oil was chromatographed on silica gel with benzene to give **18** (40 mg, 40%) and **19** (31 mg, 33%).

Registry No.—**1**, 69381-70-0; **2**, 60914-90-1; *cis*-**4a**, 69381-72-2; *trans*-**4a**, 69381-74-4; *cis*-**4b**, 69381-76-6; *trans*-**4b**, 69381-78-8; *trans*-**4c**, 69381-80-2; **5**, 69381-81-3; **10**, 261-31-4; **11**, 492-22-8; **15a**, 69381-82-4; **15b**, 69381-83-5; **15c**, 69381-84-6; **16**, 69381-70-0; **17**, 69381-85-7; **18**, 60914-90-1; **19**, 69381-86-8; **20**, 63076-58-4; **21**, 69381-87-9; 9-methoxy-9-methylthioxanthene, 69381-88-0; 2-chlorothioxanthene *N*-(*p*-toluenesulfonyl)sulfilimine, 69381-89-1; 2-chlorothioxanthene, 92-38-6; MSH, 36016-40-7; chloramine T, 127-65-1.

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(10) The Experimental Section of ref 9 should be corrected as follows: page 2994, column 1, line 8. "*cis*-**5**" should be *trans*-**5**. Line 18. "*trans*-**5**" should be *cis*-**5**. Line 37. "*cis*-**6**" should be *trans*-**6**. Column 2, line 4. "*trans*-**8**" should be *cis*-**8**. (A private communication from Professor A. L. Ternay, Jr.).
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(22) It should be noted here that *trans*-**6c** exchanged deuterium at C-9 upon treatment with potassium hydroxide in deuteriomethanol at room temperature. This implies the intervention of the carbanion **22** (R = *i*-C_3H_7) in the rearrangement of *trans*-**6c**.
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Optically Active Amines. 26.[1] Spectral Observations on Chiral Schiff Bases[2]

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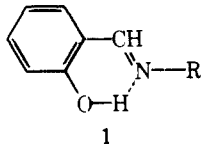
Received October 26, 1978

Examination of the isotropic electronic absorption (EA) and circular dichroism (CD) spectra of the Schiff base [*N*-benzylidene, *N*-(*o*-methoxybenzylidene), and *N*-salicylidene] derivatives of (*S*)-α-phenylethylamine, (*S*)-α-benzylethylamine, and 17β-amino-5α-androstan-3α-ol indicates that for the salicylidenimino chromophore, the lowest energy n → π* transition of the azomethine group occurs at about 275 nm. Although no absorption maximum can be observed in the EA spectrum for this transition, it gives rise to a moderately intense Cotton effect near 275 nm in the CD spectrum of the *N*-salicylidene derivatives of some amines. Since this Cotton effect occurs between those associated with absorption bands I and II at about 315 and 255 nm, respectively, and since it is generally opposite in sign to that of those associated with absorption bands I and II, its identification makes the application of the salicylidenimino chirality rule less ambiguous for the deduction of the absolute configuration of chiral primary amines.

The isotropic electronic absorption (EA) spectra of the *N*-salicylidene derivatives of chiral primary amines in hexane exhibit characteristic absorption bands at about 315 (log ϵ_{max} 3.68–3.73), 255 (4.12–4.21), and 215 nm (4.36–4.49), designated as bands I, II, and III, respectively,[4] which are assigned to transitions of the intramolecularly hydrogen-bonded salicylidenimino chromophore (**1**).[5] In polar solvents such as dioxane, ethanol, and methanol, a broad band at about 400 nm (log ϵ_{max} 1.32–1.89 in dioxane[6] and 3.06–3.38 in methanol[4] and ethanol[6]) and a shoulder near 280 nm (log ϵ_{max} 3.49–3.67 in ethanol[6]) become evident, and the other three bands show a slight decrease in intensity.[4,6] The two additional bands are attributed to the presence of a quinoid tautomer (**2**) in the polar solvents.[5] The corresponding circular dichroism (CD) spectra usually show for bands I and II corresponding Cotton effects of the same sign which can be correlated with the absolute configuration of the amine moiety by application of the salicylidenimino chirality rule.[4,7-11]



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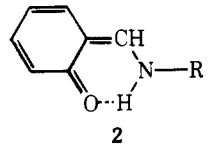

