LEY and CARDWELL[3] were not able to utilize the relatively low D line rotation of anolobine (XIV) for a configurational assignment. However, it should be pointed out that so far rotatory dispersion measurements bear out their assumption[3] that a positive D line rotation is associated with absolute configuration I. We shall refrain from attempting to correlate at this time the rotatory dispersion behavior of the presently discussed aporphines and the previously investigated[12] elagitannin-derived polyalkoxy-biphenyls, since we are aware of the complexity in the relationship of rotatory dispersions and stereochemistry in these structural types[17].

Résumé. Les configurations absolues de certains alkaloïdes de l'aporphine ont été détérminées à partir de leurs courbes de dispersion rotatoire.

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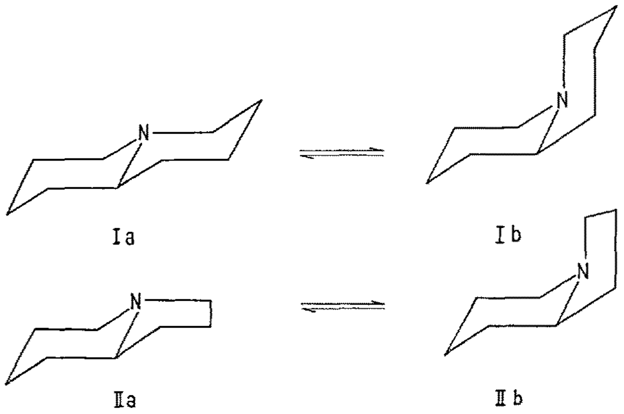
[17] *Acknowledgement.* We are indebted to the National Institutes of Health (grant CRTY-5061) of the U.S. Public Health Service and the National Science Foundation (grant G-10032) for financial assistance and to Mrs. RUTH RECORDS for the optical rotatory dispersion measurements. Thanks are also due to the following investigators for supplying samples of aporphine alkaloids: Drs. R. H. F. MANSKE, M. TOMITA, T. NAKANO, T. R. GOVINDACHARI, J. SCHMUTZ, and A. RUEGGER, and Sandoz Ltd.

The Stereochemistry of Quinolizidine and Octahydropyrocoline

In quinolizidine and octahydropyrocoline, due to easy inversion of the nitrogen atom, the energy barrier between *cis* and *trans*-fused forms[1] is low, and they may be termed as conformations. Conformational arguments attributing greater stability to the *trans*-fused forms (Ia and IIa) have been put forward by analogy with decalin and hydrindane systems[2-5]. However, if the findings of ARONEY and LE FEVRE[6] (the volume requirements of a nitrogen lone pair exceed those of hydrogen and approach the methyl group) are taken into consideration, these bases are more likely to resemble the corresponding carbocyclic systems with an angular methyl group.



Assigning, to the lone pair of the bridgehead nitrogen, an angular effect[7] of 0.8 kcal/*M* in favour of *cis*-fusion, we have estimated the enthalpy of the conversion I b $\rightleftharpoons$ I a to be roughly − 1.9 kcal/*M*. For octahydropyrocoline the enthalpy of conversion II b $\rightleftharpoons$ II a comes to be − 0.3 kcal/M. It is assumed that the replacement of carbon by nitrogen does not alter the geometry and consequently the thermodynamic constants for the corresponding carbocyclic systems[8] have been used in these estimations. The equilibrium, in the latter case at least, should lie further in favour of the *cis*-fused conformation, due to its greater entropy. This entropy effect may, however, be less prominent when bigger fused systems like E/F ring of solanidane nucleus are considered[9].

Several naturally occurring bases with these systems have substituents whose position (axial or equatorial) alters with the *cis* $\rightleftharpoons$ *trans* conversion, and this should be taken into consideration when predicting the position of the equilibrium. In cevine[10] ring E/F, for example, the C-25 methyl group is axial in the *trans* (IIIa) and equitorial in the *cis*-fused (IIIb) conformation. Using a destabilisation value of 2.4 kcal/*M*[11] for putting an axial methyl group *cis* to the nitrogen lone pair, the *cis*-fused conformation comes to be more stable by 0.5 kcal/*M*. In the case of lupinine[2], however, hydrogen bonding which is possible only in the *trans*-fused (IVa) conformation may shift the equilibrium in its favour.

BOHLMANN[3] has demonstrated that *trans*-fused quinolizidines, in which the nitrogen lone pair is *trans* to at least two axial hydrogen atoms on carbon adjacent to it, show a prominent band in the 2800–2700 cm^{-1} region. This criterion has often been used to assign *trans*-fused conformations to such systems[3-5,12]. Further MOYNEHAN et al.[5], on the basis of I.R. and N.M.R. evidence, have

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[1] In systems where one of the rings is frozen only one of the two possible *cis* isomers (with N–C bond axial with respect to the frozen ring) is easily convertible to the *trans* form.

