SYNTHESIS OF (±)-LUPININE AND (±)-EPILUPININE UTILIZING THE ANODIC OXIDATION OF LACTAMS

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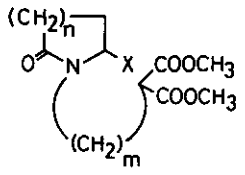
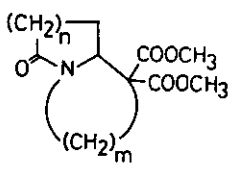
It was previously reported that the anodic oxidation of N-primary-alkyl lactams regioselectively occurred at the endocyclic methylene-α-carbon of nitrogen in five- and six-membered rings to furnish the hydroxylated lactams and imides, and this method was applied to the synthesis of various heterocycles, 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.

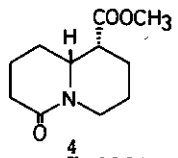


1 X= H
2 X= OCH_3



3

a: m=3, n=1
b: m=2, n=1
c: m=3, n=2



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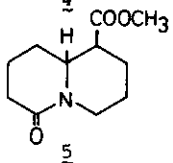

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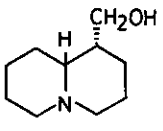
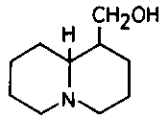


lupinine



epilupinine