2

In the course of these CD studies, we have noted the occasional appearance of an additional CD maximum, opposite in sign to that of bands I and II and centered at about 275 nm (cf. Figure 1 in ref 7). In the past, this band has been assigned to a transition of an aryl group of the amine moiety[7] or to the quinoid tautomer[4,9,11] or it has been unassigned.[10,11] Cotton effects near 280 and 400 nm can be assigned to the quinoid tautomer since these disappear using hexane as the solvent, but there are a few *N*-salicylidene derivatives for which the CD maximum near 275 nm persists in hexane and in which the chiral amine does not have a transition in the 275-nm region, notably the *N*-salicylidene derivatives of 1-alkyl-2-propynyl-

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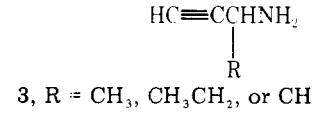
Table I. Spectral Data for the Schiff Bases of (*S*)-α-Phenylethylamine

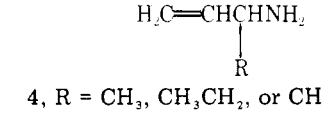
compd	registry no.	solvent	band assignment[a]	EA max, λ, nm (ε[b])	CD max, λ, nm ([θ][c])
N-benzylidene [(*S*)-**7a**]	69350-13-6	hexane	I	287 (1000)	289 (−2300)
				277 (1400)	281 (−2100)
					276 (−400)[d]
			^1L_b		268 (+7500)
					261 (+2700)[d]
			II	255 (15 000)[d]	255 (+46 000)[d]
				247 (22 000)	245 (+74 000)
				240 (19 000)[d]	
			^1L_a	210 (27 000)[d]	213 (−100 000)
			III	205 (35 000)	
		MeOH	I	287 (1100)[d,e]	288 (−2900)[d]
				278 (1900)[d]	281 (−4300)
					277 (−4000)
			II	249 (21 000)	248 (+60 000)
				240 (17 000)[d]	
			^1L_a		213 (−110 000)
N-(*o*-methoxybenzylidene) [(*S*)-**7b**]	69292-05-3	hexane	I	*f*	314 (−9000)
					305 (−9600)[d]
					303 (−11 000)
			^1L_b		268 (+12 000)[d]
					261 (+31 000)[d]
			II		252 (+40 000)
			^1L_a and III		221 (+52 000)
		MeOH	I	304 (6300)[e]	310 (−7300)
			n → π*		280–295 (−5100)[d]
			^1L_b		268 (+11 000)[d]
					260 (+28 000)[d]
			II	251 (16 000)	253 (+37 000)
			^1L_a and III	209 (31 000)	225 (+43 000)
N-salicylidene [(*S*)-**7c**]	69350-14-7	hexane	I	320 (5000)[g]	319 (+40 000)[g,h]
			n → π*		274 (−4000)
			II	262 (13 000)[d]	253 (+58 000)
				255 (15 000)	
		MeOH	quinoid	403 (730)[i]	397 (+1700)[i]
			I	315 (4000)	316 (+16 000)
			quinoid	283 (2400)[d]	
			n → π*		275 (−2300)
			II	255 (14 000)	252 (+33 000)
			III	215 (28 000)	222 (−41 000)

[a] Bands designated I, II, III, and n → π* are associated with the benzylidenimino or substituted benzylidenimino moiety; bands designated ^1L_b and ^1L_a are associated with the phenyl group of the parent amine. [b] Molar absorptivity. [c] Molecular ellipticity with *c* 2.65×10^{-4} to 2.65×10^{-2} g/100 mL. [d] Shoulder. [e] For this spectrum absolute ethanol was the solvent. [f] Not measured. [g] Data for this spectrum from ref 15. [h] For this spectrum isooctane was the solvent. [i] Data for this spectrum from ref 7.

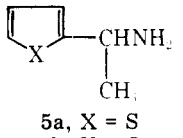
(**3**) and 1-alkyl-2-propenylamines (**4**),[10] α-(2-thienyl)-[11] (**5a**) and α-(2-furanyl)ethylamine[12] (**5b**), and 1-(2-thienyl)-2-aminopropane[11] (**6**). Therefore this CD maximum must



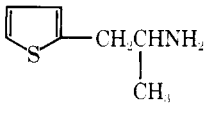
3, R = CH_3, CH_3CH_2, or $CH_3CH_2CH_2$



4, R = CH_3, CH_3CH_2, or $CH_3CH_2CH_2$



5a, X = S
b, X = O



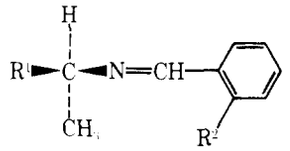
6

originate from the salicylidenimino chromophore, and its sign and intensity in some compounds are such as to make the application of the salicylidenimino chirality rule sometimes ambiguous.[9]

