# Aromatic Nucleophilic Substitution Reactions of 1-Dialkylamino-2,4-dinitronaphthalene with Primary or Secondary Amines in Organic Solvents: Facile Amine–Amine Exchange[1]

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The dialkylamino group, (e.g., dimethyl-, diethyl-, and N-n-butyl-N-methylamino, piperidino, and pyrrolidino) of 1-dialkylamino-2,4-dinitronaphthalenes is rapidly replaced by primary amines, particularly in dimethyl sulphoxide; however, substitution does not occur for secondary amines except in the case of pyrrolidine.

Although various nucleofuges, e.g. halogeno, alkoxy or aryloxy, arylsulphinyl or -sulphonyl, nitro, pyrido groups, etc., have been used in activated aromatic nucleophilic substitution reactions ($S_NAr$), dialkylamino groups have seldom been considered.[2,3] We have recently found that the dialkyl group of 1-dialkylamino-2,4-dinitronaphthalene (1) is readily replaced with primary amines and pyrrolidine at 30 °C, simply by mixing the reactants; whereas such substitution occurs only to a limited extent with other secondary amines such as diethyl- and N-n-butyl-N-methylamine and piperidine (Scheme 1). We believe that these reactions have been overlooked by many chemists interested in $S_NAr$ reactions, and are highly useful in elucidating base catalysis in the use of amines as nucleophiles.[4—10]

The results in Table 1 can be summarized as follows: i, the dialkyl groups are readily replaced by various primary amines (runs 1—12); ii, the reaction with methylamine is almost complete in several minutes at 30 °C (run 6) and occurs easily,

although the dialkyl group is very bulky (runs 10—12); iii, the yield decreases in the case of isopropylamine (runs 5 and 9), which can be attributed to the steric effect as discussed below; iv, the reaction with secondary amines, except in the case of pyrrolidine, is much slower than with a primary amine (runs 13—18, 23—27, and 29); v, the yield decreases in MeCN, $C_6H_6$, and EtOH (runs 21—24).

Amino-2,4-dinitronaphthalenes (2) formed in the substitution reactions with corresponding primary amines (runs 1—12) were found to exist as conjugate bases, produced through amino proton abstraction of (2) by excess primary amines after termination of the reactions, from measurement of absorption spectra. For example, upon addition of di-isopropylamine (2.68 × $10^{-2}$ M), a dimethyl sulphoxide (DMSO) solution of (1) ($R^1R^2N$ = MeHN) (2.5 × $10^{-5}$ M) turned red instantly, exhibiting two maximum absorptions at 392 (ε 14 600) and 522 nm (ε 24 000), very similar to those of (4).[11]
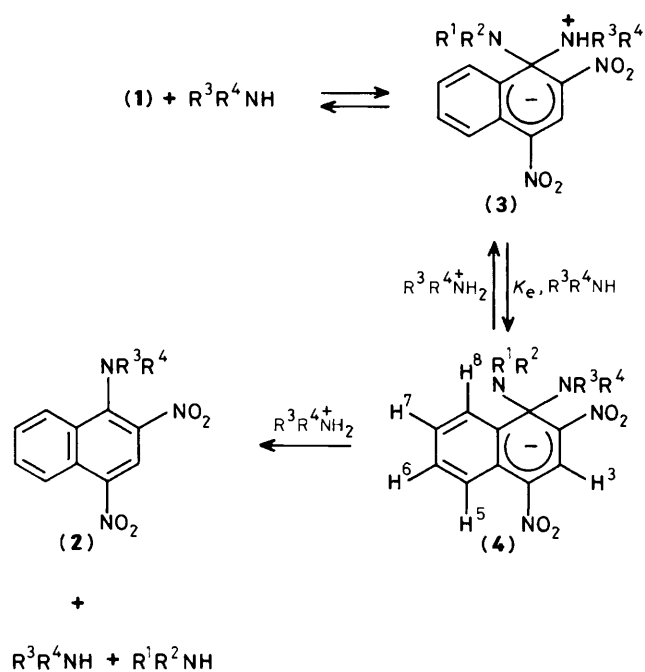
**Table 1.** Exchange reactions of 1-dialkylamino-2,4-dinitronaphthalenes (1) with various amines.[a]

