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SHORT COMMUNICATION

# ISOLATION OF ISODIHYDROQUINAMINE FROM *ISERTIA HYPOLEUCA**

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Abstract-A new dihydroindole alkaloid, isodihydroquinamine, has been isolated from the leaves of *Isertia hypoleuca* Benth. Chemical and spectroscopic data show it to be a stereoisomer of dihydroquinamine, which was previously isolated from the same plant.

## INTRODUCTION

IN A PRECEDING communication[1] we reported the isolation and characterization of the alkaloid dihydroquinamine from the leaves of *Isertia hypoleuca* Benth. This communication discusses the isolation of another alkaloid, isodihydroquinamine, and the evidence which shows it to be a stereoisomer of dihydroquinamine.

## RESULTS AND DISCUSSION

Isolation of the alkaloids of *Isertia hypoleuca* was accomplished by column chromatography of a crude alkaloid fraction using silicic acid as adsorbant and chloroform-methanol mixtures of increasing polarity as eluant. Dihydroquinamine and a new alkaloid, alkaloid C, were both eluted in fractions collected from chloroform-methanol (98 : 2), with alkaloid C appearing first. However, in most fractions the two were admixed. Those richest in alkaloid C were combined and recrystallized from hot acetone to yield reasonably pure alkaloid. The compound was further purified by preparative TLC on silica gel GF 254 plates developed with chloroform-methanol (7: 3), followed by repeated crystallizations from boiling acetone. The free base was obtained as colorless prisms, m.p. 185–187°, $[\alpha]_D$ = -70° (c = 1, EtOH).

The u.v. spectrum of alkaloid C was typical of unsubstituted dihydroindoles:[2] $\lambda_{max}^{MeOH}$ (log $\epsilon$) 242 (3.48) and 300 nm (3·04), unaffected by acid or alkali. The absorption maxima are identical to those of dihydroquinamine and the extinction coefficients are of the same order of magnitude.

The i.r. spectrum (KBr) showed the presence of OH or NH (3300 $cm^{-1}$), an unassigned broad band (2550-2700 cm-'), aromatic ring (1600 and 1462 $cm^{-1}$), cyclic ether (1105 $cm^{-1}$) cyclic tertiary OH (1047 $cm^{-1}$) and a 1,2 disubstituted phenyl ring (749 cm-$^{1}$). A comparison with the spectrum of dihydroquinamine showed that the major peaks, with the

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[1] H. BOHRMANN, C. LAU-CAM, J. TASHIRO, and H. W. YOUNGKEN, JR., *Phytochem.* 8,645 (1969).

[2] A. I. SCOTT, *Interpretation of the Ultra-Violet Spectra of Natural Products,* p. 297, Macmillan, New York (1964).

exception of the unassigned 2550-2700 $cm^{-1}$ band which is missing in the spectrum of dihydroquinamine, are essentially superimposable. Furthermore, the observed close similarity extends to the fingerprint region of the two spectra.

The NMR spectrum was rather complex and resembled that of dihydroquinamine. The few assignments which could be made were a triplet centered at 0·90 δ, 3H (J = 6·5 Hz), indicating an aliphatic ethyl side chain, a singlet at 4·75 δ (concentration dependent), 1 H, assigned to an aliphatic hydroxyl group and a multiplet in the aromatic region 6·4–7·4 δ, 4H.

The major peaks in the mass spectra of dihydroquinamine and alkaloid 3 along with their relative abundances are reproduced in Table 1. Here again the similarity between alkaloid C and dihydroquinamine is evident, even to the relative abundance of the major fragment ions.

TABLE 1. RELATIVE ABUNDANCE OF MAJOR FRAGMENT IONS IN DIHYDROQUINAMINE AND ALKALOID C

| | Relative abundance (% of base peak) | |
|---|---|---|
| *m/e* | Dihydroquinamine | Alkaloid C |
| 110 | 55 | 54 |
| 123 | 100 | 100 |
| 138 | 18 | 20 |
| 166 | 14 | 9 |
| 283 | 7 | 8 |
| 296 | 8 | 4 |
| 313 | 11 | 12 |
| 314 | 49 | 45 |
| 315 | 11 | 10 |

The chemical conversions which were utilized to characterize dihydroquinamine were also applied to alkaloid C. These included $LiAlH_4$ reduction and reoxidation of the reduction product with perbenzoic acid, acetylation and dehydration. Although we were able to effect these conversions, more stringent conditions were required. We attribute this to stereochemical differences which make the functional groups less accessible in alkaloid C.

