Moscowitz and Moffitt's case I where the ellipticity curve is simply proportional to the absorption curve.[10] The fitted rotatory strengths seem to be in accord with the points enumerated above.

We have observed that the spectrum of hexahelicene above 2200 Å. red-shifts with increasing hydrocarbon solvent density as do the spectra of other nonpolar polynuclear aromatics.[11] Thus, if the solvent dependence arises from shifting spectrum, the decrease of rotation cannot be accounted for by red-shifts of the positive Cotton curves. Most likely the decrease depends on a strong red-shifting negative Cotton curve centered at a wave length shorter than 3100 Å. Indeed, the m.o. calculation predicts such a rotational strength for a higher energy transition. In addition, the experimental rotatory dispersion measurements of Drs. Newman and Tsai out to 2750 Å.[12] are consistent with such a situation. That the change in optical activity arises from distortion of the helical pitch cannot be completely discounted but, to be sure, is not completely separable in theory from the origins of the spectral shift.

Certainly this study underscores the usefulness that parallel solvent effect studies on spectra and rotation might have in the interpretation of optical rotatory dispersion curves, especially were the latter measurements carried to the absorbing region. It also demonstrates what must be a contribution to environmental effects in more complex systems, one observable in the wings of the Cotton curve where nearly all characterizing measurements of protein and polypeptide systems are made,[13] and one not accounted for by the Lorentz field factor.

Acknowledgments.—Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for partial support of this research. A grant from the National Science Foundation under its Undergraduate Research Participation Program is also gratefully acknowledged by the participants (N. C. K., N. J. K., and T. C. C.).

(10) W. Moffitt and A. Moscowitz, *J. Chem. Phys.*, **30**, 648 (1959).

(11) O. E. Weigang, Jr., *J. Chem. Phys.*, **33**, 892 (1960). Shifts in polar solvents may be treated similarly; O. E. Weigang, Jr., and D. D. Wild, submitted to *J. Chem. Phys.*

(12) M. S. Newman and Lin Tsai, private communication of unpublished measurements.

(13) For several reviews see: (a) I. Tinoco, R. W. Woody and K. Yamaoka, *Tetrahedron*, **13**, 134 (1961); (b) J. T. Yang, *ibid.*, **13**, 143 (1961); (c) B. Jirgensons, *ibid.*, **13**, 166 (1961); (d) J. Strem, Y. S. R. Krisna-Prasad and J. A. Schellman, *ibid.*, **13**, 176 (1961); (e) J. R. Fresco, *ibid.*, **13**, 185 (1961); (f) P. O. P. Ts'o and G. Helmkamp, *ibid.*, **13**, 198 (1961).

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RECEIVED JANUARY 22, 1962

THE STEREOCHEMISTRY OF THE HETEROYOHIMBINE ALKALOIDS

Sir:

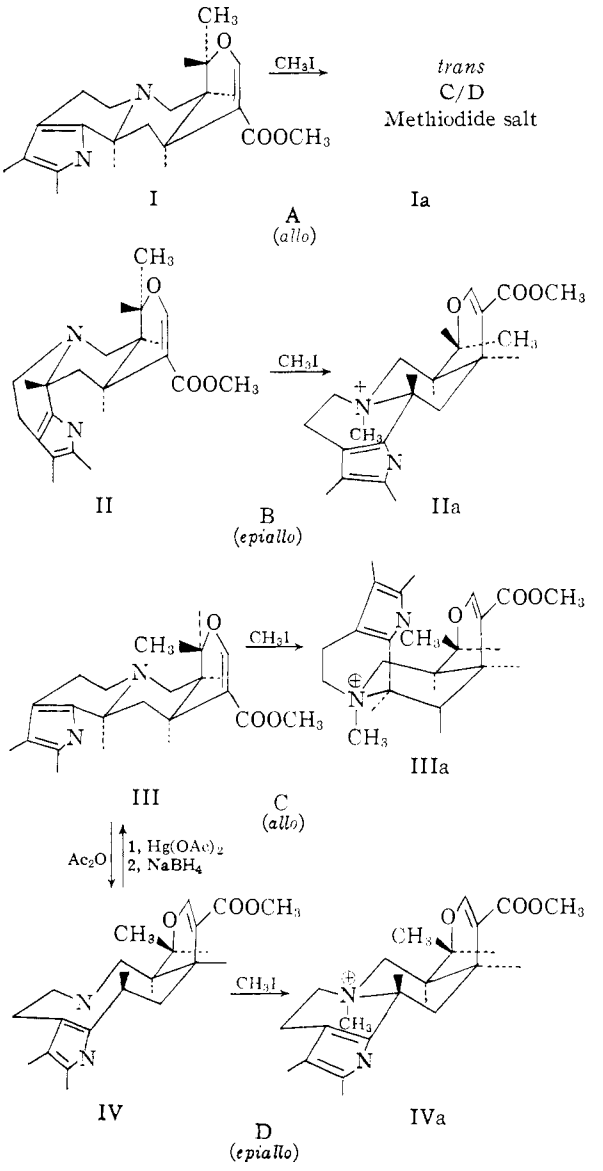
We here describe the complete stereochemistry of the alkaloids rauniticine, raunitidine, isoraunitidine, mayumbine, and raumitorine.[1,2]

