35.162, 44.378, 60.983, 72.923, 87.785, 128.021, 129.137, 131.013 (2 C), 131.708 (2 C), 164.825, 212.395.

(5*SR*,6*RS*)-5-Hydroxy-6-methoxy-2,2-dimethyl-6-phenylhexan-3-one Oxime (16). A solution of 25 mg (0.10 mmol) of aldol **11e**, 100 mg (1.50 mmol) of hydroxylamine hydrochloride, and 50 mg (0.50 mmol) of sodium hydroxide in 1 mL of 95% ethanol was refluxed for 3 days. The mixture was poured into 10 mL of 1 *N* aqueous HCl and extracted with ether (3 × 15 mL). The combined organics were washed with 5-mL portions of saturated $NaHCO_3$ and brine and dried over $MgSO_4$. The mixture was concentrated, and the crude product was flash chromatographed on 1.3 g of silica gel eluted with 20% ether/hexanes to yield 16 mg (60%) of the desired oxime: mp 97–98 °C;[41] IR ($CDCl_3$) 3490, 3270, 2361, 1469, 1458, 1369, 1198, 1131 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.01 (s, 9), 2.52 (dd, 1, J = 13.8, 2.3), 2.78 (dd, 1, J = 13.8, 10.0), 3.32 (s, 3), 3.85 (d, 1, J = 4.3), 3.97 (m, 1), 4.21 (d, 1, J = 5.2), 7.29–7.37 (m, 5), 9.35 (s, 1); ^{13}C NMR (126 MHz, $CDCl_3$) δ 27.663 (3 C), 28.184, 37.868, 57.358, 74.152, 87.234, 127.340 (2 C), 127.810, 128.324 (2 C), 138.730, 166.444.

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Far Ultraviolet Circular Dichroism Observations on the Substituted Benzene Chromophore[1]

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Abstract: The electronic absorption (EA) and circular dichroism (CD) of two chiral α-phenylalkylamines and five chiral α-phenylalkylamine hydrochlorides were measured far into the vacuum ultraviolet region. The EA for all seven compounds is similar to that of benzene, showing transitions assigned to the B_{2u}, the B_{1u}, and the E_{1u} states. In addition to the Cotton effects (CEs) associated with the B_{2u} transition at 245–270 nm, there are two or more CEs associated with electronic transitions at shorter wavelengths. When only two of these shorter wavelength CEs are observed, they are easily assigned to the corresponding electronic transitions. As the alkyl group on the chiral substituent becomes bulkier, the CD spectrum becomes more complex, and there is increased intensity. These changes explain the earlier observation of a negative background optical rotatory dispersion (ORD) from 240–225 nm for (*S*)-α-phenylethylamine but a positive background curve for (*S*)-α-phenylneopentylamine. In contrast to the B_{2u} CEs which for a particular configuration may change sign on para substitution of the benzene ring, the CD associated with the strongly allowed E_{1u} transition is independent of para substitution and therefore is valuable for determining absolute configuration when an α-phenylalkylamine has a para substituent. However, when the CD spectrum is complex, it becomes difficult to recognize which CE is associated with this transition.

The benzene chromophore shows three well-defined electronic absorption (EA) bands above 175 nm (Table I).[3] Each is the result of a $\pi \rightarrow \pi^*$ transition, but only the B_{2u} band shows in solution a well-defined vibrational fine structure. The E_{1u} transition centered near 180 nm is doubly degenerate and, as shown by its high molar absorptivity (ϵ), is strongly allowed. Both the B_{1u} and B_{2u} transitions are dipole forbidden for the static molecule. Their intensities are lower than that of the E_{1u} transition and are due to molecular vibration.

If the benzene 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.[3] More importantly, the transitions are now optically active, and Cotton effects (CEs) are associated with the absorption bands.[7] This optical activity is determined by the configuration and conformation of the molecule and can be observed as the dispersive spectroscopic property, optical rotatory dispersion (ORD), and as the absorptive spectroscopic property, circular dichroism (CD). For laboratories interested in the synthesis of asymmetric, organic molecules, optical activity in either its dispersive or absorptive form is the obvious method for determining absolute configuration.

Table I. Benzene Spectral Data

designation[a]	absorption band maximum: λ,[b] nm	ϵ[c]
B_{2u} (^1L_b)	254[d]	204
B_{1u} (^1L_a)	203.5[d]	7400
E_{1u} ($^1B_{ab}$)	183.5[e]	46000

[a] Reference 4. [b] Wavelength. [c] Molar absorptivity. [d] Reference 5, water as solvent. [e] Reference 6, *n*-heptane as solvent.

Attempts to relate the configuration of chiral benzene compounds to their CD have focused almost exclusively on utilization of the sign and magnitude of the easily observed CEs associated with the B_{2u} transition.[8] In terms of the *S* enantiomers, ORD measurements[9] in methanol reveal a number of positive CEs associated with this transition for α-phenylalkylamines (*S*)-**1**–**3** and their hydrochlorides (*S*)-**1**–**3**·HCl.

