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Optically Active Amines. 40.[1] Application of the Benzene Sector Rule to the Circular Dichroism of Chiral Benzylcarbinamines and Benzylcarbinols

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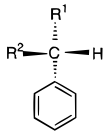
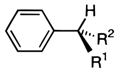
Abstract: The sign of the ${}^1L_b$ Cotton effects (CEs) from about 240 to 270 nm in the circular dichroism (CD) of enantiomers of chiral benzylcarbinamines and benzylcarbinols is correlated with their absolute configurations using the benzene sector rule and a consideration of the equilibrium between their two conformers of lowest energy and of oppositely signed rotatory powers. For chiral benzylalkylcarbinamines, carbinamine salts, and carbinols, which show a single sign for their ${}^1L_b$ CEs, a shift in the conformational equilibrium can explain a sign reversal of the CEs with a change in solvent, (*R*)-2-amino-1-phenylpropane showing negative ${}^1L_b$ CEs in methanol but positive ones in cyclohexane. L-Phenylalanine in water shows positive ${}^1L_b$ CEs, but in methanol it shows both negative and positive CD maxima. In methanol, the two longest wavelength maxima comprise a double CE associated with the band origin absorption maximum at 267 nm, the conformational equilibrium shifted from the positive conformer of L-phenylalanine to its negative one and the greater amount of the latter is now detected at slightly longer wavelength in the CD spectrum.

Previous reports[3,4] outlined a sector rule to correlate the sign of the Cotton effects (CEs) from about 240 to 270 nm in the circular dichroism (CD) spectra of enantiomers of phenylcarbinamines, such as (*R*)-α-phenylethylamine[5] [(*R*)-**1a**] and L-phenylglycine[6] (L-**1b**), phenylcarbinols, such as (*R*)-α-phenylethyl alcohol[7] [(*R*)-**1c**] and L-mandelic acid[8] (L-**1d**), the hydrochloride salts of (*R*)-**1a**[5] and L-**1b**,[6] and the potassium salt of L-**1d**,[8] with their absolute configurations. The CEs are 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 of the benzene chromophore[9,10] and are the result of vibronic borrowing[11,12] from allowed transitions at shorter wavelength.[5]



(*R*)-**1a**, $R^1 = CH_3$; $R^2 = NH_2$
L-**1b**, $R^1 = CO_2H$; $R^2 = NH_2$
(*R*)-**1c**, $R^1 = CH_3$; $R^2 = OH$
L-**1d**, $R^1 = CO_2H$; $R^2 = OH$

For benzene compounds with a contiguous hydrogen-substituted chiral center with a hydrogen substituent, empirical potential function and molecular orbital calculations and various spectroscopic measurements indicate that the preferred conformation in both the gas phase and in solution is such that the hydrogen atom at the chiral center eclipses the benzene ring plane (**2**).[3,13] This conformational preference and the CD data for a substantial number of enantiomers of chiral benzene compounds without an additional ring substituent give the quadrant projection **3**, which shows the sign of the rotatory contributions to the ${}^1L_b$ CEs by an atom or group attached to the contiguous chiral center and lying in a particular sector. The sector boundaries shown in **3** are defined by the attachment bond of the chiral center and the benzene ring plane, and the sum of the rotatory contributions gives the sign to the observed ${}^1L_b$ CEs. For compounds with additional ring substituents, an induced rotatory contribution influences the sign of the ${}^1L_b$ CEs,[14] and its sign may be the same or different from that of the nonsubstituted parent, depending on the spectroscopic moment[15] and ring positions of the additional substituents.[4,14]



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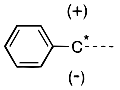
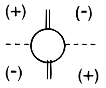


near sectors

3a



all sectors

3b

The signs for the sectors in **3** follow from the observed negative ${}^1L_b$ CEs for (*R*)-α-phenylethyl alcohol [(*R*)-**1c**] in methanol, the preferred conformation of (*R*)-**1c** (**2**, $R^1 = CH_3$; $R^2 = OH$), and the assumption of a larger rotatory contribution of a methyl group than that of an hydroxyl group.[3] This latter assumption is supported by the calculation of a larger effective

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Table 1. Chiral Benzylcarbinamines and Benzylcarbinols

compd	name	$[\alpha]_D^{23}$, deg (solvent)[a]	characterization or vendor[b]
(*R*)-**5a**·HCl	(*R*)-2-amino-1-phenylpropane hydrochloride	−23 (H_2O)	ref 28
L-**5b**	L-phenylalanine	−30 (H_2O)	A
(*R*)-**5c**	(*R*)-1-phenyl-2-propanol	−36 (benzene)	F
L-**5d**	L-3-phenyllactic acid	−19 (H_2O)	A
L-**6b**	L-phenylalaninol	−22 (1 M HCl)	A
L-**7a**	*N*-methyl-L-phenylalanine	+20 (1 M HCl)	S
L-**7b**·HCl	methyl L-phenylalaninate hydrochloride	+29 (abs EtOH)	A
L-**7c**	*N*-acetyl-L-phenylalanine	+33 (MeOH)	A
L-**7d**	ethyl *N*-acetyl-L-phenylalaninate	+12 (MeOH)	S

[a] Concentration: 1.0−5.7 g/100 mL of solvent. [b] Vendor: A, Aldrich; F, Fluka; S, Sigma.

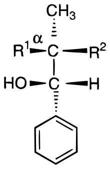
bond transition moment for a carbon−carbon bond as compared to that of a carbon−oxygen bond.[16] Using the CD data for the enantiomers of other benzene compounds with a single chiral substituent, sequences for the rotatory contributions of attached groups and atoms have been established:[3,17]

$$\mathrm{SH,\ CO_2^-,\ C(CH_3)_3 > CH_3 > NH_2,\ {}^+NH_3,\ {}^+N(CH_3)_3,\ OH,\ OCH_3,\ Cl,\ F}$$

and

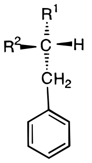
$$\mathrm{CH_3 > CO_2H > {}^+NH_3,\ OH,\ OCH_3}$$

These sequences when used in connection with the sector signs in **3** have a general usefulness for the establishment by CD measurement of the absolute configurations of chiral benzene compounds in which one substituent at a contiguous chiral center is a hydrogen atom, the sign of the ^1L_b CEs depending 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.[18]

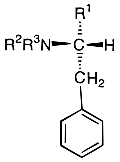


(α*R*,β*S*)-**4a**, R¹ = NH₃Cl; R² = H
(α*S*,β*S*)-**4b**, R¹ = H; R² = NH₃Cl

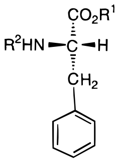
A chiral center separated by a methylene group from a benzene ring also results in ^1L_b CEs, and substantial optical rotatory dispersion[19−24] (ORD) and CD[5,6,9,10,20,24−27] data for otherwise unsubstituted benzylcarbinamines and benzylcarbinols have been reported. Using these data and those obtained in connection with this work using the compounds in Table 1, we now report the application of the benzene sector rule to the circular dichroism of chiral benzylcarbinamines and benzylcarbinols (**5**−**8**).