(1) E. Wenkert, B. Wickberg and C. L. Leight, *J. Am. Chem. Soc.*, **83**, 5037 (1961).

(2) M. Shamma and J. B. Moss, *ibid.*, **83**, 5038 (1961).

The chemical shifts of the C-19 methyl groups in the n.m.r. spectra,[3] together with the known method of infrared analysis near 8.4 μ,[4] can be used to classify the heteroyohimbines into six stereochemical groups (represented by groups A to F in Table I).[5]

Despite the retention of the *trans*-quinolizidine system, the raunitidine to isoraunitidine isomerization involves only the asymmetric center at C-3,[6,7] since in our hands treatment of isoraunitidine with mercuric acetate and subsequent reduction of the Δ^3-perchlorate salt with sodium borohydride yielded only raunitidine.



(3) Measured with a 40 Mc. Varian NMR unit using deuteriochloroform as solvent and TMS as an internal standard.

(4) N. Neuss and H. E. Boaz, *J. Org. Chem.*, **22**, 1001 (1957).

(5) Although akuammigine was not in our possession, it can be placed in group B since it has been shown to be epimeric at C-3 with tetrahydroalstonine.

(6) R. Salkin, N. Hosansky and R. Jaret, *J. Pharm. Soc.*, **50**, 1038 (1961).

(7) F. Bohlmann, *Chem. Ber.*, **92**, 1798 (1959); and W. E. Rosen, *Tetrahedron Letters*, No. 14, 481 (1961).

TABLE I

THE HETEROYOHIMBINE ALKALOIDS

Groups and stereochemistry	Alkaloids	Free bases: C/D quinolizidine fusion (from infrared at 3.4μ)	Free bases: C-19 methyl chemical shift (and J in c.p.s.)	Free bases: ^{+}N-CH_3 chemical shift	Methiodide salts[a]: C/D fusion	Methiodide salts[a]: C-19 chemical shift (and J in c.p.s.)	Δ p.p.m. C-19 methyl base − salt
A (*allo*) C-19 CH_3:	Tetrahydroalstonine (I)	*trans*	1.38 (6.1)	3.42	*trans*	1.46 (5.8)	−0.08
α and e	Aricine		1.37 (6.3)	3.43		1.47 (5.4)	−0.10
	Reserpinine		1.38 (6.1)	3.39		1.48 (5.4)	−0.10
	Isoreserpiline		1.39 (6.2)	3.41		...	...
B (*epiallo*) C-19	Akuammigine (II)	*cis*	...	...	...	...	...
CH_3: α and e	Isoreserpinine		1.32 (6.5)	3.32	*trans*	1.39 (6.2)	−0.07
	Reserpiline		1.32 (6.3)	3.35		1.39 (5.7)	−0.07
C (*allo*) C-19 CH_3:	Rauniticine (III)	*trans*	1.42 (6.7)	3.50	*cis*	1.40 (6.5)	+0.02
β and a	Raunitidine		1.42 (7.1)	3.49		1.41 (6.1)	+0.01
D (*epiallo*) C-19	Mayumbine (IV)	*trans*	1.35 (6.3)	...	...	...	...
CH_3: β and e	Isoraunitidine		1.35 (6.8)	3.31	*trans*	1.43 (6.0)	−0.08
E (*normal*) C-19	Ajmalicine[b]	*trans*	1.16 (6.7)	3.35	*trans*	1.26 (6.2)	−0.10
CH_3: α and a	Tetraphylline		1.16 (6.5)	3.36		1.26 (6.2)	−0 10
F (*normal*) C-19	Raumitorine[c]	*trans*	...	...	...	...	...
CH_3: β and e							

