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OPTICALLY ACTIVE AROMATIC CHROMOPHORES—IV

CIRCULAR DICHROISM STUDIES OF SOME OPEN-CHAIN SYSTEMS[1,2]

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Abstract—CD measurements in the spectral region from ca. 200 to 300-nm are reported for two α-substituted phenylacetic acids, two α-substituted 3-phenylpropionic acids, and some related compounds. The Ph substituted compounds exhibit two Cotton effects shown to be due to the ^1L_b and ^1L_a transitions of the Ph ring. Inversion of the sign of the 260-nm Cotton effect is observed when the aromatic chromophore is separated from the asymmetric center by a methylene group. For the aromatic carboxylic acids in the series, a positive ^1L_a Cotton effect can be correlated with the S-configuration.

With the advent of instruments capable of measuring optical activity to below 200-nm, the Cotton effects of many chromophores previously considered to be "transparent"[4] may be measured directly. One of the potentially powerful uses of optical activity measurements is the possibility of correlating the sign of an appropriate Cotton effect of a molecule with absolute configuration. Much work along these lines has been done by Djerassi[5] and others,[6] chiefly in rigid systems such as steroids. In contrast, relatively little has been done in open-chain systems which comprise a large and important group of optically active molecules.

In this paper we report the results of a CD study of several α-substituted phenylacetic and 3-phenylpropionic acids and related compounds in the spectral region from 300 to ca. 200-nm.

The compounds investigated are (+)-α-hydroxyphenylacetic acid, (+)-**1**; (−)-2-hydroxy-3-phenylpropionic acid, (−)-**2**; (−)-methyl 2-hydroxy-3-phenylpropionate, (−)-**3**; (−)-2-hydroxy-4-methylpentanoic acid, (−)-**4**, (+)-α-aminophenylacetic acid, (+)-**5**; (−)-2-amino-3-phenylpropionic acid, (−)-**6**; and (−)-2-amino-3-phenylpropanol-1, (−)-**7**. The absolute configurations are given in the stereoformulas.

RESULTS AND DISCUSSION

Monosubstituted benzene rings exhibit three major transitions in the accessible isotropic absorption region: a weak band termed ^1L_b in the Platt notation[7] in the 255–275-nm region corresponding to a symmetry-forbidden π–π^* transition, and two stronger bands near 210 and 190-nm. The 210-nm band, classified ^1L_a, is also forbidden but probably involves a contribution from the first allowed π–π^* transition which overlaps it at shorter wavelength.[8] Upon appropriate ring substitution both of these latter bands may shift to longer wavelength.

The UV and CD spectra of compounds **1**, **2**, **4**, and **7** are shown in Figs 1–4.*

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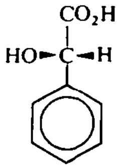
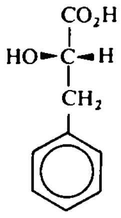
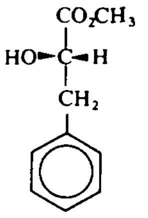
* Because the long wavelength Cotton effects are, in general, much weaker than those below ca. 240-nm, the CD curves (*which are continuous*) were divided into two parts: the right-hand ordinate refers to the longer wavelength Cotton effect while the left-hand scale refers to the bands below about 240-nm. The log ε scale corresponds to the isotropic absorption spectrum.



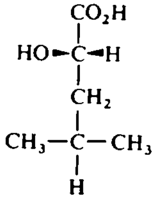
(+)-1



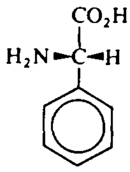
(−)-2



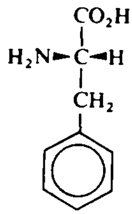
(−)-3



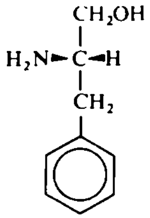
(−)-4



(+)-5



(−)-6



(−)-7

Compound 4 was included as an example of a molecule containing a carboxyl group which is structurally related to the other compounds in the series but which lacks an aromatic group. The aminoalcohol (−)-7 is important as a model for an aromatic amino acid in which the electronic effect of the carboxyl group is removed.

Compounds 1 and 5 differ only by the replacement of an α-hydroxy by an α-amino group. The CD spectra of the two compounds were very similar so that it was not

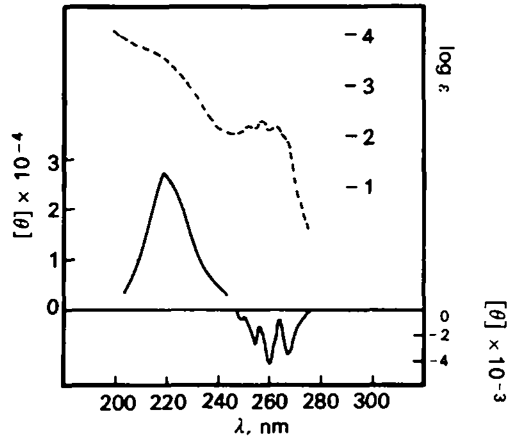


FIG. 1 CD and UV spectra of S-(+)-α-hydroxyphenylacetic acid, (+)-1, in water. See footnote 9 for explanation of the ordinate scales.