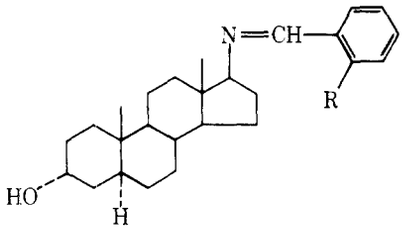
We have now investigated the origin of the 275-nm band using the EA and CD spectra of the Schiff base [*N*-benzylidene, *N*-(*o*-methoxybenzylidene), and *N*-salicylidene] derivatives of (*S*)-α-phenylethylamine [(*S*)-**7**], (*S*)-α-benzylethylamine [(*S*)-**8**], and 17β-amino-5α-androstan-3α-ol (**9**), and we now assign the CD maximum near 275 nm in the *N*-salicylidene derivatives to the n → π* transition of the azomethine group.

Results and Discussion

(*S*)-α-Phenylethylamine Derivatives (Table I). The EA spectrum of (*S*)-*N*-benzylidene-α-phenylethylamine [(*S*)-**7a**] can be understood in terms of the combined contributions of the phenyl and benzylidenimino chromophores. The maxima at 287 and 277, 247, and 205 nm in hexane, designated as bands I, II, and III, respectively, are due to transitions of the benzylidenimino group,[13] while the shoulder at 210 nm is that of the ^1L_a transition of the phenyl group.[14] The phenyl ^1L_b transition cannot be discerned in the EA spectrum but can be clearly seen at 268 and 261 nm in the CD spectrum. The 247-nm band can be regarded as a red-shifted ^1L_a transition of the benzylidenimino group or a charge-transfer transition from the benzene ring to the carbon–nitrogen double bond.[13]

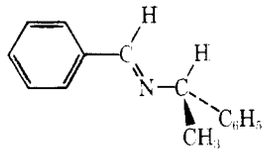


(*S*)-**7a**, $R^1 = C_6H_5$; $R^2 = H$
b, $R^1 = C_6H_5$; $R^2 = OCH_3$
c, $R^1 = C_6H_5$; $R^2 = OH$
(*S*)-**8a**, $R^1 = C_6H_5CH_2$; $R^2 = H$
b, $R^1 = C_6H_5CH_2$; $R^2 = OCH_3$
c, $R^1 = C_6H_5CH_2$; $R^2 = OH$



9a, R = H
b, R = OH

Either interpretation gives a transition moment lying roughly along the benzene ring–methine carbon bond which in the preferred conformation for (*S*)-**7a** (**10**) has a positive chirality



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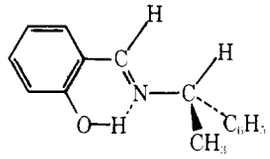

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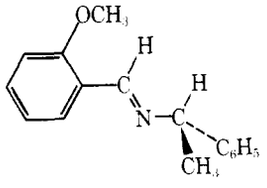
with the phenyl group attachment bond.[7] Thus the interaction of this benzylidenimino group transition with the ^1L_a and ^1B_a transitions of the phenyl group gives the observed positive Cotton effect at about 247 nm. The 277- and 287-nm EA maxima can be regarded as the ^1L_b transition of the benzylidenimino group whose polarization should be roughly perpendicular to the benzene ring–methine carbon bond. This is supported by the corresponding negative CD maxima, indicating a polarization different from that of the 247-nm band. The strong negative CD maximum at 213 nm is that of the ^1L_a transition of the phenyl group at 210 nm which exciton splits with the 205-nm transition of the benzylidenimino group. According to exciton theory, if two interacting transition moments have positive chirality when the dipole interaction is positive, the longer wavelength transition should exhibit a positive Cotton effect.[7] Since the benzene ring–methine carbon bond in the benzylidenimino chromophore has a positive chirality with the phenyl group attachment bond in **10**, the 205-nm transition moment cannot be along the benzene ring–methine carbon bond. Consequently, the 205-nm band is identified as the ^1B_b rather than the ^1L_a transition of the chromophore. This conclusion is reasonable since conjugation of the azomethine group with the benzene ring is expected to lower its transition energies. No clear evidence is found in the spectra of (*S*)-**7a** for the existence of an n → π* transition of the benzylidenimino group, although, in the CD spectrum, there is a slight indication of such a transition at about 310 nm, buried under the 287-nm band.

