Mendeleev Commun., 2002, 12(5), 196–197

Substitution for a nitro group in 1,3,5-trinitrobenzene and *meta*-substituted 1,3-dinitrobenzenes under the action of oximes

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10.1070/MC2002v012n05ABEH001639

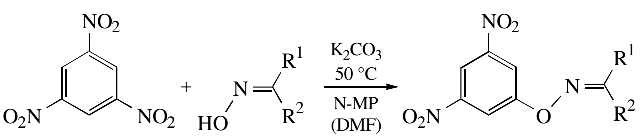
The title reaction was performed with 1,3,5-trinitrobenzene and 1-X-3,5-dinitrobenzenes (X = CF_3, ArO) in the presence of K_2CO_3 in *N*-methylpyrrolidone or DMF solutions to form *O*-3,5-dinitrophenyl oximes or *O*-3-X-5-nitrophenyl oximes, respectively.

1,3,5-Trinitrobenzene (TNB) is a good model for studying competition between nucleophilic substitution for an aromatic nitro group activated by only *meta* substituents and nucleophile addition to an aromatic nucleus. Indeed, TNB adds nucleophiles at the *ortho* position with respect to a nitro group to form stable anionic σ-complexes.[1–4] However, conditions under which anionic O-, S- and N-nucleophiles can replace one or two nitro groups in TNB were found.[5–9] Note that the substitution products were unavailable previously; thus, it is also of preparative interest to study nucioleophilic substitution in TNB.

In the case of anionic O-nucleophiles, the nitro group in TNB can be smoothly replaced with the use of compounds whose O-anions combine a comparatively low basicity with a satisfactory nucleophilicity in the reactions of aromatic substitution (phenols[5,6] and fluorinated alcohols[7] like R^FCH_2OH).

We studied substitution for a nitro group in TNB under the action of ketone and aldehyde oximes in the presence of a base. It is well known that oximate anions exhibit an increased nucleophilicity as compared with the O-anions with an analogous basicity[10] because of the α-effect (the presence of *p*- or π-electrons at the atom adjacent to the nucleophilic centre). In our opinion, this is of importance for the O-arylation of oximes under the action of TNB.

We found that TNB reacts with ketone and benzaldehyde oximes **1** in the presence of solid K_2CO_3 in *N*-methylpyrrolidone or DMF solutions at 50 °C (1–5 h). The nitro group was replaced by an oximate unit, and *O*-3,5-dinitrophenyl oximes (3,5-DNPO) **2** were formed in high yields (70–95%) (Scheme 1). This can be a preparative procedure for the synthesis of previously unknown O-aryl oximes. Compounds **2** were isolated as individual isomers (^{1}H NMR data); only compounds **2j**,**k** contained an impurity of the second isomer (5 and 8%, respectively) because of the presence of such impurities in parent oximes **1j**,**k** (the configurations were not determined).†



TNB **1a–m** **2a–m**

a $R^1 = R^2 =$ Me
b $R^1 = R^2 =$ Ph
c $R^1 = R^2 = 4\text{-}FC_6H_4$
d $R^1 = R^2 = 4\text{-}BrC_6H_4$
e $R^1 = R^2 = 2\text{-}MeOC_6H_4$
f $R^1 = R^2 = 3\text{-}MeOC_6H_4$
g $R^1 = R^2 = 2,5\text{-}(MeO)_2C_6H_3$
h $R^1 = R^2 = 3,4\text{-methylenedioxy-}C_6H_3$
i $R^1 = R^2 =$ 4-pyridyl
j $R^1 = R^2 =$ 2-furyl
k $R^1 = R^2 =$ 2-thienyl
l $R^1 =$ H, $R^2 =$ Ph
m $R^1 + R^2 = (CH_2)_5$

Scheme 1

A temperature of 50 °C is optimum for preparing **2**. The reaction performed at 80 °C resulted in the products of cyclization to 4,6-dinitrobenzofurans in addition to **2** (*cf.* ref. 11). These data will be published elsewhere.

With the use of a number of examples, we found that in principle a nitro group in 1-X-3,5-dinitrobenzenes (1-X-3,5-DNB) can be replaced under the action of oximes to form *O*-3-X-5-nitrophenyloximes (3-X-5-NPO) under the same conditions as in TNB. Thus, 1,3-dinitro-5-trifluoromethylbenzene **3**, which can be considered as an analogue of TNB, reacts with acetophenoxime to give substitution product **4** (93% yield; reaction time, 4 h) (Scheme 2). 1-Aroxy-3,5-dinitrobenzenes **5**, **7**, which were prepared previously by substitution for a nitro group in TNB under the action of corresponding phenols,[5] analogously react with acetophenoxime. However, in this case, the yields of substitution products **6**, **8** are lower (45–50%), and the reaction time is much longer (30–35 h at 50 °C) (Scheme 2).†

Note that the reaction of TNB with benzaldoxime afforded corresponding 3,5-DNPO **2l** in a high yield (Scheme 1), whereas with the use of acetaldoxime the resulting **2** decomposed *in situ*

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† The compounds were characterised by ^{1}H NMR spectroscopy, electron-ionisation mass spectrometry (the spectra of all compounds exhibited peaks due to molecular ions M^+) and elemental analysis. The ^{1}H NMR spectra (in [$^2H_6$]DMSO) were measured on a Bruker AC-200 instrument. The mass spectra were measured on a Kratos MS-30 mass spectrometer.

