Optically Active Amines. 31.[1] Spectral Observations on the Substituted Benzene Chromophore[2]

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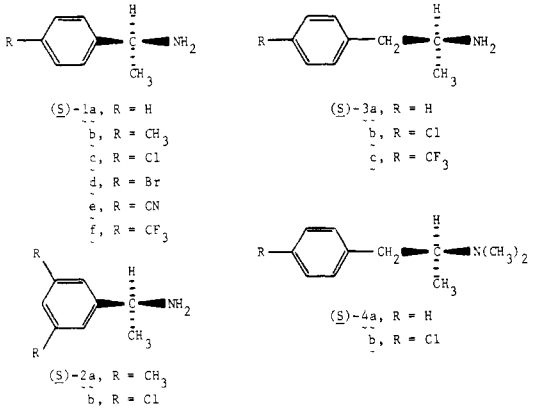
Abstract: Examination of the isotropic absorption and circular dichroism spectra of para-substituted and 3,5-disubstituted α-phenyl- and α-benzylethylamines and their hydrochlorides indicates that the sign of the ^1L_b Cotton effects (CEs) of the benzene chromophore of the unsubstituted amines and amine hydrochlorides is determined by vibronic borrowing from the ^1B_b-allowed transition. Thus, both (*S*)-α-phenylethylamine and its hydrochloride show positive ^1L_b CEs although the spectroscopic moment of the chiral group in the amine and amine hydrochloride is positive and negative, respectively. On substitution by groups with either a positive (CH_3, Cl, and Br) or a negative (CN and CF_3) spectroscopic moment, transition moments are induced in the benzene ring bonds adjacent to the attachment bond of the chiral group, resulting in enhanced coupling of the ^1L_b transition with the chiral grouping. The sign reversal of the ^1L_b CEs on para substitution of α-phenylethylamine and its hydrochloride by a group with a positive spectroscopic moment can thus be viewed as the overshadowing of the vibronic rotational strength by the induced contribution. Further, the lack of correlation of molar absorptivity with molecular ellipticity suggests that the contribution from the induced electric transition moment is less important than that of the induced magnetic transition moment.

Para substitution of the phenyl ring in norephedrine,[4] norpseudoephedrine,[4] and other chiral phenylcarbinols[5-8] with halogen, hydroxyl, and methoxyl groups causes the sign of the benzene ^1L_b Cotton effects (CEs) in their circular dichroism (CD) spectra to be opposite to that in the CD spectra of the unsubstituted phenylcarbinols. Earlier we suggested[4] that in the unsubstituted compounds the one-electron mechanism[9] is dominant but on substitution, when the ^1L_b transition moment becomes larger, the oppositely signed contribution of the coupled oscillator mechanism[9] overshadows that of the one-electron mechanism.

The possibility of the dominance of the coupled oscillator mechanism as an explanation for the sign change of the ^1L_b CEs on para substitution of (*S*)-α-phenylethylamine [(*S*)-**1a**] with



methyl (**1b**), chloro (**1c**), and bromo groups (**1d**) was also considered by Gottarelli and Samori[10] but was abandoned by them because of their difficulty in interpreting the sign of the ^1L_b CEs of (*S*)-α-(*p*-cyanophenyl)ethylamine [(*S*)-**1e**]. This compound, with a ^1L_b absorption band as intense as those of (*S*)-**1b-d**,[10] has ^1L_b CEs of the same sign as those of (*S*)-**1a**.

This difficulty may be resolved if one considers the possibility of vibronic dominance[11,12] of the ^1L_b band in the *p*-cyano compound. An alternate explanation could be that the presence of the cyano group on the benzene chromophore results in a low-lying $\sigma \rightarrow \pi^*$ transition of the cyano group[13] which may interact with the ^1L_b transition to produce, by perturbation, a strong one-electron contribution.

These observations led us to investigate in more detail the effect of substituents on the sign of the benzene ^1L_b CEs, and we report the chiroptical properties of a series of α-phenyl- (**1a-d,f** and **2a,b**) and α-benzylethylamines (**3a-c** and **4a,b**) and their hydrochlorides. The trifluoromethyl group (**1f** and **3c**) has a negative spectroscopic moment, the same sign as that of the cyano group and opposite in sign to that of the chiral substituent in **1a** and **3a**.[10,14] The methyl (**1b**), chloro (**1c**, **3b**, and **4b**), and bromo substituents (**1d**) have positive spectroscopic moments, but the combined effect of 3,5-disubstitution (**2a,b**) by the methyl and chloro groups will be a resulting spectroscopic moment of opposite sign to that of the corresponding para substituent.[14]

Results and Discussion

Chiral Amines. The particular samples of chiral amines and amine hydrochlorides used are shown in Table I. When the free base or the hydrochloride was not available for spectroscopic measurements, it was formed in situ by treatment of the hydrochloride with sodium hydroxide or the amine with hydrochloric acid.

The racemic modifications of some of these amines (**1b,c,f** and **2a,b**) were prepared by reductive amination (Leuckart reaction) of the corresponding ketones[18] while (±)-**3c**[19] was a gift.[20] The racemates were resolved by the separation of diastereomeric salts by fractional crystallization.

The absolute configurations of the enantiomers of **1b-d** were assigned earlier on the basis of the CD of their *N*-phthaloyl

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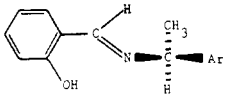
Table I. α-Phenyl- and α-Benzylethylamines and α-Phenyl- and α-Benzylethylamine Hydrochlorides Used for Spectral Measurements

compd	name	$[\alpha]^{25-26}_D$,[a] deg	% ee	ref[b]
(*S*)-**1a**	(*S*)-α-phenylethylamine	−27	95[c]	10
(*S*)-**1b**	(*S*)-α-(*p*-methylphenyl)ethylamine	−25	87[c]	10
(*S*)-**1b**·HCl	(*S*)-α-(*p*-methylphenyl)ethylamine hydrochloride	−22[d]	>95[e]	*f*
(*R*)-**1c**	(*R*)-α-(*p*-chlorophenyl)ethylamine	+23	86[c]	10
(*S*)-**1d**	(*S*)-α-(*p*-bromophenyl)ethylamine	−20	94[c]	10
(*S*)-**1f**	(*S*)-α-(*p*-(trifluoromethyl)phenyl)ethylamine	−13	60[e]	*f*
(*R*)-**2a**·HCl	(*R*)-α-(3,5-dimethylphenyl)ethylamine hydrochloride	+17[g]	78[e]	*f*
(*S*)-**2b**	(*S*)-α-(3,5-dichlorophenyl)ethylamine	−24	>95[e]	*f*
(*S*)-**3a**	(*S*)-α-benzylethylamine	+33.1[h]	93[i]	15
(*S*)-**3a**·HCl	(*S*)-α-benzylethylamine hydrochloride	+21.6[j]	87[i]	15
(*S*)-**3b**·HCl	(*S*)-α-(*p*-chlorobenzyl)ethylamine hydrochloride	+22[k]	>95[e]	16
(*R*)-**3c**	(*R*)-α-(*p*-(trifluoromethyl)benzyl)ethylamine	−19	>95[e]	*f*
(*R*)-**4a**	(*R*)-*N*,*N*-dimethyl-α-benzylethylamine	+7.8	98[l]	17
(*S*)-**4b**·HCl	(*S*)-*N*,*N*-dimethyl-α-(*p*-chlorobenzyl)ethylamine hydrochloride	+11[m]	100[n]	16