[a] The n.m.r. spectra of the methiodide salts were obtained in formamide solution with TMS as an internal solvent. All spaces left blank signify that insufficient samples were available for the spectral measurements. [b] An early suggestion that the stereochemical proposals of Wenkert for the heteroyohimbine alkaloids needed to be modified was made by Professor E. E. van Tamelen at the 139th meeting of the American Chemical Society held in St. Louis, Missouri. [c] The C-3 hydrogen in raumitorine is *alpha* and axial as indicated originally by J. Poisson in his Docteur-ès-Sciences thesis, "Recherches sur les Alkaloides des Racines du *Rauwolfia vomitaria*," Department of Pharmacy, University of Paris, p. 46 (1959).

To settle whether the above isomerization was of the *allo* to *epiallo* type or *vice versa*, we had resort to a new criterion based on the n.m.r. chemical shifts of the ^{+}N-CH_3 protons of the corresponding methiodide salts. We found that, in analogy with Katritzky's original findings in a series of N-methylquinolizidinium cations,[8] the ^{+}N-CH_3 protons absorb at lower fields in salts with *cis*-fused C/D rings than in the *trans*-fused analogs. Hence raunitidine must be as in III, and must undergo a conformational change before methylation to yield ultimately IIIa which has a *cis*-fused C/D system. In other words, *it is the conformer with the less hindered nitrogen atom that undergoes methylation*. On the other hand, isoraunitidine must be represented by IV which methylates directly to the quaternary salt IVa. The conversion of raunitidine to isoraunitidine therefore involves an *allo* to *epiallo* isomerization.

To determine the stereochemistry of the C-19 methyl group, two lines of reasoning were used. First, it can be seen that the alkaloids of groups B and D although belonging to the *epiallo* series exist in different conformations, namely, II and IV, so that they can in each case accommodate the C-19 methyl group in the preferred equatorial configuration.

The second criterion is based on the chemical shifts of the C-19 methyl doublets in the n.m.r. spectra after treatment of the free bases with methyl iodide. As can be seen from Table I, the C-19 methyl groups of the methiodide salts experienced a downfield shift in relation to the corresponding free bases, due to the deshielding of the C-methyl protons by the net positive charge on the nitrogen. However, in group C a small upfield shift (~0.015 p.p.m.) was recorded. This apparent anomaly can be explained in terms of the immediate proximity of the C-19 methyl protons in III to Nb which leads to some hydrogen bonding and a consequent diamagnetic shift for the protons in question.

We have now defined the complete stereochemistry of two groups of *allo* and two of *epiallo* heteroyohimbines. The remaining two stereochemical groups are E and F. The alkaloids of group E are now known to be of the *normal* configuration with the C-19 methyl group *alpha* and axial.[1] Hence by a simple process of elimination raumitorine[9] in group F must also be *normal* but with the methyl group *beta* and equatorial.

Acknowledgments.—The authors wish to thank S. B. Penick and Co. for a most generous gift of rauniticine, raunitidine, and isoraunitidine, and Dr. R. Goutarel for providing samples of the rare mayumbine and raumitorine. We are grateful to the National Science Foundation for financial support (Grant No. NSF-G19876).

(8) A. R. Katritzky, private communication. This work on the stereochemistry of the quinolizidines will appear in the *Journal of the Chemical Society*.

(9) There was insufficient sample of raumitorine for an n.m.r. spectrum, but the infrared spectrum in carbon disulfide solution near 8.4μ clearly indicated this alkaloid to be different from any other heteroyohimbine here discussed.

(10) Recipient of pre-doctoral fellowship No. GF-17,292 from the Division of General Medical Sciences of the National Institutes of Health.

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RECEIVED FEBRUARY 2, 1962

ALKYLATION OF PHENOL WITH A HOMOALLYLIC CHLORIDE

Sir:

We wish to report on the uncatalyzed alkylation of phenol with 5-chloro-2-methyl-2-pentene (I). This reaction has uncommon features among which are the facile formation of a seven-membered cyclic