Organic Chemistry

Regioselective replacement of nitro groups in 2,4,6-trinitrotoluene under the action of alkanethiols. Synthesis of *ortho*-(alkylthio)-substituted nitrotoluenes and their oxidation to sulfoxides and sulfones

O. V. Serushkina, M. D. Dutov, and S. A. Shevelev*

N. D. Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences, 47 Leninsky prosp., 117913 Moscow, Russian Federation. Fax: +7 (095) 135 5328. E-mail: shevelev@cacr.ioc.ac.ru

The reactions of 2,4,6-trinitrotoluene with alkanethiols in the presence of K_2CO_3 (the molar ratio of the reactants is 1 : 1 : 1) in dipolar aprotic solvents result in selective replacement of the *ortho*-nitro group to form 2-alkylthio-4,6-dinitrotoluenes, which can be oxidized to the corresponding sulfoxides or sulfones. The second *ortho*-nitro group can be replaced under the action of one more equivalent of alkanethiol on sulfides as exemplified in $PhCH_2SH$.

Key words: trinitrotoluene, alkanethiols, replacement of the nitro group.

Previously,[1—4] we have demonstrated that benzenethiols replace a nitro group in 2,4,6-trinitrotoluene (TNT) in dipolar aprotic solvents in the presence of alkali metal carbonates, only the *ortho*-nitro group being replaced to form sulfides. The latter can be selectively oxidized to the corresponding sulfoxides or sulfones.

We found that the reactions of TNT with various alkanethiols **1** under analogous conditions (*N*-methylpyrrolidone (*N*-MP) or DMF are the solvents of choice) in the presence of solid K_2CO_3 (the molar ratio of the reactants is 1 : 1 : 1) are also regioselective, *viz.*, the *ortho*-nitro group is primarily replaced to form the corresponding 2-alkylthio-4,6-dinitrotoluenes **2** (Scheme 1, Table 1).

It was shown that *ortho*-replacement is accompanied by *para*-replacement which occurs to a small extent. Generally, the fraction of the *para* isomer is no higher than 5—6% of the total amount of the *ortho* and *para* isomers. Only in the cases of **1c** and **1e**, the fraction of the *para* isomer reaches 10% (^{1}H NMR spectral data). Single crystallization from the solvents listed in Table 1 is usually sufficient to remove the *para* isomer. Only in the cases of sulfides **2c** and **2e**, double crystallization is required.

Under these conditions, the reactions proceed at 20 °C. However, in some cases it is more convenient to carry out the reactions at 50 °C (see Table 1).

Using sulfide **2a** as an example, it was demonstrated that the second nitro group can also be replaced (under the action of $PhCH_2SH$ + K_2CO_3), the *ortho*-nitro group also being selectively replaced to form bis-sulfide **3** (see Scheme 1). The best results were obtained in HMPA at ~20 °C (see Table 1).

It should be noted that only one example of replacement of the nitro group in TNT under the action of an alkanethiol has been described previously. Thus the re-

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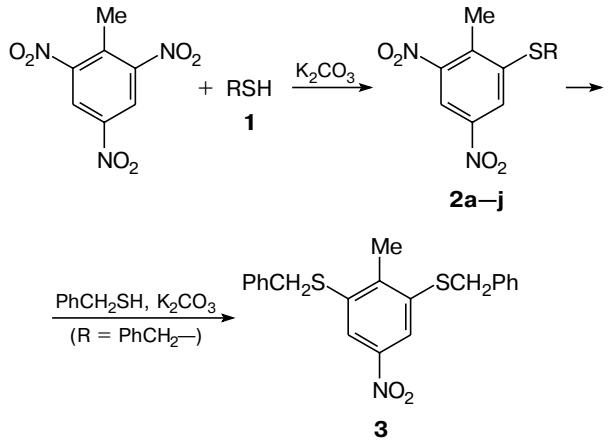
Scheme 1



