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OPTICAL ROTATORY DISPERSION AND ABSOLUTE CONFIGURATION—X

α- AND β-PHENYLETHYLAMINE S[1]

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Abstract—ORD and CD measurements on α- and β-phenylethylamines and a cyclic analogue possessing the benzoquinolizidine structure indicate that the absolute configuration of the asymmetric center may be assigned from the ORD curve. Compounds of S-configuration exhibit a positive multiple Cotton effect between 270 and 250 mμ.

NUMEROUS α- and β-phenylethylamines of general structure (I) and (II) exist, either as synthetic products or of natural origin, in which the carbon atom attached to the basic nitrogen forms a center of asymmetry. Of the two possible enantiomers, frequently only one occurs in nature or, in cases where a synthetic material has been resolved, only one mirror image possesses powerful pharmacological activity. The determination of the absolute configuration of these compounds is therefore of considerable interest, and usually entails a multiple-step sequence of chemical operations, each of which must itself be stereospecific in nature, to correlate the compound with a substance of known configuration. It was therefore desirable to examine the use of optical rotatory dispersion to assign the absolute configuration of these compounds directly from the ORD curve without the necessity of carrying out chemical degradations.

This has not hitherto been possible, only plain dispersion curves being obtained in the accessible range extending to 275 mμ, and only the first extremum (at 275 mμ) of a Cotton effect could be reached in the two previous investigations[2,3] of α- and β-phenylethylamines reported in the literature. The use of ORD for the assignment of absolute configuration for these compounds necessitated the preparation of their N-benzylidene or N-salicylidene derivatives,[4] in which a dissymmetric chromophore gave Cotton effects in the 300–400 mμ region which permitted a configurational assignment. However, with the availability of instruments which allow the measurement of rotatory dispersion in the 200–275 mμ region, a re-investigation of this problem was opportune, and we now wish to record ORD measurements in this

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[1] Supported by research grant HE-5881 from the National Institutes of Health, U.S. Public Health Service.

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

[3] V. M. Potapov and A. P. Terentev, *Zh. Obshch. Khim.* **31**, 1003 (1961).

[4] [a] H. E. Smith, S. L. Cook, and M. E. Warren, Jr., *J. Org. Chem.* **29**, 2265 (1964).

[4] [b] M. E. Warren, Jr., and H. E. Smith, *J. Am. Chem. Soc.* **87**, 1757 (1965).

[4] [c] H. E. Smith and T. C. Willis, *J. Org. Chem.* **30**, 2654 (1965).

region, supported by circular dichroism data, which make possible the rapid assignment of absolute configuration using the free α- or β-phenylethylamines themselves.

Since the weak $n \rightarrow \sigma^*$ transitions of the non-bonding electrons of aliphatic nitrogen are located[5] below 200 mμ, the UV spectra of α- and β-phenylethylamines may be expected to show the aromatic absorption bands of an alkylbenzene[6] in which the (local excitation) transitions of the benzene at 184, 203·5 and 254 mμ (log ε 4·78, 3·87 and 2·31) have been displaced to 188, 208 and 261 mμ (log ε 4·73, 3·89 and 2·34), with considerable fine structure between 250 and 270 mμ. Moreover, protonation of the nitrogen would not be anticipated to exert much effect on the UV spectrum, in view of the much greater intensity of the benzenoid absorption in the 200 mμ region, and this is confirmed by the virtual identity of the UV spectra of α-phenylethylamine and its hydrochloride (Table 1).

In spite of the widespread occurrence of the benzene ring in many natural products possessing optical activity, the rotational effects of this chromophore appear little investigated and conflicting reports exist in the literature. The sole data on the rotatory dispersion of a compound of type (I) or (II) in the 200 to 275 mμ region is that of Potapov and Terentev[3] who found only a plain curve for (+)-α-phenylethylamine (III) down to 245 mμ in iso-octane solution. On the other hand, Verbit[7] reports a positive multiple Cotton effect of relatively small magnitude for the similarly constituted (−)-methylphenylcarbinol in the 240 to 280 mμ region, for which a previous investigation[8] had recorded the absence of a Cotton effect.

The UV spectrum of (−)-α-phenylethylamine (Table 1) shows the expected aromatic absorption bands at 207 and 258 mμ, the latter exhibiting fine structure between 242 and 267 mμ. The ORD curve down to 255 mμ (Fig. 1) is in complete agreement with the UV spectrum, and indicates four successive positive Cotton effects centred at 252, 257, 262 and 268 mμ, superimposed on a strong negative background curve. Confirmatory evidence is afforded by the circular dichroism (Fig. 1), which reveals that additional smaller negative Cotton effects between 250 and 230 mμ are hidden under the steeply falling negative ORD background. To ensure complete validity for the conclusions, regardless of rising end-absorption by the solvent or of scattered light in the 200 to 225 mμ region, the spectrum of the enantiomeric (+)-α-phenylethylamine was recorded and gave the expected exact mirror image curve.

The curve for (−)-α-phenylethylamine previously reported[2] shows a negative Cotton effect centred between 290 and 275 mμ both for the base and the hydrochloride. In view of this discrepancy we have examined the (−)-hydrochloride, and find this to give an ORD curve of the same shape, and of unchanged sign of Cotton effects and circular dichroism maxima (see Experimental), as that of the parent base (III, R′ = R″ = H). The earlier observations[2] may have been caused by stray light in a region of increasing absorption near the limit of the instrument used.