[a] *c* 1.45–2.56 g/100 mL CH_3OH or as noted otherwise. [b] For characterization. [c] On the basis of comparison of the rotatory power with that in ref 10 of the amine with its % ee determined by the ^1H NMR method. [d] *c* 2.24 g/100 mL NaOH–CH_3OH. [e] By the ^1H NMR method. [f] This work. [g] *c* 0.654 g/100 mL 0.2 M KOH–CH_3OH. [h] Neat. [i] On the basis of the rotatory power in ref 15 corresponding to 100% ee. [j] *c* 9.0 g/100 mL H_2O. [k] *c* 2.10 g/100 mL H_2O. [l] On the basis of the rotatory power of the starting amine, (*R*)-**3a**. [m] *c* 2.09 g/100 mL H_2O. [n] On the basis of the rotatory power in ref 16 corresponding to 100% ee.

derivatives.[10] These assignments are now confirmed by application of the salicylidenamino chirality rule[16,21] to the CD spectra of their respective *N*-salicylidene derivatives (Experimental Section), those derivatives with the *S* configuration [(*S*)-**5**] showing strong,



(S)-5, Ar = phenyl or benzyl group

positive CEs near 255 and 315 nm. For those derivatives with the *R* configuration, the CEs are negative. Similarly, the absolute configurations are also assigned on the basis of the CD spectra of the *N*-salicylidene derivatives of those resolved amines (**1f**, **2a,b**, and **3c**) not previously reported.

The percent enantiomeric excess (% ee) of each amine and amine hydrochloride was determined by comparison of its rotatory power with that for a sample of known or assumed optical purity or by the proton nuclear magnetic resonance method of Jacobus, Raban, and Mislow.[22] For those substances that had 95% ee or less, the reported molecular ellipticities ([θ]) in their respective CD spectra have been adjusted to 100% ee.

Spectra of α-Phenylethylamines. The isotropic electronic absorption (EA) and CD maxima for the ^1L_b transition of the benzene chromophore from the band origin (0 ← 0 transition) to about 250 nm for (*S*)-α-phenylethylamine [(*S*)-**1a**] and its substituted derivatives (**1b–f** and **2a,b**) in cyclohexane and methanol are shown in Table II. Similar data are shown in Table III for (*S*)-α-phenylethylamine hydrochloride [(*S*)-**1a**·HCl] and its substituted derivatives (**1b–d,f**·HCl and **2a,b**·HCl) in methanol and 10% hydrochloric acid. In both tables, the data are given for the enantiomers with the *S* configuration regardless of the configuration of the substance actually used, and as shown in the tables, the observed ^1L_b CEs of the benzene chromophore generally arise by transitions from the totally symmetric vibrational mode (a_1) in the ground state to totally symmetric vibrational modes (a_1) in the excited state.[4] Only for (*S*)-**1b** and (*S*)-**1d** were additional CEs associated with transitions from the ground state to non-totally symmetric vibrational modes (b_2) in the excited state observed.

Since the combined effect of 3,5-disubstitution is a spectroscopic moment opposite in sign to that of the corresponding single para substituent, the slightly larger molar absorptivities (ε) of the ^1L_b band maxima of (*S*)-**2a,b**, as compared to those of the corresponding maxima of the unsubstituted parent amine [(*S*)-**1a**] in contrast to the much enhanced absorption of the para-substituted amines [(*S*)-**1b,c**], show that the combined effect of the 3,5-disubstitution is a spectroscopic moment not only of opposite sign but also of larger magnitude than that of the chiral substituent of (*S*)-**1a**. Thus the four amines [(*S*)-**1e,f** and (*S*)-**2a,b**] with substituent spectroscopic moments of opposite sign to that of the chiral substituent have ^1L_b CEs of the same sign as those of (*S*)-**1a**. Those amines [(*S*)-**1b–d**] with substituents with spectroscopic moments of the same sign as the chiral substituent show ^1L_b CEs with an opposite sign to those of (*S*)-**1a**.

Although the CD sign patterns for the amines and amine hydrochlorides are similar, there are features in the EA and CD spectra of the hydrochlorides that are different from those of the free bases. The molar absorptivities (ε) of ^1L_b band maxima for the 3,5-disubstituted amine hydrochlorides [(*S*)-**2a,b**·HCl] are higher than those for the corresponding maxima of (*S*)-**2a,b**, but the molar absorptivities for the para-substituted amine hydrochlorides [(*S*)-**1b–d**·HCl] are lower than those for the respective amines [(*S*)-**1b–d**]. Thus the EA shows that the chiral substituent in the amines has a spectroscopic moment opposite in sign to that of the chiral substituent in the amine hydrochlorides. A reversal in the overall spectroscopic moment of the chiral substituent on going from (*S*)-**1a** to (*S*)-**1a**·HCl then does not produce a change in sign of the ^1L_b CEs. Further, the enhanced CD intensities associated with the weak EA band in the *p*-trifluoromethyl and 3,5-disubstituted amines indicate that a sign reversal of the ^1L_b CEs on para substitution as a consequence of an enhanced coupled oscillator contribution overtaking a one-electron contribution[4] is too simplistic and that the spectroscopic observations in Tables II and III must be accommodated in another way. To do this, the origin of the ^1L_b CEs will be divided into contributions derived from vibronic borrowing, induced electronic transition moments, and induced magnetic transition moments.

In benzene, the ^1L_b transition is both electrically and magnetically forbidden with its EA intensity coming from vibronic borrowing from the $^1B_{a,b}$-allowed transitions. Upon substitution, however, an electronic transition moment normal to the substituent attachment bond and concomitantly a magnetic transition moment perpendicular to the ring are induced in the ^1L_b transition. These induced transition moments can give rise to ^1L_b CEs in chiral benzene compounds through dynamic and static coupling with dissymmetric substituents. Furthermore, as in EA, the rotational strengths of the CEs can be influenced by the $^1B_{a,b}$ transitions by vibronic interaction.[11,12]

The magnitude of the induced electronic transition moment is related to the spectroscopic moment[14,23] of the substituent of the benzene ring. This moment can be decomposed into bond transition moments[24,25] as shown in Figure 1. Such a decomposition