R = $PhCH_2$— (**a**); —CH_2—(furan) (**b**); —CH_2—CH(Me)—Me (**c**); —$CH_2CHOHCH_2OH$ (**d**); —(cyclohexane) (**e**); R′$OOCCH_2$— (R′ = H (**f**), Et (**g**), Me (**h**)); R″OOCCHMe (R″ = H (**i**), Et (**j**))

Table 1. Reaction conditions, melting points, and yields of *ortho*-S-alkylthio-substituted nitrotoluenes

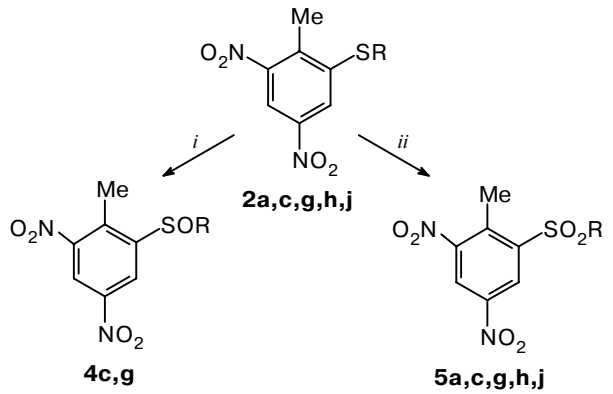
Compound	Reaction conditions		Yield* (%)	M.p./°C (solvent)
	T/°C	*t*/h		
2a	50	3	68	111—112 (MeCN)
2b	50	2	81	51—52 (EtOH)
2c	20	11	58	98—99 (CCl_4/$CHCl_3$)
2d	20	5	55	109—110 (H_2O)
2e	20	18	27	99—100 (CCl_4/$CHCl_3$)
2f	20	18	37	137—138 (EtOH)
2g	20	18	59	73—74 (EtOH)
2h	20	24	88	70—71 (EtOH)
2i	20	48	43	138—139
2j	20	24	86	31—32 (EtOH)
3	20	280	36	141—142 (MeCN)
4c	20	53	84	116—117 (CCl_4)
4g	20	20	60	21—22
5a	118**	0.5	94	167—168
5c	118**	0.5	83	107—108
5g	118**	3	45	107—108 (AcOH/H_2O)
5h	118**	1	77	113—114 (AcOH/H_2O)
5j	118**	3.5	13	123—124 (MeOH)

* With respect to the individual product isolated.
** Boiling AcOH.

action with the EtSH—LiOH system in HMPA led primarily to *ortho* replacement.[5] We demonstrated that the approach proposed in the present study is more efficient. Thus the yield of sulfide **2a** prepared according to our procedure was 68%, whereas under conditions of the cited work[5] it was 40%. The yields of bis-sulfide **3** were 36 and 9%, respectively. Analogous results were obtained in other cases as well.

In several examples, we demonstrated that sulfides **2** can be selectively oxidized under the action of H_2O_2 + AcOH to form either the corresponding sulfoxides or sulfones depending on the reaction conditions. The reactions with the use of a nearly equimolar amount of H_2O_2 at ~20 °C afforded sulfoxides **4**, whereas the reactions with the use of a large excess of H_2O_2 in boiling AcOH gave rise to the corresponding sulfones **5** (Scheme 2, see Table 1). Earlier, we have used an analogous procedure for the selective oxidation of the replacement products of the *ortho*-nitro group in TNT under the action of benzenethiols.[1—4]

Scheme 2



Regents and conditions. *i.* from **2c,g**; 20 °C, the molar ratio **2** : H_2O_2 ≈ 1 : 1.
ii. from **2a,c,g,h,j**; 118 °C, nearly fourfold molar excess of H_2O_2.

Thus, we developed a procedure for the preparation of 2-alkylthio-, 2-alkylsulfinyl-, and 2-alkylsulfonyl-4,6-dinitrotoluenes.

