Replacement of the nitro groups in 1,3,5-trinitrobenzene on treatment with polyfluorinated alcohols

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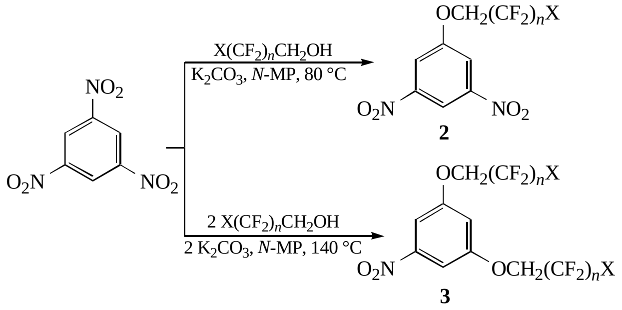
Depending on the conditions, polyfluorinated alcohols R_fCH_2OH [$R_f = CF_3$, $H(CF_2)_n$; $n = 2, 4, 6, 8$] replace one or two nitro groups in 1,3,5-trinitrobenzene in the presence of K_2CO_3 in *N*-methylpyrrolidone to give the previously unknown 1-polyfluoroalkoxy-3,5-dinitrobenzenes or 1,3-di(polyfluoroalkoxy)-5-nitrobenzenes; the reaction is successful due to the high acidity of R_fCH_2OH ($pK_a \approx 12$).

1,3,5-Trinitrobenzene (TNB) and its analogues incorporating *meta*-arranged nitro groups readily react with nucleophiles to give products of nucleophilic addition to the aromatic ring at the *ortho*/*para* positions with respect to the nitro groups — stable anionic σ-complexes. The basic kinetic and thermodynamic features of these processes are well known. They occur particularly readily in dipolar aprotic solvents.[1,2] Much more scant data are available on the prospects and conditions for the replacement of weakly activated nitro groups in 1,3,5-trinitrobenzene on treatment with nucleophiles. Systematic studies into this problem in the case of 1,3,5-trinitrobenzene[4,5,6] and its analogues[7,8] started only recently for, *e.g.*, phenols and thiophenols. For instance, it was shown that the nitro groups in 1,3,5-trinitrobenzene are readily replaced with the corresponding aroxyl fragments on treatment with various phenols in amide-type dipolar aprotic solvents [of which *N*-methylpyrrolidone (*N*-MP) is the best] in the presence of K_2CO_3 at 80–90 °C (replacement of one nitro group) or at 150 °C (replacement of two nitro groups).[4,5]

We found in a study of reactions of 1,3,5-trinitrobenzene with *O*-nucleophiles of another type — aliphatic alcohols in the presence of bases — that this method is completely suitable for polyfluorinated alcohols $X(CF_2)_nCH_2OH$ **1**: 2,2,2-trifluoroethanol (X = F, $n = 1$, **1a**) and telomeric alcohols, *i.e.* products of telomerisation of tetrafluoroethylene with methanol, $H(CF_2)_nCH_2OH$ ($n = 2$, **1b**; $n = 4$, **1c**; $n = 6$, **1d**; $n = 8$, **1e**). The reaction of compounds **1** with 1,3,5-trinitrobenzene in the presence of K_2CO_3 (molar ratio of the reagents 1:1:1) in *N*-methylpyrrolidone at 80 °C for several hours gives products from the replacement of one nitro group in 1,3,5-trinitrobenzene by a polyfluoroalkoxyl fragment, namely, 1-polyfluoroalkoxy-3,5-dinitrobenzenes **2a–d**,[†] representatives of a previously unknown structural type of substituted benzenes, in 65–80% yield. These products were characterised by ^{1}H and ^{19}F NMR spectroscopy,[‡] mass spectrometry (the presence of a molecular ion), IR spectroscopy (absorption corresponding to an aromatic nitro group) and satisfactory elemental analysis.

The replacement of a nitro group in 1,3,5-trinitrobenzene on treatment with fluorinated alcohols also occurs at room temperature (in *N*-methylpyrrolidone in the presence of K_2CO_3), although very slowly. For example, the formation of compound **2b** from **1b** started with an equimolar ratio of the reagents but required 48 h to complete (yield of **2b** 65%).



