SYNTHESIS OF LACTAMS FROM N-ACYLATED CYCLIC AMINES BY RuO_4 OXIDATION METHOD

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In order to develop a general, versatile method for synthesis of lactams from cyclic amines, the RuO_4 oxidation of N-acylated cyclic amines was investigated. This oxidation method was earlier utilized by Sheehan to simple amines.

The oxidation of N-acylated piperidines bearing substituents at the 3-position such as the methyl, ethyl, isopropyl, benzyl, phenyl, or ethoxycarbonyl group which were easily synthesized from 3-substituted piperidines by acylation with acyl chlorides such as acetyl, propionyl, trimethylacetyl, cyclohexanecarbonyl, or ethoxycarbonyl chloride was carried out at 20° in carbon tetrachloride using catalytic amount of RuO_2 and excess 10% aqueous $NaIO_4$ in a two-phase system to produce the corresponding 2- and 6-piperidones in good yields. In the all cases, the 6-position oxidation predominated over the 2-position oxidation. It was suggested that the unfavoured oxidation at the 2-position may be due to steric and electronic repulsion between the substituent at the 3-position and the oxidant approaching to the 2-position.

Next, the RuO_4 oxidation of N,N'-diacyl derivatives of six-membered cyclic amines containing two nitrogen atoms in ring was examined. When N,N'-diacetyl- and N,N'-diethoxycarbonylpiperazines were oxidized under the same manner, the corresponding 2-oxo and 2,3-dioxo compounds were obtained. In the oxidation of 2,5- and 2,6-dimethylpiperazine derivatives, and hexahydropyridazine derivative, the monooxidation products were obtained. However, the cleavage of ring was caused at the 2-position in the case of hexahydropyrimidine system.

These N-acylated lactams obtained in the above oxidation can be converted into the NH-type lactams by common method of deacylation, which might be useful as synthetic intermediates of various heterocyclic compounds.