These CEs are superimposed on a strong background curve which is the sum of the long wavelength wings of CEs below 240 nm.[9] The contributions from the short wavelengths far override

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(1) This is part 32 in the Vanderbilt University series Optically Active Amines. Part 31 is ref 11.

(2) (a) Oregon State University. (b) Vanderbilt University.

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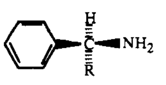
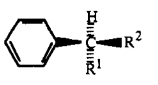


(*S*)-**1**, R = CH_3

(*S*)-**2**, R = CH_3CH_2

(*S*)-**3**, R = $(CH_3)_3C$



D-**4**, $R^1 = CO_2^-$; $R^2 = NH_3^+$

D-**5**, $R^1 = CO_2H$; $R^2 = NH_3Cl$

D-**6**, $R^1 = CO_2Na$; $R^2 = OH$

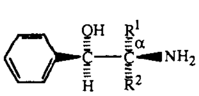
D-**7**, $R^1 = CO_2H$; $R^2 = OH$

(*S*)-**8**, $R^1 = CH_3$; $R^2 = OH$

(*S*)-**9**, $R^1 = (CH_3)_3C$; $R^2 = OH$

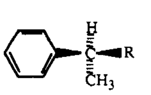
the rotatory contribution of the B_{2u} transition at 240–270 nm, and although the rotatory power at the sodium D line is always negative for the *S* configuration, the background curves may be either positive or negative in the region of the B_{2u} transition.

Extensive CD studies have also been reported for the B_{2u} transition for α-phenylethylamine[10,11] (**1**) and its hydrochloride [11,12] (**1**·HCl) and for related chiral amines and alcohols (**4**–**9**).[13-17] Positive B_{2u} CEs are observed from the ground state to the totally symmetric vibrational state in the excited state[12,18] for (*S*)-**1** and its hydrochloride,[10-12] for D-**4**–**7**,[13-16] and (*S*)-**8** and **9**.[14,17] Chiral substitution on the methyl group of (*S*)-α-phenylethyl alcohol [(*S*)-**8**] does not change the sign of these CEs,[19] and both (αS)-norephedrine [(αS,βR)-**10**] and and (αR)-norpseudoephedrine [(αR,βR)-**11**] and their hydrochlorides all show positive CD maxima from 240–270 nm.[19] Alkyl substitution on the amino group also does not cause a great change in the B_{2u} CEs, and both (*S*)-*N*,*N*-dimethyl-α-phenylethylamine [(*S*)-**12**] and its methyl iodide [(*S*)-**13**] show B_{2u} CEs of the same sign as those of the primary amine (*S*)-**1** and its hydrochloride (*S*)-**1**·HCl.[20]



(αS,βR)-**10**, $R^1 = H$; $R^2 = CH_3$

(αR,βR)-**11**, $R^1 = CH_3$; $R^2 = H$



(*S*)-**12**, R = $N(CH_3)_2$

(*S*)-**13**, R = $N(CH_3)_3I$

Substitution on the benzene ring, however, may change the sign of the B_{2u} CEs.[10,11,19,21-24] Para substitution of (*S*)-α-phenylethylamine [(*S*)-**1**] and its hydrochloride [(*S*)-**1**·HCl] with a bromo, chloro, or methyl group causes the sign of these CEs to be opposite to that of the unsubstituted amine and amine hydrochloride.[10,11] Substitution with a para cyano or trifluoromethyl group does not alter the sign of these CEs from that of the unsubstituted amine and amine hydrochloride.[10,11] Thus the sign of the CEs for the B_{2u} transition is not a priori indicative of the absolute configuration of these molecules.

However, the absolute configurations of α-phenylalkylamines and their hydrochlorides can be determined from the sign of the B_{2u} CEs, if the spectroscopic moment of any other substitutent is taken into account. As shown by Sklar some time ago,[25] the intensity of the forbidden B_{2u} transition can be divided into two parts. One part is attributed to vibronic borrowing from nearby allowed transitions. The second part of the intensity of the B_{2u} transition is attributed by Sklar[25] to a migration moment (spectroscopic moment), induced in the ring by a substitution on the ring of any group which destroys the symmetry of the ring. Earlier work[11] indicates that the sign of the B_{2u} CEs of the unsubstituted amine and amine hydrochloride is determined by vibronic borrowing from transitions at shorter wavelength.[26,27] Both (*S*)-**1**

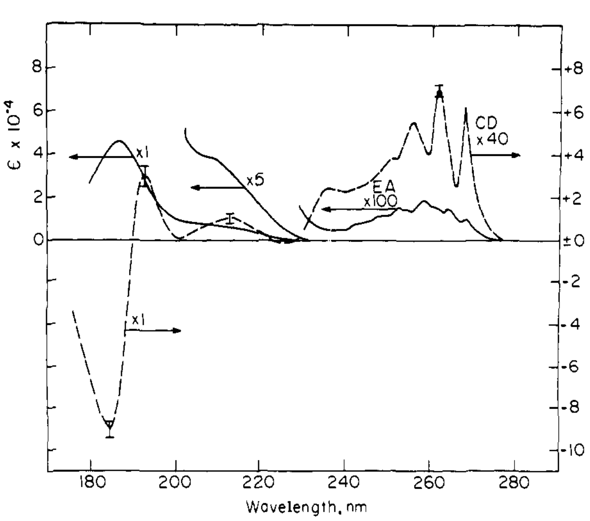


Figure 1. Electronic (EA) and circular dichroism (CD) spectra of (*S*)-α-phenylethylamine [(*S*)-**1**] in isooctane.