It was shown for compounds **1b** and **1d** as examples that, as with the reaction of phenols with 1,3,5-trinitrobenzene,[2] when the reaction was carried out with a double molar amount of polyfluorinated alcohols and K_2CO_3 at 140 °C, two nitro groups in 1,3,5-trinitrobenzene are replaced for polyfluoroalkoxyl fragments to give substituted benzenes of another type, 1,3-bis(polyfluoroalkoxy)-5-nitrobenzenes **3**. The corresponding products **3b** and **3d** are formed in 50–60% yields.[§]

It was found that the conditions for nitro group replacement

[†] *General procedure*. A mixture of 1,3,5-trinitrobenzene (0.025 mol), **1** (0.025 mol) and K_2CO_3 (0.025 mol) in *N*-methylpyrrolidone (20 ml) (intense red colour) was stirred until the 1,3,5-trinitrobenzene was consumed completely (HPLC, TLC). The reaction mixture was poured into water and the crystals that formed were separated, washed with 3% hydrochloric acid on the filter, washed with water and recrystallized from methanol.

[‡] Spectra were recorded on Bruker WM-250, AM-300, AC-200. Standards $SiMe_4$ (^{1}H) and $CFCl_3$ (^{19}F).

2a, 1-CF_3CH_2O-3,5-$(NO_2)_2C_6H_3$: yield 81% (1.5 h), mp 49–50 °C. ^{1}H NMR ($CDCl_3$) δ: 8.7 (t, 1H, H-4, J = 2 Hz), 8.16 (d, 2H, H-2 and H-6, J = 2 Hz), 4.63 (q, 2H, CH_2, J = 8 Hz). ^{19}F NMR ($CDCl_3$) δ: –73.09 (s).

2b, 1-$H(CF_2)_2CH_2O$-3,5-$(NO_2)_2C_6H_3$: yield 76% (5 h), mp 75–76 °C. ^{1}H NMR ($CDCl_3$) δ: 8.68 (t, 1H, H-4, J = 2 Hz), 8.16 (d, 2H, H-2 and H-6, J = 2 Hz), 6.36–5.82 (t, 1H, CF_2H, J = 52 Hz), 4.63 (t, 2H, CH_2, J = 12.5 Hz). ^{19}F NMR ($CDCl_3$) δ: –123.19 (s, 2F, F-2′), –137.21 (d, 2F, F-3′, J = 56 Hz).

2c, 1-$H(CF_2)_4CH_2O$-3,5-$(NO_2)_2C_6H_3$: yield 66% (4 h), mp 36–37 °C. ^{1}H NMR ($CDCl_3$) δ: 8.71 (t, 1H, H-4, J = 2 Hz), 8.17 (d, 2H, H-2 and H-6, J = 2 Hz), 6.37–5.85 (t, 1H, CF_2H, J = 52 Hz), 4.73 (t, 2H, CH_2, J = 12.5 Hz). ^{19}F NMR ($CDCl_3$) δ: –118.81 (s, 2F, F-2′), –124.23 (s, 2F, F-3′), –129.13 (s, 2F, F-4′), –136.47 (d, 2F, F-5′, J = 56 Hz).

2d, 1-$H(CF_2)_6CH_2O$-3,5-$(NO_2)_2C_6H_3$: yield 75% (3 h), mp 30–32 °C. ^{1}H NMR ([$^2H_6$]DMSO) δ: 8.53 (t, 1H, H-4, J = 2 Hz), 8.33 (d, 2H, H-2 and H-6, J = 2 Hz), 7.41–6.90 (t, 1H, CF_2H, J = 52 Hz), 5.23 (t, 2H, CH_2, J = 12.5 Hz). ^{19}F NMR ([$^2H_6$]DMSO) δ: –117.99 (s, 2F, F-2′), –121.19 (s, 2F, F-3′), –121.84 (s, 2F, F-4′), –122.21 (s, 2F, F-5′), –128.10 (s, 2F, F-6′), –137.88 (d, 2F, F-7′, J = 56 Hz).