It has been previously shown[9] that (−)-α-phenylethylamine is configurationally

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[5] E. Tannenbaum, E. M. Coffin and A. J. Harrison, *J. Chem. Phys.* **21**, 311 (1953); L. W. Pickett, M. E. Corning, G. M Wieder, D. A. Semenov and J. M. Buckley, *J. Am. Chem. Soc.* **75**, 1618 (1953).

[6] cf. A. I. Scott, *Interpretation of the Ultraviolet Spectra of Natural Products* pp. 90–94, Pergamon Press, Macmillan, New York (1964).

[7] L. Verbit, *J. Am. Chem. Soc.* **87**, 1617 (1965).

[8] W. Kuhn and H. Biller, *Z. physik. Chem.* **B29**, 1 (1935).

[9] [a] W. Leithe, *Chem. Ber.* **64**, 2827 (1931).

[9] [b] M. B. Watson and G. W. Youngson, *J. Chem. Soc.* 2145 (1954).

TABLE 1. ULTRAVIOLET ABSORPTION OF α- AND β-PHENYLETHYLAMINES IN 95% ETHANOL

Compound	λ_{max} mμ (log ε)									
α-Phenylethylamine	207 sh (3·96)	211 sh (3·91)	—	242 sh (2·17)	247 (2·24)	252 (2·30)	258 (2·33)	261·5 sh (2·22)	264 (2·18)	267 (2·01)
α-Phenylethylamine hydrochloride	206 (3·95)	210 sh (3·88)	215 sh (3·53)	241 sh (2·20)	247 (2·27)	251 (2·33)	257 (2·36)	260·5 (2·20)	263 (2·23)	267 (2·01)
N,N-Dimethyl-α-phenylethylamine	205 (3·61)	—	217 sh (3·23)	—	246 (2·40)	252 (2·38)	258 (2·35)	—	264 (2·21)	267 sh (1·93)
N,N-Dimethyl-α-phenylethylamine hydrochloride	207 (3·58)	—	217 sh (3·23)	—	246 (2·27)	251 (2·35)	257 (2·41)	262 (2·37)	264 sh (2·33)	268 (2·24)
1,3,4,6,7,11b-Hexahydro-2H-benzo[a]quinolizine hydrochloride	207 (4·01)	211 (4·01)	215 sh (3·91)	243 sh (2·14)	251 (2·26)	256 sh (2·36)	262 (2·45)	264 (2·46)	268 (2·35)	272 (2·41)
N,N-Dimethyl-α-phenylethylamine methiodide	—	215 sh (4·20)	222 (4·25)	—	—	252 sh (2·41)	257 (2·47)	262·5 (2·54)	265 sh (2·42)	269 (2·45)
α-Methyl-β-phenylethylamine	207 sh (3·93)	217 sh (3·66)	—	242 sh (2·46)	248 (2·50)	254 (2·58)	258 (2·62)	262 (2·59)	264 (2·54)	268 (2·49)
α-Methyl-β-phenylethylamine sulfate	207 (4·53)	211 sh (4·48)	216 sh (4·12)	242·5 sh (2·44)	247 (2·62)	252·5 (2·77)	258 (2·87)	261 sh (2·72)	264 (2·77)	267 (2·54)
N,α-Dimethyl-β-phenylethylamine	206 sh (4·04)	217 sh (3·70)	—	243 (2·00)	248 (2·16)	253 (2·30)	258 (2·38)	262 (2·34)	264 (2·28)	268 (2·22)
N,α-Dimethyl-β-phenylethylamine hydrochloride	—	216 sh (4·43)	227 (4·25)	242 sh (2·62)	248 (2·61)	253 (2·66)	258 (2·69)	262 sh (2·63)	264 (2·61)	268 (2·52)
N,N,α-Trimethyl-β-phenylethylamine	—	217 sh (3·16)	228 (3·03)	242 sh (2·24)	248 (2.24)	254 (2·31)	259 (2·36)	262 (2·33)	264 (2·28)	269 (2·19)
N,N,α-Trimethyl-β-phenylamine hydrochloride	—	216 sh (3·12)	227 (2·95)	242 (1·86)	248 (2·03)	253 (2·18)	258 (2·24)	262 sh (2·13)	264 (2·18)	268 (1·91)
N,N,α-Trimethyl-β-phenylethylamine methiodide	—	216 sh (4·66)	—	—	—	252 (2·31)	258 (2·32)	261 sh (2·15)	264 (2·21)	268 (1·94)
α-Methyl-β-(3,4-dimethoxyphenyl)-ethylamine	—	—	230 (4·08)	—	—	—	—	277 (3·51)	280 (3·53)	291 (3·45)

