product ratios and indicated the presence of 4–5% of 1-methyladamantane. The products of **3b** and **3d** were separated by three successive chromatographies on a neutral alumina (activity II/III) column with pentane as the eluent.

The products were identified by ^{13}C NMR (see Table I), ^1H NMR, IR, and mass spectra.

For the mixture of **3-methyl-2,4-didehydroadamantane (8a)** and **1-methyl-2,4-didehydroadamantane (9a)** obtained from **4a**: ^1H NMR (C_6D_6) δ 2.3–1.2 (complex m, maximums at δ 2.2, 1.7, 1.3), 1.11 (s, CH_3), and 0.95 (s, CH_3); IR (film) 3040 (m–w), 2930 (s), 2840 (s), 1450 (w) cm^{-1}; mass spectrum, *m/e* (relative intensity) 148 (M^+, 37), 133 (11), 119 (13), 93 (51), 92 (60), 91 (92), 79 (100), 77 (43), 70 (40). Anal. Calcd for $C_{11}H_{16}$: C, 89.19; H, 10.81. Found: C, 88.99; H, 10.83.

For the mixture of **1-methyl-2,4-didehydroadamantane (9a)** and **7-methyl-2,4-didehydroadamantane (10a)**: ^1H NMR (C_6D_6) δ 2.4–1.0 [complex m, maximums at δ 2.26, 1.52, 1.12, 1.11 (s, CH_3), and 0.75 (s, CH_3)]; IR (film) 3030 (w–m), 2990 (w), 2920 (s), 2840 (s), 1450 (m) cm^{-1}; mass spectrum, *m/e* (relative intensity) 148 (M^+, 100), 133 (48), 106 (78), 105 (67), 93 (77), 91 (94), 79 (95), 78 (30), 77 (41). Anal. Calcd for $C_{11}H_{16}$: C, 89.19; H, 10.81. Found: C, 89.12; H, 10.95.

1-Chloro-2,4-didehydroadamantane (9b): ^1H NMR ($CDCl_3$) δ 2.8–0.7 (complex m, maximums at δ 2.7, 2.0, 1.9, 1.8, 1.3, and 1.2); IR (film) 3040 (m), 2930 (s), 2860 (m), 1460 (w) cm^{-1}; mass spectrum, *m/e* (relative intensity) 170 (M^+ + 2, 11), 168 (M^+, 31), 133 (40), 126 (19), 93 (35), 92 (55), 91 (100), 81 (31), 79 (56). Anal. Calcd for $C_{10}H_{13}Cl$: C, 71.43; H, 7.74; Cl, 20.83. Found: C, 71.47; H, 7.48; Cl, 20.54.

3-Chloro-2,4-didehydroadamantane (8b): ^1H NMR ($CDCl_3$) δ 2.6–0.7 (complex m, maximums at δ 2.4, 2.2, 2.0, 1.9, 1.4, and 1.3); IR (film) 3030 (m), 2920 (s), 2850 (s), 1450 (w), 720 (w) cm^{-1}; mass spectrum, *m/e* (relative intensity) 170 (M^+ + 2, 10), 168 (M^+, 32), 133 (39), 126 (32), 113 (37), 92 (25), 91 (100), 81 (47), 79 (49). Anal. Calcd for $C_{10}H_{13}Cl$: C, 71.43; H, 7.74; Cl, 20.83. Found: C, 71.41; H, 7.69; Cl, 20.76.

7-Chloro-2,4-didehydroadamantane (10b): ^1H NMR ($CDCl_3$) δ 2.7–1.3 (complex m, maximums at δ 2.5, 2.2, 1.9, 1.8, and 1.5); IR (KBr) 3030 (m), 2940 (s), 2860 (s), 1450 (w), 1440 (w), 1315 (w), 1025 (s), 850 (s), 795 (s), 740 (m), 630 (s) cm^{-1}; mass spectrum, *m/e* (relative intensity) 170 (M^+ + 2, 4), 168 (M^+, 13), 133 (11), 126 (11), 92 (17), 91 (83), 79 (100), 78 (70), 77 (36). Anal. Calcd for $C_{10}H_{13}Cl$: C, 71.43; H, 7.74; Cl, 20.83. Found: C, 71.33; H, 7.65; Cl, 20.53.

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Registry No. 1a, 26832-19-9; **1b**, 81315-72-2; **1c**, 21365-84-4; **1d**, 20098-17-3; **2a**, 81315-73-3; **2b**, 81315-74-4; **2c**, 81315-75-5; **2d**, 81315-76-6; **3a**, 81315-77-7; **3b**, 81315-78-8; **3c**, 81315-79-9; **3d**, 81315-80-2; **4a**, 81315-81-3; **4b**, 81315-82-4; **4c**, 81315-83-5; **4d**, 81315-84-6; **5**, 27567-85-7; **6**, 28996-05-6; **7**, 81315-85-7; **8a**, 81315-86-8; **8b**, 81315-87-9; **9a**, 81315-88-0; **9b**, 81315-89-1; **10a**, 81315-90-4; **10b**, 81315-91-5; 1-chloro-2-hydroxyadamantane, 81315-92-6; 1-methyladamantane, 768-91-2; 5-hydroxy-2-adamantanone, 20098-14-0.

Optically Active Amines. 30.[1a] Application of the Salicylidenimino Chirality Rule to Aliphatic and Alicyclic Amines[1b]

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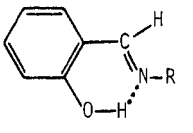
The salicylidenimino chirality rule can be used to correlate the sign of the observed Cotton effects near 315 and 255 nm in the circular dichroism spectra of the *N*-salicylidene derivatives of aliphatic and alicyclic amines with their absolute configurations. The rule is based on the model that the Cotton effects originate from interaction of the respective transition moments of the hydrogen-bonded salicylidenimino chromophore with bond transition moments in the rest of the molecule. Carbon–carbon and carbon–oxygen bonds vicinal and homovicinal to the salicylidenimino attachment bond are the dominant contributors to the Cotton effects, and the sign of the Cotton effects depends on the algebraic sum of these contributions. Since the polarizability of a carbon–oxygen bond is smaller than that of a carbon–carbon bond, the contribution of a vicinal or homovicinal carbon–oxygen bond is less than that of a corresponding carbon–carbon bond. The sign of a particular contribution usually can be determined by the chirality that the bond has with the attachment bond of the salicyclidenimino group, a positive contribution for positive chirality (right-handed screw) and a negative contribution for negative chirality (left-handed screw).

