Peyote and Related Alkaloids XIV: Mescaloxylic Acid and Mescaloruvic Acid, the Novel Amino Acid Analogs of Mescaline

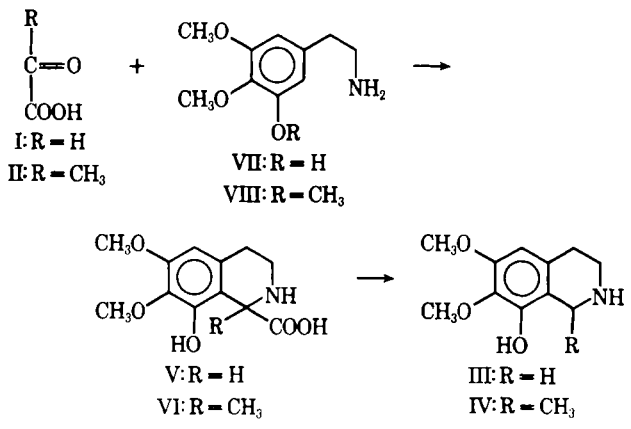
Keyphrases ☐ Peyote alkaloids—synthesis of new amino acid analogs of mescaline, mescaloxylic and mescaloruvic acids ☐ Mescaline amino acid analogs—synthesis of mescaloxylic and mescaloruvic acids ☐ Mescaloxylic acid—synthesized as amino acid analog of mescaline ☐ Mescaloruvic acid—synthesized as amino acid analog of mescaline ☐ NMR spectroscopy—characterization, synthetic amino acid analogs of mescaline

Sir:

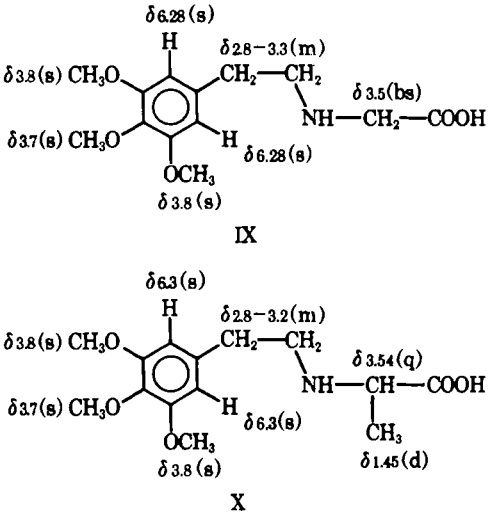
In our recent biosynthetic studies (1) on the peyote tetrahydroisoquinoline alkaloids, we showed that glyoxylate (I) and pyruvate (II) could account for the origin of the C-1 carbon and C-1/C-9 two-carbon units in anhalamine (III) and anhalonidine (IV), respectively, *via* peyoxylic (V) and peyoruvic acids (VI) (Scheme I). The reductive amination of I and II by 3-demethylmescaline (VII) apparently leads to the formation of the acids V and VI, the *N*-alkyl α-amino acid analogs of glycine and alanine.

In a continuation of studies on the peyote constituents, we considered the involvement of mescaline (VIII), the major base of the cactus, in the reductive amination of glyoxylate and pyruvate. If this reaction were to occur, the formation of two types of products appears likely. First, the more obvious products would be the *O*-methyl ethers of V and VI formed by a Pictet–Spengler type of reaction. Since mescaline lacks an activating phenolic group, the formation of the C-1 carboxytetrahydroisoquinolines V and VI could be expected to a less extent than in the case of 3-demethylmescaline. Earlier, however, we encountered (2) several Krebs cycle conjugates of mescaline in the peyote cactus.

On the other hand, the second possibility involves the less apparent reaction of mescaline with glyoxylate and pyruvate to form the open-chain analogs of glycine and alanine, IX and X, respectively. In the present communication, we report the synthesis and identification of IX and X, designated mescaloxylic and mescaloruvic



Scheme I



Scheme II

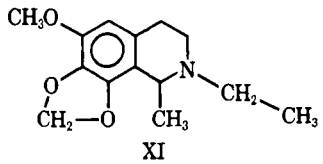
acids, respectively, as trace constituents of the peyote cactus.

Mescaloxylic acid (IX)[1] was synthesized by reacting glyoxylic acid and mescaline in methanol at pH 5 in the presence of the reducing agent $NaBH_3CN$ (yield 63%). Under identical conditions, reductive amination of pyruvic acid by mescaline gave racemic mescaloruvic acid (X)[1] (yield 57%). Alternatively, X could also be obtained by refluxing α-chloropropionic acid and mescaline in dioxane (yield 37%).

The synthetic acids IX and X were characterized by NMR (CD_3OD solvent) and mass spectrometry (Schemes II and III). The noncyclic nature of the two acids is substantiated by the presence of two equivalent aromatic protons in their NMR spectra and the dominant β-bond cleavage with respect to the aromatic ring in the mass spectra of their ditrimethylsilyl (di-TMS) derivatives, IX*a* and X*a*.