2e, 1-$H(CF_2)_8CH_2O$-3,5-$(NO_2)_2C_6H_3$: yield 69% (6 h), mp 51–53 °C. ^{1}H NMR ([$^2H_6$]acetone) δ: 8.62 (t, 1H, H-4, J = 2 Hz), 8.35 (d, 2H, H-2 and H-6, J = 2 Hz), 7.08–6.57 (t, 1H, CF_2H, J = 52 Hz), 5.18 (t, 2H, CH_2, J = 12.5 Hz). ^{19}F NMR ([$^2H_6$]acetone) δ: –116.99 (s, 2F, F-2′), –121.44 (s, 6F, F-3′, F-4′ and F-5′), –122.36 (s, 2F, F-6′), –122.74 (s, 2F, F-7′), –128.96 (s, 2F, F-8′), –137.88 (d, 2F, F-9′, J = 56 Hz).

[§] **3b**, 1,3-$[H(CF_2)_2CH_2O]_2$-5-$NO_2C_6H_3$: yield 60% (10 h), mp 78–79 °C. ^{1}H NMR ($CDCl_3$) δ: 7.51 (d, 2H, H-4 and H-6, J = 2 Hz), 6.86 (t, 1H, H-2, J = 2 Hz), 6.31–5.76 (t, 2H, CF_2H, J = 52 Hz), 4.44 (t, 4H, CH_2, J = 12.5 Hz). ^{19}F NMR ($CDCl_3$) δ: –123.41 (s, 2F, F-2′), –137.46 (d, 2F, F-3′, J = 56 Hz).

3d, 1,3-$[H(CF_2)_6CH_2O]_2$-5-$NO_2C_6H_3$: yield 53% (6.5 h), mp 39–41 °C. ^{1}H NMR ([$^2H_6$]DMSO) δ: 7.61 (d, 2H, H-4 and H-6, J = 2 Hz), 7.35 (t, 1H, H-2, J = 2 Hz), 7.31–6.92 (t, 2H, CF_2H, J = 52 Hz), 5.03 (t, 4H, CH_2, J = 12.5 Hz). ^{19}F NMR ([$^2H_6$]DMSO) δ: –118.04 (s, 2F, F-2′), –121.28 (s, 2F, F-3′), –121.90 (s, 2F, F-4′), –122.30 (s, 2F, F-5′), –128.23 (s, 2F, F-6′), –137.53 (d, 2F, F-7′, J = 56 Hz).

in 1,3,5-trinitrobenzene on treatment with polyfluorinated alcohols are unsuitable for aliphatic and alicyclic alcohols. For example, in the case of *n*-butanol, although the product of nitro group replacement (1-butoxy-3,5-dinitrobenzene) is formed, its yield is no higher than 10% even on prolonged heating at 100 °C in *N*-methylpyrrolidone in the presence of K_2CO_3. In the case of cyclohexanol, the substitution product is not formed at all.

The acidity of the polyfluorinated alcohols and non-fluorinated alcohols studied differs significantly: for polyfluorinated alcohols, $pK_a \approx 12.4–12.8$,[9] while for *n*-butanol and cyclohexanol, $pK_a > 16$.[10,¶]

At first glance, the result obtained seems paradoxical: a decrease in basicity of the reagent (alkoxide) facilitates nucleophilic substitution. The simplest explanation of this effect is the insufficient basicity of K_2CO_3 under the specified conditions (solid K_2CO_3 is insoluble in *N*-methylpyrrolidone) for the formation of a noticeable amount of alkoxides from the non-fluorinated alcohols studied. A fact supporting this viewpoint is that the addition of cyclohexanol alcoholate to an unsubstituted position of 1,3,5-trinitrobenzene in the system cyclohexanol–1,3,5-trinitrobenzene–K_2CO_3 in *N*-methylpyrrolidone at room temperature is not observed (^{1}H NMR data; *cf.* ref. 1), while only gradual formation of a known complex $TNB\cdot OH^-$ is produced upon addition of OH^- to an unsubstituted position of 1,3,5-trinitrobenzene (identified by ^{1}H NMR spectroscopy according to refs. 12 and 13). The formation of the $TNB\cdot OH^-$ σ-complex can occur due to either hydrolysis of K_2CO_3 or addition of CO_3^{2-} to 1,3,5-trinitrobenzene (*cf.* ref. 14) followed by CO_2 elimination, as was assumed in the case of 4,6-dinitrobenzofuroxan.[15] When 2 mol of K_2CO_3 is used, 1,3,5-trinitrobenzene is completely transformed into the $TNB\cdot OH^-$ σ-complex (in 24 h at 20 °C).