| Run no. | $R^1$ | $R^2$ | $R^3$ | $R^4$ | Reaction temp./°C | Reaction time/h | Yield[b]/% |
|---|---|---|---|---|---|---|---|
| 1 | Me | Me | Me | H | 30 | 2 | 90 |
| 2[c] | Me | Me | Me | H | 30 | 2 | 87 |
| 3 | Me | Me | Et | H | 30 | 2 | 89 |
| 4[d] | Me | Me | Et | H | 30 | 2 | 98 |
| 5 | Me | Me | $Pr^i$ | H | 30 | 2 | 80 |
| 6[c] | Et | Et | Me | H | 30 | 5 min | 90 |
| 7[c] | Et | Et | Me | H | 30 | 1 | 97 |
| 8[d] | Et | Et | Et | H | 30 | 1 | 100 |
| 9 | Et | Et | $Pr^i$ | H | 30 | 1 | 61 |
| 10[c] | $Bu^n$ | Me | Me | H | 30 | 1 | 100 |
| 11[c] | $-(CH_2)_5-$ | | Me | H | 30 | 1 | 100 |
| 12[c] | $-(CH_2)_4-$ | | Me | H | 30 | 1 | 98 |
| 13 | Me | Me | Et | Et | 80 | 0.5 | 0 |
| 14 | Me | Me | $Bu^n$ | Me | 80 | 0.5 | 0 |
| 15 | Et | Et | Me | Me | 80 | 0.5 | 0 |
| 16 | $Bu^n$ | Me | Me | Me | 80 | 0.5 | 0 |
| 17 | $-(CH_2)_5-$ | | Me | Me | 80 | 0.5 | 0 |
| 18 | $-(CH_2)_5-$ | | Me | Me | 80 | 0.5 | 0 |
| 19 | Me | Me | $-(CH_2)_4-$ | | 30 | 0.5 | 67 |
| 20 | Me | Me | $-(CH_2)_4-$ | | 80 | 0.5 | 71 |
| 21[e] | Me | Me | $-(CH_2)_4-$ | | 50 | 0.5 | 51 |
| 22[e] | Me | Me | $-(CH_2)_4-$ | | 80 | 0.5 | 60 |
| 23[f] | Me | Me | $-(CH_2)_4-$ | | 80 | 0.5 | 3 |
| 24[g] | Me | Me | $-(CH_2)_4-$ | | 80 | 0.5 | 3 |
| 25 | Me | Me | $-(CH_2)_5-$ | | 80 | 0.5 | 0 |
| 26 | Me | Me | $-(CH_2)_5-$ | | 80 | 5 | 5 |
| 27 | Me | Me | $-(CH_2)_5-$ | | 80 | 24 | 14 |
| 28 | $-(CH_2)_5-$ | | $-(CH_2)_4-$ | | 50 | 24 | 51 |
| 29 | $-(CH_2)_4-$ | | $-(CH_2)_5-$ | | 50 | 24 | 6 |

[a] $[1]_0$ 0.5 mmol; $[amine]_0/[1]_0$3 (molar ratio); solvent 10 ml. [b] Determined by HSLP and based on the substrate. [c] An aqueous solution of methylamine (40%) was used. [d] An aqueous solution of ethylamine (70%) was used. [e] Solvent MeCN. [f] Solvent $C_6H_6$. [g] Solvent $C_2H_5OH$.

