

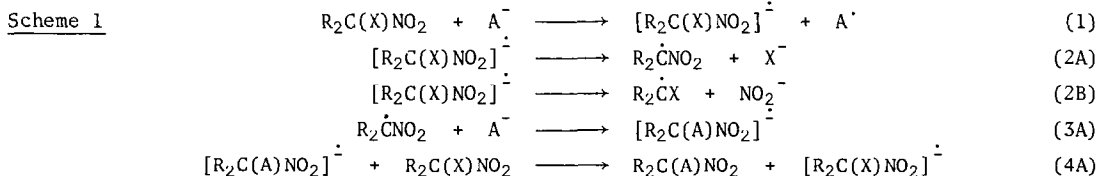
RADICAL-NUCLEOPHILIC SUBSTITUTION ( $S_{RN}1$ ) REACTIONS OF  $\alpha$ -NITRO-THIOCYANATES

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*Summary:*  $\alpha$ -Nitro-thiocyanates undergo substitution by a  $S_{RN}1$  mechanism with a range of anions to give loss of thiocyanate, corroborating behaviour observed for the intermediate  $\alpha$ -nitro-thiocyanato radical-anions by e.s.r. spectroscopy.

$\alpha$ -Substituted nitroalkanes have been reported<sup>1,2</sup> to undergo substitution via a radical radical-anion chain mechanism ( $S_{RN}1$ ) with an increasing number of anions. Loss of the  $\alpha$ -substituent (Scheme 1, route A) has been observed for X = I, Br, Cl,  $SO_2R$ , S(O)R, and SR; and loss of nitrite (equation 2B) in an equivalent  $S_{RN}1$  mechanism has been observed for X = COR,  $CO_2R$ ,  $NO_2$ , CN,  $N_3$ , and R. To our knowledge, there are no reports of thiocyanate acting as a leaving group in  $S_{RN}1$  reactions.



Electron spin resonance (e.s.r.) spectroscopy<sup>3</sup> has been used to show that 2-nitro-2-thiocyanatopropane, at low temperature in solid matrices, is able to capture an electron to form a stable radical-anion  $[Me_2C(SCN)\dot{N}O_2^-]$  which dissociates to yield  $Me_2\dot{C}NO_2$  and thiocyanate (Equation 2A, X = SCN). One of the purposes of this study is to show that e.s.r. spectroscopy can be used to predict the behaviour of radical-anions in solution reactions at room temperature e.g. their stability, and the direction of dissociation (Equation 2A versus 2B). The radical-anion of nitro-thiocyanatomethane has also been observed<sup>4</sup> recently by e.s.r. spectroscopy. Electrochemical studies<sup>5</sup> have shown that thiocyanato radical-anions can dissociate by loss of thiocyanate and/or cyanide.

2-Nitro-2-thiocyanatopropane and 1-nitro-1-thiocyanatocyclohexane were prepared in good yield (40 and 43% resp.) by the oxidative addition of thiocyanate to the anion of 2-nitropropane (Scheme 2). The best yields were obtained when the anion of 2-nitropropane (1 equiv.) was added to a  $CH_2Cl_2/H_2O$  solution of thiocyanate (1 equiv.) and ferricyanide (2 equiv.).

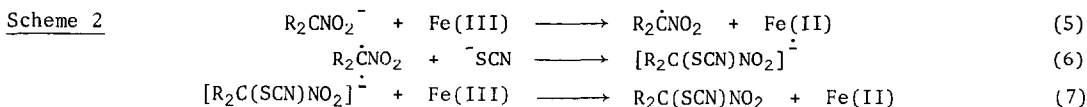


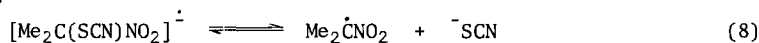
Table 1 :  $\text{Me}_2\text{C}(\text{SCN})\text{NO}_2 + \text{A}^- \longrightarrow \text{Me}_2\text{C}(\text{A})\text{NO}_2 + ^-\text{SCN}$ 

