THE REACTION OF HETEROAROMATIC AMINE OXIDES WITH $TiCl_4/NaBH_4$

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Abstract ——— Treatment of 2-, 3-, 4-picoline N-oxides and 2,6-dimethylpyridine N-oxide with $TiCl_4/NaBH_4$ in dimethoxyethane afforded the corresponding picolines and 2,6-dimethylpyridine in acceptable yields. The same reaction of quinaldine N-oxide and benzo[h]quinoline N-oxide successfully gave quinaldine and benzo[h]quinoline, respectively. In the case of quinoline N-oxide, 1,2,3,4-tetrahydroquinoline and quinoline were obtained. On the other hand, lepidine N-oxide and isoquinoline N-oxide afforded the corresponding 1,2-dihydro derivatives. Similarly, papaverine N-oxide gave 1,2-dihydropapaverine as a major product accompanying with papaverine.

Deoxygenation of heteroaromatic amine oxides has been the subject of the extensive research and various conditions and many preparatively useful methods have been reported[1-4]. Generally, the nitrogen-oxygen bond has been reduced by catalytic hydrogenation, complex hydrides, trivalent phosphorus compounds, various sulfur containing compounds, dissolving metals, metal iron and electrolysis[1-4]. Recently, deoxygenation of heteroaromatic amine oxides by aqueous titanium trichloride[5], sulfoxide[6] and chromous chloride[7] has been reported. We have investigated the deoxygenation of heteroaromatic amine oxides with low-valent titanium borane complex[8], easily obtained by mixing $TiCl_4$ (1.1 equi mole) and $NaBH_4$ (2.2 equi mole) in dimethoxyethane (DME), and this reducing species has been found to effective for the deoxygenation of heteroaromatic amine oxides. Herein we wish to report these results.

Treatment of 2-, 3-, 4-picoline and 2,6-dimethylpyridine N-oxides with $TiCl_4$/$NaBH_4$ in anhydrous DME at room temperature for 1 hr afforded the corresponding picolines and 2,6-dimethylpyridine, respectively, in greater than 90 % yield. The reaction readily took place and the blue colored reaction mixture , characteristic of low-valent titanium borane complex, turned to colorless at the end of the reaction. The same reaction of N-oxides of quinoline and isoquinoline derivatives was carried out. In the cases of quinaldine N-oxide and benzo[h]quinoline N-oxide, deoxygenation smoothly occurred to yield quinaldine and benzo[h]quinoline. *However, quinoline N-oxide gave 1,2,3,4-tetrahydroquinoline as a major* product accompanying with quinoline. Lepidine N-oxide and isoquinoline N-oxide were converted to 1,2-dihydrolepidine and 1,2-dihydroisoquinoline[9], respectively, by the reduction with $TiCl_4$/$NaBH_4$. In addition, papaverine N-oxide was also subjected to this deoxygenation to give 1,2-dihydropapaverine[10,11] and papaverine in 67 and 37 % yield, respectively. Table 1 lists the products thus obtained and their yields based upon the amounts of the isolated ones. The structure of these products was established by comparison of their spectral data with those of the authentic samples.

Heteroaromatic compounds such as pyridine, quinoline and isoquinoline are reduced neither to the corresponding dihydro derivatives, nor to the tetrahydro anlogues with $TiCl_4$/$NaBH_4$ and the starting materials remain unchanged. Therefore, the deoxygenated heteroaromatic compounds are not intermediates for the formation of dihydro- and tetrahydroquinoline or isoquinoline derivatives.

Thus, $TiCl_4$/$NaBH_4$ was found to be effective for the deoxygenation of heteroaromatic amine oxides, especially, for the deoxygenation of N-oxides of pyridine and α-alkylquinoline derivatives.

Table 1. Deoxygenation of Pyridine, Quinoline and Isoquinoline N-Oxides[a]

N-Oxides	Products	Yield (%)[b]
2-Picoline N-Oxide	2-Picoline	95
3-Picoline N-Oxide	3-Picoline	95
4-Picoline N-Oxide	4-Picoline	90
2,6-Dimethylpyridine N-Oxide	2,6-Dimethylpyridine	93
Quinaldine N-Oxide	Quinaldine	87
Lepidine N-Oxide	1,2-Dihydrolepidine	90
Quinoline N-Oxide	Quinoline	32
	1,2,3,4-Tetrahydroquinoline	65
Benzo[h]quinoline N-Oxide	Benzo[h]quinoline	91
Isoquinoline N-Oxide	1,2-Dihydroisoquinoline	89
Papaverine N-Oxide	Papaverine	32
	1,2-Dihydropapaverine	67

[a] Molar ratios of Sub/$TiCl_4$/$NaBH_4$ is 1/1.1/2.2. [b] Based upon the amounts of isolated products.

References and Notes

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