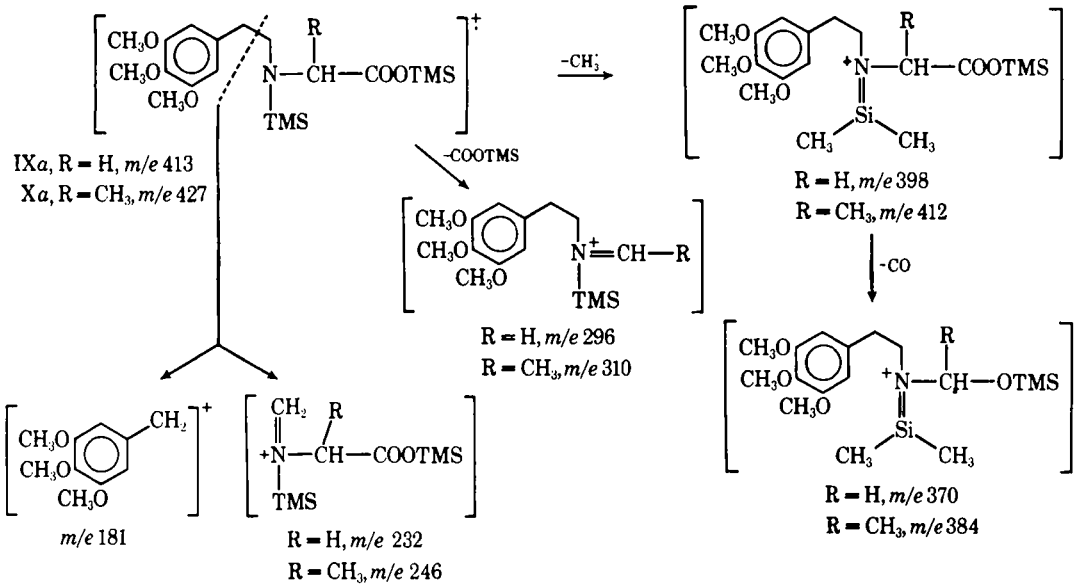
Paper chromatography of the peyote amino acid fraction (1) indicated the presence of mescaloxylic and mescaloruvic acids, which were then separated from other amino acids by preparative paper chromatography. The identity of the isolated acids IX and X was established by GC–mass spectrometry (1) of their ditrimethylsilyl derivatives.

Currently, we are investigating the role, if any, of the new amino acids IX and X in the biogenesis of the peyote alkaloids. In particular, it is of interest to test whether mescaloruvic acid (X) or its *O*-methyl analog would serve as the precursor to the rare *N*-ethyl group containing alkaloid, peyophorine (XI) (3). Also, the



XI

[1] Analytical samples of the synthetic new acids were obtained by recrystallization from ethanol to yield colorless crystals, IX, m.p. 187–189°, and X, m.p. 235–236.5°. Both new compounds gave satisfactory analyses.



Scheme III

plausible involvement of mescaloxylic acid (IX) in the biogenesis of *N*-methylmescaline is being considered. In both of these cases, the decarboxylation of the acids IX and X is an essential step. Finally, we are also currently evaluating the biological activity of the reported new compounds.

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(3) G. J. Kapadia and H. M. Fales, *J. Pharm. Sci.*, **57**, 2017 (1968).

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Received December 20, 1971.
Accepted for publication April 19, 1972.
Presented in part to the APhA Academy of Pharmaceutical Sciences, San Francisco meeting, March 1971.
The authors are grateful to Dr. Henry M. Fales for valuable discussions. Studies at Howard University were generously supported by the National Institute of Mental Health, Grant MH 15573.

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BOOKS

REVIEWS

Dispensing of Medication, 7th ed. (Formerly Husa's Pharmaceutical Dispensing). Edited by E. W. MARTIN. Mack Publishing Co., 20th and Northampton Sts., Easton, PA 18042, 1971. 1223 pp. 18.5 × 26 cm. Price $19.00.

The editor's intent is clearly stated in the Preface: "...this new edition has directed its emphasis toward the new concept of clinical pharmacy as it relates to every pharmacist whether he serves in a community or hospital practice, in governmental or private practice, in an extended care facility, a community health center, or some other environment where he works closely with both physicians and patients." Let us pause for a minute to consider the Promise of the Preface and ask ourselves what is to be expected from such a textbook. First of all, since clinical pharmacy is the goal, one would expect an in-depth exploration of this shadowy concept. Furthermore, one might expect a detailed description of the various drug distribution systems (including automated dispensing) as they apply to community pharmacies, institutional pharmacies, and extended care facilities. Additionally, a how-to-do-it discussion of extemporaneous sterile technique (including i.v. additives) would appear to be appropriate. Patient medication profiles are here to stay, and thus one might expect at least a chapter on the various types, their utilization, and some evaluation of the various designs. The list of potential *in-depth* topics is long (*e.g.*, the various automated or computerized information systems, third-party payment, novel methods of receiving compensation) but let us end it here and crack open the book to see what it contains.

The Table of Contents is not encouraging. At first glance, it looks like a traditional dispensing textbook, a potpourri of the various pharmaceutical sciences (physical pharmacy, pharmaceutics, pharmaceutical technology, *etc.*). But no, there are a few new chapters which did not appear in the previous edition: Hospital Phar-