Mendeleev Commun., 2000, 10(2), 72–73

Regioselectivity of the substitution for the nitro group in 2,4,6-trinitrobenzonitrile under the action of thiols. The synthesis of 4,6-dinitro derivatives of benzo-annelated sulfur-containing heterocycles

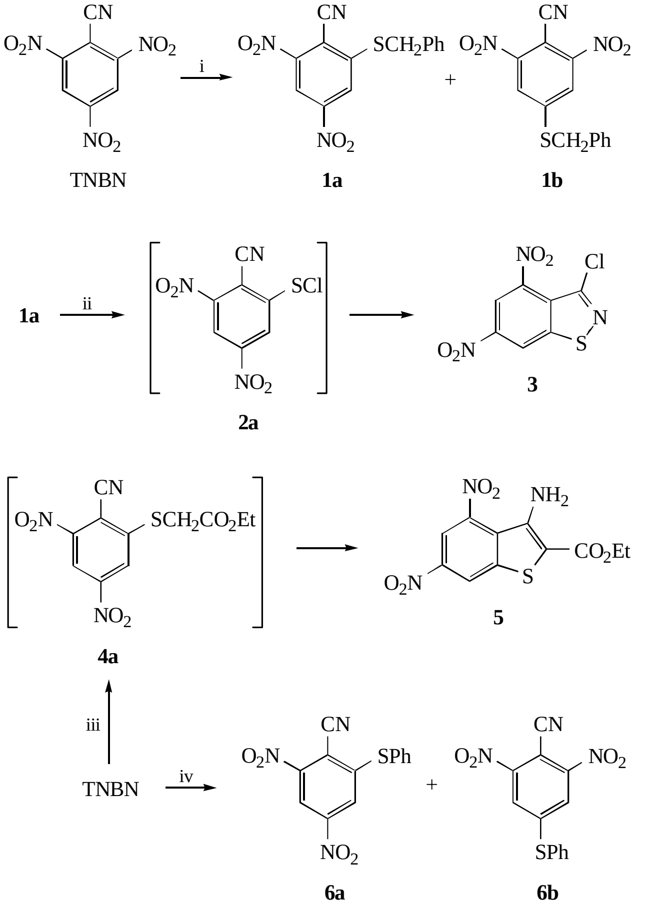
Igor L. Dalinger, Tat'yana I. Cherkasova, Valerian M. Khutoretskii and Svyatoslav A. Shevelev*

N. D. Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences, 117913 Moscow, Russian Federation.
Fax: +7 095 135 5328; e-mail: shevelev@cacr.ioc.ac.ru

DOI: 10.1070/MC2000v010n02ABEH001220

Conditions for the regioselective substitution for a nitro group in the *ortho*-position in 2,4,6-trinitrobenzonitrile under the action of thiols ($PhCH_2SH$, $HSCH_2CO_2Et$ or PhSH) in the presence of K_2CO_3 or KOH were found, and the intramolecular cyclization of the *ortho*-fragments –SX and –CN (X = Cl or CH_2CO_2Et) was performed to afford 3-chloro-4,6-dinitrobenzo[*d*]isothiazole and 3-amino-2-ethoxycarbonyl-4,6-dinitrobenzo[*b*]thiophene, respectively.

We are concerned with the chemistry of primary conversion products of 2,4,6-trinitrotoluene (TNT) in the context of the utilisation of this explosive.[1] These products include 2,4,6-trinitrobenzonitrile (TNBN), which can be easily prepared from TNT by the treatment with nitrosyl chloride.[2] One of the promising synthetic applications of TNBN is the production of benzo-annelated heterocycles, which can be performed, in particular, by the selective replacement of a nitro group in the *ortho*-position with a unit capable of intramolecular cyclization with the nitrile group.



Scheme 1 *Reagents, conditions and results*: i, 1 equiv. $PhCH_2SH$ + 1.8 equiv. K_2CO_3; i$_1$, DMF/H_2O (4:1, v/v; 0.42 M $PhCH_2SH$), 0–2 °C, 3 h, 91% yield of **1a** + **1b**, **1a**:**1b** = 2:1; i$_2$, MeCN (0.42 M $PhCH_2SH$), 80 °C (boiling), 3 h, 90% yield of **1a** + **1b**, **1a**:**1b** = 3:1; i$_3$, toluene (0.25 M $PhCH_2SH$), 110 °C (boiling), 8 h, 40% yield of **1a** + **1b**, **1a**:**1b** = 5:1; ii, **1a**:**1b** = 5:1, 7 equiv. SO_2Cl_2/DCE, boiling, 8 h, 50% yield of **3** (in terms of **1a**); iii, 1 equiv. $HSCH_2CO_2Et$ + 1.8 equiv. KOH, MeCN/H_2O (4:1, v/v, 0.42 M $HSCH_2CO_2Et$), 0 °C, 0.5 h, 20 °C, 3 h, 54% yield of **5**; iv, 1 equiv. PhSH + 1.8 equiv. K_2CO_3; iv$_1$, DMF/H_2O (4:1, v/v; 0.42 M PhSH) 0–2 °C, 3 h, 76% yield of **6a** + **6b**, **6a**:**6b** = 2:1; iv$_2$, toluene, (0.25 M PhSH), 110 °C (boiling), 4 h, 80% yield of **6a**.