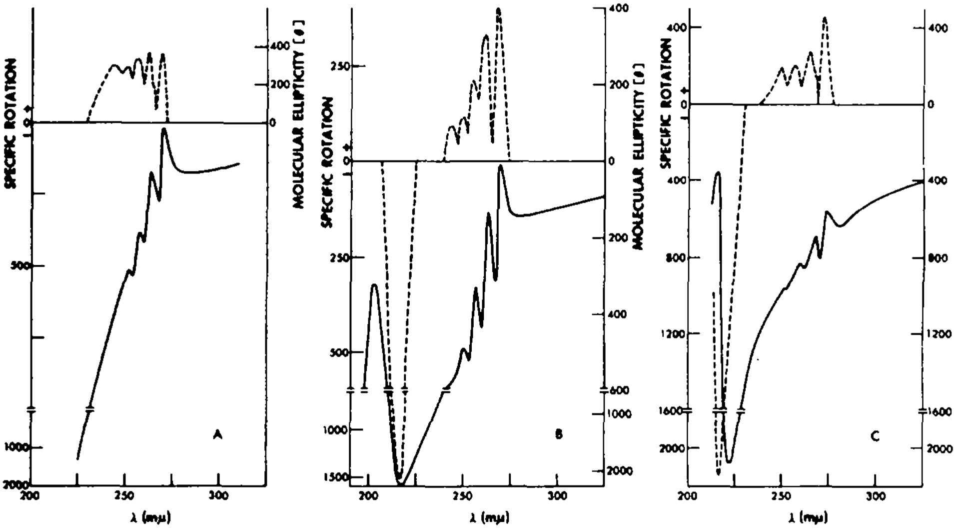

Fig. 1. Rotatory dispersion (———) and circular dichroism (- - - - -) curves of S-α-phenylethylamine (A), S-N,N-dimethyl-α-phenylethylamine hydrochloride (B), and S-1,3,4,6,7,11b-hexahydro-2H-benzo[a]quinolizine hydrochloride (C).

related to L-(+)-alanine; it is thus correctly described[10a] as S-(−)-α-phenylethylamine (III).[10b]

The phenyl Cotton effect will be expected to show important conformational influences due to the dissymmetric distribution, in the regions of space between and among the planes of symmetry of the phenyl group, of the rest of the atoms in the molecule. It is therefore possible that conformational changes might even occasionally produce opposite rotatory properties in closely related compounds having the same configuration. The optical properties of the tertiary and quaternary derivatives of the parent base (III, $R' = R'' = H$) were therefore examined. Eschweiler–Clarke methylation of S-(−)-α-phenylethylamine gave S-(−)-N,N-dimethyl-α-phenylethylamine (III, $R' = R'' = Me$).[11] This base, its hydrochloride (Fig. 1), and the corresponding S-(−)-methiodide[11] all showed closely similar ORD curves for the 260 mμ Cotton effects, proved to be of positive sign by CD measurements (see Experimental). In the case of the tertiary amine and its hydrochloride it was possible to see the second aromatic Cotton effect at ca. 216 mμ, shown to be negative by CD.

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[10] [a] R. S. Cahn, C. K. Ingold and V. Prelog, *Experientia* **12**, 81 (1956);

[b] S-(−)-α-phenylethylamine (III), which on degradation afforded L-(+)-alanine, can be written in the L-configuration if the phenyl group is placed at the top in the Fischer projection formula. However, if the requirements of the Fischer convention for C-1 (methyl group) of the main carbon chain to be at the top are obeyed, the symbolism is reversed and the compound falls into the D-series.[10c] This semantic difficulty in structures containing an aromatic ring directly attached to an asymmetric carbon atom[10d] is avoided by the use of the R-S system;[10a]

[c] E. L. Eliel, *Stereochemistry of Carbon Compounds*, p. 90, McGraw-Hill, New York (1962);

[d] J. A. Mills and W. Klyne in W. Klyne, *Progress in Stereochemistry* Vol. 1; p. 186, Academic Press, New York (1954).

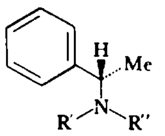
[11] A. C. Cope, E. Ciganek, L. J. Fleckenstein, and M. A. P. Meisinger, *J. Am. Chem. Soc.* **82**, 4651 (1960).

$Ph.CHR.NR'R''$

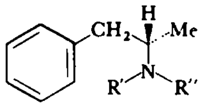
I

$PhCH_2.CHR.NR'R''$

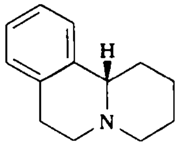
II



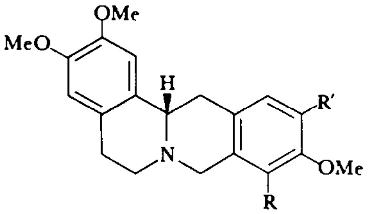
III



VII



IV



V R = OMe, R' = H
VI R = H, R' = OMe

It was of interest to examine a cyclic analogue of (III). A (+)-benzoquinolizidine was obtained from the degradation of the alkaloid securinine,[13] and the enantiomeric (−)-benzoquinolizidine (IV) from the isomeric virosecurinine.[12] A sample of the (−)-benzoquinolizidine hydrochloride[13] gave a UV spectrum (Table 1) closely resembling that of α-phenylethylamine, with only the anticipated[6] slight shift to longer wavelengths of an *ortho*-xylene versus a toluene derivative. Thus it showed two additional low wavelength transitions (at 211 and 215 mμ), and the main peak of the high wavelength absorption region was now at 264 mμ. The ORD spectrum, down to 270 mμ, of the enantiomeric (+)-quinolizidine has already been recorded[12b, 14] and shows a positive ORD curve with what appear to be two *positive* Cotton effects in the 270 to 290 mμ region. This ORD curve had been compared[12b] with those from 700 to 300 mμ, obtained for S-(−)-tetrahydropalmatine[2] (V) and S-(−)-norcoralydine[15] (VI). Since both V and VI showed a *negative* Cotton effect at ca. 300 mμ, the asymmetric center of the (+)-quinolizidine was assigned the R-configuration.[12b]

