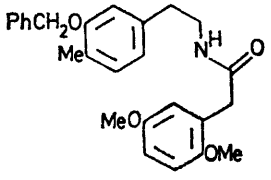
Convenient Method for Syntheses of Erythrinan Alkaloids

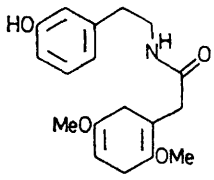
By MITSUMASA HARUNA* and KAZUO ITO
(*Faculty of Pharmacy, Meijo University, Yagoto, Tempaku-ku, Nagoya, Japan*)

Summary A new synthetic route to erythrinan alkaloids was developed, *via* the *cis*-C/D-ring fused 15-methoxy-16-hydroxydioxoerythrinan-2,8-dione (III) as the key intermediate, from the enol methyl derivative (II) which was obtained by Birch reduction of the benzyl amide (I).

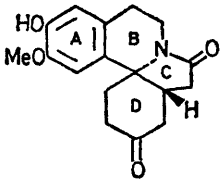
WE have already reported the preparation of a key intermediate in the syntheses of erythrinan alkaloids, the indoledione (IV).[1] We now report a simple synthesis of the erythrinen-one (X), which is a potential intermediate in the synthesis of erysotrine (XII), the most common alkaloid occuring in *Erythrina* species (Leguminosae).



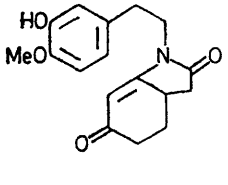
(I)



(II)



(III)



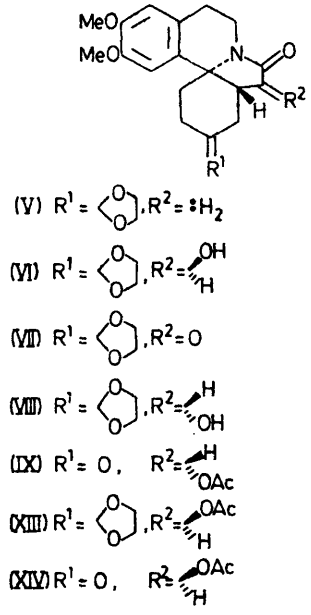
(IV)

Birch reduction of the benzyl-amide (I), m.p. 125—127 °C, followed by treatment of the resulting dihydro-compound (II) with 10% H_2SO_4 in dimethylformamide (DMF) afforded the desired tetracyclic compound, (III) with a *cis*-C/D ring junction [overall yield 90% from (I)], m.p. 211—212 °C; *m/e* 301 (M^+), 244 (100%), and 230; ν_{max} ($CHCl_3$) 3580 (OH), 1730 (C=O), and 1690 (N–C=O) cm^{-1}; δ ($CDCl_3$) 6·64 (1H, s, 17-H), 6·67 (1H, s, 14-H), 4·32 (1H, m, 10*eq*-H), and 4·89 (3H, s, OMe).

Acetalization of (III) with BF_3–Et_2O in ethylene glycol, followed by methylation (MeI, anhyd.K_2CO_3 in DMF), gave the acetal lactam (V) [95% from (III)], ν_{max} ($CHCl_3$) 1680 (N–C=O) cm^{-1}.

Hydroxylation[2] of the lithium enolate of (V) with molecular oxygen afforded the 7β-hydroxy acetal lactam† (VI) (70%), m.p. 202—202·5 °C; ν_{max} ($CHCl_3$) 3360 (OH) and 1690 (N–C=O) cm^{-1}; δ($CDCl_3$) 4·77 (1H, d, *J* 9 Hz, 7α-H), along with the 7-oxo derivative (VII)‡ (5%), ν_{max} ($CHCl_3$) 1780 (C=O) and 1708 (N–C=O) cm^{-1}.

Oxidation of (VI) with Collins reagent, followed by reduction of the resulting oxo-compound (VII) with $NaBH_4$ gave the 7α-hydroxy derivative (VIII), ν_{max} ($CHCl_3$) 3300—3600 (OH) and 1700 (N–C=O) cm^{-1}, which, upon acetylation with Ac_2O–pyridine, yielded the acetoxy acetal lactam, readily convertible into the 7α-acetoxy-2-oxo-lactam (IX) [63% from (VI)], ν_{max} ($CHCl_3$) 1760 (OAc), 1730 (C=O), and 1710 (N–C=O) cm^{-1}; δ ($CDCl_3$) 5·52 (1H, d, *J* 8 Hz, 7β-H) and 2·08 (3H, s, OAc), upon deacetalization with 2%-HCl–acetone.



(V) R^1 = , R^2 = :H_2

(VI) R^1 = , R^2 =

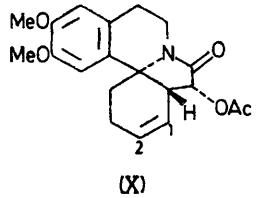
(VII) R^1 = , R^2 = O

(VIII) R^1 = , R^2 =

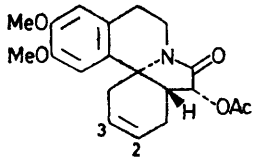
(IX) R^1 = O, R^2 =

(XIII) R^1 = , R^2 =

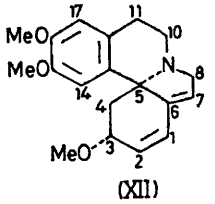
(XIV) R^1 = O, R^2 =



(X)



(XI)



(XII)

Treatment of (IX) with toluene-α-thiol and BF_3–Et_2O in AcOH, followed by desulphurisation with Ni_2B[3] in EtOH for 1 h gave the erythrinenone (X) (35%), ν_{max} ($CHCl_3$) 1760 (OAc) and 1690 (N–C=O) cm^{-1}; δ ($CDCl_3$) 6·10 and 5·90 (each 1H, m, vinyl-H), 5·63 (1H, d, *J* 7·5 Hz, 7β-H), and 2·09 (3H, s, OAc), along with its positional isomer (XI) (55%), δ ($CDCl_3$) 5·93 (2H, m, vinyl-H) and 5·60 (1H, d, *J* 6·5 Hz, 7β-H).

The structure of (X) was identified by comparison of its i.r. and ^{1}H-n.m.r. spectra with those of an authentic sample.

The conversion of (X) into erysotrine has already been reported by Mondon *et al.*,[4] so the formal synthesis of erysotrine is now established.

We thank Professor A. Mondon, Institut für Organische Chemie der Universität Kiel, for a specimen of compound (X).

(*Received*, 23*rd February* 1976; *Com.* 195.)

† The β configuration of the C-7 hydroxy-group was indicated by the high-field shift of the 7-H signal in the n.m.r. spectrum of (XIV) (δ 5·04, 1H, d, *J* 8 Hz), compared with that for (XIII) (δ 5·88, 1H, d, *J* 6 Hz).

‡ Keto–enol equilibrium was observed in this compound.

[1] K. Ito, M. Haruna, and H. Furukawa, *J.C.S. Chem. Comm.*, 1975, 681.
[2] H. H. Wasserman and B. H. Lipshutz, *Tetrahedron Letters*, 1975, 1731.
[3] R. B. Boar, D. A. Hawkins, J. F. McGhie, and D. H. R. Barton, *J.C.S. Perkin I*, 1973, 654.
[4] A. Mondon and N. J. Nestler, *Angew. Chem.*, 1964, **76**, 651.