that is, the contribution to binding to the surface might be relatively small and constant. Thus the calculated reaction mechanisms and activation energies in this paper may be more accurate than the adsorption energies of CH_4, CH_3, CH_2, C_2H_2, and C_2H_4.

Activation and stabilization energies for dehydrogenation of CH, CH_2, CH_3, and CH_4 are shown in Table XIII. The activation energies to hydrogenation and dehydrogenation decrease on going from CH to CH_2 to CH_3. Energetically, C is the prefered surface species, and at high temperatures H desorbs. However, when H_2 is maintained at a sufficient pressure it can combine with surface carbon to form gases[25] and gasoline.[31] Statistical considerations will be important in determining what species exist on an iron surface at various temperatures and H_2 pressures. Once an alkane forms it is likely to desorb as its bond to the surface is much weaker than for the unsaturated hydrocarbons. Should two CH_3 fragments collide, ethane might desorb, and so on. The relationships between concentrations of surface species and temperature and pressure are thermodynamic problems beyond the reach of quantum chemistry as applied to the calculation of energy surfaces in this paper.

Appendix

The theory used in this paper is derived in ref 1. Further applications are in ref 2 and 4–9. Parameters used in this paper are in Table XIV.

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# Optically Active Amines. 22.[1] Application of the Salicylidenimino Chirality Rule to α-Amino Acids

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Abstract: The sign of the Cotton effects near 255 and 315 nm in the circular dichroism (CD) spectra of the N-salicylidene derivatives formed in situ using sodium salicylaldehyde and chiral amine hydrochlorides, α-amino acids, and α-amino ester hydrochlorides correlates with their absolute configurations. The Cotton effects are generated by the coupled oscillator mechanism and their sign is the same as the chirality (right-handed screw for positive chirality) of the interaction of the dominant oscillator of the amine moiety with those of the salicylidenimino chromophore, the chirality of the interaction being deduced by conformational analysis.

The salicylidenimino chirality rule[5] correlates the absolute configurations of the N-salicylidene (**1a**) and N-5-bromosalicylidene (**1b**) derivatives (Schiff bases) of a wide variety of chiral primary amines with the sign of the Cotton effects near 255 and 315 nm in their circular dichroism (CD) spectra. Included are α- and β-arylalkylamines[5,6] and cyclic terpene[7] and steroidal amines.[1]

The electron (isotropic) absorption (EA) spectra of the

1a, X = H
b, X = Br
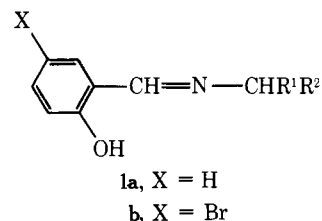
N-salicylidene derivatives (**1a**) in hexane exhibit bands at about 315, 255, and 215 nm,[7-10] designated bands, I, II, and III, respectively, which are assigned to transitions of the intramolecularly hydrogen-bonded salicylidenimino chromophore (**2**). In polar solvents a broad band at about 400 nm and

2   3
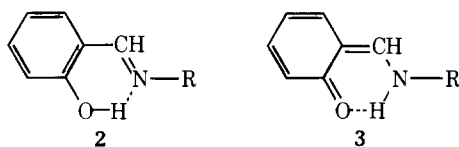
in methanol and ethanol a shoulder near 280 nm[7-12] become evident, and the other three bands show a slight decrease in intensity. The two additional bands are attributed to the presence of a quinoid tautomer[13,14] (**3**) in the polar solvents. The EA spectra of the N-5-bromosalicylidene derivatives (**1b**) are essentially the same except that the two longest wavelength bands are at about 328 and 415 nm.[5,6,8,12,15] Corresponding CD maxima are observed for bands I and II and for the band near 400 nm in methanol and ethanol.[5-12,15] In all solvents the anisotropy factor ($\Delta\epsilon/\epsilon$) of band III is such that its associated CD is difficult to measure and is frequently not observed.

For α- and β-arylalkylamine derivatives, the magnitudes of the observed Cotton effects and the general features of the CD spectra indicate that the dominant mechanism operative in generation of the Cotton effects is the coupled oscillator in which there is electric dipole–dipole coupling of the transition moments of the aryl group with the salicylidenimino chromophore.[16] Positive chirality (right-handed screw) for this coupling results in positive Cotton effects near 255 and 315 (328) nm.[5] For derivatives of cyclic terpene[7] and steroidal[1] amines, the sign of the Cotton effects, also generated by the coupled oscillator mechanism, is the same as the chirality of a single nearby carbon–carbon bond and the attachment bond of the salicylidenimino chromophore.

In previous work, Schiff bases were formed by reaction of salicylaldehyde and 5-bromosalicylaldehyde with the chiral amine in methanol and were isolated and characterized prior to spectral measurements. We now have examined the CD spectra of N-salicylidene derivatives formed in situ by mixing sodium salicylaldehyde[17] (**4**) (10–30% molar excess) with chiral amine hydrochlorides (10–15 μmol) (Table I) in methanol (Scheme I) and have compared these spectra with

Scheme I
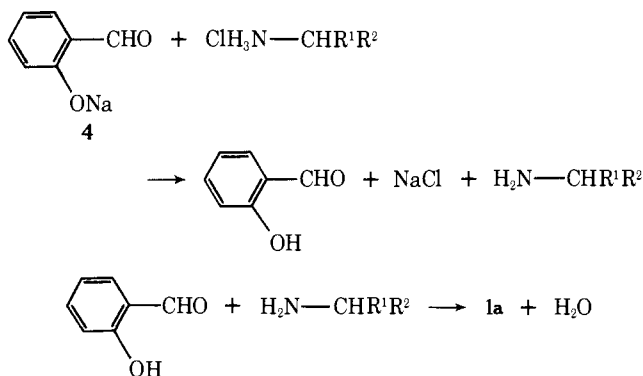
those of the isolated Schiff bases in methanol. This procedure obviates the conversion of a crystalline amine hydrochloride to a usually noncrystalline free base, and since both reactants are solids, one to two milligram amounts can be conveniently weighed before mixing.

