A Stereospecific Synthesis of (±)-Cataline

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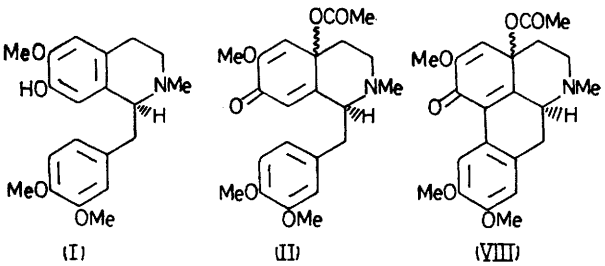
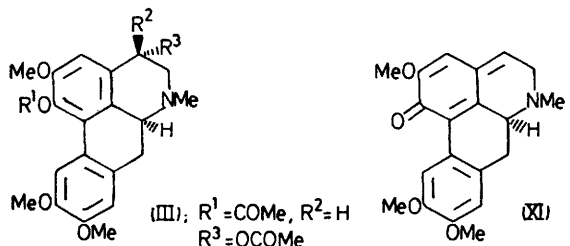
Summary (±)-Thaliporphine (VI) was readily oxidized with lead tetraacetate in acetic acid to give amorphous (±)-4β-acetoxythaliporphine (VIII), which was converted into (±)-cataline (V) in 86·5% overall yield.

WE have previously reported that $Pb(OAc)_4$ oxidation of (±)-codamine (I)[1] gives a *p*-quinol acetate (II), which when treated with acetic anhydride–conc. sulphuric acid gave (±)-4-acetoxy-*O*-acetylthaliporphine (III)[2] and (±)-

O-acetylthaliporphine (IV).[2] (III) is a potential intermediate for the synthesis of 4-hydroxyaporphine, (+)-cataline (V),[3] from *Glaucium flavum Cr. var. vestitum*. We now report that in contrast with (I) the oxidation of (±)-





thaliporphine (VI)[4] gave (±)-4β-acetoxythaliporphine (VII) as the sole product rather than the *p*-quinol acetate (VIII) and that the first stereospecific synthesis of (±)-cataline (V) has been achieved.

Reaction of (VI) with $Pb(OAc)_4$ (1·2 equiv.) in AcOH at room temperature for 0·5 h produced an amorphous product (VII) {quantitative yield, ν_{max}† 3510 (OH) and 1720 (C=O) cm^{-1}; δ† 2·10 (3H, s, OCO*Me*) and 5·90 [1H, t (br), half-band width 5·0 Hz, C(4)-H]}. Acetylation of (VII) with Ac_2O–pyridine led to the (±)-diacetate (IX),‡ m.p. 257—259° (decomp.) (from benzene–n-hexane) {δ 2·14, 2·19 (each 3H, s, OCO*Me*) and 5·92 [1H, t(br), half-band width 5·0 Hz, C(4)-H]}, which was diasteroisomeric with (III),[2] m.p. 236—238° (decomp.) (from benzene–n-hexane) {δ 6·20 [1H, dd, *J* 7·5, 10 Hz, C(4)-H]}. From the spectral data (n.m.r.), the structure of (VII) was found to be (±)-4β-acetoxythaliporphine, in which an acetoxyl group possessed the same orientation as a hydroxyl group in (+)-cataline (V).

Hydrolysis of the amorphous substance (VII) with 10% hydrochloric acid at room temperature for 0·5 h gave (±)-4β-hydroxythaliporphine (X), m.p. 167—168° (decomp.) (from ether) {quantitative yield, δ 4·44 [1H, t(br), half-band width 5·0 Hz, C(4)-H]}. Successive methylation of (X) with diazomethane–ether (excess) in methanol at room temperature (overnight) afforded (±)-cataline (V), m.p. 149—150° (decomp.) (from ether–n-hexane) {86·5% overall yield from (VI), δ 4·46 [1H, t(br), half-band width 5·0 Hz, C(4)-H], 6·73, 6·88 (each 1H, s, arom-H) and 8·06 [1H, s, C(11)-H]; *m/e*† 371 (M^+), 370 ($M^+ - 1$), 356, 340 and 328 (base peak)}, which was identical with natural (+)-cataline by comparison of their i.r. spectrum and t.l.c.§

We suggest that compound (VII) is formed by stereospecific acetoxylation of the quinone methide (XI) in which AcOH is hydrogen bonded to the nitrogen atom. This is analogous to the epoxidation of cyclic allylic alcohols (the Henbest rule[5]).

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† The i.r. spectrum was measured using a Hitachi 215 spectrometer in $CHCl_3$ solution. The n.m.r. spectra were measured with a JEOL 4H-100 (100 MHz) spectrometer in $CDCl_3$ solution (5—10%). The mass spectrum was measured with a Hitachi RMU-7M mass spectrometer.

‡ Satisfactory analytical data were obtained for all new compounds described.

§ T.l.c. was performed using the following absorbents and developing solvents; (1) Silica gel GF_{254} (type 60) (Merck); $CHCl_3$-ethanol (9 : 1) and benzene–ethyl acetate–diethylamine (7 : 2 : 1); (2) aluminium oxide G (type E) (Merck); acetone-petroleum ether (7 : 3) and (1 : 1).

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[2] O. Hoshino, T. Toshioka, and B. Umezawa, *Chem. Comm.*, 1971, 1533; *Chem. Pharm. Bull.* (*Tokyo*), 1974, **22**, 1302. The stereochemical structure of (III), though not described previously, was proved to be (±)-4α-acetoxy-*O*-acetylthaliporphine by comparison of its n.m.r. spectrum with that of (±)-diacetate (IX) obtained in the present reaction.
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