Antirhine, a New Indole Alkaloid from *Antirhea putaminosa* (F.v.Muell.) Bail.

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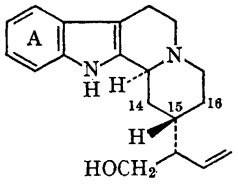
ANTIRHINE, the major base isolated from the leaves of *Antirhea putaminosa* (F. v. Muell.) Bail. (Rubiaceae), has been shown to be (I), and may be regarded as the parent member of the small group of indole alkaloids which possess a 15β-hydrogen, and were previously represented only by the quaternary hunterburnine methiodides (IIa, IIb),[1] and vallesiachotamine.[2] Antirhine, m.p. 112—114° ($CHCl_3$ adduct), $[\alpha]_D$ −2° in chloroform, $C_{19}H_{24}N_2O$ (from elemental analysis and molecular ion *m/e* 296) is an indole alkaloid [λ_{max} 225 mμ (ϵ 25,900), 282 (6300), $\lambda_{inflect}$ 289 (ϵ 4800), ν_{max}($CHCl_3$) 3510 cm^{-1} (NH)] unsubstituted in ring-A (four-proton multiplet between 420—456 c./sec.). Two protons are exchangeable with deuterium (two-proton peak at δ 8·32; molecular ion *m/e* 298 after exchange with D_2O) and are assigned to the indolic NH and an aliphatic alcohol group. Reduction over Adams catalyst affords dihydroantirhine (III), hydrate m.p. 106—108°, $[\alpha]_D$ + 23°, isomeric with dihydrocorynantheol[3,4] and corynantheidol[4] and similar in properties to, but not identical with, either. A complex three-proton multiplet at 294—354 c./sec. in the n.m.r. spectrum of (I) and a three-proton triplet at δ 0·90 in the spectrum of (III) indicates the conversion of a vinyl into an ethyl group on hydrogenation of (I). The signals from the C-21 methylene protons in the spectrum of (I) comprise the AB portion of an ABX system (δ_A 3·77, δ_B 3·56; J_{AB} 10·5 c./sec.; J_{AX} 4·8 c./sec.; J_{BX} 6·5 c./sec.), and the nonequivalence of the methylene protons is

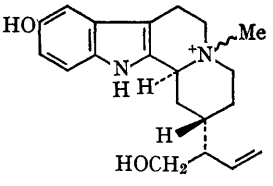
attributed to their proximity to an asymmetric centre and to differential shielding by the C-18–C-19 double bond. Acetylation of (I) produces an average "acylation shift" of 0·6 p.p.m. in the signals from the C-21 methylene protons, in accord with shift normally observed in the spectra of primary alcohols. A major peak in the mass spectrum of (I) at *m/e* 225 (*M*−71) involves a single elimination of the C-15 side chain (metastable ion *m** 171·0, calc. 171·0). Corresponding (*M*−73) and (*M*−74) ions in the spectra of (III) and deuterated (III) respectively confirm the presence of the double bond and hydroxyl group in the side chain. The base peak in the mass spectrum of (I) at *m/e* 223, derived from the (*M*−1) ion (*m** 168·3, calc. 168·6) involves a McLafferty type rearrangement and no corresponding major peak is observed in the spectrum of (III) which lacks the C-18–C-19 double bond. Peaks at *m/e* 197, 184, 169, and 156, typical of tetrahydrocarboline derivatives, support structure (I).

Selenium dehydrogenation of (III) affords a 3 : 1 mixture of (IVa) and (IVb) (λ_{max} 328 mμ) in which the C-6 proton resonates as a doublet at δ 8·50 ($J_{5,6}$ 4·5 c./sec.) thus confirming an unsubstituted C-16 position in (I). Unequivocal proof of structure was obtained by the formation of (V) from (III) by reaction with toluene-*p*-sulphonyl chloride–pyridine and subsequent refluxing in dimethylformamide. (V), m.p. 318—320°, $[\alpha]_D$ −67° (90% methanol) is identical with the product obtained from tosylation and cyclisation of dihydrocorynantheol or dihydrocinchonamine.[5,6]

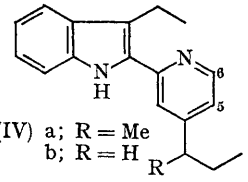
The 15β-configuration for C-15–H in (I), established by the formation of (V), is in accord with the biosynthetic hypothesis of Wenkert and Bringi,[6,7] as the formal transposition of bonds required to convert (I) into a normal corynane type (C-15 proton α) would involve rotation about the C-14–C-15 bond with consequent inversion of the configuration at C-15.



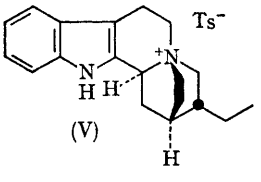
(I)



(II) a; α — Me
b; β — Me



(IV) a; R = Me
b; R = H



(V)

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