U-shaped glass column (2.5 mm × 2 m) was packed with 3% OV-101 on Gas-Chrom Q.

Nitrogen was used as carrier gas at a flow rate of 45 ml/min. Column temperature was kept constant at 210°.

***N*-*tert*-Butyloxycarbonyl-N^{β}-*p*-methoxybenzyl-L-asparagine Benzyl Ester [Boc-Asn(pmb)-OBzl].** This compound was prepared similarly to the Dmb analogue in 64% yield: mp 105–106° (from ethyl acetate); R_f(A) 0.74, R_f(B) 0.62.

Anal. Calcd for $C_{24}H_{30}N_2O_6$: C, 65.14; H, 6.83; N, 6.33. Found: C, 65.19; H, 6.87; N, 6.42.

***N*-*tert*-Butyloxycarbonyl-N^{β}-*p*-methoxybenzyl-L-asparagine [Boc-Asn(pmb)-OH].** Boc-Asn(pmb)-OBzl (2.21 g, 5 mmol) was hydrogenated in ethanol (50 ml) over 10% palladium on charcoal (0.6 g) for 10 h. The catalyst was then filtered off and the solvent evaporated. Crystallization from ethyl acetate gave the product (1.41 g, 80%): mp 132–133°; R_f(C) 0.71, R_f(B) 0.63; $[\alpha]^{20}D$ +9.92° (*c* 1.0, methanol).

Anal. Calcd for $C_{17}H_{24}N_2O_6$: C, 57.94; H, 6.86; N, 7.95. Found: C, 57.87; H, 6.84; N, 7.91.

***N*-*tert*-Butyloxycarbonyl-N^{γ}-*p*-methoxybenzyl-L-glutamine Benzyl Ester [Boc-Gln(pmb)-OBzl].** This compound was prepared similarly to the Dmb analogue in 88% yield: mp 108–109° (from ethyl acetate); R_f(A) 0.80, R_f(B) 0.59.

Anal. Calcd for $C_{25}H_{32}N_2O_6$: C, 65.77; H, 7.06; N, 6.13. Found: C, 65.64; H, 7.10; N, 6.12.

***N*-*tert*-Butyloxycarbonyl-N^{γ}-*p*-methoxybenzyl-L-glutamine [Boc-Gln(pmb)-OH].** This compound was prepared similarly to the asparagine analogue in 94% yield: mp 97–98° (from ethyl acetate); R_f(C) 0.80, R_f(B) 0.72; $[\alpha]^{20}D$ −2.66° (*c* 1.0, methanol).

Anal. Calcd for $C_{18}H_{26}N_2O_6$: C, 59.00; H, 7.15; N, 7.64. Found: C, 59.06; H, 7.13; N, 7.68.

Action of 1 N HCl–Acetic Acid. The protected amides (0.1 mmol) were placed in test tubes and treated with 1 N HCl in CH_3COOH (1.5 ml). The tubes were stoppered and kept in a desiccator and the reaction was allowed to proceed for the required time at 25°. Then the reagent was evaporated under nitrogen and the residue was dissolved in 1 N HCl (100 ml).

Action of 50% Trifluoroacetic Acid–Methylene Chloride and Trifluoroacetic Acid. The protected amides (0.1 mmol) were placed in test tubes and treated with 50% trifluoroacetic acid in methylene chloride (v/v) or trifluoroacetic acid (2 ml) in the presence of anisole (0.2 ml) for the desired time at 25°. After the evaporation under nitrogen of the reagent the residue was quantitatively transferred to a 25-ml funnel with 1 N HCl and extracted twice with ether (5 ml each). The solution was diluted with 1 N HCl to a constant volume (100 ml).

Action of Hydrofluoric Acid. The protected amides (0.1 mmol) were treated with HF and anisole[7] for 1 h at 0°. The HF was then evaporated under nitrogen within 1 h and the residue was quantitatively transferred to a 25-ml funnel with 1 N HCl (10 ml). The solution was extracted twice with ether (5 ml) and then brought to 100 ml with 1 N HCl.