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} 3.7), 255 (4.1–4.2), and 215 nm (4.4–4.5), designated as bands I–III, respectively,[5] which were assigned to the $\pi \rightarrow \pi^*$ transitions of the intramolecularly hydrogen-bonded salicylidenimino (SI) chromophore (**1**).[6]



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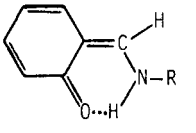

2

In polar solvents, a broad band at about 400 nm (log ϵ_{max} 1.3–1.9 in dioxane[7] and 3.1–3.4 in methanol[5] and ethanol[7]) and a shoulder near 280 nm (log ϵ_{max} 3.5–3.7 in ethanol[7])

(1) (a) Part 29: Smith, H. E.; Chen, F.-M. *J. Org. Chem.* **1981**, *46*, 185–187. (b) Some of this work was taken from the Ph.D. Thesis of A.F.M., Vanderbilt University, Jan 1967.

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

(3) Supported by United States Public Health Service Training Grant in Reproductive Biology HD-07043.

(4) Supported by National Institutes of Health Grant HD-05797.

(5) Smith, H. E.; Burrows, E. P.; Massey, E. H.; Chen, F.-M. *J. Org. Chem.* **1975**, *40*, 2897–2901.

(6) Alexander, P. W.; Sleet, R. J. *Aust. J. Chem.* **1970**, *23*, 1183–1190.

(7) Ripperger, H.; Schreiber, K.; Snatzke, G.; Ponsold, K. *Tetrahedron* **1969**, *25*, 827–836.

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Table I. Circular Dichroism Data for the *N*-Salicylidene Derivatives of Some Chiral Aliphatic Amines

amine	solvent	CD max, λ, nm ([Θ][a]) quinoid	band I	band II
(*S*)-3a	MeOH[b]	395 (+630)	313 (+1600)	253 (+4900)
(*S*)-3b[c]	MeOH[d]	395 (+550)	315 (+1800)	260 (+3800)
(*S*)-3c[e]	MeOH[d]	395 (+700)	313 (+2300)	258 (+4300)
(*R*)-3d	MeOH[b]	400 (−1100)	315 (−2500)	261 (−6200)
(*S*)-3e	MeOH[b]	396 (+710)	312 (+2700)	269 (−1900), 248 (+6300)
	n-hexane[b,f]		315 (+1800)	267 (−3800), 251 (+8300)
5a	dioxane[g]		315 (+10 000)	
5b	dioxane[g]		315 (−15 000)	
(*R*)-8a	MeOH[h]	400 (−590)	316 (−1800)	252 (−2000)[i]
(*R*)-8b	MeOH[b]	388 (−160)	315 (−450)	267 (+6000), 248 (−2300)
	n-hexane[b,f]		316 (+1100)	267 (+6500), 248 (−2900)

[a] Molecular ellipticity. [b] Data from ref 19. [c] $[\alpha]^{27}_D$ +8.7° (neat). For the absolute configuration see ref 20. [d] Formed in situ. [e] $[\alpha]^{27}_D$ +6.3° (neat). For the absolute configuration see ref 20 and 21. [f] An additional weak maximum near 418 nm. [g] Data adapted from ref 22. [h] Data from ref 14. [i] Band III maximum at 220 nm ([Θ] +2400).

become evident, and the three other bands show a slight decrease in intensity.[5,7] The two additional bands are attributed to the presence of a quinoid tautomer (**2**) in polar solvents.[6] The corresponding circular dichroism (CD) spectra usually show Cotton effects (CEs) for bands I–III as well as one near 400 nm for the quinoid tautomer. In some of these spectra, there is an additional, comparatively weak CD maximum of opposite sign to that of bands I and II and centered between bands I and II at about 275 nm which is assigned to an n → π* transition of the azomethine group.[8,9]

The sign of CD bands I and II can be correlated with the absolute configurations of a wide variety of chiral *N*-salicylidene derivatives by application of the SI chirality rule.[1,5,10-15] The rule is based on the model that the coupled oscillator mechanism[16] can account for the observed CEs, the electric transition moments of bands I and II being coupled to electric transition moments in the amine moiety.

Application of the rule to *N*-salicylidene derivatives of chiral amines with groups having strong π → π* transitions is straightforward and gives good stereochemical correlations.[10,11,13-15] For the *N*-salicylidene derivatives of amino sugars[1] and cyclic terpene[5] and steroidal amines,[12] the CEs arise from coupling of C–C and C–O bond transition moments[17,18] with the transition moments of the SI chromophore. The effect due to C–H bonds is negligible, and C–C and C–O bonds vicinal and homovicinal to the SI chromophore are the dominant contributors to the CEs. Since the polarizability of a C–O bond is smaller than that of a C–C bond,[17,18] the contribution of a vicinal or homovicinal C–O bond is less than that of a corresponding C–C bond.

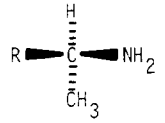
For the SI chromophore, the transition moment directions of bands I and II, although slightly different in direction,[10] are approximately parallel to the attachment bond of the SI chromophore, and the sign of the contribution to the CEs of bands I and II by a particular vicinal or homovicinal bond can usually be determined from the chirality that the bond has with the attachment bond of the SI group, a positive contribution for positive chirality (right-handed screw) and a negative contribution for negative chirality (left-handed screw). In carbocyclic and oxacyclic amine derivatives, contributions from C–C and C–O ring bonds can usually be assumed to be nil due to the symmetry of the ring and/or mutual cancellation. This assumption is certainly valid for the chair conformation of six-membered carbocyclic systems but may be poor for six-membered oxacyclic systems or for five-membered rings.

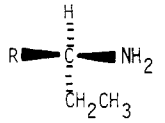
The sign of the observed CEs for bands I and II is due to the algebraic sum of all bond contributions, and the sign of this sum for a particular configuration can usually be deduced by conformational analysis.

We now outline additional applications of the salicylidenimino chirality rule for the correlation of the CD spectra of the *N*-salicylicylidene derivatives of aliphatic and alicyclic amines with their absolute configurations. In some cases, the assignment of the CEs to bands I and II or the algebraic sum of the bond contributions are ambiguous, and predictions as to the sign of the CEs for a particular configuration are uncertain without use of CD spectra of model compounds of similar structures and known absolute configurations.