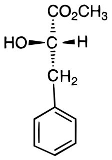
(*R*)-**5a**, R¹ = CH₃; R² = NH₂
L-**5b**, R¹ = CO₂H; R² = NH₂
(*R*)-**5c**, R¹ = CH₃; R² = OH
L-**5d**, R¹ = CO₂H; R² = OH



(*S*)-**6a**, R¹ = *c*-C₆H₁₁; R² = R³ = H
L-**6b**, R¹ = CH₂OH; R² = R³ = H
(*R*)-**6c**, R¹ = CH₃; R² = CH₃; R³ = H
(*R*)-**6d**, R¹ = CH₃; R² = R³ = CH₃

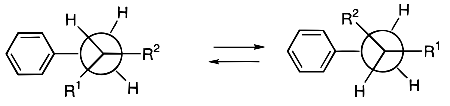


L-**7a**, R¹ = H; R² = CH₃
L-**7b**, R¹ = CH₃; R² = H
L-**7c**, R¹ = H; R² = CH₃CO
L-**7d**, R¹ = CH₂CH₃; R² = CH₃CO

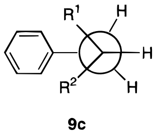


L-**8**

For application of the benzene sector rule to the circular dichroism of phenylcarbinamines and phenylcarbinols, only conformer **2** 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 (−)-**9a** and (+)-**9b** 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 chiral benzylcarbinamines and benzylcarbinols (**5**−**8**) follow from the



(-)-**9a** (+)-**9b**



9c

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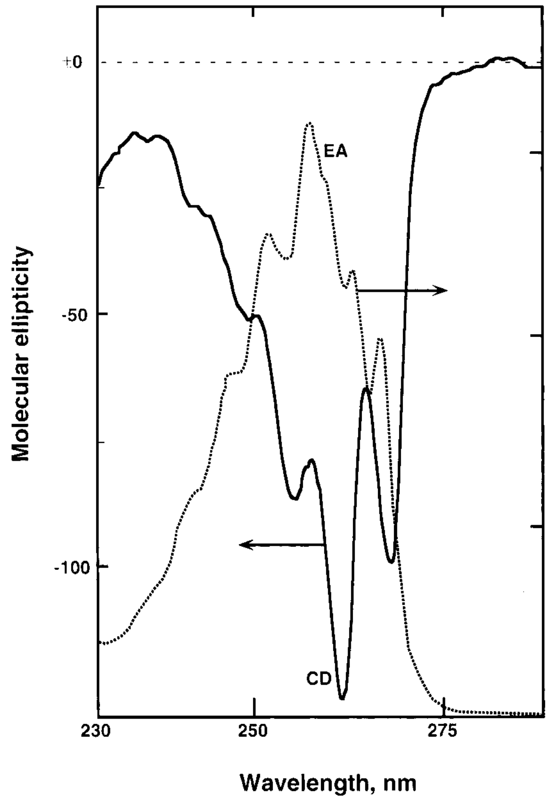

Figure 1. Electronic absorption (EA) and circular dichroism (CD) spectra of (*R*)-2-amino-1-phenylpropane hydrochloride [(*R*-**5a**·HCl] in 0.1 M KOH in methanol. For the EA spectrum, the concentration was 3.3×10^{-3} M.

preferred conformation determined by supersonic molecular jet laser[29] and microwave[30] spectroscopy of various alkylbenzenes including ethylbenzene[29] and of 2-phenylethylamine in the gas phase,[30] in which the carbon−carbon bond α,β to the benzene ring is orthogonal to the benzene ring plane. Conformer **9c** need not be considered because the gauche interactions of R^1 and R^2 with the benzene ring make it of higher energy than either (−)-**9a** or (+)-**9b**. Since the rotatory contribution of a hydrogen atom attached at the chiral center is insignificant[16] and of a group in a sector boundary is also small, sector rule **3** gives the rotatory contribution of **9a** and **9b**, 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 **5**−**8** was investigated in detail.

Results and Discussion

Benzylalkylcarbinamines, Carbinamine Salts, and Carbinols. Figure 1 shows the electronic absorption (EA) and circular dichroism (CD) spectra of (*R*)-2-amino-1-phenylpropane [(*R*)-**5a**] in methanol from 230−290 nm. As discussed earlier in connection with the ^1L_b absorption band in the EA spectra of other monosubstituted benzene compounds,[10] the longest wavelength maxima at 267 nm (band origin) in the EA spectrum of (*R*)-**5a** in methanol corresponds to the 0−0 transition which in toluene is a $B_2 \leftarrow A_1$ electronic transition. For (*R*)-**5a**, this electronic transition 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 2) 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 2, 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 $(10 + 9) \times 10^2$ cm^{-1}. A corresponding EA absorption maximum is observed at $(375 + 10) \times 10^2$ cm^{-1}, but one at $(375 + 10 + 9) \times 10^2$ 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 (A_1) with the first vibrational level $^vB_2$ nontotally 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 2). In the EA spectrum of (*R*)-**5a**, three of these transitions are seen as maxima separated from the band origin by 4×10^2, $(4 + 9) \times 10^2$, and $(4 + 9 + 7) \times 10^2$ cm^{-1}, respectively. Since CD minima are near these EA maxima, the CEs associated with these EA maxima are weak.

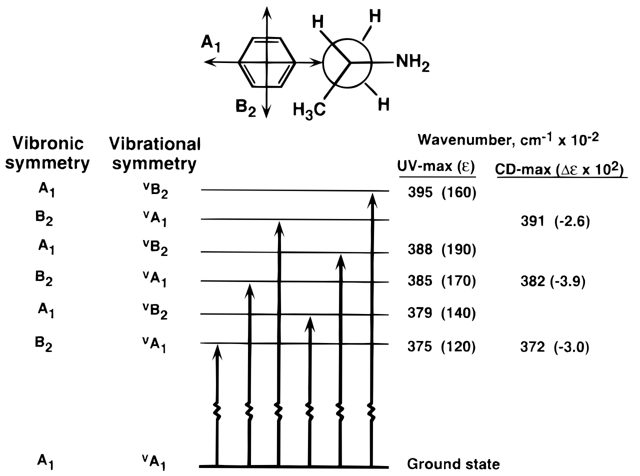

Figure 2. Schematic diagram of the electronic absorption (EA) and circular dichroism (CD) maxima observed with (*R*)-2-amino-1-phenylpropane hydrochloride [(*R*)-**5a**·HCl] in 0.1 M KOH in methanol. The A_1 and B_2 axes are in the plane of the benzene ring.

Since (*R*)-2-amino-1-phenylpropane [(*R*)-**5a**] in methanol shows negative ^1L_b CEs, the conformational equilibrium for (*R*)-**5a** in methanol is such that its CD spectrum is the result of the greater rotatory contribution of (−)-**9a** ($R^1 = CH_3$, $R^2 = NH_2$) as compared to (+)-**9b**, both the greater rotatory contribution of a methyl group than that of an amino group[3] and the respective mole fractions of (−)-**9a** and (+)-**9b** coming into play. The negative sign for the ^1L_b CEs of (*R*)-**5a** is in agreement with the positive sign for the longest wavelength CE previously reported for (*S*)-**5a** in methanol,[5,21] 95% ethanol,[20] and isopropyl alcohol.[21] When the solvent is cyclohexane, however, the sign of ^1L_b CEs for (*R*)-**5a** is positive,[27] and Table 2 compares the position and molar absorptivity (ϵ) and molar dichroic absorption ($\Delta\epsilon$) of the ^1L_b band origin of (*R*)-**5a** in

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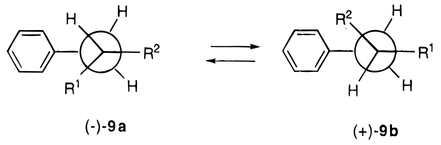
Table 2. ^1L_b Band Origin Maxima for Benzylalkylcarbinamines, Carbinamine Salts, and Carbinols



