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Efficient Conversion of Thiols to *S*-Nitrosothiols with the 18-Crown-6 Complex of N_2O_4 as a New Nitrosating Agent†

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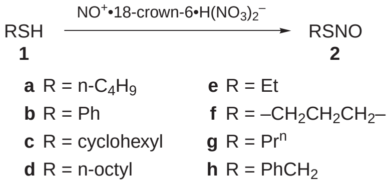
Gaseous N_2O_4 reacts with 18-crown-6 to afford a stable ionic complex of $NO^+\cdot$18-crown-6$\cdot H(NO_3)_2{}^-$; this complex is an efficient nitrosating agent for the conversion of thiols to their corresponding *S*-nitrosothiols in different organic solvents.

S-Nitrosothiols are an interesting class of organic compounds[1] and are becoming increasingly useful not only as a source of thiyl radicals[2] or as nitrosating reagents[3] but also as vasodilatory drugs due to their therapeutic use and their remarkable physiological importance.[4] One of the problems encountered in the synthesis of *S*-nitrosothiols is their low stability and their ease of conversion to the corresponding disulfides due to the oxidative ability of the reaction media.[2,5–8]

As a source of nitrosonium ion, gaseous dinitrogen tetroxide (N_2O_4) has also been used for this transformation. However, control of the reaction with this gas is important and the intermediate *S*-nitrosothiol can be converted to disulfides or other oxidative products. In our recent report on the use of $Cu(NO_3)_2\cdot N_2O_4$ as a nitrosating agent, the presence of Cu^{II} enhances the rapid conversion of the resulting *S*-nitrosothiol to the disulfide.[6] In order to eliminate this problem, a study upon the use of dinitrogen tetroxide derivatives as a source of nitrosonium ion is important. We have recently demonstrated the applicability of the crystalline ionic complex of $NO^+\cdot$18-crown-6$\cdot H(NO_3)_2{}^-$[9] for the selective nitration of phenols.[10] We now report that $NO^+\cdot$18-crown-6$\cdot H(NO_3)_2{}^-$ in solvents such as ethyl acetate, diethyl ether, *tert*-butanol, carbon tetrachloride and dichloromethane reacts immediately with thiols at room temperature and produces the corresponding *S*-nitrosothiol. The reaction in *tert*-butanol is more advantageous than the other solvents in this study in which the reaction mixture solidifies on freezing and can be stored for days without change.[11] UV and IR spectral analysis of the products in solution showed the characteristic bands for the thionitrite group which are similar to those reported in the literature[8] (Scheme 1 and Table 1).



Scheme 1

In conclusion, the present reagent is an efficient, stable and solid source of N_2O_4 for the conversion of thiols to the corresponding *S*-nitrosothiols. The reactions can proceed in a variety of solvents under mild reaction conditions. The handling of the reagent is also very easy.

Table 1 Reaction of thiols with $NO^+\cdot$18-crown-6$\cdot H(NO_3)_2{}^-$ in *tert*-butanol at room temperature[a]

Thiol	Product[b]	λ_{max}/nm/Absorbance[c]
1a	$Me[CH_2]_3SNO$	339/1.99, 551.2/0.09
1b	PhSNO	378/0.91, 572/0.16
1c	Cyclohexyl-SNO	342/0.76, 557/0.06
1d	$Me[CH_2]_6CH_2SNO$	339/2.89, 551/0.12
1e	EtSNO	337/2.8, 552/0.12
1f	$ONSCH_2CH_2CH_2SNO$	339/1.4, 551/0.11
1g	PrSNO	343/1.67, 600/0.14
1h	$PhCH_2SNO$	341/2.65, 550.4/0.07

[a] The reactions occurred immediately. [b] The products were not isolated and were identified by comparison of their UV and IR spectral data with the literature. [c] All products show a weak absorption band at about 520 nm.

Experimental

Products were characterised by comparison of their UV and IR spectral data with those of known samples in the appropriate solvent without isolation. UV spectra were recorded on a Pye Unicam 8725 spectrometer and samples were taken from the reaction mixture in *tert*-butanol. IR spectra were recorded on a Perkin Elmer IR-157 G or a Perkin Elmer 781 spectrometer and the samples were taken from the reaction mixture using CCl_4 as solvent.

Typical Procedure.—To a stirred solution of thiophenol (0.11 g, 1 mmol) in *tert*-butanol (5 ml), $NO^+\cdot$18-crown-6$\cdot (NO_3)_2{}^-$ (0.42 g, 1 mmol) was added at room temperature. The reaction was completed immediately and a bright red solution was obtained. UV and IR spectral data of the product in *tert*-butanol were compared with the reported data in the literature. The frozen mixture can be stored for several days without any change.

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† This is a **Short Paper** as defined in the Instructions for Authors, Section 5.0 [see *J. Chem. Research (S)*, 1999, Issue 1]; there is therefore no corresponding material in *J. Chem. Research (M)*.

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