compounds near 185 and 205 mμ.[14]

In Tables 1 and 2 are given rotatory powers at cut-off which indicate the shape of the apparent plain curves observed below about 245 mμ. For the amines Ia–IVa, these curves are only slightly sensitive to changes in solvent, in general increasing in strength as the solvent becomes less polar, but are exceedingly sensitive to changes in structure (cf Ia and IIIa) and salt formation (cf IIa and IIb). For the α-phenylalkylamine salts Ib–IIIb, again the curves are not highly sensitive to changes in solvent, but for IVb the plain positive curve in water or methanol becomes plain negative in isopropyl alcohol. In this case the sign of the rotation at 589 mμ, $[\phi]_D$, changes from positive to negative as the solvent is changed from water to isopropyl alcohol.

The two contributions to the far UV component, and their variability, make reliable correlations of the configurations of amines of this type with the sign of rotation in the visible[18,19] or with the shape of the plain dispersion curve above 300 mμ[20–22] exceedingly questionable.* Also, since we were generally unable to measure the dispersion curves below 225 mμ, we could not determine the effect of these far UV components on the dispersion curve in the 200–225 mμ region, the

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* It is to be noted that because of the respective signs of the near and far UV contributions to the ORD, IIa, IIIa, IIb and IIIb exhibit a broad peak in the 300–600 mμ region. Measurements using a Rudolph recording spectropolarimeter, Model 260/685/850/810–614, revealed these at 302 ($[\phi]$ +42°), 540 ($[\phi]$ +4·9°), 360 ($[\phi]$ +32°) and 410 mμ ($[\phi]$ +24°), respectively, for IIa, IIIa, IIb and IIIb in absolute ethanol.

direction of which has recently been suggested[16] as a means of assigning the absolute configurations of amines and amine hydrochlorides such as Ia–IVa and Ib–IVb. Sharp changes in some of these present curves, for which there is no indication down to cut-off, would be necessary to give such correlations for some of the amines in some of the solvents used.

EXPERIMENTAL

M.ps were taken in sealed capillary tubes and are corrected. Microanalyses were done by Galbraith Laboratories, Inc., Knoxville, Tenn. Electronic absorption spectra were measured using an Applied Physics Corp. Cary Model 14 spectrophotometer. Rotatory power measurements at the sodium D-line were obtained using a visual polarimeter and a 1-dm sample tube.

ORD measurements. These were recorded at room temperature from 225 to 295 mμ using a Durrum-Jasco Model ORD/UV-5 spectropolarimeter. Sample concentrations, 0·2–0·6 g/100 ml, and path lengths, 1–10 mm, were selected such that the absorbance was not greater than 2 at the maximum of the Ph absorption at 258 mμ. The absorbance of the longest wavelength component of the band was less than this, and the corresponding Cotton effect could be traced accurately. Under conditions such that the generally weak intensity of this Cotton effect was even lower than average, as with some of the hydrochlorides, more absorption was allowed, so long as the absorbance at the longest wavelength component did not exceed 2.

(R)-α-*Phenylethylamine* (Ia),[23] $[\alpha]_D^{23}$ +39·9° (neat).

(R)-α-*Phenylethylamine hydrochloride* (Ib). Addition of Ia to conc HCl and two recrystallizations of the resulting ppt from acetone gave Ib as white, silky needles, mp 171–173°, $[\alpha]_D^{25}$ +6·7° (*c* 2·0, abs EtOH) [lit.[24] m.p. 171°, $[\alpha]_D^{15}$ +7·2° (*c* 16, EtOH)].

(R)-α-*Phenyl-n-propylamine* (IIa),[25] $[\alpha]_D^{24}$ +21·2° (neat).

(R)-α-*Phenyl-n-propylamine hydrochloride* (IIb). Addition of IIa to conc HCl and three recrystallizations of the resulting ppt from MeOH–acetone gave IIb as the monomethanolated compound, colorless, clear plates, sublimes without melting near 175°, $[\alpha]_D^{26}$ +5° (*c* 1·9, abs EtOH). (Found: Cl, 17·67. $C_9H_{14}ClN \cdot CH_3OH$ requires: Cl, 17·41%.)