Results and Discussion

Aliphatic Amines (Table I). Application of the SI chirality rule to the *N*-salicylidene derivatives of (*S*)-2-aminobutane [(*S*)-**3a**], (*S*)-2-aminopentane [(*S*)-**3b**], and



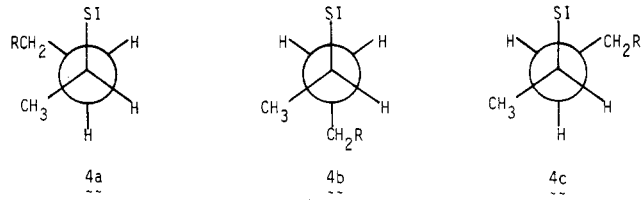


(S)-3a, R = CH_3CH_2
b, R = $CH_3CH_2CH_2$
c, R = $CH_3(CH_2)_3CH_2$
d, R = $(CH_3)_3C$
e, R = $HOCH_2$

(S)-8a, R = $CH_3CH_2CH_2$
b, R = $HOCH_2$

(8) Smith, H. E.; Padilla, B. G.; Neergaard, J. R.; Chen, F.-M. *J. Org. Chem.* **1979**, *44*, 1690–1695.
(9) Smith, H. E.; Chen, F.-M. *J. Org. Chem.* **1979**, *44*, 2775–2779.
(10) Smith, H. E.; Neergaard, J. R.; Burrows, E. P.; Chen, F.-M. *J. Am. Chem. Soc.* **1974**, *96*, 2908–2916.
(11) Smith, H. E.; Burrows, E. P.; Chen, F.-M. *J. Org. Chem.* **1975**, *40*, 1562-1567.
(12) Smith, H. E.; Burrows, E. P.; Chen, F.-M. *J. Org. Chem.* **1976**, *41*, 704–706.
(13) Smith, H. E.; Burrows, E. P.; Marks, M. J.; Lynch, R. D.; Chen, F.-M. *J. Am. Chem. Soc.* **1977**, *99*, 707–713.
(14) Ringdahl, B.; Smith, H. E.; Chen, F.-M. *J. Org. Chem.* **1977**, *42*, 4184–4187.
(15) Smith, H. E.; Cozart, W. I.; de Paulis, T.; Chen, F.-M. *J. Am. Chem. Soc.* **1979**, *101*, 5186–5193.
(16) Schellman, J. A. *Acc. Chem. Res.* **1968**, *1*, 144–151.
(17) Inskeep, W. H.; Miles, D. W.; Eyring, H. *J. Am. Chem. Soc.* **1970**, *92*, 3866–3872.
(18) Snyder, P. A.; Johnson, W. C., Jr. *J. Am. Chem. Soc.* **1978**, *100*, 2939–2944.
(19) Smith, H. E.; Ensley, H. E. *Can. J. Chem.* **1971**, *49*, 2902–2906.
(20) Halpern, B.; Ricks, J.; Westley, J. W. *Chem. Commun.* **1966**, 679–680.
(21) Mazur, R. H. *J. Org. Chem.* **1970**, *35*, 2050–2051.

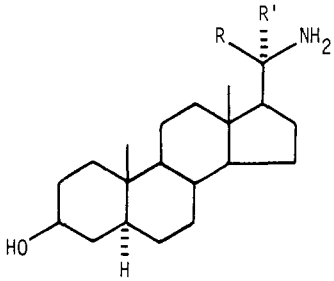
(*S*)-2-aminoheptane [(*S*)-**3c**] proceeds by consideration of their three conformers of lowest energy (**4a–c**) resulting



R = H, CH_3, or $CH_3CH_2CH_2$

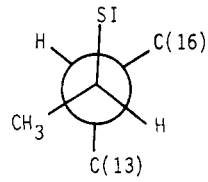
from rotation about the C(2)–C(3) bond. Conformer **4a** is that of highest energy due to steric interaction and will be unimportant compared to the other two. Conformer **4b** will also contribute negligible rotational strength to the CD spectrum because of the nearly anticolinearity and large separation of the SI group attachment bond and the C(3)–C(4) bond. Conformer **4c** is the principal contributor to the CD spectrum, and the positive chirality that the C(3)–C(4) bond, vicinal to the SI group attachment bond, has with this bond unambiguously predicts the positive sign for CD bands I and II for these derivatives, contributions from the homovicinal and other C–C bonds being unimportant compared to that of the vicinal C(3)–C(4) bond.

A similar prediction can be made for the CE at 315 nm shown by the *N*-salicylidene derivatives of 20-amino steroids. Those with the 20α(*S*) configuration (four reported[22,23]) such as that of 20α-amino-5α-pregnan-3β-ol[22] (**5a**) are predicted, by using Newman projection **6**, to show



5a, R = H; R' = CH_3

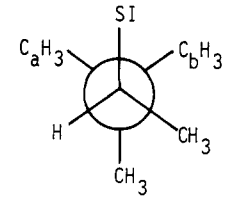
b, R = CH_3; R' = H



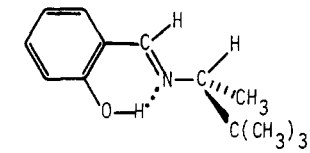
6

positive CEs for bands I and II although only a CE at 315 nm was reported. The other conformers resulting from rotation about the C(17)–C(20) bond are less stable than **6** due to steric interaction and do not make a significant contribution to the CEs. Those with the 20β(*R*) configuration (three reported[22,23]) such as that of 20β-amino-5α-pregnan-3β-ol[22] (**5b**) are predicted to show negative CEs.

The negative sign for CD bands I and II for the *N*-salicylidene derivative of (*R*)-2-amino-2,2-dimethylbutane [(*R*)-**3d**] cannot be predicted by using Newman projection **7a** without considering the relative position of the methyl groups with respect to the transition moments of the SI chromophore itself. In the preferred conformation of the SI group about its attachment bond (**7b**),[10,13] the C_aH_3 group in **7a** is closer to the major axis of the chromophore than is the C_bH_3 group, and thus the negative chirality that the C_aH_3 group attachment bond has with the SI group transition moments makes a greater contribution to the



7a



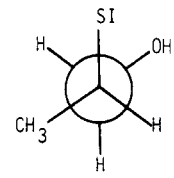
7b

CEs than does the positive chirality which the C_bH_3 group attachment bond has with these moments, and the observed CEs are negative.

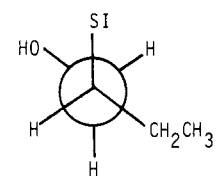
For the *N*-salicylidene derivative of (*R*)-3-aminohexane [(*R*)-**8a**], the negative CEs arise by contributions from the chiralities that C–C bonds, vicinal and homovicinal to the SI group attachment bond, have with the transition moments of the SI chromophore. The algebraic sum of these contributions is not readily deduced by using molecular models, and no prediction as to the sign of the CEs shown by the derivative of (*R*)-**8a** is possible.