carbinamines				carbinamine salts				carbinols			
solute	substituents	solvent	λ, nm (ε[a]) [λ, nm (Δε[b] × 10²)]	solute	substituents	solvent	λ, nm (ε[a]) [λ, nm (Δε[b] × 10²)]	solute	substituents	solvent	λ, nm (ε[a]) [λ, nm (Δε[b] × 10²)]
(*R*)-**5a**·HCl	$R^1 = CH_3$ $R^2 = NH_2$	0.1 M KOH in MeOH	267 (120) [269 (−3.0)]	(*R*)-**5a**·HCl	$R^1 = CH_3$ $R^2 = N^+H_3$	H_2O	[266 (−1.3)]	(*R*)-**5c**	$R^1 = CH_3$ $R^2 = OH$	H_2O	[268 (−2.3)]
(*R*)-**5a**[c,d]	$R^1 = CH_3$ $R^2 = NH_2$	cyclohexane	268 (150) [268 (+4.5)]	(*R*)-**5a**·HCl	$R^1 = CH_3$ $R^2 = N^+H_3$	MeOH	266 (77)[e] [267 (−3.3)]	(*R*)-**5c**	$R^1 = CH_3$ $R^2 = OH$	MeOH	267 (120) [268 (−5.5)]
(*S*)-**6a**[d,f]	$R^1 = c\text{-}C_6H_{11}$ $R^2 = NH_2$	cyclohexane	[269 (+4.5[g])]	(*R*)-**5a**·$^1/_2H_2(SO_4)$[d,j]	$R^1 = CH_3$ $R^2 = N^+H_3$	95% EtOH	267 (350) [268 (−20)]	(*R*)-**5c**[h]	$R^1 = CH_3$ $R^2 = OH$	MeOH	269[i] [271 (−0.6[g])]
(*R*)-**6c**[d,j]	$R^1 = CH_3$ $R^2 = NHCH_3$	95% EtOH	268 (170) [268 (−9.2)]	(*R*)-**6c**·HCl[d,j]	$R^1 = CH_3$ $R^2 = N^+H_2CH_3$	95% EtOH	268 (330) [268 (−7.1)]	(*R*)-**5c**	$R^1 = CH_3$ $R^2 = OH$	dioxane	[269 (−4.5)]
(*R*)-**6d**[d,j]	$R^1 = CH_3$ $R^2 = N(CH_3)_2$	95% EtOH	269 (150) [268 (−10)]	(*R*)-**6d**·HCl[d,j]	$R^1 = CH_3$ $R^2 = N^+H(CH_3)_2$	95% EtOH	268 (81) [267 (−9.1)]	(*R*)-**5c**	$R^1 = CH_3$ $R^2 = OH$	THF	[269 (−5.5)]
(*R*)-**6d**[c]	$R^1 = CH_3$ $R^2 = N(CH_3)_2$	cyclohexane	272 (190) [272 (−7.3)]	(*R*)-**6d**·methiodide[d,j]	$R^1 = CH_3$ $R^2 = N^+(CH_3)_3$	95% EtOH	268 (87) [273 (−13)]	(*R*)-**5c**	$R^1 = CH_3$ $R^2 = OH$	cyclohexane	[269 (−1.7)]

[a] Molar absorptivity. [b] Molar dichroic absorption; $\Delta\epsilon = [\theta]/3300$ where $[\theta]$ is the molecular ellipticity. [c] Data from ref 5. [d] Enantiomer used. [e] Shoulder. [f] Data from ref 23. [g] Molecular amplitude for the longest wavelength ^1L_b Cotton effect in the ORD curve. [h] Data from ref 22. [i] Molar absorptivity not reported. [j] Data from ref 20.

both methanol and cyclohexane.[31] The positive sign for ^1L_b CEs for (*R*)-**5a** in cyclohexane confirms an earlier observation[27] of negative ^1L_b CEs for (*S*)-**5a** in cyclohexane and is the result of shift in the equilibrium from (−)-**9a** to (+)-**9b** 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.[30] The positive sign in the ORD curve for the ^1L_b CEs for (*S*)-1-cyclohexyl-2-phenylethylamine [(*S*)-**6a**] in cyclohexane is explained on a similar basis,[31] the cyclohexyl group larger in effective size than the methyl group and thus stabilizing conformer (+)-**9b** as compared to (−)-**9a** to a greater extent than in the case of (*R*)-**5a**.

As shown in Table 2,[31] (*R*)-*N*-methyl- and (*R*)-*N*,*N*-dimethyl-2-amino-1-phenylpropane [(*R*)-**6c** and (*R*)-**6d**] in 95% ethanol, and as reported for (*R*)-**6d** in methanol,[5] 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*)-**6d** also shows negative ^1L_b CEs even in cyclohexane.

Using this same interpretation, the sign of the ^1L_b CEs of (*R*)-2-amino-1-phenylpropane hydrochloride [(*R*)-**5a**·HCl] in water, methanol, and 0.1 M HCl in methanol[32] is also predicted to be negative, confirming earlier reports of a negative sign for ^1L_b CEs for (*R*)-**5a**·HCl in water,[10,21] methanol,[5,10,21,26] and isopropyl alcohol,[10,21] and of (*R*)-**5a**·$^1/_2(H_2SO_4)$ in 95% ethanol.[20] Similarly, the ^1L_b CEs for (*R*)-*N*-methyl- and (*R*)-*N*,*N*-dimethyl-2-amino-1-phenylpropane hydrochloride [(*R*)-**6c**·HCl and (*R*)-**6d**·HCl] in 95% ethanol, (*R*)-**6d**·HCl in methanol,[32] and (*R*)-**6d**·methiodide in 95% ethanol are also negative.

As shown in Table 2,[31] (*R*)-1-phenyl-2-propanol [(*R*)-**5c**] in water, methanol, dioxane, and tetrahydrofuran (THF) also shows negative ^1L_b CEs. When the solvent is change from water to cyclohexane the intensity of the ^1L_b CEs is reduced, but the sign remains negative. The equilibrium shown at the top of Table 2 can be assumed to shift from (−)-**9a** and (+)−**9b** but not enough to cause a change in sign of the ^1L_b CEs.

L-Phenylalanines with Postive, Neutral, and Acetylated Nitrogen. In contrast to the enantiomers of a benzylalkylcarbinamine, carbinamine salt, and carbinol, each of which show a single sign for its ^1L_b CEs, L-phenylalanine and some of its derivatives in some solvents show oppositely signed ^1L_b CEs in their CD spectra. Thus, L-phenylalanine (L-**5b**) in water shows positive ^1L_b CEs (Table 3),[31] but in methanol, the CD spectrum (Figure 3) is more complex and shows both negative and positive CD maxima. These observations are in agreement with an earlier report[9] of positive ^1L_b CEs for L-**5b** in water and negative and positive ^1L_b CEs for L-**5b** in glycerol−methanol, the positive CEs being assigned in the latter solvent to electronic transitions from the ground state to nontotally symmetric vibronic excited states.[9] Based on the data in Table 3, however, the two longest wavelength CD maxima in the spectrum of L-**5b** in methanol are assigned differently and comprise a double CE,[33] 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 slightly from (+)-**9b** to (−)-**9a**, and the greater amount of (−)-**9a** is now detected in the CD spectrum. Thus the positive and negative ^1L_b CEs centered at 267 nm arise from conformers (+)-**9b** and (−)-**9a**, respectively. The negative CD maxima at 269 nm results from a small bathochromic shift of the EA absorption of the phenyl group in (−)-**9a** due to the influence

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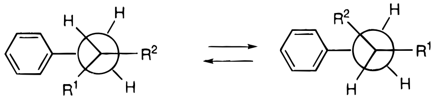
(31) Complete EA and CD data are given in the Experimental Section or in previous reports shown as footnotes in the tables.

(32) See Experimental Section.

(33) Wellman, K. M.; Laur, P. H. A.; Briggs, W. S.; Moscowitz, A.; Djerassi, C. *J. Am. Chem. Soc.* **1965**, *87*, 66−72.

