

TOTAL SYNTHESIS OF THE MORPHINANDIENONE ALKALOIDS, ( $\pm$ )-AMURINE,  
( $\pm$ )-FLAVINANTINE, AND ( $\pm$ )-PALLIDINE BY ANODIC OXIDATION

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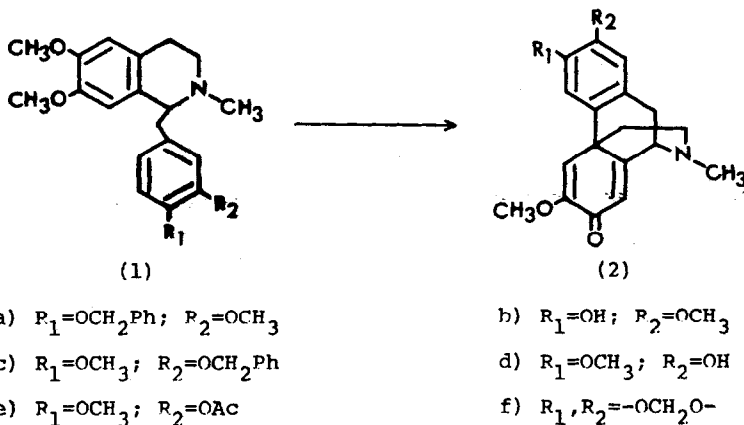
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In the preceding communication<sup>1</sup>, intramolecular oxidative coupling reaction of N-phenethyl benzylamine derivatives by electrochemical method are superior than other chemical oxidative coupling methods in several respects and crinine-type alkaloids of Amarvllidaceae were synthesized using those method. The electrolyte in electrochemical reaction is a dominant factor and we also found fluoroboric acid  $\text{HBF}_4$  was a sufficient electrolyte in those reaction.

Recently, Miller and his collaborators have reported the synthesis of morphinandienone alkaloids, ( $\pm$ )-O-methylflavinantine (2) ( $R_1=R_2=\text{OCH}_3$ ), ( $\pm$ )-O-benzylflavinantine (2a), and ( $\pm$ )-O-benzylpallidine (2c) by anodic oxidation of corresponding 1-benzyltetrahydroisoquinolines<sup>2</sup>. They reported that it is necessary to set rather strict condition for the electrolysis of those compounds, namely, the oxidation was carried out at a platinum electrode in a three compartment cell at 1.1 V in purified acetonitrile at 0° with either tetramethylammonium tetrafluoroborate or lithium perchlorate as electrolyte in the presence of  $\text{Na}_2\text{CO}_3$ .

This paper deals with the synthesis of morphinandienone alkaloids, ( $\pm$ )-flavinantine (2b), and ( $\pm$ )-pallidine (2d) by anodic oxidation using  $\text{HBF}_4$  as electrolyte in higher yield than previous report<sup>2</sup>, and a new synthesis of ( $\pm$ )-amurine (2f).

In general, the reactions were carried out with an H-type one compartment glass cell at room temperature in a concentration of reactant 0.02 M in acetonitrile using a Hg-Hg<sub>2</sub>Cl<sub>2</sub> reference electrode. In all cases, electrolysis was done at the current 100-120 mA maintaining the potential at 1.10 V<sub>i</sub> (SCE) for 15 min. using platinum electrodes. After the reaction mixture had been worked up as usual, the residue was subjected to chromatography on Al<sub>2</sub>O<sub>3</sub>. 1-Benzyltetrahydroisoquinolines (1a), (1c), and (1f) were synthesized by the usual methods<sup>2,4</sup>. Benzyl group in (2a) and (2c) was hydrolysed by the method of Marsh and Goodman<sup>3</sup>, namely, a solution of 200 mg of (2a) or (2c) in 2 ml of CF<sub>3</sub>CO<sub>2</sub>H was allowed to stand at room temperature for 10 hr.



(1a) was oxidized in the manner described above to give (2a) as colorless crystals, m.p. 142-144° (from acetone; lit.<sup>2,5</sup> as colorless syrup) in 86 % yield<sup>6</sup> (98 % based on recovered starting material)<sup>7</sup>. (2a) was hydrolysed in the method described above to give (±)-flavinantine (2b) as colorless crystals, m.p. 138-140°<sup>8</sup> (from acetone) in 63 % yield. The uv, ir, nmr, and mass spectra of (2b) were completely identical with those of natural flavinantine, kindly donated by Prof. K. L. Stuart.

Electrolysis of (1c) in the described fashion gave (2c) as colorless crystals, m.p. 165-167° (from acetone; lit.<sup>2,4f</sup> as an oil) in yield 74 %<sup>9</sup> (90 % based on recovered starting material)<sup>7</sup>. (2c) was hydrolysed in the manner

described above to give ( $\pm$ )-pallidine (2d) as colorless crystals, m.p. 120-122° (lit.<sup>4f</sup> as an oil) in 50 % yield, acetate (2e), m.p. 208-210° (lit.<sup>4f,11</sup> m.p. 203-204°). All physical data of (2d) and (2e) were identical with those of natural pallidine<sup>10,11</sup>.

(1f) was electrolysed in the same manner to yield ( $\pm$ )-amurine (2f) as a colorless syrup (lit.<sup>12</sup> as a pale yellow viscous svrup) in 70 % yield (80 % based on recovered starting material). The physical data of (2f) showed the completly same spectra with natural authentic spectra of amurine<sup>13</sup>. The methiodide of (2f) was cvrstallized from methanol as colorless prisms, m.p. 202-206° (dec.) (lit.<sup>13</sup> colorless prisms, m.p. 202-206° (dec.); lit.<sup>12</sup> pale yellow needles, m.p. 222-224°).

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6. The yield obtained by previous authors in an analogous anodic and chemical oxidative coupling reactions from (1a) to (2a) are 53 %<sup>2</sup> and 8.5 %<sup>5</sup>.
7. All physical data, uv, ir, nmr, and mass spectra were identical with those of previous reports.
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The recorded melting point of flavinantine is 130-132° in this communication. However, the melting point of natural and synthetic flavinantine showed the same as 138-140° using block melting point apparatus.
9. The yield obtained by previous authors in an analogous anodic and chemical oxidative coupling reactions from (1c) to (2c) are 43 %<sup>2</sup> and 10 %<sup>4f</sup>.
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