In (*S*)-*N*-(*o*-methoxybenzylidene)-α-phenylethylamine [(*S*)-**7b**], the methoxyl group substitution has bathochromically shifted bands I, II, and III to 304, 251, and 209 nm, respectively, in ethanol with the corresponding CD maxima appearing at 310, 253, and 225 nm in methanol. The 225-nm CD maximum is clearly the result of exciton splitting of the 209-nm EA band consisting of transitions from both the *o*-methoxybenzylidenimino and the phenyl groups. The positive Cotton effect for band II at about 253 nm, the same sign as that for band II in (*S*)-**7a**, indicates that the transition moment for band II in (*S*)-**7b** is still approximately along the benzene ring–methine carbon bond in the *o*-methoxybenzylidenimino group despite the presence of the ortho substituent. Since the sign of band I is the same for both (*S*)-**7a** and (*S*)-**7b**, while that of band III is different, the ortho methoxyl substituent, must affect the transition moment directions of bands I and III differently.

The interesting feature of the CD spectrum of (*S*)-**7b** in methanol is the appearance of a broad shoulder from 280 to 295 nm which is not evident in the CD spectrum of (*S*)-**7b** in hexane. This band is assigned as the n → π* transition of the azomethine group. In hexane solution it is partially submerged under band I, but it is hypsochromically shifted in methanol away from band I as the result of hydrogen bonding.

In (*S*)-*N*-salicylidene-α-phenylethylamine [(*S*)-**7c**], the ortho hydroxyl substituent makes possible an intramolecular hydrogen bond (**11**) and further complicates the matter by allowing the formation of a quinoid tautomer (**2**) in polar solvents. Thus in methanol the EA spectrum of (*S*)-**7c** exhibits a band at 403 nm and a shoulder at 283 nm in addition to the characteristic bands I, II, and III which are further bathochromically shifted from their respective positions in the spectrum of the *o*-methoxyl derivative. The additional bands at 403 and 283 nm are assigned to quinoid tautomer transitions.[5] The sign of CD band II is the same as that for the *N*-benzylidene and *N*-(*o*-methoxybenzylidene) derivatives and again indicates that the transition moment for band II is approximately along the benzene ring–methine carbon bond of the chromophore. An identical sign for the CD maxima of bands I and II in the spectrum of (*S*)-**7c** also suggests that the transition moment for band I is roughly parallel to the benzene ring–methine carbon bond, this orientation for the transition moments of bands I and II being the basis of the salicylidenimino chirality rule.[7] The CD maxima at 222 nm is again a consequence of exciton interaction of the 214-nm transition of the salicylidenimino group with the ^1L_a transition of the phenyl group near 210 nm. The sign difference between the *N*-salicylidene [(*S*)-**7c**] and *N*-(*o*-methoxybenzylidene) [(*S*)-**7b**] derivatives for band III may reflect a difference in transition moment direction resulting from different conformations of the benzene group about its attachment bond. In (*S*)-**7c** the hydroxyl substituent is syn (**11**) to the carbon–nitrogen double bond while in (*S*)-**7b** it may be anti as in **12**.



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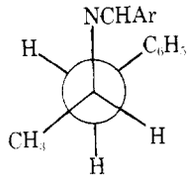

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In the CD spectrum of (*S*)-**7c** in methanol the CD maximum at 397 nm is due to the quinoid tautomer but that at 275 nm cannot be so assigned since it persists in hexane. Furthermore this 275-nm maximum cannot be assigned to the ^1L_b transition of the phenyl chromophore since this transition has CD maxima at 261 and 268 nm in (*S*)-**7a** and (*S*)-**7b**. Thus the 275-nm maximum in (*S*)-**7c** is assigned to the azomethine n → π* transition which as the result of intramolecular hydrogen bonding is hypsochromically shifted to 275 nm from 280–295 nm in (*S*)-**7b**. The moderately strong Cotton effect for the transition may originate from dynamic coupling of its magnetic transition moment with the electric transition moments for the phenyl group.

