Tetrahedron Letters No. 38, pp 3429 - 3430, 1974. Pergamon Press. Printed in Great Britain.

ADINA ALKALOIDS: 5α-CARBOXYCORYNANTHINE.

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(Received in UK 7 August 1974; accepted for publication 15 August 1974)

Further work on the amino-acid constituents of Adina rubescens has now yielded a carboxy indole alkaloid assigned the yohimbine type structure 1c which complements the Corynanthe and heteroyohimbine examples obtained previously[1,2]. After treatment with CH_2N_2 a small quantity (5 mg) was isolated as the methyl ester, $C_{23}H_{28}N_2O_5$, m.p. 235-7° $[\alpha]_D^{25}$ -29° ($CHCl_3$). Its UV spectrum was indolic, and IR bands at 1745 and 3480 cm^{-1} indicated saturated ester and NH/OH functions. These features were substantiated b NMR signals at τ 2.06(indolic NH) and 2.5 - 3.1 (4 aromatic H), and methoxyl spikes at τ 6.22 and 6.26 suggested two methyl esters; significantly, there were no absorptions attributable to olefinic or C-methyl groups.

Dominant mass spectral fragments at m/e 353 (M-CO_2Me), 351 (M-CO_2Me-H_2), 242, 169 and 168 were characteristic of a tetrahydro-β-carboline substituted at C-5 by a carbomethoxy group and were immediately reminiscent of methyl adirubine[1]. The resemblance extended to substantial ions at m/e 221, 195, 182 and 156 consistent with a fourth ring linked to C-3 and N-4, but unlike adirubine derivatives there were no intense peaks due to loss of the β-hydroxypropionate unit by facile cleavage of the 15-16 bond. This difference was explicable by a 17-18 bond forming a fifth ring as in yohimbine alkaloids (e.g. 1a), and a close relationship with the latter was supported by common mass spectral fragments, particularly those retaining the pentacyclic skeleton at m/e 293 ($C_{19}H_{21}N_2O$) and 277 ($C_{19}H_{21}N_2$).

The presence of a hydroxyl group was confirmed when Ac_2O in pyridine afforded two monoacetates $[\alpha]_D^{25}$ -40° and -44° ($CHCl_3$). An acetamide was excluded by the IR spectra and deacetylation with NaOMe, both acetates affording the same alcohol, isomeric but non-identical with the starting material. Oxidation with Me_2SO/Ac_2O gave a β-keto ester as shown by a large base shift in the UV absorption (λ_{max} 275 nm) an thus fixed the relative position of the hydroxyl group. Subsequent reduction with $NaBH_4$ yielded yet another stereoisomer of the starting material. The only gross structure compatible with the above data and genera biogenetic considerations was a 5-carboxy-yohimbine.

Since the CD spectrum exhibited a positive Cotton effect between 250 and 300 nm, the absolute configuration at C-3 must be a α(S); trans-quinolizidine IR bands in the 2700-2800 cm^{-1} region and lack of a H-3 NMR absorption below τ 6.2 showed that H-15 was cis to H-3 and hence α as expected.[1] It was reasonable to assume that H- 5 was also α in accordance with biogenesis from L-tryptophan and a favourable equatorial conformation for the carboxyl group. The remaining asymmetric centres at 16, 17 and 20 could be correlated with those of corynanthine (1a) on the basis of identical behaviour in the sequence 1 to 4. Thus only corynanthine of the known yohimbine isomers has an axial ester function at C-16 which is readily and irreversibly epimerised by base to give yohimbine (2a) in which it is equatorial[3]: the present alkaloid is likewise epimerised, partially by pyridine and fully by NaOMe. Oxidation of (2a) gives yohimbinone (3a) which is reduced by $NaBH_4$ to β-yohimbine (4a) with an equatorial hydroxyl group at C-17 rather than yohimbine[4]: again, this would explain the isomeric alcohols formed above. Examination of models indicates that for both of these inversions to occur the configuration at C-20 should also be the same as in corynanthine.

Hence the available chemical and spectroscopic evidence is consistent with structure 1b for the methyl ester, and the natural product is 5α-carboxycorynanthine (5α-carboxy-3α,15α,16α,17β, 20β-yohimbine)(1c).

References

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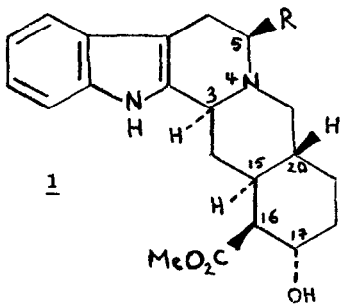
3. M.-M. Janot, R. Goutarel, A. Le Hir, H. Amin and V. Prelog, Bull. Soc. Chim. France, 1085(1952); R. C. Cookson, Chem. and Ind., (London) 337(1953).
4. M.-M. Janot, R. Goutarel, E. W. Warnhoff and A. Le Hir, Bull. Soc. Chim. France, 637(1961).



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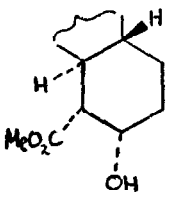

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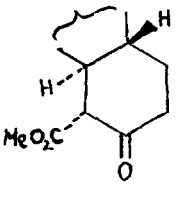

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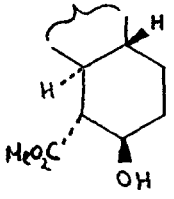

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	a	b	c
R :	H	CO_2Me	CO_2H