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Chiroptical Properties of the Benzene Chromophore. A Method for the Determination of the Absolute Configurations of Benzene Compounds by Application of the Benzene Sector and Benzene Chirality Rules

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Contents

I. Introduction

A. Historical Development

In the early part of this century, two reviews of early work on the measurement and interpretation optical rotatory dispersion (ORD) and circular dichroism (CD) of chiral organic compounds appeared, respectively, in 1935[1] and 1938.[2] Because of the difficulties associated with such measurements at that time, only a small number of ORD and CD curves were measured in the visible (380−780 nm) and an even a smaller number were measured in the ultraviolet (200−380 nm) spectral region. The earlier review was out of print after the Second World War of 1939−1945, and the latter was not updated and was not included as part of the second edition of the book in which it had appeared earlier.[3] This situation change dramatically about 1953 with the introduction of a photoelectric spectropolarimeter developed by Erwin Brand in cooperation with O. C. Rudolph and Sons of Caldwell, NJ.[4] This spectropolarimeter utilized a Western Union K-100 zirconium arc lamp in a quartz envelope, a Beckman DU monochromator, and a photoelectric analyzer[5] attached to a Rudolph precision polarimeter. Using this instrument and before his untimely death in July 1953, Brand and his associates were able to measure the optical rotatory dispersion (ORD) from 240 to 750 nm of several steroids, amino acids, and peptides.[4] Only plain dispersion curves were observed, measurements not being made through the electronic absorption (EA) bands of cortisone acetate and L-tyrosine. In 1953, Carl Djerassi and his group received the second spectropolarimeter and shortly thereafter reported anomalous ORD curves showing a Cotton effect (CE) associated with the EA of the carbonyl group of steroidal ketones.[6] By 1958, the

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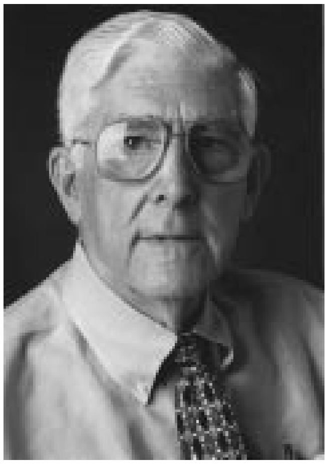


Howard E. Smith retired as a Professor of Chemistry, Emeritus from Vanderbilt University in 1993 where he joined the faculty in 1959. He was born and grew up in San Francisco, CA. After receiving his B.S. degree (1951) from the University of California at Berkeley and his M.S. degree (1954) and Ph.D. degree (1957) from Stanford University for work with Richard H. Eastman, Professor Smith had postdoctoral training as a National Institutes of Health Fellow at Wayne State University with Carl Djerassi and at the Swiss Federal Institute of Technology, Zurich, with Vladimir Prelog. Professor Smith's major research interests are concerned with stereochemistry and the interaction of chiral molecules, natural and synthetic, with biological receptor systems. He was recently elected as a Fellow of the American Association for the Advancement of Science.

Djerassi group had measured over 2000 anomalous ORD curves.[7]

Circular dichroism measurements were not routinely performed until 1960 when the description of the first recording circular dichrograph[8] led to a rapid development in this field[9] and to the commercial availability of instruments capable of routine measurements of CD in the visible and near-ultraviolet spectral regions.

Since then, measurements of ORD curves and CD spectra have led to reliable rules for the correlation of the sign and magnitude of observed CEs with the absolute configurations of enantiopure chiral compounds.[7,9,10] Among the best known and the most widely used are the octant rule,[11] the dibenzoate chirality rule,[12] and the salicylidenamino chirality rule.[13] Initially, the octant rule related the sign of the CEs associated with the carbonyl $n \rightarrow \pi^*$ transition at about 300 nm with the absolute configurations of chiral, alkyl-substituted cyclohexanones, but subsequently, the rule has been extended for use with other types of carbonyl compounds.[14,15] The dibenzoate chirality rule was first applied to the exciton coupling of the $\pi \rightarrow \pi^*$ transitions at about 230 nm of the benzoate groups in the dibenzoate derivatives of chiral vicinal diols, but currently similar exciton coupling methods utilizing aryl ester derivatives have wide applications to other polyols,[16] including acyclic 1,3-diols,[17] and exciton coupling has been used to interpret the CD spectra of a wide variety of other chiral compounds containing unsaturated and aromatic groups.[18] The salicylidenamino chirality group, first used to establish the absolute configurations of α- and β-phenylalkylamines on the basis of the sign of the observed CEs at 255 and 315 nm in the CD spectra of their *N*-salicylidene derivatives, has evolved into a general method for the establishment of the absolute configurations of various primary amines, including α-amino acids and aliphatic and alicyclic amines.[19]

The utility of these rules resides in the wide occurrence of carbonyl, polyol, and primary amine groups in chiral natural products and synthetic materials. Other widely occurring structural features in such compounds are aromatic groups, and very early it was hoped that the sign of the CEs associated with such groups could be correlated with the absolute configurations of these substances. Various aromatic substances were investigated,[9,20] but the vast majority of work starting in 1935,[21] proceeding in 1960 with a photoelectric spectropolarimeter,[22] and continuing to the present,[23] focused on the easily observed CEs at about 230−270 nm associated with the ^1L_b transition of the benzene chromophore. As part of this work, Snatzke and Ho[24] proposed sector rules to correlate the signs of the CEs of chiral benzene compounds with their absolute configurations. Subsequently, Snatzke, Kajtar, and Werner-Zamojska[25] extended the rules and utilized modified spectroscopic moments[26,27] of substituents to explain the changes in the sign of the ^1L_b CEs when substituents are introduced at various positions of the benzene ring of a chiral substance. Complete clarity was frustrated, however, by the inability of these rules to account for many experimental observations.[28]

B. Scope of the Review

As outlined below, an alternative benzene sector rule[29] has been formulated which correlates the absolute configuration of a chiral center contiguous[29] to or separated by a methylene group[30] from an otherwise unsubstituted benzene ring with the sign of its ^1L_b CEs. For some chiral benzene compounds, however, substitution on the benzene ring may cause the sign of these CEs to be different from that of the unsubstituted parent, and the benzene chirality rule[31] relates these changes to both the ring position and the nature of the subsistent. This review then outlines the use of the benzene sector rule and the benzene chirality rule to assign the absolute configuration at a chiral center contiguous or homocontiguous to a benzene ring, the latter with or without an additional substituent. Application of these rules to nonplanar perhydrobenzoalkenes evolves into sector sign projections suggested by Snatzke and Ho[24] to correlate the signs of chiral 1,2,3,4-tetrahydronaphthalenes and 1,2,3,4-tetrahydroisoquinolines with their absolute configurations.[32]

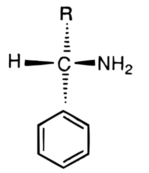
This review is complete in itself with many examples of the application of the benzene sector and benzene chirality rules to the correlation the absolute configurations of a wide variety of chiral benzene compounds with the sign of the ^1L_b CEs in their CD spectra. Much EA and CD spectral data for these compounds are given in the tables in the body of the review. The rotatory power ($[\alpha]_D$) and more complete spectral data for these compounds, as well as the same data for additional chiral benzene compounds, are given in the Supporting Information. In the Supporting Information, the data are collected into

48 tables on 93 pages with appropriate literature citations range from 1965 to early 1997. The signs of the observe ^1L_b CEs of these additional compounds can frequently be correlated with their absolute configurations using the benzene sector and benzene chirality rules.

II. Chiroptical Observations

A. Benzene Chromophore

Benzene shows three well-defined electronic absorption (EA) bands at longer wavelength than 175 nm.[33] These bands are centered at 184, 204, and 254 nm with intensities and designations shown in Table 1. Each band is the result of a $\pi \rightarrow \pi^*$ transition, but only the B_{2u} (^1L_b) band centered at 254 nm shows vibrational fine structure. If the ring is substituted with a chiral group, the position of the absorption bands may be somewhat shifted and their intensities slightly altered, but the spectrum is essentially unchanged.[33] More importantly, the transitions are now optically active, and as shown in Figure 1 for the EA and CD spectra of (*S*)-α-phenylethylamine [(*S*)-**1a**] in isooctane, CEs are associated with these absorption bands.[37] The series of positive CEs from 236 to 268 nm are associated with the B_{2u} (^1L_b) transition of the benzene ring, the positive one at 213 nm with the B_{1u} (^1L_a) transition, and the negative one at 184 nm with the E_{1u} ($^1B_{a,b}$) transition.[34,37] The two additional CD maxima at 225 and 193 nm, negative and positive, respectively, are associated with $n \rightarrow \sigma^*$ transitions of the amino chromophore and are not observed in the CD spectrum of the hydrochloride of (*S*)-**1a**.[37] The CE associated with the doubly degenerate E_{1u} ($^1B_{a,b}$) transition in the vacuum ultraviolet is observed only with very special instrumentation,[38] and a CE as the result of the B_{1u} (^1L_a) transition is difficult to observe except when an auxochromic group is present. As a practical matter then, most work for the purpose of establishment of the absolute configurations has been concerned with the CEs associated with the B_{2u} (^1L_b) transition.



(*S*)-**1a**, R = CH_3
2a, R = CH_2CH_3
3a, R = $C(CH_3)_3$

Table 1. Benzene Spectral Data

band designation[a]	absorption band maximum λ, nm[b]	ϵ[c]
B_{2u} (^1L_b)	254[d]	204
B_{1u} (^1L_a)	203.5[d]	7 400
E_{1u} ($^1B_{a,b}$)	183.5[e]	46 000

[a] Reference 34. [b] Wavelength. [c] Molar absorptivity. [d] Reference 35, water as the solvent. [e] Reference 36, *n*-heptane as the solvent.

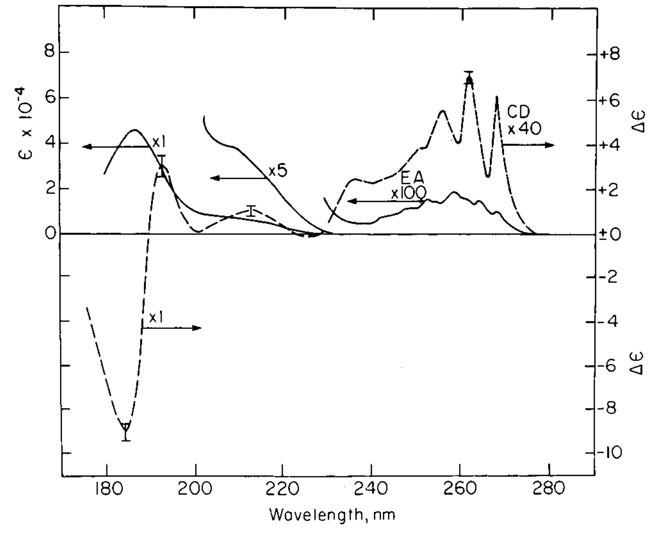


Figure 1. Electronic absorption (EA) and circular dichroism (CD) spectra of (*S*)-α-phenylethylamine [(*S*)-**1a**] in isooctane. Reprinted from *J. Am. Chem. Soc.* **1987**, *109*, 3361. Copyright 1987 American Chemical Society.

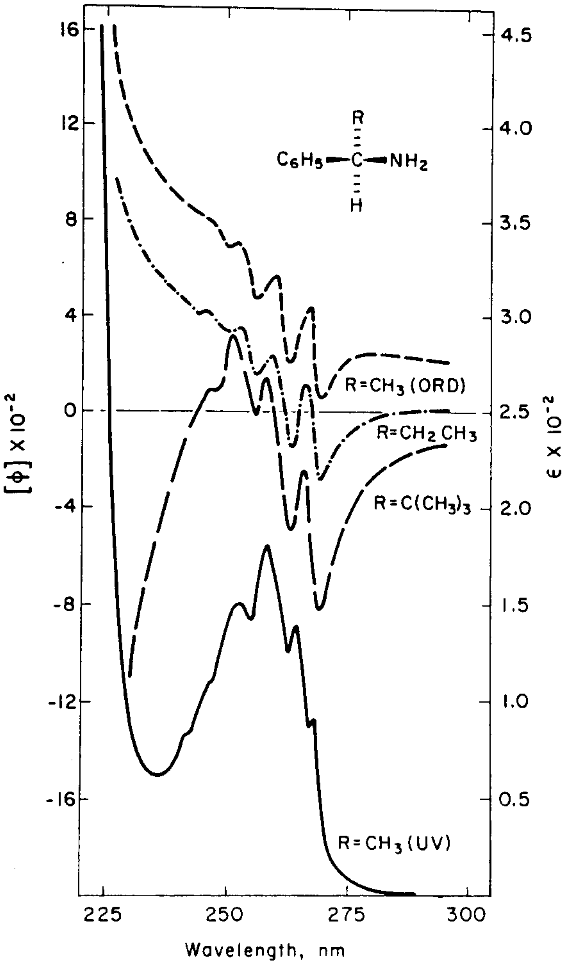


Figure 2. Electronic absorption spectrum (UV) of (*R*)-α-phenylethylamine [(*R*)-**1a**, R = CH_3] in absolute ethanol and optical rotatory dispersion curves (ORD) of (*R*)-α-phenylethylamine [(*R*)-**1a**, R = CH_3), (*R*)-α-phenyl-*n*-propylamine [(*R*)-**2a**, R = CH_2CH_3], and (*R*)-α-phenylneopentylamine [(*R*)-**3a**, R = $C(CH_3)_3$] in methanol. Reprinted with permission from *Tetrahedron* **1968**, *24*, 1327. Copyright 1968 Elsevier Science Ltd.

B. Optical Rotatory Dispersion

In early attempts to assess the suitability of CEs associated with the ^1L_b transition of the benzene chromophore for absolute configuration assignments, the ORD curves of a series of (*R*)-α-phenylalkylamines [(*R*)-**1a**-**3a**] and their hydrochlorides [(*R*)-**1b**-**3b**] were examined.[39] As seen in Figure 2, these amines with the *R* configuration display in methanol a number of negative CEs associated with the ^1L_b transition which are superimposed on a strong plain background curve. For (*R*)-α-phenylethylamine [(*R*)-**1a**] and (*R*)-α-phenyl-*n*-propylamine [(*R*)-**2a**], the plain dispersion curve from 225 to 240 nm is positive, and the rotatory power in methanol using sodium D light is positive. Below 240 nm, the plain dispersion curve for (*R*)-α-phenylneopentylamine [(*R*)-**3a**] is negative, but the rotatory power in methanol using sodium D light is also positive, indicating both positive and negative CEs below 225 nm. The ORD curves for the corresponding (*R*)-α-phenylalkylamine hydrochlorides [(*R*)-**1b**-**3b**] (Figure 3) are similar to those of the respective free bases, except that the amplitudes of the ^1L_b CEs are somewhat reduced, and the plain background curve for (*R*)-α-phenyl-*n*-propylamine hydrochloride [(*R*)-**2b**] is now negative. All of the hydrochlorides in methanol, however, are dextrorotatory at 589 nm.[39]

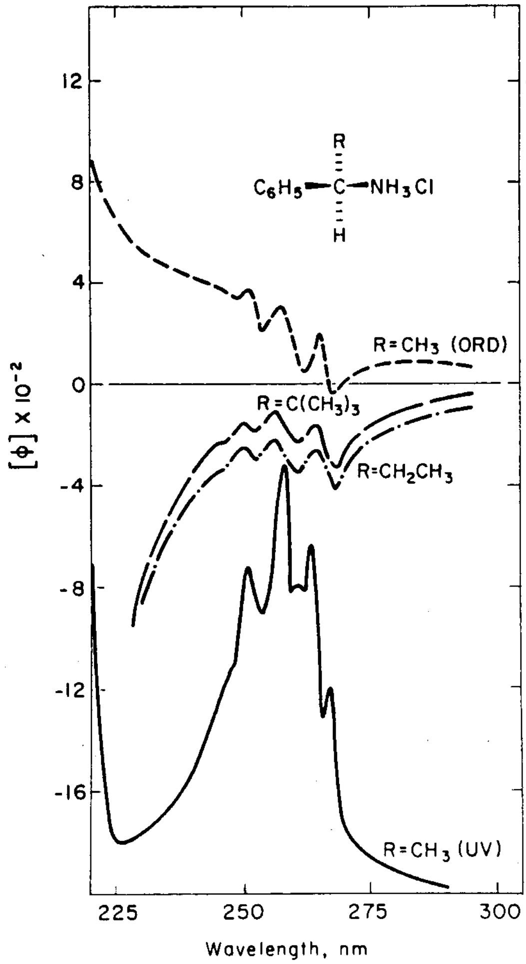


Figure 3. Electronic absorption spectrum (UV) of (*R*)-α-phenylethylamine hydrochloride [(*R*)-**1b**, R = CH_3] in absolute ethanol and optical rotatory dispersion curves (ORD) of (*R*)-α-phenylethylamine hydrochloride [(*R*)-**1b**, R = CH_3], (*R*)-α-phenyl-*n*-propylamine hydrochloride [(*R*)-**2b**, R = CH_2CH_3], and (*R*)-α-phenylneopentylamine hydrochloride [(*R*)-**3b**, R = $C(CH_3)_3$] in methanol. Reprinted with permission from *Tetrahedron* **1968**, *24,* 1327. Copyright 1968 Elsevier Sciene Ltd.

In subsequent work,[37] the EA and the CD spectra of some of these α-phenylalkylamines and their hydrochlorides were measured in the vacuum ultraviolet region. It became easy to understand in a qualitative way why the background ORD curve at the ^1L_b transition is positive for some of these α-phenylalkylamines and their hydrochlorides and negative for others of the same absolute configuration. The background curve at 225−240 nm is the sum of the long wavelength wings for all of the CEs at shorter wavelengths, and thus the background curves in Figures 2 and 3 are the sum of a number of positive and negative plain dispersion curves associated with positive and negative CEs in the vacuum ultraviolet region. For some of the amines and amine hydrochlorides, these sums are positive; for others, they are negative as the result of variations in the positions and intensities of the short wavelength CEs.

C. Circular Dichroism

In the ORD curves of both the (*R*)-α-phenylalkylamines [(*R*)-**1a**−**3a**] and their hydrochlorides [(*R*)-**1b**−**3b**], there appear to be CEs associated with the ^1L_b band origin and then only with some of the ^1L_b vibrational absorption bands at shorter wavelength. When the CD spectra of these amines and amine hydrochlorides are examined, greater resolution of the CEs is achieved, and the CD spectrum of (*R*)-**1b** in water (Figure 4) shows three distinct, well-resolved CD maxima between 270 and 250 nm.[40] The EA spectrum of this compound in methanol (Figure 3), however, shows at least five EA maxima in this same wavelength interval, and thus only some of the ^1L_b EA maxima are associated with observable CEs. This is shown in Figure 5 for the EA and CD spectra for (*S*)-α-phenylethylamine [(*S*)-**1a**] in methanol and schematically in Figure 6 for (*R*)-α-phenylethylamine hydrochloride [(*R*)-**1b**] in water. In the EA spectra of the α-phenylalkylamines and their hydrochlorides, the longest wavelength maximum near 268 nm corresponds to the 0−0 vibrational transition which

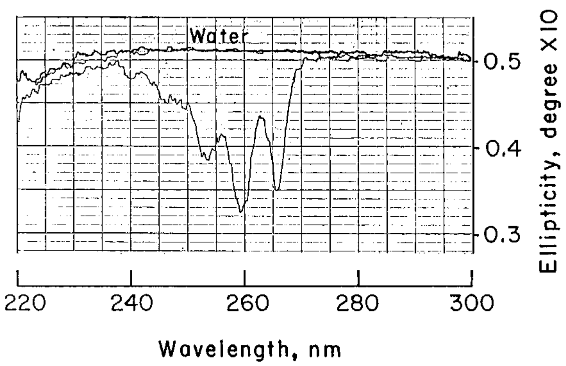


Figure 4. Circular dichroism spectrum of (*R*)-α-phenylethylamine hydrochloride [(*R*)-**1b**] in water (*c* 0.105 g/100 mL, path 1 cm). Reprinted from *J. Am. Chem. Soc.* **1971**, *93,* 2282. Copyright 1971 American Chemical Society.

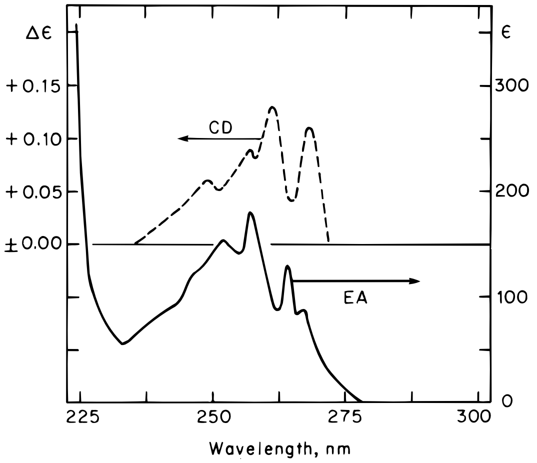


Figure 5. Electronic absorption (EA) and circular dichroism (CD) spectra of (*S*)-α-phenylethylamine [(*S*)-**1a**] in methanol. Reprinted with permission from *Croat. Chem. Acta* **1989**, *62*, 201. Copyright 1989 Croatian Chemical Society.

in toluene is a $B_2 \leftarrow A_1$ electronic transition.[41,42] This electronic transition has allowed and forbidden components, and as seen in Figure 6, only for the allowed transitions for which the electric dipole transition moment is in the plane of the benzene ring and perpendicular to the bond between the substituent and the ring are CD maxima observed. These transitions connect the ground-state zeroth vibrational level (${}^{v}A_1$) with the zeroth and higher totally symmetric levels (also ${}^{v}A_1$) of the ring-breathing vibration in the first electronic excited state.[43] For (*R*)-α-phenylethylamine hydrochloride [(*R*)-**1b**], the first two of these higher totally symmetric vibronic states are seen as CD maxima separated from the band origin at 376×10^2 cm^{-1} (266 nm) by 9×10^2 and $(9 + 9) \times 10^2$ cm^{-1}. A corresponding EA maximum was observed at $(375 + 10) \times 10^2$ cm^{-1}, but one at $(375 + 9 + 9) \times 10^2$ cm^{-1} was not observed, obscured by other absorption (Figure 3).