Table II. Spectral Data for the Schiff Bases of (*S*)-α-Benzylethylamine

compd	registry no.	solvent	band assignment[a]	EA max, λ, nm (ε[b])	CD max, λ, nm ([θ][c])
N-benzylidene[d] [(*S*)-**8a**]	69350-15-8	hexane	I	287 (950)	292 (+760)
					284 (+1100)
				277 (1300)	276 (+1600)
			II	255 (13 000)[e]	
				248 (19 000)	246 (+81 000)
				241 (18 000)[e]	
			^1L_a	210 (24 000)[e]	213 (−65 000)
		MeOH	I	287 (1100)[e]	291 (+1900)[e]
					284 (+2600)[e]
				277 (1900)[e]	277 (+4000)[e]
			II	247 (18 000)	247 (+77 000)
			^1L_a		213 (−52 000)
N-(*o*-methoxybenzylidene)[d] [(*S*)-**8b**]	69350-16-9	hexane	I	313 (5000)	
				302 (6500)	295 (−2000)
				293 (4700)[e]	
			II	258 (11 000)[e]	258 (+28 000)[e]
				251 (17 000)	251 (+44 000)
				246 (16 000)	247 (+40 000)[e]
			^1L_a and III	208 (31 000)	223 (+43 000)
		MeOH	I	305 (5600)[f]	308 (−1600)
			II	252 (16 000)	252 (+46 000)
			^1L_a and III	210 (28 000)	223 (+42 000)
N-salicylidene [(*S*)-**8c**]	3082-83-5	hexane	I	318 (4700)[g]	317 (+24 000)[g,h]
			II	262 (13 000)[e]	253 (+30 000)
				255 (14 000)	
		95% EtOH	quinoid	402 (1000)[g]	399 (+2000)[f,g]
			I	315 (3800)	312 (+15 000)
			quinoid	280 (2800)[e]	
			II	253 (12 000)	251 (+39 000)

[a] Bands designated I, II, III, and n → π* are associated with the benzylidenimino or substituted benzylidenimino moiety; bands designated ^1L_b and ^1L_a are associated with the phenyl group of the parent amine. [b] Molar absorptivity. [c] Molecular ellipticity with *c* 2.58×10^{-4} to 5.48×10^{-2} g/100 mL. [d] Enantiomer used. [e] Shoulder. [f] For this spectrum absolute ethanol was the solvent. [g] Data for this spectrum from ref 15. [h] For this spectrum isooctane was the solvent.

(*S*)-α-Benzylethylamine Derivatives. (Table II). A similar spectral analysis of the EA and CD spectra of the Schiff bases of (*S*)-α-benzylethylamine [(*S*)-**8**] results in band assignments as shown in Table II. No indication of the n → π* transition of the azomethine group was found. Introduction of the methylene group between the phenyl group and the chiral center results in a larger separation of the phenyl group and Schiff base chromophores as well as additional conformational mobility and reduces the impact of their dynamic coupling. The sign of the CD maxima associated with band II for the three derivatives and that of band I for the *N*-salicylidene derivative [(*S*)-**8c**] is the same as the chirality between the benzene ring–methine carbon bond of the Schiff base chromophore and the phenyl group attachment bond in the most rotationally significant conformation (**13**).[7]

17β-Amino-5α-androstan-3α-ol Derivatives (Table III). In the CD spectrum of 17β-salicylidenimino-5α-androstan-3α-ol (**9b**) in hexane, a 273-nm maximum is clearly evident although no pertubing phenyl chromophore is present in the amine moiety. The rigidity and large dissymetry of the five-membered ring may contribute to the appearance of this band which is assigned to the n → π* transition of the azomethine group. Band II of both **9a** and **9b** as well as band I of **9b** again have the same sign in agreement with the conclusion that their transition moments are roughly parallel to the benzene ring–methine carbon bond of the Schiff base group.

Other Chiral Amine Derivatives. Similar to (*S*)-*N*-salicylidene-α-phenylethylamine [(*S*)-**7c**], the *N*-salicylidene derivatives of other chiral α-phenylalkylamines show a Cotton effect near 275 nm[15] of opposite sign to that of bands I and II. Earlier this Cotton effect was attributed to the ^1L_b transition of the phenyl group but is now reassigned to the n → π* transition of the azomethine group. For *N*-salicylidene derivatives containing aromatic groups with transitions near 275 nm in the amine moiety, the 275-nm CD maximum may conceivably be due to the aromatic group. This is definitely the case for (*S*)-α-(1-naphthyl)ethylamine[15] in which the strong negative Cotton effect at 285 nm is due to the ^1L_a transition of the naphthalene group. The same is true for (*S*)-*N*-salicylidene-1-aminoindan in which a strong negative CD maximum is observed at 271 nm[16] whose magnitude ([θ] −24 000) and wavelength position suggest it is mainly due to the relatively strong ^1L_b transition of the indanyl group with partial contribution from the azomethine n → π* transition. The negative Cotton effect at 274 nm in the spectrum of (*S*)-*N*-(5-bromosalicylidene)-α-(4-pyridyl)ethylamine,[17] however, is more likely due to the n → π* transition of the azomethine group. For the *N*-salicylidene derivatives of α-(2-thienyl)-[11] (**5a**) and α-(2-furanyl)ethylamine[12] (**5b**) and 1-(2-thienyl)-2-aminopropane[11] (**6**), the Cotton effect at about 275 nm results from dynamic coupling of the azomethine n → π* transition with the strong electrically allowed transition of the thienyl and furanyl chromophores at about 225 nm.[18]

