

## A TRANSFORMATION OF TETRAHYDROBERBERINE TO A RETROPROTOBERBERINE

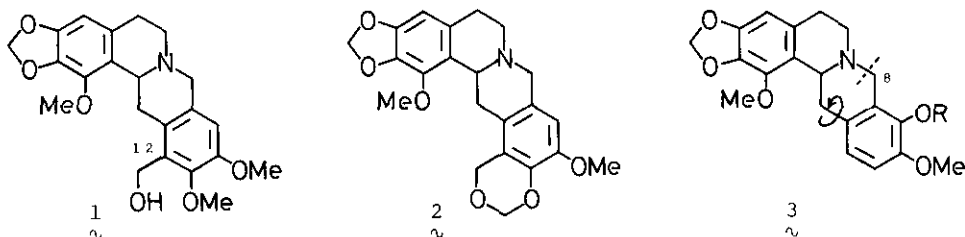
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*Abstract*— The retroprotoberberine (8) was synthesized from tetrahydroberberine (4) via the urethane (6) and the amino-alcohol (7).

Retroprotoberberine alkaloids,<sup>1,2</sup> e.g. mecambidine (1) and orientalidine (2), are characterized by the presence of one extra carbon at C<sub>12</sub> of the protoberberine skeleton and have been proposed to be biosynthesized from the corresponding protoberberine alkaloid (3) via C<sub>8</sub>-N bond cleavage.<sup>3,4</sup> The extra carbon, therefore, must originate from C-8 of 3. In previous papers, we reported a regioselective

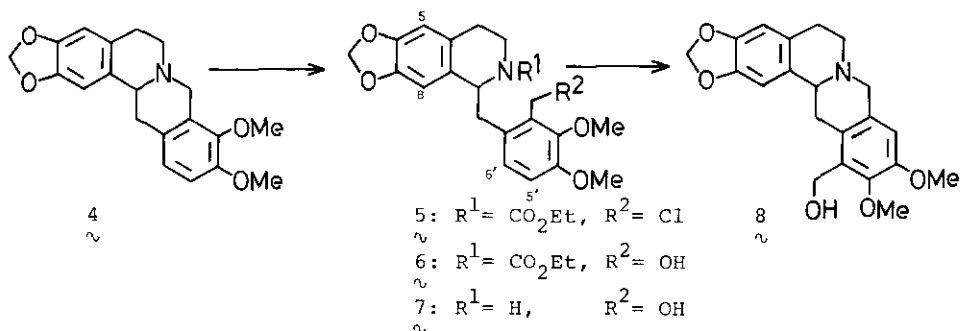


C<sub>8</sub>-N bond cleavage of tetrahydroprotoberberine using ethyl chloroformate and its application to the syntheses of (±)-canadaline,<sup>5,6</sup> (±)-α-, and (±)-β-hydrastine.<sup>7</sup>

This communication deals with the conversion of tetrahydroberberine (4) to the retroprotoberberine (8) according to the above biogenetic assumption.

Hydrolysis of the urethane (6),<sup>5</sup> derived from 4 via 5, with potassium hydroxide in aqueous ethanol in a sealed tube at 140~145° for 46 hr gave the amino-alcohol (7) [mp 157~158°, m/e 339 (M<sup>+</sup>-18), ν<sup>8</sup>) 3300, 3150, δ<sup>8</sup>) 7.01 and 6.86 (2H, AB-q, J=8.5, H-5' and H-6'), 6.80 (1H, s, H-8), 6.56 (1H, s, H-5), 5.93 (2H, s, OCH<sub>2</sub>O), 4.84 and 4.47 (2H, AB-q, J=11.5, CH<sub>2</sub>OH), 3.90 (3H, s, OCH<sub>3</sub>), 3.87 (3H, s, OCH<sub>3</sub>)] in 67% yield (86% yield based on consumed 6). The Mannich reaction of 7 with 37%

aqueous formaldehyde in acetic acid at 100° for 3.5 hr afforded the retroprotoberberine (8) [mp 195~196°,  $m/e$  369 ( $M^+$ ),  $\nu$  3350,  $\delta$  6.78, 6.60, and 6.58 (each 1H, s, Ar-H), 5.92 (2H, s, OCH<sub>2</sub>O), 4.73 (2H, br-s, CH<sub>2</sub>OH), 3.86 (3H, s, OCH<sub>3</sub>), 3.85 (3H, s, OCH<sub>3</sub>)] as a sole product in 90% yield.



The above biogenetic-type conversion will provide a new general method for the synthesis of the retroprotoberberine alkaloids.

#### REFERENCES AND FOOTNOTES

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