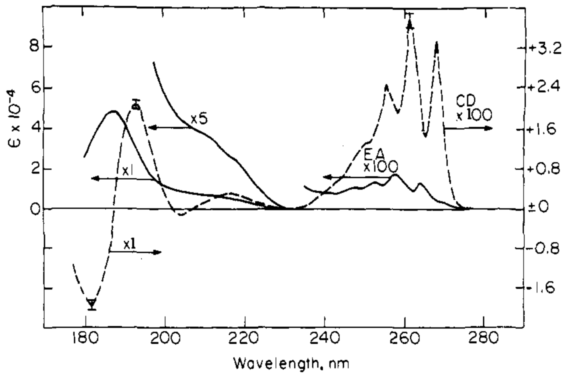


Figure 2. Electronic (EA) and circular dichroism (CD) spectra of (*S*)-α-phenylneopentylamine [(*S*)-**3**] in isooctane.

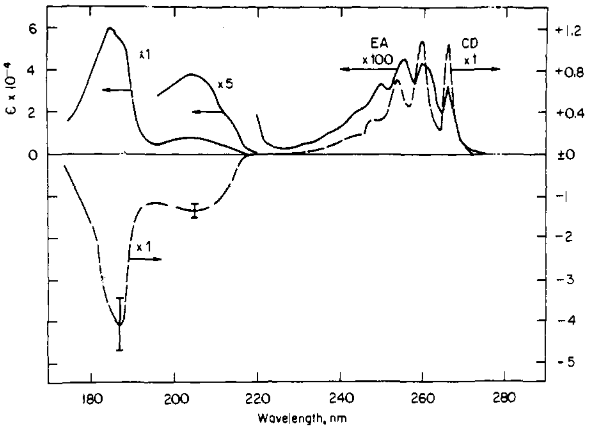


Figure 3. Electronic absorption (EA) and circular dichroism (CD) spectra of (*S*)-α-phenylethylamine hydrochloride [(*S*)-**1a**·HCl] in 1,1,1,3,3,3-hexafluoro-2-propanol.

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Table II. α-Phenylalkylamines and Amine Hydrochlorides

compd	name	$[\alpha]^{22-26}{}_D$, deg	% ee	ref[a]
(*S*)-**1**	(*S*)-α-phenylethylamine	−27[b]	95	11
(*S*)-**1**·HCl	(*S*)-α-phenylethylamine hydrochloride	−21[c]	95	*d*
(*R*)-**2**·HCl	(*R*)-α-phenyl-*n*-propylamine hydrochloride[e]	+5[f]	*g*	9
(*S*)-**3**	(*S*)-α-phenylneopentylamine	−5.4[h]	*i*	*d*
(*S*)-**3**·HCl	(*S*)-α-phenylneopentylamine hydrochloride	−5[j]	*k*	*d*
(*S*)-**14**·HCl	(*S*)-α-(*p*-methylphenyl)-ethylamine hydrochloride	−22[l]	>95	11
(*S*)-**15**·HCl	(*S*)-α-(*p*-(trifluoromethyl)-phenyl)ethylamine hydrochloride	−3.3[m]	60	11

[a] For characterization and percent enantiomeric excess (% ee). [b] *c* 2.00 g/100 mL of CH_3OH. [c] *c* 1.15 g/100 mL of 0.1 M KOH in 4:1 CH_3OH-H_2O. [d] This work. [e] Methanolate. [f] *c* 1.9 g/100 mL of absolute CH_3CH_2OH. [g] Not established but has the highest rotatory power reported. [h] Neat. [i] Not established but with 96% of the highest rotatory power reported. [j] *c* 1.6 g/100 mL of CH_3CH_2OH. [k] Not established but with 90% of the highest rotatory power reported. [l] *c* 2.24 g/100 mL of NaOH–CH_3OH. [m] *c* 1.40 g/100 mL of CH_3OH.

