Tetrahedron Letters No.36, pp. 3169-3174, 1965. Pergamon Press Ltd.
Printed in Great Britain.

STUDIES ON THE ALKALOIDS OF PACHYSANDRA TERMINALIS SIEB. ET ZUCC. (5). : STRUCTURE OF EPIPACHYSAMINE-D, -E, and -F.[1]

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(Received 13 July 1965)

In Part (3)[2] of this series we described the isolation of base IV from the weakly basic alkaloid fraction of Pachysandra terminalis SIEB. et ZUCC. However, later study revealed that base IV is a mixture of two new bases, epipachysamine-D and epipachysamine-E. Moreover, another new alkaloid, named epipachysamine-F, was isolated from the strongly basic fraction of the same plant. This communication deals with structure elucidation of these three bases.

Epipachysamine-D (I), $C_{30}H_{46}ON_2$,[3] m.p. 245-248°,[4] $[\alpha]_D$ +13°,[5] showed IR $\nu_{max}^{CHCl_3}$ 3400, 1655, 1515 cm^{-1} (conjugated sec. amide), 1600, 1580, 1490 cm^{-1} (phenyl), and NMR signals at 2.1-2.8 (5H, phenyl), 7.81 (6H, $N(CH_3)_2$), 9.10 (3H, d., J 6 c.p.s.; sec. CH_3), and 9.17 and 9.33 τ(6H, two tert. CH_3)[6].

On hydrolysis with conc. HCl-AcOH mixture followed by N-methylation, it gave 3β, 20α-dimethylamino-5α-pregnane (III), $C_{25}H_{46}N_2$, m.p. 105-

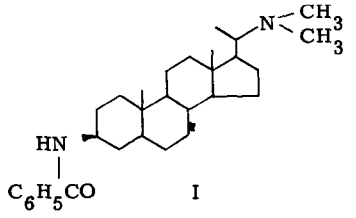
108°, $[\alpha]_D$+ 7°, whose identity was confirmed by direct comparison with an authentic sample (IR and mixed melting point). When the above hydrolysed product was acetylated, an acetate (IIb), $C_{25}H_{44}ON_2$, m.p. 267-268°, $[\alpha]_D$+ 12°, was obtained. This was identified with an authentic sample of chonemorphine acetate (IIb)[7] by IR comparison (KBr) and mixed melting point determination.

The N-acetate obtained was again hydrolysed with conc. HCl-AcOH and the subsequent benzoylation of the resulting amine (IIa) gave rise to an N-benzoate (I), $C_{30}H_{46}ON_2$, m.p. 247-249°, $[\alpha]_D$+13°, which was shown to be identical with epipachysamine-D by IR comparison (KBr) and mixed melting point determination. Therefore the structure of epipachysamine-D is completely proved to be I.

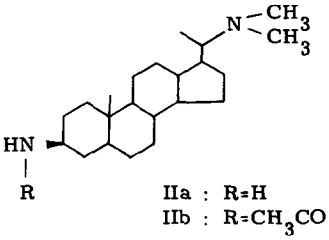
Epipachysamine-E (IV), $C_{28}H_{48}ON_2$ (molecular ion peak at m/e 428 in mass spectrum[8]), m.p. 210-212°, $[\alpha]_D$+20°, showed IR $\nu_{max}^{CHCl_3}$ 3420, 1665, 1635, 1500 cm^{-1} (conjugated sec. amide). Its NMR spectrum exhibited signals attributable to $(CH_3)_2C{=}CHCO$ grouping (one oleffinic proton at 4.46-4.78 and two CH_3 groups at 7.83 and 8.18 τ) along with two tert. methyl, one sec. methyl, and one N-dimethyl signals.

Acid hydrolysis of epipachysamine-E gave an N-desacyl compound (IIa) whose IR spectrum ($CHCl_3$) was identical with that of authentic chonemorphine (IIa). Thus epipachysamine-E would be chonemorphine β,β-dimethyl-

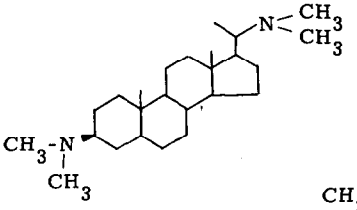
acrylate (IV). This was confirmed by the treatment of chonemorphine (IIa)[9] with β,β-dimethylacrylyl chloride according to the Schotten-Baumann method to afford an amide (IV), $C_{28}H_{48}ON_2 \cdot 1/2\ H_2O$, m.p. 200-205°, $[\alpha]_D^{+19°}$. The IR spectrum (KBr) of this compound was superimposable with that of epipachysamine-E and mixed melting point did not depress.