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Table II. ^1L_b Absorption Band Data for α-Phenylethylamines

compd	substituent	spectrum	λ_{max}, nm (ε or [θ][a])				
			a_1	b_2	a_1	b_2	a_1
			In Cyclohexane				
(*S*)-**1a**		EA	268 (99)	264 (150)		258 (190)	
		CD	268 (+450)		262 (+570)		256 (+450)
(*S*)-**1b**[b]	*p*-CH_3	EA	273 (320)			265 (350)	
		CD	275 (−110)	272 (+73)	269 (−67)	264 (+89)	
(*S*)-**1c**[c]	*p*-Cl	EA	276 (270)		268 (340)		261 (280)
		CD	277 (−250)		269 (−230)		263 (−46)
(*S*)-**1d**	*p*-Br	EA	276 (220)		268 (310)		261 (270)
		CD	278 (−220)		271 (−220)	267 (+50)	264 (−61)
(*S*)-**1e**[d]	*p*-CN	EA	279 (383)	274 (451)	273 (479)	269 (519)[e]	
		CD	279 (+350)		271 (+380)		261 (+570)
(*S*)-**1f**	*p*-CF_3	EA	268 (200)		263 (290)		258 (310)
		CD	269 (+610)		263 (+660)		259 (+540)
(*S*)-**2a**[b,c]	3,5-$(CH_3)_2$	EA	274 (140)[f]	272 (190)	267 (210)[f]	265 (230)	263 (190)[f]
		CD	276 (+1 100)		268 (+990)		262 (+600)[f]
(*S*)-**2b**	3,5-Cl_2	EA	280 (150)	277 (160)	272 (200)[f]	270 (210)	264 (170)
		CD	280 (+1 300)		272 (+1 300)		265 (+780)
			In Methanol				
(*S*)-**1a**		EA	267 (86)	264 (130)			257 (180)
		CD	268 (+350)		261 (+440)		257 (+300)
(*S*)-**1b**	*p*-CH_3	EA	273 (310)		267 (310)[f]	264 (340)	
		CD	273 (−90)		268 (−49)	263 (+40)	
(*S*)-**1c**[c]	*p*-Cl	EA	276 (240)		268 (310)		261 (250)
		CD	276 (−200)		269 (−190)		263 (−76)
(*S*)-**1d**	*p*-Br	EA	276 (180)		267 (270)		260 (250)
		CD	277 (−180)		270 (−170)		263 (−82)
(*S*)-**1f**	*p*-CF_3	EA	268 (240)		263 (340)		
		CD	269 (+580)		262 (+610)		258 (+470)[f]
(*S*)-**2a**[b,c]	3,5-$(CH_3)_2$	EA	274 (170)	271 (200)	267 (230)	265 (240)	262 (210)[f]
		CD	275 (+860)		267 (+730)	265 (+620)[f]	262 (+460)[f]
(*S*)-**2b**	3,5-Cl_2	EA	278 (140)[f]	276 (160)		269 (210)	263 (170)
		CD	280 (+1 200)		272 (+1 300)		264 (+750)

[a] Molecular ellipticity adjusted to 100% ee. [b] Formed in situ from the amine hydrochloride. [c] Enantiomer used. [d] Data adapted from those in ref 10. [e] An additional maximum at 267 nm (ε 582). [f] Shoulder.

Table III. ^1L_b Absorption Band Data for α-Phenylethylamine Hydrochlorides

compd	substituent	spectrum	λ_{max}, nm (ε or [θ][a])				
			a_1	b_2	a_1	b_2	a_1
			In Methanol				
(*S*)-**1a**·HCl[b]		EA	267 (120)	263 (180)	260 (160)	257 (210)	
		CD	267 (+270)		261 (+290)		255 (+220)
(*S*)-**1b**·HCl	*p*-CH_3	EA	271 (170)		267 (180)		262 (250)
		CD	271 (−200)		265 (−160)		260 (−110)[c]
(*S*)-**1c**·HCl[b,d]	*p*-Cl	EA	274 (140)		269 (160)[c]	265 (220)	258 (200)
		CD	274 (−200)		268 (−200)		261 (−110)
(*S*)-**1d**·HCl[b]	*p*-Br	EA	274 (120)		269 (160)[c]	264 (230)	258 (210)
		CD	275 (−200)		268 (−150)		262 (−84)
(*S*)-**1f**·HCl[b]	*p*-CF_3	EA	268 (480)		263 (550)		257 (420)
		CD	268 (+540)		262 (+580)		257 (+360)[c]
(*S*)-**2a**·HCl[d]	3,5-$(CH_3)_2$	EA	275 (370)	270 (320)[c]	267 (380)	265 (360)	262 (300)[c]
		CD	275 (+740)		268 (+630)		
			In 10% Hydrochloric Acid				
(*S*)-**1a**·HCl[e]		EA	267 (120)	262 (180)	260 (180)	256 (220)	
		CD	267 (+270)		261 (+320)		254 (+240)
(*S*)-**1b**·HCl	*p*-CH_3	EA	271 (170)		266 (190)[c]		262 (260)
		CD	272 (−150)		265 (−120)		
(*S*)-**1c**·HCl[d,e]	*p*-Cl	EA	272 (130)		268 (170)[c]		263 (230)
		CD	274 (−160)		267 (−150)		262 (−90)
(*S*)-**1d**·HCl[e]	*p*-Br	EA	273 (120)[c]		268 (180)[c]		264 (240)
		CD	274 (−140)		268 (−110)		262 (−32)
(*S*)-**1f**·HCl[e]	*p*-CF_3	EA	268 (530)		262 (630)		257 (500)
		CD	268 (+610)		262 (+620)		257 (+430)[c]
(*S*)-**2a**·HCl[d]	3,5-$(CH_3)_2$	EA	274 (380)	270 (350)[c]	267 (410)	265 (390)[c]	262 (330)[c]
		CD	276 (+720)		267 (+640)		
(*S*)-**2b**·HCl[e]	3,5-Cl_2	EA	281 (340)		273 (410)		266 (290)
		CD	280 (+660)		273 (+640)		265 (+410)

[a] Molecular ellipticity adjusted to 100% ee. [b] Formed in situ from the amine. [c] Shoulder. [d] Enantiomer used. [e] Amine in 10% hydrochloric acid.

is not only useful in the determination of the induced magnetic transition moment direction[25] but may be more realistic for a large chromophore whose size is comparable to intergroup distances. The direction of the induced magnetic transition moment can be

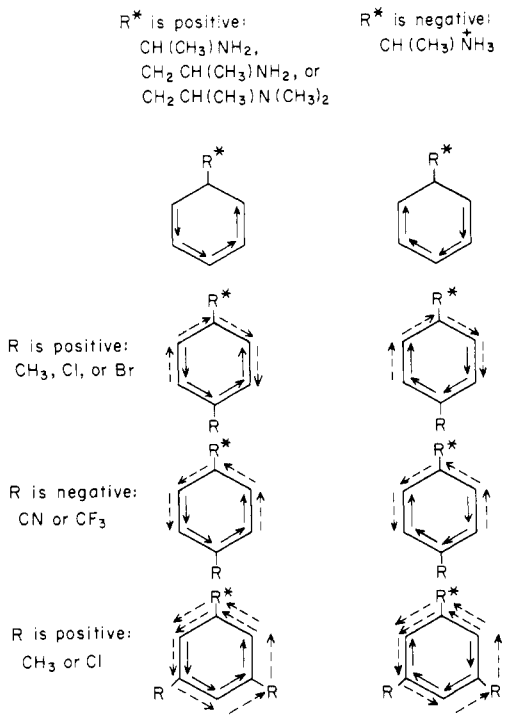

Figure 1. Induced bond moment directions for chiral benzene compounds substituted with groups having positive and negative spectroscopic moments.

determined by the sense of rotation of the bond transition moments, pointing up for the bond transition moments in the counterclockwise sense.

