STEREOSELECTIVE SYNTHESIS OF AN ALKENOID-TYPE ERYTHRINAN ALKALOID, (±)-ERYTHRATIDINE[1)]

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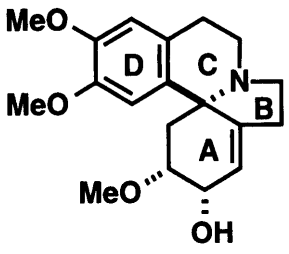
Oxidation of (±)-demethylerysotramidine (**2**) with mCPBA gave the α-1,2-epoxide (**3**) as a single product, which was methylated to **4**, then treated with SmI_2 in THF-MeOH to give 8-oxoerythratidine (**5**) in good yield. Finally, **5** was reduced with a $LiAlH_4$-$AlCl_3$ combination to the natural alkaloid, (±)-erythratidine (**1**).

KEY WORDS erythratidine; stereoselective epoxidation; samarium iodide; alkenoid-type erythrinan alkaloid; total synthesis

Erythrinan alkaloids possessing a D-aromatic ring are classified into two groups based on the structures of A/B rings: the dienoid type and alkenoid type. Although several total syntheses of the former type of alkaloids have been achieved,[2)] total synthesis of the latter type of alkaloids (35 species are known) is still elusive except for the simplest alkaloid, 3-demethoxyerythratidinone.[3)] Here we report the total synthesis of a representative of the latter, erythratidine[4)] (**1**), which has three chiral centers, from a key intermediate in the synthesis of dienoid-type alkaloids. In this conversion, radical reduction with samarium iodide was effective for construction of the desired allylic alcohol from an epoxy-enone system.



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Oxidation of (±)-demethylerysotramidine (**2**)[5)] with *m*-chloroperbenzoic acid (mCPBA) afforded an epoxide **3** as a single product in 70% yield.[6)] On the other hand, erysotramidine (**2**: OMe instead of OH) was recovered unchanged in a similar oxidation. The ^{1}H-NMR spectrum of **3** proved that it is the 1,2-epoxide, since only one olefinic proton at δ 6.48 was observed. The stereochemistry of the epoxide group was assigned as α (the same side as the hydroxy group) based on the Henbest rule,[7)] and finally confirmed from non-identity with the alternatively synthesized β-epoxide isomer.[8)]

Compound **3** was methylated with iodomethane and NaH in the presence of a phase-transfer catalyst (Bu_4NHSO_4) to the *O*-methyl derivative (**4**)[6)] in 62% yield.[9)] Conversion of **4** to the desired allylic alcohol (**5**) with opening of the epoxide ring and migration of the double bond to the unconjugated position from the conjugated position were achieved by radical reduction with SmI_2. Thus treatment of **4** with samarium iodide in THF-MeOH at -90°C afforded the expected allylic alcohol **5**[6)] in 74% yield.[10)] The structure and stereochemistry of **5** were confirmed from the detailed analysis of its NMR spectra. Finally, the lactam group was removed by reduction with a $LiAlH_4$-$AlCl_3$ combination[11)] in 79% yield.[12)] The base thus obtained was confirmed to be identical to

