XMP to GMP reactions occurred with no extensive dilution of specific activity.

The mechanisms of the amination reactions are being investigated. Carter and Cohen[5] have reported the formation of adenylosuccinic acid from AMP and fumaric acid. It seems likely that this compound is an intermediate in AMP formation from IMP, and that the corresponding guanyloglutaric acid is an intermediate in GMP formation from XMP.

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(5) C. E. Carter and L. H. Cohen, THIS JOURNAL, **77**, 499 (1955).

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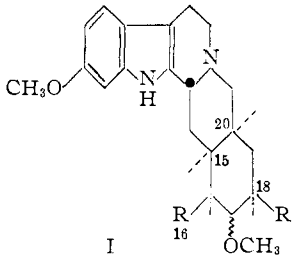
RAUWOLFIA ALKALOIDS. XXII. FURTHER OBSERVATIONS OF THE STEREOCHEMISTRY OF RESERPINE

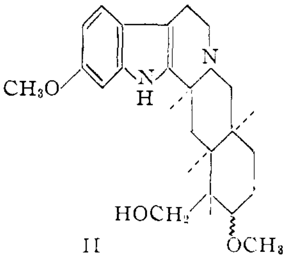
Sir:

Four lines of evidence have been offered recently in support of Ia as representing the stereochemistry of reserpine[1,2]: (1) the C-3 epimerization of reserpine, (2) molecular rotational differences indicating β-orientation of the C-3 hydrogen, 16-carbomethoxyl and 18-acyloxy groups, (3) the inability of 3-isoreserpic acid to lactonize and (4) data strengthening the presently accepted structures of allo- and 3-epialloyohimbane. We now wish to describe new findings demonstrating conclusively the validity of Ia.

When 3-iso-reserpinol (II)[3] was treated with *p*-toluenesulfonyl chloride in pyridine at room temperature overnight, a substance crystallized directly from the reaction mixture in high yield. An inspection of its properties made it evident that the substance must be a quaternary salt. It has a high melting point (320–330° (dec.)) and is virtually insoluble in chloroform. Analysis indicated it to be a mixed tosylate–chloride salt. *Anal.* Calcd. for $C_{22}H_{29}N_2O_2^+ \cdot 0.6\ SO_3C_7H_7^- \cdot 0.4Cl^-$: C, 66.86; H, 7.09; N, 5.96; S, 4.09; Cl, 3.02. Found: C, 66.64; H, 7.10; N, 6.02; S, 3.89; Cl, 2.87. Addition of an excess of sodium iodide to a hot aqueous solution gave an immediate precipitate of the crystalline iodide salt (m.p. 360–365° (dec.)). *Anal.* Calcd. for $C_{22}H_{29}N_2O_2^+ \cdot I^-$: C, 54.98; H, 6.10. Found: C, 55.33; H, 6.17. A free base extractable in chloroform could not be liberated from the salt with dilute ammonia. The infrared spectrum of the mixed tosylate–chloride salt showed the bands characteristic of the *p*-tosylate ion[4] and the presence of chloride ion was revealed by an instantaneous precipitate with silver nitrate. Formulation of this quaternary salt as III requires a *cis* relationship of the hydrogens at C-15 and C-16 restricting the stereochemistry of reserpine to Ia. Similarly, reserpinol (Ib)[5] gave a quaternary tosylate best characterized as its iodide salt (m.p. 315–316° (dec.)).

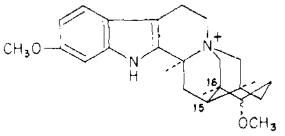


I



II

a: R = —COOCH$_3$, R′ = —OCOC$_6$H$_2$(OCH$_3$)$_3$
b: R = —CH$_2$OH, R′ = H.



III

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(1) C. F. Huebner, H. B. MacPhillamy, E. Schlittler and A. F. St. André, *Experientia*, in press.

(2) E. Wenkert and L. H. Liu, *ibid.*, in press.

(3) H. B. MacPhillamy, C. F. Huebner, E. Schlittler, A. F. St. André and P. R. Ulshafer, THIS JOURNAL, in press.

(4) P. A. Diassi, F. H. Weisenborn, C. M. Dylion and O. Wintersteiner, *ibid.*, **77**, 2028 (1955).

(5) C. F. Huebner, H. B. MacPhillamy, A. F. St. André and E. Schlittler, *ibid.*, **77**, 472 (1955).

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STUDIES IN THE SYNTHESIS OF THE ANTIRACHITIC VITAMINS. III. THE SYNTHESIS OF 1-CYCLOHEXYLIDENE-2-[5′-METHOXY-2′-METHYLENECYCLOHEXYLIDENE-1′]-ETHANE

Sir:

Several years ago we reported[1] the synthesis of a simple model (I) of vitamin D. However, subsequent work in this Laboratory[2] showed that the method used was impractical for the synthesis of vitamin D_2 or D_3. In view of work undertaken in other laboratories[3] we wish to report at this time the synthesis of 1-cyclohexylidene-2-[5′-methoxy-2′-methylenecyclohexylidene-1′]-ethane (III) using a method which can easily be adapted for the synthesis of all vitamin Ds.

Cyclohexylidene acetaldehyde (6.8 g.)[4,5] prepared by the chromic acid oxidation[6] of 1-ethenylcyclohexanol-1 was allowed to condense with 14 g. of 4-methoxycyclohexanone with stirring under nitrogen in 900 cc. of methanol containing 4 g. of sodium hydroxide and 10 cc. of water. After twelve hours the mixture was acidified and from it was obtained 6.1 g. (58.6%) of the ketone (II), recrystallized from ligroin, m.p. 79.5–80.5°. *Anal.* Calcd. for (II): C, 76.92; H, 9.46; mol. wt., 234. Found: C, 76.77; H, 9.45; mol. wt. (in exaltone), 224; ϵ (309 mμ), 29,100. The infrared spectrum shows strong bands for the dienone. 2,4-Dinitrophenylhydrazone, m.p. 178–179°. *Anal.* Calcd. for $C_{21}H_{26}N_4O_5$: C, 60.86; H, 6.33; N, 13.52. Found: C, 61.05; H, 6.68; N, 13.66.

The ketone (II) was allowed to react with freshly

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(1) N. A. Milas and W. L. Alderson, Jr., THIS JOURNAL, **61**, 2534 (1939).

(2) Unpublished results.

(3) I. T. Harrison, B. Lythgoe and S. Trippett, *Chem. and Ind.*, April, 507 (1955).

(4) J. B. Aldersley, G. N. Burkhardt, A. E. Gillam and N. C. Hindley, *J. Chem. Soc.*, 10 (**1940**).

(5) V. K. Paranjpe, N. L. Phalnikar and B. V. Bhide, *J. Univ. Bombay*, **28**, 38 (1949–50).

(6) R. Kuhn and C. Grundmann, *Ber.*, **70**, 1897 (1937).