The CD spectra for the *N*-salicylidene derivative of (*S*)-2-amino-1-propanol [(*S*)-**3e**] and (*R*)-2-amino-1-butanol [(*R*)-**8b**] are unusual in that both show two CEs from 245 to 270 nm. In the absence of exciton splitting, bisignate CD curves associated with a single electronic transition have been attributed to conformational equilibria, the oppositely signed maxima being due to different conformers,[24,25] to solution equilibria involving different solvated species,[24,25] or to vibronic coupling.[26,27] The conformational mobility of (*S*)-**3e** and (*R*)-**8b** suggests that the bisignate CD curve for band II is best explained on the basis of an equilibrium between two conformers having slightly different transition energies associated with band II.[25]

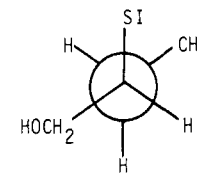
Conformational analysis for (*S*)-**3e** suggests that conformer **9** is the most important contributor to the CD.



9



10a



10b

Consideration of this conformer predicts positive CEs for both bands I and II in conformity with the observed positive CEs at 312 and 248 nm in methanol and 315 and 251 nm in *n*-hexane. The smaller negative CE at 269 nm in methanol and 267 nm in *n*-hexane indicates that the contribution due to a less favored negatively contributing conformer with the hydroxyl group juxtaposed between the methyl and SI groups may be significant. A slight intensity increase for both bands I and II is to be expected when a polar solvent is changed to a nonpolar solvent. For the derivative of (*S*)-**3e**, however, the twofold increase in intensity for the 267-nm negative CD maximum and the substantial decrease in the 312-nm positive CD maximum on changing the solvent from methanol to *n*-hexane is attributed to an increase in the importance of the nega-

(22) Bertin, D.; Legrand, M. *C. R. Hebd. Seances Acad. Sci.* **1963**, *256*, 960–962.
(23) Velluz, L.; Legrand, M.; Grosjean, M. "Optical Circular Dichroism"; Academic Press: New York, 1965; pp 240–241.
(24) Crabbé, P. "Optical Rotatory Dispersion and Circular Dichroism in Organic Chemistry", Holden-Day: San Francisco, CA, 1965; pp 79–83.
(25) Wellman, K. M.; Laur, P. H. A.; Briggs, W. S.; Moscowitz, A.; Djerassi, C. *J. Am. Chem. Soc.* **1965**, *87*, 66–72.
(26) Weigang, O. E., Jr. *J. Chem. Phys.* **1965**, *43*, 3609–3618.
(27) Caldwell, D. J. *J. Chem. Phys.* **1969**, *51*, 984–988.

Table II. Circular Dichroism Data for the *N*-Salicylidene Derivatives of Some Chiral Alicyclic Amines

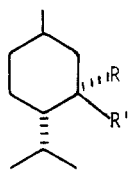
amine	solvent	CD max, λ, nm ([Θ][a]) quinoid	band I	band II
11a	MeOH[b]	400 (−150)	315 (−1400)[c]	267 (−12 000), 245 (+3500)
11b	MeOH[b]	396 (+860)	314 (+710)[c]	264 (+6500)
13a	MeOH[d]		318 (+3800)	271 (−18 000), 250 (+9200)[e]
13b	MeOH		324 (−1800)	271 (+13 000)[f]
15a	MeOH	398 (−820)	315 (−1500)	253 (−4900)
15b	EtOH[g]	409 (+200)	314 (−1300)	255 (+4100)[h]
16	dioxane[g]		315 (−6600)	270 (−11 000)[i]
17a	hexane		315 (+4100)	252 (+5500)
17b	MeOH	402 (+540)	315 (+1700)	252 (+2400)
18	EtOH[g]	405 (−500)	314 (−1800)	250 (−3000)
19	dioxane[g]		330 (−5000)	285 (+13 000)
20a	MeOH	402 (+6600)	315 (+15 000)	254 (+26 000)
20b	dioxane[j]		315 (−15 000)	
21	MeOH	400 (+6300)	315 (+14 000)[k]	254 (+26 000)
22[l]	MeOH[m]	395 (−660)	312 (−2100)[n]	251 (−6200)

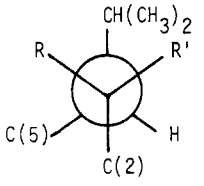
[a] Molecular ellipticity. [b] Data from ref 5. [c] Shoulder. [d] CD similar to that in ref 7 with dioxane as the solvent. [e] Band III at 232 nm ([Θ] +4400). [f] Band III at 234 nm ([Θ] +2600). [g] Data adapted from ref 7. [h] Band III at ~220 nm ([Θ] +5600). [i] Maximum not reached. [j] Data adapted from ref 23. [k] Maximum at 274 nm ([Θ] −2000) assigned to the n → π* transition of the SI chromophore. [l] A gift from Professor D. W. Mathieson, University of Bradford, Bradford, England. For preparation and characterization see ref 30. [m] Formed in situ. [n] Maximum at 272 ([Θ] +1500) assigned to the n → π* transition of the SI chromophore.

tively contributing conformer.

For correlation of the absolute configuration of the *N*-salicylidene derivative of (*R*)-**8b** with its CD curve, the preferred chirality that both the C(1)–O and C(3)–C(4) bonds have with the SI group attachment bond must be considered. In conformer projections **10a** and **10b**, the contribution from the C(1)–O bond is negative, and that from the C(3)–C(4) bond is positive. Since the contribution from a vicinal C–O bond is less than that from vicinal C–C bond,[17,18] the derivative of (*R*)-**8b** is predicted to show positive CEs for bands I and II in agreement with the observed positive CD maxima at 316 and 267 nm in *n*-hexane. The dependence of conformational equilibrium on the solvent is dramatically demonstrated by the sign reversal for band I when the solvent is changed to methanol.

Alicyclic Amine Derivatives (Table II). Earlier the salicylidenimino chirality rule was used to correlate the sign of the CEs associated with bands I and II of the *N*-salicylidene derivatives of a series of cyclic terpene amines.[5] Thus for those of (−)-menthylamine (**11a**) and (+)-neomenthylamine (**11b**), both with preferred chair





11a, R = H; R' = NH_2

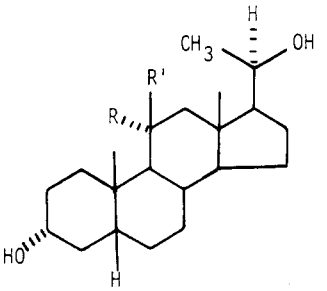
b, R = NH_2; R' = H

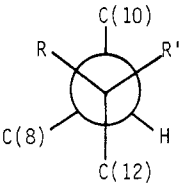
12a, R = H; R' = SI

b, R = SI; R' = H

conformations, the chirality of the attachment bond of the isopropyl group with the SI group attachment bond is negative (**12a**) and positive (**12b**), respectively, and the *N*-salicylidene derivatives of **11a** and **11b** show negative and positive CEs, respectively, for band I and the allowed component of band II, band II for the derivative of **11a** showing a bisignate CD curve. The latter is presumed to be a manifestation of the combined effect of an allowed progression of a totally symmetric vibrational mode and a forbidden progression of a nontotally symmetric mode whose differential dichroic absorption maximum occurs at a shorter wavelength and borrows its intensity chiefly by vibronic coupling from the nearby intense band III.[26,27]