Densitometry. The spots were scanned at 490 nm and the areas under the densitometric curve were measured by the relationship area = peak height × width at half height. By reading from standard graphs for glycine amide, L-asparagine, and L-glutamine, the areas were related to the amounts of amino acid amide present.

Acidolysis and Gas Chromatography. H-Gly-NHDmb or H-Gly-NHpmb (0.5 mmol) were treated with trifluoroacetic acid (18.5 ml) and anisole (1.5 ml) or with 1 N HCl–CH_3COOH (20 ml), respectively. At fixed times portions of the reaction mixture were evaporated under nitrogen. The residue was treated with trifluoroacetic anhydride (0.5 ml) and methylene chloride (2 ml) for 30 min at room temperature. The solution was evaporated under nitrogen and the residue dissolved in ethyl acetate (0.5 ml) containing 0.2 mg of methyl stearate as internal standard; 1 μl was injected in the gas chromatograph. The retention times relative to methyl stearate for N-TFA-Gly-NHDmb and N-TFA-Gly-NHpmb were 1.11 and 0.72, respectively. The peak areas were calculated as peak height × width at half height and corrected against the peak area of the internal standard. The values of these areas were then related to the amounts of glycine amide produced at time *t* using the relationship $100 - (A_t/A_0)100$ where A_0 and A_t are the initial corrected area of N-TFA-Gly-NHDmb (or pmb) and that at time *t*, respectively.

Registry No.—Boc-Asn(pmb)-OBzl, 27482-84-4; Boc-Gln(pmb)-OBzl, 27482-67-3; HCl, 7647-01-0; acetic acid, 64-19-7; trifluoroacetic acid, 76-05-1; HF, 7664-39-3.

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Optically Active Amines. XXI.[1] Application of the Salicylidenimino Chirality Rule to Cyclic Steroidal Amines

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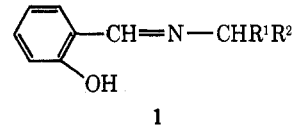
The salicylidenimino chirality rule[3] has been used to correlate the absolute configuration of *N*-salicylidenimino derivatives (1) of cyclic terpene amines (menthane, thujane,



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and fenchane ring systems) with the signs of the observed Cotton effects near 255 and 315 nm in their circular dichroism (CD) spectra.[1] The Cotton effects are generated by the coupled oscillator mechanism, demonstrated earlier to account for most of the observed optical activity in pyrimidine nucleosides.[4,5] For the *N*-salicylidene derivative the signs of the Cotton effects are determined by the chirality (right-handed screw for positive chirality) of vicinal carbon–carbon bonds and the attachment bond of the salicylidenimino chromophore.

We now apply similar consideration of a coupled oscillator mechanism to the interpretation of the CD spectra of the *N*-salicylidene derivatives of steroidal cyclic amines (Table I). These spectra were reported earlier,[6–9] but until now there has been no simple interpretation.

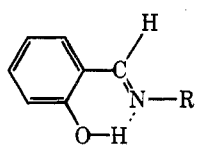
The electronic (isotropic) absorption (EA) spectra of *N*-salicylidene derivatives in hexane exhibit absorption bands at about 315 (log ϵ_{max} 3.68–3.73), 255 (log ϵ_{max} 4.12–4.21), and 215 nm (log ϵ_{max} 4.36–4.49),[1] designated as bands I, II, and III,[3] respectively, assigned to transitions of the intramolecularly hydrogen-bonded salicylidenimino chromophore[3] (2). In polar solvents such as dioxane, ethanol, and methanol a broad band at 400 nm (log ϵ_{max} 1.32–1.89 in dioxane[9] and log ϵ_{max} 3.06–3.38 in ethanol[9] and methanol[1]) and in ethanol a shoulder near 280 nm (log ϵ_{max} 3.49–3.67[9]) become evident, and the other three bands show a slight decrease in intensity.[1,9] The two additional bands are at-

Table I
Circular Dichroism for the *N*-Salicylidene Derivatives of Steroidal Cyclic Amines