Using sodium salicylaldehyde, a convenient measurement of the CD spectra of the N-salicylidene derivatives of α-amino acids and α-amino esters formed in situ is also possible, and we report a correlation of the CD spectra of the N-salicylidene derivatives of a number of α-amino acids (Table II) and α-

Table I. Circular Dichroism Data for N-Salicylidene Derivatives of α- and β-Arylalkylamines in Methanol

Code	Name	R	Method[b]	CD max, λ, nm ($[\theta]$[a]) Quinoid	I	II	III
(S)-Ia	(S)-α-Phenylethylamine hydrochloride	C_6H_5	Derivative[c]	397 (+1700)	316 (+16 000)	252 (+33 000) / 275 (−2300)	222 (−41 000)
			In situ[d,e]		316 (+16 000)	252 (+28 000) / 275 (−1900)	
(S)-Ib	(S)-α-Benzylethylamine hydrochloride	$C_6H_5CH_2$	Derivative[f,g]		313 (+16 000)	253 (+38 000)	
			In situ[e]		313 (+12 000)	253 (+28 000)	
(αS)-Ic	(αS)-Norephedrine hydrochloride	(βR)-$C_6H_5C(OH)H$	Derivative[d,h,i]	417 (+1300)	327 (+10 000)	256 (+21 000)	
			In situ[d,j]		316 (+11 000)	256 (+16 000)	
(S)-Id	(S)-1-(2-Thienyl)-1-aminoethane hydrochloride	2-C_4H_3S	Derivative	402 (+810)	316 (+18 000)	256 (+34 000) / 276 (−15 000)	228 (−53 000)
			In situ		316 (+15 000)	256 (+25 000) / 276 (−10 000)	
(S)-Ie	(S)-1-(2-Thienyl)-2-aminopropane hydrochloride	2-$C_4H_3SCH_2$	Derivative[d,h]	415 (+690)	325 (+4000)	256 (+16 000) / 272 (−570)	228 (−40 000)
			In situ[d]		316 (+6000)	255 (+16 000)	

[a] Molecular ellipticity calculated for in situ formed derivatives on the basis of complete formation of the Schiff base. [b] For in situ formed derivatives, spectra not examined above 360 nm. [c] CD data from ref 5. [d] Enantiomer used. [e] Salt characterized in H. E. Smith, M. E. Warren, Jr., and L. I. Katzin, *Tetrahedron*, **24**, 1327 (1968). [f] Schiff base characterized in ref 8. [g] Spectrum not examined above 360 nm. [h] N-5-Bromosalicylidene derivative. [i] CD data from ref 12. Absolute ethanol as solvent. [j] Salt characterized in ref 12.

Table II. Circular Dichroism Data for N-Salicylidene Derivatives of α-Amino Acids Formed in Situ in Methanol^a

$$\begin{array}{c} CO_2^- \\ | \\ H_3\overset{+}{N}\blacktriangleright C \blacktriangleleft H \\ | \\ R \end{array}$$

Code	Name	R	CD max, λ, nm ([θ]^b)			
			I	Quinoid	II	III
L-IIa	L-Alanine^c	CH_3	314 (+6400)	273 (−5000)	252 (+5100)	229 (−16 000)
L-IIb	L-α-Amino-n-butyric acid	CH_3CH_2	315 (+4500)	273 (−9300)	252 (+8800)	228 (−15 000)
L-IIc	L-Valine	$(CH_3)_2CH$	316 (+3900)	275 (−12 000)	253 (+9100)	232 (−14 000)
L-IId	L-Leucine	$(CH_3)_2CHCH_2$	315 (+3200)	274 (−13 000)	253 (+8500)	232 (−13 000)
L-IIe	L-Isoleucine	$CH_3CH_2C(CH_3)H$	317 (+4100)	275 (−16 000)	253 (+14 000)	232 (−15 000)
L-IIf	L-Alloisoleucine^d	allo-$CH_3CH_2C(CH_3)H$	317 (+3400)	275 (−16 000)	253 (+10 000)	232 (−12 000)
L-IIg	L-Serine	$HOCH_2$	313 (+4000)	272 (−3000)	249 (+1600)	229 (−21 000)
L-IIh	L-Threonine	$CH_3C(OH)H$	317 (+6000)	273 (−8200)	252 (+5300)	229 (−26 000)
L-IIi	L-(S)-Methylcysteine	CH_3SCH_2	317 (−2500)		264 (−15 000) 246 (+4600)	228 (−12 000)
L-IIj	L-Methionine	$CH_3SCH_2CH_2$	315 (+300)	274 (−15 000)	251 (+10 000)	228 (−15 000)
L-IIk	L-Cysteine^e	$HSCH_2$		288 (+3000)	260 (−4600)	
L-IIl	L-Aspartic acid^e	HO_2CCH_2			254 (−5000)	
L-IIm	L-Glutamic acid^e	$HO_2CCH_2CH_2$		270 (−6300)		
L-IIn	L-Asparagine monohydrate	NH_2COCH_2	315 (+1400)		268 (−6000) 248 (+2300)	229 (−13 000)
L-IIo	L-Phenylglycine^d	C_6H_5	313 (−6000)	277 (−5800)		
L-IIp	L-Phenylalanine	$C_6H_5CH_2$	313 (−6600)	272 (−14 000) 266 (−18 000) 261 (−19 000)	256 (−17 000)	
L-IIq	L-Tyrosine	p-$HOC_6H_4CH_2$	314 (−11 000)		262 (−31 000)	
L-IIr	L-Histidine	[imidazol-4-ylmethyl]	315 (−2100)		262 (−11 000) 244 (+2300)	229 (−12 000)
L-IIs	L-(2-Thienyl)glycine^d	2-C_4H_3S	313 (−3500)	275 (+1800)		

