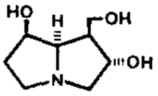
STEREOSELECTIVE TOTAL SYNTHESIS OF PYRROLIZIDINE ALKALOID BASES, (-)-ROSMARINECINE AND (-)-ISORETRONECANOL

Kuniaki Tatsuta, Hideaki Takahashi, Yoshiya Amemiya and Mitsuhiro Kinoshita

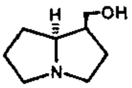
Department of Applied Chemistry, Keio University
Hiyoshi, Kohoku, Yokohama 223, Japan

The first, stereoselective total synthesis of pyrrolizidine "necine" bases, (-)-rosmarinecine[1] (**1**) and (-)-isoretronecanol[2] (**2**) is reported, starting from D-glucosamine. The furanose **3**, which was derived in 6 steps from methyl α-D-glucosaminide via the stereospecific skeletal-rearrangement[3] of the N,O-o-benzenesulfonyl derivative, was silylated to **4** and subjected to the Grignard reaction with allylmagnesium bromide to afford stereoselectively the *threo* amido alcohol **5** (92%), which was in turn converted to the monomesylated γ-lactam **6** in 7 steps. Treatment of **6** with borane-methylsulfide to give the pyrrolizidine skeleton with intramolecular S_N2 displacement of the intermediary pyrrolidine derivative, followed by cleavage of MOM protecting group afforded (-)-rosmarinecine [**1**: $[\alpha]_D^{21}$ -121° (EtOH); picrate (needles from EtOH): mp 175°C] identical in all respects with that obtained from natural sources.

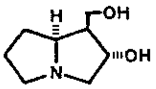
In the similar manner, the natural (-)-isoretronecanol (**2**) and (-)-7-deoxyrosmarinecine (**7**) were stereoselectively synthesized from the common intermediate **3** through the unsaturated ester **8**.



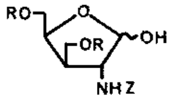
(-)-Rosmarinecine (**1**)



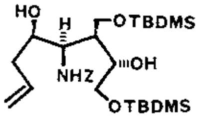
(-)- Isoretronecanol (**2**)



(-)-7-Deoxyrosmarinecine (**7**)



3: R=H
4: R=TBDMS



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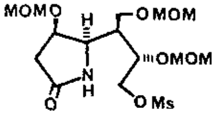

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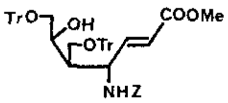

8

References:

1) M. F. Richardson & F. L. Warren, *J. Chem. Soc.*, 1943, 452.

2) R. Adams & K. E. Hamlin, Jr., *J. Am. Chem. Soc.*, 64, 2597 (1942).

3) K. Tatsuta, S. Miyashita, K. Akimoto & M. Kinoshita, *Bull. Chem. Soc. Jpn.*, 55, 3254 (1982).