Examination of the ORD spectrum of the (−)-quinolizidine (IV) hydrochloride[13] (Fig. 1) gave a curve which was indeed the mirror image of that reported[12b] for its (+)-enantiomer between 600 and 270 mμ. The curve then descends steeply to large, and hitherto unreported, negative rotations, and the expected second aromatic

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[12] [a] Z. Horii, M. Ikeda, Y. Yamawaki, Y. Tamura, S. Saito and K. Kodera, *Chem. Pharm. Bull., Tokyo* **11**, 817 (1963);
[b] *Idem, Tetrahedron* **19**, 2101 (1963);
[c] T. Nakano, T. H. Yang, and S. Terao, *Chem. & Ind.* 1651 (1962).

[13] We are indebted to Professor Z. Horii for a sample of this material.

[14] The legends below Figs 1 and 2 in Ref. 12*b* should be interchanged.

[15] A. Brossi, M. Baumann, F. Burkhardt, R. Richle, and J. R. Frey, *Helv. Chim. Acta* **45**, 2219 (1962).

Cotton effect is observed at ca. 214 mμ. However, whereas circular dichroism confirmed the latter to be of negative sign, the CD curve in the 240–280 mμ region clearly shows all the fine-structure Cotton effects in that region to be *positive*, a point which is further confirmed by the agreement between the UV transitions and the maxima of the CD curve at ca. 272, 265, 257 and 250 mμ. It is clear that the erroneous negative appearance of these Cotton effects is, in fact, due to the steep descent of the negative background curve and that great care has to be exercised in such cases. The ORD and CD curves of the free base (IV) closely resembled those of the salt (see Experimental).

Although this finding reverses the sign of the 240 to 280 mμ Cotton effects described[12b] for the (+)-quinolizidine and therefore makes these uniformly negative, it appears by good fortune that this does not invalidate the assignment of the R-configuration[12b] to the (+)-quinolizidine. The asymmetric center in this compound has been independently proved to belong to the R-series by degradation to R (or D)-(+)-N-benzoylpipecolic acid.[12b] It therefore appears that the comparison of a single Cotton effect from the ORD spectrum of a tetraoxygenated protoberberine structure such as (V) and (VI) with those of the simpler α-phenylethylamines such as (III) or (IV), is not valid. On the other hand, the absolute configuration of the (−)-benzoquinolizidine (IV) may be reasonably assigned from Fig. 1 as belonging to the S-series, since the hydrochloride exhibits a positive multiple Cotton effect between 270 and 250 mμ, and the ORD curve shows a steeply descending "tail" below 240 mμ.

As a typical β-phenylethylamine compound, both enantiomers of α-methyl-β-phenylethylamine (II, R = Me, R′ = R″ = H) were examined as their sulfates, and gave curves which were exact mirror images. The ORD curve of the (+)-enantiomer (Fig. 2), deduced[16] to have the S-(or L) configuration (VII), shows at least five positive Cotton effects between 240 and 270 mμ, with a strongly negative background curve. This is in full agreement with the UV spectrum (Table 1) and is corroborated by the circular dichroism (Fig. 2) which again indicates the presence of several smaller positive Cotton effects not discernible in the ORD curve. It is clear that the ORD curve of Potapov and Terentev[3] for the parent base (VII) represents correctly the overall *envelope* of the curve without showing the fine-structure Cotton effects embedded therein.

However, the free primary amine S-(+)-α-methyl-β-phenylethylamine (VII) revealed a startling and unexpected difference in its background absorption (Fig. 2) which had become positive due to the inversion of the sign of the 215 mμ Cotton effect. Nevertheless, CD measurements showed that the 260 mμ Cotton effect had retained the positive sign found so far in all compounds of type I or II for the S-configuration.

In the case of the analogous secondary base S-(or L-)-(+)-deoxyephedrine[16] (VII, R′ = H, R″ = Me), the corresponding tertiary S-(+)-N,N,α-trimethyl-β-phenylethylamine[17] (VII, R′ = R″ = Me), and the derived methiodide,[18] the ORD and CD curves (Fig. 2 and Experimental) of the bases, their hydrochlorides, and

[16] W. Leithe, *Chem. Ber.* **65**, 660 (1932).

[17] [a] S. Senoh and I. Mita, *J. Pharm. Soc. Japan* **72**, 1096 (1952);
[b] S. Senoh, *J. Pharm. Soc. Japan* **72**, 1098 (1952).

[18] W. E. Parham, W. T. Hunter, R. Hanson, and T. Lahr, *J. Am. Chem. Soc.* **74**, 5646 (1952).