For the $B_2 \leftarrow A_1$ electronic transition, the forbidden progression combines the ground-state zeroth vibronic state (${}^{v}A_1$) with the first vibrational level of a nontotally symmetric vibrational state (${}^{v}B_2$). The vibronic symmetry of these excited states is A_1.[43] The electric dipole transition moment is also in the plane of the benzene ring but is parallel to the substituent attachment bond.[43] In the EA spectrum of (*R*)-**1b** (Figure 6), three of these transitions are seen as absorption maxima separated from the band origin by 5×10^2, $(5 + 9) \times 10^2$, and $(5 + 9 + 11) \times 10^2$ cm^{-1}, respectively. Since there are CD minima at these wavelengths (Figure 4) the CEs associated with these transitions are weak.

III. Benzene Correlation Rules

A. ${}^{1}L_b$ Cotton Effects

In benzene, the ${}^{1}L_b$ transition is both electrically and magnetically forbidden, with its isotropic electronic absorption intensity coming from vibronic borrowing from an allowed transition at shorter wavelength. Upon substitution of the ring, an additional intensity is attributed to an induced electric transition moment normal to the substituent attachment bond, and concomitantly a magnetic transition moment perpendicular to the ring is induced in the ${}^{1}L_b$ transition. This second part of the intensity is attributed by Sklar[44] to a migration moment (spectroscopic moment) induced in the ring by a substituent on the ring which destroys its symmetry. These induced transition moments can give rise to ${}^{1}L_b$ CEs in chiral benzene compounds through dynamic and static coupling with dissymmetric substituents.[45] Furthermore, as in EA, the rotational strength of the ${}^{1}L_b$ CEs is influenced by the ${}^{1}B_{a,b}$ transitions through vibronic interaction.[46,47]

The magnitude of the induced electronic transition moment is related to the spectroscopic moment[26,27]

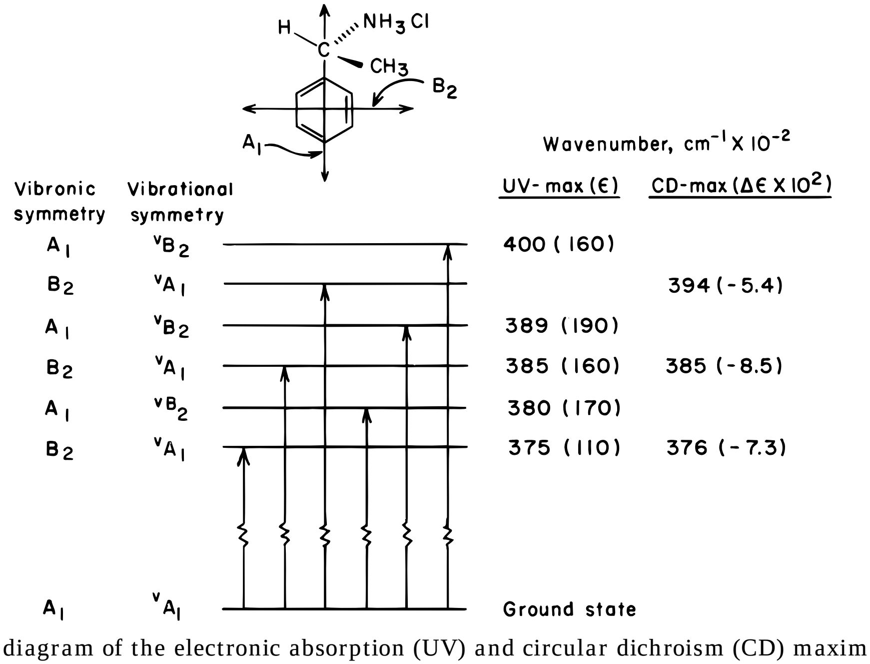


Figure 6. Schematic diagram of the electronic absorption (UV) and circular dichroism (CD) maxima observed with (*R*)-α-phenylethylamine hydrochloride [(*R*)-**1b**] in water. The A_1 and B_2 axes are in the plane of the benzene ring. Reprinted from *J. Am. Chem. Soc.* **1971**, *93*, 2282. Copyright 1971 American Chemical Society.

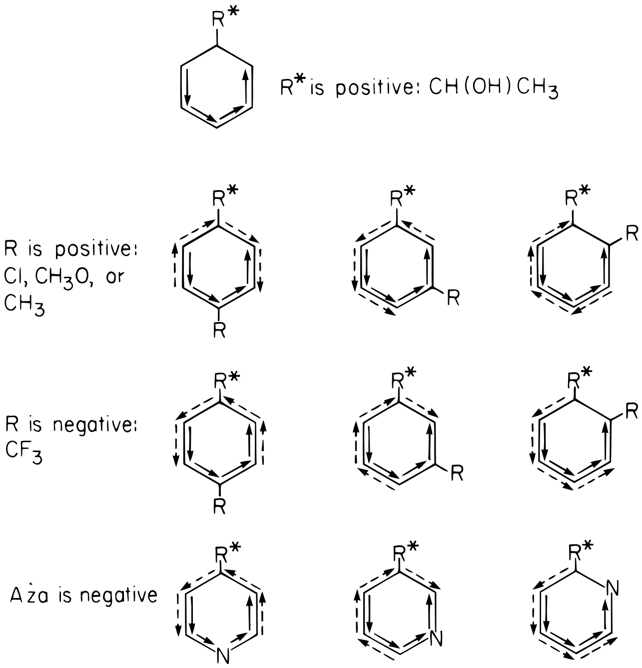


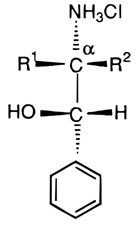
Figure 7. Induced bond moment directions for chiral benzene compounds substituted with groups having positive and negative spectroscopic moments. Solid arrows represent the bond moments induced by the chiral group, whereas the dashed arrows represent those induced by the additional ring substituent. Reprinted from *J. Org. Chem.* **1987**, *52*, 3386. Copyright 1987 American Chemical Society.

of the substituent of the benzene ring. This moment can be resolved into bond transition moments [48,49] as shown in Figure 7. Such a resolution is useful in the determination of the induced magnetic transition moment direction,[49] and the direction of the induced magnetic transition can be determined by the sense of rotation of the bond transition moments, pointing up for transition moments in the counterclockwise sense.

The relative importance of the induced contribution to the ^1L_b CEs as compared to the vibronic contribution can be seen in Figure 7. The chiral substituent (R*) does not induce transition moments in ring bonds adjacent to its attachment bond, and thus there is negligible chiral interaction of the ^1L_b transition moment with the chiral substituent. The negative ^1L_b CEs for (*R*)-α-phenylethylamine [(*R*)-**1a**] are dominated by vibronic borrowing from CEs at shorter wavelength.[45] The importance of the vibronic coupling mechanism in (*R*)-**1a** is underscored by the presence of a non-totally symmetric vibrational progression in the EA spectra of benzene compounds with a single substituent.[28,37,40,45,50] The dominance of a vibronic contribution to the ^1L_b CEs also affords a rationale for the observation of negative ^1L_b CEs for both (*R*)-α-phenylethylamine [(*R*)-**1a**] and (*R*)-α-phenylethylamine hydrochloride [(*R*)-**1b**], despite the difference in sign of the spectroscopic moments for their chiral groups, positive and negative, respectively.[45] Since a vibronically borrowed CE will have the same sign as the allowed rotational strength from which borrowing occurs, protonation of the amine moiety reverses the spectroscopic moment direction of the chiral group but has little effect on the CE associated with the allowed transitions at shorter wavelength and consequently on the ^1L_b CEs.

B. Benzene Sector Rule

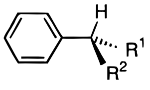
For chiral benzene compounds with a contiguous chiral center such as (*S*)-α-phenylethylamine [(*S*)-**1a**] in which the alkyl and amino groups are replaced by different atoms or groups, the CEs from about 255 to 270 nm are also due to vibronic borrowing. These CEs are also associated with transitions from the lowest energy vibrational mode in the ground state to totally symmetric vibrational modes in the ^1L_b electronically excited state, the lowest energy CD maximum being the band origin (0−0 vibrational transition). In addition, for chiral benzene compounds without an additional ring substituent, the sign of the ^1L_b CEs depends only on the chirality of the chiral center immediately attached to the benzene ring. Thus both (α*R*)-norephedrine hydrochloride [(α*R*,β*S*)-**4a**] and (α*S*)-norpseudoephedrine hydrochloride [(α*S*,β*S*)-**4b**] show negative ^1L_b CEs,[28] and this sign is the same as that observed in the ORD and CD spectra of other phenylalkylcarbinols with a contiguous chiral center of the same generic configuration.[51−54] The sign of these ^1L_b CEs can be predicted provided the conformation of the chiral group about its attachment bond to the benzene ring is known, and an empirical sector rule allows the summation of the rotatory contribution of the groups attached to the chiral center. For the formulation of such a rule, the CD data in Table 2 were used.



(α*R*,β*S*)-**4a**, $R^1 = H$; $R^2 = CH_3$
(α*S*,β*S*)-**4b**, $R^1 = CH_3$; $R^2 = H$

For benzene compounds with a contiguous chiral center incorporating a hydrogen atom, empirical potential function[65] and molecular orbital calculations[66−68] as well as X-ray,[66,69] proton nuclear magnetic resonance,[67,70−72] gas electron diffraction,[73] and jet laser[74] spectroscopy indicate that the preferred conformation (**5**) is such that the hydrogen atom at the carbon center eclipses or almost eclipses the phenyl ring plane (Table 2). Thus the CD data in Table 2 suggest the quadrant projections in Figure 8A which show the sign of the vibronic contribution to the ^1L_b CEs of a monosubstituted benzene chromophore by atoms or groups attached to a chiral center and lying in sectors in front of the benzene ring plane (near sectors). The sector boundaries are defined by the attachment bond of the chiral center and the benzene ring plane.[32] For atoms or groups in sectors behind the plane of the benzene ring plane (far sectors) in Figure 8A, the signs of the vibronic contributions are reversed, and for those groups and atoms lying in sector boundaries, there is no contribution to the CEs. The sum of the contributions gives

Table 2. $^{1}L_{\mathrm{b}}$ Band Origin Spectral Data for Chiral Compounds[a]



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			electronic absorption (EA): $\lambda_{\max}$, nm (ϵ[b]) circular dichroism (CD): $\lambda_{\max}$, nm [$\Delta\epsilon$[c] $\times 10^2$] {ref[d]}				
code	R^1		(*R*)-**1**, $R^2 = CH_3$	(*R*)-**3**, $R^2 = C(CH_3)_3$	(*S*)-**6**, $R^2 = CO_2H$	(*S*)-**7**, $R^2 = CO_2Na$	(*S*)-**8**, $R^2 = CO_2CH_3$
a	NH_2	EA:	267 (86)	269 (50)[f,g]			
		CD:	268 [−11][e] {45}	268 [−34][e,g] {37}			
b	NH_3Cl	EA:	267 (120)	266 (180)[h]	268 (130)[i]		
		CD:	267 [−8.2][e] {45}	266 [−3.6][e,h] {37}	268 [−22][e,i] {42}	268 [−23][j,k] {55}	
c	$N(CH_3)_3I$	EA:	269 (280)[i]	269 (280)			
		CD:	269 [−21][e,i] {56}	269 (−24)[e] {29}			
d	OH	EA:	267 (90)	267 (130)[i]	267 (79)	268 (75)[l]	
		CD:	268 [−17] {57}	268 [−39][i] {58}	269 [−6.7][e] {59}	268 [−2.4][e,l] {59}	262 [−8.2][e,i,m] {60}
e	OCH_3	EA:			267		
		CD:	268 [−7.5][e,i] {61}		267 [−6.1][e] {62}	261 [−17][e,j,m] {60}	262 [−7.6][e,i,m] {60}
f	CH_3	EA:		268 (110)[n]	267 (79)	268 (120)[l]	
		CD:		267 [−160][e,o] {63}	268 [+2.9] {64}	269 [−12][l] {64}	261 [+9.1][i,m] {60}
g	$C(CH_3)_3$	EA:					
		CD:			260 [+8.1][i,m] {60}	262 [−6.5][j,m] {60}	261 [+13][i,m] {60}
h	CF_3	EA:					
		CD:			261 [−7.3][i,m] {60}	261 [−7.6][j,m] {60}	260 [−7.1][i,m] {60}
i	Cl	EA:	272 (110)				
		CD:	273 [−3.3][e] {29}				
j	F	EA:			268 (88)	267 (120)[l]	
		CD:			268 [−18][e] {64}	268 [−12][e,l] {64}	
k	SH	EA:	271 (100)[f]				
		CD:	270 [+27][e] {29}				

[a] Methanol as the solvent or as otherwise noted. [b] Molar absorptivity. [c] Molar dichroic absorption. $\Delta\epsilon = [\theta]/3300$ where $[\theta]$ is the molecular ellipticity. [d] Original report of the complete electronic absorption (EA) and circular dichroism (CD) data. [e] Enantiomer used. [f] Shoulder. [g] Isooctane as the solvent. [h] 1,1,1,3,3,3-Hexafluoro-2-propanol as the solvent. [i] Ethanol as the solvent. [j] Water as the solvent. [k] Sodium and chloride ions not present. [l] Potassium cation. [m] Center maximum of three $^{1}L_{\mathrm{b}}$ CEs. [n] *n*-Heptane as the solvent. [o] Methylcyclohexane−isopentane 1:3 as the solvent.

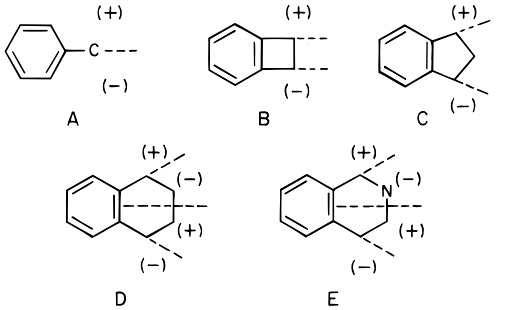


Figure 8. Near sector signs giving the vibronic contribution to the $^{1}L_{\mathrm{b}}$ Cotton effects for atoms or groups at chiral centers for various substituted benzene chromophores. For far sectors, the signs are reversed. Reprinted from *J. Am. Chem. Soc.* **1992**, *114,* 2181. Copyright 1992 American Chemical Society.

the sign to the observed CEs of the $^{1}L_{\mathrm{b}}$ band since for benzene compounds with only a single substituent the CEs are solely the result of vibronic borrowing.[45]

The signs for the sectors follow from the observed negative $^{1}L_{\mathrm{b}}$ CEs for (*R*)-α-phenylethyl alcohol [(*R*)-**1d**], the preferred conformation of (*R*)-**1d**, and the assumption of a larger rotatory contribution for a methyl group than that of an hydroxyl group.[29] This latter assumption is supported by the calculation of a larger effective bond transition moment for a carbon−carbon bond as compared to that of a carbon−oxygen bond.[75]

By using the CD data for the enantiopure compounds in Table 2, in which one substituent at the contiguous chiral center is a hydrogen atom and for which the absolute configurations are known, a sequence for the summation of the rotatory contributions to the $^{1}L_{\mathrm{b}}$ CEs is established as the ranking of rotatory contributions shown in Table 3. This sequence when used in connection with the sector signs in Figure 8A has a general usefulness for the establishment by CD measurement of the absolute

Table 3. Ranking of Rotatory Contributions

compound	ranking of groups
(*R*)-**1**	SH > $\mathbf{CH_3}$ > NH_2, N^+H_3, $N^+(CH_3)_3$, OH, OCH_3, Cl
(*R*)-**3**	$\mathbf{C(CH_3)_3}$ > NH_2, N^+H_3, $N^+(CH_3)_3$, OH, CH_3
(*S*)-**6**	CH_3, $C(CH_3)_3$ > $\mathbf{CO_2H}$ > N^+H_3, OH, OCH_3, CF_3, F
(*S*)-**7**	$\mathbf{CO_2^-}$ > N^+H_3, OH, OCH_3, CH_3, $C(CH_3)_3$, CF_3, F
(*S*)-**8**	CH_3, $C(CH_3)_3$ > $\mathbf{CO_2CH_3}$ > OH, OCH_3, CF_3
summary	CO_2^- > SH,[a] $C(CH_3)_3$ > CH_3 > CO_2H, CO_2CH_3 > NH_2, N^+H_3, $N^+(CH_3)_3$, OH, OCH_3, CF_3, Cl, F

[a] The thiol group may not rank below the carboxylate group.

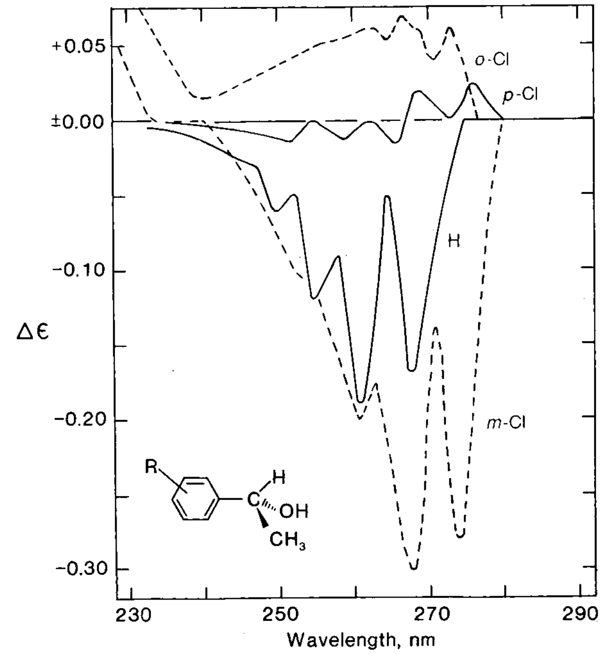


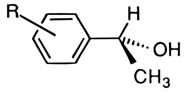
Figure 9. Circular dichroism spectra of (*R*)-α-phenylethyl alcohol [(*R*)-**1d**], (*R*)-α-(*p*-chlorophenyl)ethyl alcohol [(*R*)-**9a**], (*R*)-α-(*m*-chlorophenyl)ethyl alcohol [(*R*)-**9c**], and (*R*)-α-(*o*-chlorophenyl)ethyl alcohol [(*R*)-**9d**] in methanol. Reprinted from *J. Am. Chem. Soc.* **1990**, *112*, 5741. Copyright 1990 American Chemical Society.

configurations of related chiral benzene compounds in which one substituent at the contiguous chiral center is a hydrogen atom.

C. Benzene Chirality Rule

For enantiomers of chiral benzene compounds with attached groups with contiguous chiral centers and with additional ring substituents, an induced rotatory contribution influences the sign of the ^1L_b CEs,[31] and the sign may be the same or different from that of the nonsubstituted parent, depending on the spectroscopic moment[26,27] and ring positions of the additional substituents.[31,45,57] The reversal of the sign for the ^1L_b CEs on para substitution of (*R*)-α-phenylethyl alcohol [(*R*)-**1d**] by an atom or group with a positive spectroscopic moment can be viewed as the overshadowing of the negative vibronic rotational strength by a positive induced contribution, and (*R*)-α-(*p*-chlorophenyl)ethyl alcohol [(*R*)-**9a**] has positive ^1L_b CEs (Table 4 and Figure 9). On para substitution by a group with a negative spectroscopic moment, the induced contribution to the ^1L_b rotational strength has the same sign as the vibronic contribution. Thus (*R*)-α-(*p*-trifluoromethylphenyl)ethyl alcohol [(*R*)-**9b**] has negative ^1L_b CEs. Meta substitution by an atom or group will result in an induced contribution with an opposite sign from that caused by the same group in the para position. Thus for (*R*)-α-(*m*-chloromethylphenyl)ethyl alcohol [(*R*)-**9c**], both the vibronic and induced contribution to the ^1L_b CEs are negative, and (*R*)-**9c** shows strong negative ^1L_b CEs. For meta substitution by a trifluoromethyl group with a negative spectroscopic moment, the induced contribution is of opposite sign to that of the vibronic contribution. Since for a *m*-trifluoromethyl group, the latter contribution is more important than the former, the sign of the ^1L_b CEs of (*R*)-**9d** is unchanged from that of (*R*)-**1d**. Ortho substitution again reverses the sense of the induced bond transition moments from that induced by the same meta substitution, and (*R*)-α-(*o*-chlorophenyl)ethyl alcohol [(*R*)-**9e**] shows positive ^1L_b CEs while those of (*R*)-α-(*o*-trifluoromethyl) analogue and [(*R*)-**9f**] are negative. These various induced contributions are summarized in Table 5 for a benzene compound with a single chiral substituent giving a negative vibronic contribution to the ^1L_b CEs. For a chiral substituent giving a positive contribution to the ^1L_b CEs, the signs for the induced rotatory contributions to the CEs are reversed from those as shown in Table 5.

Table 4. ^1L_b Band Origin Maxima for (*R*)-Phenylmethylcarbinols in Methanol



solute	R	EA: λ, nm (ϵ[a])	CD: λ, nm ($\Delta\epsilon$[b] × 10^2)	ref[c]
(*R*)-**1d**	H	267 (90)	268 (−17)	57
(*R*)-**9a**[d]	*p*-Cl	275 (240)	276 (+2.5)	57
(*R*)-**9b**[d]	*p*-CF_3	269 (280)	268 (−12)	57
(*R*)-**9c**	*m*-Cl	274 (200)	274 (−28)	31
(*R*)-**9d**	*m*-CF_3	270 (600)	271 (−15)	31
(*R*)-**9e**	*o*-Cl	273 (160)	273 (+6.7)	31
(*R*)-**9f**[d]	*o*-CF_3	271 (940)	270 (−13)	31

[a] Molar absorptivity. [b] Molar dichroic absorption. [c] Report giving complete EA and CD spectral data. [d] Enantiomer used.

Table 5. Rotational Contributions to the ^1L_b Cotton Effects for a Benzene Compound with a Single Chiral Substituent Giving a Negative Vibronic Contribution to the ^1L_b Cotton Effects

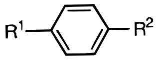
	substituent		
contribution[a]	ortho	meta[b]	para
No Additional Ring Substituent			
vibronic	−	−	−
induced	±0	±0	±0
Substitution by a Group with a Positive Spectroscopic Moment[c]			
vibronic	−	−	−
induced	+	−	+
Substitution by a Group with a Negative Spectroscopic Moment[c]			
vibronic	−	−	−
induced	−	+	−

[a] For a similar compound giving a positive vibronic contribution to the ^1L_b, the signs for the induced contributions are reversed. [b] The signs are the same for the 3,5-disubstituted compounds. [c] See refs 26 and 27 for the spectroscopic moments.

