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Mendeleev Commun., 1996, **6(4)**, 155–157

Mendeleev Communications

A general method for the synthesis of 1,3-diaryloxy-5-nitrobenzenes

Svyatoslav A. Shevelev,* Mikhail D. Dutov, Irina A. Vatsadze, Maksim A. Korolev and Aleksandr L. Rusanov

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 1,3-diaryloxy-5-nitrobenzenes by the condensation of phenols with 1,3,5-trinitrobenzene or aryl 3,5-dinitrophenyl ethers in the presence of solid K_2CO_3 in amide-type dipolar aprotic solvents has been developed.

We have previously developed a general method for the synthesis of aryl 3,5-dinitrophenyl ethers (3,5-DNPEs) of types **1** and **2** based on the substitution of the nitro group in 1,3,5-trinitrobenzene (TNB) under the action of phenols and bis-phenols.[1]

3,5-DNPEs synthesized with various substituents in the aryl fragment are of interest for studying the problem of nucleophilic substitution of the aromatic nitro group activated by electron-withdrawing *meta*-substituents. The substitution of a *meta*-nitro group, unlike the well studied substitution of a nitro group activated by *ortho*- and *para*-substituents,[2,3] has been insufficiently studied, which is probably because of its considerably lesser mobility. In the former case, activation is caused only by the I-effect, while in the latter it is also caused by the more efficient M-effect.

In this work, the possibility of substituting the nitro group in a 3,5-DNPE under the action of phenols and bis-phenols was studied in order to develop a general method for the preparation of the previously unknown 1,3-diaroxy-5-nitrobenzenes (1,3-DA-5-NB) of types **3** and **4** (diaryl 5-nitroresorcinol ethers **3** and their bis-analogs **4**). These compounds may be of interest, for example, for preparing anilines of a previously unknown type, 3,5-diaryloxyanilines, based on **3** and the corresponding diamines, probably *via* the conden-

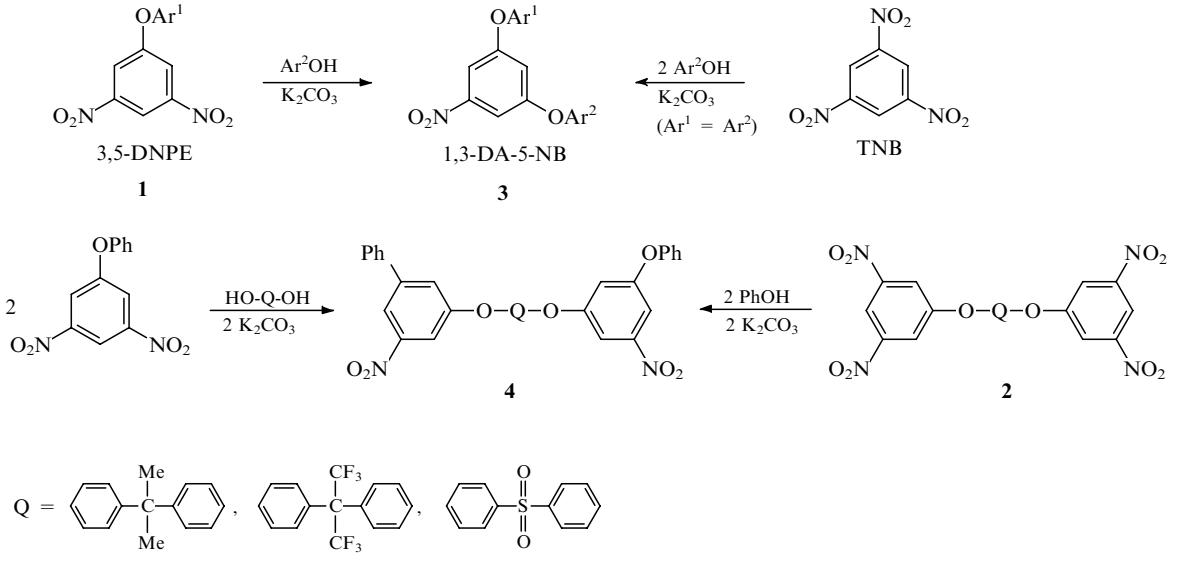
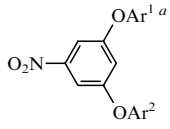
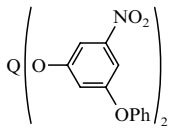
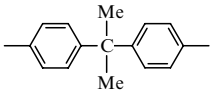
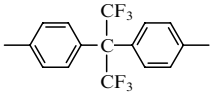
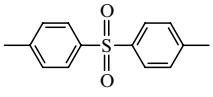


Table 1 1,3-Diaryloxy-5-nitrobenzenes.