The moderately strong Cotton effects between 267 and 272 nm for the *N*-salicylidene derivatives of 1-alkyl-2-propynyl- (**3**) and 1-alkyl-2-propenylamines (**4**)[10] arise by dynamic coupling of the azomethine n → π* transition with the π → π* transition of the acetylene or ethylene group below 200 nm.[19]

Finally, the CD spectra of the *N*-salicylidene derivatives of the sodium salts of L-α-amino acids in methanol usually show strong negative CD maxima at about 275 nm between the positive maxima of bands I and II.[11] This band was as-

Table III. Spectral Data for the Schiff Bases of 17β-Amino-5α-androstan-3α-ol

compd	registry no.	solvent	band assignment	EA max, λ, nm (ε[a])	CD max, λ, nm ([θ][b])
N-benzylidene (**9a**)	69292-06-4	hexane	I	287 (1100)	288 (−5600)
					282 (−6200)
				277 (1600)	275 (−4700)[c]
			II	258 (14 000)[c]	
				247 (22 000)	247 (+61 000)
			III	211 (21 000)[c]	214 (−14 000)
		MeOH			293 (+550)[d]
			I	287 (1400)[c]	
				278 (2400)[c]	277 (−1600)
			II	249 (21 000)	247 (+55 000)
			III	212 (18 000)[c]	214 (−28 000)
N-salicylidene (**9b**)	69350-17-0	hexane	I	319 (5100)	316 (+16 000)
			n → π*		273 (−4800)
			II	263 (13 000)[c]	
				258 (15 000)	253 (+25 000)
			III	222 (23 000)[c]	
				217 (25 000)	
		MeOH	quinoid	401 (2400)	402 (+6500)
			I	315 (3600)	315 (+13 000)
			quinoid	278 (5800)[c]	
			n → π*		275 (−3300)
			II	262 (12 000)[c]	
				257 (13 000)	254 (+21 000)
			III	222 (23 000)[c]	226 (−17 000)
				218 (24 000)	

[a] Molar absorptivity. [b] Molecular ellipticity with c 9.08×10^{-4} to 9.08×10^{-2} g/100 mL. [c] Shoulder. [d] Taken to be the start of the Cotton effect centered at 247 nm.

signed to the quinoid tautomer although CD measurements were not made in other solvents. The CD maximum, however, is probably due to the n → π* transition of the azomethine group strongly coupled to the electrically allowed π → π* transitions of the carboxylate group below 210 nm.[20]

Experimental Section

Boiling points are corrected. Melting points were taken in open capillary tubes and are also corrected. Optical rotations were measured at the sodium D line using a visual polarimeter and a 1-dm sample tube. Isotropic electronic absorption (EA) spectra were obtained with a Cary Model 14 spectrophotometer using the normal variable slit and matched 1-cm cells. Circular dichroism (CD) spectra were measured with a Cary Model 60 spectropolarimeter with a CD Model 6001 accessory at 25–28 °C using a 1-cm cell. The slit was programmed for a spectral band width of 1.5 nm, and cut-off was indicated when the dynode voltage reached 400 V. The Schiff base derivatives were prepared as previously reported,[21] and the elemental analyses were done by Galbraith Laboratories, Inc., Knoxville, Tenn.

(*S*)-*N*-Benzylidene-α-phenylethylamine [(*S*)-7a]: bp 124–128 °C (1.0 mm); n^{28}_D 1.5839, and $[\alpha]^{25}_D$ +71° (c 1.21, absolute C_2H_5OH) [lit.[21] $[\alpha]^{22}_D$ −76° (c 1.3, absolute C_2H_5OH) for (*R*)-**7a**].

(*S*)-*N*-(*o*-Methoxybenzylidene)-α-phenylethylamine [(*S*)-7b]: bp 140–143 °C (0.25 mm); n^{28}_D 1.5884, and $[\alpha]^{25}_D$ −17° (c 1.04, absolute C_2H_5OH) [lit.[21] $[\alpha]^{26}_D$ +20° (c 1.0, absolute C_2H_5OH) for (*R*)-**7b**].