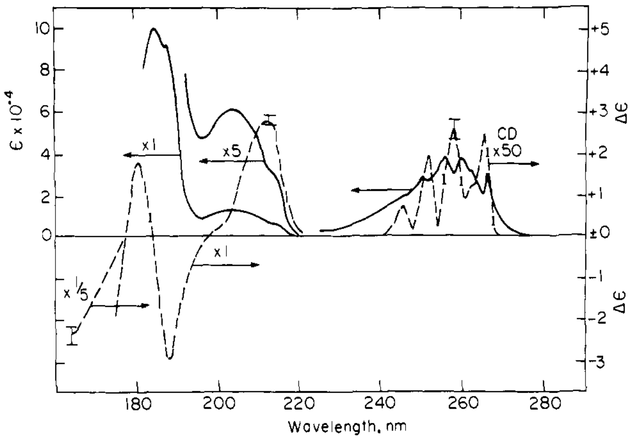

Figure 4. Electronic (EA) and circular dichroism (CD) spectra of (*S*)-α-phenyl-*n*-propylamine hydrochloride [(*S*)-**2**·HCl] in 1,1,1,3,3,3-hexafluoro-2-propanol. These spectra recorded for the *R* isomer, and the signs of the CD are reversed for presentation here.

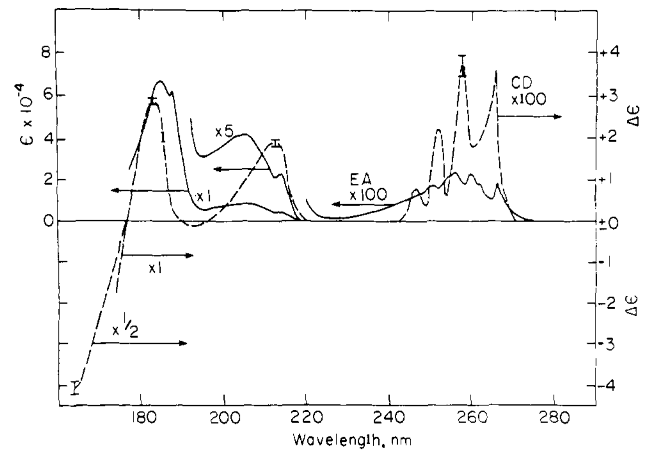

Figure 5. Electronic (EA) and circular dichroism (CD) spectra of (*S*)-α-phenylneopentylamine hydrochloride [(*S*)-**3**·HCl] in 1,1,1,3,3,3-hexafluoro-2-propanol.

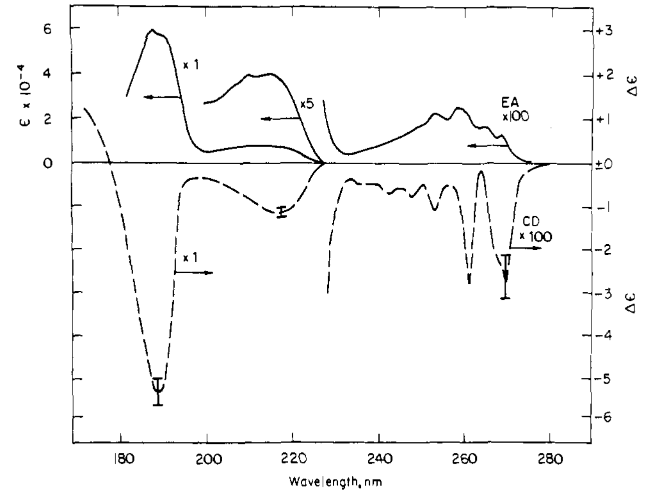

Figure 6. Electronic absorption (EA) and circular dichroism (CD) spectra of (*S*)-α-(*p*-methylphenyl)ethylamine hydrochloride [(*S*)-**14**·HCl] in 1,1,1,3,3,3-hexafluoro-2-propanol.

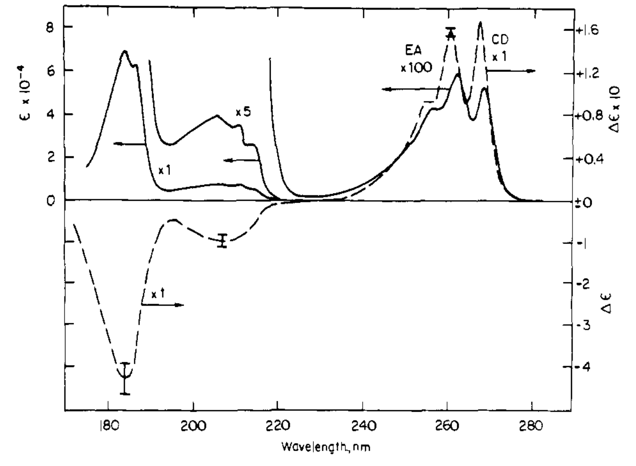

Figure 7. Electronic absorption (EA) and circular dichroism (CD) spectra of (*S*)-α-(*p*-(trifluorormethyl)phenyl)ethylamine hydrochloride [(*S*)-**15**·HCl] in 1,1,1,3,3,3-hexafluoro-2-propanol.

