

SYNTHESIS OF (+)-LUPININE AND (+)-EPI-LUPININE
UTILIZING THE ANODIC OXIDATION OF LACTAMS

Makoto Okita, Takeshi Wakamatsu and Yoshio Ban
Faculty of Pharmaceutical Sciences, Hokkaido University
Sapporo, 060 Japan

It was previously reported that the anodic oxidation of N-primary-alkyl lactams regioselectively occurred at the endocyclic methylene- α -carbon of nitrogen in five- and six-membered rings to furnish the hydroxylated lactams and imides, and this method was applied to the synthesis of various heterocycles, including the natural alkaloids. We wish to report a new synthesis of (+)-lupinine, (+)-epilupinine and related heterobicyclic compounds by anodic oxidation of lactams(1) bearing the malonate group at the terminal position of N-alkyl side chain.

The anodic oxidation of the lactams(1) was also regioselectively carried out at the endocyclic methylene- α -carbon in methanol, which provided the corresponding methoxylated lactams(2). The methylene chloride solution of 2 was reacted with TiCl_4 to give the heterobicyclic compounds(3) in good yields, possibly through generation of α -acyliminium cation as a crucial transition state in the intramolecular C-C bond formation.

The required lactam(1c) for the synthesis of the lupine alkaloids was prepared from dimethyl (3-iodopropyl)-malonate by heating with 2-ethoxy-3,4,5,6-tetrahydropyridine. A solution of the lactam(1c) in methanol electrolyzed by constant current, gave the product(2c) in high yield. The treatment of the compound(2c) with TiCl_4 yielded the quinolizidine derivative(3c). Decarboxylation of 3c gave two products, 4 and 5. The lithium aluminum hydride reduction of 4 afforded (+)-lupinine. By the same reduction of 5, (+)-epilupinine was obtained.