As can be seen in Figure 1, the respective directions of the induced ^1L_b electric and magnetic transition moments are opposite for (*S*)-α-phenylethylamine [(*S*)-**1a**] as compared to those for (*S*)-α-phenylethylamine hydrochloride [(*S*)-**1a**·HCl], yet the observed ^1L_b CEs for both (*S*)-**1a** and (*S*)-**1a**·HCl are positive. On the other hand, a para substituent with a large spectroscopic moment (**1b–d**) results in the same ^1L_b transition moment direction for both the amines and amine hydrochlorides although the magnitudes of the respective transition moments are different. The negative ^1L_b CEs observed for (*S*)-**1b-d** suggest that the contribution from the induced effect may be important in these amines but not in (*S*)-**1a**. Assuming that protonation does not greatly alter the conformation of the chiral substituent about its attachment bond or the chiral interactions, the same is true for the corresponding amine hydrochlorides.

The relative importance of the induced effect can be rationalized by using Figure 1. A chiral substituent does not induce transition moments in bonds adjacent to its attachment bond and thus there is negligible chiral interaction of the ^1L_b transition moment with the chiral substituent. The ^1L_b CEs for (*S*)-**1a** and (*S*)-**1a**·HCl can thus be regarded as dominated by vibronic borrowing from the ^1B_b-allowed transition. On para substitution, transition moments are induced in bonds adjacent to the attachment bond of the chiral group, resulting in enhanced coupling of the ^1L_b transition with the chiral grouping. The sign reversal upon para substitution by a group (CH_3, Cl, or Br) with a positive spectroscopic moment can thus be viewed as the overshadowing of the vibronic rotational strength by the induced contribution.

The importance of the vibronic coupling contribution in monosubstituted benzene compounds such as (*S*)-**1a** and (*S*)-**1a**·HCl is underscored by the everpresence of a non-totally symmetric vibrational (b_2) progression observed in their EA spectra.[4,10,26] The dominance of a vibronic contribution to the ^1L_b CEs also affords a rationale for the observation of positive ^1L_b CEs for both (*S*)-**1a** and (*S*)-**1a**·HCl despite the difference in sign of the spectroscopic moment for their respective chiral groups. 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 ^1B_b CE and consequently on the ^1L_b CEs.

As shown in Figure 1, substitution at the 3 and 5 positions in (*S*)-**1a** and (*S*)-**1a**·HCl with groups with positive spectroscopic moments will induce double-strength moments in a counterclockwise sense along bonds adjacent to the attachment bond of the chiral group. Thus enhanced positive ^1L_b CEs, in comparison to the corresponding para-substituted derivatives, are predicted and indeed are observed. Partial cancellation of transition moments in more remote bonds may account for the reduced intensity of the ^1L_b CEs of (*S*)-**2a,b**·HCl as compared to those of (*S*)-**2a,b**.

The relative importance of the two induced contributions, electric vs. magnetic, to the ^1L_b CEs may be estimated from a comparison of the molar absorptivity vs. the molecular ellipticity. The lack of correlation of molar absorptivity with molecular ellipticity suggests that the contribution from the induced electric transition moment is less important than that of the induced magnetic transition moment in agreement with the conclusion reached by Schoenfelder and Snatzke[27] from CD studies of benzene derivatives with several identical chiral substituents. The 1,4-disubstituted compounds have an enhanced induced electric transition moment but no magnetic transition moment. The 1,3,5-trisubstituted derivatives have a strong induced magnetic transition moment but no electric transition moment. Observation[27] shows strong ^1L_b CEs for the 1,3,5-trisubstituted derivatives but very weak dichroic absorption for the 1,4-disubstituted derivatives.

Spectra of α-Benzylethylamines. As shown in Table IV, the EA intensity variations on para substitution of (*S*)-α-benzylethylamine [(*S*)-**3a**] and (*S*)-*N*,*N*-dimethyl-α-benzylethylamine [(*S*)-**4a**] with a group with a positive (chloro) and a negative (trifluoromethyl) spectroscopic moment are analogous to those on substitution of (*S*)-α-phenylethylamine [(*S*)-**1a**]. Thus the chiral substituents in (*S*)-**3a** and (*S*)-**4a** also have positive spectroscopic moments.

For (*S*)-**3a** in cyclohexane, the ^1L_b CD sign variations (Table IV) on para substitution are also similar to those with (*S*)-**1a**. A positive spectroscopic moment of the substituent [(*S*)-**3b**] reverses the sign of the ^1L_b CEs while a negative spectroscopic moment [(*S*)-**3c**] does not. Again the interplay of vibronic vs. induced contributions can be used to rationalize such sign changes.

In methanol, (*S*)-**3a** exhibits positive ^1L_b CEs in contrast to the negative ones in cyclohexane. For (*S*)-**3b** in methanol, the ^1L_b CEs are more positive than those for (*S*)-**3a** in methanol, but the *p*-(trifluoromethyl) group reverses the sign. Such a trend is similar to that observed when cyclohexane is the solvent. The gross variation of the ^1L_b CEs for (*S*)-**3a** in different solvents is assumed to be a consequence of conformational change. Conformational change can also occur as a consequence of N-methylation of (*S*)-**3a**. Thus the ^1L_b CEs of (*S*)-**3a** and (*S*)-**4a** are of opposite sign in cyclohexane but have the same sign in methanol.

For (*S*)-α-benzylethylamine hydrochloride [(*S*)-**3a**·HCl], the EA intensity variation on para substitution (Table V) is not such as to allow the assignment of the sign of the spectroscopic moment of the chiral substituent. This moment is expected, however, to be quite small, and although the ^1L_b CEs do not change sign on para substitution of (*S*)-**3a**·HCl with a group with either a positive (**3b**) or negative (**3c**) spectroscopic moment, (*S*)-**3c**·HCl has much weaker ^1L_b CEs than does (*S*)-**3b**·HCl (Table V). This indicates that contributions from an induced magnetic transition moment may be responsible for the intensity variation of the ^1L_b CEs on para substitution of (*S*)-**3a**·HCl.