^a Except for that of the derivative of L-IIa, spectra not measured above 360 nm. ^b Molecular ellipticity calculated on the basis of complete formation of the Schiff base. ^c Longest wavelength examined was 500 nm. Quinoid band at 402 nm ([θ] +3600). ^d Enantiomer used. ^e Two molar equivalents plus a 10–30% molar excess of 4.

Table III. Circular Dichroism Data for N-Salicylidene Derivatives of α-Amino Ester Hydrochlorides Formed in Situ in Methanol^a

$$\begin{array}{c} CO_2R^2 \\ | \\ ClH_3N\blacktriangleright C \blacktriangleleft H \\ | \\ R^1 \end{array}$$

Code	Name	R^1	R^2	CD max, λ, nm ([θ]^b)		
				I	II	III
L-IIIa	Methyl L-alaninate hydrochloride^c	CH_3	CH_3	315 (+1900)	262 (−3600)	229 (−7600)
L-IIIb	Methyl L-valinate hydrochloride	$(CH_3)_2CH$	CH_3		266 (−8500)	
L-IIIc	Methyl L-leucinate hydrochloride	$(CH_3)_2CHCH_2$	CH_3		264 (−5900)	229 (−4000)
L-IIId	Ethyl L-leucinate hydrochloride	$(CH_3)_2CHCH_2$	CH_3CH_2		265 (−11 000)	230 (−5400)
L-IIIe	Methyl L-phenylalaninate hydrochloride	$C_6H_5CH_2$	CH_3	316 (−13 000)	261 (−36 000)	
L-IIIf	Ethyl L-p-nitrophenylalaninate hydrochloride^d	p-$NO_2C_6H_4CH_2$	CH_3CH_2	316 (−3400)^e	268 (−2800) 252 (+4000)	
L-IIIg	Methyl L-tryptophanate hydrochloride	[indol-3-ylmethyl]	CH_3	320 (−3400)	261 (−4900)	

^a Except for that of the derivative of L-IIIa, spectra not measured above 360 nm. ^b Molecular ellipticity calculated on the basis of complete formation of the Schiff base. ^c Longest wavelength examined was 500 nm. ^d Enantiomer used. ^e Additional CD maximum at 282 nm ([θ] + 1200) assigned to a transition of the free α-amino ester.

amino ester hydrochlorides (Table III) formed in situ with their absolute configurations.

Results and Discussion

In Situ Formation of Schiff Bases. Table I shows a comparison of the CD spectra of N-salicylidene derivatives formed in situ from five α- and β-arylalkylamine hydrochlorides (Ia–e) in the presence of 10–30% molar excess of sodium salicylaldehyde (4) with those of the pure derivatives.

Application of the salicylidenimino chirality rule[5] to the data in Table I for the Schiff base of (S)-1-(2-thienyl)-1-aminoethane hydrochloride [(S)-Id] confirms the previously assigned S configuration to the levorotatory free base.[18] The amine was obtained in higher optical purity using D-N-acetylleucine[19] than that achieved earlier using O-nitrotartranilic acid as resolving agent.[18] The CD data also allow assignment of the R configuration to (−)-1-(2-thienyl)-2-aminopropane hydrochloride obtained by resolution with L-N-acetylleucine.
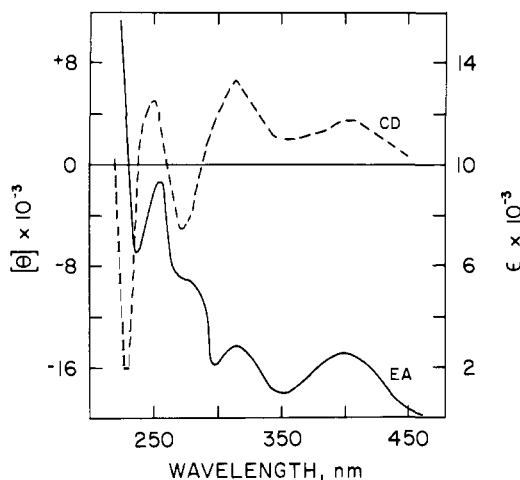
Figure 1. Electronic absorption (EA) and circular dichroism (CD) spectra of L-alanine (L-IIa) with a 15% molar excess of sodium salicylaldehyde (4) in methanol.
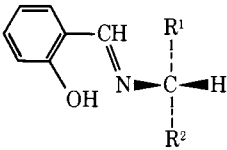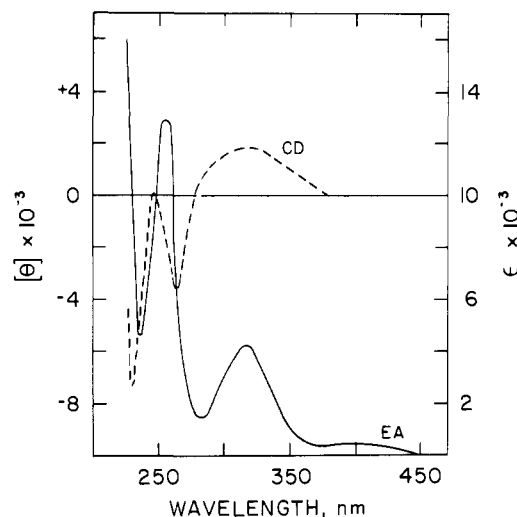