(*S*)-*N*-Benzylidene-α-benzylethylamine [(*S*)-8a]: bp 121–122 °C (0.6 mm); n^{28}_D 1.5705, and $[\alpha]^{25}_D$ −261° (c 1.23, absolute C_2H_5OH) [lit.[21] $[\alpha]^{20}_D$ +255° (c 1.2, absolute C_2H_5OH) for (*S*)-**8a**].

(*S*)-*N*-(*o*-Methoxybenzylidene)-α-benzylethylamine [(*S*)-8b]: bp 131–135 °C (1.0 mm); n^{28}_D 1.5749, and $[\alpha]^{25}_D$ −166° (c 1.22, absolute C_2H_5OH) [lit.[21] $[\alpha]^{24}_D$ +171° (c 1.2, absolute C_2H_5OH) for (*S*)-**8b**].

17β-Amino-5α-androstan-3α-ol. A mixture of 5α-androstan-3α-ol-17-one (2.9 g, 10 mmol), aluminum turnings (1.5 g), mercuric chloride (0.5 g), hydrazine hydrate (1.3 g), ethanol (75 mL), and water (7.5 mL) was boiled with stirring for 2 h.[22] More hydrazine hydrate (1.3 g) and water (2.5 mL) were added, and boiling was continued for 2.5 h. The mixture was evaporated at reduced pressure to a paste and then was made strongly basic by the addition of ice and solid potassium hydroxide. The resulting mixture was extracted with ether. The ether solution was washed with water and saturated aqueous sodium chloride and was dried (Na_2SO_4). Evaporation of the ether gave crude amine (2.8 g), mp 181–185 °C. The amine was converted to the hydrochloride salt with concentrated hydrochloric acid in ethanol. This salt was washed with ether and then was mixed with ethanol (15 mL). This mixture was made basic with solid potassium hydroxide, was diluted with water (100 mL), and finally was extracted with ether. The ether extracts were washed with water, dried (Na_2SO_4), and evaporated. Sublimation of the residue at 140 °C (0.03 mm) gave the pure amine (1.7 g, 59%): mp 188–190 °C (lit.[23] mp 187–188 °C); $[\alpha]^{25}_D$ +17° (c 1.1, $CHCl_3$); $[\alpha]^{25}_D$ +30° (c 1.1, CH_3OH).

Treatment of a sample of the amine with acetic anhydride in pyridine gave 17β-acetamido-3α-acetoxy-5α-androstane (58%), recrystallized from benzene–cyclohexane: mp 250–253 °C; $[\alpha]^{25}_D$ −27° (c 1.5, CH_3OH).

Anal. Calcd for $C_{23}H_{37}NO_3$: C, 73.56; H, 9.93; N, 3.73. Found: C, 73.36; H, 9.73; N, 3.75.

Evaporation of a solution of a sample of the amine in dry acetone gave *N*-isopropyliden-17β-amino-5α-androstan-3α-ol (92%), recrystallized from acetone and then cyclohexane: mp 195 °C dec; $[\alpha]^{25}_D$ +11° (c 1.0, $CHCl_3$).

Anal. Calcd for $C_{22}H_{37}NO$: C, 79.70; H, 11.25; N, 4.23. Found: C, 80.14; H, 11.34; N, 4.23.

***N*-Benzyliden-17β-amino-5α-androstan-3α-ol (9a)** was formed in benzene and was recrystallized from absolute ethanol as white platelets (89%), mp 191–192 °C.

Anal. Calcd for $C_{26}H_{37}NO$: C, 82.27; H, 9.83; N, 3.69. Found: C, 82.70; 82.65; H, 9.80; 9.88; N, 3.68, 3.74.

***N*-Salicyliden-17β-amino-5α-androstan-3α-ol (9b)** was formed in absolute ethanol and was recrystallized from methanol as yellow platelets (73%), mp 195–196 °C. The analytical sample was obtained by sublimation at 145 °C (0.04 mm): mp 195–196 °C; $[\alpha]^{25}_D$ +119° (c 1.0, $CHCl_3$).

Anal. Calcd for $C_{26}H_{37}NO_2$: C, 78.94; H, 9.43; N, 3.54. Found: C, 79.01; H, 9.36; N, 4.34.

Acknowledgment. We thank the National Science Foundation for generous grants (CHE77-04608 and CHE77-24293) supporting this work.

Registry No.—17β-Amino-5a-androstan-3a-ol, 69350-18-1; 5a-androstan-3a-ol-17-one, 53-41-8; 17β-acetamide-3a-acetoxy-5a-

androstane, 69292-07-5; *N*-isopropyliden-17β-amino-5a-androstan-3a-ol, 69309-42-8; acetone, 67-64-1.

