Novel Method of Activating Thiols by their Conversion into Thionitrites with Dinitrogen Tetroxide

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Summary The reaction of thiols with N_2O_4 in an inert organic solvent such as CCl_4 or ether at low temperatures afforded aryl and alkyl thionitrites in quantitative yields; the thionitrites thus obtained reacted very readily with other thiols or sulphinic acids to give unsymmetrical disulphides or thiolsulphonates in nearly quantitative yields.

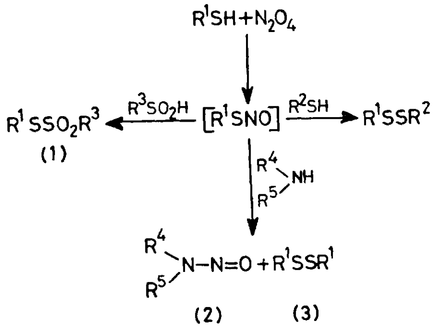
Alkyl thionitrites have been prepared by the reaction of thiols with either alkyl nitrites,[1] nitrosyl chloride,[2] or nitrogen trioxide.[3] Attempts to prepare aryl thionitrites have failed.[4] Since thionitrites are generally unstable, most of the known alkyl thionitrites of low molecular weight were characterized mainly by i.r. spectroscopic analysis in the gas phase and hence the yields and purities of these thionitrites have never been reliably determined because of their easy decomposition.

We found that both arene- and alkane-thiols reacted rapidly with an equimolar amount of N_2O_4† at low temperatures (*ca.* −10 °C) and afforded the corresponding thionitrites quantitatively when the temperature was kept sufficiently low. N_2O_4 is known to be in equilibrium with NO^+ and NO_3^-.[5] Probably the electrophilic attack of NO^+ on the sulphur atom of the thiol forms the corresponding thionitrite and nitric acid.

A solution of N_2O_4 (20 mmol) in CCl_4 (1 ml) at *ca.* −20 °C was carefully added to a solution of the thiol (20 mmol), in ether or CCl_4 (50 ml) at −20 °C with vigorous stirring in the dark. Immediately the mixture became bright red, characteristic of alkyl thionitrites (RSNO), except for t-butyl thionitrite which was dark green. Where the alkyl thionitrites were comparatively stable, the reaction mixture was washed with cold aq. $NaHCO_3$ solution (5%) and then with water to remove unchanged N_2O_4 and nitric acid formed. The organic layer was separated and dried over $MgSO_4$. Since even t-butyl and n-butyl thionitrites are sensitive to oxidation and light, the distillation was carried out in an evacuated system at low temperatures (*ca.* −10 °C) in the dark. All the thionitrites were prepared and i.r. and u.v. spectral data were obtained at *ca.* −2 °C.§

Decomposition of the thionitrites is markedly faster at higher concentrations in solution. The half lives of various thionitrites obtained by u.v. measurements (at *ca.* −2 °C in CCl_4) are as follows: Bu^nSNO: 100 ($9{\cdot}7 \times 10^{-3}$ M) and 17 min ($6{\cdot}5 \times 10^{-2}$ M); Bu^tSNO: 350 ($2{\cdot}6 \times 10^{-3}$M) and 180 min ($6{\cdot}4 \times 10^{-2}$ M); PhSNO: 1·5 min ($4{\cdot}5 \times 10^{-4}$ M) and *ca.* 2 s ($1{\cdot}9 \times 10^{-2}$ M). Decomposition gives nitric oxide and the corresponding disulphide, which is considered to be formed by the intermolecular reaction of the thionitrite with a thiyl radical by homolytic fission of the sulphur–nitrogen bond as suggested by Barrett *et al.*[6]

The thionitrites thus obtained were found to react with various nucleophiles such as thiols, sulphinic acids, and amines to give unsymmetrical disulphides, thiolsulphonates, and *N*-nitrosoamines, respectively.



A typical preparation of an unsymmetrical disulphide is as follows. When an equimolar amount of Bu^tSH or Bu^nSH (2·0 mmol) in ether (10 ml) was slowly added to an ethereal solution of phenyl thionitrite (2·0 mmol) in ether (20 ml) at *ca.* −5 °C, the characteristic red colour of the thionitrite disappeared gradually. The mixture was kept at *ca.* 0 °C for 0·5—1·0 h until the colour had disappeared completely, washed with $NaHCO_3$ solution (5%) to remove the nitric acid formed and then dried. Phenyl t-butyl disulphide (*ca.* 98%) and phenyl n-butyl disulphide (*ca.* 85%), respectively were obtained from the ethereal solutions.

By treating the thionitrites with sulphinic acids or secondary amines, unsymmetrical thiolsulphonates (**1**) or *N*-nitrosoamines (**2**) were similarly obtained in good yields.

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† N_2O_4 gas was trapped in a cold flask containing P_2O_5 at *ca.* −20 °C. The liquid N_2O_4 was then evaporated off by warming at *ca.* 30 °C into another flask containing P_2O_5 cooled at *ca.* −20 °C. The liquid N_2O_4 was finally trapped in cold CCl_4, and this solution was used for the reaction.

‡ The CCl_4 solution of N_2O_4 (0·1 ml) was quenched in cold water (10 ml) and then gradually warmed to *ca.* 20 °C. The resulting nitric acid solution was titrated with 0·1N NaOH solution. The amount of N_2O_4 was then calculated according to the following equation: $3\,N_2O_4 + H_2O \rightarrow 4\,HNO_3 + 2\,NO$ (P. Gray and A. D. Yoffe, *Quart. Rev.*, 1955, **9**, 383; Z. Abel, *Phys. Chem.*, 1930, 148).

§ The yields of alkyl thionitrites were determined by liquid–liquid chromatography, while those of aromatic thionitrites were estimated from the yields of the unsymmetrical disulphides obtained from the reaction of the thionitrites with other thiols. Yields of the thionitrites RSNO: R = Et, Bu^n, Bu^t, $Me[CH_2]_7$, and $Me[CH_2]_9$, all *ca.* 100%; R = $PhCH_2$, 96%; aromatic thionitrites, R = Ph, 97%; R = *p*-MeC_6H_4, 91%. I.r. and u.v. spectra of all these thionitrites were measured at −2 °C. Typical spectra are as follows: ν_{max} (CCl_4): Bu^nSNO, 1910, 1530—1500, 795, and 770 cm⁻¹; PhSNO, 1910—1900, 1670—1580, and 695 cm⁻¹; $PhCH_2SNO$, 1660, 1530—1500, 840, and 695 cm⁻¹; λ_{max} (n-hexane–CCl_4, 100 : 1): Bu^nSNO, 342 (ϵ 780), 519 (13), and 550 (27) nm; PhSNO, 261 (ϵ *ca.* 1000), 380 (*ca.* 260), 530 (*ca.* 27), and 570 (*ca.* 42) nm.

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