SYNTHESIS OF SUBSTITUTED PYRIDINES FROM N-tert-BUTYLIMINE AND ENAMINES

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As one of applications of de-tert-butylation which we often observe during heterocyclic syntheses, we have found one step synthesis of 3,5-disubstituted pyridines from N-tert-butylimine (Ia) and enamines II. Treatment of Ia with β-substituted vinylpiperidines (IIa-d) or vinylmorpholine (IIe) (substituent R) in benzene at 200°C (in a sealed tube) for 6-9 hr gave 3,5-di-R-pyridines IIIa-e: IIIa, R = Me, 48%; IIIb, R = Et, 34%; IIIc, R = i-Pr, 53%; IIId, R = c-C_6H_{11}, 84%; IIIe, R = Ph, 73%.

Although a few reactions between imines and enamines are reported, such heteroaromatization has not been known. Mechanistic study in detail clarified that 1-tert-butyl-3-R-1-azabuta-1,3-diene (IV) is initially formed by cycloaddition of Ia and II followed by elimination of an amine (moiety of II) and rearrangement. Indeed the azabutadiene IV was isolated under certain conditions (R = Me, Et). Then eliminations of the amine (moiety of II), isobutene (checked by GLC), and hydrogen from the cycloadduct of the azabutadiene IV and II lead to the pyridine III. Hence the imine Ia constitutes 1- and 4-positions of III.

Preparation of unsymmetrically di-substituted or poly-substituted pyridines are also discussed. By treating 1-tert-butyl-3-ethyl-1-azabuta-1,3-diene (IVb) with II, 3-ethyl-5-isopropyl- and 3-ethyl-5-phenylpyridines were obtained in 45 and 53% yields, respectively. Formation of tri-substituted pyridine was detected by NMR in the reaction of IVb with 1-piperidino-1-cyclohexene, but N-tert-butylethylideneamine (IIb) gave no pyridines when treated with enamines.

Further investigation especially on reaction conditions is in need to obtain poly-substituted pyridines.