Reaction of 1,3,5-Trinitrobenzene with Phenols: Synthesis of 3,5-Dinitrophenyl Aryl Ethers

Svyatoslav A. Shevelev,* Mikhail D. Dutov, Irina A. Vatsadze, Olga V. Serushkina, Aleksandr L. Rusanov and Aleksandr M. Andrievskii

N. D. Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences, 117913 Moscow, Russian Federation. Fax: +7 095 135 5328

A general method for the synthesis of 3,5-dinitrophenyl aryl ethers by condensation of phenols with 1,3,5-trinitrobenzene in the presence of solid K_2CO_3 in dipolar aprotic amide-type solvents has been elaborated.

Within the scope of work on the chemical conversion of explosive compounds of the aromatic series we have been studying systematically the nucleophilic substitution of nitro groups in the explosive 2,4,6-trinitrotoluene (TNT) and in the product of its demethylation, 1,3,5-trinitrobenzene (TNB), with the aim of obtaining new or inaccessible compounds which are of interest for creating valuable products for civil purposes.

In the present work we have studied the possibility of replacing the nitro group in TNB by phenols and their analogues in order to obtain the corresponding 3,5-dinitrophenyl aryl ethers (3,5-DNPAE).

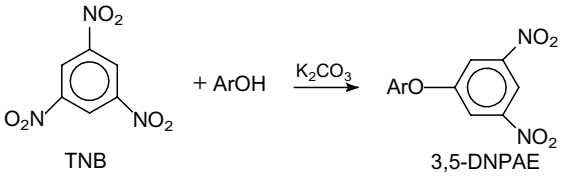
A thorough analysis of the literature shows that 3,5-DNPAE, *i.e.*, aryl and heteroaryl ethers of 3,5-dinitrophenol, are an almost unknown type of compound, since no general methods for their synthesis are available. On the other hand, 3,5-DNPAE could be of interest for obtaining, *e.g.*, the corresponding diamines – potential condensation monomers.

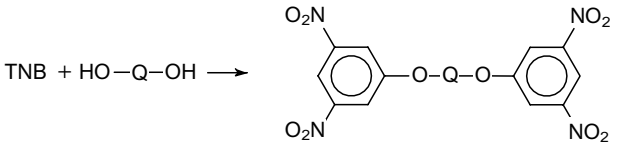
In our opinion, a general approach for obtaining 3,5-DNPAE may involve the condensation of TNB with phenols and their analogues in an alkaline medium through nucleophilic substitution of the nitro group by phenolate anions. However, reactions of various nucleophiles with TNB generally do not give substitution products, but instead, result in stable anionic σ-complexes through addition of nucleophiles to the aromatic ring,[1,2] although separate cases of substitution of the nitro group in TNB, *e.g.*, by MeO[3,4] and $PhCH_2O$ [5] are also known. Phenolate anions also form σ-complexes with TNB;[1,2] it has been reported only once[6] that the reaction of potassium 2,4,6-trimethylphenolate in DMSO results not only in a σ-complex but also in a product of nitro group substitution. Similar transformations were recently reported[7] for reactions of TNB with some potassium phenoxides (ArOK, Ar = C_6H_5, 3,5-$Bu^t_2C_6H_3$, 2,4,6-$Me_3C_6H_2$) in the acetonitrile–glyme† system and in DMSO. However, it turned out that these conditions are unsuitable for creating a general preparative method for 3,5-DNPAE synthesis.

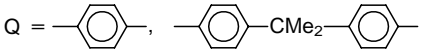
We found that the general method for 3,5-DNPAE synthesis involves the reaction of various hydroxyarenes with TNB in dipolar aprotic amide-type solvents (DMF, DMA, *N*-methylpyrrolidin-2-one, *etc.*), preferably in *N*-methylpyrrolidin-2-one (*N*-MP), in the presence of solid K_2CO_3 at 80–90 °C for several hours.† Non-amide dipolar aprotic solvents, such as DMSO, have low efficiency, as the yields of 3,5-DNPAE are often low.

Phenols containing either electron-donating or electron-withdrawing substituents can be successfully used in this reaction (Table 1).

Using 2-naphthol and 3-hydroxypyridine as examples, we showed that not only can phenols be used, but other types of aromatic hydroxy derivatives as well.







The same reaction can be carried out with phenols containing two hydroxy groups [TNB:$Q(OH)_2$ ratio 2:1], see Table 1.

Preliminary data show that electron-withdrawing substituents in phenol slow down the process.

The compounds obtained in this work are new.§ They were characterized by ^{1}H NMR spectroscopy (Table 1), mass spectrometry (the presence of a molecular ion), IR spectroscopy (absorption corresponding to aromatic NO_2) and satisfactory elementary analyses.

Phenolates are ambident ions, which can react with electrophiles to give not only *O*- but also *C*-derivatives.[8] In our case, they undergo *O*-3,5-dinitrophenylation.

References

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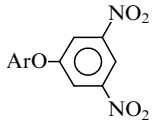
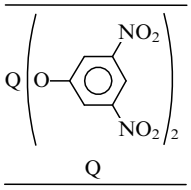
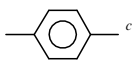
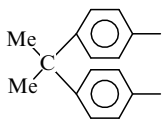
† Glyme = ethylene glycol dimethyl ether.

