Reactions of Thionitrites or Thionitrates with Carbanions

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(Received November 10, 1980)

Synopsis. Reaction of several thionitrites (RSNO) or thionitrates ($RSNO_2$) with carbanions such as Grignard reagents, alkyllithium, or the carbanion of diethyl malonate gave *C*-alkylthio derivatives such as sulfides or diethyl (alkylthio)malonates.

In the course of our studies on the synthetic applications of thionitrites (RSNO)[1] and thionitrates ($RSNO_2$),[2] the two initial key intermediates in the oxidation of thiols with dinitrogen tetraoxide (N_2O_4), we found that both thionitrites and thionitrates reacted rapidly with carbanionic species such as Grignard reagents, alkyllithium, and the carbanion of diethyl malonate below room temperature. This paper deals with these reactions.

When thionitrites (**1**) or *t*-butyl thionitrate (**2a**) were treated with phenylmagnesium bromide (**3a**) or methylmagnesium iodide (**3b**) in diethyl ether, the corresponding sulfides (**4**) were obtained as the main products, besides small amounts of disulfides (**5**) and thiols (**6**).

RSNO or $RSNO_2$ + R′MgX ⟶

1 **2** **3**

1a: R = *p*-Tol **2a**: R = *t*-Bu **3a**: R′ = Ph, X = Br

1b: R = *t*-Bu **3b**: R′ = CH_3, X = I

RSR′ + $(RS-)_2$ + RSH

4 **5** **6**

4a: R = *p*-Tol, R′ = Ph **5a**: R = *p*-Tol **6a**: R = *p*-Tol

4b: R = *p*-Tol, R′ = CH_3 **5b**: R = *t*-Bu **6b**: R = *t*-Bu

4c: R = *t*-Bu, R′ = Ph

When thionitrite **1a** was treated with methyllithium (**7a**) or benzyllithium (**7b**)[3] in diethyl ether, nearly the same results were obtained as in the reaction with the Grignard reagents. Sulfide **4b** and benzyl *p*-tolyl sulfide (**4d**) were the major products, as summarized in Table 1.

These reactions were considered to proceed *via* the nucleophilic attack of the carbanionic species on the sulfur atoms of **1** or **2a**. The carbanions do not seem

p-TolSNO + RLi ⟶

1a **7**

7a: R = CH_3

7b: R = $PhCH_2$

p-TolSR + $(p\text{-TolS-})_2$ + *p*-TolSH

4 **5a** **6a**

4b: R = CH_3

4d: R = $PhCH_2$

to attack the nitrogen atom, in view of the lack of formation of the *C*-nitroso or *C*-nitro compound. **1** and **2a** were found to decompose during the reaction to give small amounts of the corresponding disulfides **5**. The thiols **6** are considered to be formed by the reaction of disulfides **5** with carbanions.

When **2a** was treated with diethyl malonate (**8**) in the presence of potassium hydroxide, diethyl (*t*-butylthio)-malonate (**9**) was obtained in a good yield. This reaction did not proceed without potassium hydroxide. The reaction of **1b** with diethyl malonate (**8**) in the presence of potassium hydroxide did not give **9** but uncharacterized products.

$$t\text{-BuSNO}_2 + CH_2(CO_2Et)_2 \xrightarrow[\text{in EtOH}]{\text{KOH}} t\text{-BuSCH}(CO_2Et)_2$$

2a **8** **9**

Meanwhile, treatment of 1.4 equiv. of *p*-chlorophenyl thionitrate (**2b**) with diethyl malonate (**8**) in the presence of potassium hydroxide gave diethyl bis(*p*-chlorophenylthio)malonate (**10**) as the major product. However, when this reaction was carried out in the presence of a large amount of potassium hydroxide, ethyl (*p*-chlorophenylthio)acetate (**12**), which might be formed by partial hydrolysis of diethyl (*p*-chloro-

$$p\text{-Cl-C}_6H_4\text{-SNO}_2 + CH_2(CO_2Et)_2 \xrightarrow[\text{in EtOH}]{\text{KOH}}$$

2b **8**

$$(p\text{-Cl-C}_6H_4S-)_2C(CO_2Et)_2 + p\text{-Cl-C}_6H_4SCH(CO_2Et)_2$$

10 **11**

$$+\ p\text{-Cl-C}_6H_4SCH_2CO_2Et$$

12

Table 1. Reactions of thionitrites **1a—b**, or thionitrate **2a** with carbanions **3a—b** or **7a—b**

