Total Synthesis of the Alkaloids (±)-Oxocrinine and (±)-Oxomaritidine *via* Anodic Oxidation

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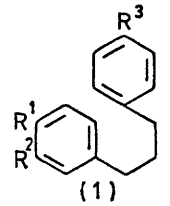
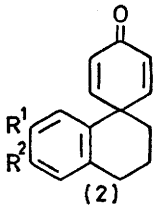
Summary (±)-Oxocrinine (**5a**) and (±)-oxomaritidine (**5b**) were synthesized by anodic oxidation of the trifluoroacetyl derivatives of *N*-(4-methoxyphenethyl)-3,4-methylenedioxybenzylamine (**3a**) and *N*-(4-methoxyphenethyl)-3,4-dimethoxybenzylamine (**3b**) followed by hydrolysis.

(±)-CRININE (**6a**) and (±)-maritidine (**6b**), Amaryllidaceae alkaloids which have the 5,10-ethanophenanthridine ring system, have been synthesized by various routes.[1] Recent reports of electro-oxidation of tetrahydroisoquinolines[2] suggested that this process has wide applicability for intramolecular oxidative coupling. We were interested to use anodic oxidation for the transformation of compounds (**1**) into (**2**),[3] in connection with the synthesis of crinine, maritidine, and other natural products which have a methylenedioxy-group, and now report new total syntheses of (±)-oxocrinine (**5a**) and (±)-oxomaritidine (**5b**) by this method. These compounds can readily be transformed to (±)-crinine[4] (**6a**) and (±)-maritidine[1d] (**6b**).



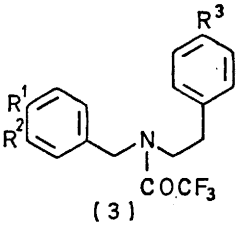
(1)

a ; $R^1, R^2 = OCH_2O$, $R^3 = OMe$
b ; $R^1 = R^2 = R^3 = OMe$
c ; $R^1, R^2 = OCH_2O$, R^3 OH



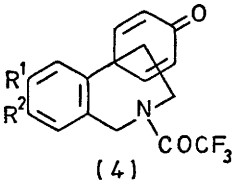
(2)

a ; $R^1, R^2 = OCH_2O$
b ; $R^1 = R^2 = OMe$



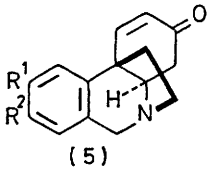
(3)

a ; $R^1, R^2 = OCH_2O$, $R^3 = OMe$
b ; $R^1 = R^2 = R^3 = OMe$
c ; $R^1, R^2 = OCH_2O$, $R^3 = OH$
d ; $R^1 = OMe$, $R^2 = R^3 = OH$



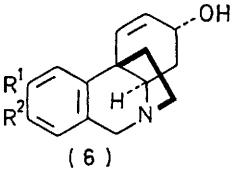
(4)

a ; $R^1, R^2 = OCH_2O$
b ; $R^1 = R^2 = OMe$
c ; $R^1 = OMe$, $R^2 = OH$



(5)

a ; $R^1, R^2 = OCH_2O$
b ; $R^1 = R^2 = OMe$



(6)

a ; $R^1, R^2 = OCH_2O$
b ; $R^1 = R^2 = OMe$

The preliminary investigations were done with (**1a**) and (**1b**), prepared from the corresponding chalcones. In general, the reactions were carried out with an H-type glass cell at room temperature in a concentration of reactant 0·02 M in acetonitrile using a $Hg–Hg_2Cl_2$ reference electrode. The electrodes were varied with the electrolytes; when tetraethylammonium perchlorate was the electrolyte (0·1 M), a carbon anode and platinum cathode were used, (b) with fluoroboric acid as electrolyte (0·1 M), both electrodes were platinum. In the oxidation of (**1a**) by procedure (b), the current (0·98 V, SCE) was dropped smoothly from 120 mA to 10 mA in 1 h and the spiro-dienone (**2a**), m.p. 169—171°,[3] was obtained in a yield of $> 95\%$.†‡ Similarly, when (**1b**) in acetone§ was oxidized by procedure (b) (**2b**), m.p. 95·5—96·5°, 90%, was obtained after 15 min.

These results prompted the use of anodic oxidation for a biogenetic-type synthesis of crinine and maritidine. Compound (**3a**) (prepared from piperonal and *O*-methyltyramine in two steps) was oxidized by procedure (b) at a current of 1·10—1·18 V (SCE) in 1 h and the oxidation product (**4a**), m.p. 181—182°,¶ was obtained in 62% yield.†‡ Alkaline hydrolysis of (**4a**) by K_2CO_3 in methanol–H_2O afforded (±)-oxocrinine (**5a**), m.p. 176—177° (lit.[1a,3] 172—173° and 171—174°), 95%, which was identical in all respects with an authentic sample. A similar transformation was carried out with (**3b**) by procedure (b) at a current of 1·10—1·20 V in 1 h and the dienone (**4b**), m.p. 159—160° was obtained in 62% yield.†‡ Alkaline hydrolysis of (**4b**) gave (±)-oxomaritidine (**5b**), m.p. 145—147°,[1c] identical with an authentic sample in all respects.

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† Yields of the oxidation products following procedure (a) were generally low: *e.g.* (**1a**) → (**2a**) 17%, (**3a**) → (**4a**) 39%, and (**3b**) → (**4b**) 52%.

‡ The yields obtained by previous authors in an analogous chemical oxidative couplings are: (i) (**1c**) → (**2a**) by oxidation with thallium(III) trifluoroacetate 87%;[3] (ii) (**3c**) → (**4a**) by oxidation with thallium trifluoroacetate 19%,[3] (**3d**) → (**4c**) with $VOCl_3$ 24%,[1c] and (**3d**) → (**4c**) with $[Fe(DMF)_3Cl_2][FeCl_4]$ 35%.[5]

§ The yield of the spiro-dienone (**2b**) from (**1b**) in acetonitrile by procedure (b) was 60%.

¶ The m.p. of (**4a**) prepared by us differs from that reported,[3] (138—142°) but structure (**4a**) is the only one which fits the analytical and spectral data.

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