Table 3. ^1L_b Band Origin Maxima for Phenylalanines with Positive, Neutral, and Acetylated Nitrogen



(-)-**9a** (+)-**9b**

positive nitrogen				neutral nitrogen				acetylated nitrogen			
solute	substituents	solvent	λ, nm (ϵ^a) [λ, nm ($\Delta\epsilon^b \times 10^2$)]	solute	substituents	solvent	λ, nm (ϵ^a) [λ, nm ($\Delta\epsilon^b \times 10^2$)]	solute	substituents	solvent	λ, nm (ϵ^a) [λ, nm ($\Delta\epsilon^b \times 10^2$)]
L-**5b**	$R^1 = CO_2^-$ $R^2 = N^+H_3$	H_2O	[265 (+1.1)]	L-**5b**	$R^1 = CO_2^-$ $R^2 = NH_2$	1 M NaOH in H_2O	[271 (−0.12)] [266 (+1.5)]	L-**7c**	$R^1 = CO_2^-$ $R^2 = NHCOCH_3$	1 M NaOH in H_2O	[267 (−3.0)]
L-**5b**	$R^1 = CO_2^-$ $R_2 = N^+H_3$	MeOH	267 (77)^c [269 (−0.64)] [265 (+0.14)]	L-**5b**	$R^1 = CO_2^-$ $R^2 = NH_2$	0.1 M KOH in MeOH	268 (110) [270 (−0.64)] [266 (+0.82)]	L-**7c**	$R^1 = CO_2^-$ $R_2 = NHCOCH_3$	0.1 M KOH in MeOH	267 (100) [269 (−2.1)] [264 (+0.82)]
L-**7a**	$R^1 = CO_2^-$ $R^2 = N^+H_2CH_3$	H_2O	[266 (+1.9)]	L-**7a**	$R^1 = CO_2^-$ $R^2 = NHCH_3$	1 M NaOH in H_2O	[268 (−0.52)] [265 (+0.58)]	L-**7c**	$R^1 = CO_2H$ $R^2 = NHCOCH_3$	H_2O	[268 (−2.8)]
L-**7a**	$R^1 = CO_2^-$ $R^2 = N^+H_2CH_3$	MeOH	267 (150)^c [270 (−0.39)] [266 (+0.73)]	L-**7b**·HCl	$R^1 = CO_2CH_3$ $R^2 = NH_2$	1 M NaOH in H_2O	[266 (+1.6)]	L-**7c**	$R^1 = CO_2H$ $R^2 = NHCOCH_3$	MeOH	267 (83)^c [268 (−2.8)] [265 (+0.06)]
L-**5b**	$R^1 = CO_2H$ $R^2 = N^+H_3$	1 M HCl in H_2O	[265 (+1.4)]	L-**7b**·HCl	$R^1 = CO_2CH_3$ $R^2 = NH_2$	0.1 M KOH in MeOH	267 (100) [270 (−0.33)] [266 (+1.1)]	L-**7c**	$R^1 = CO_2H$ $R^2 = NHCOCH_3$	dioxane	[269 (−0.42)] [265 (+1.8)]
L-**5b**	$R^1 = CO_2H$ $R^2 = N^+H_3$	0.1 M HCl in MeOH	266 (70)^c [266 (+1.1)]					L-**7c**	$R^1 = CO_2H$ $R^2 = NHCOCH_3$	THF	[269 (−0.97)] [265 (+1.4)]
L-**7a**	$R^1 = CO_2H$ $R^2 = N^+H_2CH_3$	1 M HCl in H_2O	[266 (+3.3)]					L-**7d**	$R^1 = CO_2CH_2CH_3$ $R^2 = NHCOCH_3$	H_2O	[267 (−2.1)]
L-**7a**	$R^1 = CO_2H$ $R^2 = N^+H_2CH_3$	0.1 M HCl in MeOH	267 (66)^c [266 (+3.0)]					L-**7d**	$R^1 = CO_2CH_2CH_3$ $R^2 = NHCOCH_3$	MeOH	267 (87)^c [268 (−2.8)]
L-**7b**·HCl	$R^1 = CO_2CH_3$ $R^2 = N^+H_3$	H_2O	[266 (+1.8)]					L-**7d**	$R^1 = CO_2CH_2CH_3$ $R^2 = NHCOCH_3$	THF	[269 (−1.3)] [265 (+0.85)]
L-**7b**·HCl	$R^1 = CO_2CH_3$ $R^2 = N^+H_3$	MeOH	267 (73)^c [265 (+0.94)]					L-**7d**	$R^1 = CO_2CH_2CH_3$ $R^2 = NHCOCH_3$	cyclohexane	[269 (−0.45)] [265 (+1.6)]

[a] Molar absorptivity. [b] Molar dichroic absorption; $\Delta\epsilon = [\theta]/3300$ where $[\theta]$ is the molecular ellipticity. [c] Shoulder.

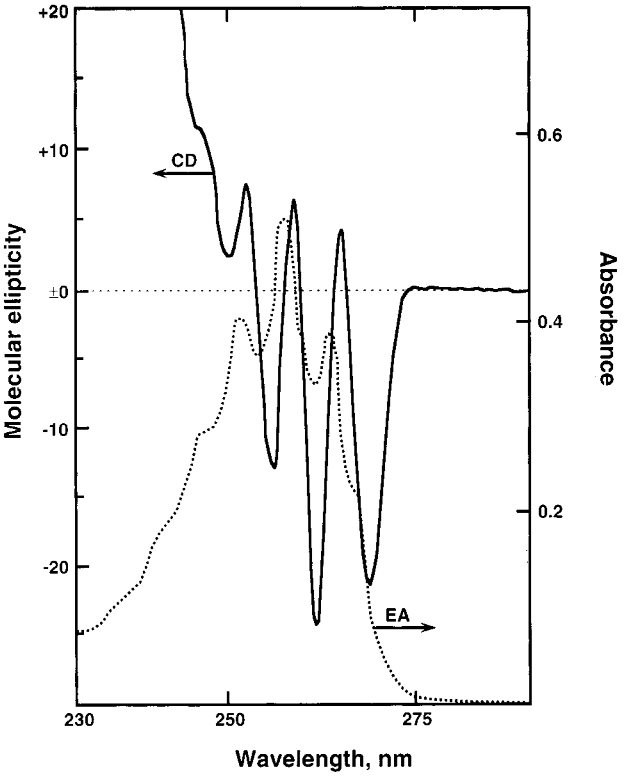


Figure 3. Electronic absorption (EA) and circular dichroism (CD) spectra of L-phenylalanine (L-**5b**) in methanol. For the EA spectrum, the concentration was 3.0 × 10^{-3} M.

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-**7a**) shows positive ^1L_b CEs in water but double ^1L_b CEs in methanol (Table 3[31]). In both water and methanol, the hydrochlorides of L-phenylalanine and *N*-methyl-L-phenylalanine (L-**5b** and L-**7a** in 1 M HCl in H_2O and 0.1 M HCl in MeOH) and methyl L-phenylalanine hydrochloride (L-**7b**·HCl) show only positive ^1L_b CEs. For each of these compounds with a positive nitrogen atom, conformer (+)-**9b** gives the sign of the ^1L_b CEs. With the exception of L-**7b** in water (L-**7b**·HCl in 1 M NaOH in H_2O), the L-phenylalanines L-**5b**, L-**7a**, and L-**7b** with a neutral nitrogen atom show double CEs for the ^1L_b band origin (Table 3) in both water and methanol, but at shorter wavelength only positive ^1L_b CEs are observed.[32] The less intense, negative CEs associated with the EA band origin is due to the presence of conformer (−)-**9a**, but at shorter wavelength, negative CEs are not observed in the presence of the stronger positive CEs displayed by conformer (+)-**9b**.

Acetylation of L-phenylalanines and ethyl L-phenylalaninate 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-**7c** in 1 M NaOH in H_2O), *N*-acetyl-L-phenylalanine (L-**7c**) in water, and ethyl *N*-acetyl-L-phenylalaninate (L-**7d**) in water and methanol is shifted toward conformer (−)-**9a**, and only negative ^1L_b CEs are observed. In less polar solvents, both positive and negative ^1L_b CEs associated with conformers (−)-**9a** and (+)-**9b** are observed, potassium *N*-acetyl-L-phenylalaninate in methanol (L-**7c** in 0.1 M KOH in MeOH), *N*-acetyl-L-phenylalanine in methanol, dioxane, and tetrahydrofuran, and L-**7d** in tetrahydrofuran and in cyclohexane showing double CEs for the ^1L_b band origin. As expected, the longer wavelength component of the double CEs (Table 3) is negative and is associated with the EA transition of (−)-**9a**, bathochromically shifted when a carboxylate, carboxyl, or ethoxycarbonyl group is gauche to the benzene ring chromophore.