(R)-α-*Phenylneopentylamine* (IIIa),[25] $[\alpha]_D^{21}$ +5·6° (neat).

(R)-α-*Phenylneopentylamine hydrochloride* (IIIb). Addition of IIIa to conc HCl and three recrystallizations of the resulting ppt from abs EtOH–ether gave IIIb, sublimes without melting near 200°, $[\alpha]_D^{26}$ +5·5° (*c* 2·0, abs EtOH). (Found: Cl, 17·65. $C_{11}H_{18}ClN$ requires: Cl, 17·75%.)

(S)-α-*Benzylethylamine* (IVa),[23] $[\alpha]_D^{25}$ +34·1° (neat).

(S)-α-*Benzylethylamine hydrochloride* (IVb). Commercially available salt, $[\alpha]_D^{25}$ +21·6° (*c* 9·0, water), was used without further purification [lit.[26] $[\alpha]_D^{15}$ +24·8° (*c* 9·0, water)], and was the same material used to prepare IVa.[23]

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REFERENCES

[1] Paper VII: H. E. Smith, J. C. D. Brand, E. H. Massey and L. J. Durham, *J. Org. Chem.* **31**, 690 (1966).

[2] Presented in part at the 151*st National Meeting of the American Chemical Society. Division of Organic Chemistry*, Abstract No. 106. Pittsburgh, Pa., March (1966).

[3] Present address: Department of Chemistry, Peabody College, Nashville, Tennessee.

[4] T. M. Hooker, Jr., and C. Tanford, *J. Am. Chem. Soc.* **86**, 4989 (1964).

[5] L. Verbit, *Ibid.* **87**, 1617 (1965).

[6] A. Moscowitz, A. Rosenberg and A. E. Hansen, *Ibid.* **87**, 1813 (1965).

[7] A. Yogev and Y. Mazur, *Chem. Comm.* 388 (1965).

[8] A. La Manna, V. Ghislandi, P. M. Scopes and R. J. Swan, *Farmaco, Pavia, Ed. Sci.* **20**, 842 (1965).

[9] J. C. Craig and S. K. Roy, *Tetrahedron* **21**, 1847 (1965).

[10] L. Verbit, S. Mitsui and Y. Senda, *Ibid.* **22**, 753 (1966).

[11] J. H. Brewster and J. G. Buta, *J. Am. Chem. Soc.* **88**, 2233 (1966).

[12] L. Verbit, *Ibid.* **88**, 5340 (1966).

[13] Absolute configuration: [a] M. E. Warren, Jr., and H. E. Smith, *Ibid.* **87**, 1757 (1965); [b] H. E. Smith and T. C. Willis, *J. Org. Chem.* **30**, 2654 (1965); or as indicated therein.

[14] H. H. Jaffé and M. Orchin, *Theory and Applications of Ultraviolet Spectroscopy* p. 247. Wiley, New York, N.Y. (1962).

[15] I. P. Dirkx and Th. J. De Boer, *Rec. Trav. Chim.* **83**, 535 (1964).

[16] J. C. Craig and S. K. Roy, *Tetrahedron* **21**, 401 (1965).

[17] Absolute configuration: J. A. Mills and W. Klyne, *Progress in Stereochem.* **1**, 177 (1954).

[18] J. H. Brewster, *J. Am. Chem. Soc.* **81**, 5475 (1959).

[19] J. H. Brewster, *Tetrahedron Letters* No. **20**, 23 (1959).

[20] G. G. Lyle, *J. Org. Chem.* **25**, 1779 (1960).

[21] G. G. Lyle and W. Gaffield, *Tetrahedron Letters* No. **21**, 1371 (1963).

[22] A. La Manna and V. Ghislandi, *Farmaco, Pavia, Ed. Sci.* **19**, 377 (1964).

[23] For the source and a more complete characterization of this amine see H. E. Smith, S. L. Cook and M. E. Warren, Jr., *J. Org. Chem.* **29**, 2265 (1964).

[24] W. Leithe, *Monatsh. Chem.* **51**, 381 (1929).

[25] For the source and a more complete characterization of this amine see Ref. 13a.

[26] W. Leithe, *Ber. Dtsch. Chem. Ges.* **65**, 660 (1932).