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# Preparation of *N*-alkyl-substituted 3,5-dinitroanilines by amination of 1,3,5-trinitrobenzene

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Highly efficient amination of 1,3,5-trinitrobenzene by a number of simple aliphatic amines to form the corresponding *N*-alkyl-substituted 3,5-dinitroanilines has been achieved.

**Keywords:** amination, 1,3,5-trinitrobenzene, *N*-alkyl-substituted 3,5-dinitroanilines

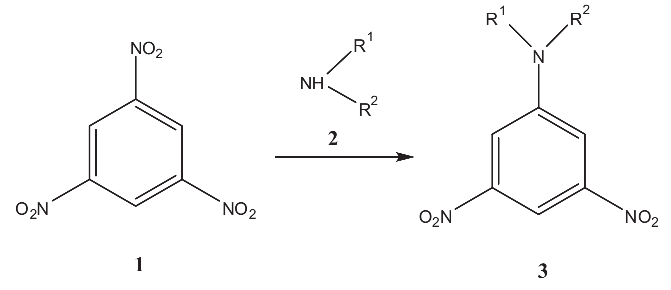
*N*-Alkyl-substituted 3,5-dinitroanilines are valuable industrial intermediates in the manufacture of dyes, plastics, pharmaceuticals and agrochemicals. Traditionally, these compounds are prepared in the liquid phase using mineral acids as catalysts and alkyl halides or dimethyl sulfate as alkylating agents.[1-7] Though various new heterogeneous catalysts and non-toxic alkylating agents, such as methanol[8] and dimethyl carbonate,[9,10] have been introduced, yields or product selectivity are, with few exceptions, low and depend on the nature of the catalysts and on the reaction conditions. The major synthetic problem is competing over-alkylation, which leads to mixtures of secondary and tertiary amines and quaternary ammonium salts. The difficulty in preventing over-alkylation is especially true when highly reactive electrophilic compounds are used, such as methyl, ethyl, benzyl and allyl alkylating agents. Besides the *N*-alkylation,[11,12] other general methods for the synthesis of secondary amines are amide reduction[13] and reductive amination.[14] Although these methods are quite reliable, there is also in these cases the necessity of controlling the concomitant over-alkylations when the amine is employed as the limiting substrate, which often reduces the application of these methods.

We report here the synthesis of *N*-alkyl-substituted 3,5-dinitroanilines using 1,3,5-trinitrobenzene and lower aliphatic amines under mild reaction conditions and with water as solvent (see Scheme 1). This method not only shows gives *N*-alkyl-substituted 3,5-dinitroanilines with high conversions and chemoselectivities, but also eliminates the formation of overalkylation products.

Table 1 illustrates the generality of this amination procedure in the trinitrobenzene system. Note that the second and third aromatic nitro groups are unaffected under these conditions.

From a series of experiments we found that eight equivalents of amine were required for completion of the reaction. An increase in the amount of amine did reduce the time required. Experiments show that a catalyst was unnecessary.

In an effort to elucidate the mechanism, amination of nitrobenzene was attampted by reacting with amine **2a**. We found that only starting material was recovered. We conclude that the activity of the nitro group on the aromatic ring increased because of the electron-withdrawing effect of the other two nitro groups. Furthermore, the activity of the remaining nitro groups decreased because of the electron-



**a** R$^1$=H, R$^2$=Me;
**b** R$^1$=H, R$^2$=Et;
**c** R$^1$=H, R$^2$=n-Pr;
**d** R$^1$=H, R$^2$=n-Bu;
**e** R$^1$=Me, R$^2$=Me;
**f** R$^1$=Et, R$^2$=Et.

**Scheme 1**

**Table 1** Amination of 1,3,5-trinitrobenzene

| Compound | $^1$H NMR (δ) | IR/cm$^{-1}$/KBr$^{disks}$ | M.p./°C/Lit.[15] | Yield[a]/% |
|---|---|---|---|---|
| **3a** | 2.64(3H, d,*J* = 4.1 Hz), 6.89(1H, m, *J* = 4.1 Hz), 7.73(2H, s), 7.92(1H, s) | 3366, 2928, 1623, 1587, 1338 | 156.5–157.4 (158) | 88.2<br>91.2 |
| **3b** | 1.23(3H, t,*J* = 7.2 Hz), 3.38(2H, m), 7.74(2H, s), 7.92(1H, s), 7.98(1H, m, *J* = 3.7 Hz) | 3376, 2986, 1626, 1520, 1336 | 184.9–185.6 (185–186) | |
| **3c** | 0.95(3H, t,*J* = 7.3 Hz), 1.45(2H, m, *J* = 9.2 Hz), 3.32(2H, m, *J* = 4.3 Hz), 6.42(1H, t, *J* = 4.2 Hz), 7.76(2H, s), 7.94(1H, s) | 3383, 2984, 1626, 1514, 1330 | 130.1–130.5 (129–130) | 87.6 |
| **3d** | 0.90(3H, t,*J* = 7.1 Hz), 1.30(2H, m, *J* = 11.3 Hz), 1.41(2H, m, *J* = 8.4 Hz), 3.32(2H, m, *J* = 7.5 Hz), 6.38(1H, m, *J* = 4.3 Hz), 7.77(2H, s), 7.95(1H, s) | 3387, 2980, 1629, 1501, 1331 | 97.1–98.2 (99) | 84.3 |
| **3e** | 3.15(6H, m), 7.72(2H, s), 8.21(1H, s) | 3425, 2938, 1630, 1545, 1366 | 161.5–162.1 (164) | 89.3 |
| 3f | 1.18(6H, t, *J* = 7.2 Hz), 3.51(4H, m), 7.74(2H, s), 8.23(1H, s) | 3444, 2941, 1643, 1587, 1351 | 111.1–111.9 (112) | 86.9 |

[a] Isolated yield.

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donating effect of the substituent amino group, so there were no multiamino compounds observed.

In conclusion, a new method has been developed for the synthesis of *N*-alkyl-substituted 3,5-dinitroanilines. The materials are inexpensive and the yields are high. The method described herein compares very favourably with known methods and should be a valuable addition to amination methodology.

## Experimental

$^1$H NMR spectra were obtained in $CDCl_3$ with a Bruker AC-400 instrument. Chemical shifts are given in ppm, with respect to internal TMS; *J* values are quoted in Hz. IR spectra were obtained with a Nicolet NEXUS-670 spectrophotometer; only the most significant absorptions in $cm^{-1}$ are indicated. Melting points were determined by using a Gallenkamp heated-block apparatus.

**CAUTION:** 1,3,5-trinitrobenzene is an explosive compound and should be stored and handled using appropriate precautions for the amounts involved.

*General procedures for preparation of N-alkyl-3,5-dinitroanilines* **3a–f**.

1,3,5-Trinitrobenzene (6.4 g, 30 mmol) and amine (240 mmol) **2a–f** were taken up in 15 ml water in a 25 ml autoclave. The mixture was heated at 180°C for 4 h after which time the starting material had been consumed as evidenced by thin layer chromatographic (developing solvent, EtOAc/hexanes = 3:1, V/V) analysis. The mixture was then cooled, filtered and the solvent removed under reduced pressure to give the crude product. Recrystallisation with ethanol:water = 3 : 1 (V/V) afforded *N*-alkyl-3,5-dinitroanilines **3a–f**. The yields obtained were in the range of 84–91%.

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