Figure 2. Electronic absorption (EA) and circular dichroism (CD) spectra of methyl L-alaninate hydrochloride (L-IIIa) with a 15% molar excess of sodium salicylaldehyde (4) in methanol.

Because of the somewhat lower values for the molecular ellipticities ($[\theta]$) generally observed in situ (Table I), polarimetric studies were undertaken to determine rates of formation and optical stabilities of the derivatives in the presence of measured excesses of 4. Observation of the mutarotations of solutions of (S)-α-benzylethylamine hydrochloride [(S)-Ib] and of L-phenylalanine (L-IIp) (11–20 mmol/l.) with 5–58% molar excesses of 4 showed that equilibrium was achieved within 45 min and that the rotatory powers of the solutions, $[\phi]^{25}$ D +510 and −850°, respectively, with a 5% molar excess of 4, remained unchanged for an additional 18 h. The molecular rotation of the solution prepared with (S)-Ib and a 5% molar excess of 4 was lower than the known molecular rotation of the Schiff base[8] due to incomplete formation of the derivative. Increases in the molar excess of 4 increased the rotatory power of the solution due to increasing formation of the sodium salt of the Schiff base [(S)-5] which is also strongly dextrorotatory in methanol.

(S)-5
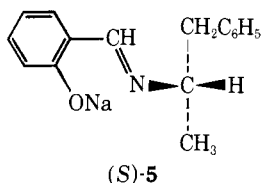
A comparison of the EA and CD spectra of a methanolic solution of L-alanine (L-IIa) and a 15% molar excess of 4 (Figure 1) with those of (S)-N-salicylidene-sec-butylamine[10] [(S)-IVa] (Table IV) shows that the Schiff base (L-IVb) of the amino acid gives rise to the spectra observed in situ. However, the magnitudes of the molecular ellipticities for this Schiff base and for those of the other α-amino acids given in Table II must be considered as minimum values due to incomplete formation of the derivatives in situ.

Polarimetric studies of methyl L-alaninate hydrochloride (L-IIIa) and methyl L-phenylalaninate hydrochloride (L-IIIe) (49 and 5–7 mmol/l., respectively) each with 6–32% molar excesses of 4 showed that the rate of Schiff base formation was slower than for (S)-α-benzylethylamine hydrochloride [(S)-Ib] and L-phenylalanine (L-IIp). With the esters 2 h were required to reach maximum molecular rotation and, contrary to what might have been expected,[20] little if any racemization took place in 12 subsequent hours even at the highest excess of 4. A comparison of the EA and CD spectra of a methanolic solution of L-methyl alaninate hydrochloride (L-IIIa) and a 15% molar excess of 4 (Figure 2) with those of (S)-N-sali-

cylidene-sec-butylamine [(S)-IVa] (Table IV) shows that it is the Schiff base L-IVc formed in situ which gives rise to the spectra. The noncrystalline methyl L-N-salicylideneleucinate (L-IVd) was prepared from methyl L-leucinate and salicylaldehyde as outlined earlier,[9] and its CD spectrum was measured in both methanol and hexane (Table IV). Again, the lower molecular ellipticities observed in situ with methyl L-leucinate hydrochloride (L-IIIc) and excess 4 (Table III) indicate that the molecular ellipticities in Table III for the Schiff bases of the other α-amino esters formed in situ must be considered minimum values.

CD Spectra. α- and β-Arylalkylamines (Table I). For prediction of the sign of the Cotton effects of bands I and II of the N-salicylidene derivative of a chiral amine, the chirality of the dominant coupled oscillators must be deduced by conformational analysis. The three conformers of lowest energy of a β-arylalkylamine derivative of configuration 6 are depicted

Sa = Salicylidene

(−)   (∼0)   (+)
6a   6b   6c
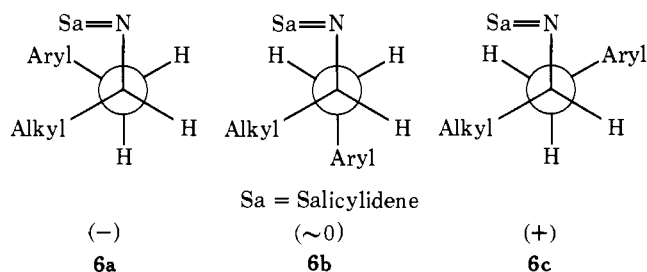
as 6a–c. For each conformer the sign, as shown, of its contribution to the CD of bands I and II is determined by the chirality of the attachment bonds of the salicylidenimino chromophore and the aryl group.[5] The transition moments of bands I and II of the chromophore do not deviate greatly from the phenyl group–methine carbon bond which in turn is parallel to the chromophore attachment bond.[5] The effective transition moments of the aryl group are also along its attachment bond as a result of ring mobility about this bond. Since 6a will be of highest energy due to steric interactions and 6b will contribute negligible rotational strength due to the near anticolinearity and/or large separation between the effective transition moments, 6c will be the principal contributor to the CD spectrum. In 6c the chirality of the attachment bonds of the chromophore and the aryl group is positive (right-handed screw), and positive Cotton effects for bands I and II are predicted. Thus the N-salicylidene derivatives of (S)-Ib, (S)-Ic, and (S)-Ie all show