L-3-Phenyllactic Acid Derivatives and (*S*)-Phenylalaninol and Its Hydrochloride. The CD of sodium L-3-phenyllactate in water (L-**5d** in 1 M NaOH in H_2O) shows negative ^1L_b CEs but double ^1L_b CEs in methanol (L-**5d** in 0.1 M KOH in MeOH) (Table 4[31]). Protonation of the carboxylate group shifts the conformational equilibrium of L-**5d** more toward (+)-**9b**, and L-**5d** in water, methanol, and tetrahydrofuran shows double ^1L_b CEs, although earlier reports[6,24] of the CD spectrum of L-**5d** in water and methanol give a single CE for the ^1L_b band origin, in water, positive,[6] in methanol, negative.[24] That the negative component of the double band origin CE in L-**5d** in water, methanol, and tetrahydrofuran is due to conformer (−)-**9a** follows from its position at a longer wavelength than that of the positive component, the benzene ring chromophore transition always slightly shifted bathochromically when it is gauche to a carboxylate group rather than gauche to an ammonium or amino group.

The CD spectrum of the methyl esters of L-3-phenyllactate (L-**8**) was reported earlier to show substantial solvent effects,[6,24] but double ^1L_b CEs were not observed. Thus L-**8** in water and methanol gave positive CEs,[6] but in hexane their sign was negative,[24] the sign reversal suggesting the dominance of (+)-**9b** in the hydrogen bonding solvents and an increased amount of (−)-**9a** in hexane.

The CD spectrum of (*S*)-phenylalaninol [(*S*)-**6b**] can also be interpreted in terms of a conformational equilibrium of the two conformers (−)-**9a** and (+)-**9b**, L-**6b** in water, methanol, and tetrahydrofuran showing negative ^1L_b CEs, similar to those shown by (*R*)-**5a** in methanol. In cyclohexane, there is a shift in the conformational equilibrium from (−)-**9a** in which the hydroxymethylene group is gauche to the benzene chromophore toward conformer (+)-**9b**, and the greater amount of (+)-**9b** 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-**6b**·HCl shows negative ^1L_b CEs, much the same as shown by (*R*)-2-amino-1-phenylpropane hydrochloride [(*R*)-**5a**·HCl] in water and methanol. In these cases, (−)-**9a** is the dominant conformer as a result of the interaction of the ammonium group with the polar solvents.

Experimental Section

The solutes were purchased as indicated in Table 1 and were used without further purification. They had rotatory powers as shown in Table 1 in agreement with those reported by the supplier and as noted below. Rotatory powers at the sodium D line were measured with a Rudolph Research Autopol III automatic polarimeter using a 1-dm sample tube. Electronic absorption (EA) spectra were measured using a Varian Cary 2300 spectrophotometer and matched 1-cm cells. Circular dichroism (CD) were observed with a Jasco J-720 spectrophotometer, using a 1-cm sample cell. Solutions for these measurements were prepared by diluting 4.6 to 11.9 mg of solute to 10.0 mL with solvent, and for each spectrum the concentration (*c*) is given in g per 100 mL of solution.

(*R*)-2-Amino-1-phenylpropane hydrochloride [(*R*)-5a·HCl) had $[\alpha]^{23}_{\mathrm{D}}$ −23° (*c* 1.0, H_2O) [lit.[28] $[\alpha]^{15}_{\mathrm{D}}$ + 24.8° (*c* 9.00, H_2O) for the enantiomer]: EA max (0.1 M KOH in MeOH) 267 nm (ϵ 120), 264 (140), 260 (170) (sh), 258 (190), 253 (160), 248 (110), 243 (73) (sh), 238 (44) (sh); CD (*c* 0.061, 0.1 M KOH in MeOH) $[\theta]_{278}$ ±0, $[\theta]_{269}$

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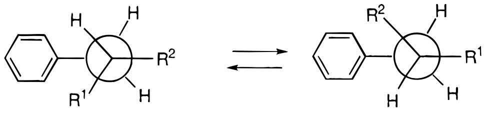
Table 4. ^1L_b Band Origin Maxima for L-3-Phenyllactic Acid Derivatives and L-Phenylalaninol and Its Hydrochloride



(-)-**9a** (+)-**9b**

phenyllactic acid derivatives				phenylalaninol and its hydrochloride			
solute	substituents	solvent	λ, nm (ϵ^a) [λ, nm ($\Delta\epsilon^b \times 10^2$)]	solute	substituents	solvent	λ, nm (ϵ^a) [λ, nm ($\Delta\epsilon^b \times 10^2$)]
L-**5d**	$R^1 = CO_2^-$ $R^2 = OH$	1 M NaOH in H_2O	[269 (−0.67)]	L-**6b**	$R^1 = CH_2OH$ $R^2 = NH_2$	H_2O	[269 (−1.2)]
L-**5d**	$R^1 = CO_2^-$ $R^2 = OH$	0.1 M KOH in MeOH	267 (110) [271 (−0.27)] [267 (+0.36)]	L-**6b**	$R^1 = CH_2OH$ $R^2 = NH_2$	MeOH	267 (130) [269 (−3.3)]
L-**5d**	$R^1 = CO_2H$ $R^2 = OH$	H_2O	[269 (−0.39)] [265 (+0.25)]	L-**6b**	$R^1 = CH_2OH$ $R^2 = NH_2$	THF	[271 (−2.6)]
L-**5d**^{c}	$R^1 = CO_2H$ $R^2 = OH$	H_2O	269 (100) [263 (+1.0)]	L-**6b**	$R^1 = CH_2OH$ $R^2 = NH_2$	cyclohexane	[271 (−1.4)] [267 (+0.91)]
L-**5d**	$R^1 = CO_2H$ $R^2 = OH$	MeOH	267 (94) [270 (−0.39)] [265 (+0.36)	L-**6b**	$R^1 = CH_2OH$ $R^2 = N^+H_3$	1 M HCl in H_2O	[267 (−2.0)]
L-**5d**^{e}	$R^1 = CO_2H$ $R^2 = OH$	MeOH	268^f [269 (−3.0)]	L-**6b**	$R^1 = CH_2OH$ $R^2 = N^+H_3$	0.1 M HCl in MeOH	266 (82)^d [268 (−5.8)]
L-**5d**	$R^1 = CO_2H$ $R^2 = OH$	THF	[271 (−0.21)] [267 (+0.67)]				
L-**8**^{c}	$R^1 = CO_2CH_3$ $R^2 = OH$	H_2O	[264 (+1.0)]				
L-**8**^{c}	$R^1 = CO_2CH_3$ $R^2 = OH$	MeOH	[266 (+0.76)]				
L-**8**^{e}	$R^1 = CO_2CH_3$ $R^2 = OH$	hexane	[269 (−2.1)]				

[a] Molar absorptivity. [b] Molar dichroic absorption; $\Delta\epsilon = [\theta]/3300$ where $[\theta]$ is the molecular ellipticity. [c] Data from ref 6. [d] Shoulder. [e] Data from ref 24. [f] Molar absorptivity not reported.

−99, $[\theta]_{266}$ −65, $[\theta]_{262}$ −130, $[\theta]_{258}$ −79, $[\theta]_{256}$ −87, $[\theta]_{250}$ − 51 (sh), $[\theta]_{245}$ −30 (sh), $[\theta]_{238}$ −15, $[\theta]_{230}$ −28; CD (*c* 0.061, H_2O) $[\theta]_{274}$ ±0, $[\theta]_{266}$ −42, $[\theta]_{263}$ −25, $[\theta]_{259}$ −51, $[\theta]_{256}$ −30, $[\theta]_{253}$ −38, $[\theta]_{245}$ −15 (sh), $[\theta]_{238}$ −6.1, $[\theta]_{235}$ −9.4, $[\theta]_{230}$ −2.8; EA max (MeOH) 266 nm (ϵ 77) (sh), 263 (130), 257 (180), 251 (140), 247 (96), 242 (63) (sh), 237 (38) (sh); CD (*c* 0.063, MeOH) $[\theta]_{275}$ ±0; $[\theta]_{267}$ −110, $[\theta]_{265}$ −64, $[\theta]_{261}$ −130, $[\theta]_{257}$ −80, $[\theta]_{255}$ −87, $[\theta]_{250}$ −49 (sh), $[\theta]_{243}$ −22 (sh), $[\theta]_{232}$ ±0, $[\theta]_{230}$ −4.6; CD (*c* 0.056, 0.1 M HCl in MeOH) $[\theta]_{277}$ ±0, $[\theta]_{268}$ −140, $[\theta]_{265}$ −80, $[\theta]_{261}$ −170, $[\theta]_{258}$ −100, $[\theta]_{255}$ −110, $[\theta]_{250}$ −64 (sh), $[\theta]_{244}$ −30 (sh), $[\theta]_{230}$ −5.9.

