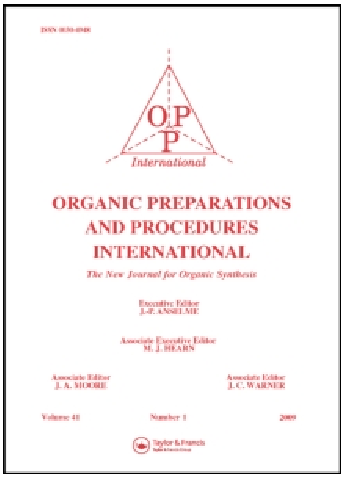

Organic Preparations and Procedures International
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t902189982

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To cite this Article Bertini, F. , Caronna, T. and Cecere, M.(1973) '*tert*-ALKYLATION OF PYRIDINE N-OXIDE', Organic Preparations and Procedures International, 5: 3, 109 — 112

To link to this Article: DOI: 10.1080/00304947309355556

URL: http://dx.doi.org/10.1080/00304947309355556

ORGANIC PREPARATIONS AND PROCEDURES INT. 5(3), 109-112 (1973)

tert-ALKYLATION OF PYRIDINE N-OXIDE

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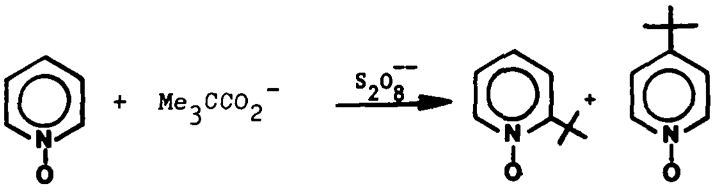
The protonation of heteroaromatic bases increases their electron-deficient nature and makes possible new homolytic substitution reactions with nucleophilic radicals, which are of particular synthetic interest.[1] N-Oxidation also increases the reactivity of heteroaromatic bases toward nucleophilic agents[2] so that high selectivity in the 2- and 4-positions would be anticipated in the homolytic substitution of aromatic N-oxides with nucleophilic radicals. Moreover, a nitroxide-type structure(V) could contribute to the selectivity of attack of free radicals on aromatic N-oxides.



III IV

V

However, several of our attempts to achieve homolytic alkylation of pyridine N-oxide with various radical sources had resulted in the deoxygenation of the reaction products. We now report a new procedure for the homolytic alkylation of pyridine N-oxide with very high selectivity and little loss of oxygen. The alkyl radicals were generated by the oxidation of alkyl carboxylate ions with peroxydisulfate as shown below.

$$S_2O_8^{--} \longrightarrow 2\ SO_4^{-\cdot} \xrightarrow{R-CO_2^-} R\cdot + CO_2 + SO_4^{--}$$

Although the reaction gives good results with tertiary alkyl radicals, only poor yields(10-15%) are obtained with primary and secondary alkyl radicals. The very high nucleophilic character of t-alkyl radicals[3] is presumably responsible for this behavior. The activation exerted by N-oxidation is thus apparently lower than that resulting from protonation of heteroaromatic bases. Poor results are also obtained by using as radical source, the silver(II)-catalyzed decarboxylation of acids with peroxydisulfate which is usually a more effective source of alkyl radicals.[4]

EXPERIMENTAL

All melting points are uncorrected. The nmr spectra were recorded on a Varian A-60 spectrometer; the chemical shifts are reported in ppm(δ) from TMS as an internal standard. Mass spectra were obtained on a Hitachi-Perkin Elmer RMU 6D at 70 eV. The samples were introduced by means of an "all glass heated inlet system" at 200°. The gas chromatographic analyses were carried out with a Hewlett-Packard 5751 G instrument with a flame inonization detector, ss column 5' x 1/8" packed with 10% silicone UCC-W-982 on Chromosorb W-AW DMCS 100-200 mesh; N_2: 25 ml./min. The analyses were performed at programmed temperatures from 158°-240°, program rate 6°/min.; the total time was 9'. Preparative glp chromatography was carried out with a Varian Aerograph 90 P3, thermal conductivity detector, 5' x 1/4" 20% XE on Chromosorb W, 60-80 mesh; He: 55 ml./min. Temperature from 140° -175°.

4-t-Butyl pyridine N-oxide.- To a mixture of 0.05 mole of pyridine N-oxide, 0.15 mole of pivalic acid and 0.10 mole of sodium hydroxide in 30 ml. of boiling water, was added over a period of 15 min. a solution of 0.05 mole of ammonium proxydisulfate in 15 ml. of water. Heating was continued for an additional 30 min. The solution was then stronly basified and extracted with chloroform. Removal of the solvent left a residue(4.1 g.) which was analyzed by glc.[5] Four peaks were present; the first(2%) and the second(6%) were identified as 2-t-butylpyridine(I) and 4-t-butylpyridine(II) by comparison with authentic samples.[4] The third(40%) and the fourth(52%) were identified as the corresponding N-oxides III and IV by reduction[6] to I and II and by their spectral data(nmr and mass spectra). 4-t-butylpyridine N-oxide(IV) was isolated by distillation of the reaction mixture as the fraction boiling at 135-140°/1 mm.; it crystallized on cooling. After collection and washing with diethyl ether, it melted at 103-104°, lit.[7] mp. 103.9-104.3°. The purity of the compound was shown to be 99% by glc.

nmr: δ 1.3(s, 9H), 7.2-8.3(m, 4H)

mass spectrum: M^+ 151; other peaks: 136, 120, 108, 92.

2-t-Butylpyridine N-oxide was isolated by preparative glc as a viscous liquid.

Anal. Calcd for $C_9H_{13}NO$: C, 71.49; H, 8.67; N, 9.26
Found: C, 71.63; H, 8.52; N, 9.18.

nmr: δ 1.4(s, 9H), 7.0-8.2(m, 4H)

mass spectrum: M^+ 151; other peaks: 136, 120, 108, 96, 79.

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(Received April 2, 1973; in revised form June 28, 1973)