Table IV. Spectral Data for N-Salicylidene Derivatives

Compd	R¹	R²	Spectrum (solvent)	Quinoid	I		II	III
(S)-IVa	CH₃CH₂	CH₃	EA (methanol)ᵇ	400 (1700)	314 (3300)	277 (4000)	258 (10 000)ᶜ	
							252 (11 000)	
			CD (methanol)ᵇ	395 (+630)	313 (+1600)		253 (+4900)	
L-IVbᵈ	CO₂Na	CH₃	EA (methanol)	403 (2600)	315 (2900)	275 (5500)	254 (9400)	
L-IVcᵉ	CO₂CH₃	CH₃	EA (methanol)	393 (410)	318 (4300)		256 (13 000)	
L-IVd	CO₂CH₃	(CH₃)₂CHCH₂	CD (methanol)				265 (-13 000)	230 (-8500)
			CD (hexane)		315 (+2100)		264 (-14 000)	232 (-15 000)
(S)-IVe	2-C₄H₃S	CH₃	EA (methanol)	403 (330)	316 (4200)		256 (14 000)	215 (28 000)
			EA (hexane)		321 (5100)		257 (15 000)	216 (27 000)
			CD (hexane)		320 (+21 000)	275 (-15 000)	256 (+35 000)	230 (-47 000)
(S)-IVfᶠ·ᵍ	2-C₄H₃SCH₂	CH₃	EA (methanol)	417 (930)	327 (3600)		252 (12 000)ᶜ	222 (39 000)
							242 (17 000)ᶜ	
			EA (hexane)		331 (4300)		255 (10 000)ᶜ	222 (36 000)
			CD (hexane)		330 (+6700)	278 (-1300)	257 (+26 000)	
L-IVgᶠ	CO₂CH₂CH₃	p-NO₂C₆H₄CH₂	EA (methanol)	403 (140)	315 (5500)		259 (21 000)	213 (28 000)
			CD (methanol)	402 (-500)	317 (-21 000)		267 (-17 000)	
							251 (+13 000)	

ᵃMolar absorptivity (ε) and molecular ellipticity ([θ]) calculated for in situ formed derivatives on the basis of complete formation of the Schiff base. ᵇData from ref 10. ᶜShoulder. ᵈPrepared in situ using L-IIa and a 15% molar excess of 4. ᵉPrepared in situ using L-IIIa and a 15% molar excess of 4. ᶠEnantiomer used. ᵍN-5-Bromosalicylidene derivative.

positive CD maxima near 255 and 315 nm. The negative maximum near 275 nm observed for the Schiff base of (S)-Ie, (S)-N-(5-bromosalicylidene)-1-(2-thienyl)-2-aminopropane [(S)-IVf], cannot be attributed to the quinoid tautomer since the maximum persists in hexane (Table IV). No corresponding band was detected in the EA spectrum of (S)-IVf in methanol or hexane (Table IV). It is worth noting that a recent electron impact investigation of thiophene has identified a singlet → triplet transition in this spectral region.[21]

Since the attachment bonds of the chromophore and the aryl group in a chiral α-arylalkylamine derivative merge to the same carbon atom, the chirality of the phenyl group–methine carbon bond of the chromophore and the attachment bond of the aryl group is used to determine the sign of CD bands I and II. The three conformers of lowest energy for an α-arylalkylamine derivative of configuration 7 are shown as 7a–c.[11]


(+)
7a

(~0)
7b

(−)
7c
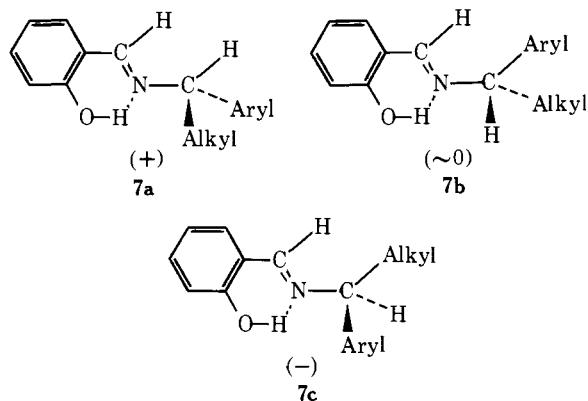
As shown, conformer 7a makes a positive contribution to the CD spectrum since the chirality of the relevant transition moments is positive while 7b makes a negligible contribution due to near coplanarity of these moments. The contribution of 7c is negative but less than that of 7a because the latter is more stable.[11] Thus the N-salicylidene derivatives of (S)-Ia and (S)-Id show positive Cotton effects associated with band I and II. In the spectrum of the (S)-Id derivative, (S)-N-sal-

icylidene-1-(2-thienyl)-1-aminoethane [(S)-IVe], the strong negative maximum at 275 nm again cannot be assigned to the quinoid tautomer since the maximum persists in hexane (Table IV). Again no corresponding band was found in the EA spectrum in methanol or hexane (Table IV). The negative maximum at 275 nm in the CD spectrum of the Schiff base derivative of (S)-Ia (Table I), also persisting in isooctane,[10] was attributed to the ^1L_B transition of the phenyl group and indicates that the rotational averaging process for the short axis polarization is not complete.[5]