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Neighboring Group Interaction in Ortho-Substituted Heterocycles. 2. 1,2,4-Oxadiazolylpyridines and Pyrido[2,3-*d*]pyrimidine 3-Oxides[1]

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Received November 2, 1978

Various synthetic methods have been elaborated to prepare pyrido[2,3-*d*]pyrimidines and their 3-oxides from *o*-aminocyanopyridine. Conversion of these 3-oxides into 1,2,4-oxadiazolylpyridines, *s*-triazolo[1,5-*a*]pyridines, and pyrazolo[3,4-*b*]pyridines as well as other transformations are described.

In our previous report[2] neighboring group interactions in ortho-substituted aminopyridines were described. Among other reactions, the preparation of pyrido[2,3-*d*]pyrimidines via intermediate 1,3,4-oxadiazolypyridines was investigated. This paper deals mainly with a study of interconversions of pyrido[2,3-*d*]pyrimidine 3-oxides and 1,2,4-oxadiazolyl-3-pyridines.

As staring material 2-amino-3-cyanopyridine (**1**) was used. With an ethanolic solution of hydroxylamine it was transformed into the amidoxime (**2**, R = H). Attempted cyclization of this compound in poly(phosphoric acid) failed and 2,3-diaminopyridine was formed. However, the amidoxime (**2**, R = H) could be acetylated and the product (**2**, R = COMe), when heated in water, was transformed into a compound analyzing for $C_8H_8N_4O$. Since from its IR spectrum the absence of a carbonyl group was evident, the compound could have either structure **3** (R = Me; R_1 = H) or structure **18**. On the basis of the NMR spectrum a differentiation between these structures is not possible. Based on further chemical transformations and in particular on the X-ray analysis[3] the structure of this compound as 2-amino-3-(5′-methyl-1′,2′,4′-oxadiazolyl-3′)pyridine (**3**, R = Me; R_1 = H) was unequivocally established. The compound is transformed back into the amidoxime **2** (R = H) in hot aqueous sodium hydroxide solution. It is known that the stability of 1,2,4-oxadiazoles varies with the number of substituents. Whereas disubstituted compounds are thermally stable and do not hydrolyze, the monosubstituted derivatives readily undergo hydrolysis by ring opening.[4-6]

The same oxadiazolylpyridine **3** (R = Me; R_1 = H) could be prepared also by hydrolysis of the formyl drivative **3** (R = Me; R_1 = CHO), obtained by treatment of 4-aminopyrido[2,3-*d*]pyrimidine 3-oxide (**4**, R = H) with acetic anhydride. This transformation parallels the ring opening of adenine 1-oxide which proceeds through the *O*-acetyl derivative which subsequently undergoes ring opening and recyclization into a oxadiazole derivative.[7] Finally, if the amidoxime **2** (R = H) was heated with triethyl orthoformate, compound **3** (R = R_1 = H) was obtained as byproduct (1%) together with **4** (R = H) as the main product (89%). Since one may postulate that the *N*-oxide (**4**, R = H) in this reaction may be formed from **3** (R = R_1 = H) in a thermal reaction, we have performed a separate experiment and established that this conversion does not occur under the conditions of the above reaction. Since other amidoximes react readily with triethyl orthoformate to give 1,2,4-oxadiazoles,[8] we anticipate that the *o*-amino group of **2** (R = H) must play an important role in this transformation. Evidently, this *o*-amino group participates more readily in ring closure than the amino group from the amidoxime function. The reverse transformation, i.e., **3** into **4**, was never observed during our experiments.

4-Aminopyrido[2,3-*d*]pyrimidine 3-oxide (**4**, R = H) could be prepared by two additional methods. In one of them, compound **1** was treated with *N*,*N*-dimethylformamide dimethyl acetal to give **5**, which upon treatment with methanolic hydroxylamine hydrochloride at room temperature gives the bicyclic structure **4** (R = H) in reasonable yield. According to the second procedure, compound **5** was first transformed into **6** with free hydroxylamine in methanol at room temperature and cyclization to **4** (R = H) may then be accomplished either in the presence of poly(phosphoric acid) or thermally. In the last case, also a small amount of **8** (R = R_1 = H) could be isolated and identified. The bicyclic compound **4** (R = H) is decomposed in hot dilute hydrochloric acid into the amidoxime **2** (R = H) which was also obtained in admixture with **1** after treatment with hot aqueous sodium hydroxide solution.

0022-3263/79/1944-1695$01.00/0