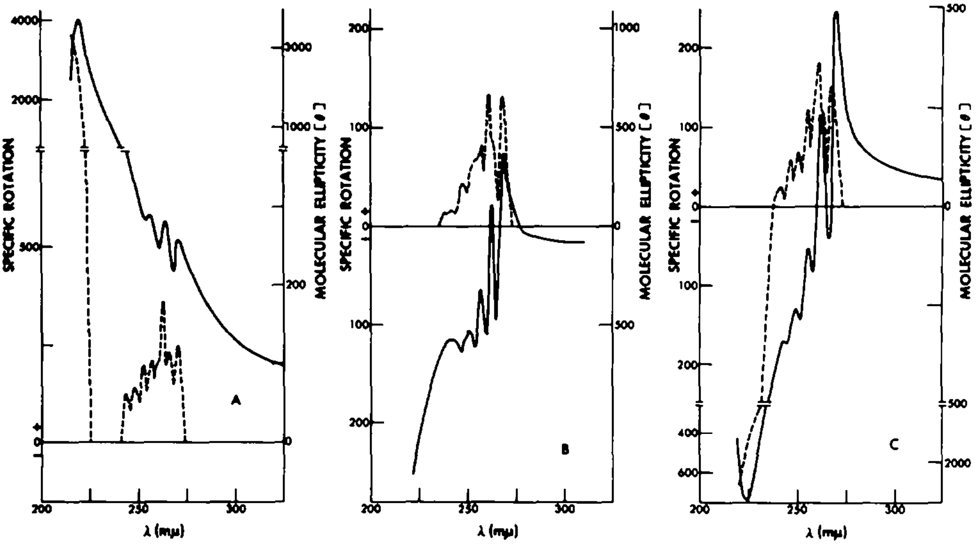

FIG. 2. Rotatory dispersion (———) and circular dichroism (-----) curves of S-α-methyl-β-phenylethylamine (A), S-α-methyl-β-phenylethylamine sulfate (B), and S-deoxyephedrine (C).

the methiodide were identical in the positions and signs of the Cotton effect at 260 mμ and also for the background.

The anomalous positive background curve for the primary amine S-(+)-α-methyl-β-phenylethylamine can only be ascribed to a conformational change (such as was mentioned above) involving possibly the rotational transposition of the methyl and amino moieties attached to the asymmetric carbon, which occurs on protonation or methylation of the (sterically least demanding) primary amine, and may thus be due to either electric or steric effects or both. In the corresponding α-phenylethylamines, no such steric compression exists, and the primary, secondary, tertiary, and quaternary compounds can remain conformationally unchanged.

On the basis of the preceding results we can, therefore, conclude that the absolute configuration of an α- or β-phenylethylamine, or its salt, may be assigned from the ORD curve on the basis that compounds possessing the S-configuration exhibit a positive multiple Cotton effect for the 260 mμ band. The salts also show a steeply descending negative background curve below 240 mμ, in agreement with the rule formulated earlier[19] for other amines.

It was of interest to see whether a substituted β-phenylethylamine would differ in any way from the unsubstituted molecules, and the 3,4-dimethoxy derivative of (VII, R′ = R″ = H) was examined. The UV spectrum of (+)-α-methyl-β-(3,4-dimethoxyphenyl)-ethylamine (Table 1) is shifted in the expected manner on the introduction of the 3,4-dimethoxy substituents, but the ORD and CD curves (see Experimental) are fully analogous to those of the unsubstituted compound, with the usual

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

[20] A. H. Beckett, G. Kirk, and A. J. Sharpen, *Tetrahedron* **21**, 1489 (1965);
A. W. Schrecker and J. L. Hartwell, *J. Am. Chem. Soc.* **79**, 3827 (1957)

loss of fine structure in the 280 mμ band. The compound has been related to L-(+)-alanine and shown[20] to have the S-configuration. Its hydrochloride also gave a positive Cotton effect and CD maximum for the 280 mμ band.[21] In view of the findings reported above in the case of S-(+)-α-methyl-β-phenylethylamine and its 3,4-dimethoxy analogue and their salts, and of the misleading comparisons (quoted above) between S-(−)-norcoralydine and the benzoquinolizidine (IV), it is clear that caution must be exercised in such instances in view of possible conformational influences on the phenyl Cotton effects, and that only compounds of closely similar structure should be compared.

EXPERIMENTAL

ORD curves were determined with a Bendix model 460-C or a JASCO spectropolarimeter in 95% ethanol at 25°. A number of spectra were determined on both instruments and agree within 5%. Rotations are given below only for (1) the highest and lowest wavelengths measured, (2) peaks and troughs. Since ORD curves of enantiomeric pairs agreed within 5%, only one isomer is described. CD was measured at 25° on a JASCO instrument, and is recorded in molecular ellipticity units $[\theta]$.[22]

S-(−)-α-Phenylethylamine. $[\alpha]_D$ −30·2° (*c* 7·0, EtOH). ORD (*c* 0·977, EtOH) $[\alpha]_{310}$ −143°, $[\alpha]_{270}$ −40·9° (pk), $[\alpha]_{267}$ −276° (tr), $[\alpha]_{263\cdot5}$ −169° (pk), $[\alpha]_{259}$ −422° (tr), $[\alpha]_{257}$ −379° (pk), $[\alpha]_{253}$ −537° (tr), $[\alpha]_{252}$ −517° (pk), $[\alpha]_{225}$ −1700°. CD $[\theta]_{272}$ 0, $[\theta]_{269}$ 357, $[\theta]_{266}$ 59·5, $[\theta]_{262}$ 365, $[\theta]_{259\cdot5}$ 198, $[\theta]_{256}$ 337, $[\theta]_{252\cdot5}$ 198, $[\theta]_{251}$ 297, $[\theta]_{248}$ 198, $[\theta]_{243}$ 309, $[\theta]_{230}$ 0.