The structures of the resulting compounds were established by ^{1}H NMR spectroscopy (Table 2), mass spectrometry in the electron impact mode (in all cases, except for sulfones **5a**, **5d**, and **5h**, the formation of molecular ions was observed), and IR spectroscopy (ν_{as} (NO_2), 1550—1580 cm^{-1}; ν_s, 1350—1380 (NO_2) cm^{-1}; ν (SO), 1070—1030 cm^{-1}; ν_{as} (SO_2), 1300—1340 cm^{-1}; ν_s (SO_2), 1120—1160 cm^{-1}) and were confirmed by the data from elemental analysis (see Table 2).

Experimental

The melting points were determined on a Boetius stage (the rate of heating was 4 deg min^{-1}). The IR spectra were recorded on a Specord M-80 spectrometer in KBr pellets. The mass spectra were obtained on an MS-30 spectrometer (Kratos). The course of the reactions was monitored by HPLC on a Liquochrom (Model 2010) instrument on a column with Silasorb-18 as the reversed phase using the 3 : 1 MeCN—H_2O system as the eluent. The ^{1}H NMR spectra were recorded on a Bruker AC-200 spectrometer.

Table 2. ^{1}H NMR spectra and data of elemental analysis of *ortho*-substituted nitrotoluenes

Compound	Found / Calculated (%)				Molecular formula	^{1}H NMR (solvent; δ, *J*/Hz)
	C	H	N	S		
2a	55.07 55.26	3.73 3.97	9.33 9.21	10.71 10.53	$C_{14}H_{12}N_2O_4S$	Acetone-d_6; 2.51 (s, 3 H); 4.51 (s, 2 H); 7.32 (m, 3 H); 7.47 (m, 2 H); 8.38 (d, 1 H, *J* = 2); 8.42 (d, 1 H, *J* = 2)
2b	48.92 48.98	3.41 3.42	9.61 9.52	10.94 10.89	$C_{12}H_{10}N_2O_5S$	$CDCl_3$; 2.54 (s, 3 H); 4.29 (s, 2 H); 6.26 (dd, 1 H, *J* = 3, 1.5); 6.33 (d, 1 H, *J* = 3); 7.37 (d, 1 H, *J* = 1.5); 8.37 (d, 1 H, *J* = 2); 8.42 (d, 1 H, *J* = 2)
2c	48.59 48.88	5.08 5.22	10.48 10.36	11.98 11.86	$C_{11}H_{14}N_2O_4S$	$CDCl_3$; 1.15 (d, 6 H, *J* = 10); 2.04 (nonet, 1 H, *J* = 10); 2.58 (s, 3 H); 2.88 (d, 2 H, *J* = 11); 8.21 (d, 1 H, *J* = 2); 8.34 (d, 1 H, *J* = 2)
2d	41.45 41.67	4.09 4.20	9.81 9.72	11.22 11.12	$C_{10}H_{12}N_2O_6S$	Acetone-d_6; 2.53 (s, 3 H); 3.27 (dd, 1 H, *J* = 14, 8); 3.48 (dd, 1 H, *J* = 14, 6); 3.66 (t, 2 H, *J* = 10); 3.96 (m, 2 H); 4.38 (d, 1 H, *J* = 8); 8.40 (d, 1 H, *J* = 2); 8.52 (d, 1 H, *J* = 2)
2e	52.55 52.69	5.38 5.44	9.51 9.45	10.89 10.82	$C_{13}H_{16}N_2O_4S$	Acetone-d_6; 1.49 (m, 6 H); 1.65 (m, 2 H); 1.79 (m, 2 H); 2.56 (s, 3 H); 3.51 (m, 1 H); 8.40 (d, 1 H, *J* = 2); 8.45 (d, 1 H, *J* = 2)
2f	39.61 39.71	2.89 2.96	10.35 10.29	11.87 11.78	$C_9H_8N_2O_6S$	Acetone-d_6; 2.51 (s, 3 H); 4.13 (s, 2 H); 8.47 (d, 1 H, *J* = 2); 8.52 (d, 1 H, *J* = 2)