General procedure for the synthesis of 3,5-DNPO **2** *and* 3-X-5-NPO **4**, **6**, **8**. A solution of 0.1 mol of TNB or 1-X-3,5-DNB **3**, **5** or **7** in 50 ml of *N*-methylpyrrolidone was added to a mixture of 0.1 mol of a corresponding oxime and 0.1 mol of K_2CO_3 in 30 ml of *N*-methylpyrrolidone with intense stirring. The mixture was held at 50 °C until the complete conversion of TNB or 1-X-3,5-DNB (1–5 h for TNB and **3** or 30–35 h for **5** and **7**, TLC monitoring). The reaction mixture was poured into water; the resulting precipitate was filtered off, washed with water and ethanol and dried in a vacuum oven. The resulting compounds do not require additional purification.

The reaction times, yields, melting temperatures and ^{1}H NMR spectra are given for the prepared compounds.

2a (4 h, 96%, 108–110 °C): 8.45 (t, 1H), 8.28 (d, 2H), 2.13 (s, 3H), 2.06 (s, 3H).

2b (1 h; 95%; 177–178 °C): 8.50 (t, 1H), 8.42 (d, 2H), 7.85 (m, 2H), 7.51 (s, 3H), 2.49 (s, 3H).

2c (3 h; 95%; 166–167 °C): 8.50 (t, 1H), 8.12 (d, 2H), 7.90 (dd, 2H), 7.33 (dd, 2H), 2.52 (s, 3H).

2d (5 h; 80%; 180 °C): 8.50 (t, 1H), 8.40 (d, 2H), 7.80 (d, 2H), 7.70 (d, 2H), 2.50 (s, 3H).

2e (2,5 h; 94%; 138–139 °C): 8.50 (t, 1H), 8.35 (d, 2H), 7.45 (m, 2H), 7.10 (m, 2H), 3.86 (s, 3H), 2.43 (s, 3H).

2f (5 h; 96%; 115–116 °C): 8.52 (t, 1H), 8.42 (d, 2H), 7.45 (m, 2H), 7.35 (s, 1H), 7.12 (m, 1H), 3.84 (s, 3H), 2.53 (s, 3H).

2g (4 h; 92%; 126–127 °C): 8.52 (t, 1H), 8.42 (d, 2H), 7.45 (m, 2H), 7.35 (s, 1H), 7.12 (m, 1H), 3.84 (s, 3H), 2.53 (s, 3H).

2h (3 h; 90%; 189–190 °C): 8.50 (t, 1H), 8.40 (d, 2H), 7.40 (s, 1H), 7.35 (d, 2H), 7.05 (d, 2H), 6.10 (s, 2H), 2.51 (s, 3H).

2i (1.5 h; 93%; 184–185 °C): 8.72 (t, 2H), 8.52 (d, 1H), 8.43 (s, 2H), 7.10 (d, 2H), 2.53 (s, 3H).

2j (5 h; 90%; 149–150 °C): 8.49 (t, 1H), 8.39 (d, 2H), 7.93 (s, 1H), 7.23 (d, 1H), 6.70 (m, 1H), 2.42 (s, 3H) (major isomer).

2k (3 h; 92%; 175–176 °C): 8.50 (t, 1H), 8.39 (d, 2H), 7.75 (d, 1H), 7.72 (d, 1H), 7.20 (dd, 1H), 2.52 (s, 3H) (major isomer).

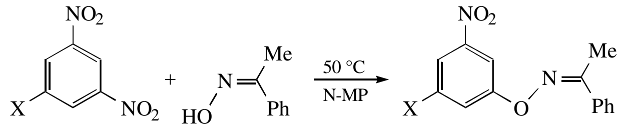
2l (1.5 h; 72%; 163–164 °C): 8.89 (s, 1H), 8.52 (t, 1H), 8.38 (d, 2H), 7.85 (m, 2H), 7.51 (m, 3H).

2m (3 h; 94%; 114 °C): 8.46 (t, 1H), 8.32 (d, 2H), 2.71 (t, 2H), 2.15 (t, 2H), 1.65 (m, 6H).

4 (5 h; 93%; 106–107 °C): 8.30 (s, 1H), 8.13 (s, 1H), 8.05 (s, 1H), 7.85 (m, 2H), 7.50 (m, 3H), 2.50 (s, 3H).