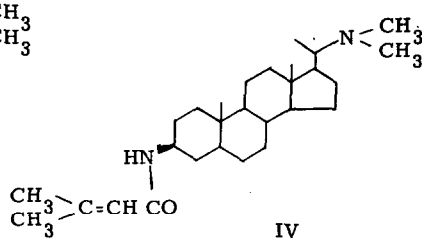
I



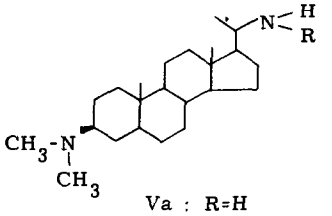
IIa : R=H
IIb : R=CH_3CO



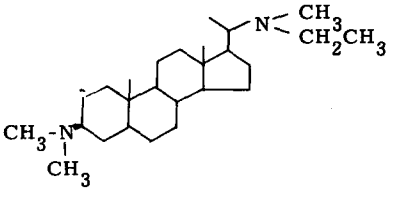
III



IV



Va : R=H
Vb : R=CH_3CO



VI

Epipachysamine-F (Va) is a minor alkaloid obtained as its N-acetate from the acetylated product of strongly basic alkaloid fraction. The acetate (Vb), $C_{25}H_{44}ON_2 \cdot H_2O$ (molecular ion peak at m/e 388 in mass spectrum), m.p. 250-253°, $[\alpha]_D$+6°, showed IR $\nu_{max}^{CHCl_3}$ 3420, 1660, 1510 cm^{-1} (sec. amide) and NMR signals which could be asigned to one acetyl, one N-dimethyl, one sec. methyl, and two tert. methyl groups.

The mass spectrometry provided an important information about the gross structure of epipachysamine-F acetate. The intense peaks at m/e 84 ($(CH_3)_2N^+=CH-CH=CH_2$) and 110 ($(CH_3)_2N^+=CH-CH=CH-CH=CH_2$) together with the characteristic peaks at m/e 373 (M^+-CH_3), 345 (M^+-CH_3CO), and 302 ($M^+-CH_3-CH-NHCOCH_3$) suggested strongly the structure Vb for the base[10].

Acid hydrolysis of the acetate and the subsequent N-methylation yielded an amine (III), $C_{25}H_{46}N_2$, m.p. 106-108°, $[\alpha]_D$+28°, identified with an authentic N,N-dimethylchonemorphine (III) (IR, mixed melting point).

The acetate (Vb) was then reduced with $LiAlH_4$ and the resulting amine was subjected to N-methylation to afford an $N(CH_3)CH_2CH_3$ compound (VI), m.p. 105-107°, $[\alpha]_D$+38°. This was identified by direct comparison (IR in KBr and mixed melting point) with the compound VI, $C_{26}H_{48}N_2$, m.p. 109.5-111°, derived from the already determined alkaloid, epipachysamine-A[2], by $LiAlH_4$ reduction.

The structure of epipachysamine-F is therefore assigned to Va.

Acknowledgement The authors express their deep gratitude to Prof. M. Tomita of this Faculty for his guidance and hearty encouragement.

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2. T. Kikuchi, S. Uyeo, M. Ando, and A. Yamamoto, Tetrahedron Letters, 1817 (1964).
3. All the compounds with cited empirical formulas gave satisfactory elemental analyses.
4. All the melting points are uncorrected.
5. All the optical rotations reported in this communication were taken in chloroform solutions at 10-28°C.
6. All NMR spectra were measured in deuterated chloroform and chemical shifts are reported in τ values, using tetramethylsilane as the internal reference.
7. The authors thank Dr. A. Chatterjee for the sample of chonemorphine acetate.
8. The mass spectra were measured on a Hitachi Mass Spectrometer Model RMU-6D, using an all-glass intet system.
9. We are indebted to Dr. A. W. Burgstahler for a gift of synthetic chonemorphine.

10. H. Budzikiewicz, C. Djerassi, and D. W. Williams, "Interpretation of Mass Spectra of Organic Compounds", Holden-Day, Inc., San Francisco, p. 74, 1964.; A. Chatterjee, B. Das, C. P. Dutta, and K. S. Mukherjee, Tetrahedron Letters, 67 (1965).