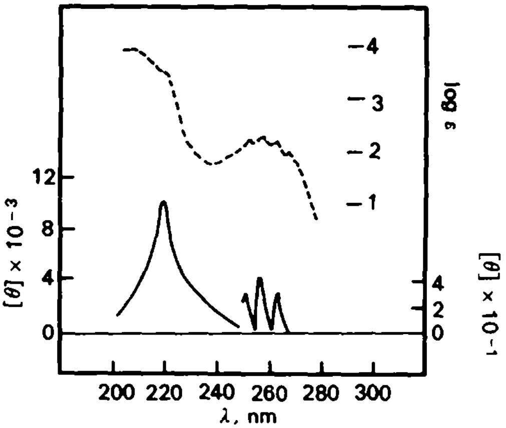


FIG. 2 CD and UV spectra of S-(−)-2-hydroxy-3-phenylpropionic acid, (−)-2, in water. See footnote on p. 1231 for explanation of the ordinate scales.

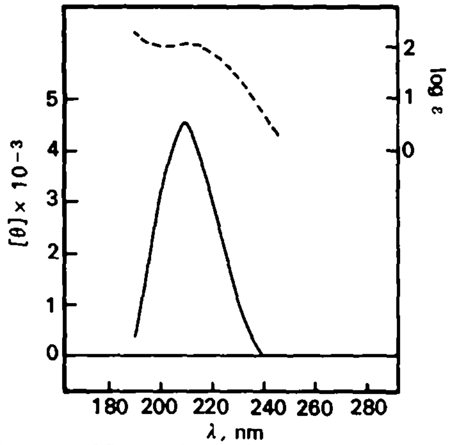


FIG. 3 CD and UV spectra of S-(−)-2-hydroxy-4-methylpentanoic acid, (−)-4, in water.

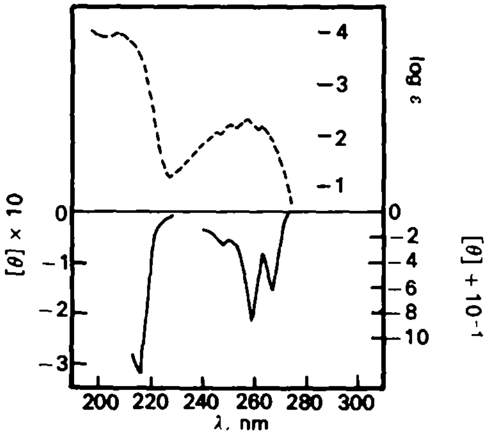


FIG. 4 CD and UV spectra of S-(−)-2-amino-3-phenylpropanol-1, (−)-7, in 0·1N HCl solution. See footnote on p. 1231 for explanation of the ordinate scales.

necessary to include a graph of the data for the latter compound. The same situation occurs with the hydroxy and amino analogs **2** and **6**. In addition, the CD spectrum of the methyl ester **3** was very similar to that of the parent acid **2** so that graphical presentation of the data is not given. However, CD data for all compounds are included in the Experimental.

An examination of the CD data for compounds **1–3** and **5–7** indicates that two distinct Cotton effects occur in the spectral region from 300 to 200-nm. A weak band containing fine structure occurs in the 260–290 nm region and is associated with the ^1L_b transition of the aromatic chromophore.[9] If the arylcarboxylic acids are considered as two groups, one having the Ph ring attached directly to the asymmetric center ((+)-**1** and (+)-**5**) and the other having the aromatic ring one carbon removed from the asymmetric center ((−)-**2**, (−)-**3**, and (−)-**6**), then the sign of the ^1L_b Cotton effect may be correlated with the absolute configuration. It is negative for the S-compounds of the first group but inverts in sign when the Ph ring is separated from the center of asymmetry by a CH_2 group. Similar inversion of the Cotton effect has been found for the carbonyl chromophore[10] and analyzed in terms of a conformational equilibrium change.[11] It is well established that in conformationally mobile systems, the observed CD curve is composed of the population-weighted contributions of the Cotton effects of all rotameric species present.[12]