It is interesting to note in this relation that $CH_3OCH_2CH_2OH$, whose acidity ($pK_a = 14.82$)[9,10] lies between that of polyfluorinated alcohols and the unsubstituted alcohols studied, can replace a nitro group in 1,3,5-trinitrobenzene under the conditions used by us (1,3,5-trinitrobenzene, K_2CO_3 in *N*-methylpyrrolidone, 100 °C, 7 h) to give a known compound, 1-($CH_3OCH_2CH_2O$)-3,5-$(NO_2)_2C_6H_3$,[16] but in only 30% yield, whereas on treatment of 1,3,5-trinitrobenzene with $CH_3OCH_2CH_2OK$ in $CH_3OCH_2CH_2OH$ (90 °C, 3 h), the yield of this product is up to 80%.[16]

We also observed a side reaction: on heating 1,3,5-trinitrobenzene with K_2CO_3 in *N*-methylpyrrolidone to 80–100 °C, the 1,3,5-trinitrobenzene is consumed completely in 5–10 h (depending on the temperature) to give 3,5-dinitrophenol (in the form of the corresponding phenolate), which was isolated in 25% yield. This result was obtained both when the reaction was started from the $TNB\cdot OH^-$ σ-complex preliminarily obtained at 20 °C on treatment with K_2CO_3 and when the components were heated at once. It is clear in this relation why, *e.g.*, 1,3,5-trinitrobenzene is consumed completely in the case of cyclohexanol (100 °C, 5 h), despite the absence of a reaction product.

Thus, we observe some correlation between the acidity of an alcohol and its ability to replace a nitro group in 1,3,5-trinitrobenzene in the presence of K_2CO_3 (in *N*-methylpyrrolidone). The chosen reaction conditions are at an optimum for polyfluorinated alcohols, at least those with the acidity specified above.

The products of replacement of a nitro group in 1,3,5-trinitrobenzene synthesised in this work by its treatment with polyfluorinated alcohols **2** may be of interest for the synthesis of the corresponding diamines, 1-$X(CF_2)_nCH_2O$-3,5-$(NH_2)_2C_6H_3$ **4**, based on them. The latter can be considered as promising monomers for the preparation of high-molecular heterochain polymers possessing a number of valuable properties. In fact, it is known that polyimides containing polyfluorinated alkoxide substituents (PAS) have smaller relative permittivities, refraction coefficients and moisture absorption than their analogues containing no PAS.[17] Such polyimides are obtained from diamines of the type 1-$X(CF_2)_nCH_2O$-2,4-$(NH_2)_2C_6H_3$ **5** synthesised by treatment of polyfluorinated alcohols with 1-fluoro-2,4-dinitrobenzene followed by reduction of the dinitro compounds obtained.[17] However, the amino groups in diamines **5** are non-equal, since one of them is shielded by an *ortho*-PAS. Diamines **4** do not suffer this drawback, which circumstance will supposedly make it possible to obtain higher-molecular condensation polymers, including polyimides, that incorporate PAS. Products of replacement of two nitro groups in 1,3,5-trinitrobenzene on treatment with polyfluorinated alcohols can provide the basis for the synthesis of a new type of substituted anilines with free *ortho*/*para* positions, 1,3-bis(polyfluoroalkoxy)anilines, which might be interesting *e.g.* for the synthesis of various polyheterocyclic systems with fluorine-containing substituents.

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[¶] The pK_a values in H_2O at 25 °C are given. Although the pK_a values change on transition to aprotic dipolar solvents, the relative series of acidity remains the same.[11]