‡ *General procedure:* ArOH (0.025 mol) [or $Q(OH)_2$ (0.0125 mol)] was mixed with K_2CO_3 (0.025 mol) in *N*-MP (20 ml), then TNB (0.025 mol) in *N*-MP (5 ml) was added at 80 °C. The mixture was stirred at 80 °C until the TNB disappeared (TLC, HPLC), poured into water and recrystallized or reprecipitated from a suitable solvent. The reaction times and solvents for purification are specified in Table 1.

§ Quite recently, compound **1** (Table 1) was obtained by treatment of PhOK with TNB in DMSO in 7.6% yield.[7]

Table 1 3,5-Dinitrophenyl aryl ethers.

Entry	 Ar	Reaction time (at 80 °C)	Yield (%) with respect to the purified product	M.p./°C (solvent)	^{1}H NMR δ/ppm (solvent)
1	Ph	4 h	80.5	119.5–120.5[a]	([$^2H_6$]acetone): 8.71t-1H, 8.09d-2H, 7.49tm-2H, 7.33tm-1H, 7.13dm-2H
2	3-MeC_6H_4	3 h	50.0	87–88[a]	([$^2H_6$]acetone): 8.60t-1H, 8.10d-2H, 7.37t-1H, 7.14d-1H, 7.01br.s-1H, 7.00dd-1H, 2.38s-3H
3	2-MeC_6H_4	3 h	63.0	112–113[a]	([$^2H_6$]DMSO): 8.51t-1H, 8.00d-2H, 7.40dd-1H, 7.33ddd-1H, 7.25ddd-1H, 7.14dd-1H, 2.20s-3H
4	4-FC_6H_4	3 h	68.9	118[a]	([$^2H_6$]DMSO): 8.56t-1H, 8.12d-2H, 7.36d-2H, 7.33d-2H
5	4-BrC_6H_4	3 h	68.0	123.5–124.5 (EtOAc)	([$^2H_6$]DMSO): 8.59t-1H, 8.18d-2H, 7.69d-2H, 7.22d-2H
6	4-IC_6H_4	3 h	64.2	126–127[a]	([$^2H_6$]DMSO): 8.57t-1H, 8.14d-2H, 7.79d-2H, 7.04d-2H
7	3-ClC_6H_4	3 h	52.3	69.0–70.0 (EtOAc/MeOH)	([$^2H_6$]DMSO): 8.61t-1H, 8.22d-2H, 7.53t-1H, 7.39dt-1H, 7.36t-1H, 7.22dt-1H
8	4-(HO)C_6H_4[b]	1.5 h	60.0	79.0–79.5 (diethyl ether)	([$^2H_6$]DMSO): 9.50br.s-1H, 8.47t-1H, 7.97d-2H, 7.01d-2H, 6.84d-2H
9	4-EtOC_6H_4	2 h	78.0	112–113[a]	([$^2H_6$]DMSO): 8.49t-1H, 8.02d-2H, 7.15d-2H, 7.01d-2H, 4.04q-2H, 1.35t-3H
10	4-$NH_2C_6H_4$	3 h	40.8	129–130 (MeOH)	([$^2H_6$]DMSO): 8.46t-1H, 7.99d-2H, 6.93d-2H, 6.66d-2H, 5.24br.s-2H
11	3-$Et_2NC_6H_4$	2 h	77.0	72–73 (Pr^iOH)	($CDCl_3$): 8.63t-1H, 8.11d-2H, 7.24dd-1H, 6.59dd-1H, 6.38s-1H, 6.29dd-1H, 3.37q-4H, 1.20t-6H
12	4-MeCONHC_6H_4	3 h	78.5	223–224 (acetone)	([$^2H_6$]DMSO): 10.07br.s-1H, 8.52t-1H, 8.07d-2H, 7.70d-2H, 7.19d-2H, 2.07s-3H
13	4-(COOH)C_6H_4	3 h	40.0	198–200 ($CHCl_3$)	([$^2H_6$]DMSO): 12.98br.s-1H, 8.64t-1H, 8.28d-2H, 8.03d-2H, 7.29d-2H
14	4-$NO_2C_6H_4$	6 h	35.2	140–142 ($CHCl_3$/MeOH)	($CDCl_3$): 8.86t-1H, 8.38d-2H, 8.22d-2H, 7.23d-2H
15	2-naphthyl	2.5 h	46.6	173–174 ($CHCl_3$)	([$^2H_6$]DMSO): 8.59t-1H, 8.19d-2H, 8.08d-1H, 7.98dd-1H, 7.91dd-1H, 7.71d-1H, 7.55m-2H, 7.42dd-1H
16	3-pyridyl	4 h	70.0	92–93 (MeOH)	($CDCl_3$): 8.80t-1H, 8.62m-1H, 8.54m-1H, 8.14d-2H, 7.48m-2H
	 Q				
17	 [c]	7 h	60.0	208.0–209.5 ($CHCl_3$/dichloroethane)	([$^2H_6$]DMSO): 8.59t-2H, 8.22d-4H, 7.41s-4H
18		6 h	50.0	161–162 ($CHCl_3$/MeOH)	($CDCl_3$): 8.70t-2H, 8.11d-4H, 7.40dm-4H, 7.08dm-4H, 1.80s-6H

[a] Dissolved in the minimum amount of chloroform and precipitated with MeOH. [b] 1,4-$(HO)_2C_6H_4$:TNB:K_2CO_3 = 1:1:1.
[c] 1,4-$(HO)_2C_6H_4$:TNB:K_2CO_3 = 0.5:1:1.

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