Available online at www.sciencedirect.com
ScienceDirect
*Mendeleev Commun.*, 2006, **16(4)**, 230–232
Mendeleev Communications

# Reactions of *ortho*-aminophenols and *ortho*-aminothiophenols with 1,3,5-trinitrobenzene

**Mikhail D. Dutov, Sergei S. Vorob'ev, Ol'ga V. Serushkina, Svyatoslav A. Shevelev,* Bogdan I. Ugrak and Vadim V. Kachala**

*N. D. Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences, 119991 Moscow, Russian Federation. Fax: +7 495 135 5328; e-mail: shevelev@ioc.ac.ru*

DOI: 10.1070/MC2006v016n04ABEH002257

1,3-Dinitrophenoxazine and 1,3-dinitrophenothiazine derivatives were prepared by the reactions of *ortho*-aminophenols and *ortho*-aminothiophenols with 1,3,5-trinitrobenzene.

This study on the use of 1,3,5-trinitrobenzene as a multipurpose synthon is a part of a programme for the chemical utilization of 2,4,6-trinitrotoluene.[1,2] 1,3,5-Trinitrobenzene can be easily prepared from 2,4,6-trinitrotoluene by two-step oxidative demethylation.[3] A technologically attractive procedure for the oxidation of the methyl group in 2,4,6-trinitrotoluene with 80% $HNO_3$ at elevated temperatures and pressures was proposed and optimised.[4]

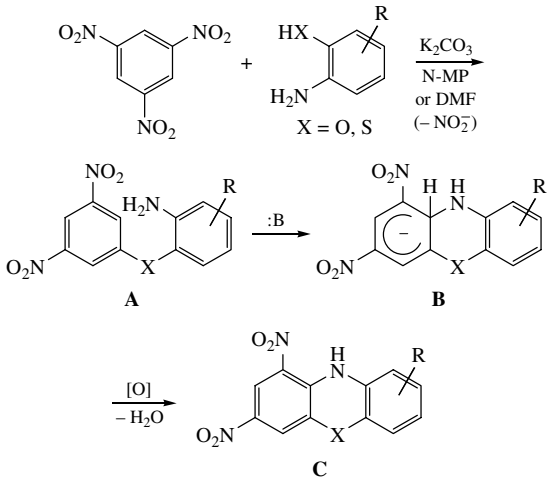
1,3,5-Trinitrobenzene is characterised by the ability of adding nucleophiles at the *ortho*/*para* positions with respect to nitro groups with the formation of stable anionic σ-H complexes.[5–8] At the same time, it was found that, under certain conditions, a number of O, S, and N nucleophiles, including phenols and thiophenols, substitute for nitro groups in 1,3,5-trinitrobenzene in the presence of organic bases.[9–14]

In our opinion, the products of substitution for the nitro group in 1,3,5-trinitrobenzene can be used for the synthesis of condensed polycyclic structures. Thus, we believed that, under conditions developed previously for phenols and thiophenols, that is, in the presence of $K_2CO_3$ in N-MP or DMF, *ortho*-aminophenols and *ortho*-aminothiophenols can serve as anionic O and S nucleophiles to form substitution products **A** (Scheme 1).†

We believed that, under specially chosen conditions, products **A** undergo intramolecular oxidative substitution for hydrogen by the formation of cyclic σ-H complex **B** followed by oxidation to target products **C**, that is, 1,3-dinitrophenoxazines and 1,3-dinitrophenothiazines (Scheme 1).

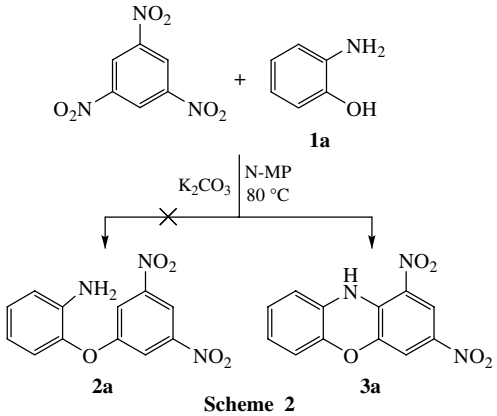
We found that the interaction of 1,3,5-trinitrobenzene with *ortho*-aminophenol **1a** in N-MP in the presence of an equimolar amount of $K_2CO_3$ at 80 °C did not afford substitution product **2a** (that is, compound **A**) and cyclic σ-H complex **B**. The only reaction product was 1,3-dinitrophenoxazine **3a**, which was isolated in 52% yield (Scheme 2).