S-(−)-α-Phenylethylamine Hydrochloride. ORD (*c* 1·30, EtOH) $[\alpha]_{300}$ −61·0°, $[\alpha]_{269}$ 11·5° (pk), $[\alpha]_{266}$ −145° (tr), $[\alpha]_{263}$ −68·7° (pk), $[\alpha]_{259}$ −214° (tr), $[\alpha]_{256}$ −153° (pk), $[\alpha]_{253}$ −236·5° (tr), $[\alpha]_{251}$ −229° (sh), $[\alpha]_{220}$ −763°. CD $[\theta]_{272}$ 0, $[\theta]_{267}$ 238, $[\theta]_{265}$ 0, $[\theta]_{261}$ 190, $[\theta]_{258}$ 79·3, $[\theta]_{255}$ 135, $[\theta]_{250}$ 71·4, $[\theta]_{247}$ 87·2, $[\theta]_{242}$ 0.

S-(−)-N,N-Dimethyl-α-phenylethylamine. $[\alpha]_D$ −67° (neat). ORD (*c* 2·0) $[\alpha]_{350}$ −200°, $[\alpha]_{270}$ −588° (pk), $[\alpha]_{267}$ −744° (tr), $[\alpha]_{264}$ −738° (pk), $[\alpha]_{259}$ −925° (tr), $[\alpha]_{256\cdot5}$ −931° (sh), $[\alpha]_{217}$ −6,250° (tr), $[\alpha]_{212}$ −3250°. CD $[\theta]_{273}$ 0, $[\theta]_{268}$ +85, $[\theta]_{264}$ 0, $[\theta]_{261}$ +94, $[\theta]_{256}$ +17, $[\theta]_{253}$ +51, $[\theta]_{250}$ 0.

S-(−)-N,N-Dimethyl-α-phenylethylamine Hydrochloride. ORD (*c* 2·56, 95% ethanolic 0·1 N–HCl) $[\alpha]_{350}$ −63°, $[\alpha]_{270}$ −12° (pk), $[\alpha]_{267}$ −315° (tr), $[\alpha]_{263\cdot5}$ −133° (pk), $[\alpha]_{260}$ −437° (tr), $[\alpha]_{2\text{[illegible]}7}$ −328° (pk), $[\alpha]_{253}$ −525° (tr), $[\alpha]_{250}$ −485 (pk), $[\alpha]_{216}$ −1600° (tr), $[\alpha]_{203}$ −320° (pk), $[\alpha]_{198}$ −696°. CD $[\theta]_{274}$ 0, $[\theta]_{269}$ +401, $[\theta]_{266}$ +43, $[\theta]_{262}$ +332, $[\theta]_{258}$ +154, $[\theta]_{255}$ +213, $[\theta]_{253}$ +77, $[\theta]_{251}$ +120, $[\theta]_{247\cdot5}$ +43, $[\theta]_{244}$ +85, $[\theta]_{240}$ 0, $[\theta]_{225}$ 0, $[\theta]_{216}$ −2130, $[\theta]_{207}$ 0.

S-(−)-N,N-Dimethyl-α-phenylethylamine Methiodide. $[\alpha]_D$ −19° (*c* 5·0, EtOH). ORD (*c* 1·0) $[\alpha]_{360}$ −85°, $[\alpha]_{270}$ −80° (pk), $[\alpha]_{267}$ −365° (tr), $[\alpha]_{264}$ −235° (pk), $[\alpha]_{260}$ −510° (tr), $[\alpha]_{257}$ −440° (pk), $[\alpha]_{253}$ −610° (tr), $[\alpha]_{251}$ −600° (pk), $[\alpha]_{247}$ −706° (sh), $[\alpha]_{225}$ −1800°. CD $[\theta]_{273}$ 0, $[\theta]_{269}$ +678, $[\theta]_{266}$ +178, $[\theta]_{262}$ +710, $[\theta]_{259}$ +196, $[\theta]_{255\cdot5}$ +338, $[\theta]_{251}$ +71, $[\theta]_{248}$ +124, $[\theta]_{244}$ 0.

S-(−)-1,3,4,6,7,11b-Hexahydro-2H-benzo[*a*]*quinolizine.* (IV). ORD (*c* 0·092) $[\alpha]_{350}$ −530°, $[\alpha]_{274}$ −835° (pk), $[\alpha]_{270}$ −1260° (tr), $[\alpha]_{267}$ −1195° (pk), $[\alpha]_{263}$ −1583° (tr), $[\alpha]_{260}$ −1596 (sh), $[\alpha]_{230}$ −3800 (tr), $[\alpha]_{212}$ −108°. CD $[\theta]_{278}$ 0, $[\theta]_{272}$ +430, $[\theta]_{270}$ +242, $[\theta]_{265}$ +670, $[\theta]_{261}$ +335, $[\theta]_{258}$ +455, $[\theta]_{254}$ +242, $[\theta]_{252}$ +268, $[\theta]_{244}$ 0.