2g	43.89 44.00	3.97 4.03	9.50 9.33	10.71 10.68	$C_{11}H_{12}N_2O_6S$	Acetone-d_6; 1.22 (t, 3 H, *J* = 9); 2.56 (s, 3 H); 4.12 (s, 2 H); 4.18 (q, 2 H, *J* = 10); 8.44 (d, 1 H, *J* = 2); 8.48 (d, 1 H, *J* = 2)
2h	41.91 41.96	3.49 3.52	9.80 9.79	11.22 11.20	$C_{10}H_{10}N_2O_6S$	DMSO-d_6; 2.44 (s, 3 H); 3.66 (s, 3 H); 4.28 (s, 2 H); 8.31 (d, 1 H, *J* = 2); 8.51 (d, 1 H, *J* = 2)
2i	41.82 41.96	3.36 3.52	9.91 9.79	11.29 11.20	$C_{10}H_{10}N_2O_6S$	Acetone-d_6; 1.61 (d, 3 H, *J* = 10); 2.64 (s, 3 H); 4.29 (q, 1 H, *J* = 9); 8.55 (d, 1 H, *J* = 2); 8.68 (d, 1 H, *J* = 2)
2j	45.69 45.86	4.33 4.49	9.08 8.91	10.32 10.20	$C_{12}H_{14}N_2O_6S$	$CDCl_3$; 1.25 (t, 3 H, *J* = 9); 1.65 (d, 3 H, *J* = 10); 2.63 (s, 3 H); 4.00 (q, 1 H, *J* = 9); 4.20 (q, 2 H, *J* = 9); 8.45 (d, 1 H, *J* = 2); 8.54 (d, 1 H, *J* = 2)
3	65.98 66.11	4.96 5.02	3.72 3.67	16.91 16.81	$C_{21}H_{19}NO_2S_2$	DMSO-d_6; 2.33 (s, 3 H); 4.34 (s, 4 H); 7.32 (m, 10 H); 7.91 (s, 2 H)
4c	46.03 46.15	4.79 4.93	9.81 9.78	11.29 11.20	$C_{11}H_{14}N_2O_5S$	$CDCl_3$; 1.14 (d, 3 H, *J* = 9); 1.26 (d, 3 H, *J* = 9); 2.42 (nonet, 1 H, *J* = 6); 2.61 (s, 3 H); 2.79—2.55 (m, 2 H); 8.80 (d, 1 H, *J* = 2); 9.08 (d, 1 H, *J* = 2)
4g	41.63 41.77	3.74 3.82	8.98 8.86	10.22 10.14	$C_{11}H_{12}N_2O_7S$	Acetone-d_6; 1.20 (t, 3 H, *J* = 9); 2.67 (s, 3 H); 3.88 (d, 1 H, *J* = 18); 4.17 (q, 2 H, *J* = 10); 4.28 (d, 1 H, *J* = 18); 8.88 (d, 1 H, *J* = 2); 8.92 (d, 1 H, *J* = 2)
5a	49.89 50.00	3.53 3.60	8.47 8.33	9.71 9.53	$C_{14}H_{12}N_2O_6S$	Acetone-d_6; 2.68 (s, 3 H); 4.80 (s, 2 H); 7.32 (m, 5 H); 8.72 (d, 1 H, *J* = 2); 8.90 (d, 1 H, *J* = 2)
5c	43.59 43.71	4.57 4.67	9.33 9.27	10.81 10.61	$C_{11}H_{14}N_2O_6S$	$CDCl_3$; 1.15 (d, 6 H, *J* = 9); 2.42 (nonet, 1 H, *J* = 10); 2.92 (s, 3 H); 3.15 (d, 2 H, *J* = 9); 8.70 (d, 1 H, *J* = 2); 9.12 (d, 1 H, *J* = 2)
5g	39.78 39.76	3.52 3.64	8.59 8.43	9.33 9.65	$C_{11}H_{12}N_2O_8S$	Acetone-d_6; 1.14 (t, 3 H, *J* = 10); 2.93 (s, 3 H); 4.12 (q, 2 H, *J* = 10); 4.74 (s, 2 H); 9.00 (d, 1 H, *J* = 2); 9.04 (d, 1 H, *J* = 2)
5h	37.69 37.74	3.09 3.17	8.87 8.80	10.12 10.07	$C_{10}H_{10}N_2O_8S$	$CDCl_3$; 2.92 (s, 3 H); 3.73 (s, 3 H); 4.32 (s, 2 H); 8.84 (d, 1 H, *J* = 2); 9.11 (d, 1 H, *J* = 2)
5j	41.49 41.62	4.01 4.07	8.13 8.09	9.33 9.26	$C_{12}H_{11}N_2O_8S$	Acetone-d_6; 1.08 (t, 3 H, *J* = 9); 1.68 (d, 3 H, *J* = 10); 2.91 (s, 3 H); 4.08 (q, 2 H, *J* = 10); 4.76 (q, 1 H, *J* = 9); 8.96 (d, 1 H, *J* = 2); 9.05 (d, 1 H, *J* = 2)

