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OXIDATIVE DEMETHYLATION OF SOME METHYLNITROPYRIDINE 1-OXIDES

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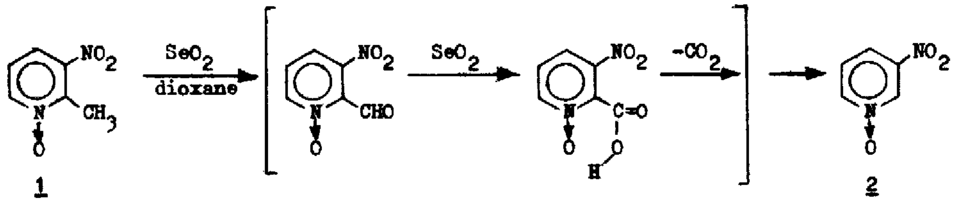
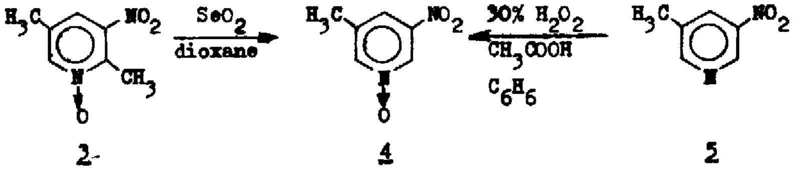
Summary: 3-Nitropyridine 1-oxide and 5-methyl-3-nitropyridine 1-oxide are produced readily by oxidative demethylation using SeO_2 of 2-methyl- and 2,5-dimethyl-3-nitropyridine 1-oxides.

During studies on the synthesis of formylnitropyridine 1-oxides by oxidation of methyl groups of methylnitropyridine 1-oxide with SeO_2 in dioxane, we observed an unusual course of reaction in the case of 2-methyl-3-nitropyridine 1-oxide (1). 3-Nitropyridine 1-oxide (2) was obtained in 70% yield instead of the expected 2-formyl-3-nitropyridine 1-oxide. Changes of the reaction conditions (ratio of substrates, solvent, temperature) did not influence the result. Trace amounts of aldehyde in the reaction mixture and liberation of CO_2 indicate that the reaction proceeds through acid which is extremely easily decarboxylated. This is an interesting example of neighbouring group participation.



In the case of oxidation of analogous compound, 2,5-dimethyl-3-nitropyridine 1-oxide (3) (the 5-methyl group is resistant to SeO_2), removal of the 2-methyl group also took place and 5-methyl-3-nitropyridine 1-oxide (4) was formed in 63% yield.



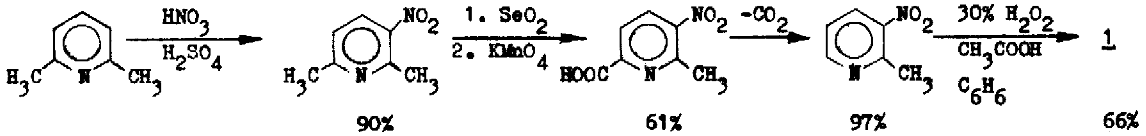
A mixture of 1-oxide 1[1] or 3 (32 mmol), dioxane (25 ml), SeO_2 (8.3 g, 75 mmol), and water (1 ml) was refluxed for 7 h. Selenium was removed by filtration (in the case of oxidation of 1, product 2 crystallized after cooling dioxane solution) and solvents were evaporated in vacuo. To the residue, the concentrated aqueous solution of $NaHCO_3$ was added and the mixture was extracted with chloroform. The extract was dried over $MgSO_4$ and evaporated to dryness. The residue was recrystallized from absolute ethanol to yield pure product. Yield of 2 - 69.6%; m.p. 171-172°C (lit[2] 172-173°C). IR(KBr) ν_{max} 1257 cm^{-1}. The identity of the compound obtained was additionally confirmed by its ^{1}H-NMR spectrum.[3] Yield of 4 - 62.8%; m.p. 139-140°C. IR (KBr) ν_{max} 1290 cm^{-1}. The structure of 1-oxide 4 was proved by its synthesis by direct oxidation of 5-methyl-3-nitropyridine (5)[4] with H_2O_2 in acetic acid and benzene (yield 66%) by the method described previously.[1]

2,5-Dimethyl-3-nitropyridine 1-oxide (3) was obtained by direct oxidation of 2,5-dimethyl-3-nitropyridine[4] as described above; yield 68%; m.p. 115.5--116.5°C. IR (KBr) ν_{max} 1292 cm^{-1}. Calcd for $C_7H_8N_2O_3$: C 50.0%, H 4.8%, N 16.7%. Found: C 50.4%, H 4.9%, N 16.8%.

Oxidation of 2,6-dimethyl-3-nitropyridine 1-oxide, however, did not result in demethylation but gave 6-formyl-2-methyl-3-nitropyridine 1-oxide (29%) contaminated with small amounts of other aldehydes.[5]

The novel synthesis of 1-oxides is especially convenient for the preparation of 1-oxide 2, since the best hitherto method of its synthesis (in 40% yield) includes oxidation of 3-nitropyridine with 40% peracetic acid.[2] Furthermore, the described methods of synthesis of 3-nitropyridine[6] give small yields of frequently contaminated product.

The starting compound 1 can be easily obtained from commercial 2,6-dimethyl pyridine by the described method[1,7], following the scheme:



References and Notes

1. L. Achremowicz, L. Syper, Roczniki Chem., 46, 409 (1972).
2. E.C. Taylor, J. Org. Chem., 25, 1716 (1960).
3. ^{1}H-NMR(CF_3COOH): δ 7.98 (dd, 1H, 5-H, $J_{5,4}$= 8.6 Hz, $J_{5,6}$= 6.4 Hz), 8.81 (d, 1H, 4-H, $J_{4,5}$= 8.6 Hz), 8.95 (d, 1H, 6-H, $J_{6,5}$= 6.4 Hz), 9.44 (s, 1H, 2-H).
4. L. Achremowicz, Roczniki Chem., 47, 2367 (1973).
5. L. Achremowicz, J. Koncewicz, Polish J. Chem. in press.
6. G.B. Barlin, Org. Proced. Int., 4, 63 (1972).
7. L. Achremowicz, Roczniki Chem., 46, 307 (1972).

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