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Synthesis of the Ochotensine Type 1-Spiroisoquinoline. Dimsylsodium-induced Rearrangement of N-Methyltetrahydroprotoberberinium Salts

The Stevens rearrangement of the N-methyltetrahydroprotoberberinium iodide (3) in the presence of sodium methylsulfinylmethanide afforded the ochotensine type 1-spiroisoquinoline (4), the structure of which was determined by the chemical and spectroscopic methods.

Although several works on the syntheses of ochotensine type 1-spiroisoquinolines through base-induced rearrangement of the phenolic protoberberinium salts were reported,[1–4] the non-phenolic protoberberinium salts were quite stable to these reagents. Recently, Kondo

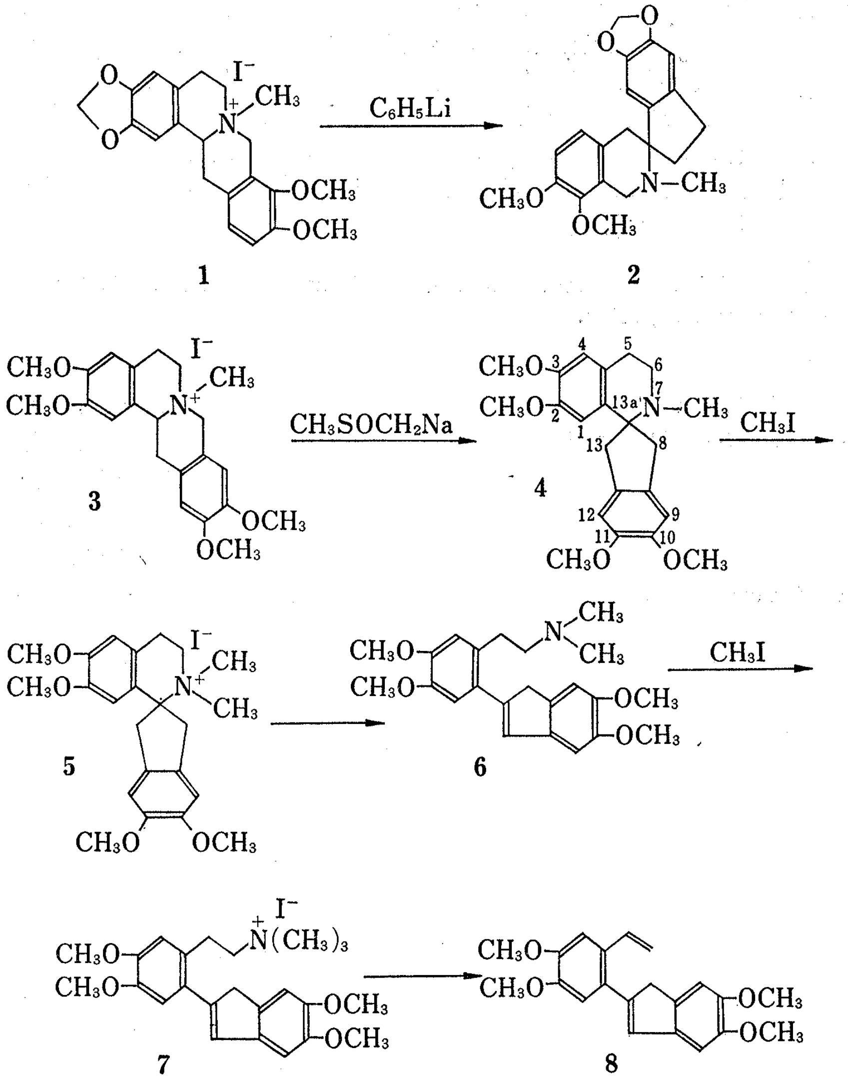

Chart 1

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1) M. Shamma and C.D. Jones, *J. Am. Chem. Soc.*, **91**, 4009 (1969); *idem, ibid.*, **92**, 4943 (1970).

2) M. Shamma and J.F. Nugent, *Tetrahedron Letters*, **1970**, 2625.

3) M. Shamma and J.F. Nugent, *Chem. Commum.*, **1971**, 1642.

4) M. Shamma and J.F. Nugent, *Tetrahedron*, 29, 1265 (1973).

and his co-workers reported the formation of the 3-spiroisoquinoline system (**2**) by the Stevens rearrangement of the N-methyltetrahydroberberinium salt (**1**) with phenyllithium.[5] We have independently examined the Stevens rearrangement of the N-methyltetrahydroprotoberberinium iodide (**3**).[6] Their results[5] prompted us to report the synthesis of the ochotensine type 1-spiroisoquinoline (**4**) by the base-induced rearrangement in this paper.

The reaction of **3** with sodium methylsulfinylmethanide in dimethyl sulfoxide (DMSO) afforded the 1-spiroisoquinoline (**4**) in 80% yield, mp 122—123°, the molecular formula, $C_{22}H_{27}NO_4$, of which was established by mass spectral (M^+, *m/e* 369) and elemental analysis. Its nuclear magnetic resonance (NMR) ($CDCl_3$) spectrum showed two singlets at 3.20 and 3.33 ppm attributable to C_8–H_2 and C_{13}–H_2. The N–CH_3 signal appeared at 2.22 ppm. The ^{13}CNMR ($CDCl_3$) spectrum also supported the structure (**4**); 26.95 (C_5), 38.21 (N–CH_3), 45.96 (C_8 and C_{13}), 48.34 (C_6), 56.03 ($4\times OCH_3$), 69.01 ppm (C_{13a}). Treatment of the methiodide (**5**), mp 204—205°, prepared by the usual way, with sodium methylsulfinylmethanide gave the methine base (**6**). The NMR ($CDCl_3$) spectrum of **6** showed a methylene signal at 3.67 ppm and olefinic and aromatic signals at 6.75 (2H), 6.80 (1H), 6.92 (1H), and 7.02 (1H) ppm. These signals indicated the presence of a indene system in the methin base (**6**). The methiodide (**7**), obtained on treatment of **6** with methyl iodide, was heated in ethanolic sodium hydroxide to give **8**, mp 104—105°, $C_{21}H_{22}O_4$ (M^+, *m/e* 338). The structure of the des-N methine (**8**) was supported by a methylene signal at 3.70 ppm and two pairs of doublets, characteristic of styrens, at 5.17 (1H, $J=10$, 2 Hz) and 5.53 ppm (1H, $J=17$, 2 Hz) observed in its NMR ($CDCl_3$) spectrum. Therefore the product from the N-methyltetrahydroprotoberberinium iodide (**3**) was proved to be the 1-spiroisoquinoline (**4**).

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[5] Y. Kondo, T. Takemoto, and K. Kondo, *Heterocycles*, **2**, 659 (1974).

[6] S. Kano, T. Ogawa, E. Komiyama, T. Yokomatsu, Y. Takahagi, and S. Shibuya, Abstracts of the 7th ongress of Heterocyclic Chemistry, Chiba, Japan, 1974, p. 181.