Aliphatic α-Amino Acids (Table II). In the CD spectra of the N-salicylidene derivatives of aliphatic α-amino acids (IIa–IIf), the strong band near 273 nm is assigned to the quinoid tautomer (3) while bands I, II, and III arise primarily by transition moment dipole–dipole coupling of the carboxylate group with the salicylidenimino chromophore. Thus on replacement of the methyl group of (S)-N-salicylidene-sec-butylamine [(S)-IVa] by a carboxylate group to give the N-salicylidene derivative of D-α-amino-n-butyric acid [D-IIb], the sign of the Cotton effects of bands I and II is reversed. The positive Cotton effects for (S)-IVa arise by the coupled oscillator mechanism,[16] and their sign is determined by the chirality of these oscillators. Since the polarizability of a carbon–hydrogen bond is negligible compared with that of a carbon–carbon bond,[22] only the carbon–carbon bond vicinal to the chromophoric group attachment bond need be considered as inducing dichroic absorption in the chromophore.

The dominant conformer for the generation of Cotton effects of (S)-IVa is 8, and the observed Cotton effects are positive

8

9
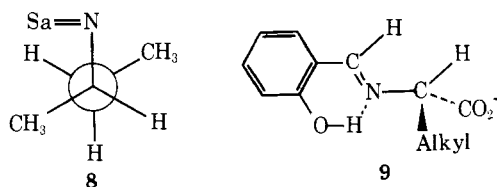
(Table IV). The rotatory contribution of any vicinal carbon–carbon bond in an aliphatic α-amino acid N-salicylidene derivative is overshadowed by the interaction of the carboxylate

group with the chromophore which is analogous to that in an α-arylalkylamine derivative.[5] For an N-salicylidene derivative of an L-α-amino acid, the most important conformer for dichroic absorption is **9**,[5] and the N-salicylidene derivatives of L-IIa–L-IIf display positive Cotton effects for bands I and II (Table II).

The longest wavelength absorption band of the carboxylate group occurs at about 210 nm, and its identity as n $\rightarrow$ π*[23] or π $\rightarrow$ π*[24] transition has been of some controversy. If it is an n $\rightarrow$ π* transition, the possibility of magnetic dipole–electric dipole coupling of the carboxylate group with the salicylidenimino chromophore cannot be eliminated. It is reasonable to assume, however, that electric dipole–dipole coupling is operative. The electric transition moments of the doubly degenerate π $\rightarrow$ π* transitions[25] of the carboxylate group at 210 nm, or at shorter wavelength if the 210 nm band is an n $\rightarrow$ π* transition, will form components along and perpendicular to the group's symmetry axis. The perpendicular component is deemed ineffective because of rotational averaging about the axis. Thus the sign for bands I and II in the CD spectrum of an aliphatic α-amino acid derivative can be predicted from the chirality of the carboxylate group attachment bond and the phenyl group–methine carbon bond in the salicylidenimino chromophore. The CD maximum near 230 nm (Table II), bathochromically shifted from the corresponding EA maximum (Figure 1), is interpreted as the long wavelength portion of the couplet resulting from exciton splitting, electric dipole–dipole or magnetic dipole–electric dipole coupling depending on the nature of the carboxylate transition, between band III of the chromophore and the carboxylate group transition since both occur near 215 nm.

A β-hydroxyl substituent on an aliphatic α-amino acid (L-IIg and L-IIh) derivative has little effect on its CD spectrum since the polarizability of a carbon–oxygen bond is smaller than that of a carbon–carbon bond.[22] A sulfur-containing substituent at this position, however, has a dramatic effect. The sign of band I in the spectrum of the L-S-methylcysteine (L-IIi) derivative is opposite to that in the L-alanine (L-IIa) derivative, and no CD maximum near 275 nm was detected. These changes are a consequence of the additional interaction of the salicylidenimino chromophore with the sulfide group which for band I overshadows that with the carboxylate group. A similar interaction in the L-methionine (L-IIj) derivative only partially compensates for the carboxylate contribution since the sulfide group is separated from the chromophore by an additional σ bond. In this derivative, the sign of band I is positive but substantially reduced in rotational strength, and a negative maximum near 275 nm is observed. The couplet structure for band II in the derivative of L-IIi confirms this interpretation. The longest wavelength transition for the sulfide group has been located at about 240 nm and is electric dipole forbidden but magnetic dipole allowed.[26] The absence of a couplet structure for band II in the L-IIj derivative is further evidence that the sulfide group–chromophore interaction has been weakened by the intervention of an additional σ bond.

We have also examined a solution of L-cysteine (L-IIk) with a slight excess of 2 equiv of **4**. No CD maximum associated with band I was detected and the remainder of the spectrum is somewhat difficult to interpret. Thus a thiolate group vicinal to the chromophore also overshadows the carboxylate group contribution.