By using the EA data in Table 6 for phenylmethylcarbinamine [R^1 = H; R^2 = $CH(NH_2)CH_3$] and its hydrochloride [R^1 = H; R^2 = $CH(NH_3Cl)CH_3$] together with similar data for the para-substituted amines and their amine hydrochlorides, the spectroscopic moments of the para substituents (m_i) and of the chiral groups (m_j) were calculated and are shown in Table 7.

The former values are in excellent agreement with those found earlier.[26] Those of the free base group and the hydrochloride group, however, are of opposite sign, on average +2 and −2 [(cm mol)/L]$^{1/2}$, respectively, and thus the sign of the spectroscopic moment

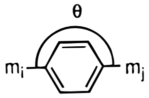
Table 6. Electronic Absorption ^1L_b Band Origin Maxima for Phenylmethylcarbinamines and Their Hydrochlorides in Methanol



	λ, nm (ϵ^a) [ref^b]		
R^1	$R^2 = H$	$R^2 = CH(NH_2)CH_3$	$R^2 = CH(NH_3Cl)CH_3$
H		267 (86) [45]	267 (120) [45]
CH_3	268 (230) [59]	273 (310) [45]	271 (170) [45]
Cl	272 (200) [57]	276 (240) [45]	274 (140) [45]
Br	271 (119) [76]	276 (180) [45]	274 (120) [45]
CF_3	266 (380) [57]	268 (240) [45]	268 (480) [45]
CN	(607)^c [50]	279 (383) [50]	

[a] Molar absorptivity. [b] Report giving complete EA spectral data. [c] Cyclohexane as the solvent.

Table 7. Spectroscopic Moments[a]



	m_i		m_j	
group	this work^c	Platt^d	$CH(NH_2)CH_3$	$CH(NH_3Cl)CH_3$
CH_3	+7^e	+7	+1	−1
Cl	+7	+6	0	−1
Br	+5	+4	+1	0
H	0	0	+4	−5
CF_3	−9	−15	+2	−1
CN	−11	−19	+2	

[a] In units of $[(\text{cm mol})/\text{L}]^{1/2}$. [b] Reference 77. [c] These values of m_i used for the calculation of m_j values. [d] Reference 26. [e] Value of m_i assumed for the calculation of $K = 4.7$ in the equation above.

of the chiral group does not change the sign of the observed ^1L_b CEs.

If the vibronic and induced contributions to the ^1L_b CEs have the same sign, the sign of a particular ring-substituted benzene compound can be predicted with certainty. When the vibronic and induced contributions to the ^1L_b CEs are of opposite sign, a prediction to the sign of the ^1L_b CEs shown by a particular enantiomer is somewhat ambiguous. However, all of the phenylalkylcarbinamines and carbinols so far reported that are ortho- and para-substituted with an atom or group having a positive spectroscopic moment (CH_3, Cl, Br, OH, OCH_3) show ^1L_b CEs of opposite sign to that of the unsubstituted parent.[28,31,37,45,50,57,62,65,78−81] For phenylalkylcarbinamines and carbinols having a group with a negative spectroscopic moment (CN, CF_3) in the meta position, the sign of the ^1L_b CEs is not changed from that of the unsubstituted parent.[31]

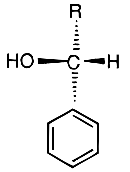
IV. Applications

A. Unsubstituted Benzene Rings

1. Phenylcarbinamines, Phenylcarbinamine Salts, and Phenylcarbinols

Since a methyl group makes a larger contribution to the ^1L_b CEs than does an amino, ammonium, hydroxyl, and methoxyl group [(*R*)-**1a**−**e**, Table 2], the preferred conformation **5** for chiral phenylalkylcarbinamines, phenylcarbinamine salts, and phenylcarbinols and their *N*-alkyl and *O*-alkyl derivatives with the same generic configuration as (*R*)-**1a** and **d** are also predicted to show negative ^1L_b CEs using sector projection A in Figure 8. Considerations of the preferred conformation **5** also predict that changes in solvent will not change the sign of the ^1L_b CEs shown by an enantiomer of a particular benzene compound. These predictions are confirmed by the circular dichroism data for chiral phenylcarbinamines and *N*-substituted phenylcarbinamines and their salts, and negative signs are observed for the ^1L_b CEs of (*R*)-*N*,*N*,*N*-trimethyl-α-phenylethylammonium iodide [(*R*)-**1c**, Table 2] and (*R*)-α-phenylneopentylammonium chloride [(*R*)-**3b**, Table 2], the trimethylammonium group being larger in effective bulk size than a methyl group and a *tert*-butyl group being larger than an ammonium group.

Chiral phenylalkylcarbinamines, phenylalkylcarbinols, and their *N*- and *O*-substituted derivatives which have a hydroxyl group, a halogen atom, or an amino group substituent on the carbon atom attached to the chiral center will show ^1L_b CEs with the same sign as that of the unsubstituted carbinamine, carbinol, and their *N*-alkyl and *O*-alkyl derivatives. Thus (*S*)-2-hydroxy-,[42] (*S*)-2-bromo-,[29] and (*S*)-2,2,2-trifluoro-1-phenylethanol[60] [(*S*)-**10a**−**c**], and (1*S*,2*S*)-2-(dichloroacetamido)-1-phenyl-3-propanediol[81] [(1*S*,2*S*)-**10d**] all show negative ^1L_b CEs.



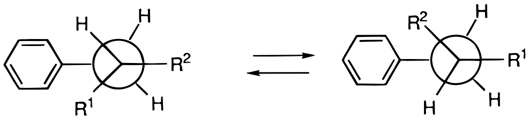
(*S*)-**10a**, R = CH_2OH
b, R = CH_2Br
c, R = CF_3
(1*S*,2*S*)-**10d**, R = $CH(CH_2OH)NHCOCHCl_2$

2. Benzylcarbinamines, Benzylcarbinamine Salts, and Benzylcarbinols

A chiral center separated by a methylene group from a benzene ring also results in ^1L_b CEs, and substantial ORD[39,56,62,82−84] and CD[23,28,30,40,41,45,55,56,62,85,86] data have been reported, and for otherwise unsubstituted benzylcarbinamines and benzylcarbinols, such as (*R*)-2-amino-1-phenylpropane [(*R*)-**11a**] and (*R*)-1-phenyl-2-propanol [(*R*)-**11b**], the benzene sector rule correlates the sign of the ^1L_b CEs with their absolute configurations.[30]

For application of the benzene sector rule to the circular dichroism of phenylcarbinamines and phenylcarbinols, only conformer **5** in which the hydrogen atom at the chiral center eclipses the benzene ring plane need be considered. For benzylcarbinamines and benzylcarbinols, however, there is a greater conformational mobility of the attached group with respect to the benzene ring, and an equilibrium between conformers (−)-**12a** and (+)-**12b** (Table 8) must be considered when relating the sign of the ^1L_b CEs to the absolute configurations of such compounds. The two lowest energy conformations of

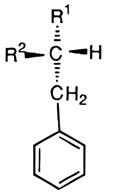
Table 8. ^1L_b Band Origin Maxima for Benzylcarbinamines, Benzylcarbinamine Salts, and Benzylcarbinols



(-)-**12a** (+)-**12b**

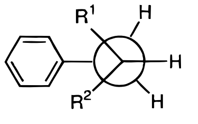
solute	R^1	R^2	solvent	EA: λ, nm (ε[a])	CD: λ, nm (Δε[b] × 10^2)	ref[c]
(*R*)-**11a**·HCl	CH_3	NH_2	0.1 M KOH in MeOH	267 (120)	269 (−3.0)	30
(*R*)-**11a**[d]	CH_3	NH_2	cyclohexane	268 (150)	272 (−0.1) 268 (+4.5)	45
(*R*)-**11a**·HCl	CH_3	N^+H_3	H_2O		266 (−1.3)	30
(*R*)-**11a**·HCl	CH_3	N^+H_3	MeOH	266 (77)[e]	267 (−3.3)	30
(*R*)-**11b**	CH_3	OH	MeOH	267 (120)	268 (−5.5)	30
(*R*)-**11b**	CH_3	OH	cyclohexane		269 (−1.7)	30
(*S*)-**11c**[d]	C_6H_{11}-*c*	NH_2	cyclohexane		269 (+4.5)[f]	84
(*R*)-**11d**[d]	CH_3	$NHCH_3$	95% EtOH	268 (170)	268 (−9.2)	56
(*R*)-**11d**·HCl[d]	CH_3	$N^+H_2CH_3$	95% EtOH	268 (330)	268 (−7.1)	56
(*R*)-**11e**[d]	CH_3	$N(CH_3)_2$	95% EtOH	269 (150)	268 (−10)	56
(*R*)-**11e**	CH_3	$N(CH_3)_2$	cyclohexane	272 (190)	272 (−7.3)	45
(*R*)-**11e**·HCl[d]	CH_3	$N^+H(CH_3)_2$	95% EtOH	268 (81)	267 (−9.1)	56
(*R*)-**11f**[d]	CH_3	$N^+(CH_3)_3$	95% EtOH	268 (87)	273 (−13)	56

[a] Molar absorptivity. [b] Molar dichroic absorption. [c] Report giving complete EA and CD spectral data. [d] Enantiomer used. [e] Shoulder. [f] Reduced amplitude (*a*) of the CE in the ORD spectrum. $a = [\phi]_{\text{long wavelength extremum}} - [\phi]_{\text{short wavelength extremum}}/100$.



(*R*)-**11a**, $R^1 = CH_3$; $R^2 = NH_2$
b, $R^1 = CH_3$; $R^2 = OH$
(S)-**11c**, $R^1 = C_6H_{11}$-*c*; $R^2 = NH_2$
(*R*)-**11d**, $R^1 = CH_3$; $R^2 = NHCH_3$
e, $R^1 = CH_3$; $R^2 = N(CH_3)_2$
f, $R^1 = CH_3$; $R^2 = N(CH_3)_3I$

chiral benzylcarbinamines and benzylcarbinols **12a** and **b** follow from the preferred conformation determined by supersonic molecular jet laser[74] and microwave[87] spectroscopy of various alkylbenzenes including ethylbenzene[74] and of 2-phenylethylamine[87] in the gas phase, in which the carbon−carbon bond α,β to the benzene ring is orthogonal to the benzene ring plane. Conformer **12c** need not be considered because the gauche interactions of R^1 and R^2 groups with the benzene ring make it of higher energy than either (−)-**12a** or (+)-**12b**.



12c

Since the rotatory contribution of a hydrogen atom attached at the chiral center is insignificant[75] and that of a group in a sector boundary is also small, sector rule A in Figure 8 gives the rotatory contribution of **12a** and **12b**, negative and positive, respectively. The sign of the observed ^1L_b CEs depends on the rotatory contribution and relative amount of each conformer in a particular solvent. To determine the possible importance of this equilibrium in the application of the benzene sector rule to the CD spectra of benzylcarbinamines and benzylcarbinols, the effect of solvent on the observed CD spectra of the carbinamines and carbinols such as **11** was investigated in detail.[30]

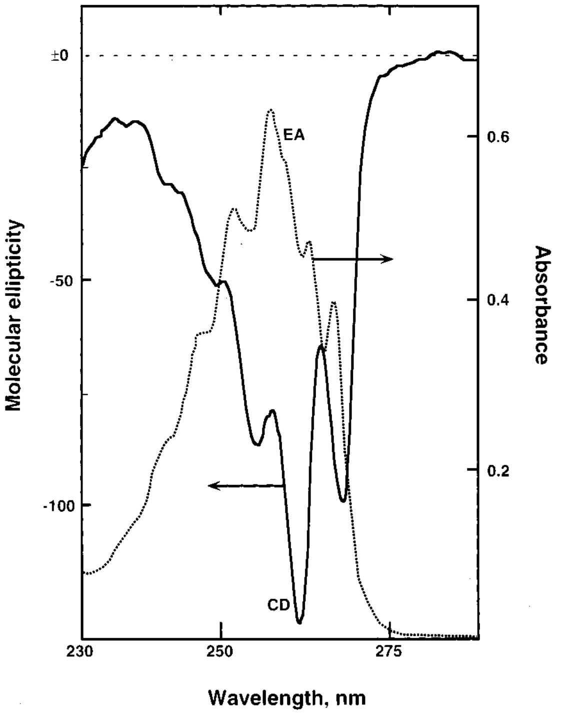


Figure 10. Electronic absorption (EA) and circular dichroism (CD) spectra of (*R*)-2-amino-1-phenylpropane hydrochloride [(*R*)-**11a**·HCl] in 0.1 M KOH in methanol. Reprinted from *J. Am. Chem. Soc.* **1996**, *118*, 7694. Copyright 1996 American Chemical Society.

Figure 10 shows the electronic absorption (EA) and circular dichroism (CD) spectra of (*R*)-2-amino-1-phenylpropane [(*R*)-**11a**] in methanol from 230 to 290 nm. As discussed above for the EA spectrum of (*R*)-α-phenylethylamine hydrochloride [(*R*)-**1b**], the long-

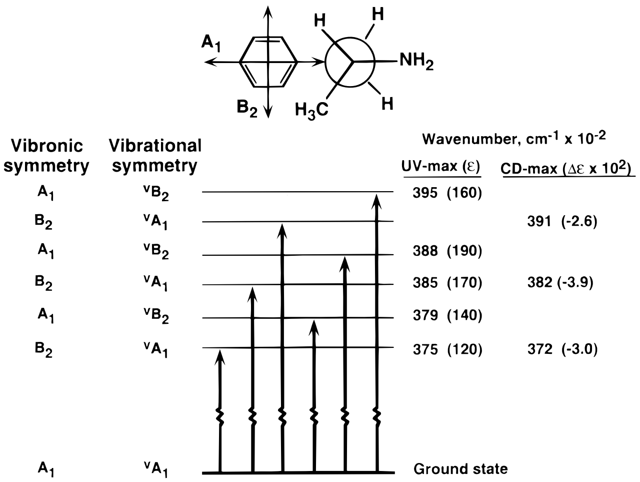


Figure 11. Schematic diagram of the electronic absorption (UV) and circular dichroism (CD) maxima observed with (*R*)-2-amino-1-phenylpropane hydrochloride [(*R*)-**11a**·HCl] in 0.1 M KOH in methanol. The A_1 and B_2 axes are in the plane of the benzene ring. Reprinted from *J. Am. Chem. Soc.* **1996**, *118*, 7694. Copyright 1996 American Chemical Society.

est wavelength maxima at 267 nm (band origin) corresponds to the 0−0 transition for a $B_2 \leftarrow A_1$ electronic transition (Figure 6). For (*R*)-**11a**, this electronic transition also has allowed and forbidden vibronic components, but only for the allowed components for which the electronic dipole transition moment is in the plane of the benzene ring and perpendicular to the substituent attachment bond (B_2 axis in Figure 11) are CD maxima observed. These transitions connect the ground-state zeroth vibrational level ($^vA_1$) with the zeroth and higher totally symmetric levels (also $^vA_1$) of the ring-breathing vibration in the electronically excited state. The vibronic symmetry of these higher energy states is B_2, and as shown in Figure 11, the excitations to the first two of these higher totally symmetric vibronic states are seen as negative CD maxima separated from the band origin CE at 372 × 10^2 cm^{-1} (269 nm) by 10 × 10^2 cm^{-1} and (10 + 9) × 10^2 cm^{-1}. A corresponding EA absorption maximum is observed at (375 + 10) × 10^2 cm^{-1}, but one at (375 + 10 +9) × 10^2 cm^{-1} was obscured by other absorption bands and was not observed. For the $B_2 \leftarrow A_1$ electronic transition, the forbidden vibronic component combines the ground zeroth vibronic state ($^vA_1$) with the first vibrational level $^vB_2$ non-totally symmetric ring deformation vibration, and thence with higher totally symmetric vibrational states. The vibronic symmetry of these states is also A_1, and the electric dipole transition moment is also in the plane of the benzene ring but is coincident with the substituent attachment bond (A_1 axis in Figure 11). In the EA spectrum of (*R*)-**11a**, three of these transitions are seen as maxima separated from the band origin by 4 × 10^2, (4 + 9) × 10^2, and (4 + 9 + 7) × 10^2 cm^{-1}, respectively. Since CD minima are near these EA maxima, the CEs associated with these EA maxima are weak.

Since (*R*)-2-amino-1-phenylpropane [(*R*)-**11a**] in methanol shows negative ^1L_b CEs, the conformational equilibrium is such that its CD spectrum is the result of the greater rotatory contribution of conformer (−)-**12b** ($R^1 = CH_3$, $R^2 = NH_2$) as compared to conformer (+)-**12b** (Table 8), both the greater rotatory contribution of a methyl group than that of an amino group[29] and the respective mole fractions of (−)-**12a** and (+)-**12b** coming into play. The negative sign for the ^1L_b CEs of (*R*)-**11a** is in agreement with the positive sign for the longest wavelength CE previously reported for (*S*)-**11a** in methanol,[39,45] 95% ethanol,[56] and 2-propanol.[39] When the solvent is cyclohexane, however, the sign of ^1L_b CEs for (*R*)-**11a** is positive with a weak negative CD maximum at a slightly longer wavelength (272 nm) than that of the EA band origin, and Table 8 compares the position and molar absorptivity (ϵ) and molar dichroic absorption ($\Delta\epsilon$) of the ^1L_b band origin of (*R*)-**11a** in both methanol and cyclohexane.[45] The intense positive band for ^1L_b CEs at 268 nm for (*R*)-**11a** in cyclohexane confirms an earlier observation[86] of a negative ^1L_b CEs for (*S*)-**11a** in cyclohexane and is the result of a shift in the equilibrium from (−)-**12a** to (+)-**12b** due to diminished hydrogen bonding of the solvent to the amino group and a stabilizing interaction of the amino group with the benzene ring moiety.[87] The positive sign in the ORD curve for the ^1L_b CEs for (*S*)-1-cyclohexyl-2-phenylethylamine [(*S*)-**11c**] in cyclohexane[84] is explained on a similar basis, the cyclohexyl group being larger in effective size than the methyl group and thus stabilizing conformer (+)-**12b** as compared to (−)-**12a** to a greater extent than in the case of (*R*)-**11a**.

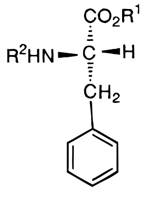
As discussed in detail in section IV.A.3 in connection with the CD spectrum of L-phenylalanine (L-**13a**) in methanol, the negative CD maximum at 272 nm in the CD spectrum of (*R*)-2-amino-1-phenylpropane [(*R*)-**11a**] in cyclohexane is assigned to conformer (−)-**12a**, whereas the intense positive maximum at 268 nm is assigned to conformer (+)-**12b**, conformer (+)-**12b** being somewhat more stabilized by the nonpolar solvent.

As shown in Table 8, (*R*)-*N*-methyl- and (*R*)-*N*,*N*-dimethyl-2-amino-1-phenylpropane [(*R*)-**11d** and (*R*)-**11e**] in 95% ethanol are also correctly predicted to show negative ^1L_b CEs. Because of the larger effective size of a dimethylamino group as compared to an amino group, (*R*)-**11e** also shows negative ^1L_b CEs even in cyclohexane.[45]

By using this same interpretation, the sign of the ^1L_b CEs of (*R*)-2-amino-1-phenylpropane hydrochloride [(*R*)-**11a**·HCl] in water and methanol is also correctly predicted to be negative, confirming earlier reports of a positive sign for ^1L_b CEs for (*S*)-**11a**·HCl in water,[40] methanol,[28,39,40,45] and 2-propanol,[39,40] and of (*S*)-**11a**·$^1/_2(H_2SO_4)$ in 95% ethanol.[56] Similarly, the ^1L_b CEs for (*R*)-*N*-methyl- and (*R*)-*N*,*N*-dimethyl-2-amino-1-phenylpropane hydrochloride [(*R*)-**11d**·HCl and (*R*)-**11e**·HCl] and (*R*)-**11e**·methiodide [(*R*)-**11f**] in 95% ethanol are also negative.

As shown in Table 8, (*R*)-1-phenyl-2-propanol [(*R*)-**11b**] in methanol and in cyclohexane and in other solvents also shows negative ^1L_b CEs. When the solvent for (*R*)-**11b** is changed from water to cyclohexane, the intensity of the ^1L_b CEs is reduced, but the sign remains the same. The equilibrium shown at the top of Table 8 can be assumed to shift from (−)-**12a** toward (+)-**12b**, but not enough to cause a change in sign of the ^1L_b CEs.

3. L-Phenylalanines with Positive, Neutral, and Acetylated Nitrogen Atoms



L-**13a**, $R^1 = H$; $R^2 = H$
b, $R^1 = H$; $R^2 = CH_3$
c, $R^1 = CH_3$; $R^2 = H$
d, $R^1 = H$; $R^2 = CH_3CO$
e, $R^1 = CH_3CH_2$; $R^2 = CH_3CO$

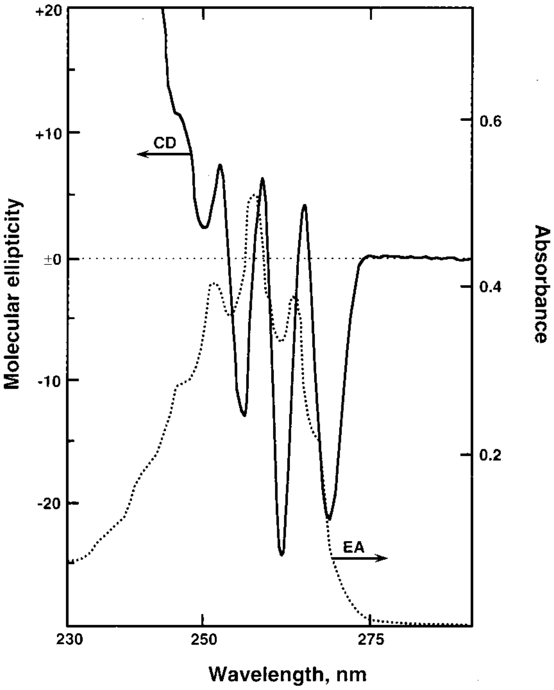
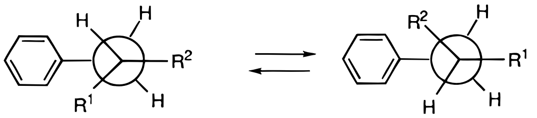


Figure 12. Electronic absorption (EA) and circular dichroism (CD) spectra of L-phenylalanine (L-**13a**) in methanol. Reprinted from *J. Am. Chem. Soc.* **1996**, *118*, 7694. Copyright 1996 American Chemical Society.

