Synthesis of (±)-Kreysigine *via* a *p*-Quinol Acetate

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Summary Treatment with acid of a *p*-quinol acetate derived from (±)-1,2,3,4-tetrahydro-6-methoxy-2-methyl-1-[β-(3,4,5-trimethoxyphenyl)ethyl]isoquinolin-7-ol gave (±)-*O*-acetylkreysigine in 18% yield.

To explore the scope of the method used in the preparation of (±)-thaliporphine from (±)-codamine,[1] we have applied the same method to the (±)-tetrahydroisoquinoline† (I) in a synthesis of (±)-kreysigine‡ (II).[2-4]

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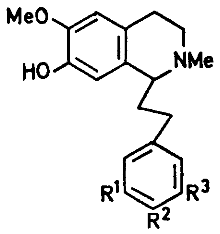
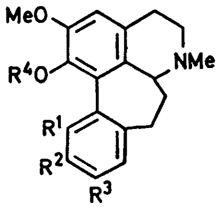
† Satisfactory spectra (i.r., n.m.r.) were obtained for all compounds described. Analytical data for (IV) and the styphnate of (I) confirmed their structures.

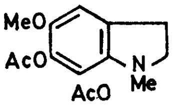
‡ Structures (II), (IV) or (VI) were confirmed by mass spectra.



(I) $R^1 = R^2 = R^3 = OMe$
(III) $R^1 = H, R^2 = R^3 = OMe$



(II) $R^1 = R^2 = R^3 = OMe, R^4 = H$
(IV) $R^1 = H, R^2 = R^3 = OMe, R^4 = Ac$
(V) $R^1 = R^2 = R^3 = OMe, R^4 = Ac$



(VI)

The (±)-tetrahydroisoquinoline (III), an oil, was first oxidized [$Pb(OAc)_4$] and then treated with conc. H_2SO_4–Ac_2O to give the desired (±)-homoaporphine (IV) [16%, m.p. 163—164° (from benzene–n-hexane)]. The method could thus be used for the synthesis of homoaporphines.

Similarly, a solution of (I), an oil, was oxidized [$Pb(OAc)_4$; with water cooling] for 0·5 h to give an amorphous *p*-quinol acetate which was treated with conc. H_2SO_4–Ac_2O and chromatographed [both column ($CHCl_3$–MeOH) and thin layer] to give (±)-*O*-acetylkreysigine (V) (18%) as an amorphous mass. The indoline (VI) [1·5%, m.p. 145—146° (from benzene–n-hexane)] was isolated from the $CHCl_3$ eluate.

Hydrolysis of (V) in 4N-HCl–MeOH at 80° for 1·5 h gave (II) [56%, m.p. 185·5—186·5°[3,4] (from benzene–n-hexane), which was identical with an authentic sample (i.r. and n.m.r. spectra).

Indoline (VI) was presumably originated from the *o*-quinol acetate produced during the course of oxidation.

We thank Professor T. Kametani for i.r. and n.m.r. spectra for (II).

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