Compounds **1**, **2**, **3**, **5**, and **6** are all of the S-configuration and all exhibit a positive Cotton effect in the 215–225 nm region. In addition to the ^1L_a phenyl ring transition these molecules possess an optically active carboxyl chromophore which absorbs in a spectral region close to the ^1L_a transition. The CD spectrum of (−)-**4**, which is structurally similar to **1**, **2**, and **3** but which lacks the aromatic ring, exhibits only one band in the region from 300 to 190-nm (Fig. 3), $[\theta]_{max}$ at 209-nm, which is assigned to the optically active carboxyl group.* It is well established that two overlapping Cotton effects give a resultant curve which is shifted in position from either of the component bands.[14] The question arises whether the short wavelength Cotton effect in the CD spectra of **1**, **2**, **3**, **5** and **6** is composed of overlapping ^1L_a and carboxyl chromophore bands. Legrand and Viennet[15] have stated that the CD band under discussion is due to the carboxyl group and not to a transition involving the phenyl ring. However, these authors did not indicate how they arrived at their conclusion. The results presented below are significantly different from those of Legrand and Viennet.

The aromatic α-aminoalcohol (−)-**7** is identical in structure to (−)-**6** except that it possesses a CH_2OH group in place of a CO_2H function. Even though the carboxyl group is absent in (−)-**7** the CD spectrum (Fig. 4) still exhibits two Cotton effects, similar in shape and position although of opposite sign, to those found for the aromatic carboxylic acids in this series. The CD spectrum of the related compound S-(−)-2-amino-4-methylpentanol-1 was measured and no Cotton effects found down to 209-nm. The absence of a CD band above this wavelength in the aminopentanol indicates that the 216-nm Cotton effect of (−)-**7** is due mainly to a transition associated with the aromatic ring.

It is not yet possible to establish why the ^1L_b, but not the ^1L_a transition changes

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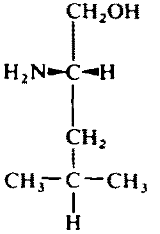
* A longer wavelength band, $[\theta]_{244}$ −2000, has recently been discovered for this compound.[13]

sign when the phenyl chromophore is moved one carbon away from the asymmetric center. This important point requires further investigation as does the change in in sign of the CD bands on going from (−)-6 to (−)-7.



EXPERIMENTAL

CD measurements were made using a JASCO Model ORD/UV/CD-5 instrument operating at a sample compartment temp of 27°.[16] Isotropic absorption spectra were measured on the JASCO and on a Cary Model 14 spectrophotometer.

S-(+)-α-*Hydroxyphenylacetic acid*, (+)-1 (Fig. 1). $[\alpha]_D^{27^\circ}$ +154° (*c* 1·3, water); CD in water, 1·19 × 10^{-3} M; $[\theta]_{267}$ −350 (max), $[\theta]_{260}$ −430 (max), $[\theta]_{254}$ −280 (max), $[\theta]_{247}$ 0, $[\theta]_{230}$ +12,000, $[\theta]_{219}$ +27,000 (max), $[\theta]_{210}$ +10,000.

S-(−)-2-*Hydroxy-3-phenylpropionic acid*, (−)-2 (Fig. 2). $[\alpha]_D^{27^\circ}$ −17·9° (*c* 1·1, water); CD in water, 3·31 × 10^{-3} M; $[\theta]_{263}$ +33 (max), $[\theta]_{256}$ +44 (max), $[\theta]_{251}$ +33 (max), $[\theta]_{240}$ +2000, $[\theta]_{219}$ +10,000 (max), $[\theta]_{202}$ +1700.

S-(−)-*Methyl 2-hydroxy-3-phenylpropionate*, (−)-3. $[\alpha]_D^{27^\circ}$ −17·8° (*c* 0·7, water); CD in water, 1·40 × 10^{-2} M; $[\theta]_{264}$ +33 (max), $[\theta]_{257}$ +47 (max), $[\theta]_{251}$ +38 (max), $[\theta]_{240}$ +60, $[\theta]_{230}$ +1400, $[\theta]_{218}$ +9500 (max), $[\theta]_{210}$ +240.

CD in MeOH, 6·11 × 10^{-3} M; $[\theta]_{266}$ +25 (max), $[\theta]_{258}$ +66 (max), $[\theta]_{252}$ +66 (max), $[\theta]_{240}$ +230, $[\theta]_{225}$ +8800, $[\theta]_{219}$ +15,000 (max), $[\theta]_{216}$ +7800.

S-(−)-2-*Hydroxy-4-methylpentanoic acid*, (−)-4 (Fig. 3). $[\alpha]_D^{27^\circ}$ −13·1° (*c* 0·6, water); CD in water, 7·96 × 10^{-3} M; $[\theta]_{230}$ +760, $[\theta]_{209}$ +4500 (max), $[\theta]_{190}$ +400.

CD in 0·1N HCl, 7·61 × 10^{-2} M; $[\theta]_{230}$ +770, $[\theta]_{209}$ +5200 (max), $[\theta]_{190}$ +900.