In contrast to the enantiomers of benzylalkylcarbinamines, benzylalkylcarbinamine salts, and benzylalkylcarbinols, each of which, except for (*R*)-2-amino-1-phenylpropane [(*R*)-**11a**] in cyclohexane, shows a single sign for its ^1L_b CEs, L-phenylalanine (L-**13a**) and some of its derivatives in some solvents show a number of oppositely signed ^1L_b CEs in their CD spectra. Thus, L-**13a** in water shows positive ^1L_b CEs (Table 9), but in methanol, the CD spectrum (Figure 12) is more complex and shows both negative and positive CD maxima. These observations are in agreement with an earlier report[41] of positive ^1L_b CEs for L-**13a** in water and negative and positive ^1L_b CEs for L-**13b** in glycerol-methanol, the positive CEs being assigned in the latter solvent to electronic transitions from the ground state to non-totally symmetric

Table 9. ^1L_b Band Origin Maxima for L-Phenylalanines with Positive, Neutral, and Acetylated Nitrogen Atoms[a]



(-)-**12a** (+)-**12b**

solute	R^1	R^2	solvent	EA: λ, nm (ϵ^b)	CD: λ, nm ($\Delta\epsilon^c \times 10^2$)
L-**13a**	CO_2^-	N^+H_3	H_2O		265 (+1.1)
L-**13a**	CO_2^-	N^+H_3	MeOH	267 (77)[d]	269 (−0.64) 265 (+0.14)
L-**13a**	CO_2H	N^+H_3	1 M HCl in H_2O		265 (+1.4)
L-**13a**	CO_2H	N^+H_3	0.1 M HCl in MeOH	266 (70)[d]	266 (+1.1)
L-**13a**	CO_2^-	NH_2	1 M NaOH in H_2O		271 (−0.12) 266 (+1.5)
L-**13a**	CO_2^-	NH_2	0.1 M KOH in MeOH	268 (110)	270 (−0.64) 266 (+0.82)
L-**13b**	CO_2^-	$N^+H_2CH_3$	H_2O		266 (+1.9)
L-**13b**	CO_2^-	$N^+H_2CH_3$	MeOH	267 (150)[d]	270 (−0.39) 266 (+0.73)
L-**13b**	CO_2H	$N^+H_2CH_3$	1 M HCl in H_2O		266 (+3.3)
L-**13b**	CO_2H	$N^+H_2CH_3$	0.1 M HCl in MeOH	267 (66)[d]	266 (+3.0)
L-**13b**	CO_2^-	$NHCH_3$	1 M NaOH in H_2O		268 (−0.52) 265 (+0.58)
L-**13c**·HCl	CO_2CH_3	N^+H_3	H_2O		266 (+1.8)
L-**13c**·HCl	CO_2CH_3	N^+H_3	MeOH	267 (73)[d]	265 (+0.94)
L-**13c**·HCl	CO_2CH_3	NH_2	1 M NaOH in H_2O		266 (+1.6)
L-**13c**·HCl	CO_2CH_3	NH_2	0.1 M KOH in MeOH	267 (100)	270 (−0.33) 266 (+1.1)
L-**13d**	CO_2^-	$NHCOCH_3$	1M NaOH in H_2O		267 (−3.0)
L-**13d**	CO_2^-	$NHCOCH_3$	0.1 M KOH in MeOH	267 (100)	269 (−2.1) 264 (+0.82)
L-**13d**	CO_2H	$NHCOCH_3$	H_2O		268 (−2.8)
L-**13e**	$CO_2C_2H_5$	$NHCOCH_3$	H_2O		267 (−2.1)
L-**13e**	$CO_2C_2H_5$	$NHCOCH_3$	MeOH	267 (87)[d]	268 (−2.8)
L-**13e**	$CO_2C_2H_5$	$NHCOCH_3$	THF		269 (−1.3) 265 (+0.85)
L-**13e**	$CO_2C_2H_5$	$NHCOCH_3$	cyclohexane		269 (−0.45) 265 (+1.6)
L-**14**	CH_2OH	NH_2	MeOH	267 (130)	269 (−3.3)
L-**14**	CH_2OH	NH_2	cyclohexane		271 (−1.4) 267 (+0.91)
L-**14**	CH_2OH	N^+H_3	0.1 M HCl in MeOH	262 (82)[d]	268 (−5.8)

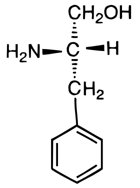
[a] Complete EA and CD spectral data given in ref 30. [b] Molar absorptivity. [c] Molar dichroic absorption. [d] Shoulder.

vibronic excited states.[41] On the basis of the data in Table 9, however, the two longest wavelength CD maxima in the spectrum of L-**13a** in methanol are assigned differently and comprise a double (bisignate) CE,[88,89] both associated with the EA band origin absorption maximum at 267 nm. On changing the solvent from water to methanol, the conformational equilibrium is shifted from (+)-**12b** toward (−)-**12a**, and the greater amount of (−)-**12a** is now detected in the CD spectrum (Table 9). The negative CD maxima at 269 nm results from a small bathochromic shift of the ^1L_b absorption of the phenyl group in (−)-**12a** due to the influence of the carboxylate group gauche (synclinal) to the benzene ring chromophore.

The CD spectra of other phenylalanines with both positive and neutral nitrogen atoms show a similar solvent effect. *N*-Methyl-L-phenylalanine (L-**13b**) shows positive ^1L_b CEs in water but double ^1L_b CEs in methanol (Table 9). In both water and methanol, the hydrochlorides of L-phenylalanine (L-**13a** in 1 M HCl in H_2O and 0.1 M HCl in MeOH), *N*-methyl-L-phenylalanine (L-**13b** in 1 M HCl in H_2O and 0.1 M HCl in MeOH), and methyl L-phenylalaninate hydrochloride (L-**13c**·HCl) show (Table 9) only positive ^1L_b CEs. For each of these compounds with a positive nitrogen atom, conformer (+)-**12b** gives the sign of the ^1L_b CEs, and with the exception of methyl L-phenylalaninate in water (L-**13c**·HCl in 1 M NaOH in H_2O), the L-phenylalanines L-**13a**−**c** with a neutral nitrogen atom show double CEs for the ^1L_b band origin in both water and methanol (Table 9), but at shorter wavelength only positive ^1L_b CEs are observed.[30] The less intense, negative CEs associated with the EA band origin are due to the presence of conformer (−)-**12a**, but at shorter wavelength, negative CEs are not observed in the presence of the stronger positive CEs displayed by conformer (+)-**12b**.

Acetylation of L-phenylalanines and ethyl L-phenylalaninate also results in CD spectra which frequently show substantial solvent effects. It is to be noted, however, that the conformational equilibrium for sodium *N*-acetyl-L-phenylalaninate (L-**13d** in 1 M NaOH in H_2O), *N*-acetyl-L-phenylalanine (L-**13d**) in water, and ethyl *N*-acetyl-L-phenylalaninate (L-**13e**) in water and methanol is shifted toward conformer (−)-**12a**, and only negative ^1L_b CEs are observed (Table 9). In less polar solvents, both positive and negative ^1L_b CEs associated with conformers (−)-**12a** and (+)-**12b** are observed, these phenylalanine derivatives, potassium *N*-acetyl-L-phenylalaninate in methanol (L-**13d** in 0.1 M KOH in MeOH) (Table 9), *N*-acetyl-L-phenylalanine in methanol, dioxane, and tetrahydrofuran,[30] and L-**13e** in tetrahydrofuran and in cyclohexane (Table 9) showing double CEs for the ^1L_b band origin.[30] As expected, the longer wavelength component of the double CEs is negative and is associated with the EA transition of (−)-**12a**, at a slightly longer wavelength than that of the absorption maximum of (+)-**12b** when a carboxylate, carboxyl, or ethoxycarbonyl group is gauche to the benzene ring chromophore.

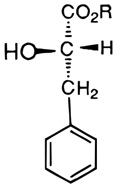
The CD spectrum of L-phenylalaninol (L-**14**) in various solvents[30] (Table 9) can also be interpreted in terms of a conformational equilibrium of the two conformers (−)-**12a** and (+)-**12b**, L-**14** in water, methanol, and tetrahydrofuran showing only negative ^1L_b CEs (Table 9), similar to those shown by (*R*)-2-amino-1-phenylpropane [(*R*)-**11a**] in methanol (Figure 10).[30] For L-**14** in cyclohexane, there is a shift in the conformational equilibrium from (−)-**12a** in which the hydroxymethylene group is gauche to the benzene chromophore toward conformer (+)-**12b**, and the greater amount of (+)-**12b** results in the appearance of double ^1L_b CEs with the positive component at slightly shorter wavelength than that of the negative component. In both water and methanol, L-**14**·HCl shows negative ^1L_b CEs, much the same as shown by (*R*)-2-amino-1-phenylpropane hydrochloride [(*R*)-**11a**·HCl] in water and methanol.[30] In these cases, (−)-**12a** is the dominant conformer as a result of the interaction of the ammonium group with the polar solvents.



L-**14**

4. L-3-Phenyllactic Acid and Its Methyl Ester

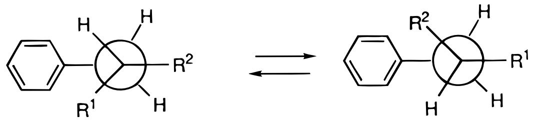
The CD of sodium L-3-phenyllactate in water (L-**15a** in 1 M NaOH in H_2O) shows negative ^1L_b CEs but double ^1L_b CEs in methanol (L-**15a** in 0.1 M KOH in MeOH) (Table 10). Protonation of the carboxylate group shifts the conformational equilibrium of L-**15a** more toward (+)-**12b**, and L-**15a** in water, methanol, and tetrahydrofuran shows double ^1L_b CEs,[30] although earlier reports[55,62] of the CD spectrum of L-**15a** in water and methanol give a single CE for the ^1L_b band origin. In water, the CEs are reported as positive,[55] and in methanol, they are reported as negative.[62] That the negative component of the double band origin CE in L-**15a** in water, methanol, and tetrahydrofuran (Table 10) is due to conformer (−)-**12a** follows from its position at a longer wavelength than that of the positive component. The benzene ring chromophore transition is always slightly shifted bathochromically when it is gauche to a carboxylate group rather than gauche to an ammonium or amino group.



L-**15a**, R = H
b, R = CH_3

The CD spectrum of methyl L-3-phenyllactate (L-**15b**) was reported earlier to show substantial solvent effects,[55,62] but double ^1L_b CEs were not observed. Thus L-**15b** in water and methanol gave positive ^1L_b

Table 10. ^1L_b Band Origin Maxima for L-3-Phenyllactic Acid and Its Methyl Ester[a]



(-)-**12a** (+)-**12b**

solute	R^1	R^2	solvent	EA: λ, nm (ε[b])	CD: λ, nm ($\Delta\epsilon$[c] × 10^2)
L-**15a**	CO_2^-	OH	1 M NaOH in H_2O		269 (−0.67)
L-**15a**	CO_2^-	OH	0.1 M KOH in MeOH	267 (110)	271 (−0.27) 267 (+0.36)
L-**15a**	CO_2H	OH	H_2O		269 (−0.39) 265 (+0.25)
L-**15a**[d]	CO_2H	OH	H_2O	269 (100)	263 (+1.0)
L-**15a**	CO_2H	OH	MeOH	267 (94)	270 (−0.39) 265 (+0.36)
L-**15a**[e]	CO_2H	OH	MeOH	268	269 (−3.0)
L-**15a**	CO_2H	OH	THF		271 (−0.21) 267 (+0.67)
L-**15b**[d]	CO_2CH_3	OH	H_2O		264 (+1.0)
L-**15b**[d]	CO_2CH_3	OH	MeOH		266 (+0.76)
L-**15b**[e]	CO_2CH_3	OH	hexane	268[f]	269 (−2.1)

[a] Complete EA and CD spectral data given in ref 30 or as otherwise noted. [b] Molar absorptivity. [c] Molar dichroic absorption. [d] Complete spectral data given in ref 55. [e] Complete spectral data given in ref 62. [f] In EPA at −185 °C.

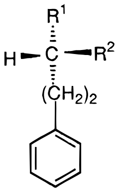
CEs,[55] but in hexane, their sign was reported as negative,[62] the sign reversal suggesting the dominance of (+)-**12b** in the hydrogen bonding solvents, and an increased amount of (−)-**12a** in hexane.

5. *γ-Phenylalkylamines, γ-Phenylalkylamine Salts, and γ-Phenylalkyl Alcohols*

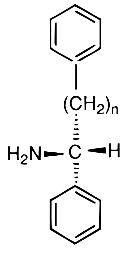
The ORD and CD of only a very small number of *γ*-phenylalkylamines and *γ*-phenylalkyl alcohols [(*S*)-**16a** and **b** and (*R*)-**16c**] have been reported.[83,84,86] In the ORD of (*S*)-α-methyl-*γ*-phenylpropylamine [(*S*)-**16a**], its hydrochloride salt [(*S*)-**16a**·HCl], and (*R*)-α-methyl-*γ*-phenylpropyl alcohol [(*S*)-**16b**] in methanol no ^1L_b CE was detected, and only plain positive ORD curves were observed from 230 to 400 nm.[83] These results are not unexpected considering great conformational mobility of the ethylene group separating the chiral center from the benzene chromophore. In the CD spectrum of (*R*)-α-cyclohexyl-*γ*-phenylpropylamine [(*R*)-**16c**] in cyclohexane a positive ^1L_b band origin CE at 270 nm ($\Delta\epsilon$ +0.03) is associated with the band origin of the ^1L_b band centered at about 262 nm.[86] The sign of this CE cannot, on the basis of the benzene sector rule, be related to the absolute configuration of [(*R*)-**16c**] because of the difficulty in the conformational analysis of the alkyl group incorporating the chiral center.

6. *α,β- and α,γ-Diphenylalkylamines*

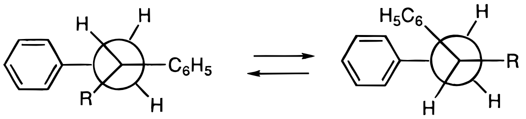
The EA and CD spectra of (*R*)-α,*β*-diphenylethylamine [(*R*)-**17a**], its hydrochloride [(*R*)**17a**·HCl], and (*R*)-α,*γ*-diphenylpropylamine [(*R*)-**17b**] were reported (Table 11),[40,86] and the sign of the observed ^1L_b CEs can be related to their absolute configuration using the benzene sector rule. The negative ^1L_b CEs shown by (*R*)-**17a** in cyclohexane[86] follows from the preferred conformation of the benzene chromophore α to the chiral center (Table 2) in which the hydrogen atom at the chiral center eclipses the plane of the benzene ring. The benzene chromophore *β* to the chiral center may also contribute to the negative sign for the ^1L_b CEs since conformer (−)-**18a** of (*R*)-**17a** in the nonpolar solvent cyclohexane is rotationally more important as compared to (+)-**18a**, both the mole fractions and rotational strengths of (−)-**18a** and (+)-**18a** coming into play.



(*S*)-**16a**, R^1 = CH_3; R^2 = NH_2
b, R^1 = CH_3; R^2 = OH
(*R*)-**16c**, R^1 = C_6H_{11}-*c*; R^2 = NH_2



(*R*)-**17a**, n = 1
b, n = 2



(-)-**18a**, R = NH_2
b, R = N^+H_3

(+)-**18a**, R = NH_2
b, R = N^+H_3

For (*R*)-α,*β*-diphenylethylamine hydrochloride [(*R*)-**17a**·HCl] in 2-propanol, the negative ^1L_b CEs[40] with the band origin at 267 nm are due to the preferred conformer of benzene ring about its attachment bond (Table 2). For (*R*)-**17a**·HCl in the hydrogen-bonding solvent 2-propanol, the equilibrium between conformer (−)-**18b** and (+)-**18b** is shifted from (−)-**18a** toward (+)-**18b**, and the latter is now detected as a positive ^1L_b CE at 270 nm.

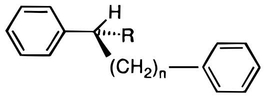
In CD spectrum of (*R*)-α,*γ*-diphenylpropylamine [(*R*)-**17b**] in cyclohexane, the negative ^1L_b CEs are the result of dominant contribution of the preferred conformer of the chiral center contiguous to the benzene ring about its attachment bond, the benzene chromophore *γ* to the chiral center being too remote to make any significant rotatory contribution to the ^1L_b CEs.

B. Ring-Monosubstituted Benzene Compounds

1. *Phenylcarbinamines and Phenylcarbinols*

As discussed above in connection with the benzene chirality rule in section III.C, for chiral phenylcar-

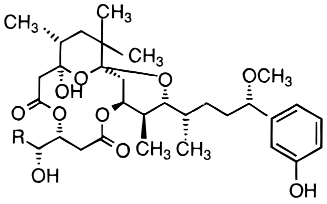
Table 11. ^1L_b Band Origin Maxima for α,β- and α,γ-Diphenylalkylamines



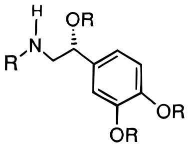
solute	R	n	solvent	EA: λ, nm (ε[a])	CD: λ, nm (Δε[b] × 10^2)	ref[c]
(*R*)-**17a**	NH_2	1	cyclohexane	268 (314)	269−268 (−22.5)	86
(*R*)-**17a**·HCl	N^+H_3	1	*i*-PrOH	267 (190)	270 (+1.8) 267 (−20)	40
(*R*)-**17b**	NH_2	2	cyclohexane	267 (251)	269−268 (−9)	86

[a] Molar absorptivity. [b] Molar dichroic absorption. [c] Report giving complete EA and CD spectral data.

binamines, phenylcarbinamine salts, and phenylcarbinols with an additional benzene ring substituent, an induced rotatory contribution influences the sign of the ^1L_b CEs, and the sign may be the same or different from that of the unsubstituted parent. Any sign reversal results from the overshadowing of the vibronic rotational contribution by an induced vibrational contribution, the sign of the latter depending on the spectroscopic moment and ring position of the substituent (Table 5). If the vibronic and induced contributions have the same sign, the sign of the ^1L_b CEs for a particular ring-substituted chiral benzene compound can be predicted with certainty. Thus the chiral center contiguous to the benzene ring in oscillatoxin A (**19a**) and debromoaplysiatoxin (**19b**), both **19a** and **b** showing positive L_b CEs, can be confirmed as having the *S* configuration.[90] This configurational assignment was originally made on the unjustified assumption that if **19a** and **b** had the same generic configuration as (*R*)-(−)-noradrenaline hydrochloride [(*R*)-**20a**·HCl] and (*R*)-(−)-calipamine hydrochloride [(*R*)-**20b**·HCl],[90] **19a** and **b** would have the same sign as the ^1L_b CEs of (*R*)-**20a**·HCl and (*R*)-**20b**·HCl. For the configuration shown in **19a** and **b**, the benzene sector rule predicts a positive vibronic contribution to the ^1L_b CEs. Since the spectroscopic moment of a hydroxyl group is positive,[26,27] the induced rotatory contribution for a group with a positive spectroscopic moment in the meta position is also positive (Table 5), and the *S* absolute configuration can thus be unambiguously assigned to the carbinol chiral center in **19a** and **b** on the basis of their positive ^1L_b CEs. Likewise, the levorotatory isomers of phenylephrine (**21a**) and its hydrochloride (**21a**·HCl) were also assigned the *R* absolute configuration because of the similarity of their ORD curves to that of (−)-adrenaline hydrochloride [(*R*)-**21b**·HCl].[91] By using the benzene sector and benzene chirality rules, both (*R*)-**21a** and (*R*)-**21a**·HCl are predicted to show positive ^1L_b CEs.