Compd	*N*-Salicylidene derivative (solvent[b])	Circular dichroism maxima[a]			Coupled oscillator	
		Quinoid[c]	Band I	Band II[d]	Bond	Chirality
4	1α-Amino-5α-cholestane-2β,3β-diol (D, E)	+	+	+[e,f]	C(9)–C(10)	+
5	4β-Aminocholestan-5α-ol (D, M)		+[g]	+	C(5)–C(6)	+
6	4β-Aminocholestane-3β,5α-diol (D)		+	+	C(5)–C(6)	+
7	6α-Amino-5α-cholestane (D, E)	—	—	+, —	C(4)–C(5)	+
8	6β-Amino-3β-acetoxycholestan-5α-ol (D, E)	—	—	—[h]	C(4)–C(5)	—
9	6β-Amino-5α-cholestane-3β,7α-diol (D)		—	—[h]	C(4)–C(5)	—
10	7α-Amino-5α-cholestane-3β,6β-diol (D)		—	—	C(8)–C(14)	—
11	7β-Amino-5α-cholestane (E, I)	+	+	+, —[f]	C(8)–C(14)	+
12	11α-Amino-5β-pregnane-3α,20β-diol (D)		+	—, +[i]	C(9)–C(10)	—
13	12α-Amino-5β-cholane (D)		—	+	C(13)–C(17)	+
14	2β-Amino-5α-cholestane-1α,3β-diol (D)		—	—[h]	C(9)–C(10)	—
15	2β-Amino-5α-cholestan-3α-ol (D)		—	—	C(9)–C(10)	—
16	3α-Amino-5α-solanidane (D, E)	—	—[g,j]	—	C(5)–C(6)	—
17	3α-Amino-5α-cholestan-2β-ol (D, E)	+	—[g]	+[i]	C(5)–C(6)	—
18	3α-Amino-5α-pregnan-20α-ol (D)		—[k]		C(5)–C(6)	—
19	3β-Amino-5β-solanidane (D, E)	+	+[l]	+	C(5)–C(6)	+
20	3α-Amino-5β-solanidane (D, E)	—	—[g,j]	—	*m*	
21	3β-Amino-5α-solanidane (D, E)	+	+[n]	+	*m*	
22	Jurubidin (D)		+[o]		*m*	
23	Jurubin (D, E)	+	+[g,o]	+	*m*	
24	Solanocapsin (D, E)	+	+[l,p]	+	*m*	
25	5α-Aminocholestane-3β,6β-diol (D)		—	+	*m*	
26	3β-Dimethylamino-16α-amino-18,20(*R*)-epoxy-5α-pregnane (E)	+	+		*q*	
27	3β-Dimethylamino-16β-amino-18,20(*R*)-epoxy-5α-pregnane (D)		—[h]		*q*	
28	17α-Amino-5α-androstan-3β-ol (D)		—[k]		*q*	
29	17β-Amino-5α-androstan-3β-ol (D)		+[k]	—	*q*	
30	17β-Amino-5α-androstan-3α-ol-11-one (D)		+[k]	—	*q*	

[a] CD from ref 9, or as noted otherwise. [b] Solvents: D, dioxane; E, ethanol; M, methanol; I, isooctane. [c] Observed only in ethanol and methanol. [d] For S-shaped curves, the sign of the maximum at the longer wavelength is shown to the left. [e] A weak positive maximum at 246 nm in ethanol also reported. [f] A negative maximum at shorter wavelength in ethanol assigned to band III. [g] Only this band in dioxane reported. [h] Maximum in dioxane not reached. [i] A positive maximum at shorter wavelength assigned to band III. [j] CD in dioxane from ref 7. [k] CD from ref 6. [l] Two positive maxima in dioxane assigned to band II. [m] No obvious carbon–carbon bond as a single coupled oscillator. [n] A negative maximum near 275 nm in dioxane assigned to the quinoid tautomer. [o] CD in dioxane from ref 8. [p] A negative maximum near 275 nm assigned to the quinoid tantomer. [q] Cyclopentylamine system.

tributed to the presence of a quinoid tautomer (3) in the polar solvents.[10]



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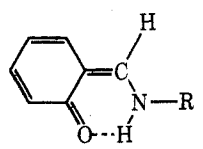