Experimental Section

Melting points were taken in open capillary tubes and are corrected. Boiling points are also corrected. Optical rotations at the sodium D line were measured with a Schmidt & Haensch visual polarimeter or an

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Table IV. ^1L_b Absorption Band Data for α-Benzylethylamines

compd	substituent	spectrum	λ_{max}, nm (ε or [θ][a])				
			a_1	b_2	a_1	b_2	a_1
			In Cyclohexane				
(*S*)-3a		EA	268 (150)	265 (160)	262 (200)	259 (210)	253 (170)
		CD[b]	268 (−150)		262 (−110)		255 (−60)
(*S*)-3a[c]		EA	268 (140)	265 (150)	262 (180)	259 (190)	253 (160)
		CD	269 (−140)		262 (−130)		256 (−70)
(*S*)-3b[c]	*p*-Cl	EA	277 (420)		269 (430)		262 (310)
		CD	278 (+260)		271 (+300)		265 (+210)
(*S*)-3c[d]	*p*-CF_3	EA	269 (160)		264 (260)		258 (310)
		CD	269 (−130)		263 (−190)		259 (−40)
(*S*)-4a[d]	*N,N*-$(CH_3)_2$	EA	272 (190)		268 (210)		265 (300)
		CD	272 (+240)		268 (+190)		265 (+190)
(*S*)-4b[c]	*N,N*-$(CH_3)_2$	EA	280 (270)[e]	277 (420)	271 (480)[e]	269 (500)	
	p-Cl	CD	282 (+480)		274 (+500)		267 (+430)
			In Methanol				
(*S*)-3a		EA	268 (140)	264 (160)	261 (180)	259 (200)	
		CD	269 (+170)		262 (+170)		257 (+110)[e]
(*S*)-3b[c]	*p*-Cl	EA	276 (320)		268 (370)		261 (280)
		CD	277 (+250)		269 (+240)		263 (+190)
(*S*)-3c[d]	*p*-CF_3	EA	269 (210)		263 (300)		258 (330)
		CD	269 (−67)		264 (−60)		
(*S*)-4a[d]	*N,N*-$(CH_3)_2$	EA	268 (170)		264 (210)	262 (240)[e]	
		CD	269 (+340)		263 (+380)		256 (+240)
(*S*)-4b[c]	*N,N*-$(CH_3)_2$	EA	277 (340)		268 (420)		262 (350)
	p-Cl	CD	277 (+330)		269 (+360)		263 (+260)

[a] Molecular ellipticity adjusted to 100% ee. [b] An additional maximum at 272 nm ([θ] +17) not assigned as the ^1L_b band origin. [c] Formed in situ from the hydrochloride. [d] Enantiomer used. [e] Shoulder.

Table V. ^1L_b Absorption Band Data for α-Benzylethylamine Hydrochlorides in Methanol

compd	substituent	spectrum	λ_{max}, nm (ε or [θ][a])				
			a_1	b_2	a_1	b_2	a_1
(*S*)-3a·HCl		EA	267 (79)	264 (140)	261 (120)[b]	258 (170)	
		CD	268 (+240)		261 (+260)		254 (+180)
(*S*)-3b·HCl	*p*-Cl	EA	276 (230)		268 (280)		261 (220)
		CD	277 (+160)		268 (+170)		262 (+140)
(*S*)-3c·HCl[c]	*p*-CF_3	EA	269 (310)		263 (400)		258 (350)
		CD	270 (+21)				
(*S*)-4a·HCl[c]	*N,N*-$(CH_3)_2$	EA	268 (80)	264 (150)		258 (190)	
		CD	268 (+280)		261 (+270)		255 (+180)
(*S*)-4b·HCl	*N,N*-$(CH_3)_2$	EA	276 (230)		268 (280)		261 (220)
	p-Cl	CD	277 (+120)		268 (+180)		261 (+160)

[a] Molecular ellipticity adjusted to 100% ee. [b] Shoulder. [c] Enantiomer used and formed in situ from the amine.

Autopol III automatic polarimeter and a 1-dm sample tube or, where noted, a 0.5- or 2-dm tube. Proton magnetic resonance (^1H NMR) spectra were observed in chloroform-*d* with tetramethylsilane as an internal standard with a JEOL JNM-MH-100 spectrometer, and all compounds had spectra consistent with their assigned structures. Isotropic electronic absorption (EA) spectra were measured with a Cary Model 14 spectrophotometer with matched 1-cm cells and the normal variable slit. Circular dichroism (CD) spectra were obtained at 25–28 °C with a Cary Model 60 spectropolarimeter with a CD Model 6001 accessory. The cell was 0.1 or 1 cm, and the slit was programmed for a spectral band width of 1.5 nm. Cutoff was indicated when the dynode voltage reached 400 V.

In some cases, for measurement of its EA and CD spectra in cyclohexane and methanol, the amine was formed in situ from the hydrochloride. The latter (10–30 mg) was mixed with 1 drop of 20% sodium hydroxide in water, and cyclohexane or methanol was added. The cyclohexane mixtures were dried ($MgSO_4$), and the solutions were made up to 10 mL and then diluted as needed for spectral measurements. Some of the amine hydrochlorides were formed in situ from the amines. One drop of concentrated hydrochloric acid was added to the amine (10–30 mg) in methanol. The solutions were made up to 10 mL with methanol and then diluted as needed for spectral measurements.

In general, hydrochlorides of the amines were prepared by treatment of methylene chloride solutions of the amines with concentrated hydrochloric acid. The salts were collected by filtration and recrystallized, if indicated, from appropriate solvents. Salts, both hydrochlorides and those of organic acids, were decomposed in 10 M sodium hydroxide, and the amine was extracted into ether. The ether solution was dried (KOH), and the ether was removed at reduced pressure. If the residual amine was distilled, its boiling point is given. Amines not distilled were free from impurities within the limits of ^1H NMR observations.

The isolated *N*-salicylidene and *N*-5-bromosalicylidene derivatives of the amines were prepared from the amines as previously reported.[28] Some *N*-salicylidene derivatives were formed in situ[29] by warming the amines (ca. 0.1 mmol) and 15–100% molar excess of salicylaldehyde in methanol (5 mL) for 10 min. The CD spectra of the derivatives are summarized in Table VI.

The percent enantiomeric excess (% ee) of the amines (Table I) was determined by comparison of their observed specific rotations with literature values of amines of known or assumed optical purity or by the ^1H NMR of the amides prepared from (*S*)-*O*-methylmandelic acid,[22] using the distinct doublets due to the α-methyl group of the amine moiety of the diastereomeric amides as the diagnostic absorption.[10] When only one such doublet was detected the ee is shown in Table I as greater than 95%.

Elemental analyses were done by Galbraith Laboratories, Inc., Knoxville, TN, and agree within 0.4% of the calculated values unless otherwise indicated.

(*S*)-α-Phenylethylamine[31] **[(*S*)-1a]** was an oil and had $[\alpha]^{26}_D$ −27° (*c* 2.00, CH_3OH) [lit.[10] $[\alpha]^{20}_D$ −28° (*c* 2, CH_3OH); 98.7% ee].