L-**Phenylalanine (**L-**5b)** had $[\alpha]^{23}{}_{D}$ −30° (*c* 2.1, H_2O): CD (*c* 0.067, H_2O) $[\theta]_{272}$ ±0, $[\theta]_{265}$ +36, $[\theta]_{262}$ +21, $[\theta]_{259}$ +43, $[\theta]_{255}$ +13, $[\theta]_{253}$ +22, $[\theta]_{249}$ +4.1, $[\theta]_{246}$ +8.8, $[\theta]_{244}$ +7.3, $[\theta]_{230}$ +480; EA max (MeOH) 267 nm (ϵ 77) (sh), 264 (130), 258 (170), 252 (140), 247 (97) (sh), 243 (67) (sh), 237 (38) (sh); CD (*c* 0.067, MeOH) $[\theta]_{274}$ ±0, $[\theta]_{269}$ −21, $[\theta]_{266}$ ±0, $[\theta]_{265}$ +4.5, $[\theta]_{264}$ ±0, $[\theta]_{262}$ −24, $[\theta]_{260}$ ±0, $[\theta]_{259}$ +6.3, $[\theta]_{258}$ ±0, $[\theta]_{256}$ −13, $[\theta]_{254}$ ±0, $[\theta]_{253}$ +7.6, $[\theta]_{250}$ +2.2, $[\theta]_{246}$ +11 (sh), $[\theta]_{230}$ +650; CD (*c* 0.071, 1 M HCl in H_2O) $[\theta]_{274}$ ±0, $[\theta]_{265}$ +47, $[\theta]_{262}$ +37, $[\theta]_{259}$ +61, $[\theta]_{255}$ +36, $[\theta]_{252}$ +52, $[\theta]_{251}$ +47, $[\theta]_{230}$ +3600; EA max (0.1 M HCl in MeOH) 266 nm (ϵ 70) (sh), 263 (130), 257 (160), 251 (130), 247 (96) (sh), 242 (72) (sh); CD (*c* 0.066, 0.1 M HCl in MeOH) $[\theta]_{271}$ ±0, $[\theta]_{266}$ +37, $[\theta]_{263}$ +16, $[\theta]_{259}$ +56, $[\theta]_{256}$ +30, $[\theta]_{252}$ +62 (sh), $[\theta]_{230}$ +4700; CD (*c* 0.069, 1 M NaOH in H_2O) $[\theta]_{272}$ ±0, $[\theta]_{271}$ −4.1, $[\theta]_{270}$ ±0, $[\theta]_{266}$ +48, $[\theta]_{263}$ +25, $[\theta]_{259}$ +61, $[\theta]_{256}$ +34, $[\theta]_{253}$ +49, $[\theta]_{250}$ +28, $[\theta]_{246}$ +34 (sh), $[\theta]_{230}$ +730; EA max (0.1 M KOH in MeOH) 268 nm (ϵ 110), 264 (150), 261 (170) (sh), 258 (200), 253 (160), 248 (120), 243 (77) (sh); CD (*c* 0.063, 0.1 M KOH in MeOH) $[\theta]_{277}$ ±0, $[\theta]_{270}$ −21, $[\theta]_{269}$ ±0, $[\theta]_{266}$ +27, $[\theta]_{263}$ ±0, $[\theta]_{260}$ +38, $[\theta]_{256}$ +10, $[\theta]_{253}$ +29, $[\theta]_{250}$ +9.4, $[\theta]_{247}$ +16, $[\theta]_{244}$ +12, $[\theta]_{230}$ +490.

(*R*)-1-Phenyl-2-propanol [(*R*(-5c] has $[\alpha]^{23}{}_{D}$ −36° (*c* 5.7, benzene) [lit.[34] $[\alpha]_D$ +41.82° (*c* 5.3, benzene): CD (*c* 0.085, H_2O) $[\theta]_{277}$ ±0, $[\theta]_{268}$ −77, $[\theta]_{264}$ −55, $[\theta]_{261}$ −100, $[\theta]_{257}$ −64, $[\theta]_{255}$ −75, $[\theta]_{251}$ −46, $[\theta]_{249}$ −47, $[\theta]_{243}$ −25 (sh), $[\theta]_{230}$ −12; EA max (MeOH) 267 nm (ϵ 120), 264 (140), 260 (170) (sh), 258 (190), 252 (160), 247 (110), 243 (74) (sh), 237 (43) (sh); CD (*c* 0.087, MeOH) $[\theta]_{278}$ ±0, $[\theta]_{268}$ −180, $[\theta]_{266}$ −100, $[\theta]_{262}$ −240, $[\theta]_{258}$ −140, $[\theta]_{256}$ −170, $[\theta]_{250}$ −89 (sh), $[\theta]_{244}$ −44 (sh), $[\theta]_{230}$ −8.2; CD (*c* 0.086, dioxane) $[\theta]_{282}$ ±0, $[\theta]_{269}$ −150, $[\theta]_{266}$ −83, $[\theta]_{263}$ −200, $[\theta]_{259}$ −120, $[\theta]_{257}$ −140, $[\theta]_{252}$ −77, $[\theta]_{250}$ −85, $[\theta]_{245}$ −38; CD (*c* 0.081, THF) $[\theta]_{278}$ ±0, $[\theta]_{269}$ −180, $[\theta]_{266}$ −94, $[\theta]_{262}$ −240, $[\theta]_{259}$ −130, $[\theta]_{256}$ −160, $[\theta]_{252}$ −88, $[\theta]_{250}$ −92, $[\theta]_{246}$ −44 (sh), $[\theta]_{230}$ −13; (*c* 0.099, cyclohexane) $[\theta]_{277}$ ±0, $[\theta]_{269}$ −56, $[\theta]_{266}$ −19, $[\theta]_{262}$ −68, $[\theta]_{258}$ −32, $[\theta]_{256}$ −50, $[\theta]_{251}$ −22, $[\theta]_{249}$ −28, $[\theta]_{243}$ −18 (sh), $[\theta]_{238}$ − 13 (sh), $[\theta]_{230}$ −11.