and (*S*)-**1**·HCl show positive B_{2u} CEs although the spectroscopic moment[28] of the chiral group in the amine and amine hydrochloride is positive and negative, respectively.[11] On para substitution by a group with either a positive or a negative spectroscopic moment, electric transition moments are induced in the benzene ring bonds adjacent to the attachment bond of the chiral group, resulting in enhanced coupling of the B_{2u} transition with the chiral group. The reversal of the sign of the ^1L_b CEs on para substitution of (*S*)-**1** and (*S*)-**1**·HCl by a group with a positive spectroscopic moment (Br, Cl, and CH_3) thus can be viewed as the overshadowing of the positive vibronic rotational strength by the negative induced contribution. For para substitution of (*S*)-**1** and (*S*)-**1**·HCl by a group with a negative spectroscopic moment (CN and CF_3), the positive vibronic rotational strength is augmented by a positive induced contribution, and para-substituted amine and amine hydrochloride have B_{2u} CEs of the same sign as (*S*)-**1** and (*S*)-**1**·HCl.

The observation concerning the reversal in the B_{2u} CEs for some ring-substituted chiral benzene compounds and the differences in the ORD background curves for the B_{2u} CEs around 260 nm for (*S*)-**1**–**3** and their hydrochlorides lead us to investigate the effect of substituents on the sign and magnitude of the B_{1u} and E_{1u} CEs which lie below 220 nm. Thus we have extended the EA and CD measurements for the amines and amine hydrochlorides in Table II into the vacuum UV region with use of modern instrumentation.[29] These measurements expand the energy region of CD measurements by a factor of more than $2^1/_2$ and increase

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Table III. Spectral Data for α-Phenylalkylamines in Isooctane

	λ_{max}, nm (ϵ^a or $\Delta\epsilon^b$)				
	B_{2u}		far ultraviolet (FUV)		
compd	EA	CD	EA	CD	assignment
(*S*)-**1**	268 (100)	268 (+0.16)		225 (−0.20)	$n \rightarrow \sigma^*$
	264 (150)		208 (7800)^c	213 (+1.0)	B_{1u}
	261 (160)^c	262 (+0.18)		193 (+3.0)	$n \rightarrow \sigma^*$, E_{2g}?
	258 (180)		187 (46000)	184 (−9.0)	E_{1u}
	255 (140)^c	256 (+0.14)			
	252 (150)				
		250 (+0.10)			
		236 (+0.06)			
(*S*)-**3**	269 (50)^c	268 (+0.34)	218 (4800)^c		B_{1u}
				217 (+3.0)	
	266 (100)^c		211 (7200)^c		
	264 (140)	262 (+0.37)		204 (−1.2)	$n \rightarrow \sigma^*$, E_{2g}?
	258 (180)			193 (+21)	
	253 (130)	255 (+0.25)	187 (48000)	182 (−19)	E_{1u}
		250 (+0.13)			
		243 (+0.05)^c			

[a] Molar absorptivity. [b] Molar dichroic absorption. [c] Shoulder.

Table IV. Spectral Data for α-Phenylalkylamine Hydrochlorides in 1,1,1,3,3,3-Hexafluoro-2-propanol

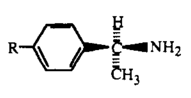
	λ_{max}, nm (ϵ^a or $\Delta\epsilon^b$)				
	B_{2u}		far ultraviolet (FUV)		
compd	EA	CD	EA	CD	assignment
(*S*)-**1**·HCl	266 (160)	266 (+0.11)	213 (3600)^c		B_{1u}
	262 (190)^c			206 (−1.3)	
	260 (220)	260 (+0.11)	205 (7700)		
	256 (230)	254 (+0.071)	187 (55000)	187 (−4.1)	E_{1u}
	250 (170)	248 (+0.034)	185 (61000)		
(*S*)-**2**·HCl^d	266 (290)	265 (+0.050)	214 (6000)^c	212 (+2.8)	B_{1u}
	262 (310)^c		204 (12000)		
	260 (370)	262 (+0.026)		200 (+0.25)^c	E_{2g}?
	256 (370)	258 (+0.055)	188 (91000)	188 (−3.0)	E_{1u}
	254 (350)	252 (+0.036)	185 (99000)		
	250 (280)			180 (+1.8)	
	246 (190)	245 (+0.015)			
(*S*)-**3**·HCl	266 (180)	266 (+0.036)	214 (4400)		B_{1u}
	262 (170)^c			212 (+1.9)	
	260 (220)	258 (+0.037)	205 (8200)		
	256 (230)				
	254 (210)	252 (+0.022)	188 (62000)		E_{1u}?
	250 (170)			192 (−0.2)	
		247 (+0.008)	185 (67000)		
				183 (+2.9)	
(*S*)-**14**·HCl	270 (130)	270 (−0.027)	216 (8200)	217 (−1.1)	B_{1u}
	266 (170)	267 (−0.022)^c	211 (8000)		
	264 (170)		191 (58000)		E_{1u}
	261 (250)^c	261 (−0.028)		189 (−5.3)	
	259 (260)		189 (60000)		
	254 (230)	253 (−0.011)			
	249 (170)^c	248 (−0.008)			
		243 (−0.007)			
(*S*)-**15**·HCl^e	268 (520)	268 (+0.17)	213 (5200)		B_{1u}
	262 (590)	261 (+0.16)	211 (6900)	207 (−1.0)	
	256 (430)	255 (+0.092)	205 (8000)		
			187 (63000)	184 (−4.2)	E_{1u}
			184 (69000)		

[a] Molar absorptivity. [b] Molar dichroic absorptivity. [c] Shoulder. [d] Enantiomer used. [e] $\Delta\epsilon$'s adjusted to 100% ee.