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For the *N*-salicylidene derivatives shown in Table I, corresponding CD maxima are reported[6-9] for bands I ($\Delta\epsilon_{max}$ ±0.13 to ±4.57) and II ($\Delta\epsilon_{max}$ ±0.9 to ±9.7) and for the band near 400 nm ($\Delta\epsilon_{max}$ ±0.05 to ±0.82) in ethanol and methanol. In dioxane a CD maximum near 400 nm was not detected,[9] and in all solvents the anisotropy factor ($\Delta\epsilon/\epsilon$) of band III is such that its CD maximum is difficult to measure and usually is not observed. The signs of the CD of bands I and II of a particular compound, however, remain unchanged with a change in solvent.

With the exception of **13**, when a single CD maximum is associated with band I and with band II, these maxima are of the same sign since the electronic transition moments of these two bands, although not coinciding exactly with each other, are almost parallel to the chromophore attachment bond.[3] In the case of **13**, the difference in sign is presumably due to the difference in orientation of these transition moments. For some of these compounds (**7**, **11**, and **12**), band II shows an S-shaped (double-humped[11]) CD curve. This may be the manifestation of the combined effect of an allowed progression of a totally symmetric vibrational mode and a forbidden progression of a possibly non-totally symmetric mode whose differential dichroic absorption maximum occurs at a shorter wavelength and borrows its intensity chiefly from band III.[12] An S-shaped CD curve for band II appears only when the two progressions have opposite signs and their rotational strengths are of approximately equal intensity. That the longer wavelength CD maximum for band II of **7** and **12** does not have the same sign as that of band I is also due to the slightly different orientation of the respective electronic transition moments.

Since in **4–19** the chromophore is symmetrically disposed with respect to the cyclohexane ring to which it is attached and the effect due to the polarizability of the carbon–hydrogen and carbon–oxygen bonds may be assumed to be small compared to a carbon–carbon bond,[4] only the carbon attachment bonds to the cyclohexane ring bearing the chromophore need be considered as inducing differential dichroic absorption. As shown in Table I for **4–13**, the sign of the CD maximum for band II (or the longer wavelength portion of band II) and with three exceptions for band I (**7**, **12**, and **13**) is the same as the chirality (right-handed screw for positive chirality) of the attachment bond of the salicylidenimino group and a carbon attachment bond to the cyclohexane ring vicinal to the chromophore. Assuming chair conformations for all cyclohexane rings, the dihedral angle for the two bonds is close to ±60°. The C(10)–C(19) bond in **4** and the C(13)–C(18) bond in **13** are essentially antiparallel to the chromophore attachment bond and have

little effect on the CD. For compounds with one hydroxyl group vicinal to the chromophore (**4, 5,** and **8–10**), the attachment bond of the hydroxyl group is nearly antiparallel to the chromophore attachment bond and has an insignificant effect on the CD. In **6** the vicinal C(5)–O bond is also antiparallel to the chromophore attachment bond, but the vicinal C(3)–O bond has a dihedral angle of about −60°. Nevertheless, the CD for both bands I and II is positive as a result of the positive chirality of the C(5)–C(6) bond.

As is also shown in Table I for **14–19,** the sign of the CD for bands I and II is determined also by the chirality of the attachment bond of the salicylidenimino group and a carbon attachment bond to the cyclohexane ring bearing the chromophore. This carbon–carbon bond and the chromophore attachment bond are separated from each other by two σ bonds and have a dihedral angle close to ±120°, again assuming chair conformations for all cyclohexane rings. The one exception is **17,** for which negative CD bands I and II are predicted. Since the C(2)–O bond in **17** is antiparallel to the chromophore attachment bond, and **16,** with an A/B ring system the same as that of **17,** shows the predicted negative CD for bands I and II, the CD of band II of **17** should be reexamined. In **14,** the vicinal C(1)–O bond is antiparallel to the chromophore attachment bond, but the vicinal C(3)–O bond has a dihedral angle of about +60°. The CD of bands I and II for **14,** however, is negative as a result of the negative chirality of the chromophore attachment bond and the C(9)–C(10) bond. In **14** and **15** the C(10)–C(19) bond is parallel with the chromophore attachment bond and will have little effect on the CD.