L-**3-Phenyllactic acid (**L-**5d)** had $[\alpha]^{23}{}_{D}$ −19° (*c* 2.2, H_2O) [lit.[35] $[\alpha]^{25-27}{}_{D}$ −20° (1−5% solution in H_2O]: CD (*c* 0.074, 1.0 M NaOH in H_2O) $[\theta]_{275}$ ±0, $[\theta]_{269}$ −22, $[\theta]_{265}$ −3.7, $[\theta]_{262}$ −31, $[\theta]_{258}$ ±0, $[\theta]_{255}$ −19, $[\theta]_{253}$ ±0, $[\theta]_{252}$ +2.1, $[\theta]_{251}$ ±0, $[\theta]_{249}$ −7.4, $[\theta]_{247}$ ±0, $[\theta]_{245}$ +8.6 (sh), $[\theta]_{230}$ +540; EA max (0.1 M KOH in MeOH) 267 nm (ϵ 110), 264 (150), 260 (170) (sh), 258 (200), 252 (160), 248 (120), 243 (80) (sh), 238 (51) (sh); CD (*c* 0.069, 0.1 M KOH in MeOH) $[\theta]_{277}$ ±0, $[\theta]_{271}$ −8.8, $[\theta]_{269}$ ±0, $[\theta]_{267}$ +12, $[\theta]_{265}$ ±0, $[\theta]_{263}$ −7.8, $[\theta]_{262}$ ±0, $[\theta]_{260}$ +21, $[\theta]_{258}$ ±0, $[\theta]_{257}$ −4.9, $[\theta]_{256}$ ±0, $[\theta]_{254}$ +19, $[\theta]_{250}$ +1.3, $[\theta]_{247}$ +10, $[\theta]_{244}$ +4.1, $[\theta]_{240}$ +13 (sh), $[\theta]_{230}$ +210; CD (*c* 0.057, H_2O) $[\theta]_{273}$ ±0, $[\theta]_{269}$ −13, $[\theta]_{266}$ ±0, $[\theta]_{265}$ +8.2, $[\theta]_{264}$ ±0, $[\theta]_{261}$ −19, $[\theta]_{260}$ ±0, $[\theta]_{256}$ ±0, $[\theta]_{255}$ −5.2, $[\theta]_{254}$ ±0, $[\theta]_{252}$ +17, $[\theta]_{249}$ +8.6, $[\theta]_{230}$ +1700; EA max (MeOH) 267 nm (ϵ 94), 264 (140), 258 (190), 252 (150), 247 (110), 242 (84); CD (*c* 0.058, MeOH) $[\theta]_{274}$ ±0, $[\theta]_{270}$ −13, $[\theta]_{267}$ ±0, $[\theta]_{265}$ +12, $[\theta]_{264}$ ±0, $[\theta]_{262}$ −12, $[\theta]_{261}$ ±0, $[\theta]_{259}$ +28, $[\theta]_{257}$ ±0, $[\theta]_{256}$ −2.0, $[\theta]_{255}$ ±0, $[\theta]_{253}$ +22, $[\theta]_{251}$ +20, $[\theta]_{230}$ +4700; CD (*c* 0.106, THF) $[\theta]_{277}$ ±0, $[\theta]_{271}$ −6.8, $[\theta]_{270}$ ±0, $[\theta]_{267}$ +22, $[\theta]_{264}$ ±0, $[\theta]_{263}$ −7.9, $[\theta]_{262}$ ±0, $[\theta]_{260}$ +36, $[\theta]_{258}$ ±0, $[\theta]_{256}$ −7.2, $[\theta]_{255}$ ±0, $[\theta]_{254}$ +11, $[\theta]_{253}$ ±0, $[\theta]_{251}$ −15, $[\theta]_{249}$ ±0, $[\theta]_{233}$ +2800.

L-**Phenylalaninol (**L-**6b)** had $[\alpha]^{23}{}_{D}$ −22° (*c* 1.5, 1 M HCl): CD (*c* 0.078, H_2O) $[\theta]_{277}$ ±0, $[\theta]_{269}$ −40, $[\theta]_{266}$ −27, $[\theta]_{262}$ −54, $[\theta]_{257}$ −40,

$[\theta]_{255}$ −47, $[\theta]_{251}$ −30, $[\theta]_{249}$ −32, $[\theta]_{242}$ −22 (sh), $[\theta]_{237}$ −17; EA max (MeOH) 267 nm (ϵ 130), 264 (150), 260 (180) (sh), 258 (200), 253 (160), 248 (120), 243 (78) (sh), 238 (48) (sh); CD (*c* 0.070, MeOH) $[\theta]_{275}$ ±0, $[\theta]_{269}$ −110, $[\theta]_{266}$ −65, $[\theta]_{262}$ −150, $[\theta]_{259}$ −89, $[\theta]_{256}$ −110, $[\theta]_{251}$ −60 (sh), $[\theta]_{244}$ −31 (sh), $[\theta]_{235}$ −18; CD (*c* 0.083, THF) $[\theta]_{279}$ ±0, $[\theta]_{271}$ −85, $[\theta]_{267}$ −4.9, $[\theta]_{264}$ −93, $[\theta]_{260}$ −32, $[\theta]_{257}$ −65, $[\theta]_{253}$ −29, $[\theta]_{250}$ −41, $[\theta]_{247}$ −27, $[\theta]_{243}$ −35 (sh), $[\theta]_{233}$ −220; CD (*c* 0.067, cyclohexane) $[\theta]_{276}$ ±0, $[\theta]_{271}$ −45, $[\theta]_{269}$ ±0, $[\theta]_{267}$ +30, $[\theta]_{266}$ ±0, $[\theta]_{264}$ −28, $[\theta]_{262}$ ±0, $[\theta]_{261}$ +20, $[\theta]_{259}$ ±0, $[\theta]_{257}$ −9.3, $[\theta]_{254}$ ±0, $[\theta]_{253.5}$ +1.8, $[\theta]_{253}$ ±0, $[\theta]_{250}$ −10, $[\theta]_{248}$ −6.5, $[\theta]_{243}$ −20, $[\theta]_{234}$ −13, $[\theta]_{230}$ −36; CD (*c* 0.101, 1 M HCl in H_2O) $[\theta]_{276}$ ±0, $[\theta]_{267}$ −65, $[\theta]_{264}$ −52, $[\theta]_{260}$ −86, $[\theta]_{256}$ −58, $[\theta]_{254}$ −61, $[\theta]_{249}$ −38 (sh), $[\theta]_{230}$ −14; EA max (0.1 M HCl in MeOH) 266 nm (ϵ 82) (sh), 263 (140), 257 (180), 252 (140), 247 (100), 242 (61) (sh), 237 (41) (sh); CD (*c* 0.050, 0.1 M HCl in MeOH) $[\theta]_{277}$ ±0, $[\theta]_{268}$ −190, $[\theta]_{265}$ −110, $[\theta]_{261}$ −230, $[\theta]_{258}$ −140, $[\theta]_{255}$ −160, $[\theta]_{251}$ −94 (sh), $[\theta]_{244}$ −53 (sh), $[\theta]_{230}$ −19.

***N*-Methyl-L-phenylalanine (L-7a)** had $[\alpha]^{23}_{D}$ +20° (*c* 1.0, 1 M HCl) [lit.[36] $[\alpha]^{20}_{D}$ +21° (*c* 3.0, 1 N HCl): CD (*c* 0.054, H_2O) $[\theta]_{276}$ ±0, $[\theta]_{266}$ +64, $[\theta]_{263}$ +46, $[\theta]_{259}$ +72, $[\theta]_{256}$ +41, $[\theta]_{253}$ +55, $[\theta]_{250}$ +26, $[\theta]_{246}$ +36, $[\theta]_{244}$ +32, $[\theta]_{230}$ +390; EA max (MeOH) 267 nm (ϵ 150) (sh), 264 (250), 258 (310), 252 (240), 248 (170) (sh), 243 (120) (sh), 237 (68) (sh); CD (*c* 0.046, MeOH) $[\theta]_{277}$ ±0, $[\theta]_{270}$ −13, $[\theta]_{268}$ ±0, $[\theta]_{266}$ +24, $[\theta]_{263}$ ±0, $[\theta]_{259}$ +34, $[\theta]_{256}$ ±0, $[\theta]_{253}$ +20, $[\theta]_{250}$ +8.6, $[\theta]_{248}$ +12, $[\theta]_{245}$ +7.8, $[\theta]_{230}$ +430; CD (*c* 0.047, 1 M HCl in H_2O) $[\theta]_{273}$ ±0, $[\theta]_{266}$ +110, $[\theta]_{263}$ +79, $[\theta]_{259}$ +130, $[\theta]_{256}$ +72, $[\theta]_{253}$ +93, $[\theta]_{250}$ +83, $[\theta]_{230}$ +3100; EA max (0.1 M HCl in MeOH) 267 nm (ϵ 66) (sh), 263 (130), 257 (170), 252 (140), 247 (96) (sh), 242 (70) (sh); CD (*c* 0.051, 0.1 M HCl in MeOH) $[\theta]_{273}$ ±0, $[\theta]_{266}$ +100, $[\theta]_{263}$ +63, $[\theta]_{260}$ +120, $[\theta]_{257}$ +74, $[\theta]_{253}$ +110 (sh), $[\theta]_{230}$ +4400; CD (*c* 0.055, 1 M NaOH in H_2O) $[\theta]_{272}$ ±0, $[\theta]_{268}$ −17, $[\theta]_{266}$ ±0, $[\theta]_{265}$ +19, $[\theta]_{263}$ ±0, $[\theta]_{262}$ −9.0, $[\theta]_{261}$ ±0, $[\theta]_{258}$ +36, $[\theta]_{256}$ +17, $[\theta]_{251}$ +37 (sh), $[\theta]_{230}$ +3200.