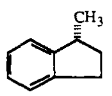
the transitions for which CEs are observed from one to three or more.

Results and Discussion

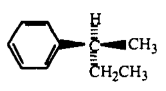
Two α-phenylalkylamines and five hydrochlorides were selected for these difficult measurements. Three hydrochlorides, (*S*)-**1**–**3**·HCl, show the effect of a progressively more bulky chiral substituent while the hydrochlorides of amines (*S*)-**14** and (*S*)-**15** show the effect of para substituents with positive and negative spectroscopic moments, respectively. The results of both EA and CD measurements are given in Figures 1–7, and Tables III and IV.



(*S*)-14, R = CH_3
(*S*)-15, R = CF_3



(*R*)-16



(*S*)-17

The EA for all seven compounds are similar in wavelength and intensity and resemble those observed for benzene. The three observed absorption bands are assigned as the B_{2u} transition at about 260 nm, the B_{1u} transition at about 210 nm, and the E_{1u} transition at about 185 nm, in analogy to the assignments for benzene (Table I).

In each of the seven CD spectra, CEs are observed that correspond to the three EA bands. Additional CEs are observed for (*S*)-**1** and **3** and (*S*)-**2** and **3**·HCl. For (*S*)-**1**·HCl, the CD mimics the EA, and thus the assignments are obviously to the $\pi \rightarrow \pi^*$

transitions of the phenyl chromophore. Para substitution, as seen in compounds (*S*)-**14** and (*S*)-**15**·HCl, does not change the features in the CD, so again the assignments are obvious. The series (*S*)-**1**–**3**·HCl progressively increases the size of the alkyl group on the chiral substituent, and the CD becomes progressively more complex. Comparing the CD spectrum of (*S*)-**2**·HCl with that of (*S*)-**1**·HCl, the CE assignments to the B_{2u} and B_{1u} transitions for (*S*)-**2**·HCl are still obvious although the B_{1u} CE is now positive rather than negative. The E_{1u} CE at about 188 nm is still negative but has lost intensity. At least some of this reduction in intensity is caused by a positive CE at about 180 nm. There is also a shoulder at about 200 nm that results from a small CE that could be either positive or negative.

Comparing (*S*)-**3**·HCl with (*S*)-**2**·HCl, assignments of CEs to the B_{2u} and B_{1u} transitions for (*S*)-**3**·HCl are straightforward, but the feature that corresponds to the E_{1u} CE is not obvious. If the E_{1u} CE corresponds to the positive maximum at 183 nm, then this maximum is blue-shifted relative to the EA, and the CE has changed sign. The 183-nm CD maximum, however, could well correspond to the E_{2g} transition of benzene that is known to be in this region[30] or to the positive CE found at 180 nm for (*S*)-**2**·HCl. The 183-nm maximum is more intense and slightly red-shifted and could be canceling a negative CE corresponding to the E_{1u} transition so that the small negative maximum at 192 nm in the CD of (*S*)-**3**·HCl is the observable remnant of the E_{1u} CE. Further, the B_{2u} transition obtains its EA and thus its CD intensity from the E_{1u} transition. Clearly, interaction with the E_{1u} transition gives positive CD intensity to the B_{2u} transition form (*S*)-**1** and **2**·HCl, and the same interaction for (*S*)-**3**·HCl would be expected. Since the latter also has positive B_{2u} CEs indicating a negative CE for the E_{1u} transition, the assignment of the negative maximum at 192 nm to E_{1u} transition is favored.

The CD spectrum of (*S*)-**1** has extra features not found in the CD spectrum of its hydrochloride. In the CD of (*S*)-**1**, the positive CEs centered around 260 nm are assigned to the B_{2u} transition, the positive CE at 213 nm to the B_{1u} transition, and the negative CE at about 184 nm to the E_{1u} transition, in analogy with the assignments for the (*S*)-**1**·HCl. Here the sign of the B_{1u} has changed, as it did when (*S*)-**2**·HCl and (*S*)-**3**·HCl are compared to (*S*)-**1**·HCl. Further, the CD of (*S*)-**1** is strikingly similar to the CD of (*S*)-**3**, so the corresponding features at about 260, 217, and 182 nm for (*S*)-**3** also receive analogous assignments. (*S*)-**1** has an extra negative band of low intensity at about 225 nm, and a positive band of moderate intensity at 193 nm, while (*S*)-**3** has a negative band of low intensity at 204 nm and a positive band of moderate intensity at 193 nm. Absorption maxima are found for trimethylamine at 227 nm and 199 nm,[31,32] and thus the extra CD maxima at 225 and 193 nm are assigned to $n \rightarrow \sigma^*$ transitions of the amino chromophore. The disappearance of these maxima on protonation of the amino group supports the conclusion that dichroic absorption in these regions is associated with amino chromophore. Another possibility for the CEs at 204 and 193 nm in the CD of the amino compounds is the benzene E_{2g} transition, which is suggested by the observation[30] of two sharp and oppositely signed bands at about 195 nm in the CD spectrum of (*R*)-1-methylindan[33] [(*R*)-**16**] in the gas phase. The existence of this pair of bands was later confirmed by observation of the same pair of CEs in the gas-phase spectrum of (*S*)-*sec*-butylbenzene [(*S*)-**17**].[34]

