Tetrahedron Letters No. 44, pp 4133 - 4134, 1971. Pergamon Press. Printed in Great Britain.

THE STRUCTURES OF SOME COMPOUNDS DERIVED FROM α-NARCOTINE

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(Received in UK 22 September 1971; accepted for publication 1 October 1971)

The tetrahydroprotoberberine alkaloid 1-methoxycanadine can be prepared from its 13,14-didehydroderivative VIII (1). It has also been reported, however, (2) that treatment of the diol I (obtained on reduction of α-narcotine) with p-toluenesulfonylchloride in pyridine yields the di-p-toluenesulfonyl ester II, which on heating with acetic anhydride in the presence of NaI is converted into VIII. Attempted repetition of this latter synthesis (2) by us was, however, unsuccessful, and the product obtained was not identical with the substance VIII obtained by the former procedure (1). Therefore, an attempt has been made to clarify this problem.

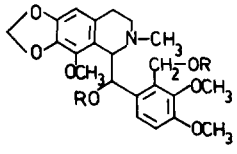
α-Narcotine-diol (I) was prepared by reduction of α-narcotine with sodium dihydro-bis-(2-methoxyethoxy)aluminate in benzene. Reaction of the diol I with an equivalent amount of p-toluenesulfonylchloride in a solution of pyridine (3) gave a quaternary chloride of m.p. 142-143° (Ref. 2, m.p. 143-145°) (4). On the basis of the NMR-spectrum, structure IV was assigned to this quaternary chloride. Alkaline hydrolysis of IV gave the 1-methoxy-13-hydroxycanadine methochloride (V), the identity of which was confirmed by comparison with an authentic sample (5).

Heating of the quaternary chloride IV with NaI in acetic anhydride gave a yellow crystalline substance, m.p. 266-268° (Ref. 2, m.p. 267-268°). λ_{max}^{EtOH} nm (log ε): 290 (4.46) and 348 (4.00). NMR ($CDCl_3$-TFA, 9:1, 60 MHz): δ 2.88s (CH_3-C(O)=), 3.27t and 4.05t, J=7.0 Hz (Ar-CH_2-CH_2-N^+), 3.93s, 3.96s (two OCH_3), 5.00s (Ar-CH_2-N^+), 6.25s (-OCH_2O-), 6.95s (Ar-H), 7.05d and 7.32d, J_{ortho}=9.0 Hz (two Ar-H). The spectral data strongly suggest structure VII for this substance. From the mother liquors, the quaternary iodide corresponding to VI, m.p. 235-237° was isolated.

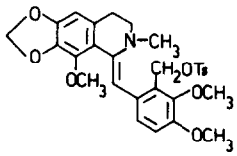
Reduction of VII with sodium borohydride in aqueous methanol gave a tertiary amine, m.p. 164-166°, M^+ 379. λ_{max}^{EtOH} nm (log ε): 238 (4.31), 271 (4.09) and 375 (4.15). NMR ($CDCl_3$): δ 1.47d and 5.43q, J=7.0 Hz (CH_3-CH(O)-), 2.4-3.3m (Ar-CH_2-CH_2-N), 3.82s, 3.85s (two OCH_3), 4.02d and 4.48d, J_{gem}= =15.0 Hz (Ar-CH_2-N), 5.92d, J_{gem}=1.0 Hz (-OCH_2O-), 6.23s (Ar-H), 6.52d and

6.73d, J_{ortho}=9.0 Hz (two Ar-H). On the basis of the spectral data, this substance was assigned structure IX.

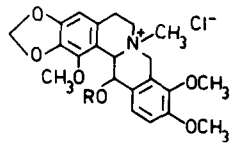
Boiling of substance IV in acetic anhydride, in absence of NaI, gave rise to N-methyl-13,14-didehydro-1-methoxycanadinium p-toluenesulfonate. This was converted into the iodide VIII, which was identical with the authentic sample (1). The substance VIII was refluxed with NaI in acetic anhydride to give the product VII. The reaction showed that enamine VIII was an intermediate product which arose on formation of the substance VII from the quaternary chloride IV. Consequently, in acetic anhydride, in the presence of NaI, selective degradation of the methoxyl group at C-1 and acetylation in the β-position of the enamino grouping took place. Closure of the pyrane ring was probably due to enolization of the 13-acetyl group, which caused a shift of the double bond from the positions 13,14 to the positions 14,7 with simultaneous cleavage of the N^+-CH_3 group. Further studies of these reactions are in progress.



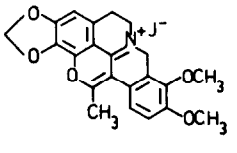
I R = H
II R = Ts



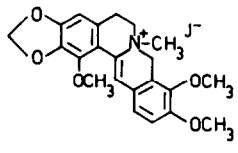
III



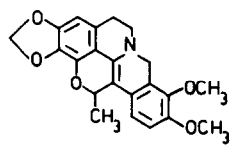
IV R = Ts
V R = H
VI R = $COCH_3$



VII



VIII



IX

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4. All the compounds gave correct elemental analyses.
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