Methyl L-phenylalaninate hydrochloride (L-7b·HCl) had $[\alpha]^{23}_{D}$ +29° (*c* 2.1, abs EtOH); CD (*c* 0.086 in H_2O) $[\theta]_{273}$ ±0, $[\theta]_{266}$ +58, $[\theta]_{263}$ +50, $[\theta]_{259}$ +69, $[\theta]_{255}$ +43, $[\theta]_{253}$ +61, $[\theta]_{249}$ +38, $[\theta]_{230}$ +2600; EA max (MeOH) 267 nm (ϵ 73) (sh), 264 (140), 258 (180), 252 (140), 248 (100) (sh), 242 (70) (sh); CD (*c* 0.077, MeOH) $[\theta]_{272}$ ±0, $[\theta]_{265}$ +31, $[\theta]_{262}$ +13, $[\theta]_{259}$ +47, $[\theta]_{256}$ +21, $[\theta]_{252}$ +44, $[\theta]_{251}$ +42, $[\theta]_{230}$ +4300; CD (*c* 0.087, 1.0 M NaOH in H_2O) $[\theta]_{271}$ ±0, $[\theta]_{266}$ +54, $[\theta]_{263}$ +21, $[\theta]_{259}$ +70, $[\theta]_{256}$ +36, $[\theta]_{253}$ +48, $[\theta]_{250}$ +32, $[\theta]_{246}$ +38 (sh), $[\theta]_{230}$ +750; EA max (0.1 M KOH in MeOH) 267 nm (ϵ 100), 264 (160), 258 (200), 252 (170), 248 (130), 242 (100); CD (*c* 0.054, 0.1 M KOH in MeOH) $[\theta]_{274}$ ±0, $[\theta]_{270}$ −11, $[\theta]_{268}$ ±0, $[\theta]_{266}$ +35, $[\theta]_{263}$ ±0, $[\theta]_{259}$ +51, $[\theta]_{256}$ +11, $[\theta]_{253}$ +31, $[\theta]_{250}$ ±0, $[\theta]_{247}$ +19 (sh), $[\theta]_{230}$ +3300.

***N*-Acetyl-L-phenylalanine (L-7c)** had $[\alpha]^{23}_{D}$ +33° (*c* 1.0, MeOH): CD (*c* 0.071, 1.0 M NaOH in H_2O) $[\theta]_{273}$ ±0, $[\theta]_{267}$ −100, $[\theta]_{264}$ −14, $[\theta]_{261}$ −74, $[\theta]_{258}$ ±0, $[\theta]_{257}$ +27, $[\theta]_{254}$ +5.6, $[\theta]_{250}$ +53, $[\theta]_{249}$ +49, $[\theta]_{245}$ +64 (sh), $[\theta]_{230}$ +1000; EA max (0.1 M KOH in MeOH) 267 nm (ϵ 100), 264 (150), 258 (200), 252 (160), 247 (120), 242 (83) (sh); CD (*c* 0.069, 0.1 M KOH in MeOH) $[\theta]_{274}$ ±0, $[\theta]_{269}$ −69, $[\theta]_{266}$ ±0, $[\theta]_{264}$ +27, $[\theta]_{263}$ ±0, $[\theta]_{262}$ −23, $[\theta]_{261}$ ±0, $[\theta]_{258}$ +81, $[\theta]_{255}$ +52, $[\theta]_{251}$ +93, $[\theta]_{249}$ +85, $[\theta]_{245}$ +100 (sh), $[\theta]_{230}$ +1500; CD (*c* 0.067, H_2O) $[\theta]_{275}$ ±0, $[\theta]_{268}$ −94, $[\theta]_{264}$ −10, $[\theta]_{261}$ −66, $[\theta]_{258}$ ±0, $[\theta]_{257}$ +30, $[\theta]_{254}$ +5.6, $[\theta]_{251}$ +40, $[\theta]_{248}$ +31, $[\theta]_{230}$ +1800; EA max (MeOH) 267 nm (ϵ 83) (sh), 264 (140), 258 (180), 252 (150), 247 (110), 241 (90) (sh); CD (*c* 0.066, MeOH) $[\theta]_{274}$ ±0, $[\theta]_{268}$ −92, $[\theta]_{265}$ ±0, $[\theta]_{264.5}$ +2.1, $[\theta]_{264}$ ±0, $[\theta]_{261}$ −67, $[\theta]_{259}$ ±0, $[\theta]_{258}$ +17, $[\theta]_{256}$ ±0, $[\theta]_{254}$ −26, $[\theta]_{252}$ −14, $[\theta]_{249}$ −41, $[\theta]_{245}$ ±0, $[\theta]_{230}$ +5600; CD (*c* 0.096, dioxane) $[\theta]_{273}$ ±0, $[\theta]_{269}$ −14, $[\theta]_{268}$ ±0, $[\theta]_{265}$ +61, $[\theta]_{262}$ +35, $[\theta]_{259}$ +97, $[\theta]_{256}$ +65, $[\theta]_{251}$ +100 (sh), $[\theta]_{249}$ +130; CD (*c* 0.064, THF) $[\theta]_{273}$ ±0, $[\theta]_{269}$ −32, $[\theta]_{267}$ ±0, $[\theta]_{265}$ +45, $[\theta]_{262}$ +13, $[\theta]_{259}$ +77, $[\theta]_{256}$ +50, $[\theta]_{253}$ +69, $[\theta]_{251}$ +65, $[\theta]_{234}$ +3000.

Ethyl *N*-acetyl-L-phenylalaninate (L-7d) had $[\alpha]^{23}_{D}$ +12° (*c* 1.0, MeOH): CD (*c* 0.078, H_2O) $[\theta]_{273}$ ±0, $[\theta]_{267}$ −68, $[\theta]_{264}$ −2.5, $[\theta]_{261}$ −48, $[\theta]_{258}$ ±0, $[\theta]_{257}$ +18, $[\theta]_{255}$ ±0, $[\theta]_{254}$ −6.6, $[\theta]_{253}$ ±0, $[\theta]_{251}$ +21, $[\theta]_{248}$ ±0, $[\theta]_{241}$ −77, $[\theta]_{238}$ ±0; EA max (MeOH) 267 nm (ϵ 87) (sh), 264 (140), 258 (190), 252 (150), 247 (110), 241 (93) (sh); CD (*c* 0.119, MeOH) $[\theta]_{273}$ ±0, $[\theta]_{268}$ −91, $[\theta]_{265}$ −13, $[\theta]_{261}$ −78, $[\theta]_{259}$ ±0, $[\theta]_{258}$ +7.0, $[\theta]_{257}$ ±0, $[\theta]_{255}$ −26, $[\theta]_{252}$ −5.0, $[\theta]_{247}$ −45, $[\theta]_{244}$ ±0; (*c* 0.076, THF) $[\theta]_{274}$ ±0, $[\theta]_{269}$ −42, $[\theta]_{267}$ ±0, $[\theta]_{265}$ +28, $[\theta]_{263}$ ±0, $[\theta]_{262}$ −8.3, $[\theta]_{261}$ ±0, $[\theta]_{258}$ +70, $[\theta]_{256}$ +60, $[\theta]_{251}$ +150 (sh), $[\theta]_{234}$ +3300; CD (*c* 0.075, cyclohexane) $[\theta]_{272}$ ±0, $[\theta]_{269}$ −15, $[\theta]_{268}$ ±0, $[\theta]_{265}$ +52, $[\theta]_{262}$ +17, $[\theta]_{259}$ +96, $[\theta]_{256}$ +69, $[\theta]_{253}$ +100, $[\theta]_{249}$ +78 (sh), $[\theta]_{245}$ +58, $[\theta]_{230}$ +3200.

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