HETEROCYCLES. Vol.12. No. 1 , 1979

QUATERNIZATION OF PYRAZINE DERIVATIVES AND REDUCTION OF THE PYRAZINIUM SALTS WITH $NaBH_4$

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The authors have reported already the synthesis of some naturally occurring pyrazines and the transformation of pyrazines to diketopiperazines. In continuation of these works, quaternization of pyrazines, pyrazinols and pyrazine 1-oxides, and reduction of the methiodides, thus obtained, will be described in the present report.

The methiodides, prepared by heating the above-mentioned pyrazine derivatives with methyl iodide at 80°, were converted to the corresponding piperazines, 2-ketopiperazines and 1-hydroxypiperazines, respectively, by the treatment with sodium borohydride in water or a mixture of methanol and water. Some 1-methyl-2-keto-1,2-dihydropyrazines, derived from pyrazinols by the treatment with diazomethane, were also submitted to the quaternization reaction and the following reduction, to afford 1-methyl-2-ketopiperazines.

Reduction of pyrazine derivatives with sodium borohydride was studied also in an acidic medium. Namely, some alkylpyrazinols and 2-hydroxypyrazine 1-oxides, dissolved in 1N hydrochloric acid, were successfully reduced to give the corresponding 2-keto-piperazines and 1-hydroxy-2-keto-piperazines in a moderate yield. The latter was characteristic for a red coloration with ferric chloride.

As shown in Tables, the quaternization of phenylpyrazines proceeded hardly. These phenomena might be caused by the steric hindrance and the electron withdrawing effect of phenyl groups. In the case of the reduction of some phenylpyrazine 1-oxide methiodides, deoxygenation occurred simultaneously, to afford the 1-methylpiperazines, because the phenyl group might weaken the basisity of the pyrazinic nitrogen.

In some cases of the reduction of pyrazinols, pyrazinol methiodides and 2-hydroxypyrazine 1-oxides, the products showed two spots on TLC plates and were separated by column chromatography from each other. Stereochemical studies of these products are now in progress.