Although the spectroscopic data point to a close relationship between alkaloid C and dihydroquinamine, the two do differ in other properties such as melting point (185-187" vs. 154–156°) specific rotation (-70" vs. +43°), solubility in acetone and chromatographic mobility on TLC. This leads us to conclude that alkaloid C is a stereoisomer of dihydroquinamine and we propose the name isodihydroquinamine for this new alkaloid.

## EXPERIMENTAL

### *Plant Material*

Leaves of ***Zsertia hypoleuca*** Benth. used in this study were obtained from S. B. Penick and Company, New York, U.S.A. and were collected in Leticia, Colombia, during the summer of 1966. The sample was authenticated by Dr. Richard E. Schultes, Curator, Botanical Museum, Harvard University, Cambridge, Massachusetts, U.S.A. Voucher specimens are deposited in the Gray Herbarium of Harvard University.

### *Extraction and Isolation of Alkaloid C*

The powdered plant material was defatted with light petroleum (b.p. 30–60°), air dried, then extracted with MeOH on a Soxhlet extractor. The MeOH extract was evaporated to dryness *in vacuo* and the residue fractionated for alkaloids as described earlier.' The alkaloid extract (Fraction C, 10·6 g) was chromatographed on a silicic acid column (550 g) and eluted with $CHCl_3$, $CHCl_3$–MeOH mixtures and MeOH.

Fractions of approximately 100-200 ml were manually collected at a moderate rate. As in the past, all fractions were monitored by means of TLC and fluorescence analysis. They were concentrated to small volumes, combined on the basis of their composition and finally evaporated to dryness and weighed.

Elution with $CHCl_3$–MeOH (98 : 2) yielded a series of fractions containing one major alkaloid, designated alkaloid C, accompanied by small amounts of several other bases. These were combined, the solvent was removed *in vacuo* and the pale yellowish brown residue crystallized from acetone as stout prisms, m.p. 183–185" (0.613 g). Recrystallization from boiling acetone gave long, colorless prisms, m.p. 185–186° with slight decomposition (0.380 g). Concentration of the mother liquors yielded an additional crop of crystals (0.060 g) melting at 183-185".

An analytical sample of alkaloid C was obtained by preparative TLC of the compound on silica gel GF254 layers (450 $\mu$) developed with $CHCl_3$–MeOH (7 : 3) followed by two recrystallizations from boiling acetone to yield colorless prisms, m.p. 185–187°, $[\alpha]_D$-70° (c = 1, EtOH), $C_{19}H_{26}N_2O_2$ (mass spectrum, M + 314); u.v. $\lambda_{max}^{MeOH}$ (log $\epsilon$) 242 (3·48) and 300 nm (3·04), unchanged on addition of 0·1 N NaOH or HCl; i.r. $\tilde{\nu}_{max}$ (KBr) 3300, 1600, 1462, 1408, 1105, 1016, 1047, and 749 $cm^{-1}$; NMR ($CDCl_3$) $\delta$ 0·9 (triplet, 3H), $\delta$ 2·0–4·2 (complex, 18H), $\delta$ 465 (singlet, 1H), $\delta$ 6·5–7·4 (multiplet, 4H); no $OCH_3$ or $NCH_2$ (Zeisel); TLC: $R_f$ 0·44 ± 0·02 ($CHCl_3$–MeOH, 6:4); 0·18 ± 0·01 ($CHCl_3$–$Me_2CO$–Pyr, 55:40:5), 024 ± 0·02 (benzene–$Me_2CO$–MeOH–Pyr, 40:20:10:2), 0·15 ± 0·02 ($CH_2Cl_2$–MeOH, 9: 1).

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