| $\text{A}^-$                | Reaction Conditions <sup>a</sup>                               | % yield of $\text{Me}_2\text{C}(\text{A})\text{NO}_2$ |
|-----------------------------|--|---|
| $\text{Me}_2\text{CNO}_2^-$ | DMSO (2h), DMF (2h)  | 72, 51  |
|                             | DMSO (2h), dark, oxygen atmosphere,                            | 42, 38  |
|                             | 5 molar % p-dinitrobenzene, 10 molar % (t-Bu) <sub>2</sub> NO· | 34, 34  |
| $\text{PhSO}_2^-$           | DMSO (2h)  | 49  |
|                             | DMSO (2h); dark, oxygen atmosphere,                            | 40, 37  |
|                             | 5 molar % p-dinitrobenzene, 10 molar % (t-Bu) <sub>2</sub> NO· | 40, 35  |
| $\text{N}_3^-$              | HMPA; fluorescent laboratory lights; 90 min, 5h                | 8 (39) <sup>b</sup> , 8 (27) <sup>b</sup>             |

(a) The reactions were carried out with 3 molar quantities of 2-nitro-2-thiocyanatopropane and the anion under an atmosphere of nitrogen and with irradiation (Tungsten 'white light' lamps, 2 x 150W), unless otherwise stated. (b) Unreacted 2-nitro-2-thiocyanatopropane.

Attempts to prepare 2-nitro-thiocyanatopropane, under various conditions, by an  $\text{S}_{\text{RN}}1$  reaction (Scheme 1,  $\text{A}^- = ^-\text{SCN}$ ,  $\text{X} = \text{I}, \text{Br}$ ) failed, leaving unreacted starting material. Even use of catalytic chain initiation<sup>6</sup> (entrainment) with catalytic amounts of the anion of 2-nitropropane yielded no  $\alpha$ -nitro-thiocyanate, but did yield traces of 2,3-dimethyl-2,3-dinitrobutane. The latter compound was also a significant impurity in the synthesis using ferricyanide, suggesting that the anion of 2-nitropropane successfully competes with thiocyanate for addition to the 2-nitropropyl radical.

Similar lack of reactivity of thiocyanate in  $\text{S}_{\text{RN}}1$  reactions with haloquinolines has been reported<sup>7</sup>. The lack of reactivity in our system is surprising because the synthesis of 2-nitro-2-thiocyanatopropane with ferricyanide shows that thiocyanate is able to add to the 2-nitropropyl radical (Equation 5) - the second step of the  $\text{S}_{\text{RN}}1$  chain (Equation 3A,  $\text{A}^- = ^-\text{SCN}$ ). Likewise results from e.s.r. spectroscopy suggest that the dissociation of  $[\text{Me}_2\text{C}(\text{SCN})\text{NO}_2]^\cdot$  is reversible (Equation 8),



but that dissociation takes place readily. Similar results for the stability of  $[\text{Me}_2\text{C}(\text{Br})\text{NO}_2]^\cdot$  and  $[\text{Me}_2\text{C}(\text{Cl})\text{NO}_2]^\cdot$  have been suggested from e.s.r. spectroscopy. Bromide and chloride have not been reported to act as nucleophiles in  $\text{S}_{\text{RN}}1$  reactions. We suggest that the equilibrium (Equation 8) lies well over on the side of dissociation thus inhibiting the chain reaction. The lack of  $\text{S}_{\text{RN}}1$  reactivity could also be due to poor electron transfer between thiocyanate and 2-iodo- or 2-bromo-2-nitropropane. The electron transfer is required for initiation of the  $\text{S}_{\text{RN}}1$  chain reaction (Equation 1,  $\text{A}^- = ^-\text{SCN}$ ,  $\text{X} = \text{Br}, \text{I}$ ).

It is of interest to note that thiocyanate is an ambident anion but only adds to the 2-nitropropyl radical via the sulphur atom (Equation 6). We suggest that this phenomena is possibly explained by kinetic control<sup>8</sup> of the addition because the sulphur-anion is more nucleophilic towards carbon than the nitrogen-anion.

