

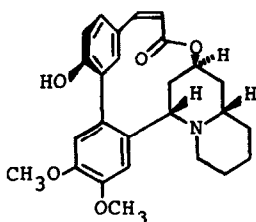
TOTAL SYNTHESIS OF (\pm)-DECALINE

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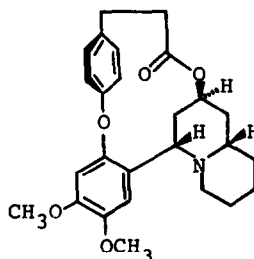
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Lythraceae alkaloids (1,2) possess the unique structures having a quinolizidine ring with a biphenyl or biphenyl ether and a twelve- or fourteen-membered lactone, as shown in lythrine (I) and decaline (II). We now report the first total synthesis of one of these alkaloids, decaline (II), which was isolated from Decodon verticillatus (L.) Ell. and characterized by Ferris et al. (3,4).

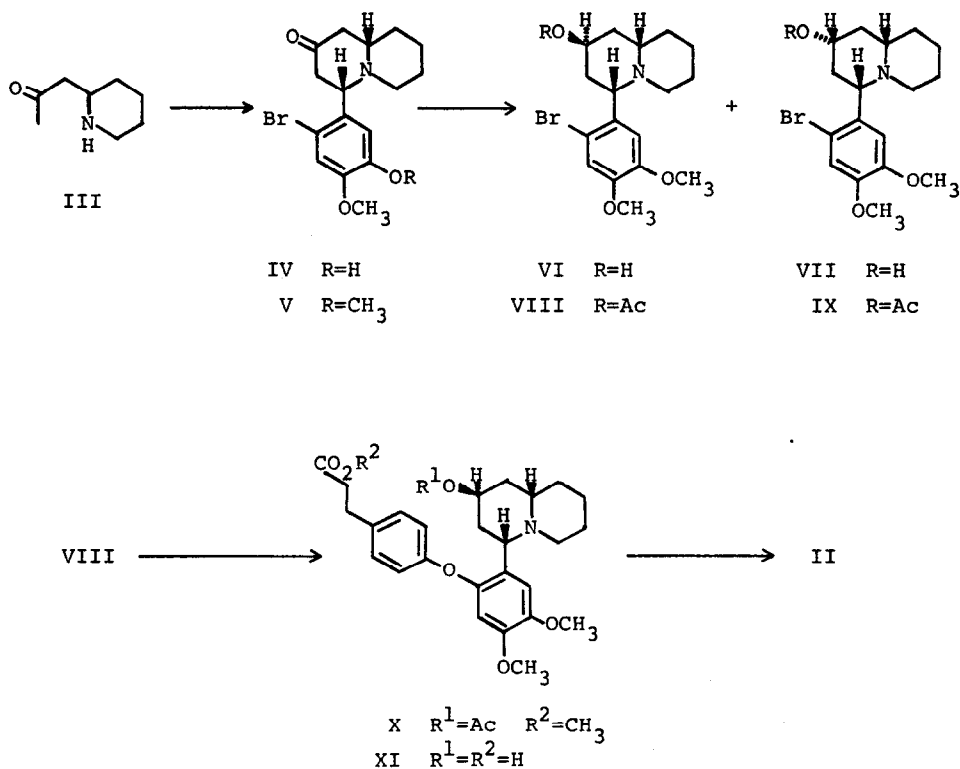


I



II

Condensation of isopelletierine (III) (5) with 6-bromoisovanillin (6) in aqueous sodium hydroxide and subsequent methylation of the product (IV) [$\underline{m/e}$: 355, 353 (M^+ , 1:1), $\nu_{\max}^{\text{CHCl}_3}$ cm^{-1} : 3530 (OH), 2780, 2750 (Bohlmann bands), 1720 (C=O)] with dimethyl sulfate and sodium hydroxide provided the quinolizidin-2-one (V) [mp 143-144°, $\underline{m/e}$: 369, 367 (M^+ , 1:1), $\nu_{\max}^{\text{CHCl}_3}$ cm^{-1} : 2800, 2760 (Bohlmann bands), 1719 (C=O)] in 76% yield from III. The stereochemistries of IV and V



were established from the presence of Bohlmann bands in their IR spectra and the NMR data of the alcohol (VII) [τ : 6.48 (1H, d-d, $J=12$; 3 Hz, CH_{Ar})] and the acetyl derivative (IX) [τ : 6.45 (1H, d-d, $J=11$; 3 Hz, CH_{Ar})] derived from V (7). Though condensation of III with benzaldehyde has been reported to give a mixture of cis- and trans-4-phenylquinolizidin-2-one (4a), only the trans isomer (IV) could be isolated in the above reaction.

For the synthesis of this alkaloid it is necessary to get the axial alcohol (VI), and this purpose was realized successfully by stereoselective reduction of V with Henbest catalyst (8). The quinolizidin-2-one (V) was heated with iridium tetrachloride and hydrochloric acid in the presence of trimethyl phosphite in aqueous 2-propanol, and the resulting crude product was separated by chromatography into the axial alcohol (VI) [mp 112-113°] and the equatorial

alcohol (VII) [mp 71-74°] in the ratio of 9:1 in 84% yield. On the other hand, reduction of V with sodium borohydride afforded VI and VII in the ratio of 3:7 in 85% yield. In order to verify the stereochemistry of the hydroxyl group unambiguously, both the alcohols (VI and VII) were acetylated with acetic anhydride in pyridine to furnish quantitatively the acetyl derivative (VIII) [τ : 4.95 (1H, m, $W_H = 7$ Hz, CHOAc)] and the epimeric acetyl derivative (IX) [τ : 5.16 (1H, t-t, $J = 11$; 4.5 Hz, CHOAc)], respectively. These NMR data well support the assigned stereochemistry of the acetoxy group in VIII and IX.

Ullmann condensation of VIII with methyl 4-hydroxyhydrocinnamate (9) in pyridine using copper oxide afforded the biphenyl ether (X) [mp 113-114.5°, m/e : 511 (M^+), $\nu_{\text{max}}^{\text{CHCl}_3} \text{ cm}^{-1}$: 2790, 2760, 2730 (Bohlmann bands), 1728 (C=O), τ : 8.15 (3H, s, OCOCH_3), 6.33, 6.23, 6.09 (each 3H, s, $\text{OCH}_3 \times 3$), 5.03 (1H, m, $W_H = 7$ Hz, CHOAc)] in 34% yield.

Finally, the ester (X) was hydrolyzed with aqueous sodium hydroxide and the resulting carboxylic acid (XI) [m/e : 455 (M^+)] was heated in benzene solution containing *p*-toluenesulfonic acid to provide (\pm)-decaline (II) [mp 196-197°, m/e : 437 (M^+), $\nu_{\text{max}}^{\text{CHCl}_3} \text{ cm}^{-1}$: 2800, 2730 (Bohlmann bands), 1720 (C=O), τ : 6.12, 6.10 (each 3H, s, $\text{OCH}_3 \times 2$), 5.11 (1H, m, $W_H = 7$ Hz, CHOCO)] in 55% yield from X.

The synthetic (\pm)-decaline was proved to be completely identical with natural decaline by IR in CHCl_3 , NMR, UV, and mass spectral comparison and t.l.c. behaviour.

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