S-(+)-α-*Aminophenylacetic acid*, (+)-5. $[\alpha]_D^{27^\circ}$ +157° (*c* 1·4, 0·1N HCl); CD in 0·1N HCl, 6·62 × 10^{-4} M; $[\theta]_{267}$ −900 (max), $[\theta]_{260}$ −1100 (max), $[\theta]_{254}$ −720 (max), $[\theta]_{245}$ 0, $[\theta]_{224}$ +23,000 $[\theta]_{218}$ +34,000 (max), $[\theta]_{204}$ +11,000.

CD in water, 2·58 × 10^{-3} M; $[\theta]_{268}$ −770 (max), $[\theta]_{261}$ −890 (max), $[\theta]_{254}$ −620 (max), $[\theta]_{241}$ 0, $[\theta]_{224}$ +12,000. $[\theta]_{210}$ +23,000 (shoulder).

S-(−)-2-*Amino-3-phenylpropionic acid*, (−)-6. $[\alpha]_D^{27^\circ}$ −34·6° (c 2·1, water); CD in 0·1N HCl, 3·28 × 10^{-3} M; $[\theta]_{266}$ +50 (max), $[\theta]_{263}$ +54 (max), $[\theta]_{257}$ +75 (max), $[\theta]_{230}$ +2500, $[\theta]_{217}$ +13,500 (max), $[\theta]_{205}$ +2400.

CD in water, 3·28 × 10^{-3} M; $[\theta]_{267}$ +45 (max), $[\theta]_{264}$ +50 (max), $[\theta]_{258}$ +60 (max), $[\theta]_{230}$ +400, $[\theta]_{218}$ +8400 (max), $[\theta]_{210}$ +5900.

S-(−)-2-*Amino-3-phenylpropanol*-1, (−)-7 (Fig. 4). $[\alpha]_D^{27^\circ}$ −18·1° (*c* 3, water); CD in 0·1N HCl, 1·59 × 10^{-2} M; $[\theta]_{267}$ −60 (max), $[\theta]_{259}$ −90 (max), $[\theta]_{248}$ −30, $[\theta]_{220}$ −800, $[\theta]_{216}$ −3200 (max), $[\theta]_{213}$ −2800.

CD in water, 2·08 × 10^{-3} M; $[\theta]_{269}$ −60 (max), $[\theta]_{262}$ −60 (max), $[\theta]_{249}$ 0, $[\theta]_{226}$ −100, $[\theta]_{216}$ −7000 (max), $[\theta]_{210}$ −6400.

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REFERENCES

[1] Part III. L. Verbit, *J. Am. Chem. Soc.* **88**, 5340 (1966).

[2] Presented in part at the 152*nd National Meeting of the American Chemical Society*, Abstract S-169. New York, N. Y., September (1966).

[3] Abstracted in part from the M.A. Thesis of P.J.H., State University of New York at Binghamton, 1967.

[4] P. Crabbe, *Optical Rotatory Dispersion and Circular Dichroism in Organic Chemistry* Chap. 11. Holden-Day, San Francisco (1965).

[5] C. Djerassi, *Optical Rotatory Dispersion: Applications to Organic Chemistry*. McGraw-Hill, New York, N.Y. (1960).

[6] L. Velluz, M. Legrand and M. Grosjean, *Optical Circular Dichroism* Chap. 4. Academic Press, New York, N.Y. (1965).

[7] J. R. Platt, *J. Chem. Phys.* **17**, 484 (1949).

[8] J. N. Murrell, *The Theory of the Electronic Spectra of Organic Molecules* p. 129. Wiley, New York, N.Y. (1963).

[9] A. Moscowitz, A. Rosenberg and A. E. Hansen, *J. Am. Chem. Soc.* **87**, 1813 (1965).

[10] C. Djerassi and L. E. Geller, *Ibid.* **81**, 2789 (1959).

[11] M. J. T. Robinson, *Chem. & Ind.* 932 (1964).

[12] W. S. Briggs and C. Djerassi, *Tetrahedron* **21**, 3455 (1965); A. Moscowitz, K. M. Wellman and C. Djerassi, *J. Am. Chem. Soc.* **85**, 3515 (1963).

[13] See also R. D. Anand and M. K. Hargreaves, *Chem. Commun.* 421 (1967); L. Verbit and P. J. Heffron, *Tetrahedron* **23**, 3865 (1967).

[14] K. M. Wellman, P. H. A. Laur, W. S. Briggs, A. Moscowitz and C. Djerassi, *Ibid.* **87**, 66 (1965).

[15] M. Legrand and R. Viennet, *Bull. Soc. Chim. Fr.* 2798 (1966).

[16] L. Verbit, *J. Am. Chem. Soc.* **89**, 167 (1967).