Table 2 :  $\text{Me}_2\text{C}(\text{SCN})\text{NO}_2 + \text{RS}^- \longrightarrow \text{Me}_2\text{C}(\text{SR})\text{NO}_2 + \text{RSSR} + \text{SCN}^- + \text{Me}_2\text{C}(\text{NO}_2)\text{C}(\text{NO}_2)\text{Me}_2$ 

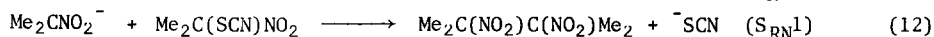
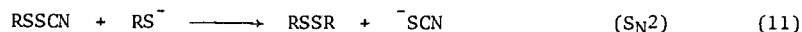
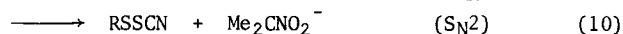
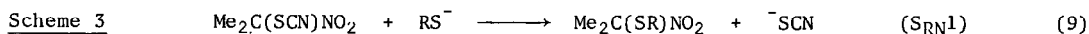
| RS <sup>-</sup> | Reaction Conditions <sup>a</sup>     | % yields                             |        |         |                                       |
|-----------------|--------------------------------------|--------------------------------------|--------|---------|---------------------------------------|
|                 |                                      | Me <sub>2</sub> C(SR)NO <sub>2</sub> | RSSR   | 'dimer' | Me <sub>2</sub> C(SCN)NO <sub>2</sub> |
| 4-chlorophenyl  | DMSO (2h)                            | 37                                   | 14     | 16      | 0                                     |
|                 | DMSO (2h); dark, oxygen atmosphere,  | 20, 12                               | 16, 4  | 20, 10  | 10, 41                                |
|                 | 40 molar % <i>p</i> -dinitrobenzene, | 17                                   | 26     | 8       | 34                                    |
|                 | 40 molar % (t-Bu) <sub>2</sub> NO·   | 26                                   | 0      | 0       | 11                                    |
| phenyl          | DMSO (2h), 10 min., 2h               | 0, 0                                 | 36, 52 | 34, 50  | 10, 0                                 |
|                 | DMSO (2h); dark, oxygen atmosphere,  | 0, 0                                 | 38, 26 | 41, 11  | 0, 24                                 |
|                 | 20 molar % <i>p</i> -dinitrobenzene, | 0                                    | 38     | 12      | 9                                     |
|                 | 20 molar % (t-Bu) <sub>2</sub> NO·   | 0                                    | 37     | 13      | 6                                     |

(a) The reaction conditions were the same as detailed in Table 1 except that irradiation was with fluorescent laboratory lights.

The results of the reaction of 2-nitro-2-thiocyanatopropane with the anion of 2-nitropropane, phenyl sulphinate, and azide (Table 1) show good yields of the corresponding  $\alpha$ -substituted nitro-compound, with loss of thiocyanate. The inhibition studies<sup>2,6</sup> indicate that a radical radical-anion light-catalysed chain mechanism ( $\text{S}_{\text{RN}}1$ ) is operative (Scheme 1 with  $\text{X} = \text{SCN}$ ). The lower yields for azide are due to the steady decomposition of 2-azido-2-nitropropane<sup>1a</sup> with time.

1-Nitro-1-thiocyanatocyclohexane also reacted (DMSO, 4h, hv) with the anion of 2-nitropropane, with loss of thiocyanate, to yield the corresponding  $\alpha$ -substituted product [1-(1-methyl-1-nitroethyl)-1-nitrocyclohexane] (61%) by an  $\text{S}_{\text{RN}}1$  mechanism and 2,3-dimethyl-2,3-dinitrobutane (16%) by a radical radical-anion non-chain mechanism<sup>1a,9,10</sup>.

The reaction of 2-nitro-2-thiocyanatopropane with thiolates yielded the corresponding  $\alpha$ -nitrosulphides and/or disulphides (Scheme 3).



4-Chlorophenylthiolate yielded largely the  $\alpha$ -nitrosulphide. Inhibition studies clearly show lowered yields of  $\alpha$ -nitrosulphide and increased recovery of starting material, indicating a  $\text{S}_{\text{RN}}1$  mechanism for the formation of  $\alpha$ -nitrosulphide (Equation 9 or Scheme 1,  $\text{X} = \text{SCN}$ ,  $\text{A}^- = \text{RS}^-$ ). The reaction with phenylthiolate yielded only disulphide, the formation of which was unaltered by *p*-dinitrobenzene, di-*t*-butylnitroxide, and the absence of light, suggesting a non-radical mechanism<sup>10</sup> (Equations 10 and 11).

