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A STABLE PYRIDINESULFENYL HALIDE

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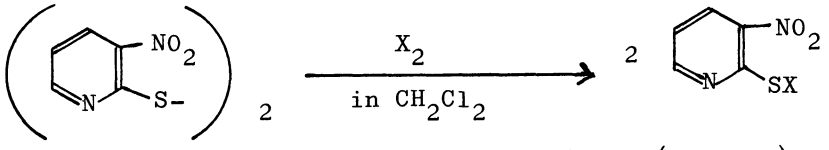
Synthesis of 3-nitro-2-pyridinesulfenyl halide (NPySX) is reported. NPySX was found to be extraordinarily stable as compared with known pyridinesulfenyl halides and contribution of the nitro group to its stabilization was indicated by X-ray diffraction investigation of one of its derivatives.

Few heterocyclic sulfenyl chlorides are known.[1] So far, pyridinesulfenyl chlorides have been little studied[2] apart from tetrafluoro-4-pyridinesulfenyl chloride[3], tetrachloro-4-pyridinesulfenyl chloride[4], tetrachloro-2-pyridinesulfenyl chloride[5], and 5-nitro-2-pyridinesulfenyl chloride[6]. However, these sulfenyl halides are so unstable that they only exist in anhydrous solution and decompose in open air to give disulfides.

This communication reports synthesis of a new stable and safely storable pyridinesulfenyl halide, 3-nitro-2-pyridinesulfenyl halide (NPySX), which is readily prepared by the reaction of its disulfide with a halogen.



In a typical experiment, to a suspension of 3.1 g (10 mmol) of bis(3-nitro-2-pyridyl) disulfide[7] in 100 ml of methylene chloride, chlorine gas was introduced with vigorous stirring at 0°C for 30 min and at room temperature for 1 hr. The reaction mixture became almost clear and the solvent was condensed in vacuo after filtration of a trace of tar in the reaction mixture. 3-Nitro-2-pyridinesulfenyl chloride was obtained in quantitative yield as yellow needles from the residue: mp 217~22°C (dec); λ_{max} (CH_3CN) 230.8 (ε 12,988), 264.5 (5,784), 372.5 nm (3,117); nmr (δ in $CDCl_3$) 7.45 (1H, dd, J=4.6 and 8.2 Hz, H-5), 8.56 (1H, dd, J=1.4 and 8.2 Hz, H-4), 8.94 (1H, dd, J=1.4 and 4.6 Hz, H-6). Found: C, 31.73; H, 1.89; N, 14.75; S, 16.77; Cl, 18.27%. Calcd for $C_5H_3N_2O_2SCl$: C, 31.50; H, 1.58; N, 14.70; S, 16.82; Cl, 18.60%. Sulfenyl bromide was also prepared by the same procedure using 3 eq of bromine: mp 195~200°C (dec).

These compounds were stable for several weeks at room temperature under dry conditions and no decomposition was observed after 6 months in a refrigerator. NPySX easily reacts with amine or alcohol in the presence of base to give sulfenamide and sulfenate, respectively. The reaction of equimolar amounts of NPySCl, methanol, and triethylamine in methylene chloride at room temperature gave methyl 3-nitro-2-pyridinesulfenate (mp 135~8°C) in 78% yield.

NPySX is extraordinarily stable[11] as compared with known pyridinesulfenyl halides and the structural difference between each other is that NPySX has a neighbouring nitro group ortho to the sulfenyl group. To examine the contribution of the nitro group to the stabilization of NPySX, X-ray diffraction of the crystal structure of methyl 3-nitro-2-pyridinesulfenate was investigated.[12] The compound crystallizes in the monoclinic, space group $P2_1/n$ with cell dimensions a=13.612, b=4.118, c=14.851Å, β=116°. These values are very similar to those of the methyl ester of o-nitrophenylsulfenic acid. This indicates that both compounds have homologous crystal and molecular structures and the distance between S and one of O atoms on the nitro group of methyl 3-nitro-2-pyridinesulfenate is found to be extraordinarily short as that of the methyl ester of o-nitrophenylsulfenic acid[13]. Therefore, the stability of NPySX may be due to a strong resonance stabilization of the molecule which results in a decrease of basicity of the nitrogen atom in the pyridine ring as well as a specific nonbonding attractive interaction between S and O.

NPySX is not only useful as an anticoccidial drug[14] but also as a chemical reagent , which may open up interesting synthetic possibilities. Its application as a protecting group for amines or alcohols as sulfenamide or sulfenate in peptide chemistry and the activation of carboxyl component via its thiol ester by the contribution of the nitrogen atom in the pyridine ring are now in progress.

References and Notes

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7) 2-Chloro-3-nitropyridine was allowed to react with thiourea according to the ordinary method[8] and 3-nitro-2-pyridinethiol was obtained in 69% yield, mp 174~5°C (lit.[9] mp 174~5°C). Subsequent oxidation of the thiol with $K_3Fe(CN)_6$[10] gave bis(3-nitro-2-pyridyl)disulfide in 96% yield, mp 249~50°C (dec) (lit.[9] mp 249 50°C).
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11) 2-Pyridinesulfenyl chlorides of non-substituted and nitro-substituted at 3, 4 and 5[6] position were investigated and only the 3-nitro derivative was isolated and found to be extraordinarily stable. It is almost equally stable to o-nitrophenylsulfenyl halide and can be stored in the same manner.
12) We are indebted to Dr. C. Tamura of our laboratories.
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