2-Alkylthio-4,6-dinitrotoluenes (2a—j). A solution of TNT (5.675 g, 0.025 mol) in *N*-MP (10 mL) was added to a mixture of the corresponding alkanethiol (0.025 mol), K_2CO_3 (3.45 g, 0.025 mol), and *N*-MP (15 mL). The reaction mixture was stirred under conditions given in Table 1. Then the mixture was poured into cold water (120 mL). The precipitate that formed was filtered off, dried, and recrystallized from the corresponding solvent (see Table 1). Compounds **2a**, **2b**, **2g**, **2h**, and **2j** were dissolved in chloroform and filtered through a silica gel layer (~20 g) before recrystallization. In the cases of compounds **2f** and **2i**, the reaction mixtures were poured into CH_2Cl_2 (120 mL). The precipitates that formed were filtered off, dried, and dissolved in water and the solution were filtered. The filtrates were acidified with HCl and the precipitates that formed were filtered off and recrystallized.

2,6-Bis(benzylthio)-4-nitrotoluene (3). A mixture of compound **2a** (6.08 g, 0.02 mol), HMPA (20 mL), $PhCH_2SH$ (2.48 g, 0.02 mol), and K_2CO_3 (2.76 g, 0.02 mol) was stirred at

~20 °C for 12 days. Then the mixture was poured into cold water (100 mL) and the precipitate that formed was filtered off, dried, and recrystallized.

Sulfoxides 4c and 4g. A mixture of sulfide **2c** or **2g** (0.025 mol), 35% H_2O_2 (2.25 mL), and glacial AcOH (45 mL) was stirred at ~20 °C over a period indicated in Table 1. Then the mixture was poured into cold water (225 mL) and the precipitate that formed was filtered off and dried (compound **4c** was recrystallized).

Sulfones 5a, 5c, 5g, 5h, and 5j. A mixture of sulfide **2** (0.03 mol), 35% H_2O_2 (10.2 mL), and glacial AcOH (70 mL) was refluxed over a period given in Table 1. Then the mixture was cooled. In the case of sulfone **5h**, the precipitate was filtered off, dried, and recrystallized. In the cases of sulfones **5g** and **5j**, the reaction mixtures were poured into cold water (350 mL) and the precipitates that formed were filtered off, dried, and recrystallized. In the case of sulfone **5j**, the precipitate was stirred in a dilute aqueous solution of KOH for 4 h before recrystallization.

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