The CD spectra of N-salicylidene derivatives of dicarboxylic α-amino acids formed by mixing L-aspartic acid (L-IIl) and L-glutamic acid (L-IIm) with a slight excess of 2 equiv of **4** illustrate the effect of two groups which strongly interact with the chromophore. For the L-IIl derivative the interaction of the vicinal carboxylate group will make a negative contribution to the CD of bands I and II whereas the contribution of the other carboxylate group will be positive. In the spectrum of this

derivative, band II is negative, indicating that at least for band II the β-carboxylate has the greater influence. In the L-IIm derivative the second carboxylate group is separated from the chromophore by an additional σ bond. No maximum associated with bands I and II was observed, and the interaction of this second carboxylate group is still substantial.

The CD spectrum of the L-asparagine (L-IIn) N-salicylidene derivative shows the influence of a β-amido substituent. The sign of band I is still positive, but its rotational strength is reduced and no 275-nm band is observed. The couplet at about 255 nm arises from interaction of the salicylidenimino chromophore with the bathochromically shifted n $\rightarrow$ π* transition[27] of the amide group.

α- and β-Aryl α-Amino Acids (Table II). In the CD spectra of N-salicylidene derivatives of α- and β-aryl α-amino acids (IIo–s) the sign of band I and band II is determined by the chirality of the interaction of the chromophore with the aryl group which overshadows that with the carboxylate group. Since conformer **10** is the most important for dichroic ab-

10   11
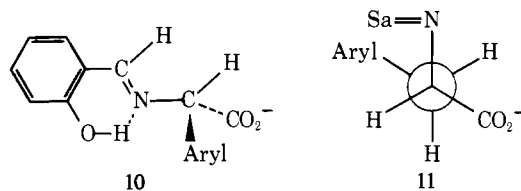
sorption, band I is negative in the CD spectrum of the Schiff base derivatives of L-phenylglycine (L-IIo) and L-(2-thienyl)-glycine[28] (L-IIs). In the spectrum of the L-IIo derivative, the band near 275 nm is negative as a result of interaction of the carboxylate group with the quinoid chromophore, while in the spectrum of the L-IIs derivative, a positive maximum at this wavelength is due to the overriding influence of the 2-thienyl group.

Conformer **11** is the most important contributor to the dichroic absorption of bands I and II of the derivatives of the β-aryl α-amino acids,[5] L-phenylalanine (L-IIp), L-tyrosine (L-IIq), L-histidine (L-IIr), and in their CD spectra bands I and II are negative. The dichroic absorption at about 275 nm assigned to the quinoid tautomer is also negative and thus combines with band II to form a broad negative maximum as in the L-IIq derivative. The fine structure from 256 to 272 nm in the spectrum of the L-IIp derivative is a combination of these two CD bands. The couplet observed for band II in the L-IIr derivative is a consequence of interaction of the salicylidenimino chromophore with a weak transition at about 256 nm of the imidazole group,[29] analogous to the pyrrole transition near 240 nm.[30]

Aliphatic α-Amino Esters (Table III). The CD spectrum of an N-salicylidene derivative of an aliphatic α-amino acid ester is typified by that of the methyl L-alaninate (L-IIIa) derivative in which maxima for bands I, II, and III are observed (Figure 2). The negative maximum near 260 nm is assigned to band II rather than to the quinoid tautomer since the maximum persists when the CD spectrum of the isolated methyl L-N-salicylideneleucinate (L-IVd) is observed in hexane (Table IV). The dominant interaction for generation of the Cotton effects for bands II and III in these derivatives and band I in the derivative of L-IIIa is interaction of the chromophore with the ester moiety. In the derivatives of L-IIIb–L-IIId the dichroic absorption associated with band I is too weak to observe due to a negative contribution of the alkyl substituent at the β carbon atom. Since the conformational preference of the ester group about its attachment bond is not well understood and a symmetry axis for the group is absent, no statement concerning the chirality of its interaction with the salicylidenimino chromophore can be made. The slight difference in transition moment directions for bands I and II of the chromophore,[5]

perhaps, produces opposite chirality with the ester group and consequently opposite signs for these two bands are observed.

β-Aryl α-Amino Esters (Table III). The signs of bands I and II for β-aryl α-amino ester (IIIe–g) derivatives are those predicted by the salicylidenimino chirality rule as applied to β-arylalkylamine derivatives, and these derivatives show negative maxima for bands I and II. The couplet for band II in the spectrum of the ethyl L-p-nitrophenylalaninate[31] (L-IIIf) derivative is a consequence of dipolar interaction between the transition moment of band II and that of a bathochromically shifted ^1L_a transition of the p-nitrophenyl group near 260 nm.[32] This spectrum as compared with that of the isolated ethyl L-N-salicylidene-p-nitrophenylalaninate (L-IVg) (Table IV) further shows that the derivative in situ is incompletely formed and the weak positive maximum at 282 nm is due to an ^1L_b transition of the free α-amino ester.[33] The absolute configuration of the parent α-amino ester, however, can be directly deduced by observation of the sign of bands I and II for the Schiff base derivative and application of the salicylidenimino chirality rule.

Experimental Section

Melting points were taken in open capillary tubes and are corrected. Boiling points are also corrected. Sodium D line rotations were obtained using a visual polarimeter and 1-dm or 2-dm tubes. Electronic absorption (EA) spectra were measured with a Cary Model 14 spectrophotometer using 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 equipped with a CD Model 6001 accessory. The slit was programmed for a spectral band width of 1.5 nm, and a 1-cm cell was used. Elemental analyses were done by Galbraith Laboratories, Inc., Knoxville, Tenn.

