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STUDIES ON THE ALKALOIDS OF PACHYSANDRA TERMINALIS SIEB. ET ZUCC. (2). : STRUCTURE OF PACHYSAMINE - A AND -B.

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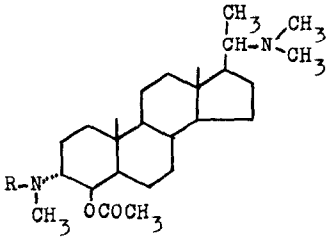
In the preceeding communication[1], structure elucidation of pachysandrine - A (Ia) and -B (Ib), new alkaloids isolated from Pachysandra terminalis SIEB. et ZUCC., was described. In this paper, structures of other two alkaloids, named pachysamine - A and -B, are presented herewith.

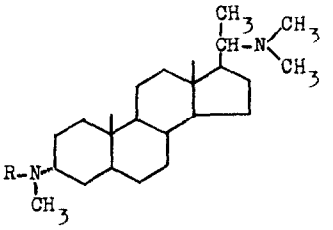
Pachysamine - A (IIa), $C_{24}H_{44}N_2$[2], m. p. 167 - 168°[3], $[\alpha]_D$ +20°[4], showed NMR signals at 7.61 (3H, N-CH_3), 7.84 (6H, $N(CH_3)_2$), 9.15 (3H, doublet, J 6 c.p.s.; sec. CH_3), and 9.20 and 9.35 τ (6H, two tert. CH_3)[5].

On treatment with acetic anhydride in pyridine it gave an N-acetate, m.p. 150 - 152°, IR $\nu_{max}^{CHCl_3}$ 1625 cm^{-1}(amide C=O) and on methylation with formalin - $NaBH_4$ it afforded N-methyl compound (IIb), $C_{25}H_{46}N_2$, m.p. 165.5 - 167°, $[\alpha]_D$ +16°, NMR signals at 7.79 and 7.85 τ (12H, two $N(CH_3)_2$). Properties of this compound are in agreement with those of 3α, 20α-bisdimethylamino-5α-pregnane (IIb)[6] and the identity was established by direct



Ia : R=C_6H_5CO-

Ib : R=$(CH_3)_2C$=CHCO-

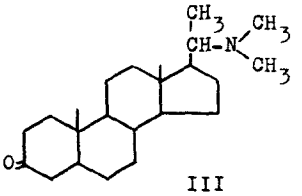


IIa : R=H

IIb : R=CH_3

IIc : R=$(CH_3)_2C$=CHCO-

IId : R=$(CH_3)_2CHCH_2CO$-



III

comparison (mixed melting point, and IR and NMR spectra) with the N,N-dimethyl compound, m.p. 165 - 167°, $[\alpha]_D$ +20°, derived from 3α-amino-20α-dimethylamino-5α-pregnane[7].

Ruschig degradation[8] of pachysamine - A yielded a keto-amine (III), m.p. 174 - 176°, $[\alpha]_D$ +43°, IR ν_{max}^{KBr} 1715 cm^{-1}, NMR signals at 7.83 (6H, $N(CH_3)_2$), 9.14 (3H, doublet, J 6 c.p.s.; sec. CH_3), and 8.99 and 9.33 τ(6H, two tert. CH_3). Its ORD curve showed a positive Cotton effect (i. e. peak : $[\Phi]_{307}$ +2880°, trough : $[\Phi]_{268}$ -2590°)[9], which is the characteristic of 3-keto-5α-steroids. When admixed with the authentic sample of funtumafrine -C (III)[10], no melting point depression was observed.

Accordingly, the structure of pachysamine - A should be 3α-methylamino-20α-dimethylamino-5α-pregnane (IIa).

Pachysamine - B (IIc), $C_{29}H_{50}ON_2$, m.p. 171 - 173°, $[\alpha]_D$ +67°, showed IR ν_{max}^{KBr} 1650, 1610 cm^{-1}(conjugated tert. amide). Its NMR spectrum exhibited signals which can be attributed to $(CH_3)_2C=CHCO$ grouping (one oleffinic proton at 4.22 (diffuse) and two CH_3 groups at 8.15 and 8.18 τ(doublet, J's 2 c.p.s.)) along with two tertiary methyl , one secondary methyl, one N-dimethyl, and one amide N-methyl signals. On catalytic hydrogenation with platinum oxide it gave a dihydro compound (IId), $C_{29}H_{52}ON_2$, m.p. 138 - 139°, $[\alpha]_D$ +54°, IR $\nu_{max}^{CHCl_3}$ 1620 cm^{-1}(amide C=O).

Although attempts to hydrolyze both pachysamine - B and its dihydro compound under drastic acid condition resulted in failure, it was considered to be β,β-dimethylacrylyl amide of pachysamine -A on the basis of the NMR spectrum and by analogy with pachysandrine - B (Ib).

Finally, we prepared the compound IIc by treating pachysamine -A (IIa) with β,β-dimethylacrylyl chloride in pyridine. The product, $C_{29}H_{50}ON_2$, m.p. 173 - 174°, $[\alpha]_D$ +55°, was found to be quite identical with pachysamine - B by IR comparison and mixed melting point determination.

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2. All compounds with cited empirical formulas gave satisfactory elemental analyses. We thank Dr. K. Konobu and Miss Y. Mano of this Faculty for these analyses.
3. All the melting points were uncorrected.
4. Optical rotations reported in this communication were measured in chloroform solutions at 10°C.
5. All NMR spectra were taken on a Varian Associates recording spectrometer (A - 60) at 60 Mc. in deuterated chloroform and chemical shifts are reported in τ values, using tetramethylsilane as the internal reference. We are indebted to Dr. T. Shingu of this Faculty for these NMR measurements.
6. M. M. Janot, F. Laine, Q. Khuong-Huu, and R. Goutarel, Bull. soc. chim. France, 111 (1962).
7. P. Chien, W. E. McEwen, A. W. Burgstahler, and N. T. Iyer, J. Org. Chem., 29, 315 (1964). We express our deep gratitude to Dr. A. W. Burgsthaler for a gift of 3α-amino-20α-dimethylamino-5α-pregnane.
8. H. Ruschig, W. Fritsch, J. Schidt-thome, and W. Haede, Chem. Ber., 88, 883 (1955); K. S. Brown, Jr. and S. M. Kupchan, J. Am. Chem. Soc., 84, 4592 (1962).
9. The optical rotatory dispersion was determined in methanol solution. We are indebted to Dr. K. Kuriyama of Shionogi & Co., Ltd. for the determination.
10. M. M. Janot, Q. Khoung-Huu, and R. Goutarel, Compt. rend., 250, 2445 (1960). Infrared spectra in KBr, however, were found to be not identical, probably due to the difference in crystal forms. We wish to thank Dr. R. Goutarel for the sample of funtumafrine-C.