

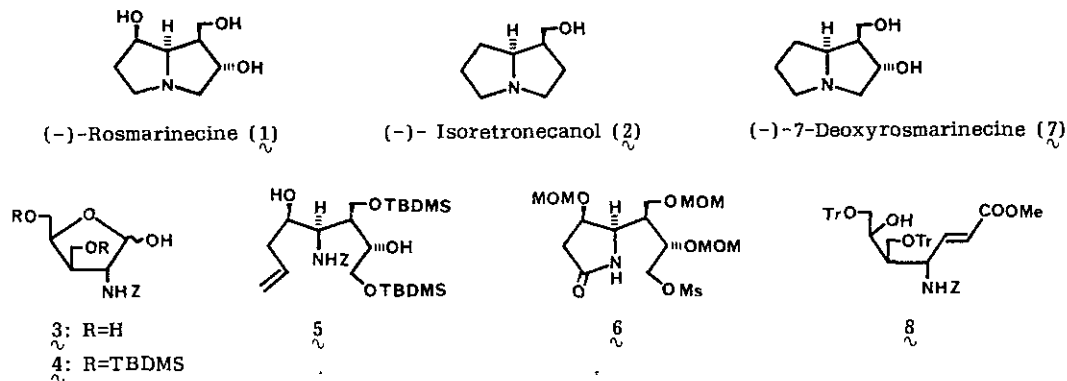
STERESELECTIVE TOTAL SYNTHESIS OF PYRROLIZIDINE ALKALOID
BASES, (-)-ROSMARINECINE AND (-)-ISORETRONECANOL

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The first, stereoselective total synthesis of pyrrolizidine "necine" bases, (-)-rosmarinine¹⁾ (1) and (-)-isoretronecanol²⁾ (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-rearrangement³⁾ 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 (-)-rosmarinine [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-deoxyrosmarinine (7) were stereoselectively synthesized from the common intermediate 3 through the unsaturated ester 8.



References:

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- 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).