The Synthesis of (±)-Mahanimbine and Bicyclomahanimbine

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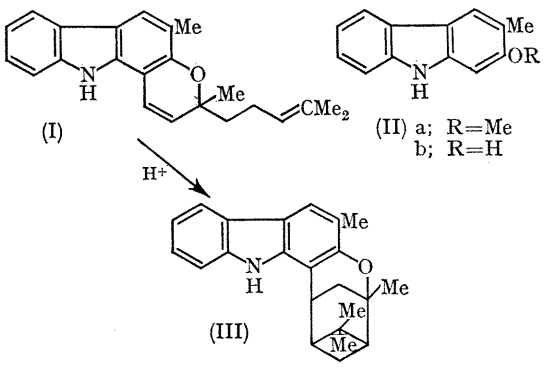
Summary A general method for the synthesis of terpenoid carbazole alkaloids of *Murraya koenigii* Spreng., as exemplified by mahanimbine, is reported.

MAHANIMBINE, $C_{23}H_{25}NO$, isolated by Chakraborty *et al.*[1] from the stem bark of *Murraya koenigii* Spreng. was assigned the structure (I) by Narasimhan *et al.*[2] We describe its synthesis, thus confirming the structure.

Ullmann condensation of 2-nitrobromobenzene with 4-bromo-2-methylanisole[3] gave 4-methoxy-3-methyl-2′-nitrobiphenyl, m.p. 76—77° in 10% yield after chromatographic purification on silica; n.m.r. (CCl_4) τ 7·79 (*s*, 3H, ar. CH_3), 6·20 (*s*, 3H, ar. OCH_3) and 7 aromatic protons between τ 2·20—3·34. The product, boiled with triethyl phosphite according to the procedure of Cadogan and Cameron-Wood,[4] cyclised neatly to give a mixture of isomeric carbazoles (45% yield), separated on a silica-gel column. The major compound was characterised as 2-methoxy-3-methylcarbazole (IIa), m.p. 218° by spectral analysis; λ_{max} (EtOH) 236, 250, 257, 302, and 331 nm. (log ϵ 4·73, 4·30, 4·26, 4·25, and 3·65 resp.), ν_{max} (KBr) 3400 (NH), 1627, and 1605 cm.$^{-1}$ (aromatic system), n.m.r. (CD_3COCD_3) τ 7·67 (*s*, 3H, ar. CH_3), 6·12 (*s*, 3H, ar. OCH_3), 3·0 (*s*, 1H, 1-*H*), 2·19 (*s*, 1H, 4-*H*). There were five protons in the region τ 1·94—2·94 (4 for ar. *H* and 1 for N*H*). The minor compound was similarly identified as 2-methoxy-1-methylcarbazole, m.p. 158—159°; λ_{max} (EtOH) 240, 253, 258, 301, 319, and 330 nm. (log ϵ 4·58, 4·45, 4·39, 4·16, 3·74, and 3·38 resp.); ν_{max} (KBr) 3415 (NH), 1615, and 1603 cm.$^{-1}$ (aromatic system); n.m.r. ($CDCl_3$) τ 7·69 (*s*, 3H, ar. CH_3), 6·14 (*s*, 3H, ar. OCH_3), 3·17 (*d*, 1H, *J* 9·0 Hz., 3-*H*), 2·19 (*d*, 1H, *J* 9·0 Hz., 4-*H*), 1·94—2·99 (*m*, 5H, 4 ar. *H* and 1 for N*H*). The former (IIa) on demethylation either with pyridine hydrochloride or with HBr–AcOH gave (yields 54 and 90%, resp.) the desired phenol (IIb), m.p. 245—247°; λ_{max} (EtOH) 236, 258, 305, and 332 nm. (log ϵ 4·64, 4·20, 4·19, and 3·62 resp.); ν_{max} (KBr) 3520 (OH phenolic), 3390



(NH), 1630, and 1600 cm.$^{-1}$ (aromatic system); n.m.r. (CD_3COCD_3) τ 7·62 (*s*, 3H, ar. CH_3), 3·00 (*s*, 1H, 1-*H*), 2·20 (*s*, 1H, 4-*H*), 1·95—2·95 (*m*, 4H, ar. *H*), 1·98 (s, 1H, O*H*). This phenol (IIb) on condensation with citral[5] (1 mol.) in refluxing pyridine (1 mol.) for 5 hr. yielded (±)-mahanimbine, m.p. 73—74° in 35% yield. The identity of the product was confirmed by mixed m.p., elemental analysis, t.l.c., u.v., i.r., and n.m.r. spectra.

Since mahanimbine has already been converted into bicyclomahanimbine (III) under mild acidic conditions,[6] this constitutes a total synthesis of the latter, also.

The alkaloids from *Murraya koenigii* Spreng. are of considerable biogenetic interest. It is suggested that the phenol (IIb) plays a key role in their biosynthesis. This intermediate or derivatives thereof on oxidative cyclisation with a C_5 unit, derived from mevalonic acid, could yield girinimbine,[7] koenigicine,[8] and koenimbin.[2,8] A similar condensation with a C_{10} unit, *viz.* geraniol, would yield mahanimbine, cyclomahanimbine,[6] and bicyclomahanimbine.[6] Tracer studies on this aspect are in hand.

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