Thus, the reaction gave compound **C** (Scheme 1) without the addition of oxidising agents. Note that atmospheric oxygen does not act as an oxidant in this process because the same result was obtained in a deoxygenated atmosphere. It is likely that the process of oxidative nucleophilic substitution occurred by so-called spontaneous or auto aromatization. At the second step, a nitro compound present in the reaction mixture can serve as an oxidizing agent.




**Scheme 1**

Substituted *ortho*-aminophenols reacted with 1,3,5-trinitrobenzene in a similar manner (Scheme 3); that is, the reaction

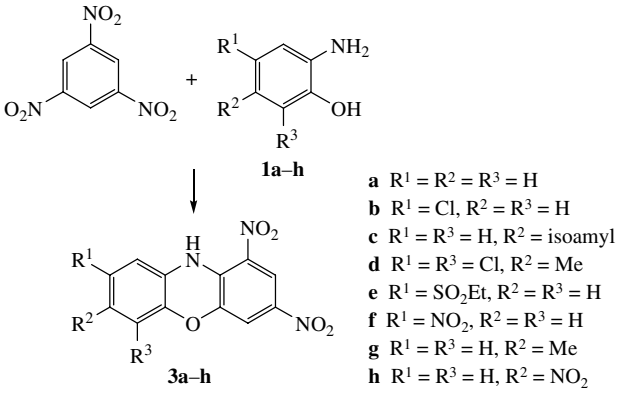



**Scheme 2**

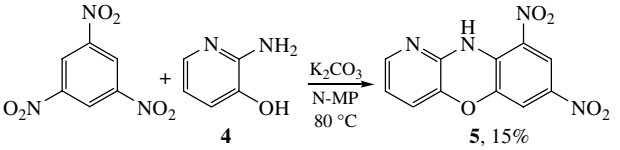
† The reaction at the amino group is improbable because aromatic amines did not replace a nitro group in 1,3,5-trinitrobenzene under the specified conditions (20–80 °C).

exhibits a general character. However, the yields of 1,3-dinitrophenoxazines dramatically decreased (to 11–15%)‡ on going from compound **1a** to substituted analogues.

2-Aminopyridin-3-ol **4**, a heterocyclic analogue of *ortho*-aminophenol, reacted with 1,3,5-trinitrobenzene in the same manner to give compound **5** (Scheme 4).‡

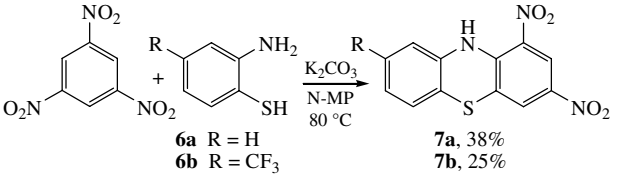



**Scheme 3**



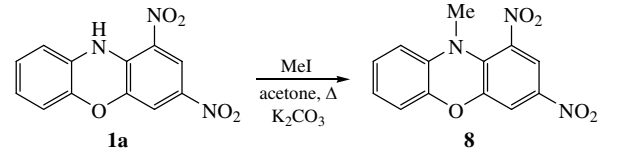

**Scheme 4**

*ortho*-Aminothiophenols **6** analogously reacted with 1,3,5-trinitrobenzene to form corresponding 1,3-dinitrophenothiazines **7** (Scheme 5).‡




**Scheme 5**

To determine the positions of nitro groups, we performed the N-methylation of 1,3-dinitrophenoxazine **1a** with the use of MeI (Scheme 6). The absence of long-range interactions between the protons of the methyl group and the protons of the dinitrobenzene moiety in resulting compound **8** was found using two-dimensional NMR spectroscopy. At the same time, the interaction with the protons of the second ring provided support for the structure of compound **1a**: the NH fragment and the nitro group occurred in the peri position with respect to each other.