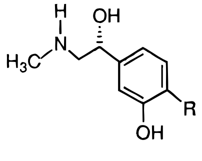


19a, R = H
b, R = CH_3

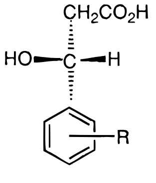


(*R*)-**20a**, R = H
b, R = CH_3

As was also discussed above, when the vibronic and induced contributions to the ^1L_b CEs are of opposite sign, a prediction as to the sign of the ^1L_b CEs shown by a particular enantiomer is somewhat ambiguous. However, all of the phenylalkylcarbinamines and phenylalkylcarbinols so far reported that are ortho or para-substituted with an atom or group with a positive spectroscopic moment show ^1L_b CEs of opposite sign to that of their unsubstituted parents,[28,31,37,45,50,57,62,65,78−81] including ortho- and para-substituted (*R*)-β-hydroxy-β-phenylpropionic acid [(*R*)-**22** , R = F, Cl, or Br].[79] For the phenylalkylcarbinamines and carbinols with a group with a negative spectroscopic moment (CN and CF_3) in the meta position, however, the sign of the ^1L_b CEs is not changed from that of the unsubstituted parent.[31]



(*R*)-**21a**, R = H
b, R = OH



(*R*)-**22**, R = *o*- and *p*-F, Cl, or Br

2. Mandelic Acids

The CD spectra of (*S*)-mandelic acid[59] [(*S*)-**6d**] and sodium (*S*)-mandelate[59] [(*S*)-**7d**] fix the vibronic contributions of the carboxyl and carboxylate groups above that of the hydroxyl group in the sequence for the vibronic contribution to the ^1L_b CEs (Table 3). A similar spectrum for methyl (*S*)-mandelate[60] [(*S*)-**8d**] shows that an alkoxycarbonyl group also gives a greater vibronic contribution to the ^1L_b CEs than does a hydroxyl group. The CD spectra of various ortho-, meta-, and para-substituted fluoro, chloro, bromo, and methoxyl derivatives of one or the other enantiomers of mandelic acid[59,62,66,80,92] (**6d**) and of methyl mandelate[62] (**8d**) have also been reported. The absolute configurations of these derivatives were established by various methods other than circular dichroism and are also correlated with the sign of the ^1L_b CEs by application of the benzene sector and benzene chirality rules.[59] When one of these substituents, each with a positive spectroscopic moment,

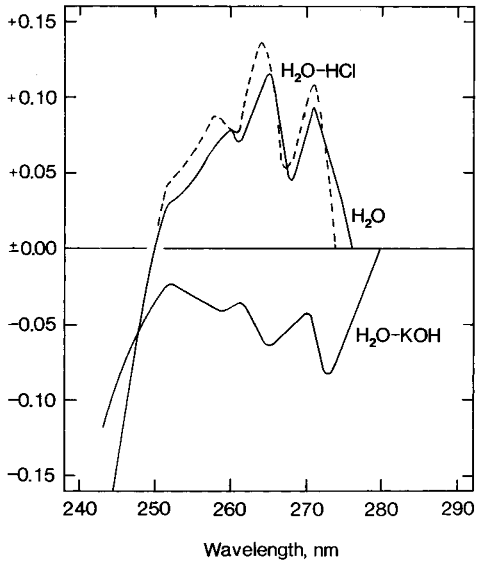
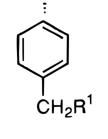


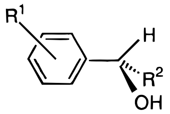
Figure 13. Circular dichroism spectra of *p*-(aminomethyl)mandelic acid [(*R*)-**23a**] in water (H_2O) and in water with added excess hydrochloric acid (H_2O−HCl) to give *p*-(aminomethyl)mandelic acid hydrochloride [(*R*)-**23b**] or aqueous potassium hydroxide (H_2O−KOH) to give potassium *p*-(aminomethyl)mandelate (*R*)-**23c**. Reprinted from *J. Org. Chem.* **1991**, *56*, 2322. Copyright 1991 American Chemical Society.

is in the meta position both the vibronic and the induced contribution to the ^1L_b CEs have the same sign, and the sign of the ^1L_b CEs is the same as the unsubstituted parent carboxylic acid. For the ortho- and para-substituted derivatives, when the sign of the induced contribution is opposite to and the magnitude is greater than that of the vibronic contribution, the sign of the ^1L_b CEs is opposite to that of the CEs of the corresponding unsubstituted acid. Thus application of the benzene sector and benzene chirality rules may be used to explain the sign of the ^1L_b CEs of (*R*)-*p*-(aminomethyl)mandelic acid [(*R*)-**23a**)] in water and aqueous hydrochloric acid or potassium hydroxide (Figure 13).[59] In water, (*R*)-*p*-(aminomethyl)mandelic acid exists as the zwitterion (*R*)-**23a**, and the para substituent has a negative spectroscopic moment. Since the benzene sector rule predicts a positive vibronic contribution to the ^1L_b CEs, the induced contribution by the *p*-ammoniomethyl group ($^+NH_3CH_2$) is also positive, and the ^1L_b CEs are positive. Addition of an excess hydrochloric acid protonates the carboxylate group [(*R*)-**23b**]. Both the vibronic and the induced contributions to the ^1L_b CEs are still positive, and, as expected, the CD spectra for (*R*)-**23a** and **b** are very similar. Addition of potassium hydroxide gives potassium *p*-(aminomethyl)mandelate [(*R*)-**23c**], and the ^1L_b CEs are now negative (Figure 13). These negative ^1L_b CEs are the result of the strong negative induced rotatory contribution of the *p*-aminomethyl group. It should be noted that the spectroscopic moment of the aminomethyl group (NH_2CH_2) was given earlier as negative[27] but subsequent examination of the electronic absorption spectra of toluene, benzylamine, and *p*-(aminomethyl)toluene and the hydrochloride salts of the latter two amines clearly shows that although the spectroscopic moment of the ammoniomethyl group is negative that of the aminomethyl group is positive.[59]



(*R*)-**23a**, $R^1 = N^+H_3$; $R^2 = CO_2^-$
b, $R^1 = NH_3Cl$; $R^2 = CO_2H$
c, $R^1 = NH_2$; $R^2 = CO_2K$

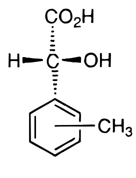
Table 12. ^1L_b Band Origin Maxima for (*R*)-Mandelic Acids and Their Potassium Salts in Methanol[a]



		(*R*)-**6d**, (*R*)-**24**, $R^2 = CO_2H$		(*R*)-**7d**, (*R*)-**25**, $R^2 = CO_2K$[b]	
R^1	solute	EA: λ, nm (ϵ[c])	CD: λ, nm (Δϵ[d] × 10^2)	EA: λ, mn (ϵ[c])	CD: λ, nm (Δϵ[d] × 10^2)
H	(*R*)-**6d**	267 (79)	269 (+6.7)	268 (75)	268 (+2.4)
o-CH_3	(*R*)-**24a**	273 (280)	275 (−3.6)	273 (250)	273 (+4.5)
m-CH_3[e]	(*R*)-**24b**	272 (340)	274 (+14)	273 (290)	274 (+20)
p-CH_3[e]	(*R*)-**24c**	273 (160)	273 (−18)	273 (240)	274 (−27)

[a] Complete EA and CD spectral data given in ref 59. [b] Formed in situ by the addition of two drops of 10% KOH to the sample cell. [c] Molar absorptivity. [d] Molar dichroic absorption. [e] Enantiomer used.

The CD observations for (*R*)-*o*-, (*R*)-*m*-, and (*R*)-*p*-methylmandelic acid [(*R*)-**24a**−**c**] and their potassium salts [(*R*)-**25a**−**c**] are summarized in Table 12 and are compared with similar data for (*R*)-mandelic acid [(*R*)-**6d**] and its potassium salt [(*R*)-**7b**]. This comparison underscores the point made earlier that when the sign of both the vibronic and induced contributions to the ^1L_b CEs is the same then the sign of the ^1L_b CEs can be predicted with certainty and, as predicted, that of (*R*)-*m*-methylmandelic acid [(*R*)-**24b**] and its potassium salt (*R*)-**25b** is the same as that of their unsubstituted parents (*R*)-mandelic acid [(*R*)-**6d**] and its potassium salt (*R*)-**7d**. If the vibronic and induced contributions to the ^1L_b CEs are of opposite sign, a prediction as to the sign of the ^1L_b CEs shown by a particular enantiomer is somewhat ambiguous. As shown in Table 12, for the *o*- and *p*-methyl-substituted mandelic acids [(*R*)-**24a** and **c**], the positive spectroscopic moment of the methyl group induces a strong negative contribution to the ^1L_b CEs which overshadows the positive vibronic contribution, and the sign of the ^1L_b CEs of both (*R*)-



(*R*)-**24a**, ortho
b, meta
c, para

24a and **c** is negative, opposite to that of (*R*)-mandelic acid [(*R*)-**6d**]. A similar interpretation is made of the CD spectra of potassium (*R*)-*p*-methylmandelate [(*R*)-**25c**], the latter having negative ^1L_b CEs, also opposite in sign to those of (*R*)-**6d**. The ^1L_b CEs of potassium (*R*)-*o*-methylmandelate [(*R*)-**25a**], however, have the same sign as that of potassium (*R*)-mandelate [(*R*)-**7d**] itself, and, as discussed in detail in section IV.F.1, it is concluded that the positive vibronic contribution to the ^1L_b CEs is still dominant and not overshadowed by the negative induced contribution of the ortho methyl group.

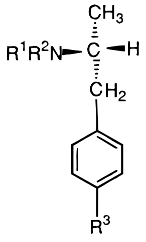
3. 2-Phenyl and 2-(3-Pyridyl) Heterocyclic Amines

As shown in Table 13, the circular dichroism has been reported for the enantiomers of a number of unsubstituted and ring-substituted analogues of (*S*)-α-phenylethylamine [(*S*)-**1a**] in which the amino group is part of a heterocyclic ring. For (*S*)-*N*-methyl-2-phenylpyrrolidine [(*S*)-**26a**] the preferred conformation of the heterocyclic ring about its attachment bond to the benzene ring is such that the tertiary amino group and the C-3 methylene group are in the same disposition with respect to the benzene ring plane as are the amino and methyl group in (*S*)-α-phenylethylamine [(*S*)-**1a**], the hydrogen atom at the chiral center eclipsing the benzene ring plane. On this basis the sign of the ^1L_b CEs are predicted to be positive as is observed (Table 13). On substitution of the benzene ring of (*S*)-**26a** and **b** with a methyl group at the ortho position, it can be safely assumed that the preferred conformation is such that the hydrogen atom at the chiral center still eclipses the benzene ring plane.[65,68] On this basis, the sign of the ^1L_b CEs for both (*S*)-*N*-methyl-2-(*o*-methylphenyl)pyrrolidine [(*S*)-**26c**] and (*S*)-*N*-methyl-2-(*o*-methylphenyl)piperidine [(*S*)-**26d**] are predicted and are observed to be negative (Table 13), the methyl group causing a negative induced contribution to the ^1L_b CEs which overshadows the positive vibronic contribution.

A similar analysis explains the negative ^1L_b CEs for (*S*)-nornicotine [(*S*)-**27a**], (*S*)-nicotine [(*S*)-**27c**], (*S*)-anabasine [(*S*)-**27b**], and (*S*)-*N*-methylanabasine [(*S*)-**27d**] (Table 13). In each of these (*S*)-3-pyridyl analogues of (*S*)-**1a**, the amino and methyl groups have dispositions with respect to the aromatic ring as that in (*S*)-**1a**. This conformation results in a positive vibronic contribution to the ^1L_b CEs which is overshadowed by a negative induced contribution by the aza group (Table 5) with a negative spectroscopic moment. Thus the observed ^1L_b CEs for (*S*)-**27a**−**d** are all negative.[95]

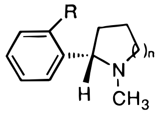
4. Benzylcarbinamines and Benzylcarbinamine Salts

In Table 14 are shown the EA and CD ^1L_b band origin maxima for a number of benzene ring-substituted benzylcarbinamines and benzylcarbinamine salts in various solvents. Conformational structures **28a** and **b** at the top of the table give the respective signs for the vibronic contribution to their ^1L_b CEs, negative and positive, respectively. As shown in Figure 14 for the EA and CD spectra of (*S*)-2-amino-1-(*p*-chlorophenyl)propane (*S*)-**29a** in methanol [(*S*)-**29a**·HCl in 0.1 M methanolic potassium hydroxide], only electronic transitions to totally symmetric vibrational states are observed, and for (*S*)-**29a**, positive CEs are associated with each of these transitions. It can be assumed that the conformational equilibrium for (*R*)-**29a** in methanol and its hydrochloride (*R*)-**29a**·HCl in methanol and water is similar that of (*R*)-2-amino-1-phenylpropane [(*R*)-**11a**] in methanol and its hydrochloride (*R*)-**11a**·HCl in methanol and water with conformer (−)-**28a** (Table 14) and (−)-**12a** (Table 8), giving the sign to the ^1L_b CEs. Since the negative sign of the ^1L_b CEs for (*R*)-**29a** in methanol is the same as that of the unsubstituted parent (*R*)-**11a** (Table 8) in methanol, the induced rotational contribution for (*R*)-**29a**, predicted to be opposite to that of the vibronic contribution on the basis of the

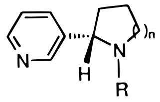


(*R*)-**29a**, $R^1 = R^2 = H$; $R^3 = Cl$
b, $R^1 = R^2 = H$; $R^3 = CF_3$
c, $R^1 = R^2 = H$; $R^3 = NH_2$
d, $R^1 = CH_3$; $R^2 = H$; $R^3 = Cl$
e, $R^1 = R^2 = CH_3$; $R^3 = Cl$

Table 13. ^1L_b Band Origin Maxima for 2-Phenyl and 2-(3-Pyridyl) Heterocyclic Amines



(*S*)-**26**

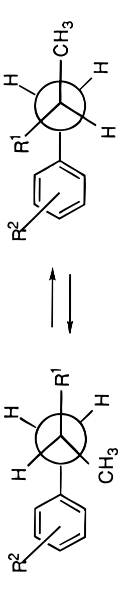


(*S*)-**27**

cmpd	*n*	R	CD: λ, nm (Δε[a] × 10^2)	ref[b]	cmpd	*n*	R	CD: λ, nm (Δε[a] × 10^2)	ref[c]
(*S*)-**26a**	1	H	266 (+3.0)	93	(*S*)-**27a**	1	H	263 (−100)	95
(*S*)-**26b**	2	H	273 (+7.9)	94	(*S*)-**27b**	2	H	266 (−52)	95
(*S*)-**26c**	1	CH_3	270 (−5.2)	93	(*S*)-**27c**	1	CH_3	263 (−110)	95
(*S*)-**26d**	2	CH_3	273 (−2.7)	94	(*S*)-**27d**	2	CH_3	266 (−100)	95

[a] Molar dichroic absorption. [b] Report giving complete CD spectral data. Cyclohexane as the solvent. [c] Report giving complete CD spectral data. Sodium phosphate buffer as the solvent.

Table 14. ^1L_b **Band Origin Maxima for Ring-Substituted (*R*)-Benzylmethylcarbinamines and Their Hydrochlorides**[a]



(−)-28a (+)-28b

neutral nitrogen				positive nitrogen			
solute	substituents	solvent	λ, nm (ϵ^b) [λ, nm ($\Delta\epsilon^c \times 10^2$)]	solute	substituents	solvent	λ, nm (ϵ^b) [λ, nm ($\Delta\epsilon^c \times 10^2$)]
(*R*)-**29a**·HCl[d]	$R^1 = NH_2$, $R^2 = p$-Cl	0.1 M KOH in MeOH	276 (320) [277 (−4.8)]	(*R*)-**29a**·HCl[d]	$R^1 = N^+H_3$, $R^2 = p$-Cl	H_2O	[CD too weak to be significant]
(*R*)-**29a**[d,e]	$R^1 = NH_2$, $R^2 = p$-Cl	cyclohexane	277 (420) [278 (−7.9)]	(*R*)-**29a**·HCl[d]	$R^1 = N^+H_3$, $R^2 = p$-Cl	MeOH	275 (240) [275 (−1.1)]
(*R*)-**29b**[e]	$R^1 = NH_2$, $R^2 = p$-CF_3	MeOH	269 (210) [269 (+2.0)]	(*R*)-**29b**·HCl[e]	$R^1 = N^+H_3$, $R^2 = p$-CF_3	MeOH	269 (310) [270 (−0.64)]
(*R*)-**29b**[e]	$R^1 = NH_2$, $R_2 = p$-CF_3	cyclohexane	269 (160) [269 (+3.9)]	(*R*)-**29c**·2 HCl[d,f]	$R^1 = N^+H_3$, $R^2 = p$-N^+H_3	dil HCl in MeOH	268 (120) [268 (−4.2)]
(*R*)-**29e**·HCl	$R^1 = N(CH_3)_2$, $R^2 = p$-Cl	0.1 M KOH in MeOH	276 (310) [277 (−7.6)]	(*R*)-**29d**·HCl[d,g]	$R^1 = N^+H_2CH_3$, $R^2 = p$-Cl	MeOH	276 (230) [277 (−4.5)]
(*R*)-**29e**[d,e]	$R^1 = N(CH_3)_2$, $R^2 = p$-Cl	cyclohexane	280 (270)[h] [282 (−15)]	(*R*)-**29e**·HCl[d,g]	$R^1 = N^+H(CH_3)_2$, $R^2 = p$-Cl	MeOH	276 (230) [277 (−3.6)]
(*R*)-**30a**·HCl	$R^1 = NH_2$, $R^2 = m$-Cl	0.1 M KOH in MeOH	274 (240) [275 (−1.7)]	(*R*)-**30a**·HCl	$R^1 = N^+H_3$, $R^2 = m$-Cl	H_2O	[273 (−2.9)]
(*R*)-**30c**·HCl	$R^1 = N(CH_3)_2$, $R^2 = m$-Cl	0.1 M KOH in MeOH	274 (240) [273 (−6.1)]	(*R*)-**30a**·HCl	$R^1 = N^+H_3$, $R^2 = m$-Cl	MeOH	274 (200) [274 (−4.5)]
(*R*)-**31**·HCl	$R^1 = NH_2$, $R^2 = o$-Cl	0.1 M KOH in MeOH	273 (190) [276 (−0.82)]	(*R*)-**30b**·HCl[d,g]	$R^1 = N^+H_2CH_3$, $R^2 = m$-Cl	MeOH	274 (220) [275 (−7.3)]
				(*R*)-**30c**·HCl	$R^1 = N^+H(CH_3)_2$, $R^2 = m$-Cl	MeOH	274 (210) [274 (−6.6)]
				(*R*)-**31**·HCl	$R^1 = N^+H_3$, $R^2 = o$-Cl	H_2O	[CD too weak to be significant]
				(*R*)-**31**·HCl	$R^1 = N^+H_3$, $R^2 = o$-Cl	MeOH	273 (150) [273 (+1.7)]

[a] Complete EA and CD spectral data given in ref 23 or as otherwise noted. [b] Molar absorptivity. [c] Molar dichroic absorption. [d] Enantiomer used. [e] Complete EA and CD spectral data given in ref 45. [f] Complete EA and CD spectral data given in ref 28. [g] Complete EA and CD spectral data given in ref 96. [h] Shoulder.

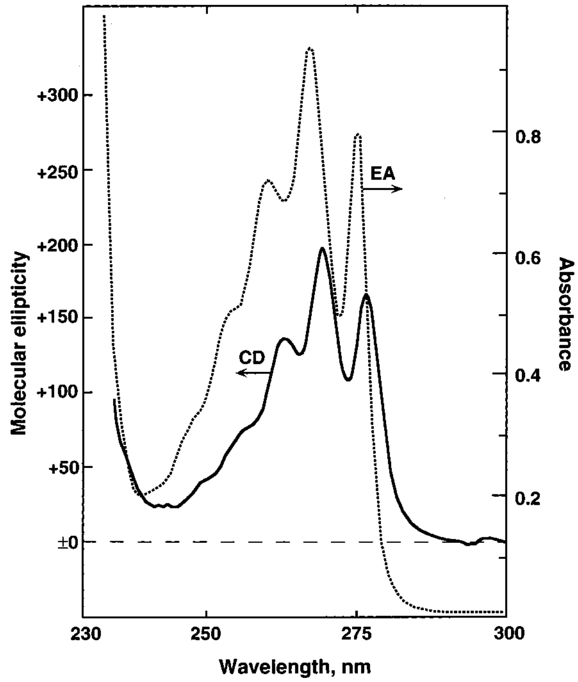


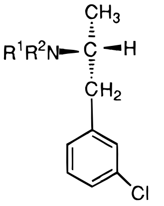
Figure 14. Electronic absorption (EA) and circular dichroism (CD) spectra of (*S*)-2-amino-1-(*p*-chlorophenyl)propane [(*S*)-**29a**] in 0.1 M methanolic potassium hydroxide. Reprinted from *J. Am. Chem. Soc.* **1997**, *119*, 116. Copyright 1997 American Chemical Society.

benzene chirality rule (Table 5), must be small compared to that of the vibronic contribution. Thus an induced contribution to the ^1L_b CEs need not be considered when predicting the sign of these CEs of chiral ring-substituted benzylcarbin-amines and benzylcarbinamine salts. Since (*R*)-**29a** in cyclohexane shows negative ^1L_b CEs whereas for (*R*)-**11a** in cyclohexane these CEs are positive, the *p*-chloro substituent in (*R*)-**29a** results in additional stabilization of conformer (−)-**28a** compared to (+)-**28b**, perhaps as a result of the positive field (σ_I) effect but a negative resonance (σ^0_R) effect of the *p*-chloro substituent.[97] On the other hand, (*R*)-2-amino-1-(*p*-trifluoromethylphenyl)propane [(*R*)-**29b**] in both methanol and cyclohexane shows positive ^1L_b CEs, the *p*-trifluoromethyl group with only a positive field effect[97] stabilizing conformer (+)-**28a** compared to (−)-**28b**. For *N*,*N*-dimethyl-2-amino-1-(*p*-chlorophenyl)propane [(*R*)-**29e**], the greater effective bulk size of the dimethylamino group, determines the sign of the observed negative ^1L_b CEs in both methanol and cyclohexane.

(*R*)-2-amino-1-(*p*-chlorophenyl)propane hydrochloride [(*R*)-**29a**·HCl] in water gave a CD spectrum too weak to be significant, but in methanol, its CD spectrum has the same sign as that of (*R*)-**11a**·HCl in methanol. The ^1L_b CEs for (*R*)-**29b**, as discussed above, are positive, but protonation of the amino group in (*R*)-**29b** shifts the conformational equilibrium from (+)-**28b** toward (−)-**28a** so that the observed ^1L_b CEs for (*R*)-**29b**·HCl in methanol are now negative.[45] As expected, the hydrochloride salts (*R*)-**29c**·2 HCl, (*R*)-**29d**·HCl, and (*R*)-**29e**·HCl show negative ^1L_b CEs in methanol.[28,96]

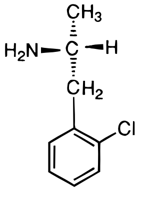
As also shown in Table 14, (*R*)-2-amino-1-(*m*-chlorophenyl)propane in methanol [(*R*)-**30a**·HCl in

0.1 M KOH in MeOH], its hydrochloride [(*R*)-**30a**·HCl] in water and methanol, *N*,*N*-dimethyl-2-amino-1-(*m*-chlorophenyl)propane in methanol [(*R*)-**30c**·HCl in 0.1 M KOH in MeOH], and the corresponding *N*-methyl and *N*,*N*-dimethyl hydrochlorides [(*R*)-**30b**·HCl and (*R*)-**30c**·HCl] in methanol all show negative ^1L_b CEs. As in the EA spectrum of (*S*)-2-amino-1-(*p*-chlorophenyl)propane [(*S*)-**30a**] in methanol (Figure 14), the EA spectra of the *m*-chloro-substituted compounds only show ^1L_b transitions to totally symmetric vibrational modes and a CE is associated with each of these transitions. Since the benzene chirality rule would predict an induced rotatory contribution of the same sign as that of the vibronic contribution to the ^1L_b CEs and since conformer (−)-**28a** is expected to dominate the CD for these compounds, the *m*-chloro-substituted compounds are predicted, as is observed, to display negative ^1L_b CEs in water and methanol.