With these assignments, consider now how the various CEs correspond to the *S* configuration and conformation of the molecules. The B_{2u} CEs were studied in earlier work[11] and discussed above. These CEs correlate with the absolute configuration of the amines and amine hydrochlorides regardless of the bulk of the alkyl group on the chiral substituent provided that the spectroscopic moment of any additional ring substituent is taken into consideration.

The B_{1u} CEs reflect only changes in the structure of the chiral substituent, the sign being negative for the amines and amine hydrochlorides only when the ethylammonium chiral group is present and positive for the others.

It is also observed, as expected, that the sign of the CE associated with strongly allowed E_{1u} transition is independent of additional ring substitution. With the bulky neopentylammonium group as the chiral substituent, however, the E_{1u} CE has either changed sign or is overwhelmed by a positive CE from another source. Thus the E_{1u} CE will not be completely reliable for the assignment of absolute configurations of an α-phenylalkylamine.

Comparing CD spectra of the five derivatives for which ORD has been measured, it becomes easy to understand in a qualitative way why the background ORD at the B_{2u} transition is positive for some compounds and negative for others. The background ORD at about 260 nm will be the sum of the long wavelength wings for all of the CEs at shorter wavelengths. The contribution of each CE will be proportional to the intensity of its CD band, but the effect is lessened by the difference between 260 nm and the wavelength at which CD occurs. For the compounds studied here, we see that the compounds with a negative ORD background at 260 nm [(*S*)-**1** and (*S*)-**1**·HCl] have more negative CD intensity to 178 nm, while the derivatives with a positive background ORD at 260 nm [(*S*)-**3**, (*S*)-**2**·HCl, and the (*S*)-**3**·HCl] have more positive CD intensity to 178 nm. Of course, the rotational strength sum rule states that the total CD intensity for all bands should sum to zero, and all the CD bands at wavelengths shorter than our observations also contribute. However, it is clear that variations in the intensity and position of the CD bands, as observed here between 240 and 178 nm, are sufficient to change the sign of the background ORD.

The sign and magnitude of the CEs associated with the transitions of the benzene chromophore above 180 nm are subject to small changes in conformation and structure and may be a sensitive probe for such changes. This same sensitivity makes individual CEs difficult to use for the determination of absolute configurations. In contrast, these changes are not greatly reflected in the rotatory power at the sodium D line, and the α-phenylalkylamines and their hydrochlorides with the *S* configuration are all levorotatory at the sodium D line (589 nm) (Table I).

Experimental Section

The melting point (capillary) and boiling point are corrected. Optical rotatory power at the sodium D line were measured with an Autopol III automatic polarimeter and a 1-dm sample tube.

Electron absorption (EA) were measured with a Cary Model 15 spectrophotometer, flushed with nitrogen to permit measurements to 175 nm. This instrument varies the slit width to keep the energy on the reference photomultiplier constant, but the sensitivity was set sufficiently high so that the spectral slit width was small compared to the structure observed for each of the absorption bands.

Circular dichroism (CD) spectra were measured from 280–190 nm on a Jasco J40 dichrograph. A 1-nm spectral slit width gave a slight improvement over the 2-nm spectral slit width for the structure observed between 270 and 240 nm. A 2-nm spectral slit width was used for the bands beginning at about 210 nm. CD spectra from 230–172 were measured on a vacuum UV CD spectrometer described elsewhere.[29] The spectral slit width was a constant 1.6 nm. Both instruments were calibrated with (+)-10-camphorsulfonic acid, $\Delta\epsilon = 2.42$ at 290.5 nm. The total absorbance of the cell, solvent, and sample did not exceed 1.0 to avoid absorption artifacts. The free amines were dissolved in isooctane and the hydrochlorides in 1,1,1,3,3,3-hexafluoro-2-propanol. The latter is a weak acid (pK_a 1.8) which is a particularly transparent in the vacuum UV region. Sample concentrations ranged from 2.2–5.3 × 10^{-3} mol/L,

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and the path length of the cell was varied to give the proper OD for each of the three bands measured. A 1-cm cell was used for the band at about 260 nm, a 0.020-cm cell for the bands at about 210 nm, and a nominal 0.005-cm cell for the bands at about 190 nm. These were standard cylindrical cells, commercially available from Helma, and the path lengths for the shorter cells were calibrated by using an infrared spectrometer.[35] In the figures the error bars on the CD spectra indicate the repeatability for two successive scans which was exact for the B_{2u} band of (*S*)-**1**·HCl (Figure 3).

