

SYNTHESIS OF DECARINE

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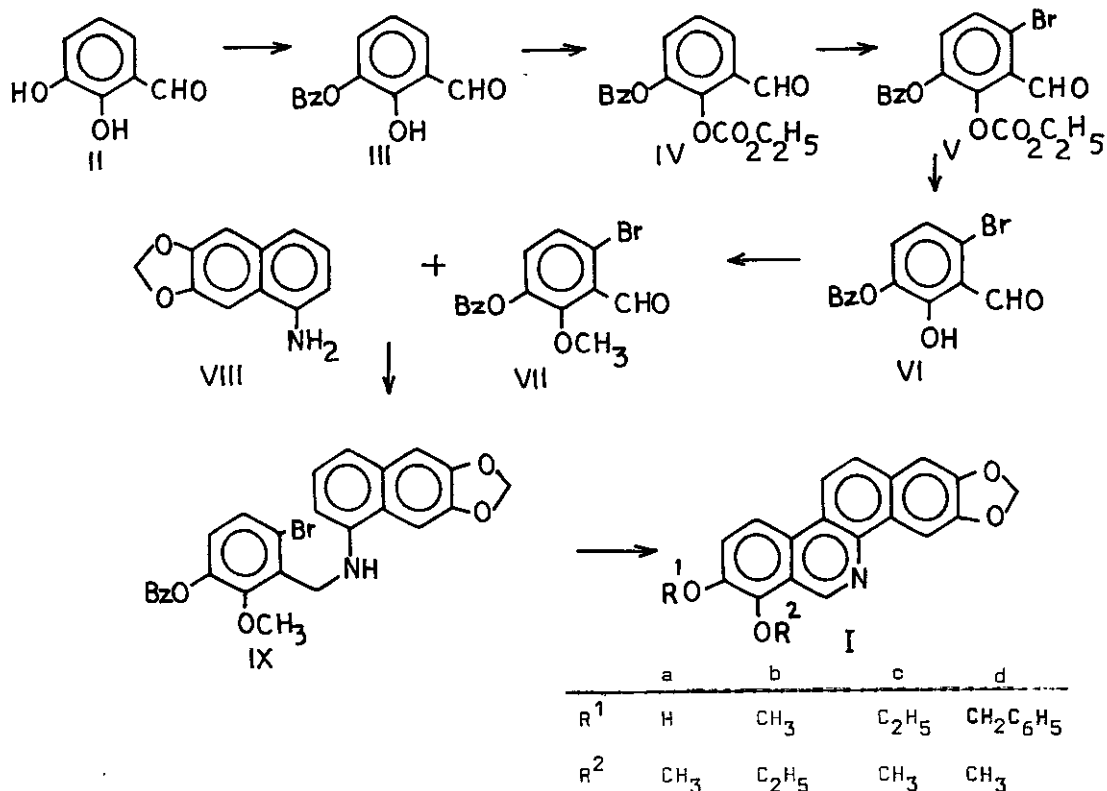
Abstract - The amine (IX), obtained by sodium borohydride reduction of the Schiff base derived from 1-amino-6,7-methylenedioxy-naphthalene (VIII) and 3-benzyloxy-6-bromo-2-methoxybenzaldehyde (VII), on treatment with potassium amide in liquid ammonia gave decarine (Ia).

For confirming the position of the free phenolic group in decarine (Ia), Ishii et al.¹ synthesised the compound (Ib) and showed it to be different from the ethoxy derivative of the alkaloid (Ic). Synthesis of decarine itself does not seem to have been achieved so far, probably because of the difficulty in obtaining a synthon with appropriate substitution pattern. In the present synthesis the requisite regioselectivity has been achieved by carrying out O-benylation of the catechol II through its dianion² and by exploiting the meta directing influence of the ester group³ in bromination of aldehyde IV.

Reaction of the catechol II⁴ with benzyl chloride (one mole) in the presence of sodium hydride (2 mole)² in DMSO gave (50%) the phenol III⁵ (C₁₄H₁₂O₃, mp 84-85°C). It was converted (98%) into the ethyl carbonate IV (C₁₇H₁₆O₅, mp 58-59°C) and treated with bromine (1 mole) in water containing potassium bromide. The crude product (V) was hydrolysed (aq NaOH, CH₃OH) to get (35%) the phenol VI (C₁₄H₁₁BrO₃, mp 61-62°C); ¹H NMR (CDCl₃) δ 5.20 (2H, s, OCH₂C₆H₅), 6.95, 7.10 (1H each, d, J = 9 Hz, ArH), 7.30-7.65 (5H, m, ArH), 10.40 (1H, s, CHO), 12.40 (1H, s, OH). Methylation led to VII (C₁₅H₁₃BrO₃, mp 74-75°C) in which the nuclear position of the bromine atom was confirmed by the downfield position⁶ of the aldehydic resonance (δ 10.40) in the ¹H NMR spectrum.

The naphthylamine VIII was obtained from piperonal in 5 steps⁷ and condensed with VII. The crude product on reduction with sodium borohydride in ethanol gave the amine IX (C₂₆H₂₂BrNO₄, mp 141-143°C) which was subjected to a benzyne cyclisation reaction⁸ with KNH₂ in liquid ammonia (40 min). The usual work

up and crystallisation ($\text{CH}_3\text{OH}/\text{CHCl}_3$) afforded Id (62%, $\text{C}_{26}\text{H}_{19}\text{NO}_4$, mp 210–211°C). Debenzylation ($\text{CH}_3\text{COOH}/\text{HCl}$) furnished decarine (Ia, $\text{C}_{19}\text{H}_{13}\text{NO}_4$, mp 242–243°C; lit.,⁹ mp 243°C), the identity of which was confirmed by comparison with an authentic sample¹⁰ (mixture mp, t.l.c. and ^1H NMR).



REFERENCES AND NOTES

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