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Table VI. Circular Dichroism Data for the *N*-Salicylidene Derivatives of Substituted α-Phenyl- and α-Benzylethylamines in Methanol

amine	Ar group[b]	CD λ_{max}, nm ([θ][a]) quinoid	band I	other[c]	band II	band III
(*S*)-**1b**	*p*-$CH_3C_6H_4$	400 (+2300)	315 (+20 000)	274 (−5600)	253 (+31 000)	
(*R*)-**1c**	*p*-ClC_6H_4	400 (−1100)	316 (−19 000)	273 (+6100)	253 (−32 000)	227 (+83 000)
(*S*)-**1d**[d]	*p*-BrC_6H_4	377 (+1700)	316 (+19 000)	274 (−13 000)	255 (+26 000)	229 (−40 000)
(*S*)-**1f**[d]	*p*-$CF_3C_6H_4$	381 (+960)	317 (+17 000)	275 (−6200)	254 (+29 000)	
(*S*)-**2a**[e]	3,5-$(CH_3)_2C_6H_3$	412 (+2800)	327 (+21 000)	282 (−3200)	258 (+45 000)[f]	225 (−125 000)
				275 (+1700)	256 (+46 000)	
			332 (+20 000)[g]	282 (−2600)	262 (+39 000)[f]	225 (−148 000)
				276 (+1900)	257 (+42 000)	
(*S*)-**2b**[d]	3,5-$Cl_2C_6H_3$	377 (+2000)	317 (+22 000)	281 (+2000)	250 (+36 000)	225 (−59 000)
				276 (−2000)		
				272 (+840)		
(*R*)-**3c**[d]	*p*-$CF_3C_6H_4CH_2$	400 (−2900)	315 (−17 000)	272 (−7200)[f]	254 (−43 000)	223 (+19 000)

[a] Molecular ellipticity. [b] As in structure **5**. [c] Assigned to the $\pi \rightarrow \pi^*$ transition of the benzene ring of the amine moiety and/or the $n \rightarrow \pi^*$ transition of the azomethine group (cf. ref 30). [d] Derivative formed in situ with molecular ellipticities adjusted to 100% ee. [e] *N*-5-Bromosalicylidene derivative. [f] Shoulder. [g] Hexane as solvent for this spectrum.

(*S*)-α-(*p*-Methylphenyl)ethylamine [(*S*)-1b]. Racemic **1b** was prepared (75%) from *p*-methylacetophenone by the Leuckart reaction[18] as outlined below for the preparation of (±)-α-(3,5-dichlorophenyl)ethylamine [(±)-**2b**] from 3,5-dichloroacetophenone and had bp 203–204 °C (lit.[32] bp 204–205 °C). Resolution[32] using *d*-camphoric acid gave (*S*)-**1b** as an oil: bp 193–203 °C; $[\alpha]^{26}_D$ −25° (*c* 2.56, CH_3OH) [lit.[10] $[\alpha]^{20}_D$ −22.2° (*c* 2, CH_3OH); 77% ee].

(*S*)-α-(*p*-Methylphenyl)ethylamine hydrochloride [(*S*)-1b·HCl] was recrystallized from acetone–ethanol: mp 189–190 °C [lit.[33] mp 170.5–171.5 °C for (±)-**1b**·HCl]; $[\alpha]^{26}_D$ −22° (*c* 2.24, NaOH–CH_3OH[34]); >95% ee.[35]

(*S*)-*N*-Salicylidene-α-(*p*-methylphenyl)ethylamine was recrystallized from methanol: mp 91–92 °C; $[\alpha]^{26}_D$ +191° (*c* 1.17, 95% C_2H_5OH). Anal. ($C_{16}H_{17}NO$) C, H, N.

(*R*)-α-(*p*-Chlorophenyl)ethylamine [(*R*)-1c]. Racemic **1c** was prepared (41%) from *p*-chloroacetophenone by the Leuckart reaction[18] as outlined below for the preparation of (±)-α-(3,5-dichlorophenyl)ethylamine [(±)-**2b**] from 3,5-dichloroacetophenone and had bp 125–126 °C (30 mm) [lit.[36] bp 104–105 °C (13 mm)]. Resolution[10] with (+)-tartaric acid gave (*R*)-**1c** as an oil: bp 124–126 °C (30 mm); $[\alpha]^{26}_D$ +23° (*c* 2.56, CH_3OH) [lit.[10] $[\alpha]^{20}_D$ +26.5° (*c* 2, CH_3OH); 99% ee].

(*R*)-*N*-Salicylidene-α-(*p*-chlorophenyl)ethylamine was a yellow oil: bp 180–184 °C (1.7 mm); $[\alpha]^{26}_D$ −152° (*c* 2.13, CH_3OH). Anal. ($C_{15}H_{14}ClNO$) C, H, N.

(*S*)-α-(*p*-Bromophenyl)ethylamine [(*S*)-1d]. Partially racemic (*S*)-**1d**,[31] $[\alpha]^{26}_D$ −14° (*c* 2.40, CH_3OH), was further resolved[10] with the use of (−)-tartaric acid. Thus (*S*)-**1d** was an oil and had $[\alpha]^{26}_D$ −20° (*c* 2.26, CH_3OH) [lit.[10] $[\alpha]^{20}_D$ −20.3° (*c* 2, CH_3OH); 95.5% ee].

(*S*)-α-(*p*-(Trifluoromethyl)phenyl)ethylamine [(*S*)-1f]. Racemic **1f** was prepared (65%) from *p*-(trifluoromethyl)acetophenone by the Leuckart reaction[18] as outlined below for the preparation of (±)-α-(3,5-dichlorophenyl)ethylamine [(±)-**2b**] from 3,5-dichloroacetophenone and had bp 88–94 °C (21 mm) [lit.[37] bp 80–86 °C (10 mm)]. Racemic **1f** (6.05 g, 3.20 mmol) and L-*N*-acetylleucine[38] (5.55 g, 3.20 mmol) were dissolved in hot ethanol (60 mL). Water (200 mL) was added, and the solution was evaporated to ca. 135 mL. On cooling, fine needles (6.23 g, 108%) were deposited. Recrystallization once from water and twice from 95% ethanol gave the salt (1.18 g, 20%): mp 189–195 °C. Decomposition of the salt gave (*S*)-**1f** (0.583 g, 19%) as an oil: $[\alpha]^{24}_D$ −13° (*c* 1.95, CH_3OH); 60% ee.[35] The hydrochloride had mp 197–222 °C and $[\alpha]^{24}_D$ −3.3° (*c* 1.40, CH_3OH).