6 (4.5 h; 46%; 91 °C): 7.80 (m, 2H), 7.50 (m, 2H), 7.25 (m, 8H), 2.48 (s, 3H).

8 (5.5 h; 50%; 97 °C): 7.76 (m, 2H), 7.50 (m, 2H), 7.20 (m, 8H), 4.05 (q, 2H), 2.40 (s, 3H), 1.35 (t, 3H).



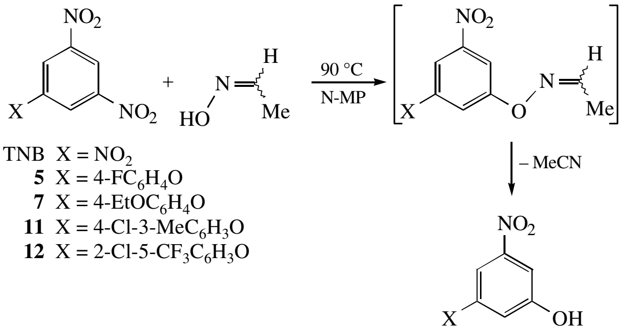
3 X = CF_3
5 X = 4-FC_6H_4O
7 X = 4-$EtOC_6H_4O$

4 X = CF_3
6 X = 4-FC_6H_4O
8 X = 4-$EtOC_6H_4O$

Scheme 2

to give 3,5-dinitrophenol **9** and acetonitrile (Scheme 3).‡ This procedure was used for the substitution of hydroxyl for one of the nitro groups in various 1-aroxy-3,5-dinitrobenzenes (the best results were obtained with the use of a double molar amount of K_2CO_3) (Scheme 3). The corresponding nitrophenols were formed in high yields (60–95%). It is of interest that 3,5-dinitrophenol **9** was obtained directly from TNB in almost 100% yield. Previously,[12] **9** was prepared from TNB by a more complicated two-stage method. Note that similar fragmentation under the action of bases was observed previously in the case of O-4-R-arylaldoximes (R is an electron-acceptor substituent).[13] In this work, we performed such a decomposition of O-arylaldoximes for *meta* substituted derivatives.

This work was supported by the International Science and Technology Center (project no. 419).



TNB X = NO_2
5 X = 4-FC_6H_4O
7 X = 4-$EtOC_6H_4O$
11 X = 4-Cl-3-MeC_6H_3O
12 X = 2-Cl-5-$CF_3C_6H_3O$

9 X = NO_2
10 X = 4-FC_6H_4O
13 X = 4-$EtOC_6H_4O$
14 X = 4-Cl-3-MeC_6H_3O
15 X = 2-Cl-5-$CF_3C_6H_3O$

Scheme 3

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Received: 12th July 2002; Com. 02/1965

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‡ *General procedure for the synthesis of* 3-X-5-nitrophenols **10**, **13**–**15**. A solution of 0.1 mol of TNB or 1-aroxy-3,5-dinitrobenzene **5**, **7**, **11**, **12** in 50 ml of *N*-methylpyrrolidone was added to a mixture of 0.1 mol of acetaldoxime and 0.2 mol of K_2CO_3 in 30 ml of *N*-methylpyrrolidone at 90 °C with intense stirring. The mixture was held at 90 °C until the complete conversion of the substrate (4 h for TNB and 6–7 h for **5**, **7**, **11**, **12**). The reaction mixture was poured into water; the mixture was acidified with dilute HCl and extracted with chloroform. The resulting solution was washed with dilute HCl and then with water and dried; the solvent was evaporated. An aqueous solution of an equimolar amount of NaOH was added to the residue; the solution was filtered, and the filtrate was acidified with dilute HCl. The resulting precipitate was filtered off, washed with water and dried in a vacuum oven. The resulting compounds do not require additional purification.

9 (3.5 h; 95%; 120–122 °C, lit.,[12] 122–123 °C): 11.50 (s, 1H), 8.28 (t, 1H), 7.95 (d, 2H).

10 (4.5 h; 77%; 100–101 °C): 11.00 (s, 1H), 7.40 (s, 1H), 7.20 (m, 5H), 6.80 (s, 1H).

13 (5 h; 75%; 166 °C): 10.50 (s, 1H), 7.25 (s, 1H), 7.10 (m, 3H), 7.00 (d, 2H), 6.70 (s, 1H), 4.05 (q, 2H), 1.34 (t, 3H).

14 (4 h; 83%; 145 °C): 10.60 (br. s, 1H), 7.45 (d, 1H), 7.32 (s, 1H), 7.15 (m, 2H), 7.00 (dd, 1H), 6.80 (m, 1H), 2.33 (s, 3H).

15 (4 h; 60%; 138 °C): 10.73 (s, 1H), 7.90 (d, 1H), 7.70 (m, 2H), 7.38 (t, 1H), 7.20 (t, 1H), 6.76 (t, 1H).