The isolated N-salicylidene and N-5-bromosalicylidene derivatives were prepared as previously reported.[8] Methyl L-N-salicylidene-leucinate (L-IVd) was prepared in methanol using methyl L-leucinate and an equivalent amount of salicylaldehyde. The solvent was removed at reduced pressure without heating.[9] Samples (3.5–13 μmol) of the isolated N-salicylidene derivatives were dissolved in 5 ml of methanol and hexane for CD measurements. Dilutions of these solutions (1:5, 1:10, and 1:25) were made as needed for observation of the reported CD maxima. For formation of the N-salicylidene derivatives in situ, amine hydrochloride, α-amino acid, and α-amino ester hydrochloride samples (10–15 μmol) were weighed into 5-ml volumetric flasks on a microgram balance. Sodium salicylaldehyde[17] (10–30% molar excess) and methanol were added, and the mixture was warmed 10–15 min with steam, cooled, and made up to 5 ml. Aliquots of these solutions were diluted for spectral measurements after 1–4 h from mixing. Dilutions (1:10 and 1:25) were required for observation of bands II and III with cut-off occurring at about 225 nm.

(S)-(−)-1-(2-Thienyl)-1-aminoethane Hydrochloride [(S)-Id]. A solution of (±)-1-(2-thienyl)-1-aminoethane (13.2 g, 0.104 mol), bp 94–97 °C (32 mm) [lit.[34] bp 83–84 °C (16 mm)], prepared by reductive amination of 2-acetylthiophene,[35] in methanol was added to a stirred solution of D-N-acetylleucine[19] (18.0 g, 0.104 mol) in methanol. The resulting salt (7.91 g) was recrystallized twice from methanol to constant specific rotation (3.90 g, 25%), $[\alpha]^{26}D \pm 0°$ (c 1.03, CH₃OH). Reworking of the mother liquors gave additional salt (4.54 g, 29%) of the same specific rotation. Decomposition of the salt gave the amine (1.93 g, 29%): bp 95–96 °C (30 mm); d^{20}_4 1.074; $[\alpha]^{26}D$ −4.9° (neat); $[\alpha]^{26}D$ −13° (c 5.00, CH₃OH) [lit.[18] $[\alpha]^{20}D$ −2.96° (neat)]. The hydrochloride [(S)-Id] had mp 194–195 °C dec and $[\alpha]^{24}D$ −14° (c 4.97, CH₃OH). (S)-N-Salicylidene-1-(2-thienyl)-1-aminoethane [(S)-IVe], recrystallized from methanol, had mp 78–79 °C and $[\alpha]^{26}D$ +155° (c 0.93, CH₃OH).

Anal. Calcd for C₁₃H₁₃NOS: C, 67.50; H, 5.67. Found: C, 67.38; H, 5.72.

(R)-(−)-1-(2-Thienyl)-2-aminopropane Hydrochloride [(R)-Ie]. A solution of L-N-acetylleucine[19] (41.0 g, 0.237 mol) in methanol (300 ml) was added dropwise to a stirred solution of (±)-1-(2-thienyl)-2-aminopropane (43.0 g, 0.304 mol), prepared by LiAlH₄ reduction of 1-(2-thienyl)-2-nitro-1-propene,[36] in methanol (300 ml). The mixture was evaporated to near dryness, isopropyl alcohol (50 ml) was

added, and the resulting crystalline salt (51.8 g) was collected and recrystallized from isopropyl alcohol yielding 25.3 g of salt, $[\alpha]^{25}D$ −15° (c 1.87, H₂O). Five additional recrystallizations from 95% ethanol were required to yield optically pure material (12.8 g, 27%), $[\alpha]^{25}D$ −21° (c 3.10, H₂O). Decomposition of the salt and treatment of the amine in ether with hydrogen chloride gave (R)-Ie: mp 147–148 °C; $[\alpha]^{25}D$ −11° (c 1.98, H₂O). (R)-N-(5-Bromosalicylidene)-1-(2-thienyl)-2-aminopropane [(R)-IVf], recrystallized from hexane, had mp 40–43 °C and $[\alpha]^{25}D$ −90° (c 1.32, CH₃OH).

α-Amino Acids and Esters. Except for D-(2-thienyl)glycine (D-α-amino-2-thienylacetic acid) (D-IIs) and ethyl D-p-nitrophenylalaninate hydrochloride (D-IIIf), the optically active α-amino acids and α-amino ester hydrochlorides were purchased [Mann Research Laboratories and ICN Pharmaceuticals, Inc. (NBCo)] and were used without further purification.

D-(2-Thienyl)glycine (D-IIs) was a gift from Dr. James W. McFarland, Pfizer Inc., and had $[\alpha]^{25}D$ −71° (c 1.00, H₂O) (lit.[37] $[\alpha]^{23}D$ −73.7° (1%, H₂O).

Ethyl D-p-nitrophenylalaninate hydrochloride (D-IIIf) was prepared in connection with other work[38] and had mp 197–199 °C dec and $[\alpha]^{25}D$ −12° (c 1.96, H₂O) [lit.[31] mp 204–205 °C, $[\alpha]^{20}D$ −12.0° (c 2.06, H₂O)]. Ethyl D-N-salicylidene-p-nitrophenylalanate (D-IVg), recrystallized from methanol, had mp 125–126 °C and $[\alpha]^{25}D$ +242° (c 0.281, CH₃OH).

Anal. Calcd for C₁₈H₁₈N₂O₅: C, 63.15; H, 5.30. Found: C, 62.48; H, 5.37.

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