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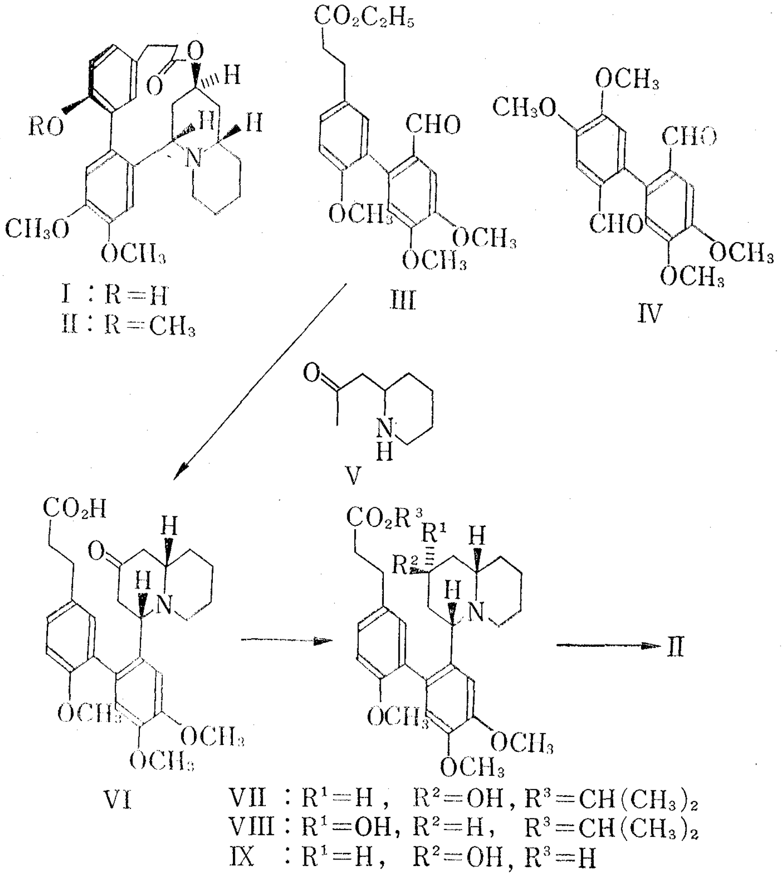
Synthesis of (±)-Methyldecinine

Decinine, a typical Lythraceae alkaloid having a biphenyl linkage, has been isolated from *Decodon verticillatus* (L.) Ell.,[1] *Lagerstroemia indica* L.,[2] and *Lythrum lanceolatum*.[3] Its structure was assigned as shown in I by J.P. Ferris, *et al.*[4] We now report the synthesis of its methyl ether, (±)-methyldecinine (II).



VII : R^1=H, R^2=OH, R^3=CH$(CH_3)_2$
VIII : R^1=OH, R^2=H, R^3=CH$(CH_3)_2$
IX : R^1=H, R^2=OH, R^3=H

Chart 1

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[1] J.P. Ferris, *J. Org. Chem.*, 27, 2985 (1962).
[2] J.P. Ferris, R.C. Briner and C.B. Boyce, *J. Am. Chem. Soc.*, **93**, 2958 (1971).
[3] H. Wright, J. Clardy and J.P. Ferris, *J. Am. Chem. Soc.*, **95**, 6467 (1973).
[4] J.P. Ferris, C.B. Boyce and R.C. Briner, *Tetrahedron Letters*, **1966**, 3641; *idem*, *J. Am. Chem. Soc.*, **93**, 2942 (1971).