We found that in the reaction of TNBN with $PhCH_2SH$ in the presence of K_2CO_3 both *ortho* and *para* nitro groups were replaced with the $PhCH_2S$ unit: an isomer mixture of *ortho* and *para* sulfides **1a** and **1b** was formed, the ratio between which depends on the polarity of the solvent (Scheme 1, i).

It can be seen that the fraction of *ortho* substitution considerably increased with decreasing polarity of solvents in the order aqueous DMF, MeCN and PhMe (Scheme 1, i, i$_1$–i$_3$). We used a mixture (5:1) of *ortho* and *para* isomers **1a** and **1b** prepared in a medium of PhMe for the intramolecular cyclization starting from **1a** (*via* **2a**). It is well known that the ArS–CH_2Ph bond is easily cleaved under the action of chlorinating agents to form ArSCl.[3] It is also known that spontaneous intramolecular cyclization with the formation of 3-chlorobenzo[*d*]isothiazoles proceeds in the presence of CN and SCl units in the *ortho* position.[4] Indeed, 3-chloro-4,6-dinitrobenzo[*d*]isothiazole **3** (Scheme 1, ii) was prepared by the treatment of the above mixture of sulfides **1a** and **1b** with SO_2Cl_2.

The substitution for the *para* nitro group was not observed in the reaction of $HSCH_2CO_2Et$ with TNBN (in the presence of KOH in aqueous acetonitrile); 3-amino-2-ethoxycarbonyl-4,6-dinitrobenzo[*b*]thiophene **5**, a representative of previously unknown 4,6-dinitrobenzo[*b*]thiophenes (Scheme 1, iii), was the only reaction product.

According to published data,[5] benzothiophene **5** is formed by base-catalysed intramolecular cyclization of *ortho*-substitution product **4a** (Scheme 1, iii).

A representative of aromatic thiols, PhSH, reacting with TNBN (in the presence of K_2CO_3) in aqueous DMF gives a mixture of isomer *ortho* and *para* sulfides **6a** and **6b** (Scheme 1, iv, iv$_1$). However, the reaction proceeds regiospecifically in a toluene medium: only a nitro group in the *ortho* position of TNBN is replaced, and the only product, *ortho*-sulfide **6a**, is formed in high yield (Scheme 1, iv, iv$_2$).

The identity of the individual products or isomer mixtures obtained was supported by ^1H and ^{13}C NMR spectroscopy, mass spectrometry, IR spectroscopy and elemental analysis. The yields in Scheme 1 are specified for isolated individual products or purified isomer mixtures. At the same time, the ratio between *ortho* and *para* isomers (^1H NMR data) is given for isolated crude reaction products. In all cases, the reaction was performed until the complete conversion of TNBN.[†]

[†] ^1H NMR spectra were recorded on a Bruker AM-300 spectrometer, solvent [$^2H_6$]DMSO.

3: mp 200–202 °C (Pr^{i}OH). ^1H NMR, δ: 8.9 (s, 1H, H^7), 9.1 (s, 1H, H^5). ^{13}C NMR, δ: 112.18, 112.73, 120.21, 129.30, 144.95, 149.42, 150.37.

5: mp 200 °C (Pr^{i}OH). ^1H NMR, δ: 1.3 (t, 3H, OEt), 4.3 (qw, 2H, OEt), 6.6 (br. s, 2H, NH_2), 8.7 (s, 1H, H^7), 9.4 (s, 1H, H^5). ^{13}C NMR, δ: 14.22, 61.25, 105.79, 116.89, 124.06, 124.93, 125.45, 141.62, 144.90, 145.89, 163.65.

6a: mp 110–112 °C (Pr^{i}OH). ^1H NMR, δ: 7.7 (m, 5H, Ph), 8.0 (s, 1H, H^3), 8.7 (s, 1H, H^5).

This work was supported by the International Science and Technology Centre (ISTC) (grant no. 419).

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 M. E. Sitzman and J. C. Dacons, *J. Org. Chem*., 1973, **38**, 4363.
3 (*a*) D. M. Tink and J. T. Strupczewski, *Tetrahedron Lett*., 1993, **34**, 6525; (*b*) N. Kharasch and R. B. Langford, *J. Org. Chem*., 1963, **28**, 1903.
4 J. R. Beck and J. A. Yahner, *J. Org. Chem*., 1978, **43**, 1604.
5 J. R. Beck, *J. Org. Chem*., 1972, **37**, 3224.

Received: 2nd November 1999; Com. 99/1548