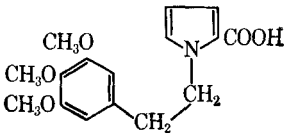
Peyote Alkaloids IV. Structure of Peyonine, Novel β-Phenethylpyrrole from *Lophophora williamsii*

Sir:

In a recent study on the peyote alkaloids, we reported (1, 2) isolation of five crystalline quaternary bases, four of which were identified. A sixth quaternary base was obtained in a purified form and a seventh crystalline compound was a nonalkaloidal substance. Further work on the peyote constituents resulted in an isolation of an eighth new compound designated peyonine.[1] Structural study on peyonine is the subject of this communication and has revealed that this is a novel β-phenethylpyrrole.

Peyonine, m.p. 131–133.5°, isolated from purified methanolic extracts of *Lophophora williamsii* (Lem.) Coult., shows a positive Ehrlich reaction, indicating the presence of an indole, a pyrrole, or a phenolic compound (3, 4). The mass spectrum (Fig. 1) is characterized by peaks at *m/e* 305 (parent), 261 (loss of a carbon dioxide), and 181 (base, evidently the trimethoxybenzyl ion, see below). The IR spectrum revealed a broad hydroxyl peak at 3600–2500 cm.$^{-1}$, a carbonyl peak at 1670, and aromatic peaks at 1595, 820, and 750 cm.$^{-1}$ The ultraviolet absorption spectrum in methanol showed a maximum at 261 mμ (ε10,000) which base shifted to 257 (9700), and acid shifted to 266 (10,700). The NMR spectrum ($CDCl_3$, TMS = 0) revealed a broad peak at 10.70 p.p.m. (1 H, COOH), 6.32 (2 H singlet, polyoxygenated aromatic), 4.35 and 2.98 (2 H each, triplets, A_2X_2, $ArCH_2CH_2$), and 3.85 (9 H, singlet, aromatic OCH_3); in benzene this last peak appeared as two singlets, 3.63 (6 H) and 3.85 [3 H, *o,o'* disubstituted aromatic methoxyl (6)]. Multiplets at 7.15, 6.70, and 6.12 (1 H each) are assigned to the protons of an *N*-substituted pyrrole-2-carboxylic acid. The spectral properties of pyrrole-2-carboxylic acid substantiated this assignment. IR (KBr) carbonyl: 1660; aromatic 1550; 750 cm.$^{-1}$; UV, $\lambda_{max.}^{MeOH}$ 261 mμ(ε 13,200) (8), shifted by base to 254 (12,000) and by acid to 263 (14,700). The spectral data and the biogenetic considerations suggested that peyonine was most likely 1-(β-3′, 4′, 5′-trimethoxyphenylethyl)-pyrrole-2-carboxylic acid (I).



I

The assigned structure I was confirmed by the synthesis of peyonine. Treatment of mescaline with methyl 2,5-dimethoxytetrahydro-2-furoate (9) in refluxing glacial acetic acid produced peyonine methyl ester. Saponification furnished crystalline peyonine identical (TLC, GLC, UV, IR, NMR, and mixed m.p. undepressed) with the isolated compound.

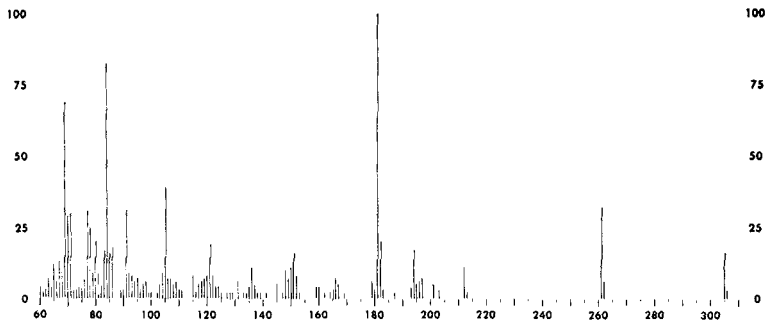


Fig. 1—Mass spectrum of peyonine.

Although proline (2-pyrrolidinecarboxylic acid) is an amino acid of wide natural occurrence, peyonine appears to be the first simple pyrrole-2-carboxylic acid derivative isolated from natural source, its structure elucidated, and the assigned structure proven by a synthesis.

It seems reasonable to speculate that the pyrrole ring of peyonine is produced in the plant by condensation of a 1,4-dicarbonyl compound such as an α-ketoglutaric acid derivative or its equivalent with mescaline or its precursors. The biosynthesis of peyonine, the preparation of com-

[1] Isolation and synthesis of peyonine have been separately reported. (See *Reference 7* for the published abstract.)

pounds related to the isolated β-phenylethylpyrrole, and pharmacological studies of peyonine and related compounds are currently being investigated.

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Keyphrases

Peyote alkaloids
Peyonine structure determination
Mass spectrometry
IR spectrophotometry—structure
UV spectrophotometry—structure
NMR spectrometry

Remarks on Synthesis of Benzofurans

Sir:

A recent note in this Journal by P. K. Sharma *et al.* (1) reported the synthesis of several substituted benzofurans. It appears, however, that there are some discrepancies in this report worthy of further mention.

The authors describe the reaction of benzyl bromide with hydroxymethyl propiophenone,[1] and *p*-nitrobenzyl bromide with 2-hydroxypropiophenone and 2-hydroxy-3-aceto-6-methylpropiophenone to yield, respectively, 4-methyl-6-phenylbenzofuran, 2-(*p*-nitrophenyl)benzofuran, and 2-aceto-5-methyl-7-nitrophenylbenzofuran. The products to be expected (2) in the first two cases, respectively, are 2-phenyl-3-ethyl-5-methylbenzofuran and 2-(*p*-nitrophenyl)-3-ethylbenzofuran, while in the third case the product might be expected to be 2-(*p*-nitrophenyl)-3-ethyl-4-methyl-7-acetylbenzofuran and/or 2-(*p*-nitrophenyl)-3,6-dimethyl-7-propionylbenzofuran. On first consideration the discrepancies appear to be one of nomenclature (2, 3), but additional contemplation reveals the problem to be an error on the part of the authors. Utilizing the reactants and conditions stated it is impossible to obtain the products alleged. Since the authors offer no analytical data or spectra to substantiate their claims, it is doubtful as to the true nature of the products. For example, the authors report the melting point of their alleged 2-(*p*-nitrophenyl)benzofuran to be 193°, while the literature value (4), substantiated by a good carbon–hydrogen analysis, is 182°. Indeed, in view of the same literature report (4), the reaction between benzyl bromide and hydroxymethyl propiophenone might *not* be expected to proceed under the *mild* conditions described, but might terminate at the benzyloxy stage.[2] Finally, the structure depicted for their alleged compound 2-aceto-5-methyl-7-nitrophenylbenzofuran is actually 1-methyl-4-acetyl-8-nitro*di*benzofuran (2).

[1] Private communication from P. K. Sharma, reveals that 2-hydroxy-5-methyl propiophenone is the "hydroxymethyl propiophenone" described.

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[2] P. K. Sharma notes in a private communication that potassium hydroxide, not potassium carbonate as reported, was used.

Keyphrases

Benzofurans—synthesis
Product identity (published) questioned