(*S*)-α-Phenylethylamine hydrochloride [(*S*)-**1**·HCl] was prepared from (*S*)-**1**, $[\alpha]^{26}_{D}$ −27° (*c* 2.00, CH_3OH) [lit.[10] $[\alpha]^{20}_{D}$ −28° (*c* 2, CH_3OH); 98.7% ee], by treatment of the latter in methylene chloride with concentrated hydrochloric acid. Recrystallization from ethanolethyl acetate gave (*S*)-**1**·HCl: mp 169–171 °C; $[\alpha]^{22}_{D}$ −21° (*c* 1.15, 0.1 M KOH in 4:1 CH_3OH-H_2O).

(*S*)-α-Phenylneopentylamine [(*S*)-**3**] was prepared by resolution of (±)-**3** by using *N*-acetyl-D-leucine as outlined earlier.[36] Recrystallization and decomposition of the diastereomeric salt gave (*S*)-**3**: bp 115–117 °C (28 mmHg); $[\alpha]^{25}_{D}$ −5.4° (neat) [lit.[36] $[\alpha]^{21}_{D}$ + 5.6° (neat) for the *R* isomer].

(*S*)-α-Phenylneopentylamine hydrochloride [(*S*)-**3**·HCl] was prepared from (*S*)-**3** as outlined for the preparation of (*S*)-**1**·HCl and had $[\alpha]^{25}_{D}$ −5° (*c* 1.60, absolute CH_3CH_2OH) [lit.[9] $[\alpha]^{26}_{D}$ +5.5° (*c* 2.0, absolute CH_3CH_2OH) for the *R* isomer].

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$^{13}C_2$ Labeling: A Means To Measure $^{12}C-^{13}C$ Isotopic Equilibria in 2-Norbornyl Cation

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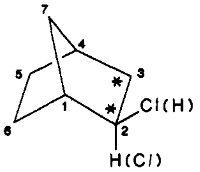
Abstract: [2,3-^{13}C]Norborn-2-yl chloride was prepared and ionized (with SbF_5) to the 2-norbornyl cation. In solution at −65 °C, rapid rearrangements occur which completely scramble the ^{13}C labels. The proton-decoupled ^{13}C NMR spectrum (62.7 MHz) contains three signals: C-4, C-1,2,6 (averaged), and C-3,5,7 (averaged). The ^{13}C labels are thus equilibrated over nonequivalent sites within the 2-norbornyl cation. This $^{12}C-^{13}C$ equilibrium isotope effect alters the proportion of di-^{13}C-labeled isomers from statistical values. The nonstatistical isotopic isomer population is manifested as an asymmetric multiplet for the averaged C-3,5,7 peak in the ^{13}C NMR spectrum. The relatively sharp lines of the multiplet can be reproduced within ±0.1 ppm, with isotopic equilibrium constants of $K_{3,5,7} = 1.010 \pm 0.005$ and $K_{1,2,6} = 1.039 \pm 0.005$.



The incorporation of ^{13}C at specific sites in organic molecules, in conjunction with ^{13}C nuclear magnetic resonance spectroscopy, can be used to obtain information about reaction mechanisms. Since the natural abundance of ^{13}C is only 1.1%, the introduced label dominates the ^{13}C NMR spectrum and label location is readily detected. ^{13}C enrichment can also aid in the study of $^{13}C-^{12}C$ kinetic[1] and/or equilibrium[2] isotope effects. Changes are also detected in ^{13}C NMR chemical shifts of nuclei[3] when they are adjacent to ^{13}C. These effects (called intrinsic shifts) are usually small, but they are experimentally measurable and useful. Most of the previous attention on ^{13}C isotope effects has been related to the kinetic isotope effects; but some results have been published on $^{13}C-^{12}C$ equilibrium isotope effects.

$^{13}C-^{13}C$ coupling constants are also of interest, since they are related to hybridization and geometry within the molecule.[4] Although methods (NMR pulse sequences exist for the observation evaluation of $^{13}C-^{13}C$ coupling in unenriched materials,[5] this approach is not without its difficulties and limitations. The introduction of ^{13}C into an organic molecule allows for determination of $^{13}C-^{13}C$ coupling constants in the molecule, with routine ^{13}C NMR spectral acquisition.[6] The couplings can be measured by

Table I. ^{13}C Chemical Shifts for the [$^{13}C_2$]Norborn-2-yl Cation[a]

carbon atom	δ at −155 °C[a,b]
1,2	124.81
3,7	36.58
4	37.86[c]
5	20.24
6	21.32

[a] In ppm, relative to Me_4Si. [b] 125.76 MHz. [c] Assigned spectral reference.

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