

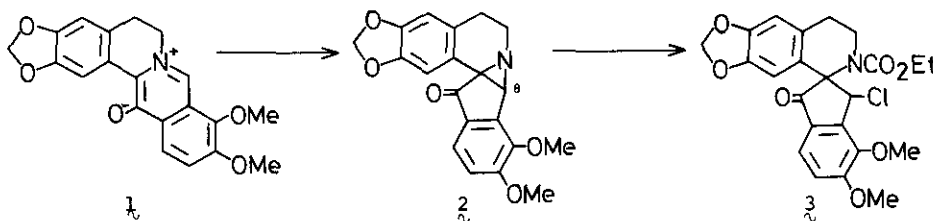
A NOVEL SYNTHESIS OF (±)-FUMARICINE

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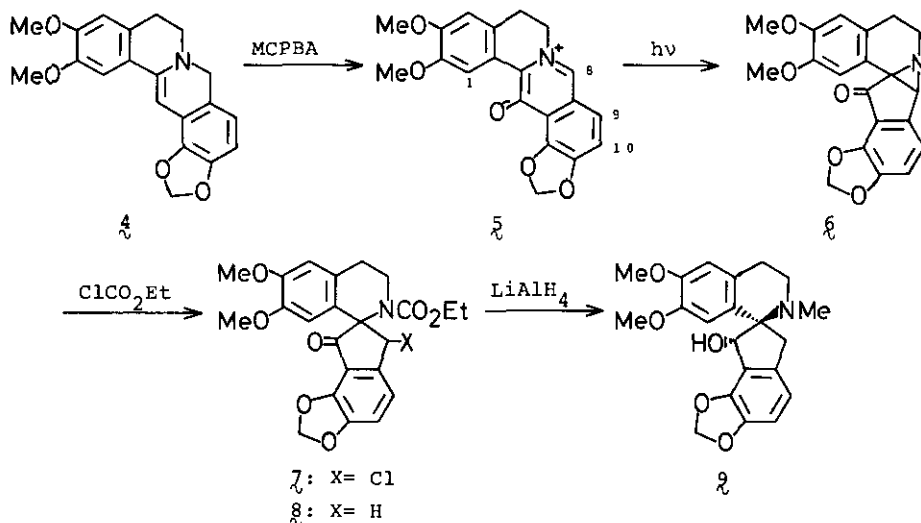
Abstract — A novel synthesis of (±)-fumaricine (9) from the phenolbetaine (5) via the 8,14-cycloberbine (6), the photochemical valence tautomer of 5, is described.

Previously, we reported a novel method for a synthesis of the spirobenzylisoquinoline (3) from berberinephenolbetaine (1) by photochemical valence tautomerization and subsequent regioselective C₈-N bond cleavage of the valence tautomer, the 8,14-cycloberbine (2).¹⁾ This communication deals with the first application of this method to a novel synthesis of a spirobenzylisoquinoline alkaloid, (±)-fumaricine (9).²⁾



Oxidation of the dehydroberbine (4)³⁾ with *m*-chloroperbenzoic acid in CH₂Cl₂ in a stream of N₂ at -20~ -30° gave the phenolbetaine (5) [69%, mp 142-143°, δ⁴⁾ 9.15 (1H, s, H-8), 7.36 (1H, s, H-1), 7.05 (2H, s, H-9 and H-10), 6.48 (1H, s, H-4)]. Irradiation (100W high pressure Hg lump, with Pyrex filter) of 5 in MeOH in a stream of N₂ for 1.5 hr at room temperature effected valence tautomerization leading to the 8,14-cycloberbine (6) [36%, ν⁴⁾ 1710, δ 3.78 (1H, s, H-8)]. Regioselective C₈-N bond cleavage of 6 with ClCO₂Et afforded the spirobenzylisoquinoline (7) [65%, mp 110-111°, *m/e*: 459, 461 (M⁺), ν 1730, 1680, δ 7.06 (2H, s, H-11 and H-12), 6.58 (1H, s, H-4), 6.11 (1H, s, H-1), 5.91 (1H, s, H-13)], which was hydrogenolyzed over 5% Pd-C to give the dechlorination product (8) in

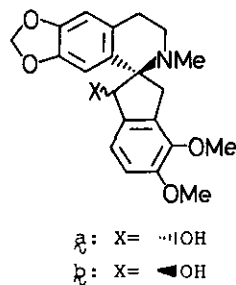
90% yield. Reduction of **8** with LiAlH_4 ⁵⁾ in THF afforded (\pm)-fumaricine (**9**) [37%, mp 148–150° (lit.²⁾ mp 147.5–149°), m/e : 369 (M^+), ν 3550, δ 6.67 (2H, s, H-11 and H-12), 6.54 (1H, s, H-4), 6.35 (1H, s, H-1), 5.88 (2H, s, OCH_2O), 5.40 (1H, s, H-8), 3.79 (3H, s, OCH_3), 3.48 (3H, s, OCH_3), 3.28 (2H, s, H-13), 2.39 (3H, s, N- CH_3)], which was proved to be identical with the authentic sample of (\pm)-fumaricine by IR and NMR spectra. The present synthesis will provide a general synthetic method for the spirobenzylisoquinoline alkaloids.



Acknowledgement: The authors are grateful to Professor H. Irie, Kyoto University, for sending the IR and NMR spectra of (\pm)-fumaricine.

REFERENCES AND FOOTNOTES

1. M. Hanaoka, S. Yasuda, K. Nagami, K. Okajima, and T. Imanishi, *Tetrahedron Letters*, 1979, 3749.
2. A synthesis of (\pm)-fumaricine has been accomplished; T. Kishimoto and S. Uyeo, *J. Chem. Soc. (C)*, 1969, 2600.
3. The synthesis of **4** will be described in a future paper.
4. All IR and NMR spectra were measured in CHCl_3 and CDCl_3 , respectively.
5. Hydrogenation of **8** over 5% Pd-C followed by LiAlH_4 reduction⁶⁾ gave stereoselectively the alcohol (**9**), while the diastereoisomeric alcohol (**10**) was stereoselectively derived from **8** by the following reaction sequence; i) NaBH_4 , ii) ClCO_2Et , iii) $\text{H}_2/\text{Pd-C}$, iv) LiAlH_4 .
6. cf. H. Irie, S. Tani, and H. Yamane, *J. Chem. Soc. Perkin I*, 1972, 2986.



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