Entry			Reaction time/h (at 150 °C)	Yield (%)	Mp/ °C	^{1}H NMR δ (ppm) (solvent)
	Ar^1	Ar^2				
1	Ph	Ph	5	48	68–69	($CDCl_3$) 7.49 (d 2H), 7.42 (t 4H), 7.24 (t 2H), 7.09 (d 4H)
2	Ph	4-Et-C_6H_4	9	39	49–50	([$^2H_6$]DMSO) 7.47 (t 2H), 7.45–7.22 (m 3H), 7.21–7.08 (m 4H), 7.03–6.95 (m 3H), 4.02 (q 2H), 1.32 (t 3H)
3	Ph	4-I-C_6H_4	8	66	69–70	([$^2H_6$]DMSO) 7.78 (d 2H), 7.52–7.40 (m 4H), 7.27 (t 1H), 7.18 (d 2H), 7.15 (t 1H), 7.00 (d 2H)
4	Ph	4-Br-C_6H_4	8	52	86–87	($CDCl_3$) 7.53 (d 2H), 7.49 (t 1H), 7.46 (t 1H), 7.43 (t 2H), 7.24 (t 1H), 7.08 (d 2H), 6.97 (d 2H), 6.96 (t 1H)
5	4-F-C_6H_4	Ph	3	71	77	($CDCl_3$) 7.51 (t,H), 7.47 (t 1H), 7.43 (t 2H), 7.24 (t 1H), 7.15–7.05 (m 6H), 6.97 (t 1H)
6	Ph	4-COOH-C_6H_4	2	55	260	([$^2H_6$]DMSO) 8.00 (d 2H), 7.53–7.38 (m 4H), 7.26 (t 1H), 7.20–7.05 (m 5H)
7	Ph	4-MeCONH-C_6H_4	5	55	144–145	([$^2H_6$]DMSO) 10.06 (br.s), 7.66 (d 2H), 7.47 (t 2H), 7.39 (t 2H), 7.26 (t 1H), 7.16 (d 2H), 7.02 (t 1H), 2.05 (s 3H)
8	Ph	3-pyridyl	9	64	84.5	([$^2H_6$]DMSO) 8.49 (d 1H), 8.47 (d.d 1H), 7.64 (d.q, 1H), 7.53–7.45 (m, 4H), 7.44 (s, 1H), 7.27 (t, 1H), 7.18 (d, 2H), 7.14 (t, 1H)
9	4-EtO-C_6H_4	4-EtO-C_6H_4	9	67	147–148	($CDCl_3$) 7.36 (d, 2H), 6.97 (d.d, 8H), 6.88 (t, 1H), 4.05 (q, 3H)
10	4-I-C_6H_4	4-I-C_6H_4	9	42	120	([$^2H_6$]DMSO) 7.78 (d, 4H), 7.47 (d, 2H), 7.16 (t, 1H), 6.99 (d, 4H)
11	4-Br-C_6H_4	4-Br-C_6H_4	3.5	40	129–130	($CDCl_3$) 7.53 (d, 4H), 7.47 (d, 2H), 7.01–6.92 (m, 5H)
12	4-HOOC-C_6H_4	4-HOOC-C_6H_4	4	40	311–312	([$^2H_6$]DMSO) 12.85 (br.s, 2H), 8.01 (d, 4H), 7.63 (d, 2H), 7.34 (t, 1H), 7.24 (d, 4H)
13	2-Me-C_6H_4	2-Me-C_6H_4	6	43	71–72	($CDCl_3$) 7.33 (d, 2H), 7.32–7.15 (m, 6H), 7.01 (d, 2H), 6.87 (t, 1H), 2.37 (s, 6H)
14	3-pyridyl	3-pyridyl	4	38	80–81.5	($CDCl_3$) 8.52 (d, 2H), 8.48 (d, 2H), 7.54 (d, 2H), 7.40 (m, 4H), 6.99 (t,1H)
15	2-naphthyl	2-naphthyl	4	25	134–135	([$^2H_6$]DMSO) 8.30–7.20 (m)
16	3-Me-C_6H_4	4-EtO-C_6H_4	6	38	52–53	([$^2H_6$]DMSO) 7.43 (t, 2H), 7.30 (t, 1H), 7.07–6.99 (m, 3H), 6.98-6.85 (m, 5H), 4.07 (q, 2H), 2.40 (s, 3H), 1.47 (t, 3H)
17	4-F-C_6H_4	4-MeCONH-C_6H_4	4	72	150–151	([$^2H_6$]DMSO) 10.05 (br.s, 1H), 7.65 (d, 2H), 7.40–7.17 (m, 6H), 7.12 (d, 2H), 7.05 (t, 1H), 2.05 (s, 3H)
18	4-EtO-C_6H_4	4-MeCONH-C_6H_4	4.5	64	198–199	([$^2H_6$]DMSO) 9.9 (br.s, 1H), 7.65 (d, 2H), 7.30 (d, 2H), 7.15–6.9 (m, 7H), 4.03 (q, 2H), 2.05 (s, 3H), 1.33 (t, 3H)
						