(±)-α-(3,5-Dimethylphenyl)ethylamine [(±)-2a]. A mixture of 3,5-dimethylacetophenone[39] (21.3 g, 0.144 mol) and formic acid (6.8 g of 97%, 0.14 mol) in formamide (45 mL) was heated at 180 °C for 2.5 h with continuous distillation of water.[18] The reaction mixture was cooled, water was added, and the mixture was extracted with ether (3 × 150 mL). The ether solution was evaporated. To the residue was added concentrated hydrochloric acid (150 mL), and this mixture was boiled for 1 h. The solution was made basic by the addition of solid potassium hydroxide and then extracted with ether (3 × 150 mL). The ether solution was dried (KOH) and evaporated. Distillation of the residue gave (±)-**2a** (16.5 g, 77%): bp 113–115 °C (28 mm) [lit.[40] bp 97–99 °C (10 mm)].

(*S*)-α-(3,5-Dimethylphenyl)ethylamine [(*S*)-2a]. Racemic **2a** (41.8 g, 0.280 mol) in 95% ethanol (0.5 L) was added to a boiling solution of L-*O*,*O*′-dibenzoyltartaric acid monohydrate (105.3 g, 0.280 mol) in 95% ethanol (1.0 L) and water (0.65 L). Cooling overnight gave a precipitate, and recrystallization of this solid (3×) from 70% ethanol in water (2.0 L) gave the L-*O*,*O*′-dibenzoyltartrate salt of (*S*)-**2a** (55.4 g, 78%): mp 186–187 °C dec; $[\alpha]^{25}_D$ −91° (*c* 0.655, CH_3OH, 2 dm). Anal. ($C_{28}H_{29}NO_8$) C, H, N.

Decomposition of the salt gave (*S*)-**2a** as an oil: $[\alpha]^{25}_D$ −21° (*c* 2.13, CH_3OH).

(*S*)-α-(3,5-Dimethylphenyl)ethylamine hydrochloride [(*S*)-2a·HCl] was recrystallized from methanol–acetone: mp 228–229 °C; $[\alpha]^{25}_D$ −16° (*c* 1.38, 0.1 M KOH in CH_3OH). Anal. ($C_{10}H_{16}ClN$) C, H, N.

(*S*)-*N*-(5-Bromosalicylidene)-α-(3,5-dimethylphenyl)ethylamine was recrystallized from 95% ethanol: mp 58–59 °C; $[\alpha]^{25}_D$ +64° (*c* 1.37, CH_3OH). Anal. ($C_{17}H_{18}BrNO$) C, N; H: calcd, 5.46; found, 5.05.

(*R*)-α-(3,5-Dimethylphenyl)ethylamine Hydrochloride [(*R*)-2a·HCl]. Partially racemic (*R*)-**2a** (19.8 g, 0.133 mol), isolated from the resolution mother liquor, was resolved further with D-*O*,*O*′-dibenzoyltartaric acid. The free base (5.2 g) from this resolution was converted directly to the hydrochloride. Recrystallization from methanol–acetone gave (*R*)-**2a**·HCl (2.4 g): mp 228–229 °C; $[\alpha]^{25}_D$ +17° (*c* 0.654, 0.2 M KOH in CH_3OH); 78% ee.[35]

(±)-α-(3,5-Dichlorophenyl)ethylamine [(±)-2b]. Methyllithium (75 mL, 1.4 M in ether, 0.11 mol) was added under an atmosphere of nitrogen to an ice-chilled solution of 3,5-dichlorobenzoic acid (19.1 g, 0.100 mol) in dry tetrahydrofuran (165 mL). The mixture was stirred for 10 min, and a second portion of methyllithium (0.11 mol) in ether (75 mL) was added. After 30 min, the reaction mixture was poured into ice and water (500 mL), and the mixture was extracted with ether (4 × 50 mL). The ether solution was extracted with saturated sodium bicarbonate (2 × 50 mL) and saturated sodium chloride (1 × 50 mL) and was dried ($MgSO_4$). Evaporation of the ether gave a crude product (15.2 g). The ^1H NMR spectrum showed this material to be mostly 3,5-dichloroacetophenone (~10.5 g) with major impurities of tetrahydrofuran (~1.2 g) and 2-(3,5-dichlorophenyl)-2-propanol (~3.5 g).

The crude ketone was mixed with formic acid (24 g, 97% in water, 0.51 mol) and formamide (100 mL), and the mixture was heated at 165–180 °C for 20 h. The mixture was cooled, diluted with water (25 mL), and extracted with benzene (2 × 25 mL). The benzene was removed by distillation, and the residue was boiled with 3 N hydrochloric acid (100 mL) for 48 h. The cooled reaction mixture was added to ether (50 mL) and then extracted with water (3 × 50 mL). The aqueous solution was washed with ether (50 mL), made basic by the addition of 20% sodium hydroxide, and extracted with ether (3 × 50 mL), and the solution was dried (KOH) and evaporated. Distillation of the residue

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gave (±)-**2b** (7.31 g, 38% from the acid): bp 129–136 °C (17 mm). Anal. ($C_8H_9NCl_2$) C, H, N.

(*S*)-α-(3,5-Dichlorophenyl)ethylamine [(*S*)-2b]. Racemic **2b** (6.95 g, 36.6 mmol) and (+)-10-camphorsulfonic acid (8.49 g, 36.6 mmol) were dissolved in hot methanol (50 mL). The methanol was removed at reduced pressure. Recrystallization (4×) of the residue from 30–50% ethanol in water gave the pure salt (1.26 g, 16%): $[\alpha]^{25}_D$ +6.8° (*c* 1.38, NaOH–CH_3OH[34]). Decomposition of the salt gave (*S*)-**2b**: $[\alpha]^{26}_D$ −24° (*c* 1.45, CH_3OH); >95% ee.[35]

(*S*)-α-Benzylethylamine [(*R*)-3a] had $[\alpha]^{22}_D$ +33.1° (neat, d^{20}_4 0.949, 0.5 dm) [lit.[15] $[\alpha]^{15}_D$ +35.6° (neat)].

(*S*)-α-Benzylethylamine hydrochloride [(*S*)-3a·HCl] had $[\alpha]^{25}_D$ +21.6° (*c* 9.0, H_2O) [lit.[15] $[\alpha]^{15}_D$ +24.8° (*c* 9.00, H_2O)].

(*S*)-α-(*p*-Chlorobenzyl)ethylamine hydrochloride [(*S*)-3b·HCl] had $[\alpha]^{25}_D$ +22° (*c* 2.10, H_2O) [lit.[16] $[\alpha]^{25}_D$ +22° (*c* 2.10, H_2O)]; >95% ee.[35]

(*R*)-α-(*p*-(Trifluoromethyl)benzyl)ethylamine [(*R*)-3c]. Racemic **3c**·HCl,[20] mp 202–204 °C (lit.[19] mp 195–197 °C) (4.83 g, 20.2 mmol), in 95% ethanol (25 mL) was mixed with 20% NaOH (4.1 g, 20 mmol). To the mixture was then added L-*N*-acetylleucine[38] (3.55 g, 20.5 mmol) in 95% ethanol (25 mL), and the mixture was heated to boiling and filtered. The solvent was evaporated, and the residue was recrystallized from methanol. A second recrystallization from methanol gave the salt (1.12 g, 29%): $[\alpha]^{26}_D$ −15° (*c* 1.47, CH_3OH). Decomposition of the salt gave (*R*)-**3c**: $[\alpha]^{26}_D$ −19° (*c* 1.76, CH_3OH); >95% ee.[35] The hydrochloride salt [(*R*)-**3c**·HCl] formed by the addition of concentrated HCl to an ether solution of the amine had mp 170–172 °C and $[\alpha]^{26}_D$ −7° (*c* 1.23, CH_3OH).