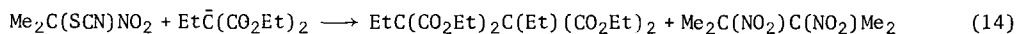
Phenylthiolate is a stronger nucleophile than 4-chlorophenylthiolate and therefore  $\text{S}_{\text{N}}2$  attack (Equation 10) by the thiolate on the thiocyanato-substituent to form an intermediate sulphenyl-thiocyanate is favoured over the slower electron-transfer required for the  $\text{S}_{\text{RN}}1$

mechanism. This competition between  $S_N2$  and  $S_{RN}1$  mechanisms for the reactions of thiolates with  $\alpha$ -substituted nitro-compounds has been described<sup>10</sup>. Sulphenyl-thiocyanates are well known to react rapidly with thiolates to yield disulphides (Equation 11).

2,3-Dimethyl-2,3-dinitrobutane was formed as a by-product in both reactions by an  $S_{RN}1$  mechanism (Equation 12) as shown by the inhibition studies. Di-(4-chlorophenyl) disulphide was formed by the abstraction route (Equation 10 and 11) as well as by an equivalent route<sup>10</sup> from the  $\alpha$ -nitrosulphide (Equation 13).

Reaction of 2-nitro-2-thiocyanatopropane with 4-nitrophenylthiolate yielded largely the corresponding  $\alpha$ -nitrosulphide as well as some disulphide but benzylthiolate yielded disulphide only.

Reaction of 2-nitro-2-thiocyanatopropane with the anion of diethyl ethylmalonate (DMSO, 5h, hv) proceeded with loss of thiocyanate by a redox reaction to give the respective dimers: 2,3-dimethyl-2,3-dinitrobutane (47%) and tetraethyl hexane-3,3,4,4-tetracarboxylate (20%). A radical radical-anion mechanism has been proposed<sup>2</sup> for redox reactions of this type.



We have shown that thiocyanate can act as a leaving group in  $S_{RN}1$  reactions with a range of different nucleophiles. The behaviour of  $\alpha$ -nitrothiocyanates and their radical-anions in solution reactions is in accordance with predictions made from e.s.r. spectroscopy. We therefore suggest that e.s.r. spectroscopy provides a good probe for predicting the reactivity of radical-anions in  $S_{RN}1$  reactions.

#### References

1. Recent references include : (a) S.I. Al-Khalil and W.R. Bowman, Tetrahedron Lett., 1982, 23, 4513; (b) G.A. Russell and B. Mudryk, J. Org. Chem., 1982, 47, 1879.
2. N. Kornblum, in 'The Chemistry of Amino, Nitroso, and Nitro-compounds and their Derivatives', ed. S. Patai, Wiley, 1982, Suppl. F, p.361.
3. W.R. Bowman and M.C.R. Symons, J. Chem. Soc., Perkin Trans. 2, 1983, 25.
4. B.C. Gilbert and R.O.C. Norman, Can. J. Chem., 1982, 60, 1379.
5. O. Hammerich and V.C. Parker, in 'The Chemistry of Cyanates and their Thio Derivatives', ed. S. Patai, Wiley, 1982, p.332.
6. M. Channon and M.L. Tobe, Angew. Chem. Int. Ed. Engl., 1982, 21, 1.
7. J.M. Saveant, Acc. Chem. Res., 1980, 13, 323.
8. L.M. Tolbert and S. Siddiqui, Tetrahedron, 1982, 38, 1079.
9. G.A. Russell, R.K. Norris and E.J. Panek, J. Am. Chem. Soc., 1971, 93, 5839.
10. W.R. Bowman and G.D. Richardson, J. Chem. Soc., Perkin Trans. 1, 1980, 1407; Tetrahedron Lett., 1981, 22, 1551.

(Received in UK 30 March 1983)