(*R*)-**30a**, R^1 = R^2 = H
b, R^1 = CH$_3$; R^2 = H
c, R^1 = R^2 = CH$_3$

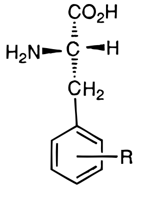
The CD spectrum of (*R*)-2-amino-1-(*o*-chlorophenyl)propane in methanol [(*R*)-**31**·HCl in 0.1 M KOH in MeOH, Table 14] also shows negative ^1L_b CEs, as predicted on the basis of the benzene sector rule and assuming an insignificant induced rotational contribution. For the hydrochloride [(*R*)-**31**·HCl] in water, the conformational equilibrium is shifted from (−)-**28a** toward (+)-**28b**, possibly by way of weak hydrogen bonding between the ammonium group and the *o*-chloro substituent, so that in the CD spectrum of (*R*)-**31**·HCl the CD maxima were too weak to be significant. For the hydrochloride in methanol, the equilibrium is shifted even more toward (+)-**28b**, and the ^1L_b CEs are now positive.



(*R*)-**31**

5. L-Phenylalanines

The CD spectra of L-*p*-chloro- and L-*p*-iodophenylalanine (L-**32a** and **b**) in water and methanol and L-**32a**·HCl and L-*p*-aminophenylalanine dihydrochloride (L-**32c**·2 HCl) in water (L-**32c** in 1 M HCl in H_2O) (Table 15) are similar to those of L-phenylalanine (L-**13a**) in water (Table 9), all showing strong positive ^1L_b CEs as a result of a larger rotational contribution by (+)-**33b** and (+)-**12b** as compared to (−)-**33a** and (−)-**12a** in these solvents. As discussed above, L-**13a** in methanol shows both negative and positive CEs due to a larger amount of conformer (−)-**12a** in methanol. For the sodium salt of L-**32a** in water (L-**32a** in 1 M NaOH in H_2O), the ^1L_b CEs are positive, but the potassium salt of L-**32a** in methanol also shows a weak negative CE at 279 nm (Figure 15) as the longer wavelength component of a double CE[89] associated with the ^1L_b band origin. This CD maximum is the result of a bathochromic shift of the ^1L_b band origin caused by the carboxyl group gauche to the benzene ring in conformer (−)-**33a**.[23,30]



L-**32a**, R = *p*-Cl
b, R = *p*-I
c, R = *p*-NH$_2$
d, R = *o*-Cl

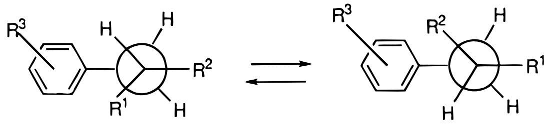
For L-*o*-chlorophenylalanine (L-**32d**) and its hydrochloride (L-**32d**·HCl) in water and methanol, the intense ^1L_b CEs are negative, the result of a shift in the conformational equilibrium from (+)-**33b** toward (−)-**33a**, due to an interaction of the carboxyl and carboxylate groups with the *o*-chloro substituent, both the increased mole fraction of (−)-**33a** and the greater rotatory contribution of the carboxyl and carboxylate groups as compared to those of the ammonium and amino group coming into play.[29] Note, however, that L-**32d**·HCl in methanol still shows a weak positive ^1L_b CE at 272 nm as the result of the presence of conformer (+)-**33b**.

6. Benzylcarbinamines with Attached Groups with Lone-Pair Electrons

When an atom having a lone pair of electrons is attached to a benzene ring, the atom can donate a lone pair of electrons to the ring, and this delocalization (resonance) shifts the position of the ^1L_b band to a longer wavelength and increases its intensity.[33] Thus L-tyrosine (L-**34a**) (Figure 16 and Table 16) in water and *O*-methyl-L-tyrosine (L-**34b**) in water and methanol show an intense ^1L_b absorption band with a maximum at about 274 nm but without vibrational fine structure. A strong positive CD maximum is associated with this transition, suggesting that as a result of the greater effective size of a carboxylate group as compared to that of an ammonium group, conformer (+)-**35b** (Table 16) being more important than (−)-**35a** in determining the sign of this CE. In contrast to these observations with the para-substituted compounds, L-*m*- and L-*o*-hydroxyphenylalanine in water were both reported to show a negative CD maximum.[98]

A positive ^1L_b CE is also observed for the hydrochloride salt of L-**34a** in water and methanol and the hydrochloride salts of L-*O*-methyltyrosine (L-**34b**·HCl) and methyl L-tyrosinate (L-**34c**) in water (Table 16). The same is true for the sodium and potassium salts of L-**34a**, L-**34b**, and L-**34c** in these same solvents and

Table 15. ^1L_b Band Origin Maxima for Ring-Substituted L-Phenylalanines[a]



(-)-**33a** (+)-**33b**

positive nitrogen				neutral nitrogen			
solute	substituents	solvent	λ, nm (ϵ^b) [λ, nm ($\Delta\epsilon^c \times 10^2$)]	solute	substituents	solvent	λ, nm (ϵ^b) [λ, nm ($\Delta\epsilon^c \times 10^2$)]
L-**32a**	$R^1 = CO_2^-$, $R^2 = N^+H_3$, $R^3 = p$-Cl	H_2O	[275 (+3.9)]	L-**32a**	$R^1 = CO_2^-$, $R^2 = NH_2$, $R^3 = p$-Cl	1 M NaOH in H_2O	[275 (+4.2)]
L-**32a**	$R^1 = CO_2^-$, $R^2 = N^+H_3$, $R^3 = p$-Cl	MeOH	275 (180) [275 (+3.9)]	L-**32a**	$R^1 = CO_2^-$, $R^2 = NH_2$, $R^3 = p$-Cl	0.1 M KOH in MeOH	276 (260) [279 (−0.33)] [275 (+3.0)]
L-**32a**	$R^1 = CO_2H$, $R^2 = N^+H_3$, $R^3 = p$-Cl	1 M HCl in H_2O	[275 (+4.8)]	L-**32d**	$R^1 = CO_2^-$, $R^2 = NH_2$, $R^3 = o$-Cl	1 M NaOH in H_2O	[275 (−1.5)]
L-**32a**	$R^1 = CO_2H$, $R^2 = N^+H_3$, $R^3 = p$-Cl	0.1 M HCl in MeOH	275 (160) [275 (+3.3)]	L-**32d**	$R^1 = CO_2^-$, $R^2 = NH_2$, $R^3 = o$-Cl	0.1 M KOH in MeOH	273 (180) [275 (−2.9)]
L-**32b**	$R^1 = CO_2^-$, $R^2 = N^+H_3$, $R^3 = p$-I	H_2O	277 (320)[d] 278 (+4.5)				
L-**32b**	$R^1 = CO_2^-$, $R^2 = N^+H_3$, $R^3 = p$-I	MeOH	277 (320)[d] [280 (+4.8)]				
L-**32c**	$R^1 = CO_2H$, $R^2 = N^+H_3$, $R^3 = p$-N^+H_3	1 M HCl in H_2O	261 (130)[d] [265 (+0.76)]				
L-**32c**	$R^1 = CO_2H$, $R^2 = N^+H_3$, $R^3 = p$-N^+H_3	0.1 M HCl in MeOH	267 (95) [267 (+1.2)]				
L-**32d**	$R^1 = CO_2^-$, $R^2 = N^+H_3$, $R^3 = o$-Cl	H_2O	[274 (−2.1)]				
L-**32d**	$R^1 = CO_2^-$, $R^2 = N^+H_3$, $R^3 = o$-Cl	MeOH	273 (140) [274 (−1.4)]				
L-**32d**	$R^1 = CO_2H$, $R^2 = N^+H_3$, $R^3 = o$-Cl	1 M HCl in H_2O	[275 (−2.0)]				
L-**32d**	$R^1 = CO_2H$, $R^2 = N^+H_3$, $R^3 = o$-Cl	0.1 M HCl in MeOH	273 (140) [276 (−1.0)] [272 (+0.67)]				

[a] Complete EA and CD spectral data given in ref 23. [b] Molar absorptivity. [c] Molar dichroic absorption. [d] Shoulder.

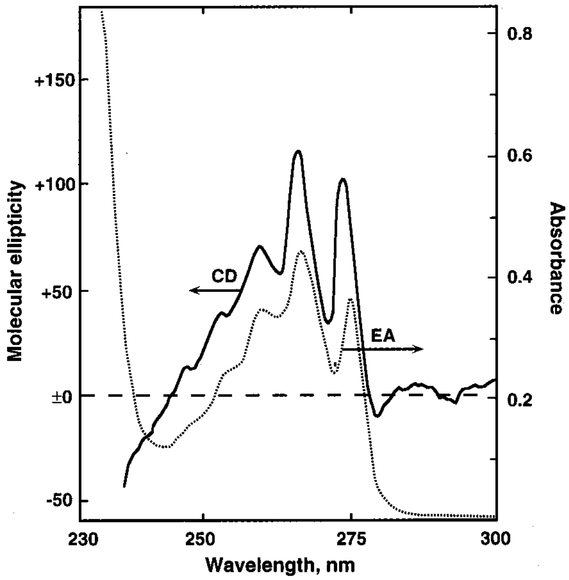


Figure 15. Electronic absorption (EA) and circular dichroism (CD) spectra of L-*p*-chlorophenylalanine (L-**32a**) in 0.1 M potassium hydroxide in methanol. Reprinted from *J. Am. Chem. Soc.* **1997**, *119*, 116. Copyright 1997 American Chemical Society.

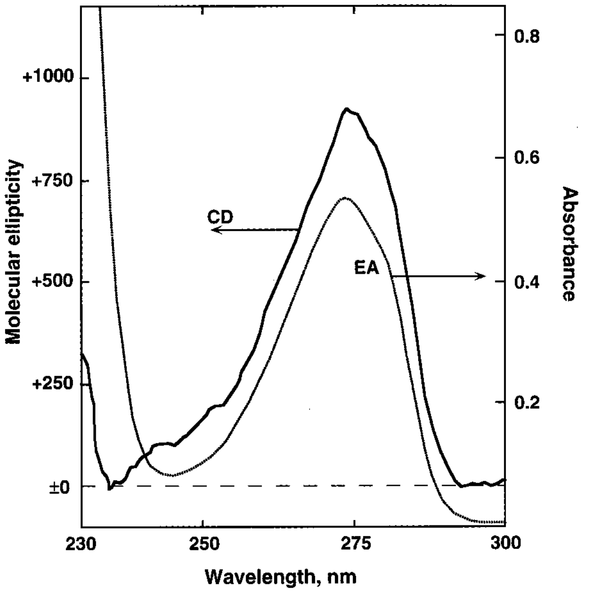
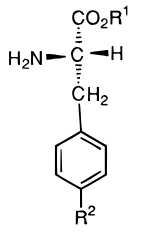


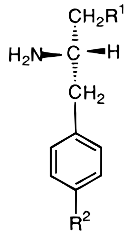
Figure 16. Electronic absorption (EA) and circular dichroism (CD) spectra of L-tyrosine (L-**34a**) in water. Reprinted from *J. Am. Chem. Soc.* **1997**, *119*, 116. Copyright 1997 American Chemical Society.

for L-**34c** in dioxane and tetrahydrofuran. A positive ^1L_b CE is also observed for L-*p*-aminophenylalanine (L-**34d**) in water and methanol, its sodium salt in water, and its potassium salt in methanol, a *p*-amino group having the same effect on the EA and CD spectra as a *p*-hydroxyl, *p*-methoxyl, and *p*-oxyl group.

As shown in Table 17, L-tyrosinol hydrochloride (L-**36a**·HCl), its sodium and potassium salts in water and methanol, and (*R*)-2-amino-1-(*p*-hydroxyphenyl)-propane hydrochloride [(*R*)-**36b**·HCl] and (*R*)-2-amino-1-(*p*-aminophenyl)propane in methanol [(*R*)-**36c**·2HCl in dilute KOH in MeOH] show a negative ^1L_b CE, conformer (−)-**35a** being more important than (+)-**35b** in determining the sign of the CE. Protonation of the two amino groups in (*R*)-**36c** [(*R*)-**29c**·2HCl in dilute HCl in MeOH, Table 14] does not cause a change in the sign of the ^1L_b CE, but does cause a decrease in its intensity and the appearance of vibrational fine structure.



L-**34a**, $R^1 = H$; $R^2 = OH$
b, $R^1 = H$; $R^2 = OCH_3$
c, $R^1 = CH_3$; $R^2 = OH$
d, $R^1 = H$; $R^2 = NH_2$



L-**36a**, $R^1 = OH$; $R^2 = OH$
(*R*)-**36b**, $R^1 = H$; $R^2 = OH$
c, $R^1 = H$; $R^2 = NH_2$

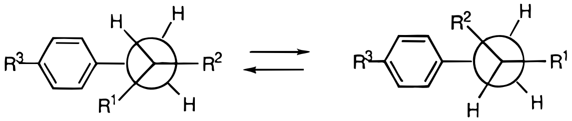
C. Ring-Disubstituted Benzene Compounds

1. 3,5-Disubstituted Phenylcarbinamines and Phenylcarbinols

Examples of 3,5-disubstituted benzene ring-substituted chiral phenylcarbinamines and phenylcarbinols for which the CD spectra are reported are (*R*)-3,5-dimethyl-, 3,5-dichloro-, and (3,5-trifluoromethylphenyl)methylcarbinamine[31,45] [(*R*)-**37a**−**c**], the salts (*R*)-**37a**·HCl and (*R*)-**37b**·HCl, and (*S*)-(3,5-dimethylphenyl)-[(1*R*,3*S*)-1,2,2,3-tetramethylcyclopentyl]carbinol[99] [(*S*)-**38a**] and (*R*)-(3,5-di(trifluoromethylphenyl)methylcarbinol[31] [(*S*)-**38b**], all of these substances showing negative ^1L_b CEs (Table 18). For (*R*)-**37a** and **b** and (*S*)-**38a**, the vibronic contribution to the ^1L_b CEs is negative (Figure 8). Since the alkyl groups and the chloro atom have a positive spectroscopic moment,[26,27] when each is at the 3- and 5-positions of the benzene ring, each makes an induced negative contributions to the ^1L_b CEs (Table 5). Thus the induced negative contribution augments the negative vibronic contribution to the ^1L_b CEs.

Although the spectroscopic moment of the trifluoromethyl group is negative,[26,27] when it is in the 3- and 5-positions it makes a positive induced contribution to the ^1L_b CEs, opposite to that of the vibronic contribution. As discussed in some detail in section III.C, the positive vibronic contribution due to the 3,5-di(trifluoromethyl) groups is less than that of the vibronic contribution, and the ^1L_b CEs for (*R*)-**37c** and (*R*)-**38b** are negative.

Table 16. ^1L_b Absorption Maxima for L-Phenylalanines with Para-Attached Oxygen and Nitrogen Atoms with Lone-Pair Electrons[a]

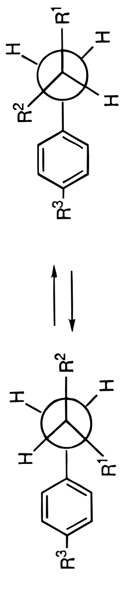


(-)-**35a** (+)-**35b**

positive nitrogen				neutral nitrogen			
solute	substituents	solvent	λ, nm (ϵ^b) [λ, nm ($\Delta\epsilon^c \times 10^2$)]	solute	substituents	solvent	λ, nm (ϵ^b) [λ, nm ($\Delta\epsilon^c \times 10^2$)]
L-**34a**	$R^1 = CO_2^-$, $R^2 = N^+H_3$, $R^3 = OH$	H_2O	274 (1300) [273 (+28)]	L-**34a**	$R^1 = CO_2^-$, $R^2 = NH_2$, $R^3 = O^-$	1 M NaOH in H_2O	292 (2400) [292 (+36)]
L-**34a**	$R^1 = CO_2H$, $R^2 = N^+H_3$, $R^3 = OH$	1M HCl in H_2O	273 (1300) [275 (+30)]	L-**34a**	$R^1 = CO_2^-$, $R^2 = NH_2$, $R^3 = O^-$	0.1 M KOH in MeOH	294 (2400) [293 (+20)]
L-**34a**	$R^1 = CO_2H$, $R^2 = N^+H_3$, $R^3 = OH$	0.1 M HCl in MeOH	277 (1700) [277 (+27)]	L-**34b**	$R^1 = CO_2^-$, $R^2 = NH_2$, $R^3 = OCH_3$	1 M NaOH in H_2O	273 (1300) [274 (+26)]
L-**34b**	$R^1 = CO_2^-$, $R^2 = N^+H_3$, $R^3 = OCH_3$	H_2O	273 (1200) [273 (+27)]	L-**34c**	$R^1 = CO_2CH_3$, $R^2 = NH_2$, $R^3 = OH$	H_2O	274 (1400) [274 (+33)]
L-**34b**	$R^1 = CO_2^-$, $R^2 = N^+H_3$, $R^3 = OCH_3$	MeOH	276 (1500) [276 (+21)]	L-**34c**	$R^1 = CO_2CH_3$, $R^2 = NH_2$, $R^3 = OH$	MeOH	273 (1200) [277 (+18)]
L-**34b**	$R^1 = CO_2H$, $R^2 = N^+H_3$, $R^3 = OCH_3$	1 M HCl in H_2O	273 (1300) [273 (+33)]	L-**34c**	$R^1 = CO_2CH_3$, $R^2 = NH_2$, $R^3 = OH$	dioxane	278 (2000) [275 (+15)]
L-**34c**	$R^1 = CO_2CH_3$, $R^2 = N^+H_3$, $R^3 = OH$	1 M HCl H_2O	273 (1300) [274 (+29)]	L-**34c**	$R^1 = CO_2CH_3$, $R^2 = NH_2$, $R^3 = OH$	THF	278 (1800) [278 (+18)]
L-**34d**[d]	$R^1 = CO_2^-$, $R^2 = N^+H_3$, $R^3 = NH_2$	H_2O	284 (1400) [284 (+24)]	L-**34c**	$R^1 = CO_2CH_3$, $R^2 = NH_2$, $R^3 = O^-$	1 M NaOH in H_2O	293 (2400) [292 (+39)]
L-**34d**[d]	$R^1 = CO_2^-$, $R^2 = N^+H_3$, $R^3 = NH_2$	MeOH	288 (1400) [291 (+21)]	L-**34d**[d]	$R^1 = CO_2^-$, $R^2 = NH_2$, $R^3 = NH_2$	1 M NaOH in H_2O	284 (1400) [285 (+23)]
				L-**34d**[d]	$R^1 = CO_2^-$, $R^2 = NH_2$, $R^3 = NH_2$	0.1 M KOH in MeOH	288 (2200) [287 (+16)]

[a] Complete EA and CD spectral data given in ref 23. [b] Molar absorptivity. [c] Molar dichroic absorption. [d] Also identified as as L-**32c** in Table 15.

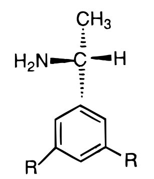
Table 17. ^1L_b Absorption Maxima for L-Phenylalaninols and (*R*)-1-Phenyl-2-aminopropanes with Para-Attached Oxygen and Nitrogen Atoms with Lone-Pair Electrons[a]



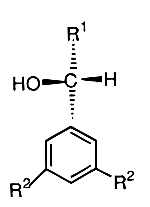
(-)-35a (+)-35b

positive nitrogen				neutral nitrogen			
solute	substituents	solvent	λ, nm (ϵ[b]) [λ, nm ($\Delta\epsilon$[c] × 10^2)]	solute	substituents	solvent	λ, nm (ϵ[b]) [λ, nm ($\Delta\epsilon$[c] × 10^2)]
L-**36a**·HCl	$R^1 = CH_2OH$, $R^2 = N^+H_3$, $R^3 = OH$	H_2O	274 (1400) [274 (−11)]	L-**36a**·HCl	$R^1 = CH_2OH$, $R^2 = NH_2$, $R^3 = O^-$	1 M NaOH in H_2O	293 (2400) [295 (−20)]
L-**36a**·HCl	$R^1 = CH_2OH$, $R^2 = N^+H_3$, $R^3 = OH$	MeOH	275 (1600) [279 (−12)]	L-**36a**·HCl	$R^1 = CH_2OH$, $R^2 = NH_2$, $R^3 = O^-$	0.1 M KOH in MeOH	294 (2300) [294 (−16)]
(*R*)-**36b**·HCl	$R^1 = CH_3$, $R^2 = N^+H_3$, $R^3 = OH$	MeOH	277 (1600) [277 (−11)]	(*R*)-**36c**·2 HCl[d-f]	$R^1 = CH_3$, $R^2 = NH_2$, $R^3 = NH_2$	dilute KOH in MeOH	289 (1500) [289 (−11)]

[a] Complete EA and CD spectral data given in ref 23 or as otherwise noted. [b] Molar absorptivity. [c] Molar dichroic absorption. [d] Enantiomer used. [e] Complete EA and CD spectral data given in ref 28. [f] Also identified as (*S*)-**29c**·2 HCl in Table 14.



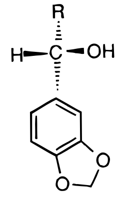
(*R*)-**37a**, R = CH_3
b, R = Cl
c, R = CF_3



(*S*)-**38a**, R^1 = (1*R*,3*S*)-tetramethylcyclopentyl
$R^2 = CH_3$
(*R*)-**38b**, $R^1 = CH_3$; $R^2 = CF_3$

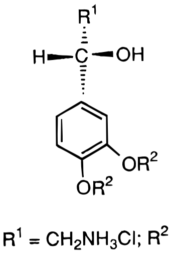
2. 3,4-Disubstituted Phenylcarbinols

For the 3,4-methylenedioxy carbinols (*R*)-**39a**−**c**, the vibronic contribution to the ^1L_b CE is positive, and (*R*)-1-(3,4-methylenedioxyphenyl)ethane-1,2-diol [(*R*)-**39a**] in methanol shows positive ^1L_b CE (Table 19).[80] A negative ^1L_b CE was observed for (*R*)-3,4-methylenedioxymandelic acid [(*R*)-**39b**], and none was observed for (*R*)-methyl 3,4-methylenedioxymandelate (*R*)-**39c**.[80] Since it is unexpected that these structural changes should result in these changes in the ^1L_b CEs for (*R*)-**39b** and **c**, the CD of these mandelic acid derivatives are in need of verification.