The CD spectra of the *N*-salicylidene derivatives of 11α- and 11β-amino-5β-pregnane-3α,20β-diol (**13a,b**) are unu-





13a, R = NH_2; R' = H

b, R = H; R' = NH_2

14a, R = H; R' = SI

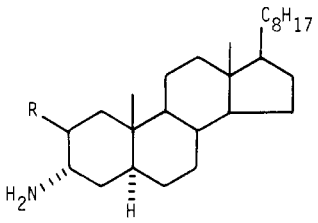
b, R = SI; R' = H

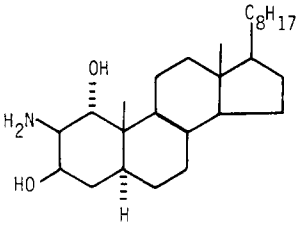
sual in that the sign of band I is different from that of band II or the long-wavelength component of band II. In each spectrum, the 271-nm CE is easily identified with band II since it is the most intense CE. When bands I and II have different signs, band II or the long-wavelength portion of band II is used for configurational correlation since its transition moment is more nearly parallel to the SI group attachment bond, and the larger magnitude of the moment and shorter wavelength for band II make dynamic coupling with perturbers more favorable.[16] Thus, the sign of band II or the allowed component of band II is the same as the chirality which the C(9)–C(10) bond has with the SI group attachment bond, negative (**14a**) for the derivative of **13a** and positive (**14b**) for that of **13b**.

Similar correlations are possible for other cyclic terpene[5] and steroidal amine derivatives[12] for which the sign of the observed CEs is the result of the chirality (±60° dihedral angle) which a single C–C bond, attached to the ring bearing the SI group and vicinal to the SI group attachment bond, has with the latter. The steroidal amine derivatives of this type for which the CD spectra have been reported[7] are those of 1α-, 4β-, 6α-, 6β-, 7α-, and 7β-amino 5α-steroids (eight examples) and a 12α-amino 5β-steroid. In many of these derivatives there is also a hydroxyl group vicinal to the SI chromphore, but the C–O bond contri-

bution is unimportant compared to that of the vicinal C–C bond.

In the *N*-salicylidene derivative of 3α-amino-5α-cholestane (**15a**), there is no carbon atom attached to ring A





15a, R = H

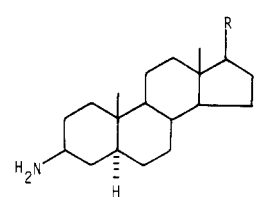
b, R = OH

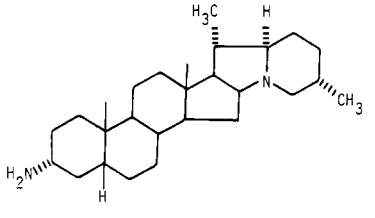
16

that is vicinal to the SI group, and the sign of CD bands I and II is determined by the chirality that a homovicinal C–C bond has with the SI chromophore attachment bond. The chirality of the homovicinal C(5)–C(6) bond is negative (−120° dihedreal angle), and negative CEs are observed. An exception to this analysis occurs with the derivative of 3α-amino-5α-cholestan-2β-ol (**15b**) for which CD band II is predicted to be negative but for which CD band II is reported to be positive[7] (Table II). the C(2)–O bond is antiparallel to the chromophore attachment bond and thus makes a negligible contribution to the CE. Since correct correlations are made for the derivative of **15a** and another *N*–salicyliden–3α–amino 5α–steroidal alkaloid,[7,28] the CD spectrum for that of **15b** should be reexamined.

By use of this model, correlations are also made for the reported[7] spectra of the *N*-salicylidene derivatives of two 2β-amino 5α-steroids and a 3β-amino 5β-steroidal alkaloid. Thus for the derivative of 2β-amino-5α-cholestane-1α,3β-diol (**16**), the chiralities of the SI attachment bond with the C(3)–O and C(9)–C(10) bonds are positive and negative, respectively. The reported[7] CEs for bands I and II are negative, the negative contribution for the homovicinal C(9)–C(10) bond being greater than the positive contribution of the vicinal C(3)–O bond. The C(1)–O bond in the derivative of **16** is antiparallel to the SI group attachment bond and makes no contribution to the CEs.

For the 3β-amino-5α-cholestane (**17a**) and 3β-amino-5α-androstan-17β-ol (**17b**) derivatives, the C(5)–C(6) bond,





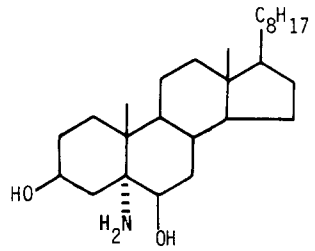
17a, R = C_8H_{17}

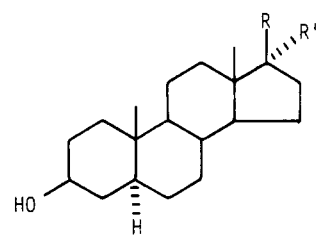
b, R = OH

18

homovicinal to the SI group attachment bond, is coplanar with the latter. The chirality of the C(5)–C(6) bond with the transition moments of the SI chromophore is deduced by consideration of the preferred conformation of the SI group about its attachment bond. In this conformation the methine hydrogen of the SI group eclipses the hydrogen atom at C-3.[10] Thus the CD spectra of the derivatives of both **17a** and **17b** show positive CEs for bands I and II since the C(5)–C(6) bond has positive chirality with the long axis of the SI chromophore. A similar analysis also predicts the observed[7,29] positive CEs for bands I and II for the derivatives of four 3β-amino 5α-steriodal alkaloids.

For the 3α-amino-5β-solanidane (**18**) derivative the C(5)–C(6) bond is coplanar with the SI attachment bond but has preferably a negative chirality with the transition moments of the SI chromophore. The observed[7] CEs for bands I and II are negative. Similarly, the chirality of the C(9)–C(11) bond with these moments predicts positive CEs for the 5α-aminocholestane-3β,6β-diol (**19**) derivative, and a positive CE is observed for band II, although this CE is reported[7] to be at an unusually long wavelength.