Ullmann reaction of 6-bromoveratraldehyde⁵⁾ and ethyl ester of 3-bromo-4-methoxyhydrocinnamic acid⁶⁾ yielded the biphenyl derivative (III) [IR $\nu_{\max}^{\mathrm{CHCl_3}}$ cm^{-1}: 1725 (ester), 1673 (CHO); NMR ($\mathrm{CDCl_3}$) δ: 9.70 (1H, s, CHO), 4.16 (2H, q, $J=7$ Hz, $\mathrm{CO_2C\underline{H}_2CH_3}$), 4.02, 3.99, 3.76 (each 3H, s, $\mathrm{OCH_3 \times 3}$), 1.23 (3H, t, $J=7$ Hz, $\mathrm{CO_2CH_2C\underline{H}_3}$); Mass spectrum m/e: 372 ($\mathrm{M^+}$)] and the dimeric aldehyde (IV) [IR $\nu_{\max}^{\mathrm{CHCl_3}}$ cm^{-1}: 1675 (CHO); Mass spectrum m/e: 330 ($\mathrm{M^+}$)]. Condensation of III with isopelletierine (V)⁷⁾ in aqueous sodium hydroxide afforded the quinolizidin-2-one (VI) [IR $\nu_{\max}^{\mathrm{CHCl_3}}$ cm^{-1}: 2780, 2740 (Bohlmann bands), 1720 (C=O); Mass spectrum m/e: 467 ($\mathrm{M^+}$)]. Treatment of VI with Henbest catalyst ($\mathrm{IrCl_4}$–HCl–$\mathrm{(CH_3O)_3P}$–iso-PrOH)⁸⁾ effected reduction and esterification, giving the axial alcohol (VII) [IR $\nu_{\max}^{\mathrm{CHCl_3}}$ cm^{-1}: 3500 (OH), 2800, 2725 (Bohlmann bands), 1720 (C=O); NMR ($\mathrm{CDCl_3}$) δ: 4.97 (1H, septet, $J=6.5$ Hz, $\mathrm{CO_2C\underline{H}(CH_3)_2}$), 1.20 (6H, d, $J=6.5$ Hz, $\mathrm{CO_2CH(C\underline{H}_3)_2}$); Mass spectrum m/e: 511 ($\mathrm{M^+}$)] and the equatorial alcohol (VIII) [IR $\nu_{\max}^{\mathrm{CHCl_3}}$ cm^{-1}: 3500 (OH), 2780, 2750 (Bohlmann bands), 1720 (C=O); Mass spectrum m/e: 511 ($\mathrm{M^+}$)] in the ratio of 5 : 1.⁹⁾ The ester (VII) was hydrolyzed with aqueous sodium hydroxide and the resulting carboxylic acid (IX) [IR $\nu_{\max}^{\mathrm{CHCl_3}}$ cm^{-1}: 2600—2000 ($\mathrm{N^+H}$), 1574 ($\mathrm{CO_2^-}$); Mass spectrum m/e: 469 ($\mathrm{M^+}$)] was heated with p-toluenesulfonic acid in benzene to provide (±)-methyldecinine (II) [mp 215—216°; IR $\nu_{\max}^{\mathrm{CHCl_3}}$ cm^{-1}: 2790, 2720 (Bohlmann bands), 1718 (C=O); NMR ($\mathrm{CDCl_3}$) δ: 4.95 (1H, m, $W_H=$ 8 Hz, CHOCO), 3.89, 3.84, 3.72 (each 3H, s, $\mathrm{OCH_3 \times 3}$); Mass spectrum m/e: 451 ($\mathrm{M^+}$)].

The synthetic (±)-methyldecinine was proved to be completely identical with the authentic sample derived from natural decinine by infrared (IR) ($\mathrm{CHCl_3}$), nuclear magnetic resonance (NMR) and mass spectral comparison and thin-layer chromatographic behaviour.

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9) *trans*-4-(2-Bromo-4,5-dimethoxy)phenylquinolizidin-2-one was reduced with Henbest catalyst to give stereoselectively the corresponding axial alcohol and the equatorial alcohol in the ratio of 9 : 1; M. Hanaoka, N. Ogawa and Y. Arata, *Tetrahedron Letters*, **1973**, 2355.