copolymer" character presumably is responsible for the variation in X-ray and physical property data observed with type III poly-(methyl methacrylate). The exact nature of the crystals themselves is under more intensive investigation.

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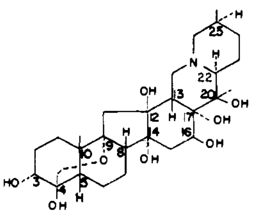
THE CONFIGURATION OF CEVINE

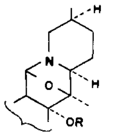
Sir:

The configurations of nine (C_3, C_4, C_5, C_9, C_{10}, C_{12}, C_{14}, C_{17}, C_{25}) of the fourteen asymmetric centers of cevine were established almost simultaneously with the climactic structure elucidation in 1954–55.[1–3] Recent work in our laboratory made possible assignment of configuration at C_{16} and C_{20} and provides support for previously considered[1] configurational assignments at C_8 and C_{13}.[4] Evidence is presented herewith for assignment of configuration at the remaining asymmetric center (C_{22}) of cevine which now can be represented completely by formula I. It is highly probable that closely related alkaloids, such as zygadenine and germine, also have this basic configuration.

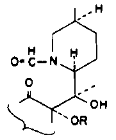
Oxidation of veracevine D-orthoacetate triacetate (IIa)[5] (pK_a' 7.4) with N-bromosuccinimide[6] yielded a dehydro compound (m.p. 280–282° dec., $[\alpha]_D$ +33° diox.; found, C, 63.51; H, 7.35; Ac, 25.52), evidently the bridged oxide IIIa for the following reasons. (1) The pK_a' (found, 3.8) was in the lower range expected for a stable carbinolamine ether.[7] (2) The infrared spectrum showed no absorption in the hydroxyl region. (3) The 16-acetate group survived prolonged treatment with methanol and triethylamine, an indication of the absence of an axial hydroxyl at C_{20} to facilitate methanolysis.[4] (4) Chromic anhydride-pyridine oxidation of IIIa afforded a neutral product (m.p. 263–264° dec., $[\alpha]_D$ +54° diox., $\lambda_{\max}^{\text{chf}}$ 6.07 μ, –NCO–, found, C, 60.59; H, 7.17), evidently the formamido ketone IVa. Acid hydrolysis afforded one mole equivalent of formic acid. Alkaline hydrolysis of the corresponding formamido ketone IVb (m.p. 288° dec., $[\alpha]_D$ +52° py., $\lambda_{\max}^{\text{chf}}$ 6.07 μ; found, C, 60.98; H, 7.08) derived from cevine gave the desacetyl-formamido-ketone IVc (m.p. 259–260° dec., $[\alpha]_D$ +22° py., found, C, 61.66; H, 7.24). In addition to the amide band, the infrared spectrum of this substance exhibited normal ketone absorption at 5.85 μ.



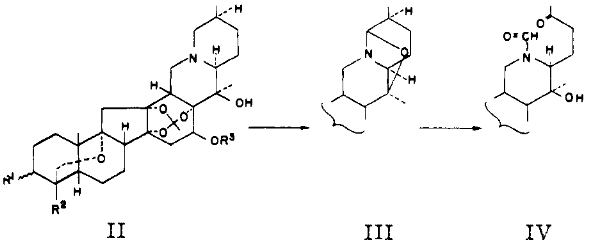
I



V



VI



II III IV

a (R^1 = β-OAc, R^2 = OAc; R^3 = Ac)
b (R^1 = α-OAc, R^2 = OAc; R^3 = Ac)
c (R^1 = α-OH, R^2 = OH; R^3 = H)

The alternative formulations V and VI for the oxide and formamido ketone were excluded on the basis of the following evidence. (1) The formamido ketone IVb derived from cevine readily formed a semicarbazone (m.p. 273–274° dec.; found, C, 57.91; H, 6.80, N, 6.93). (2) The formamido ketone IVa showed active methylene group reactivity in the Zimmermann test[8] and upon treatment in alkaline solution with furfural. (3) The corresponding formamido ketone (m.p. 253–255° dec., $[\alpha]_D$ −83° diox.; found, D, 60.96; H, 7.10) from cevagenine-C-orthoacetate diacetate[5] was, like the parent alkaloid, stable to lead tetraacetate. This behavior is characteristic of a rigid *trans* diaxial glycol system at C_{17}, C_{20}, a situation clearly not satisfied by VI.

The bridged *β-oriented* oxide structure of IIIa and b requires that the hydrogen at C_{22} be α-oriented. That the stereochemical integrity of the molecule was preserved during the oxide formation was demonstrated by catalytic hydrogenation of IIIa over platinum in acetic acid. Two mole-equivalents of hydrogen was absorbed to give a substance identical with the product of hydrogenation (one mole-equivalent uptake) of IIa, namely veracevine-D-dihydroorthoacetate triacetate (m.p. 299–300° dec., $[\alpha]_D$ +21° diox.; found, C, 63.53; H, 7.85; Ac, 19.98).[1,9]

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16α-CHLORO- AND 16α-IODOESTRONE METHYL ETHER, NEW AND POTENT LIPID-SHIFTING AGENTS

Sir:

The problem of finding estrogen-like substances capable of altering blood lipid composition, and which at the same time are not feminizing, is important in clinical treatment of atherosclerosis. A