Tetrahedron Letters No.27, pp. 2239-2244, 1965. Pergamon Press Ltd.
Printed in Great Britain.

THE ALKALOIDS OF THE BARK OF ALSTONIA VENENATA R. BR.

B. Das[1] and K. Biemann

Department of Chemistry, Massachusetts Institute of Technology
Cambridge, Massachusetts

and

(Mrs.) A. Chatterjee, A.B. Ray and P.L. Majumder

Department of Chemistry, University College of Science
Calcutta 9, India

(Received 12 April 1965; in revised form 12 May 1965)

The isolation and characterization of two new indole alkaloids of tetrahydro-β-carboline type, viz., venenatine and isovenenatine in addition to reserpine and stigmasterol from the bark of Alstonia venenata R. Br. was reported some time ago.[2,3] More recently venoxidine has been isolated and shown to be the N_b-oxide of venenatine[4]. From the petroleum ether fraction of the stem bark of this plant we have now isolated

---

1. Present address: Institut de Chimie des Substances Naturelles, Gif-sur-Yvette, France.

2. A.B. Ray and A. Chatterjee, J. Ind. Chem. Soc., 40, 1043 (1963).

3. T.R. Govindachari, N. Viswanathan, B.R. Pai, and T.S. Savitri, Tetrahedron Letters, 901 (1964).

4. A. Chatterjee, P.L. Majumder and A.B. Ray, Tetrahedron Letters, 159 (1965).

reserpine, kopsinine and three other new alkaloids which were named (i) venalstonine, (ii) venalstonidine and (iii) echitovenine. The structure of these alkaloids, largely derived from their mass spectra, is the subject of this communication.

Reserpine and kopsinine were recognized by their mass spectra and further identified by their I.R. and U.V. spectra as well as by mixed melting points.

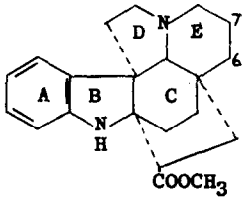
The mass spectrum of venalstonine, m.p. 140-142°, $[\alpha]_D^{30°}$-78° ($CHCl_3$), showed a molecular ion peak at m/e 336 consistent with a molecular formula $C_{21}H_{24}N_2O_2$. Its U.V. spectrum, λ_{max}^{EtoH} 245 and 292 mμ (log ε 3.87, 3.46) indicated the presence of a dihydroindole chromophore. The infrared spectrum showed bands at 3350 (NH) and 1725 cm^{-1} (ester). Reduction of venalstonine with lithium aluminum hydride gave venalstonyl alcohol, $C_{20}H_{24}N_2O$ (Mol. wt. 308), a result which requires the presence of a carbomethoxy function in the alkaloid. The strong peaks at m/e 107, 121, 122, 135 (which were retained in the spectrum of venalstonyl alcohol) in the mass spectrum of venalstonine clearly suggested an aspidospermine-like skeleton for the alkaloid with a 6,7-double bond as in tabersonine[5] and vindolinine.[6] These peaks, when considered together with those at m/e 308 (M-28), 229 and 216 (shifted

---

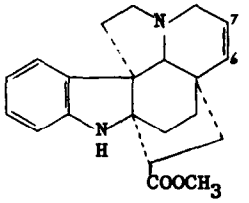
5. M. Plat, J. LeMen, M.-M. Janot, J.M. Wilson, H. Budzikiewicz, L.J. Durham, Y. Nakagawa, and C. Djerassi, Tetrahedron Letters, 271 (1962).

6. C. Djerassi, G.E. Flores, H. Budzikiewicz, J.M. Wilson, L.J. Durham, J. LeMen, M.-M. Janot, M. Plat, M. Gorman, and N. Neuss, Proc. Nat. Acad. Sci. Wash. 48, 113 (1962).

to 280, 201 and 188 respectively in the mass spectrum of venalstonyl alcohol) indicated a kopsinine (I)[7] like structure for venalstonine, containing a 6,7-double bond.



I



II

Catalytic hydrogenation of venalstonine yielded a dihydro derivative, m.p. 105°, the mass spectrum of which established its molecular weight (338; $C_{21}H_{26}N_2O_2$) as well as its identity with kopsinine (I).

The location of the 6,7-double bond in venalstonine was confirmed from its NMR spectrum which exhibited signals between 5.7 - 5.8 p.p.m. (2H at C-6 and C-7) and at 3.55 p.p.m. (2H at C-8, adjacent to the nitrogen atom).

The above results establish structure II (6,7-dehydrokopsinine) for venalstonine.

Venalstonidine, m.p. 223°-225°, exhibits a U.V. spectrum, λ_{max}^{EtOH} 244 (ε7150) and 292 mμ (ε2800), typical for dihydroindoles. The mass spectrum gave a mol. wt. of 352 (in agreement with $C_{21}H_{24}N_2O_3$) and the presence of a small peak at m/e 293 (M-59) as well as the I.R. band at 1728 cm^{-1} provided evidence for the existence of a $-COOCH_3$ function in the alkaloid.