S-(−)-1,3,4,6,7,11b-Hexahydro-2H-benzo[a]*quinolizine Hydrochloride.* $[\alpha]_D$ −140° (*c* 0·425, EtOH). ORD (*c* 0·90) $[\alpha]_{350}$ −339°, $[\alpha]_{280}$ −644°, $[\alpha]_{274}$ −560° (pk), $[\alpha]_{270}$ −806° (tr), $[\alpha]_{268}$ −694° (pk), $[\alpha]_{262}$ −860 (tr), $[\alpha]_{260}$ −830° (pk), $[\alpha]_{253}$ −970° (tr), $[\alpha]_{252}$ −965° (sh), $[\alpha]_{222}$ −2165° (tr), $[\alpha]_{216}$ −355° (pk), $[\alpha]_{213}$ −530°. CD $[\theta]_{277}$ 0, $[\theta]_{272}$ +459, $[\theta]_{269}$ 0, $[\theta]_{265}$ +311, $[\theta]_{260}$ +98·5, $[\theta]_{257}$ +213, $[\theta]_{252}$ +98·5, $[\theta]_{250}$ +197, $[\theta]_{238}$ 0, $[\theta]_{230}$ 0, $[\theta]_{217}$ −2292, $[\theta]_{205}$ 0.

S-(+)-α-Methyl-β-phenylethylamine. $[\alpha]_D$ +33·5° (*c* 10·0, EtOH). ORD (*c* 2·01) $[\alpha]_{350}$ +159° $[\alpha]_{270\ 5}$ +516° (pk), $[\alpha]_{268\cdot5}$ +437° (tr), $[\alpha]_{265}$ +562° (pk), $[\alpha]_{261}$ +497° (tr), $[\alpha]_{256}$ +578° (pk), $[\alpha]_{254}$ +568° (tr), $[\alpha]_{220}$ +4000° (pk), $[\alpha]_{216}$ +2500°. CD $[\theta]_{274}$ 0, $[\alpha]_{270}$ +124, $[\theta]_{268}$ +71, $[\theta]_{266}$ +115, $[\theta]_{2645}$ +98, $[\theta]_{263}$ +177, $[\theta]_{261}$ +106, $[\theta]_{260}$ +102, $[\theta]_{258}$ +80, $[\theta]_{257}$ +106, $[\theta]_{254}$ +62, $[\theta]_{253}$ +98, $[\theta]_{251}$ +49, $[\theta]_{248}$ +71, $[\theta]_{246}$ +35·5, $[\theta]_{244}$ +62, $[\theta]_{241}$ 0.

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[21] The ORD and CD spectrum could not be obtained below 250 mμ due to increasing light absorption. We thank Professor Beckett for a sample.

[22] C. Djerassi and E. Bunnenberg, *Proc. Chem. Soc.* 299 (1963).

S-(+)-α-Methyl-β-phenylethylamine Sulphate. $[\alpha]_{D}$ +21·5° (*c* 2·0, H_2O); $[\alpha]_{D}$ −7·1° (*c* 2·74, EtOH). ORD (*c* 1·40, EtOH) $[\alpha]_{300}$ −16·2°, $[\alpha]_{269}$ 77·1° (pk), $[\alpha]_{265}$ −95·5° (tr), $[\alpha]_{263}$ 21·6° (pk), $[\alpha]_{265}$ −95·5° (tr), $[\alpha]_{263}$ 21·6° (pk), $[\alpha]_{259}$ −111° (tr), $[\alpha]_{256}$ −64·1° (pk), $[\alpha]_{255}$ −124° (tr), $[\alpha]_{250}$ −106° (pk), $[\alpha]_{246}$ −130° (tr), $[\alpha]_{243}$ −116° (pk), $[\alpha]_{221}$ −251°. CD $[\theta]_{273}$ 0, $[\theta]_{268}$ +659, $[\theta]_{266}$ +121, $[\theta]_{261}$ +660, $[\theta]_{259}$ +277, $[\theta]_{257\cdot5}$ +416, $[\theta]_{250}$ +173, $[\theta]_{247}$ +225, $[\theta]_{244}$ +52·1, $[\theta]_{242}$ +86·7, $[\theta]_{236}$ 0.

S-(+)-Deoxyephedrine. $[\alpha]_{D}$ +10° (*c* 10·0 EtOH). ORD (*c* 2·0) $[\alpha]_{350}$ +35°, $[\alpha]_{270}$ 247·5° (pk), $[\alpha]_{267}$ −40° (tr), $[\alpha]_{263}$ 117·5° (pk), $[\alpha]_{258}$ −85° (tr), $[\alpha]_{256}$ −52·5° (pk), $[\alpha]_{251\cdot5}$ −145° (tr), $[\alpha]_{250}$ −127·5° (pk), $[\alpha]_{245}$ −172·5° (tr), $[\alpha]_{243\cdot5}$ −170° (pk), $[\alpha]_{225}$ −750° (tr), $[\alpha]_{220}$ −437·5°. CD $[\theta]_{273}$ 0, $[\theta]_{268}$ +305, $[\theta]_{265\cdot5}$ +89, $[\theta]_{261\cdot5}$ +365, $[\theta]_{257}$ +158, $[\theta]_{256}$ +246, $[\theta]_{253}$ +89, $[\theta]_{251}$ +138, $[\theta]_{248\cdot5}$ +69, $[\theta]_{247}$ +118, $[\theta]_{244}$ +20, $[\theta]_{242}$ +49, $[\theta]_{238}$ 0.