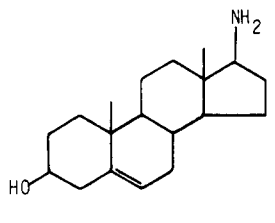


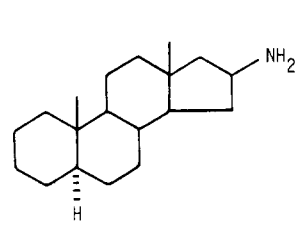
19

20a, R = NH_2; R' = H

b, R' = H; R' = NH_2

The CD of the *N*-salicylidene derivatives of 17β-amino-5α-androstan-3β-ol (**20a**) and 17β-amino-5-





21

22

androsten-3β-ol (**21**) show positive CEs associated with bands I and II, but for that of **21** there is also a weaker, negative CE at 274 nm assigned to the n → π* transition of the azomethine group.[8] The CE at 254 nm is easily assigned to band II on the basis of intensity. On the assumption of a planar cyclopentane ring and a preferred conformation of the SI group about its attachment bond such that the methine hydrogen eclipses the C(17) hydrogen atom,[10] the near proximity and positive chirality of the C(12)–C(13) bond with the SI transition moments predicts positive bands I and II. A similar analysis predicts the observed[8,23] positive CEs for the derivatives of two other 17β-amino steroids. For the derivative of 17α-amino-5α-androstan-3β-ol (**20b**), the chirality that the C(12)-C(13) bond makes with the SI group attachment bond is negative. Since the C(13)–C(18) bond makes only a negligible contribution to the CD, the CE for band I is negative, while that associated with band II has not been reported.

The *N*-salicylidene derivative of 16β-amino-5α-androstane (**22**) has negative CEs for bands I and II and a positive maximum at 272 nm for the n → π* transition

(28) Ripperger, H.; Schreiber, K.; Snatzke, G.; Heller, K. *Z. Chem.* **1965**, *5*, 62.

(29) Ripperger, H.; Budzikiewicz, H.; Schreiber, K. *Chem. Ber.* **1967**, *100*, 1725–1740.

(30) Cowall, D. B.; Davis, A. K.; Mathieson, D. W.; Nicklin, P. D. *J. Chem. Soc., Perkin Trans. 1* **1974**, 1505–1513.

of the azomethine group. It is difficult, however, to use the salicylidenimino chirality rule to predict the negative sign for bands I and II. For another 16β-amino steroid derivative, the CE for band I is reported[7] to be negative while that for a 16α-amino derivative is positive.[7]

Experimental Section

Melting points were taken in open capillary tubes and are corrected. Optical rotations were measured at the sodium D line by using a visual polarimeter and a 1-dm sample tube. Circular dichroism (CD) spectra were measured with a Cary Model 60 spectropolarimeter with a CD Model 6001 accessory at 25–28 °C by using a 1-cm cell. The slit was programmed for a spectral band width of 1.5 nm, and cutoff was indicated when the dynode voltage reached 400 V. Isolated *N*-salicylidene derivatives were prepared as outlined here or as described earlier.[31] For formation of the derivatives in situ, the amine was used with an excess of salicylaldehyde as described earlier.[13] For these derivatives the molecular ellipticies were calculated on the basis of complete formation of the derivative. All pure compounds had ^{1}H NMR spectra compatible with their assigned structures and configurations. The spectra were obtained in chloroform-*d* by using a Varian A-60 or JEOL JNM-MH-100 spectrometer with tetramethylsilane as an internal standard. Elemental analyses were done by Galbraith Laboratories, Inc., Knoxville, TN.

11α-Amino-5β-pregnane-3α,20β-diol (13a). Sodium (5.2 g, 0.23 mol) was added to 11-oximino-5β-pregnane-3α,20β-diol [350 mg (1.00 mmol), mp 217–220 °C (lit.[32] mp 227.0–228.5 °C)] in *n*-propyl alcohol (87 mL). The mixture was boiled under nitrogen for 5 h, cooled, and acidified. The solvent was evaporated at reduced pressure, and the residue was dissolved in water and filtered. The aqueous solution was made basic with 20% sodium hydroxide. The precipitate was collected by filtration, dried, and crystallized from acetonitrile. Recrystallization from acetonitrile gave a mixture of the 11α- and 11β-amines: 130 mg (39%); two spots on TLC (R_f 0.03 and 0.09, 4:6 C_2H_5OH–$CHCl_3$) with the slower moving spot being the more intense; mp ~120 °C dec.[33] Chromatography of a mixture (150 mg) on silica gel[35] with 1:1 hexanes–absolute ethanol as the eluant gave a poor recovery of **13a**: 9 mg (7%); pure by TLC (R_f 0.03, 4:6 C_2H_5OH–$CHCl_3$); mp ~165 °C dec; $[\alpha]^{27}_D$ −34° (*c* 0.73, dioxane) [lit.[32] mp 187–191 °C; $[\alpha]^{25}_D$ −10.1° (*c* 1, dioxane)].

11β-Amino-5β-pregnane-3α,20β-diol (13b). A mixture of 11-oximino-5β-pregnane-3α,20β-diol[32] (60 mg, 0.17 mmol) and platinum oxide (35 mg) in glacial acetic acid (3 mL) was stirred under hydrogen (1 atm) until the uptake of hydrogen ceased (24 h). The mixture was filtered and neutralized with 10% sodium hydroxide. The precipitate was collected by filtration, washed with water, and dried. Crystallization from acetonitrile gave (**13b**): 37 mg (64%); pure by TLC (R_f 0.09, 4:6 C_2H_5OH–$CHCl_3$); mp ~205 °C dec; $[\alpha]^{27}_D$ + 30° (*c* 1.0, dioxane) [lit.[32] mp 223–225 °C; $[\alpha]^{25}_D$ + 30° (*c* 1, dioxane)].

11α-(Salicylideneamino)-5β-pregnane-3α,20β-diol. A mixture of **13a** and **13b** (130 mg, 0.39 mmol) obtained by reduction of the oximine with sodium in *n*-propyl alcohol was mixed with salicylaldehyde (8 drops) in methanol (0.5 mL), and the resultant yellow solution was boiled for 1 h. The solvent and excess salicylaldehyde were removed at reduced pressure, and the yellow solid (160 mg) was chromatographed on silica gel. Elution with 7:3 hexanes–ethyl acetate and crystallization from hexanes–ethyl acetate gave pure 11α-(salicylideneamino)-5β-pregnane-3α,20β-diol: 110 mg (65%); as yellow cubes; pure by TLC (R_f 0.22, 3:7 hexanes–$CH_3CO_2C_2H_5$); mp 199–200 °C; $[\alpha]^{27}_D$ −48° (*c* 1.0, dioxane) [lit.[7] amorphous solid; $[\alpha]^{19}_D$ −22.3° (*c* 0.85, dioxane)].