(*R*)-**39a**, R = CH_2OH
b, R = CO_2H
c, R = CO_2CH_3

The related 3,4-dihydroxy- and 3,4-dimethoxycarbinamine hydrochlorides (*R*)-**40a**−**e** have preferred conformations such that the vibronic contribution to the ^1L_b CEs is positive and each shows a CD curves with positive ^1L_b CEs. Any induced contribution of the 3,4 -substituents does not change the sign of this CE.

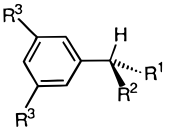


(*R*)-**40a**, $R^1 = CH_2NH_3Cl$; R^2 = H
b, $R^1 = CH_2NH_2CH_3Cl$; R^2 = H
c, $R^1 = CH_2NH_2CH_3Cl$; $R^2 = CH_3$
d, $R^1 = CH(CH_3)NH_3Cl$-(*S*); R^2 = H
e, $R^1 = CH(CH_3)NH_2CH_3Cl$-(*S*); R^2 = H

3. 3,4-Disubstituted Benzylcarbinamines

The CD spectra of only one 3,4-disubstituted benzylcarbinamine, (*S*)-α-(3,4-dimethoxybenzyl)ethylamine [(*S*)-**41**], and its hydrochloride [(*S*)-**41**·HCl] have been reported.[56] For both (*S*)-**41** and (*S*)-**41**·HCl in the hydrogen-bonding solvent 95% EtOH, the sum of the vibronic contribution to the ^1L_b CEs is positive, the rotationally more important conformers are (+)-

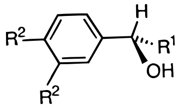
Table 18. ^1L_b Band Origin Maxima for Ring-3,5-Disubstituted Phenylcarbinamines Phenylcarbinols



solute	R^1	R^2	R^3	solvent	EA: λ, nm (ε[a])	CD: λ, nm (Δε[b] × 10^2)	ref[c]
(*R*)-**37a**·HCl	NH_2	CH_3	CH_3	MeOH−NaOH	274 (170)	275 (−26)	45
(*R*)-**37a**·HCl	N^+H_3	CH_3	CH_3	MeOH	275 (370)	275 (−22)	45
(*R*)-**37b**[d]	NH_2	CH_3	Cl	MeOH	278 (140)[e]	280 (−36)	45
(*R*)-**37b**[d]	N^+H_3	CH_3	Cl	10% HCl in H_2O	281 (340)	280 (−20)	45
(*R*)-**37c**[d]	NH_2	CH_3	CF_3	MeOH	272 (320)	271 (−7.6)	31
(*S*)-**38a**	OH	alicyclic[f]	CH_3	isooctane		276 (−102)	99
(*R*)-**38b**	OH	CH_3	CF_3	MeOH	272 (580)	273 (−15)	31

[a] Molar absorptivity. [b] Molar dichroic absorption. [c] Report giving complete EA and CD spectral data. [d] Enantiomer used. [e] Shoulder. [f] (1*R*,3*S*)-1,2,2,3-tetramethylcyclopropyl group.

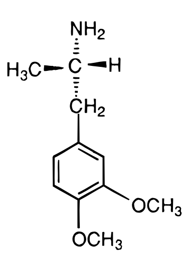
Table 19. ^1L_b Band Maxima for Ring-3,4-Disubstituted Phenylcarbinols



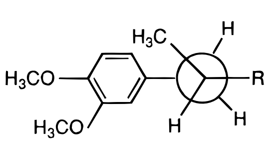
solute	R^1	R^2	solvent	EA: λ, nm (ε[a])	CD: λ nm (Δε[b] × 10^2)	ref[c]
(*R*)-**39a**	CH_2OH	OCH_2O	MeOH		288 (+18.1)	80
(*R*)-**39b**	CO_2H	OCH_2O	MeOH		278−287 (−21.3)	80
(*R*)-**39c**	CO_2CH_3	OCH_2O	MeOH		[not detected]	80
(*R*)-**40a**	$CH_2N^+H_3$	OH	H_2O−HCl	278 (2900)	277 (+8.5)	100
(*R*)-**40b**	$CH_2N^+H_2CH_3$	OH	H_2O−HCl	279 (2900)	277 (+7.3)	100
(*R*)-**40c**[d,e]	$CH_2N^+H_2CH_3$	OCH_3	95% EtOH		281 (+7.9)	61
(*R*)-**40d**	$CH(CH_3)N^+H_3$-(*S*)	OH	H_2O−HCl	278 (2600)	277 (+18)	100
(*R*)-**40e**	$CH(CH_3)N^+H_2CH_3$-(*S*)	OH	H_2O−HCl	279 (2700)	280 (+11)	100

[a] Molar absorptivity. [b] Molar dichroic absorption. [c] Report giving complete EA and CD spectral data. [d] Methoxyl group in place of the hydroxyl group at the chiral center. [e] Absolute configuration assigned on the basis of its CD spectrum.

42a and (+)-**42b**, respectively. Since the chiral center is separated from the benzene chromophore by a methylene group, the groups attached to the chiral center make an insignificant induced contribution to the sign of the ^1L_b CEs. Thus the sign of the observed CE for (*S*)-**41** and (*S*)-**41**·HCl is predicted by application of the benzene sector rule to be positive, and the sign of the observed ^1L_b CEs, without vibrational fine structure, is positive.



(*S*)-**41**

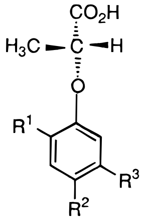


(+)-**42a**, R = NH_2
b, R = N^+H_3

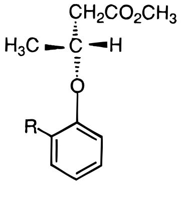
D. Phenoxy and Phenylthio Compounds

1. α-Phenoxypropionic and β-Phenoxybutyric Acids

The circular dichroism of (*R*)-α-phenoxyproprionic acid[101] [(*R*)-**43a**] and methyl (*R*)-β-phenoxybutyrate[102] [(*R*)-**44a**] and some of their ring-substituted derivatives[101−104] have been reported (Table 20). The absolute configuration of (*R*)-**43a** was related chemically to that of D-lactic acid and those of its 2-, 3-, and 4-methoxy and some of their chloro-substituted



(*R*)-**43a**, $R^1 = R^2 = R^3 = H$
b, $R^1 = C(CH_3)_3$; $R^2 = R^3 = H$
c, $R^1 = H$; $R^2 = C(CH_3)_3$; $R^3 = H$
d, $R^1 = R^2 = H$; $R^3 = C(CH_3)_3$
e, $R^1 = H$; $R^2 = Br$; $R^3 = H$
f, $R^1 = R^2 = H$; $R^3 = Br$
g, $R^1 = R^2 = R^3 = Cl$

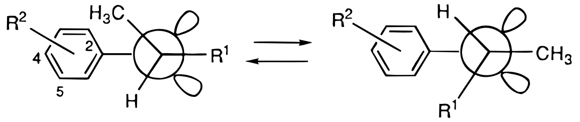


(*R*)-**44a**, R = H
b, R = NH_2

derivatives by a variety of other methods.[101] For all of these compounds in various solvents, the sign of the ^1L_b CEs is positive.[101] It appears then that (+)-**45** (Table 20) is the more important conformer. Thus the sign of the ^1L_b CE can be predicted on the basis of the benzene sector rule. Because of the remoteness of the chiral center from the benzene chromophore, no rotationally induced contribution to the ^1L_b CEs arises from the benzene ring substituents.

The absolute configuration of methyl (*R*)-β-phenoxybutyrate [(*R*)-**44a**] was assigned on the basis of the comparison of the CD curve of its enantiomer (*S*)-**44a** with that of the methyl (*S*)-(phenylthio)butyrate [(*S*)-**47a**], both (*S*)-**44a** and (*S*)-**47a** showing positive ^1L_b CEs, the absolute configuration of (*S*)-**47a** being

Table 20. ^1L_b Band Origin for Benzene Ring-Rubstituted α-Phenoxypropionic Acids and Methyl β-Phenoxybutyrates



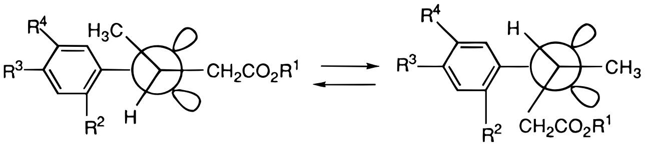
(+)-**45a**

(-)-**45b**

solute	R^1	R^2	solvent	EA: λ, nm (ε^a)	CD: λ, nm (Δε^b × 10^2)	ref^c
(*R*)-**43a**	CO$_2$H	H	MeOH	277 (1250)	276 (+97)	101
(*R*)-**43a**	CO$_2$H	H	cyclohexane	277 (1450)	277 (+140)	101
(*R*)-**43b**	CO$_2$H	2-C(CH$_3$)$_3$	MeOH	277 (1830)	277 (+140)	104
(*R*)-**43c**^{d}	CO$_2$H	4-C(CH3)$_3$	MeOH	282 (1300)	281 (+62)	104
(*R*)-**43d**^{d}	CO$_2$H	5-C(CH$_3$)$_3$	MeOH	278 (1400)	277 (+110)	104
(*R*)-**43e**^{d,e}	CO$_2$H	4-Br	EtOHl		279 (+97)^f	103
(*R*)-**43f**^{d,e}	CO$_2$H	5-Br	EtOH		272 (+140)^f	103
(*R*)-**43g**	CO$_2$H	2,4,5-(Cl)$_3$	MeOH	297 (2400)	288 (+130)^f	101
(*R*)-**44a**^{d,e}	CH$_2$CO$_2$CH$_3$	H	CH$_3$CN	280 (1060)	278 (−56)	102
(*R*)-**44b**^{d,e}	CH$_2$CO$_2$CH$_3$	2-NH$_2$	CH$_3$CN	292 (3300)	292 (−26)	102

[a] Molar absorptivity. [b] Molar dichroic absorption. [c] Report giving complete EA and CD spectral data. [d] Enantiomer used. [e] Configuration assigned on the basis of its CD spectrum. [f] Only one CD maximum reported.

Table 21. ^1L_b Band Maxima for Benzene Ring-Substituted α-(Phenylthio)butyric Acids and Methyl α-(Phenylthio)butyrates^a

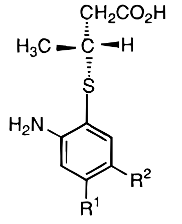


(+)-**48a**

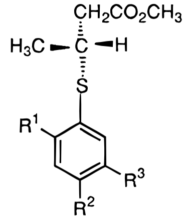
(-)-**48b**

solute	R^1	R^2	R^3	R^4	CD: λ, nm (Δε^b × 10^2)	ref^c
(*R*)-**46a**	H	NH$_2$	H	H	310 (−130)	105
(*R*)-**46b**	H	NH$_2$	CH$_3$	H	309 (−128)	105
(*R*)-**46c**	H	NH$_2$	H	CH$_3$	315 (−83)	105
(*R*)-**47a**	CH$_3$	H	H	H	264 (−48)	105
(*R*)-**47b**	CH$_3$	NH$_2$	H	H	309 (−99)	105
(*R*)-**47c**	CH$_3$	H	CH$_3$	H	266 (−42)	105
(*R*)-**47d**	CH$_3$	NH$_2$	CH$_3$	H	309 (−85)	105
(*R*)-**47e**	CH$_3$	NH$_2$	H	CH$_3$	319 (−66)	105

[a] Solvent not specified. [b] Molar dichroic absorption. [c] Report giving complete EA and CD spectral data.



(*R*)-**46a**, R^1 = R^2 = H
b, R^1 = CH$_3$; R^2 = H
c, R^1 = H; R^2 = CH$_3$



(*R*)-**47a**, R^1 = R^2 = R^3 = H
b, R^1 = NH$_2$; R^2 = R^3 = H
c, R^1 = H; R^2 = CH$_3$; R^3 = H
d, R^1 = NH$_2$; R^2= CH$_3$; R^3 = H
e, R^1 = NH$_2$; R^2 = H; R^3 = CH$_3$

deduced from X-ray and chiroptical data corroborated by chemical proofs.[102] On the basis of a preferred conformation such as (+)-**45a**, however, the benzene sector rule predicts that (*R*)-**44a** and **b** would show positive ^1L_b CEs rather than the negative ones reported (Table 20).

2. *β-(Phenylthio)butyric Acids*

For (*R*)-β-(phenylthio)butyric acid [(*R*)-**46a**] and methyl (*R*)-β-(phenylthio)butyrate [(*R*)-**47a**] and their benzene ring-substituted derivatives, the benzene sector rule would predict positive ^1L_b CEs rather than the negative ones reported (Table 21). The CD data for these compounds show that the sign of these CEs is not affected by the benzene ring substituents, presumably because of the remoteness of the chiral center from the benzene chromophore so that there is no induced contribution to the ^1L_b CE. The absolute configuration of these compounds was established by comparison of their CD spectra with that of the amide prepared from (*S*)-β-(2-nitrophenylthio)butyric acid and an enantiomer of α-phenylethylamine.[105] The absolute configuration of this amide was established by X-ray diffraction, but verification of the absolute configurations of (*R*)-**46a**−**c** and (*R*)-**47a**−**e** would be useful.

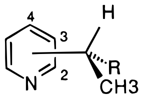
E. Pyridyl Compounds

1. *Pyridylcarbinols and Pyridylcarbinamines*

In addition to the chiroptical properties of the pyridyl compounds related to (*S*)-nicotine [(*S*)-**27c**] shown in Table 13 and discussed in section IV.B.3, the chiroptical properties of other pyridyl compounds have also been studied. The three isomeric (*R*)-α-pyridylethylamines[106] (*R*)-**49a**−**c** and (*R*)-α-pyridylethyl alcohols[107,108] (*R*)-**50a**−**c** (Table 22) may be considered ring-substituted analogues of (*R*)-α-phenylethylamine [(*R*)-**1a**)] and (R)-α-phenylethyl alcohol [(*R*)-**1d**)], the aza group having a large, negative spectroscopic moment.[26,27] Thus the sign of the observed ^1L_b CEs (Figure 17) for a particular enantiomer may be predicted using the benzene sector and benzene chirality rules.

For (*R*)-α-phenylethylamine [(*R*)-**1a**], (*R*)-α-phenylethyl alcohol [(*R*)-**1d**], (*R*)-α-(2-, 3-, and 4-pyridyl)ethylamine [(*R*)-**49a**−**c**], and (*R*)-α-(2-, 3-, and 4-pyridyl)ethyl alcohol [(*R*)-**50a**−**c**], the benzene sector rule predicts a negative vibronic contribution to the

Table 22. ^1L_b Band Origin Maxima for (*R*)-Pyridylmethylcarbinamines and Pyridylmethylcarbinols



	R = NH_2[a]			R = OH[b]		
position	cmpd	EA: λ, nm (ε[c])	CD: λ, nm ($\Delta\epsilon^d \times 10^2$)	cmpd	EA: λ, mn (ε[c])	CD: λ, nm ($\Delta\epsilon^d \times 10^2$)
2	(*R*)-**49a**[e]	267 (2900)[f]	267 (−97)	(*R*)-**50a**[e]	270 (2500)	268 (−14)
3	(*R*)-**49b**	267 (2100)[f]	268 (+88)	(*R*)-**50b**[e]	270 (1800)	270 (+110)
3	(*R*)-**49b**[e]		268 (+97)			
4	(*R*)-**49c**[e]	262 (1600)[f]	*g*	(*R*)-**50c**[e]	265 (1800)[f]	265 (−6)

[a] Complete EA and CD spectral data given in ref 106; 0.1 M methanolic potassium hydroxide as the solvent. [b] Complete EA and CD spectral data given in ref 108; methanol-glycersol 9:1 as the solvent. [c] Molar absorptivity. [d] Molar dichroic absorption. [e] Enantiomer used. [f] Shoulder. [g] An^1L_b CE not observed.

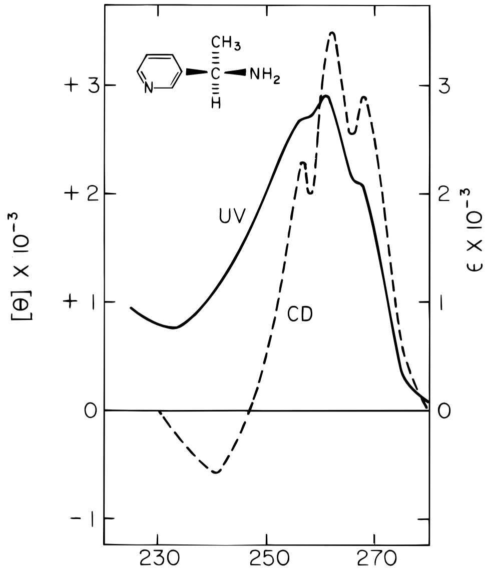
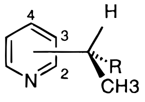


Figure 17. Electronic absorption (UV) and circular dichroism (CD) spectra of (*R*)-α-(3-pyridyl)ethylamine [(*R*)-**49b**] in 0.1 M methanolic potassium hydroxide. Reprinted from *J. Am. Chem. Soc.* **1973**, *95*, 811. Copyright 1973 American Chemical Society.



(*R*)-**49**, R = NH_2
50, R = OH

^1L_b CEs, since in all of these amines and alcohols it is presumed that the preferred conformation is such that the hydrogen atom at the chiral center nearly eclipses the aromatic ring plane, although calculations[109] using empirical potential functions suggest that the alcohols **50** deviate somewhat from this preferred conformation. Compounds (*R*)-**1a** and **d** have no induced contribution to the ^1L_b CEs, but the induced contribution for (*R*)-**49a**−**c** and (*R*)-**50a**−**c** may be positive or negative, depending on the position of the aza group with respect to the attachment bond of the chiral group (Figure 7 and Table 5). The benzene chirality rule thus predicts a negative induced contribution for the 2- and 4-pyridyl analogues of (*R*)-**1a** and **d**, and these analogues are predicted to be negative. Thus negative ^1L_b CEs are observed for (*R*)-**49a** and (*R*)-**50a** and **c** (Table 22), and no ^1L_b CE was observed for the amino analogue (*S*)-**49c** (Figure 18). Both the vibronic and induced contributions for the 3-pyridyl analogues are positive, and the sign of the ^1L_b CEs of (*R*)-**49b** contributions for the 3-pyridyl analogues are positive, and the sign of the ^1L_b CEs of (*R*)-**49b** (Figure 17) and (*R*)-**50b** is positive. More recently, the assignment of the longest wavelength maximum in the CD spectrum of (*R*)-**50c** to the ^1L_b band origin is different from that made earlier in the original report using (*S*)-**50c**.[108] In other work,[109] the positive sign for the ^1L_b CEs of the (*S*)-α-(2-pyridyl)ethyl alcohol [(*S*)-**50a**] in cyclohexane and (*R*)-α-(3-pyridyl)ethyl alcohol [(*R*)-**50b**] in methanol is in agreement with the predictions based on the benzene sector and benzene chirality rules, and no dichroic absorption associated with the ^1L_b band of the 4-pyridyl isomer [(*S*)-**49c**] in cyclohexane was observed.[109]

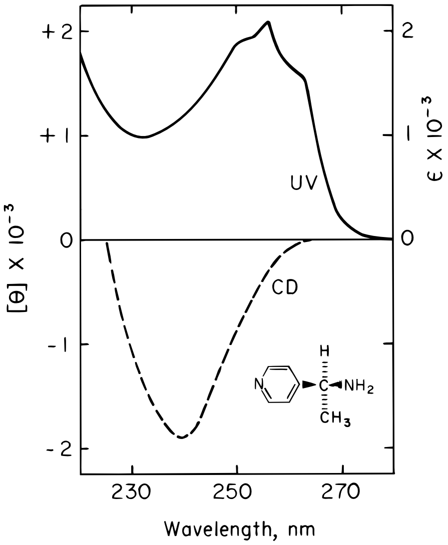
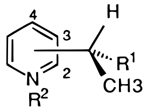


Figure 18. Electronic absorption (UV) and circular dichroism (CD) spectra of (*S*)-α-(4-pyridyl)ethylamine [(*R*)-**49c**] in 0.1 M methanolic potassium hydroxide. Reprinted from *J. Am. Chem. Soc.* **1973**, *95*, 811. Copyright 1973 American Chemical Society.

2. 2-(Pyridyl)butanes

The EA and CD spectra of a number of chiral 2-(pyridyl)butanes, (*S*)-2-, 3-, and 4-(1-methylpropyl)pyridine [(*S*)-**51a**−**c**], in hexane and hexane with

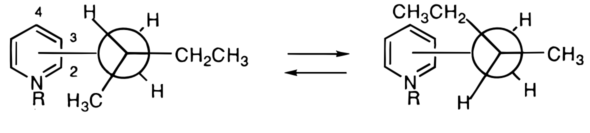
Table 23. ^1L_b Band Maxima for 2-(2-, 3-, and 4-Pyridyl)butanes and Their Salts



solute	position	R^1	R^2	solvent	EA: λ, nm (ϵ^a)	CD: λ, nm ($\Delta\epsilon^b \times 10^2$)	ref^c
(*S*)-**51a**	2	CH_2CH_3		hexane	261 (2800)	257 (+33)	110
(*S*)-**51a**	2	CH_2CH_3	H^+	hexane−TFA^d	264 (6600)	261 (−94)	110
(*S*)-**51b**	3	CH_2CH_3		hexane	261 (2500)	265 (−18)	110
(*S*)-**51b**	3	CH_2CH_3	H^+	hexane−TFA^d	264 (5400)	264 (+30)	110
(*S*)-**51c**	4	CH_2CH_3		hexane	255 (1600)	267 (−6)	110
(*S*)-**51c**	4	CH_2CH_3	H^+	hexane−TFA^d	253 (4200)	250 (+15)	110
(*S*)-**51d**^{e}	2	$C(CH_3)_3$		heptane	268 (1950)^f	270 (+260)	111
(*S*)-**51d**^{e}	2	$C(CH_3)_3$		MeOH	262 (3200)	263 (+150)	111

[a] Molar absorptivity. [b] Molar dichroic absorption. [c] Report giving complete EA and CD spectral data. [d] Trifluoroacetic acid-pyridine compound 10:1. [e] Enantiomer used. [f] Shoulder.