**Scheme 6**

Note that the well-known synthesis of nitro-substituted phenoxazines is based on the Terpin reaction.[16–18] The interaction of picryl chloride with *ortho*-aminophenols and *ortho*-thiophenols in the presence of bases is a convenient preparative procedure for the preparation of various 1,3-dinitrophenoxazines and 1,3-dinitrophenothiazines, respectively. Here, we demonstrated a specific feature of the chemistry of 1,3,5-trinitrobenzene: it is prone to the reactions of oxidative nucleophilic substitution for hydrogen without the use of external oxidizing agents, at least, in the processes of cyclisation.

‡ The compounds were characterised by $^1$H NMR spectra ([$^2H_6$]DMSO), electron-ionization mass spectra, and elemental analysis data. The $^1$H NMR spectra were measured on a Bruker AC-250 spectrometer. The mass spectra were obtained on a Kratos MS-30 instrument. All of the compounds exhibited peaks due to molecular ions ($M^+$) in the mass spectra. The course of reaction was monitored by TLC on Silufol UV-254 plates.

*General procedure for the preparation of 1,3-dinitrophenoxazines* **3a–h** *and* **5**. A mixture of 2.13 g (0.01 mol) of trinitrobenzene, 1.38 g (0.01 mol) of potassium carbonate and (0.01 mol) of *o*-aminophenol was placed in 7 cm$^3$ of *N*-methylpyrrolidone (N-MP), heated to 80 °C and continuously stirred until the complete conversion of trinitrobenzene (4–8 h; TLC monitoring; eluent, $CHCl_3$). The reaction mixture was poured into 100 cm$^3$ of 10% HCl and stirred for 20 min; the resulting precipitate was filtered off and dried on filter. The product was recrystallised from a minimum amount of 1,2-dichloroethane. Compound **5** was prepared in an analogous manner.

**3a**: yield 52.6%, mp 211–212 °C (lit.,[16] 211–212 °C). $^1$H NMR, $\delta$: 6.7 (m, 1H), 6.85 (m, 2H), 7.25 (m, 1H), 7.45 (d, 1H, $^4J$ 2 Hz), 8.30 (d, 1H, $^4J$ 2 Hz), 9.95 (s, 1H).

**3b**: yield 14%, mp 220–221 °C. $^1$H NMR, $\delta$: 6.7 (d, 1H, $^3J$ 8 Hz), 6.85 (dd, 1H, $^3J$ 8 Hz, $^4J$ 2 Hz), 7.35 (d, 1H, $^4J$ 2 Hz), 7.45 (d, 1H, $^4J$ 2 Hz), 8.25 (d, 1H, $^4J$ 2 Hz), 10.0 (s, 1H).

**3c**: yield 12.7%, mp 175–177 °C. $^1$H NMR, $\delta$: 0.65 (t, 3H, $^3J$ 8 Hz), 1.2 (s, 6H), 1.6 (q, 2H, $^3J$ 8 Hz), 6.55 (d, 1H, $^3J$ 8 Hz), 6.85 (d, 1H, $^3J$ 8 Hz), 7.45 (d, 1H, $^4J$ 2 Hz), 7.55 (d, 1H, $^4J$ 2 Hz), 8.3 (d, 1H, $^4J$ 2 Hz), 10.1 (s, 1H).

**3d**: yield 12.3%, mp 203–204 °C. $^1$H NMR, $\delta$: 2.22 (s, 3H), 7.4 (s, 1H), 7.5 (d, 1H, $^4J$ 2 Hz), 8.3 (d, 1H, $^4J$ 2 Hz), 10.1 (s, 1H).

**3e**: yield 14.2%, mp 232–234 °C. $^1$H NMR, $\delta$: 1.17 (t, 3H, $^3J$ 8 Hz), 3.22 (q, 2H, $^3J$ 8 Hz), 6.95 (d, 1H, $^3J$ 8 Hz), 7.35 (dd, 1H, $^3J$ 8 Hz, $^4J$ 2 Hz), 7.6 (d, 1H, $^4J$ 2 Hz), 7.92 (d, 1H, $^4J$ 2 Hz), 8.35 (d, 1H, $^4J$ 2 Hz), 10.25 (s, 1H).