Substrate	Carbanion	[Carbanion]/[Substrate]	Temp/°C	Time/min	Product[a]	Isolated yield/%
1a	**3a**	3	−70	3	**4a**[b,d]	57
1a	**3b**	3	−70	3	**4b**[b,e]	43
1a	**7a**	1	−70	3	**4b**[b,e]	57
1b	**3a**	1	0—5	5	**4c**[c,f]	72
2a	**3a**	1.1	0—5	5	**4c**[c,f]	79
1a	**7b**	1	−70	3	**4d**[b,g]	32

a) IR and NMR spectra of all these sulfides were identical with those of authentic samples. b) Small amounts of disulfide **5a** and thiol **6a** were also obtained. c) A small amount of disulfide **5a** was confirmed by GC-MS spectrum. d) Bp (bath temp) 135—140 °C/3 mmHg (lit,[4] 163—163.5 °C). e) Bp (bath temp) 90 °C/3 mmHg (lit,[5] 104—104.5 °C/20 mmHg). f) Bp (bath temp) 85—90 °C/3 mmHg (lit,[6] 73 °C/5 mmHg). g) Bp (bath temp) 100—110 °C/2 mmHg, mp 44 °C (lit,[7] 46 °C).

Table 2. Reactions of thionitrates **2a—b** with diethyl malonate **8** in the presence of potassium hydroxide

Thionitrate	Thionitrate: KOH: **8**	Temp °C	Time min	Product	Isolated yield/%
2a	5 : 8 : 6	25	3	**9**	79[a]
2a	10 : 16 : 5	0—5	3	**9**	74[b]
2b	7 : 8 : 5	0—5	3	**10**[d]	29[b,c]
2b	5 : 16 : 5	0—5	3	**12**[e]	72[b]

a) Based on thionitrate **2a**. b) Based on diethyl malonate **8**. c) After recrystallization from EtOH solution. d) Small amounts of compounds **11** and **12** were also formed. e) Small amounts of compounds **10** and **11** were also formed.

phenylthio)malonate (**11**) followed by decarboxylation, was obtained as the major product. These results are listed in Table 2.

Experimental

All the melting points and boiling points were uncorrected. Elemental analyses were carried out by the Chemical Analysis Center at our University. Analytical determinations by GLC were performed on a Hitachi 163 gas chromatograph fitted with the following column (3 mm o.d. × 3 m): 10% SE-30 on Chromosorb W. ^{1}H-NMR spectra were taken at 60 MHz on a Hitachi R-24 A or R-24 apparatus. IR spectra were recorded with a Hitachi 215 spectrometer. Mass spectra were recorded with a Hitachi RMU-6M spectrometer.

*Thionitrites (**1a—b**).* These compounds were prepared from the corresponding thiols with dinitrogen tetraoxide following the procedure reported by us.[1,2b] Pure thionitrite **1a** was quite unstable at room temperature, and hence this compound was used as a solution in diethyl ether immediately after preparation. Pure thionitrite **1b** was rather stable at room temperature.

*Thionitrates (**2a—b**).* Thionitrates **2a—b** were prepared from the corresponding thiols with excess dinitrogen tetraoxide.[2] Thionitrate **2a** was stable and remaining almost in pure form at room temperature for several weeks. Thionitrate **2b** was unstable at room temperature and hence was used immediately (within 30 min) after recrystallization from diethyl ether.

*Reactions of Thionitrites (**1a—b**) or Thionitrates (**2a—b**) with Grignard Reagents (**3a—b**) or Alkyllithium (**7a—b**).* The following is a typical procedure. The Grignard reagent **3a** (7 mmol) in diethyl ether (5.4 ml) was added to a stirred solution of thionitrite **1b** in dry diethyl ether (5 ml) for a few minutes at 0—5 °C. The solution was stirred further for *ca.* 3 min. The red solution of thionitrite **1b** turned to a white suspension. A cold HCl aq solution was added to the solution and then the mixture was extracted with diethyl ether. The ethereal extract was dried ($MgSO_4$), concentrated, purified by TLC (silica gel, hexane), and distilled giving 835 mg (72%) of the sulfide **4c**: bp (bath temp) 85—90 °C/3 mmHg (1 mmHg=133.322 Pa) (lit,[6] 73 °C/5 mmHg).