Elution with 3:7 hexanes–ethyl acetate and crystallization from hexanes–ethyl acetate gave pure 11β-(salicylideneamino)-5β-pregnane-3α,20β-diol: 18 mg (11%); pure by TLC (R_f 0.06, 3:7 hexanes–$CH_3CO_2C_2H_5$); mp 190–195 °C; $[\alpha]^{27}_D$ +32° (*c* 1.1, dioxane).

11β-(Salicylideneamino)-5β-pregnane-3α,20β-diol. Salicylaldehyde (4 drops) was added to 11β-amino-5β-pregnane-3α,20β-diol (**13b**); 37 mg, 0.11 mmol) in methanol (0.5 mL) and the mixture boiled for 30 min. The solvent and excess salicylaldehyde were removed at reduced pressure, and the residue was chromatographed on silica gel. Elution with 3:7 hexanes–ethyl acetate and crystallization from hexanes–ethyl acetate gave the *N*-salicylidene derivative of **13b**: 22 mg (46%); pure by TLC (R_f 0.06, 3:7 hexanes–$CH_3CO_2C_2H_5$); mp 187–192 °C.

3α-Amino-5α-cholestane (15a) was prepared by reduction of 3α-azido-5α-cholestane with lithium aluminum hydride[36] and was purified by way of its hydrochloride salt.[36] The pure amine had the following: mp 97–98 °C; $[\alpha]^{28}_D$ +28° (*c* 1.1, $CHCl_3$); $[\alpha]^{28}_D$ +36° (*c* 1.0, CH_3OH) [lit.[36] mp 87–88 °C; $[\alpha]^{26}_D$ +28.6° (*c* 1.05, $CHCl_3$)].

The *N*-acetyl derivative had a melting point of 217–218 °C (lit.[36] mp 216–218 °C).

3α-(Salicylideneamino)-5α-cholestane was recrystallized from ethanol–ethyl acetate as yellow needles: mp 98–100 and 109–110 °C; $[\alpha]^{25}_D$ +10° (*c* 1.0, $CHCl_3$). The substance has a double melting point, but when the lower melting polymorph was ground in an agate motar, it was converted to the higher melting form.

Anal. Calcd. for $C_{34}H_{53}NO$: C, 83.03; H, 10.86. Found: C, 82.73; H, 10.94.

3β-(Acetylamino)-5α-cholestane. 3-Oximino-5α-cholestane was reduced in amyl alcohol with sodium.[37] Acetylation[37] of the reduction product and recrystallization from 95% ethanol gave 3β-(acetylamino)-5α-cholestane: mp 248–251 °C; $[\alpha]^{26}_D$ +13° (*c* 1.5, $CHCl_3$) [lit.[37] mp 245–246 °C; $[\alpha]^{20}_D$ +12° (*c* 0.2, $CHCl_3$)].

3β-(Salicylideneamino)-5α-cholestane. When 3β-(acetylamino)-5α-cholestane was boiled in a mixture of concentrated hydrochloric acid and ethanol,[37] only partial hydrolysis occurred.[38] The amine in this mixture was converted to its *N*-salicylidene derivative, and the latter was purified by recrystallization from absolute ethanol as yellow plates: 58%; mp 187–188 °C (to an opaque liquid which became clear at 193 °C); $[\alpha]^{26}_D$ +40° (*c* 0.90, $CHCl_3$).

Anal. Calcd for $C_{34}H_{53}NO$: C, 83.03; H, 10.86; N, 2.85. Found: C, 82.94; H, 10.72; N, 2.88.

17β-Amino-5α-androstan-3β-ol (20a) was prepared, as described earlier[8] for the preparation of 17β-amino-5α-androstan-3α-ol, by reductive amination of 3β-hydroxy-5α-androstan-17-one with hydrazine hydrate, aluminum, and mercuric chloride in aqueous ethanol.[39] Purification by way of the amine hydrochloride and sublimation at 125 °C (0.02 mm) gave pure **20a**: 50%; mp 163–164 °C; $[\alpha]^{25}_D$ +14° (*c* 1.3, $CHCl_3$); $[\alpha]^{25}_D$ +15° (*c* 1.0, CH_3OH) (lit.[40] mp 163–164 °C).

17β-(Salicylideneamino)-5α-androstan-3β-ol was crystallized as a solvate from 95% ethanol as yellow platelets: mp 234–235 °C; $[\alpha]^{25}_D$ +115° (*c* 1.1, $CHCl_3$).

Anal. Calcd for $C_{26}H_{37}NO_2 \cdot 0.5C_2H_5OH$: C, 77.47; H, 9.63; N, 3.35. Found: C, 77.60; H, 9.76; N, 3.69.

Sublimation at 160 °C (0.03 mm) gave the pure derivative: mp 234–235 °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, 79.25; H, 9.43, N, 3.82.

17β-Amino-5-androsten-3β-ol (21) was purified by way of its hydrochloride salt. After purification and recrystallization from ethyl acetate, the pure amine had the following: mp 164–167 °C;

(31) Smith, H. E.; Cook, S. L.; Warren, M. E., Jr. *J. Org. Chem.* **1964**, *29*, 2265–2272.

(32) Rausser, R.; Weber, L.; Hershberg, E. B.; Oliveto, E. P. *J. Org. Chem.* **1966**, *31*, 1342–1346.

(33) That the 11α (equatorial) and the 11β (axial) isomers are formed predominantly by alkali metal and catalytic reduction, respectively, of the 11-oximino compound is in agreement with earlier reports in ref 32 and 34. That the 11β isomer was not removed from the major product after alkali metal reduction by recrystallization from acetonitrile is contrary to the report in ref 32.

(34) Campbell, A. C.; Maidment, M. S.; Pick, J. H.; Woods, G. F. *J. Chem. Soc., Perkin Trans. 1* **1979**, 1936–1940.

(35) Hunt, B. J.; Rigby, W. *Chem. Ind. (London)* **1967**, 1868–1869.

(36) Bose, A. K.; Kistner, J. F.; Farber, L. *J. Org. Chem.* **1962**, *27*, 2925–2927.

(37) Dodgson, D. P.; Haworth, R. D. *J. Chem. Soc.* **1952**, 67–71.

(38) Shoppee, C. W.; Ram, P.; Roy, S. K. *J. Chem. Soc. C* **1966**, 1023–1026.