[2] R. C. COOKSON, Chem. and Ind. *1953*, 337. It is suggested that compared to decalin the *cis trans* energy difference may be greater in quinolizidine because it has one less angular hydrogen.

[3] F. BOHLMANN, Chem. Ber. *91*, 2157 (1958).

[4] N. J. LEONARD and W. K. MUSKER, J. Amer. chem. Soc. *82*, 5148 (1960).

[5] T. M. MOYNEHAN et al., Proc. chem. Soc. *1961*, 218.

[6] M. ARONEY and R. J. W. LE FEVRE, Proc. chem. Soc. *1958*, 82; J. chem. Soc. *1958*, 3002; J. chem. Soc. *1960*, 2161. See also D. H. R. BARTON and R. C. COOKSON, Quart. Rev. *10*, 44 (1956).

[7] The 0.8 kcal/*M* value is arbitrarily chosen on the assumption that the effect of nitrogen lone pair is half that of the angular methyl group ($^1/_2$ × two 0.8 kcal/*M* skew interactions).

[8] N. L. ALLINGER and J. L. COKE, J. Amer. chem. Soc. *81*, 4080 (1959); *cis* decalin $\rightleftharpoons$ *trans* decalin, ΔH = −2.7 kcal/*M*; J. Amer. chem. Soc. *82*, 2553 (1960), *cis* hydrindane $\rightleftharpoons$ *trans* hydrindane, ΔH = −1.1 kcal/*M*.

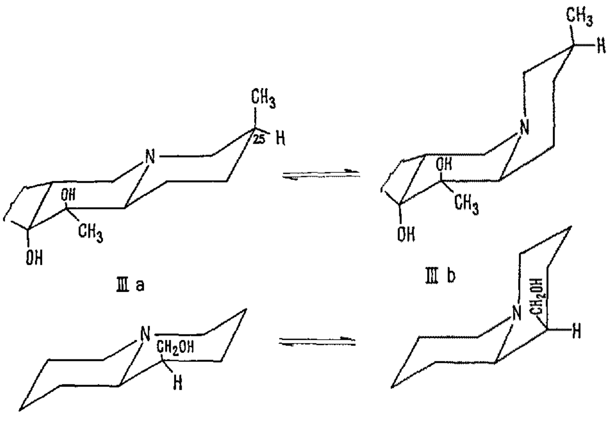
[9] N. L. ALLINGER, J. org. Chem. *21*, 915 (1956).

[10] S. M. KUPCHAN, W. S. JOHNSON, and S. RAJAGOPALAN, Tetrahedron *7*, 47 (1959).

[11] The 2.4 kcal/*M* value is arbitrarily chosen, 1.6 kcal/*M* for axial methyl and 0.8 kcal/*M* additional for its being *cis* to the nitrogen lone pair.

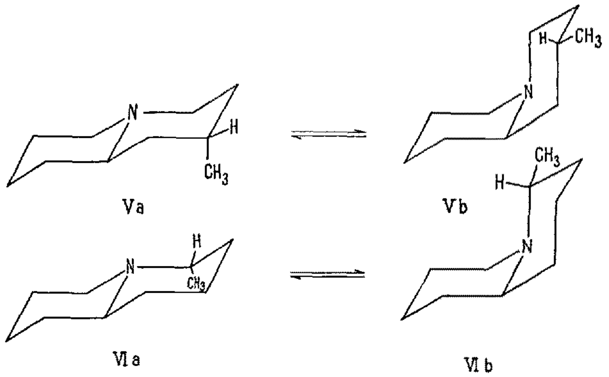
[12] Y. SATO and N. IKEKAWA, J. org. Chem. *26*, 1945 (1961).

concluded that *trans*-2-methylquinolizidine (the prefix referring to the relative configuration of 10-hydrogen atom with respect to that at position 2) exists in the *trans*-fused conformation Va, whereas for *trans*-4-methylquinolizidine the *cis*-fused conformation VI b is preferred.