*Diethyl (t-Butylthio)malonate (**9**).* A mixture of thionitrite **2a** (675 mg, 5 mmol) and diethyl malonate **8** (961 mg, 6 mmol) was added for a few minutes to a stirred solution of potassium hydroxide (450 mg, 8 mmol) in ethanol (3 ml) at room temperature. The solution was stirred further for *ca.* 3 min, and then cold HCl aq solution was added and the mixture was extracted with diethyl ether. The ethereal extract was dried ($MgSO_4$), concentrated, purified by TLC (silica gel, hexane: ether=10: 1), and distilled, giving 980 mg (79%) of the compound **9**: bp (bath temp) 100—110 °C/3 mmHg. IR (neat): 1725, 1365, 1242, 1150, 1075, and 1030 cm^{-1}. NMR (CCl_4): δ 1.28 (t, 6H, CH_3–), 1.35 (s, 9H, *t*-Bu), 4.00 (s, 1H, –C<u>H</u>), and 4.13 (q, 4H, –C<u>H</u>$_2$–). MS (70 eV), *m/e* (rel. intensity), 245 (5, M^+), 191 (41, $^+$SCH-$(CO_2Et)_2$), 159 (16, $^+CH(CO_2Et)_2$), 118 (23, $^+SCHCO_2Et$), and 57 (100, *t*-Bu$^+$). Found: C, 52.82; H, 8.18%. Calcd for $C_{11}H_{20}O_4S$: C, 53.20; H, 8.11%.

*Diethyl Bis(p-chlorophenylthio)malonate (**10**).* A mixture of thionitrate **2b** (1.41 g, 7 mmol) and diethyl malonate **8** (0.80 g, 5 mmol) was added for a few minutes to a stirred solution of potassium hydroxide 0.45 g, 8 mmol) in ethanol (3 ml) at 0—5 °C. The solution was stirred further for *ca.* 3 min, and then cold HCl aq solution was added and the mixture was extracted with diethyl ether. The crude product was purified by TLC (silica gel, hexane: ether=10: 1) and recrystallization (from ethanol) to give 643 mg (29% from diethyl malonate **8**) of compound **10**: mp 89—90 °C. IR (KBr): 1725, 1260, 1090, 1038, 1009, and 815 cm^{-1}. NMR (CCl_4): δ 1.14 (t, 6H, CH_3–), 4.01 (q, 4H, –C<u>H</u>$_2$–), 7.25 (d, J=8 Hz, 4H, ring protons), and 7.55 (d, J=8 Hz, 4H, ring protons). MS (70 eV), *m/e* (rel. intensity), 443 (16, M^+), 370 (4, $(p\text{-Cl-}C_6H_4S\text{–})_2C(CO_2Et)^+$), and 300 (100, p-Cl–$C_6H_4SC(CO_2Et)_2^+$). Found: C, 51.58; H, 4.04%. Calcd for $C_{19}H_{18}Cl_2O_4S_2$: C, 51.24; H, 4.07%.

*Ethyl (p-Chlorophenylthio)acetate (**12**).* A mixture of thionitrate **2b** (5 mmol), and diethyl malonate **8** (5 mmol) was added for a few minutes to a stirred solution of potassium hydroxide (16 mmol) in ethanol (8 ml) at 0—5 °C. The solution was stirred further for *ca.* 3 min, then cold HCl aq solution was added and the mixture was extracted with diethyl ether. Then the product was distilled giving 825 mg (72%) of compound **13**: bp 140—143 °C/2 mmHg (lit,[8] 126—130 °C/1 mmHg). IR (neat): 1720, 1260, 1140, 1085, 1020, and 820 cm^{-1}. NMR (CCl_4): δ 1.25 (t, 6H, CH_3–), 4.18 (q, 4H, –C<u>H</u>$_2$–), 4.35 (s, 1H, –C<u>H</u>), and 7.13—7.70 (m, 4H, ring protons). MS (70 eV), *m/e* (rel. intensity), 230 (55, M^+) and 157 (100, p-Cl-$C_6H_4SCH_2^+$). Found: C, 51.86; H, 4.99%. Calcd for $C_{10}H_{11}ClO_2S$: C, 52.06; H, 4.80%. Small amounts of compound **10** and **11** were also confirmed by GC-MS spectra. Compound **11**: MS (70 eV), *m/e* (rel. intensity), 302 (53, M^+), 229 (35, p-Cl-$C_6H_4SCHCO_2Et^+$), and 156 (100, p-Cl-$C_6H_4SCH^+$).

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