**3f**: yield 11.6%, mp 210–212 °C. $^1$H NMR, $\delta$: 6.9 (d, 1H, $^3J$ 2 Hz), 7.5 (dd, 1H, $^3J$ 8 Hz, $^4J$ 2 Hz), 7.7 (d, 1H, $^3J$ 8 Hz), 8.25 (d, 1H, $^4J$ 2 Hz), 8.35 (d, 1H, $^4J$ 2 Hz), 10.25 (s, 1H).

**3g**: yield 12.1%, mp 236–237 °C. $^1$H NMR, $\delta$: 2.15 (s, 3H), 6.6 (d, 1H, $^3J$ 8 Hz), 6.65 (d, 1H, $^3J$ 8 Hz), 7.1 (s, 1H), 7.35 (d, 1H, $^4J$ 2 Hz), 8.35 (d, 1H, $^4J$ 2 Hz), 9.9 (s, 1H).

**3h**: yield 11.7%, mp 207–209 °C. $^1$H NMR, $\delta$: 6.9 (d, 1H, $^3J$ 8 Hz), 7.6 (d, 1H, $^3J$ 8 Hz), 7.85 (dd, 1H, $^3J$ 8 Hz, $^4J$ 2 Hz), 8.25 (d, 1H, $^4J$ 2 Hz), 8.35 (d, 1H, $^4J$ 2 Hz), 10,25 (s, 1H).

**5**: yield 15.1%, mp 200–202 °C. $^1$H NMR, $\delta$: 6.9 (dd, 1H, $^3J$ 8 Hz), 7.2 (d, 1H, $^3J$ 8 Hz), 7.65 (d, 1H, $^3J$ 8 Hz), 7.8 (d, 1H, $^4J$ 2 Hz), 8.35 (d, 1H, $^4J$ 2 Hz), 9.7 (s, 1H).

*Synthesis of 1,3-dinitrophenothiazine* **7a**. A mixture of 1.5 g (0.007 mol) of trinitrobenzene, 0.75 cm$^3$ (0.007 mol) of 2-aminothiophenol and 0.96 g (0.007 mol) of potassium carbonate was placed in 7 cm$^3$ of *N*-methylpyrrolidone. The reaction mixture was allowed to stand at room temperature for 8 h (until the complete conversion of trinitrobenzene; TLC monitoring; eluent, $CHCl_3$). The reaction mixture was poured into 100 cm$^3$ of 10% HCl and stirred for 20 min. The resulting precipitate was filtered off and dried on filter. The product was recrystallised from 1,2-dichloroethane. Yield 38%, mp 192–193 °C (lit.,[17] 192–193 °C). $^1$H NMR ([$^2H_6$]DMSO) $\delta$: 7.1 (m, 4H), 8.0 (d, 1H, $^4J$ 2 Hz), 8.5 (d, 1H, $^4J$ 2 Hz), 10.1 (s, 1H).

*Synthesis of 1,3-dinitro-7-trifluoromethylphenothiazine* **7b**. A mixture of 2.13 g (0.01 mol) of trinitrobenzene, 1.93 g (0.01 mol) of 2-amino-4-trifluoromethylthiophenol and 1.38 g (0.01 mol) of potassium carbonate was placed in 9 cm$^3$ of *N*-methylpyrrolidone. The reaction mixture was kept at 80 °C for 16 h (until the complete conversion of trinitrobenzene; reaction monitoring by TLC; eluent, $CHCl_3$). The reaction mixture was poured into 100 cm$^3$ of 10% HCl and stirred for 20 min. The resulting precipitate was filtered off and dried on filter. The product was recrystallised from 1,2-dichloroethane. Yield 25.6%, mp 203–204 °C (lit.,[19] 205–206 °C). $^1$H NMR, $\delta$: 7.25 (m, 2H), 7.55 (d, 1H, $^4J$ 2 Hz), 8.1 (d, 1H, $^4J$ 2 Hz), 8.7 (d, 1H, $^4J$ 2 Hz), 10.12 (s, 1H).