S-Deoxyephedrine Hydrochloride. $[\alpha]_{D}$ +17·5° (*c* 1·0, H_2O); $[\alpha]_{D}$ −7·9° (*c* 12·1, 0·1N HCl in EtOH). ORD (*c* 2·38, 0·1N HCl in EtOH) $[\alpha]_{360}$ −23°, $[\alpha]_{269\cdot5}$ +57° (pk), $[\alpha]_{267}$ −132° (tr), $[\alpha]_{263\cdot5}$ −11° (pk), $[\alpha]_{260}$ −164° (tr), $[\alpha]_{256\cdot3}$ −137° (pk), $[\alpha]_{252}$ −198° (tr), $[\alpha]_{251\cdot5}$ −196° (sh), $[\alpha]_{225}$ −475°. CD $[\theta]_{274}$ 0, $[\theta]_{268}$ +233, $[\theta]_{265}$ +77, $[\theta]_{264}$ +180 (sh), $[\theta]_{261}$ +268, $[\theta]_{258}$ +119, $[\theta]_{256}$ +180, $[\theta]_{251}$ +56, $[\theta]_{249}$ +108, $[\theta]_{246\cdot5}$ +31, $[\theta]_{245}$ +67, $[\theta]_{243\cdot5}$ +26, $[\theta]_{242}$ +46·5, $[\theta]_{239}$ 0.

S-(+)-N,N,α-Trimethyl-β-phenylethylamine. $[\alpha]_{D}$ +3·4° (neat). ORD (*c* 1·0) $[\alpha]_{360}$ −30°, $[\alpha]_{269\cdot5}$ +30° (pk), $[\alpha]_{266\cdot5}$ −155° (tr), $[\alpha]_{263}$ −70° (pk), $[\alpha]_{260}$ −237·5° (tr), $[\alpha]_{257}$ −220° (pk), $[\alpha]_{252}$ −335° (tr), $[\alpha]_{250}$ −332·5 (pk), $[\alpha]_{248}$ −400° (tr), $[\alpha]_{244}$ −415° (sh), $[\alpha]_{227}$ −1700° (tr), $[\alpha]_{215}$ +3000°. CD $[\theta]_{275}$ 0, $[\theta]_{268}$ +334, $[\theta]_{266}$ +118, $[\theta]_{261}$ +345, $[\theta]_{258}$ +162, $[\theta]_{255}$ +236, $[\theta]_{250\cdot5}$ +97, $[\theta]_{248}$ +162, $[\theta]_{245}$ +65, $[\theta]_{243}$ +97, $[\theta]_{240}$ 0.

S-N,N,α-Trimethyl-β-phenylethylamine Hydrochloride. ORD (*c* 1·22) $[\alpha]_{360}$ +4°, $[\alpha]_{268}$ +110° (pk), $[\alpha]_{266}$ −24° (tr), $[\alpha]_{262}$ +68° (pk), $[\alpha]_{259}$ −40° (tr), $[\alpha]_{256}$ −12° (pk), $[\alpha]_{251}$ −52·5° (tr), $[\alpha]_{249}$ −48·5° (pk), $[\alpha]_{245}$ −60° (tr), $[\alpha]_{240}$ −56·5° (sh), $[\alpha]_{217}$ −1006° (tr), $[\alpha]_{214}$ +323°. CD $[\theta]_{272}$ 0, $[\theta]_{267}$ +301, $[\theta]_{265}$ +54, $[\theta]_{261}$ +323, $[\theta]_{258}$ +118, $[\theta]_{254}$ +215, $[\theta]_{250}$ +97, $[\theta]_{247}$ +129, $[\theta]_{242}$ +32, $[\theta]_{238}$ +76, $[\theta]_{233}$ 0.

S-N,N,α-Trimethyl-β-phenylethylamine Methiodide. $[\alpha]_{D}$ −4·4° (*c* 5·0, H_2O). ORD (*c* 1·0) $[\alpha]_{340}$ −15, $[\alpha]_{269}$ +45° (pk), $[\alpha]_{267}$ −57·5° (tr), $[\alpha]_{263}$ +2·5° (pk), $[\alpha]_{259}$ −85° (tr), $[\alpha]_{256\cdot5}$ −70° (pk), $[\alpha]_{252}$ −114·5° (tr), $[\alpha]_{249\cdot5}$ −115° (sh), $[\alpha]_{219}$ −1750°. CD $[\theta]_{273}$ +444, $[\theta]_{265}$ +141, $[\theta]_{261}$ +400, $[\theta]_{257}$ +182, $[\theta]_{254\cdot5}$ +394, $[\theta]_{250}$ +121, $[\theta]_{247}$ +222, $[\theta]_{242}$ 0.

S-(+)-α-Methyl-β-(3,4-dimethoxyphenyl)-ethylamine. ORD (*c* 0·21) $[\alpha]_{350}$ +119°, $[\alpha]_{285}$ +357° (pk), $[\alpha]_{271}$ +166° (tr), $[\alpha]_{236}$ +1540° (pk), $[\alpha]_{224}$ +770° (tr), $[\alpha]_{210}$ +2100°. CD $[\theta]_{290}$ 0, $[\theta]_{280}$ +425, $[\theta]_{260}$ 0, $[\theta]_{242}$ 0, $[\theta]_{229}$ +2750, $[\theta]_{215}$ 0.

S-(+)-α-Methyl-β-(3,4-dimethoxyphenyl)-ethylamine Hydrochloride. $[\alpha]_{D}$ +23° (*c* 1·0 in H_2O). ORD (*c* 0·26) $[\alpha]_{320}$ +76·5°, $[\alpha]_{285}$ +172° (pk), $[\alpha]_{265}$ −29·8° (tr), $[\alpha]_{250}$ 0. CD $[\theta]_{292}$ 0, $[\theta]_{278}$ +437, $[\theta]_{260}$ 0.