19			5	40	110	([$^2H_6$]acetone) 7.47 (t, 2H), 7.43 (t, 2H), 7.41 (t, 4H), 7.45–7.37 (m, 8H), 7.28–7.11 (m, 10H), 7.10 (t, 2H)
20			2.5	46	58	([$^2H_6$]DMSO) 7.57 (t, 2H), 7.47 (t, 2H), 7.45–7.37 (m, 8H), 7.28–7.11 (m, 10H), 7.10 (t, 2H)
21			3	95	54–55	([$^2H_6$]DMSO) 8.00 (d, 4H), 7.65 (d, 2H), 7.47 (d, 4H), 7.42 (s, 2H), 7.33–7.15 (m, 12H)

[a] In the case of $Ar^2 = Ar^1$, TNB + 2 Ar^2OH was used. In the case of $Ar^2 \neq Ar^1$, 1-Ar^1O-3,5-$(NO_2)C_4H_9$ + Ar^2OH was used. [b] The action of $Q(OH)_2$ upon **1** (Ar = Ph).

sation of monomers, based on **4**.

We have found that the general method for the preparation of 1,3-DA-5-NBs **3** and **4** is by the reactions of hydroxyarenes with 3,5-DNPE in amide-type dipolar aprotic solvents, best of all in *N*-methyl-2-pyrrolidone (N-MP), in the presence of solid K_2CO_3 at 150 °C for several hours (Table 1).†

As can be seen from Table 1, to perform the reaction successfully the process should be carried out under more rigorous conditions than in the case of substitution of one nitro group in TNB[1] (150 °C instead of 80–90 °C).

1,3-DA-5-NBs can also be obtained by the reactions of TNB with hydroxyarenes under the conditions mentioned above without the isolation of the intermediate 3,5-DNPE (molar ratio $TNB : Ar^2OH : K_2CO_3 = 1 : 2 : 2$, 150 °C).† To obtain 1,3-DA-5-NB with the same aryl fragments, it is more convenient to use TNB, while 3,5-DNPE should be used for the preparation of 1,3-DA-5-NB with different aryl fragments.

The 1,3-DA-5-NBs **3** and **4** so-obtained were characterized by ^{1}H NMR spectra (Table 1), mass spectra (the presence of the molecular ion), IR spectra and satisfactory elemental analysis.

We have demonstrated here the principle of possible substitution of the nitro group by hydroxyarenes in 1,3-DA-5-NB, *i.e.* without activation of the substituted nitro

group by other nitro groups: the reaction of 1,3-diphenoxy-5-nitrobenzene (**3**, $Ar^2 = Ar^1 = Ph$) with phenol in the presence of K_2CO_3 (in a ratio of 1:1:1) in N-MP at 200 °C for 3.5 h results in the formation of known 1,3,5-triphenoxybenzene[4] (yield 27%). The activating action of the *meta*-aryloxy substituent is confirmed by the fact that under similar conditions (150 °C, K_2CO_3, N-MP) compound **1** reacts with phenols 2.5–3 times faster than 1,3-dinitrobenzene (as determined by the times of conversion of initial products and the accumulation of products of the nitro group substitution); in the case of 1,3-dinitrobenzene, the known compound 1-phenoxy-3-nitrobenzene[4] is formed (yield ~ 60%).

† General procedures. *Method A*. 1,3-*DA*-5-*NB* (**3**, $Ar^2 \neq Ar^1$). Ar^2OH (0.02 mol) was mixed with K_2CO_3 (0.02 mol) in 20 ml of N-MP, a solution of 3,5-DNPE (**1**) (0.02 mol) in 10 ml of N-MP was added and the mixture stirred at 150 °C until the initial 3,5-DNPE disappeared [TLC, hexane–chloroform 3:2 (v/v)]. After cooling, the mixture was poured into water, the precipitated product was decanted or filtered off, dissolved in CCl_4 and passed through a short silica-gel column. The solvent was removed and the residue recrystallized from methanol. In the cases where the aryl fragment contained a carboxyl group, the reaction mixture was acidified by hydrochloric acid to pH 1–2 after pouring into water, and the precipitate formed was recrystallized from a $CHCl_3$–MeOH mixture [2:1 (v/v)].
Method B. 1,3-*DA*-5-*NB* (**3**, $Ar^2 = Ar^1$). Ar^2OH (0.026 mol) was mixed with K_2CO_3 (0.026 mol) in 20 ml of N-MP, and a solution of TNB (0.013 mol) in 10 ml of N-MP was added. The mixture was stirred at 150 °C until the initial TNB and the intermediate 3,5-DNPE disappeared (TLC as in Method A). The product was isolated as described in Method A.

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Received: Moscow, 23rd January 1996
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