CONVERSION OF 3-SUBSTITUTED PIPERIDINES AND PYRIDINES INTO THE CORRESPONDING N-(3,4-DIMETHOXYPHENETHYL)LACTAMS: A COMPARATIVE STUDY OF THE MERCURIC ACETATE–EDTA AND THE FERRICYANIDE OXIDATION METHODS

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The mercuric acetate–EDTA oxidation of 1-(3,4-dimethoxyphenyl)-2-piperidinoethanol to form 1-[2-(3,4-dimethoxyphenyl)-2-hydroxyethyl]-2-piperidone has been extended to include piperidine derivatives carrying the methyl, ethyl, butyl, isopropyl, phenyl, benzyl, carbamoyl, methoxycarbonyl, acetyl, or 1,1-ethylenedioxyethyl group, which have been synthesized from 3-substituted pyridines by quaternization with 3,4-dimethoxyphenacyl bromide followed by catalytic and $NaBH_4$ reductions. It has been found that the hydrocarbon group at the 3-position orients the oxidation to both the 2- and the 6-position but with advantages to the latter position and that the extent of the 6-piperidone formation is increased as the 3-substituent is changed from the lower to the higher and/or bulkier homolog. The carbonyl functions orient the oxidation to the 6-position almost exclusively.

In the alkaline ferricyanide oxidation at 32° of 3-substituted 1-(3,4-dimethoxyphenethyl)pyridinium bromides which carry the same alkyl substituents as described above, the oxidation at the 2-position is much favored over that at the 6-position. A higher and/or bulkier 3-alkyl substituent causes the extent of the 6-pyridone formation to increase. The hydroxymethyl, dimethylaminomethyl, phenyl, and carbamoyl groups at the 3-position produced the corresponding 2- and 6-pyridones in ratios of 70 : 30, 26 : 74, 13 : 87, and 50 : 50. The carboxyl, 1,1-ethylenedioxyethyl, and 1,1-ethylenedithioethyl groups at the 3-position orient the ferricyanide oxidation to the 6-position almost exclusively. The structures of the pyridones thus prepared have been assigned on the basis of their UV, IR, and NMR spectra and those of the 3- or 5-substituted 1-[2-(3,4-dimethoxyphenyl)-2-hydroxyethyl]-2-piperidones obtained by the mercuric acetate–EDTA oxidation method have been established by the chemical correlation with the corresponding pyridones through 3- or 5-substituted 1-(3,4-dimethoxyphenethyl)-2-piperidones, which are key intermediates for the synthesis of 1- or 3-substituted 9,10-dimethoxybenzo[a]quinolizidines.