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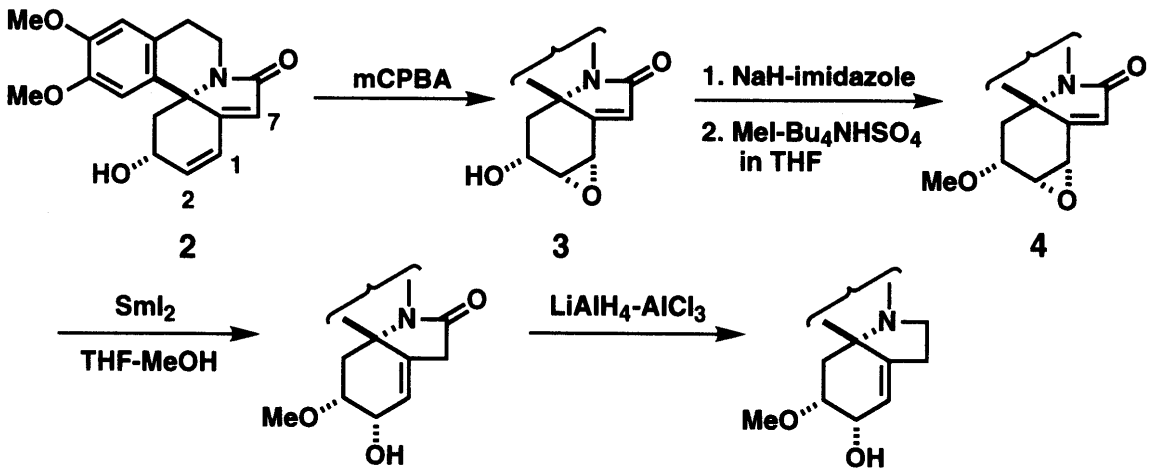
erythratidine by comparison of the ^{1}H-NMR spectral data with those of (+)-erythratidine reported by Barton *et al.*[4b]



2 3 4

5 (±)-1

Chart 1

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6) Data of new compounds. **3**: mp 258-261°C (AcOEt). IR (KBr) cm^{-1}: 3330, 1671. ^{1}H-NMR ($CDCl_3$-CD_3OD) δ: 6.75, 6.60, 6.48 (each 1H, s, 2xArH, C_7-H), 4.30 (1H, d, *J*=3.7 Hz, C_1-H), 4.06 (1H, ddd, *J*=11.2, 5.3, 1.9 Hz, C_3-H), 3.87, 3.84 (each 3H, s, OMe), 3.77 (1H, dd, *J*=3.7, 1.9 Hz, C_2-H). **4**: mp 169-170°C (AcOEt). IR (KBr) cm^{-1}: 1685. ^{1}H- NMR ($CDCl_3$) δ: 6.74, 6.59, 6.49 (each 1H, s, 2xArH, C_7-H), 4.27 (1H, d, *J*=3.9 Hz, C_1-H), 3.87, 3.84, 3.40 (each 3H, s, OMe), 3.83 (1H, dd, *J*=3.9, 1.9 Hz, C_2-H), 3.73 (1H, ddd, *J*=11.1, 5.3, 1.9 Hz, C_3-H). **5**: mp 183-185°C (AcOEt). IR (KBr) cm^{-1}: 3375, 1703. ^{1}H-NMR ($CDCl_3$) δ: 6.68, 6.48 (each 1H, s, ArH), 6.06 (1H, dd, *J*=3.6, 2.4 Hz, C_1-H), 4.53 (1H, td, *J*=3.6, 2.4 Hz, C_2-H), 3.86, 3.82, 3.35 (each 3H, s, OMe), 3.55 (1H, ddd, *J*=12.8, 4.2, 3.6 Hz, C_3-H). (±)-**1**: gum. ^{1}H-NMR ($CDCl_3$) δ: 6.62, 6.49 (each 1H, s, ArH), 5.85 (1H, m, C_1-H), 4.48 (1H, m, C_2-H), 3.86, 3.80, 3.36 (each 3H, s, OMe), 3.69 (1H, ddd, *J*=12.8, 4.3, 3.7 Hz, C_3-H). $J_{1,2}$=4.3 Hz, $J_{2,3}$=4.3 Hz by a decoupling experiment. Picrate: mp 217-219°C (acetone).

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8) All possible four stereoisomers from 3-OH and 1,2-epoxide were synthesized. Details will be described in a full paper.

9) Without Bu4NHSO4, methylation did not proceed.

10) Reduction of a similar system has been reported [Molander G. A., La Belle B. E., Hahn G., *J. Org. Chem.*, **51**, 5259-5264 (1986)].

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12) A by-product in this reduction was (±)-erysotrine (17%).

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