Table 24. ^1L_b Band Maxima for 2-Methyl-1-(2-, 3-, and 4-pyridyl)butane and Their Salts

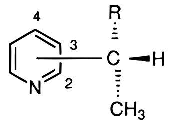


(-)-**53a** (+)-**53b**

solute	position	R	solvent	EA: λ, nm (ϵ^a)	CD: λ, nm ($\Delta\epsilon^b \times 10^2$)	ref^c
(*S*)-**52a**	2		hexane	262 (2800)	264 (+15)	110
(*S*)-**52a**	2		hexane (−85 °C)		265 (+48)	110
(*S*)-**52a**	2	H^+	hexane−TFA^d	266 (7900)	266 (+58)	110
(*S*)-**52b**	3		hexane	262 (2700)	270 (+12)	110
(*S*)-**52b**	3		hexane (−85 °C)		272 (+18)	110
(*S*)-**52b**	3	H^+	hexane−TFA^d	264 (5100)	265 (+15)	110
(*S*)-**52c**	4		hexane	256 (1700)	252 (+12)	110
(*S*)-**52c**	4		hexane (−85 °C)		254 (+15)	110
(*S*)-**52c**	4	H^+	hexane−TFA^d	254 (4100)	255 (+21)	110

[a] Molar absorptivity. [b] Molar dichroic absorption. [c] Report giving complete EA and CD spectral data. [d] Trifluoroacetic acid−pyridine compound 10:1.

added trifluoroacetic acid (TFA) were reported[110] (Table 23). In both solvents the EA and CD spectra were without vibrational fine structure, and the sign of the ^1L_b CEs is very dependent on the position of the aza group and its protonation as the result of the added TFA.



(*S*)-**51a**, position 2, R = CH_2CH_3
b, position 3, R = CH_2CH_3
c, position 4, R = CH_2CH_3
d, position 2, R = $C(CH_3)_3$

The benzene sector rule predicts a positive vibronic contribution to ^1L_b CE for both (*S*)-**51a** and **c** while the benzene chirality rule also predicts a positive induced contribution from the aza group, the latter with a negative spectroscopic moment[26,27] ortho and para to the substituent (Table 5). The ^1L_b CE for (*S*)-**51a** in hexane is in fact reported to be positive while that of (*S*)-**51c**, negative.

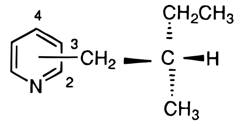
Protonation of the aza group in (*S*)-**51a** and **c** reverses the sign of the induced contribution, and the vibronic and induced contribution are predicted to be positive and negative, respectively. In agreement with prediction, the ^1L_b CE of (*S*)-**51a** is reported to be strongly negative, but that of (*S*)-**51c**, positive.

For (*S*)-**51b** in hexane, the vibronic contribution to the ^1L_b is also predicted to be positive, and the induced contribution, negative. It could not have been predicted, however, but the ^1L_b CE maximum is negative Protonation of the aza group reverses the sign of the induced contribution and the ^1L_b CEs of (*S*)-**51b** in TFA is now strongly positive (Table 23).

Finally, CD observations with (*S*)-2-(1,2,2-trimethylpropyl)pyridine[111] [(*S*)-**51d**] in methanol and hexane gave, as predicted by application of both the benzene sector and benzene chirality rules, strong positive ^1L_b CEs, both the vibronic and induced contributions being positive.

3. 2-Methyl-1-(pyridyl)butanes

The chiroptical properties of the isomeric (*S*)-2-methyl-1-(2-, 3-, and 4-pyridyl)butane [(*S*)-**52a**−**c**] in hexane at room temperature, in hexane at −85 °C, and in hexane with added trifluoroacetic acid (TFA) were reported (Table 24).[110] Since the chiral center is separated from the pyridyl chromophore, it can be expected that there is no induced contribution to the ^1L_b CEs, and as predicted, (*S*)-**52a**−**c** and their salts all show an ^1L_b CEs of the same sign. The equilibrium between conformers (−)-**53a** and (+)-**53b** would predict, on application of the benzene sector rule, a



(*S*)-**52a**, position 2
b, position 3
c, position 4

negative maximum for the *S* configuration, the maximum becoming more negative at a lower temperature as the equilibrium shifts more from (+)-**53b** toward the lower energy conformer (−)-**53a**. Thus a reexamination of the CD of the enantiomers of **52a**−**c** is important for an experimental verification of this failure of the benzene sector rule.

F. Perhydrobenzocycloalkenes

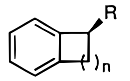
1. Planar Ring Systems

The circular dichroism spectra of a substantial number of chiral perhydrobenzocycloalkenes with planar rings have been reported,[32,40,86,112] and the benzene sector and the benzene chirality rules were used to correlate the sign of their ^1L_b CEs with their absolute configurations.[32] The CD data for (*S*)-1-amino-1,2-dihydrobenzocyclobutene [(*S*)-**54**] and some chiral 1-substituted indans [(*S*)-**55a**−**f** and (*R*)-**55g**−**i**] are shown in Table 25.

The sector diagrams for the vibronic contribution to the ^1L_b CEs for these bicyclic systems are shown in Figure 8B and C. These diagrams follow from that deduced for monosubstituted benzene compounds (Figure 8A). In sector diagrams B and C, the sector boundaries correspond to the attachment bonds of the cycloalkene to the benzene ring planes. Again the sum of the contributions of groups in the sectors gives the vibronic contribution to the ^1L_b CEs. When a hydrogen atom is at a contiguous chiral center and lies in one sector or another, it is assumed, on the basis of a very small bond transition moment for a carbon−hydrogen bond,[75] that the hydrogen atom makes no significant contribution to the vibronic contribution to the sign of the ^1L_b CEs. For the compounds in Table 25, the respective attachment bond to the benzene ring of the cycloalkene adjacent to the attachment bond of the chiral center is equivalent to the attachment of an alkyl group ortho to the attachment bond of a contiguous chiral center in a noncondensed benzene system. Since an alkyl group has a positive spectroscopic moment,[26,27] its presence induces a rotatory contribution to the ^1L_b CEs opposite to that of the vibronic contribution (Table 5).

For (*S*)-**54**, (*S*)-**55a**−**f**, and (*R*)-**55g**−**i**, each with a planar cycloalkene system, the substituents at C-1 all make a positive vibronic contribution to the ^1L_b CEs (Figure 8B and C), while the contribution of the attached hydrogen atom is insignificant. This positive vibronic contribution, however, is in general overshadowed by a negative induced contribution arising from the cycloalkene attachment adjacent to the attachment bond of the chiral group, and (*S*)-1-indanol [(*S*)-**55c**] shows strong, negative ^1L_b CEs (Figures 19), only transitions to totally symmetric vibronic states being observed.[40] For the compounds in Table 25, all with the same generic absolute configuration and a planar cycloalkene ring, the substituents at C-1 all make a positive vibronic contribution to the ^1L_b CEs while the contribution of the attached hydrogen atom is insignificant. The positive vibronic contribution, however, is overshadowed by a larger negative induced contribution arising from the cycloalkene attached adjacent to the attachment bond of the chiral group. The single exception in Table 25, as well as compared to the CD spectra of 11 other 1-substituted indans,[32] is observed with potassium (*S*)-1-indancarboxylate [(*S*)-**55f**]. The positive ^1L_b CEs for (*S*)-**55f** contrasted to the negative ones for (*S*)-1-indancarboxylic acid [(*S*)-**55e**] are similar to the CD observations with (*R*)-*o*-methylmandelic acid [(*R*)-**24a**] and potassium (*R*)-*o*-methylmandelate [(*R*)-**25a**] (Table 12).

Table 25. ^1L_b Band Origin Maxima for Planar Perhydrobenzocyclohexenes

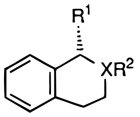


solute	R	solvent	EA: λ, nm (ε[a])	CD: λ, nm (Δε[b] × 10^2)	ref[c]
		(*S*)-**54**, *n* = 1			
	NH_2	cyclohexane	280 (414)[d]	273−274 (−)[d,e]	86
		(*S*)-**55**, *n* = 2			
a	NH_2	cyclohexane	273 (804)	273−274 (−6)[f]	86
b	NH_3Cl	MeOH	272 (1000)	271 (−39)	40
c[g]	OH	MeOH	272 (920)	271 (−44)	32
d	CH_3	MeOH	273 (1300)	274 (−39)	112
e[g]	CO_2H	MeOH	273 (850)	273 (−4.4)	32
f[g]	CO_2K[h]	MeOH	274 (1200)	276 (+21)	32
		(*R*)-**55**, *n* = 2			
g	CH_2CO_2H	MeOH	271 (1200)	272 (−53)	32
h	CH_2CO_2K[h]	MeOH	271 (1200)	272 (−31)	32
i	$C(CH_3)_3$	MeOH	272 (1300)	274 (−120)	32

[a] Molar absorptivity. [b] Molar dichroic absorption. [c] Report giving complete EA and CD spectral data. [d] Inflection. [e] The CE is negative on a strongly positive background curve. [f] A negative CE seen as a shoulder. [g] Enantiomer used. [h] Formed in situ from the corresponding carboxylic acid by the addition of methanolic potassium hydroxide.

For (*R*)-mandelic acid [(*R*)-**6d**], the preferred conformation is such that the hydrogen atom at the chiral center eclipses the benzene ring plane. Since the rotatory contribution by a carboxyl group is greater than that of an hydroxyl group (Table 3), the sum of the vibronic contributions to the ^1L_b CEs is positive (Figure 8A), and the ^1L_b CEs are positive (Table 12). For (*R*)-*o*-methylmandelic acid [(*R*)-**24a**], the ortho methyl group induces a negative contribution to the ^1L_b CEs (Table 5), which overshadows the positive vibronic contribution and results in negative ^1L_b CEs (Table 12). Treatment of (*R*)-**24a** in situ with potassium hydroxide gives the potassium salt (*R*)-**25a**, and the sign of the ^1L_b CEs is now positive, the same as that of potassium (*R*)-mandelate [(*R*)-**7d**]. It is assumed then that the vibronic contribution is no longer overshadowed by the induced contribution. This reversal in sign of the ^1L_b CEs on formation of the potassium salt (*R*)-**7d** might possibly be ascribed to a change in the preferred conformation of the chiral group about its attachment bond to the benzene ring. In the case of (*S*)-**55e** going to (*S*)-**55f**, no

Table 26. ^1L_b Band Origin Maxima for 1-Substituted (*R*)-1,2,3,4-Tetrahydronaphthalenes and (*S*)-1,2,3,4-Tetrahydroisoquinolines

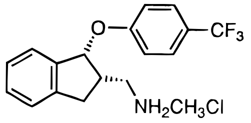


code	R¹	R²	solvent	EA: λ, nm (ε[a])	CD: λ, nm (Δε[b] × 10²)	ref[c]
			(*R*)-**57**, X = CH			
a[d]	NH_2	H	cyclohexane	274 (320)	273−274 (+14)	86
b	$N(CH_3)_2$	H	isooctane		242[e] (+24)[f]	114
c	OH	H	isooctane		264 (+15)[f]	114
d	CH_3	H	hexane	273 (289)	273 (+23)	115
e	CO_2H	H	isooctane		274 (+5.1)[f]	114
f	CO_2CH_3	H	isooctane		274 (+4.3)[f]	114
			(*S*)-**58**, X = N			
a	CH_3	H	95% EtOH		273 (+24)[f]	116
b	CH_3	H_2Cl	95% EtOH	271 (450)	272 (+11)[f]	116
c	CH_3	CH_3	95% EtOH		273 (+30)[f]	116
d	CH_3	HCH_3Cl	95% EtOH	271 (280)	272 (+9.7)[f]	116
e	CH_3	$(CH_3)_2I$	95% EtOH		269 (+5.8)[f]	116

[a] Molar absorptivity. [b] Molar dichroic absorption. [c] Report giving complete EA and CD spectral data. [d] Enantiomer used. [e] Probably a misprint and should be 272 nm. [f] Only one maximun reported.

such conformational change is possible, and the reversal in sign must be electronic in nature. In (*S*)-**55e** the induced contribution to the ^1L_b CEs overshadows the vibronic contribution, but for (*S*)-**55f**, the vibronic contribution is still the more important. Only the CD of the *o*-methylmandelic acid and the corresponding potassium salt have been reported,[59] however, and it is not known if the sign of the ^1L_b CEs is reversed on formation of the corresponding potassium salts of other ortho-substituted mandelic acids.

Finally, application of the benzene sector and chirality rules to the interpretation of the CD spectrum of (+)-*cis*-2,3-dihydro-2-[(methylamino)methyl]-1-[4-(trifluoromethyl)phenoxy-1*H*-indene hydrochloride [(1*S*,2*S*)-**56**], the more active enantiomer of a new serotonin inhibitor, gave its absolute configuration as 1*S*,2*S*, the CD spectrum of (1*S*,2*S*)-**56** showing strong positive ^1L_b CEs.[113]



(1*S*,2*S*)-**56**

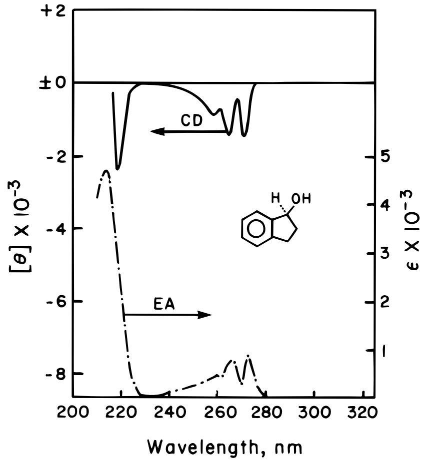


Figure 19. Electronic absorption (EA) and circular dichroism (CD) spectra of (*S*)-1-indanol [(*S*)-**55c**] in methanol. Reprinted from *J. Am. Chem. Soc.* **1992**, *114*, 2181. Copyright 1992 American Chemical Society.

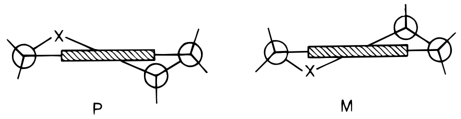
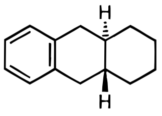


Figure 20. Conformational helicities of the cyclohexene and tetrahydropyridine moieties of substitute 1,2,3,4-tetrahydronaphthalenes (X = CH_2) and 1,2,3,4-tetrahydroisoquinolines (X = NH). Reprinted from *J. Am. Chem. Soc.* **1992**, *114*, 2181. Copyright 1992 American Chemical Society.

2. Nonplanar Ring Systems

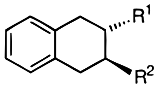
The signs of the ^1L_b CEs in the CD spectra of chiral 1-substituted 1,2,3,4-tetrahydronaphthalenes[86,114,115] [(*R*)-**57a**−**f**] and 1-methyl-1,2,3,4-tetrahydroisoquinolines[116] and their [(*R*)-**58a**−**e**] salts[116] (Table 26) may also be correlated with their absolute configurations using the benzene sector and benzene chirality rules.[32]

The cyclohexene and tetrahydropyridine moieties in the substituted 1,2,3,4-tetrahydronaphthalene (**57**) and 1,2,3,4-tetrahydroisoquinolines (**58**) are not planar,[24] and this nonplanarity must be considered in the prediction of the sign of the ^1L_b CEs. The helicity (Figure 20) of the cyclohexene and tetrahydropyridine moieties is determined by the configuration of the group at the chiral center. By using the enantiopure conformationally rigid tricyclic 1,2,3,4,5,6,7,8-octahydrophenanthrene **59**, the enantiomer of **61a** in Table 27, it was shown[24] that *P* helicity (Figure 20) of the ring attached to the benzene ring leads to positive

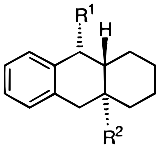


59

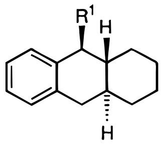
Table 27. ^1L_b Band Origin Maxima for Some Chiral 2-Substituted 1,2,3,4-Tetrahydronaphthalenes and 1,2,3,4,5,6,7,8-Octohydrophenanthrene



60



61



62

code	R^1	R^2	solvent	EA: λ, nm (ϵ^a)	CD: λ, nm ($\Delta\epsilon^b \times 10^2$)	ref[c]
				60		
a	NH_2	H	cyclohexane	273 (417)	268−271 (+13)	86
b[d]	CH_3	H	hexane	274 (746)	272 (+16)	115
c	CH_3	CH_3	hexane	274 (703)	272 (+19)	115
				61		
a	H	H	isooctane	274 (746)	273 (+27)	115
b	CH_3	H	hexane	273 (735)	273 (+57)	115
c	CH_2OH	H	MeOH	273 (619)	272 (+41)	115
d	H	CH_3	isooctane	274 (859)	273 (+30)	115
				62		
a	CH_3		hexane	273 (578)	273 (−5.8)	115
b	CH_2OH		MeOH	273 (536)	270 (+4.2)	115

[a] Molar absorptivity. [b] Molar dichroic absorption. [c] Report giving complete EA and CD spectral data. [d] Enantiomer use.

^1L_b CEs, while *M* helicity of the ring results in negative ^1L_b CEs. It was further suggested[24] that the sign of the ^1L_b CEs for **59** and the more conformationally mobile systems **57** and **58** depends only on the preferred helicity of the cyclohexene and tetrahydropyridine groups (chirality of the second sphere[24]) and can be predicted using a sector rule with signs opposite to those in Figure 8D and E.

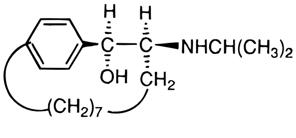
Application of the benzene sector and benzene chirality rules to **59** leads to the same prediction for the sign of the ^1L_b CEs as that of Snatzke and Ho.[24] In **59**, the *M* helicity gives a positive vibronic contribution to the ^1L_b CEs (Figure 8D). This contribution, however, is overshadowed by the negative induced contributions, and the observed ^1L_b CEs are negative.[24]

The positive ^1L_b CEs shown by the 1-substituted 1,2,3,4-tetrahydronaphthalenes (*R*)-**57a**−**f** (Table 26) and 2-substituted 1,2,3,4-tetrahydronaphthalenes **60a**−**c** (Table 27) can also be predicted using the benzene sector and benzene chirality rules. For (*R*)-1-methyl-1,2,3,4-tetrahydronaphthalene [(*R*)-**57d**], it was shown that the methyl group has preferably a quasiaxial conformation[115] and the helicity of the cyclohexene moiety is *P*. With this helicity, the sign of the vibronic contribution to the ^1L_b CEs is negative, but the induced contribution is positive. Since the latter in general overshadows the former, the sign of the ^1L_b CEs is predicted to be positive. The other substituents at C-1 in (*R*)-**57a**−**c**, **e**, and **f** also cause the cyclohexene group to have *P* helicity, and their observed ^1L_b CEs are positive. On the basis of equatorial conformation of the 2- and 3-substituents of the 1,2,3,4-tetrahydronaphthalenes **60a**−**c**, the cyclohexene moiety also has *P* helicity, and the observed ^1L_b CEs are correctly predicted to be positive (Table 27).

For the (*S*)-1-methyl-1,2,3,4-tetrahydroisoquinolines (*S*)-**58a** and **c**, a similar analysis for the free bases also predicts positive ^1L_b CEs (Table 26). When the nitrogen atom has a positive charge [(*S*)-**58b**, **d**, and **e**], the C-1 chiral group will have a negative spectroscopic moment,[45,59] and the sign of its induced contribution to the ^1L_b CEs will be negative while the induced contribution of the C-4 methylene group is still positive. Thus the overall prediction as to the sign of the induced contribution to the CEs is ambiguous. The ^1L_b CEs for the salts, however, are still positive, but their intensities, as compared to those of the free bases, are reduced. It should also be noted that any additional substitution of the benzene ring causes a change in the induced contribution to the ^1L_b CEs, depending on the position and spectroscopic moment of the additional substituent, and a prediction as to the sign of the ^1L_b CEs in these cases is at present not possible.

Application of the benzene sector and benzene chirality rules to the rigid 1,2,3,4,5,6,7,8-octahydrophenanthrenes **61a**−**d** lead to the prediction of positive ^1L_b CEs. In these compounds the *P* helicity without or with a group at C-1 gives one or two negative vibronic contributions to the ^1L_b CEs. The induced positive contribution of the attached cyclohexene ring, however, overshadows the vibronic contributions, and the observed ^1L_b CEs for **61a**−**d** are positive. For **62a** and **b**, the substituent at C-1 makes a positive vibronic contribution opposite in sign to the negative vibronic contribution of the *P* helicity of the attached cyclohexene ring. Thus the sign of the induced contribution of the attached cyclohexene ring to the sign of the ^1L_b CEs is uncertain, and a prediction as to the sign of the ^1L_b is also uncertain. In fact, **62a** shows a negative ^1L_b band origin while that of of **62b** is positive.[115]

For very flexible condensed systems, a preferred helicity of the cycloalkene attachment need not be important. The relative configuration of (+)-*threo*-1-hydroxy-2-(isopropylamino)[10]paracyclophane [(+)-**63**] was established on the basis of its proton nuclear magnetic resonance spectrum[117] and although (+)-**63** showed positive ^1L_b CEs in its CD spectrum,[117] the 1*S*,2*S* absolute configuration was established on



(1*S*,2*S*)-**63**

the basis of a comparison of the CD spectrum of the complex formed in situ from (+)-**63** and copper(II)(succinimidato)$_2$(isopropylamine)$_2$ with similar complexes of model enantiopure amines of known absolute configurations. The same absolute configuration can be assigned to (+)-**63** using the benzene sector and benzene chirality rules. The preferred conformation of (1*S*,2*S*)-**63** in which the hydrogen atom at C-1 eclipses the benzene ring plane predicts a negative vibronic contribution (Figure 8A) to the ^1L_b CEs. The latter is expected to be overshadowed by a positive induced contribution as the result of the para substitution by a group with a positive spectroscopic moment, there being no preferred helicity to the alicyclic system.

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VI. Supporting Information Availability

The rotatory power ($[\alpha]_D$) and more complete spectral data for the compounds discussed above as well as similar data for additional chiral benzene compounds are given in the Supporting Information. In the Supporting Information, the data are collected into 48 tables on 93 pages with appropriate literature citation ranging from 1965 to early 1997. See any current masthead page for ordering and Internet access instructions.

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