(39) Schmitt, J.; Panouse, J. J.; Hallot, A.; Plucket, H.; Comoy, P.; Cornu, P.-J. *Bull. Soc. Chim. Fr.* **1964**, 771–775.

(40) Kuehne, M. E.; Konopka, E. A.; Lambert, B. F. *J. Med. Pharm. Chem.* **1962**, *5*, 281–296.

$[\alpha]^{27}_D$ –61° (c 0.5, $CHCl_3$) [lit.[39] mp 158–159 °C; $[\alpha]^{25}_D$ –67.8° (c 0.5, $CHCl_3$)].

17β-(Salicylideneamino)-5-androsten-3β-ol was sublimed at 160 °C (0.02 mm); mp 224–226 °C.

Anal. Calcd for $C_{26}H_{35}NO_2$: C, 79.34; H, 8.96. Found: C, 79.09; H, 8.95.

Registry No. (*S*)-**3b** *N*-salicylidene, 81477-47-6; (*S*)-**3c** *N*-salicylidene, 81477-48-7; **13a**, 5865-17-8; **13a** *N*-salicylidene, 21934-19-0; **13b**, 5865-18-9; **13b** *N*-salicylidene, 81520-64-1; **15a**, 2206-20-4; **15a** *N*-acetyl, 40937-16-4; **15a** *N*-salicylidene, 81477-49-8; **17a**, 2206-21-5; **17a** *N*-acetyl, 1912-64-7; **17a** *N*-salicylidene, 81496-95-9; **17b** *N*-salicylidene, 81477-50-1; **20a**, 7738-80-9; **20a** *N*-salicylidene, 21934-24-7; **21**, 4350-66-7; **21** *N*-salicylidene, 81477-51-2; **22** *N*-salicylidene, 81505-43-3; 11-oximino-5β-pregnane-3α,20β-diol, 5865-16-7; salicylaldehyde, 90-02-8; 3α-azido-5α-cholestane, 15067-20-6; 3-oximino-5α-cholestane, 2735-21-9; 3β-hydroxy-5α-androstan-17-one, 481-29-8.

Irigermanal and Iridogermanal: Two New Triterpenoids from Rhizomes of *Iris germanica* L.

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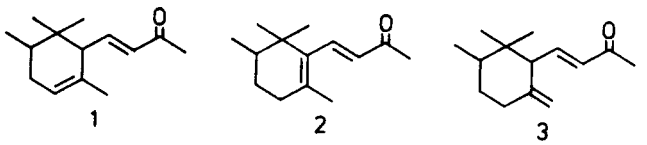
α-Irigermanal (**8a**), γ-irigermanal (**8b**), and iridogermanal (**12**) are the major extractable lipids of the rhizomes of *Iris germanica*, constituting about 1% of their fresh weight. The structure of the compounds was determined by detailed spectral analysis, chemical degradation, and X-ray crystallography. **8b** crystallizes as a methanol solvate in the space group $P2_1$ with a = 13.05 (1) Å, b = 8.84 (2) Å, c = 13.78 (1) Å, β = 105.84 (5)°, and Z = 2. The irigermanals are the first known bicyclic triterpenoids, and iridogermanal is the first monocyclic triterpenoid found so far. The compounds are closely related to ambreine.

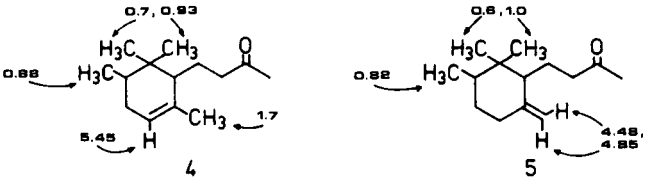
The sword-lily *Iris* has been cultivated since ancient times, and its rhizomes have been collected because they were known to contain, increasingly on storage, aromatic principles that were used to prepare perfumes and cosmetics with the fragrance of sweet violet.[1] It took some 50 years since the turn of the century and many controversies to determine the structures of the scent-carrying compounds as the three isomeric irones of 6-methylionones (**1** = α-irone, **2** = β-irone, **3** = γ-irone).[2] Just 10 years ago Rautenstrauch and Ohloff[3] published their final studies on the stereochemistry of these ketones.



1 **2** **3**

Our interest in the biosynthesis of the methylionones and the well-known fact that the irones do not occur in freshly harvested rhizomes, which have to be stored for years to contain the maximal amount,[4] led us to postulate that there have to be precursors that yield the ketones, possibly by oxidative degradation on storage.

Lipid extracts of the rhizomes of *Iris florentina* and *Iris pallida* right after their harvest do not contain irones. On treatment with various oxidizing agents ((pyridine)-chlorochromate, permanganate), however, violet-like scent is evolved, and it is possible to show the formation of irones by gas chromatography. On the other hand, the main oxidation product of such extracts from fresh *Iris germanica* rhizomes are two other compounds of slightly less polar behavior than the irones. Mass spectrometry gave a molecular ion at m/e 208. Comparison of the spectral properties and the gas chromatographic behavior with synthetic samples proved them to be α-dihydroirone (**4**)



and its γ-isomer (**5**). The presence of the corresponding precursors seems to depend on the season. We found **4** to be the major oxidation product in extracts from *I. germanica* rhizomes harvested in autumn, whereas **5** is mainly found in spring.

Isolation. To isolate the precursors of **4** and **5** the chopped rhizomes were extracted with methanol and chloroform; the combined extracts were concentrated to a viscous yellow oil. Silica gel and reversed-phase chromatography resulted in the isolation of glasslike iridogermanal and α- or γ-irigermanal, respectively.

Structure Determination. The mass spectra of α- and γ-irigermanal were almost identical. The molecular ion is m/e 472 and fragment ions are 457, 454, 439, 436, and 421 for loss of methyl groups and water. High-resolution mass measurements gave elemental compositions of $C_{31}H_{52}O_3$ for the molecular ions. The IR spectra and the loss of two molecules of water from the molecular ion implied the presence of two hydroxy groups. The third oxygen had to be an α,β-unsaturated aldehyde as shown by IR, NMR,

(1) Tschirch, A., "Handbuch der Pharmakognosie", C. H. Tauchnitz, Verlag, Leipzig, Germany, 1917.
(2) (a) Naves, Y. R., Grampoloff, A. V., and Bachmann, P., *Helv. Chim. Acta*, **30**, 1599 (1947); (b) Ruzicka, L., Schinz, H., Seidel, C. F., and Tavel, C., *ibid*, **30**, 1810 (1947).
(3) Rautenstrauch, V. and Ohloff, G., *Helv. Chim. Acta*, **54**, 1776 (1971).
(4) Crabalona, J., *Fr. Ses Parfums*, **13**, 22 (1959).

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