*Synthesis of 10-methyl-1,3-dinitrophenoxazine* **8**. A mixture of 1 g (0.0036 mol) of 1,3-dinitrophenoxazine, 0.51 g (0.0036 mol) of methyl iodide and 0.5 g (0.0036 mol) of potassium carbonate was dissolved in 15 cm$^3$ of acetone. The reaction mixture was refluxed for 26 h (until the complete conversion of the parent phenoxazine; TLC monitoring of the reaction; eluent, $CHCl_3$). The mixture was evaporated to dryness on a rotary evaporator. Yield 99%, mp 175–176 °C (lit.,[16] 176–178 °C). $^1$H NMR, $\delta$: 3.01 (s, 3H), 6.85 (d, 1H, $^4J$ 2 Hz), 7.0 (m, 3H), 7.61 (d, 1H, $^4J$ 2 Hz), 8.23 (d, 1H, $^4J$ 2 Hz).

## References

1 V. A. Tartakovsky, S. A. Shevelev, M. D. Dutov, A. Kh. Shakhnes, A. L. Rusanov, L. G. Komarova and A. M. Andrievsky, in *Conversion Concepts for Commercial Applications and Disposal Technologies of Energetic Systems*, ed. H. Krause, Kluwer Academic Publishers, Dordrecht, 1997, p. 137.

2 S. A. Shevelev, V. A. Tartakovsky and A. L. Rusanov, in *Combustion of Energetic Matirials*, ed. K. K. Kuo and L. T. DeLuca, Begell House, Inc., New York, 2002, p. 62.

3 *Organic Synthesis, Coll. Vol. 1*, ed. H. Gilman, Wiley, New York, 1946, pp. 541, 543.
4 A. Astrat'ev, V. Marchukov, V. Suschev and A. Aleksandrov, *Abstracts of the 218th American Chemical Society National Meeting, Division of Organic Chemistry*, August 1999, p. 50.
5 F. Terrier, *Chem. Rev.*, 1982, **82**, 77.
6 G. A. Artamkina, M. P. Egorov and I. P. Beletskaya, *Chem. Rev.*, 1982, **82**, 427.
7 E. Buncel, M. R. Crampton, M. J. Strauss and F. Terrier, *Electron Deficient Aromatic and Heteroaromatic Base Interaction. The Chemistry of Anionic Sigma-Complexes*, Elsevier, New York, 1984.
8 F. Terrier, *Nucleophilic Aromatic Displacement. The Influence of the Nitro Group*, VCH Publishers, Inc., New York, 1991.
9 S. A. Shevelev, M. D. Dutov, I. A. Vatsadze, O. V. Serushkina, A. L. Rusanov and M. A. Andrievskii, *Mendeleev Commun*., 1995, 157.
10 S. A. Shevelev, M. D. Dutov, I. A. Vatsadze, M. A. Korolev and A. L. Rusanov, *Mendeleev Commun*., 1996, 155.
11 S. A. Shevelev, M. D. Dutov, M. A. Korolev, O. Yu. Sapozhnikov and A. L. Rusanov, *Mendeleev Commun*., 1998, 69.
12 S. A. Shevelev, M. D. Dutov and O. V. Serushkina, *Izv. Akad. Nauk, Ser. Khim*., 1995, 2528 (*Russ. Chem. Bull*., 1995, **44**, 2424).
13 O. Yu. Sapozhnikov, M. D. Dutov, M. A. Korolev, V. V. Kachala and S. A. Shevelev, *Mendeleev Commun*., 2001, 232.
14 S. A. Shevelev, I. A. Vatsadze and M. D. Dutov, *Mendeleev Commun*., 2002, 196.
15 O. N. Chupakhin, V. N. Charushin and H. C. Van der Plas, *Nucleophilic Aromatic Substitution of Hydrogen*, Academic Press, New York, 1994.
16 V. N. Knyazev, V. N. Drozd and T. Ya. Mozhaeva, *Zh. Org. Khim*., 1980, **16**, 876 [*J. Org. Chem. USSR* (*Engl. Transl.*), 1980, **16**, 770].
17 V. N. Knyazev, V. N. Drozd and T. Ya. Mozhaeva, *Zh. Org. Khim*., 1979, **15**, 2561 [*J. Org. Chem. USSR* (*Engl. Transl.*), 1979, **15**, 2316].
18 E. A. Jauer, H. Thurm, A. Keil, H. Scheffler and L. Schwarz, *German Patent, Coden: GEXXA8 DD 10622 Z 19810909*, 1981.
19 S. Malik, M. Anand, S. S. Verma and L. Prakash, *J. Fluorine Chem.*, 1989, **42**, 201.

*Received: 24th October 2005; Com. 05/2598*