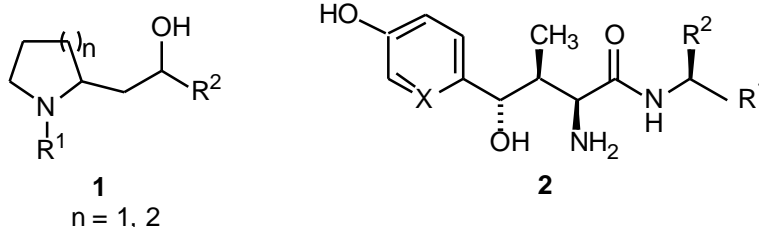


New Variants of the Mannich Reaction for the Synthesis of Alkaloids and Nikkomycins

Jeanne Delbos-Krampe

The syntheses of two independent classes of natural products are presented in this thesis: the piperidine and pyrrolidine alkaloids **1** and the Nikkomycins **2**. Both are of great interest because of their promising pharmacological properties.



Although they have very different structures, alkaloids and Nikkomycins share one common aspect: the key-step in their synthesis is the Mannich reaction yielding a *b*-aminoketone intermediate. In both cases the *b*-aminoketone is obtained by the addition of an iminium salt to a carbonyl compound. If a second stereogenic center is introduced, the diastereoselectivity of this step can be directed varying the reaction parameters. Using an enamine instead of a ketone at low temperature or employing the NaI/Me₃SiCl/NEt₃-mediated Mannich reaction gives the *anti*-products with very high diastereoselectivity.

The *b*-aminoketone can be transferred to natural and non natural derivatives by reduction and in some cases deprotection. 1,3-Aminoalcohols **1** and **2** can be obtained by this method without much preparative efforts.

This strategy provides the construction of Nikkomycine building blocks only in two steps for the first time.