**(1)**

**(2)**
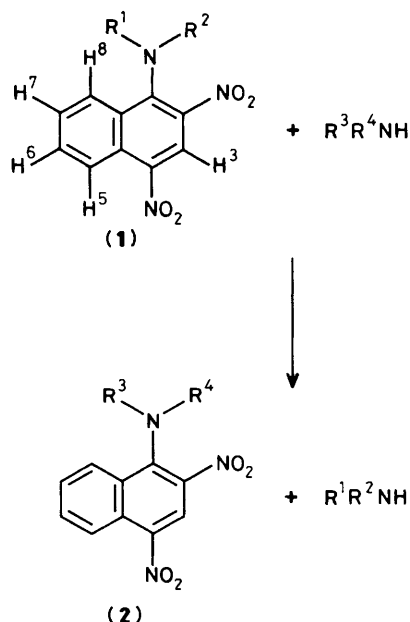
Scheme 1. **a**, $R^1 = R^2 = Me$; **b**, $R^1 = R^2 = Et$; **c**, $R^1 = Bu^n$, $R^2 = Me$; **d**, $R^1R^2 = -(CH_2)_5-$; **e**, $R^1R^2 = -(CH_2)_4-$.

$(1) + R^3R^4NH$

**(3)**

**(2)**

**(4)**

+

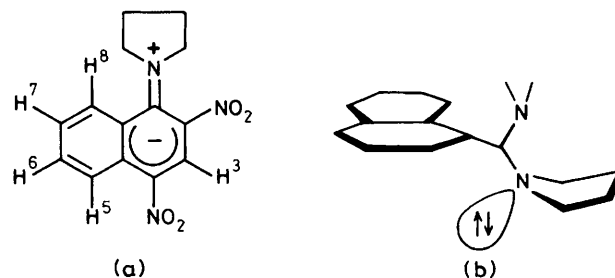$R^3R^4NH + R^1R^2NH$

**Scheme 2**

(a)　　　　(b)

**Figure 1.** Nitro groups omitted for simplicity.

Based on the kinetics of the reaction of (**1e**) and (**1d**) with pyrrolidine and piperidine in DMSO respectively,[4] Scheme 1 can be expressed as shown in Scheme 2. Whether the process from (**3**) to (**4**) is a proton transfer or acid-base equilibrium depends on the nature of the substrate, nucleophile, and solvent.[4—10]

In the reactions[4] detailed in Scheme 2, pyrrolidine was found to be very reactive compared with piperidine owing to a steric effect. This was also found to be the case with the present reactions. For this reason we propose a large contribution of the resonance structure, shown in Figure 1a, to the ground state of pyrrolidine.[4] In order to obtain conclusive evidence, the absorption spectra of the 1-amino-2,4-dinitro-naphthalenes (**1**) (secondary amine) were measured in dimethyl sulphoxide. The resonance structure (**1e**) has two maximum absorptions at 274 ($\varepsilon$ 15 000) and 438 ($\varepsilon$ 21 000), whereas compounds (**1a—d**) absorb in the range of 261—263 and 416—431 nm. These results show the considerable contribution of the resonance structure, which is also supported by the $^1$H n.m.r. spectra measured in dimethyl sulphoxide.

That is to say, the signal pattern† of (1e) alone is very similar to those of (4),[12,13] being conspicuously different from those of (1a—d).

Based on these results, it is expected that the large difference in reactivity between pyrrolidine and piperidine (runs 28 and 29) can be ascribed in part to the ease of assuming the transition state, see Figure 1b. In this transition state, the $C_1$–N (nucleofuge) and unshared electron pair on nitrogen (pyrrolidine) are antiperiplanar to the $C_1$–N (pyrrolidine) bond and, therefore, this electron pair makes the nucleofuge a better leaving group.[4] All the processes shown in Scheme 2 are much more favourable for primary amines than for secondary amines.

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† $^1H$ n.m.r. spectrum in [$^3H_6$]-dimethyl sulphoxide for (1e): δ 9.10 (s, $H^3$), 8.81 (finely-split d, $H^8$), 8.50 (finely-split d, $H^5$), 7.96 (finely-split d, $H^6$), 7.66 (finely-split d, $H^7$). The signal pattern is almost the same as that of 1,1-dipiperidino-substituted 2,4-dinitronaphthalene anionic σ-complex (4) formed from (1d) and excess piperidine in dimethyl sulphoxide.[12,13]

## References

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