---

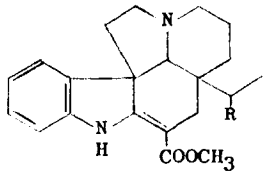
7. C. Djerassi, H. Budzikiewicz, R.J. Owellen, J.M. Wilson, W.G. Kump, D.J. LeCount, A.R. Battersby, H. Schmid, Helv. Chim. Acta, 46, 742 (1963).

The spectrum of venalstonidine was strikingly similar to that of kopsinine (I) except that the peaks at 109 and 124 in the latter[7] were displaced to 123 and 138 respectively. Venalstonidine could be reduced by $LiAlH_4$ but not by $NaBH_4$ and in the mass spectrum of the $LiAlH_4$ reduction product ($C_{20}H_{26}N_2O_2$; mol. wt. 326) these peaks were shifted to 125 and 140. These results along with the appearance of a small M-28 peak in the mass spectra of both the parent alkaloid and its reduction product require that venalstonidine has the kopsinine carbon skeleton but contains one oxygen atom in ring E (see structure I) present either as a hindered carbonyl (possibly at C-6) or as an oxide function. Attempts to assign the exact nature of this oxygen function were as yet unsuccessful due to lack of material. However, with the isolation of additional quantities this point could possibly be resolved and work in this direction is in progress.

Echitovenine, m.p. 168-170°, $[\alpha]_D^{30°}$ +640° ($CHCl_3$), exhibits an α-methylene indoline U.V. spectrum with λ_{max}^{EtOH} 228 (ε8700), 298 (ε8150) and 328 mμ (ε12,000) as in vincadifformine[8] (III; R=H). The I.R. spectrum revealed the presence of an unconjugated ester band (1728 cm^{-1}), in addition to the expected bands at 1670 and 1610 cm^{-1} for such systems. The mass spectrum of echitovenine (mol. wt. 396 in agreement with $C_{23}H_{28}N_2O_4$) showed characteristic peaks at m/e 182 (more intense), 123, 122, and 43 (CH_3CO) together with those at

8. M. Plat, J. LeMen, M.-M. Janot, H. Budzikiewicz, J.M. Wilson, L.J. Durham and C. Djerassi, Bull. Soc. Chim. France, 2237 (1962).

m/e 353 (M-43) (loss of acetyl), 337 (M-59) (loss of $COOCH_3$ or $O-CO-CH_3$), 309 (M-87) (loss of an ethyl side chain bearing an acetoxy substituent) and 279 (M-119) (loss of CH_3COOH + $COOCH_3$) suggested a vincadifformine like skeleton with an acetoxy group at C-20 (or C-21) for echitovenine (III; R=$OCOCH_3$).



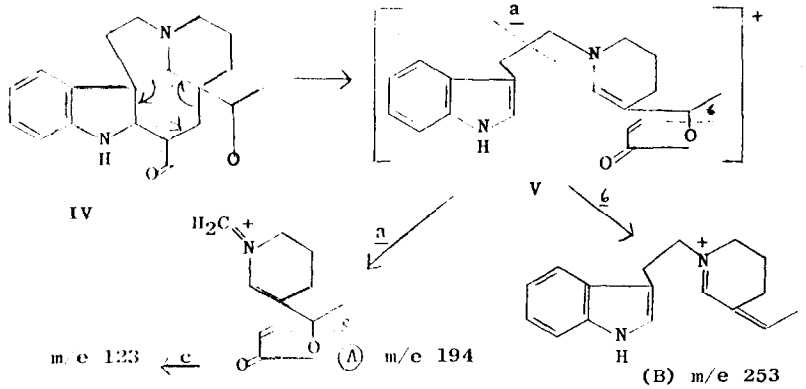
III

1) 10% Methanolic H_2SO_4

2) Aq. acid

IV

On heating of echitovenine with zinc dust and 10% methanolic sulfuric acid the 2,3-double bond is reduced and the product (mass spec. mol. wt. 398) when heated with aqueous sulfuric acid gave a compound (IV) (u.v.: λ_{max}^{EtOH} 244 and 302 mμ) of mol. wt. 324. Its mass spectrum exhibited the most intense peak at m/e 194 as well as a peak at m/e 253. These can best be rationalized as fragments A and B, respectively, derived from a lactone such as IV (M=324).



Both the facile lactone formation as well as the appearance of a peak at m/e 253 (cleavage b in V), which is expected to be stabilized when the substituent is at C-20 rather than at C-21, was strongly in favor of position 20 as the possible site of the acetoxy function in echitovenine. This alkaloid should therefore be represented by structure III ($R=OCOCH_3$).

Acknowledgment: A.B. Ray is grateful to C.S.I.R. (India) for the award of a Research Fellowship.