(*R*)-*N*,*N*-Dimethyl-α-benzylethylamine [(*R*)-4a]. A mixture of formic acid (2.4 g of 97%, 51 mmol) and formaldehyde (2.0 mL of 36%) was added with cooling to (*R*)-α-benzylethylamine [(*R*)-**9a**], $[\alpha]^{22}_D$ −35.0° (neat, d^{20}_4 0.949) (1.35 g, 10.0 mmol). The mixture was boiled for 15 h, acidified with 6 N hydrochloric acid (2.0 mL), and concentrated at reduced pressure. The concentrate was made basic with 10% sodium hydroxide (10 mL) and then extracted with ether (2 × 10 mL). The ether solution was dried (KOH) and evaporated. Distillation of the residue gave (*R*)-**4a** (0.828 g, 51%): bp 116–120 °C (32 mm) [lit.[41] bp 115–118 °C (20 mm) for (±)-**4a**]; $[\alpha]^{26}_D$ +7.8° (*c* 1.96, CH_3OH) [lit.[17] $[\alpha]_D$ +7.8° (*c* 2.6, CH_3OH)].

(*S*)-*N*,*N*-Dimethyl-α-(p-chlorobenzyl)ethylamine hydrochloride [(*S*)-4b·HCl] had $[\alpha]^{25}_D$ +11° (*c* 2.09, H_2O) [lit.[16] $[\alpha]^{25}_D$ +11° (*c* 2.09, H_2O)].

(*S*)-*O*-Methylmandelic acid was prepared as described previously[22,42] and had mp 63–66 °C $[\alpha]^{26}_D$ +161° (*c* 1.20, H_2O) [lit.[22] mp 65–67 °C and $[\alpha]^{23}_D$ −161.9° (*c* 1.66, H_2O) for the *R* isomer].

Registry No. (*S*)-**1a**, 2627-86-3; (*S*)-**1a**·HCl, 17279-30-0; (±)-**1b**, 42070-98-4; (*S*)-**1b**, 27298-98-2; (*S*)-**1b**·HCl, 84499-72-9; (±)-**1c**, 35588-60-4; (*R*)-**1c**, 27298-99-3; (*S*)-**1c**, 4187-56-8; (*S*)-**1c**-HCl, 56782-68-4; (*S*)-**1d**, 27298-97-1; (*S*)-**1d**·HCl, 84499-77-4; (*S*)-**1e**, 36244-70-9; (±)-**1f**, 84580-06-3; (*S*)-**1f**, 84499-73-0; (*S*)-**1f**·L-*N*-acetylleucine, 84499-82-1; (*S*)-**1f**·HCl, 84499-78-5; (±)-**2a**, 84580-07-4; (*S*)-**2a**, 84499-76-3; (*S*)-**2a**·L-*O*,*O*′-dibenzoyltartrate, 84520-44-5; (*R*)-**2a**·HCl, 84499-74-1; (*S*)-**2a** (*N*-5-bromosalicylidene derivative), 84499-81-0; (±)-**2b**, 84499-83-2; (*S*)-**2b**, 84499-75-2; (*S*)-**2b**·(+)-10-camphorsulfonic acid, 84580-08-5; (*S*)-**2b**·HCl, 84499-79-6; (*S*)-**3a**, 51-64-9; (*S*)-**3a**·HCl, 1462-73-3; (*S*)-**3b**, 405-46-9; (*S*)-**3b**·HCl, 16064-30-5; (*R*)-**3c**, 84580-99-4; (*R*)-**3c**·HCl, 84580-09-6; (*R*)-**3c**·L-*N*-acetylleucine, 84620-15-5; (*S*)-**3c**, 84580-04-1; (*S*)-**3c**·HCl, 84580-05-2; (*R*)-**4a**, 52691-87-9; (*S*)-**4a**·HCl, 36913-04-9; (*S*)-**4a**, 17279-39-9; (*S*)-**4b**, 84499-80-9; (*S*)-**4b**·HCl, 16064-30-5; (*R*)-**9a**, 156-34-3; *p*-methylacetophenone, 122-00-9; *p*-chloroacetophenone, 99-91-2; *p*-(trifluoromethyl)-acetophenone, 709-63-7; 3,5-dimethylacetophenone, 5379-16-8; methyllithium, 917-54-4; 3,5-dichlorobenzoic acid, 51-36-5; 3,5-dichloroacetophenone, 14401-72-0; 2-(3,5-dichlorophenyl)-2-propanol, 68575-35-9.

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Molecular Structure of Acetylacetone. A Crystallographic Determination

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Abstract: A drug complex crystallized from acetylacetone (2,4-pentanedione) was found by X-ray crystal structure determination to contain one molecule of acetylacetone per asymmetric unit in the crystal lattice. The acetylacetone does not interact with the other molecules in the crystal but displays a keto–enol configuration stabilized by an intramolecular hydrogen bond. In contrast to electron diffraction studies of acetylacetone and crystal structure studies of other β-diketones, bond distances, including the hydrogen bond, are not symmetric but are indicative of localized single and double bonds throughout the molecule. Past estimates of acetylacetone diketo/keto–enol ratios in the liquid and gas phases may be in error if they assume complete bond length symmetry for the enol form.

The β-diketones have been among the most widely studied chelating compounds because of their strong hydrogen-bonding property and their ability to form coordination complexes with almost every metal in the periodic table. Although scores of such metal chelates have been investigated crystallographically,[2] only limited structural data have been collected on β-diketones themselves. The questions of whether the diketo or enol form predominates for these molecules and whether or not the enol intramolecular hydrogen bond is symmetrical have been examined in the crystal structure determinations of bis(*m*-bromobenzoyl)-methane,[3] bis(*m*-chlorobenzoyl)methane,[4] dibenzoylmethane,[5] and tetraacetylethane.[6] All of these compounds were found to be in the enol configuration in the crystalline state and all except dibenzoylmethane are characterized by equidimensional C–O distances and a symmetric intramolecular hydrogen bond. The latter

Table I. Acetylacetone Intermolecular Contacts Less Than 3.2 Å

O(2)- - -H(C), A[a]	2.56	O(2)- - -H(C), D	2.76
O(2)- - -C, A	3.15	O(2)- - -H(C), D	3.11
O(2)- - -H(N), A	2.80	O(4)- - -H(N), A	2.95
O(4)- - -H(C), D[a]	2.91	O(4)- - -N, A	3.18

[a] A, 9-ethyladenine; D, diphenylhydantoin.

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