For **20–25,** the chromophore is 3α on a 5β ring system (**20**), 3β on a 5α ring system (**21–24**), or 5α (**25**), and in each there is no obvious single carbon–carbon bond as a coupled oscillator. Hence, no straightforward prediction as to the CD of bands I and II is possible. Also, the chromophore in **26–30** is attached to a cyclopentane ring which is not symmetrically disposed with respect to the chromophore attachment bond, and no simple interpretation of these CD spectra in terms of the coupled oscillator mechanism can be made.

Registry No.—**4,** 57525-86-7; **4** quinoid form, 57484-06-7; **5,** 57525-87-8; **6,** 57525-88-9; **7,** 57525-89-0; **7** quinoid form, 57474-17-6; **8,** 57525-90-3; **8** quinoid form, 57474-18-7; **9,** 57525-91-4; **10,** 57525-92-5; **11,** 57525-93-6; **11** quinoid form, 57474-19-8; **12,** 57525-94-7; **13,** 57526-20-2; **14,** 57572-73-3; **15,** 57525-95-8; **16,** 57525-96-9; **16** quinoid form, 57474-20-1; **17,** 57525-97-0; **17** quinoid form, 57474-21-2; **18,** 57474-22-3; **19,** 57525-98-1; **19** quinoid form, 57484-00-1; **20,** 57525-99-2; **20** quinoid form, 57474-23-4; **21,** 57526-00-8; **21** quinoid form, 57474-24-5; **22,** 57526-01-9; **23,** 57526-21-3; **23** quinoid form, 57484-08-9; **24,** 57526-02-0; **24** quinoid form, 57474-25-6; **25,** 57474-26-7; **26,** 57572-74-4; **26** quinoid form, 57474-27-8; **27,** 57526-03-1; **28,** 57526-04-2; **29,** 57526-05-3; **30,** 57474-28-9.

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A Novel Transformation of Chromone-3-carboxaldehyde to an *o*-Hydroxybenzophenone

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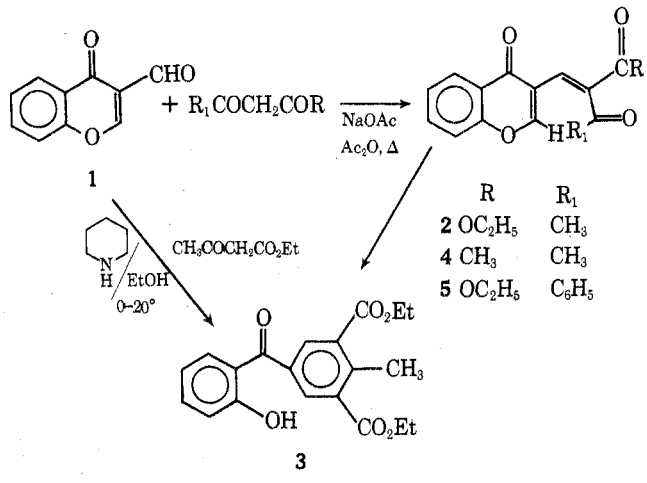
Recent publications[1–4] describing condensation reactions of 4-oxo-4*H*-1-benzopyran-3-carboxaldehyde (**1**) have prompted us to report a novel one-step transformation of **1** into an *o*-hydroxybenzophenone **3**.

Condensation of **1** with ethyl acetoacetate afforded **2** or **3** depending on reaction conditions. For example, reaction of



1 with ethyl acetoacetate in the presence of NaOAc–Ac_2O gave **2** in 62% crude yield. Similar condensations of **1** with 2,4-pentanedione and ethyl benzoylacetate gave **4** and **5** in 60 and 30% yield, respectively.

Reaction of **1** with excess ethyl acetoacetate in NaOAc–Ac_2O or pyridine–EtOH also gave **2**.

When the reaction was carried out in the presence of piperidine–EtOH the benzophenone **3** and a red oil were formed. This oil showed no trace of **3** on TLC (Et_2O–hexane, 1:1 silica gel). Upon prolonged standing it solidified. Examination of the solid by GC showed two components,