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A NOVEL NUCLEOPHILIC SUBSTITUTION OF THE PYRIDINE RING

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There are relatively few methods for direct nucleophilic substitution of the pyridine ring. The amination of pyridine using either sodium amide or sodium in liquid ammonia[1] as well as in amines[2,3] is widely known and applied. Both quinoline and isoquinoline can be hydroxylated by means of KOH[4], but pyridine itself yields only traces of 1H-2-pyridone.[5] Both the Abramovitch reaction of azaheterocyclic 1-oxides with arylimidoyl halides, nitrilium salts[6] and activated acetylenes[7,8] as well as the Abramovitch rearrangement of N-aryloxypyridinium salts[9] offer wide scope for the nucleophilic substitution of azaheterocyclic rings with various amino, alkyl and aryl substituents.

We now present a new type of intramolecular nucleophilic hydroxylation of the pyridine ring. Thus, pyridine and either anhydrous or crystalline $CuSO_4$ yield 1H-2-pyridone /95%/ when heated in an autoclave at about 300°C for 6-8 hrs.[10] 3-Picoline,[11] 3,5-lutidine, quinoline and isoquinoline also undergo hydroxylation under identical conditions, to give 3-methyl-1H-2-pyridone /3.2%/ and 5-methyl-1H-2-pyridone /6.8%/, 3,5-dimethyl-1H-2-pyridone, m.p. 117° /10%/, 1H-2-quinolone /25%/, and 2H-1-isoquinolone /17%/, respectively. The yields gi-

ven in parentheses are calculated on the basis of the bases consumed in the reaction.

The pyridones described above can easily be isolated from the reaction mixture by distillation of the unreacted base followed by extraction with benzene of the residue mixed with either silica gel or sand.

Pyridine bases bearing methyl groups in either the 2- or the 4-positions of the ring react with $CuSO_4$ in a different manner. The methyl groups are oxidized to carboxyl at 180°C within 6-8 hrs, but the corresponding pyridinecarboxylic acids undergo partial decarboxylation under the reaction conditions.

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