III a III b

IV a IV b



Va Vb

VI a VI b

On usual conformational analysis basis, the equilibria Va–Vb and VI a–VI b should have similar reaction energies and the proportion of the *trans*-fused conformation should be similar in each of the equilibria[13]. The seemingly glaring difference in the two equilibria is difficult to explain even if it is allowed, for the sake of argument, that their reaction energies differ by about 1.6 kcal/M [$\Delta\Delta F = \Delta F$ (Vb–Va) $- \Delta F$ (VI b–VI a) $= 1.6$]. In such a case, simple calculations for 27°C show that at least 50% of Vb should be present at equilibrium, the proportion of VI a at equilibrium being assumed to be less than 5% (no absorption in 2800–2700 cm^{-1} region[5]). Apparently the I.R. and the N.M.R. criteria as such are able to detect only the presence of *trans*-fused conformations and are inadequate to exclude even substantial quantities of the *cis*-conformations. Alternatively, the simple conformational analysis developed on carbocyclic systems is not applicable to nitrogen systems and special steric or electronic effects are operative[14].

Zusammenfassung. Eine Abschätzung der relativen Stabilität der *cis*- und *trans*-Konformationen von Chinolizidin, Octahydropyrocolin sowie einigen ihrer Abkömmlinge wird durchgeführt. Unter Berücksichtigung des Einflusses des isolierten Elektronenpaars am Brückenkopf-Stickstoff ergibt sich eine grössere Stabilität für die *cis*-Verbindungen.

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Department of Chemistry, Panjab University, Chandigarh (India), October 9, 1961.

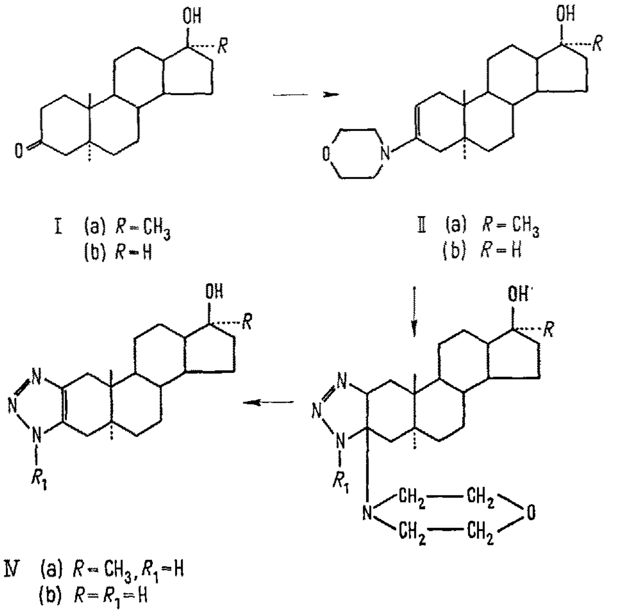
[13] Both VI a and VI b have an extra skew interaction as compared to Va and Vb.

[14] It is difficult to explain the observation of MOYNEHAN[5] et al. that, as compared to *trans*-4-methylquinolizidine, the *trans*-fused conformation is favoured for *cis*-1-methylquinolizidine and *cis*-3-methylquinolizidine (both having an axial methyl group *cis* to the nitrogen lone pair), except on the basis that the presence of three hydrogens *trans* to the nitrogen lone pair makes the latter two detectable in lower concentrations.

A New Series of Potential Anabolic Steroids: [2,3-*d*]-Triazolosteroids

FUSCO[1], in the course of an extensive research on enamines of alicyclic ketones, was able to demonstrate that different azides react with these compounds to give 1,2,3-triazoles. These results prompted us to extend this process to the enamines of some 3-ketosteroids in order to obtain steroidal molecules, in which ring A is condensed with a triazole ring.

The anabolic activities of some androstane derivatives, in which ring A is fused with various heterocyclic rings (pyrazole, isoxazole)[2–5], enhanced our interest in this



I (a) $R=CH_3$
(b) $R=H$

II (a) $R=CH_3$
(b) $R=H$

IV (a) $R=CH_3, R_1=H$
(b) $R=R_1=H$

V (a) $R=CH_3, R_1=C_6H_5$
(b) $R=H, R_1=C_6H_5$

III (a) $R=CH_3$, $R_1=C_6H_5-CH_2OCO$
(b) $R=H$, $R_1=C_6H_5-CH_2OCO$

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[1] We are indebted to Prof. Dr. R. FUSCO for the information on his results prior to publication. Our work in this field is a direct extension of this information. The contribution of Prof. R. FUSCO to this research is gratefully acknowledged.

[2] R. O. CLINTON, A. J. MANSON, F. W. STONNER, A. L. BEYLER, GR. O. POTTS, and A. ARNOLD, J. Amer. chem. Soc. *81*, 1513 (1959).

[3] Belgian patent 580, 902.

[4] A. ARNOLD, A. L. BEYLER, and G. O. POTTS, Proc. Soc. exp. Biol. Med., N.Y. *102*, 184 (1959).

[5] G. O. POTTS, A. L. BEYLER, D. F. BURNHAM, Proc. Soc. exp. Biol. Med., N.Y. *103*, 383 (1960).