Tetrahedron Vol. 46, No. 16, pp. 5567-5578, 1990
Printed in Great Britain

0040-4020/90 $3.00+.00

AROMATIC NUCLEOPHILIC SUBSTITUTION REACTIONS OF 1-DIALKYLAMINO-SUBSTITUTED ACTIVATED BENZENES WITH VARIOUS AMINES IN DIMETHYL SULFOXIDE[1]

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(*Received in Japan* 9 *March* 1990)

Abstract —— In the reactions of 1-dialkylamino-2,4,6-trinitro- and 1-dialkylamino-2,4-dinitrobenzenes with various amines in dimethyl sulfoxide, 1-dialkylamino group is easily replaced with primary n-alkylamines at room temperature, and in a low yield with pyrrolidine only among secondary amines.

INTRODUCTION

The aromatic nucleophilic substitution reactions (S_NAr) are a well-studied field.[2,3] The nucleophilic substitution reactions of dialkylamino-substituted activated aromatics with alkyl- or arylamines, however, have scarcely been investigated except for the nucleophilic addition reactions with amines giving anionic σ complexes,[4-7] because dialkylamino groups have been regarded as poor leaving ones.[8] Generally an approximate order of leaving-group ability is $F > NO_2 > OTs > SOPh > Cl, Br, I > N_3 > NR_3^+ > OAr, OR, SR, SO_2R > NR_2$, and an approximate order of nucleophilicity is $NH_2^- > Ph_3C^- > PhNH^- > ArS^- > RO^- > R_2NH > ArO^- > OH^- > ArNH_2 > NH_3 > I^- > Br^- > Cl^- > H_2O > ROH$, although these orders are greatly dependent on the kinds of substrates and nucleophiles, and reaction conditions.[8-13] On the basis of these results, it is natural that investigation such as the present amino-amine exchange reactions has been missed for a long time.

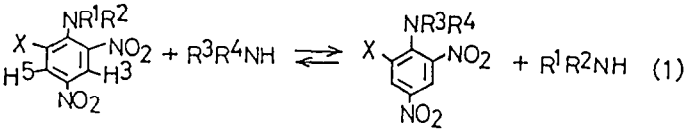
We have recently found that, in the reactions of 1-dialkylamino-2,4-dinitronaphthalenes with primary or secondary amines in dimethyl sulfoxide (DMSO), 1-dialkylamino groups, such as dimethyl-, diethyl-, and N-methylbutylamino, pyrrolidino, and piperidino groups, are easily replaced by primary n-alkylamines and pyrrolidine, but substitution by other dialkylamines, such as dimethyl-, diethyl-, diisopropyl-, and N-methylbutylamines and piperidine, hardly takes place.[1,14,15]

We have more recently expanded these reactions to benzene derivatives and found the difference between these two reactions in the detailed respects.

This paper reports the amino-amine exchange reactions (S_NAr) of 1-dialkylamino-2,4,6-trinitrobenzenes (1) or 1-dialkylamino-2,4-dinitrobenzenes (2) with primary and secondary amines in DMSO and on their reaction mechanism.

RESULTS

The present reactions are expressed as shown in equation (1). At first, we measur



$$\mathbf{1}(X = NO_2) \text{ or } \mathbf{2}(X = H) \qquad \mathbf{3}(X = NO_2 \text{ or } H) \qquad (1)$$

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

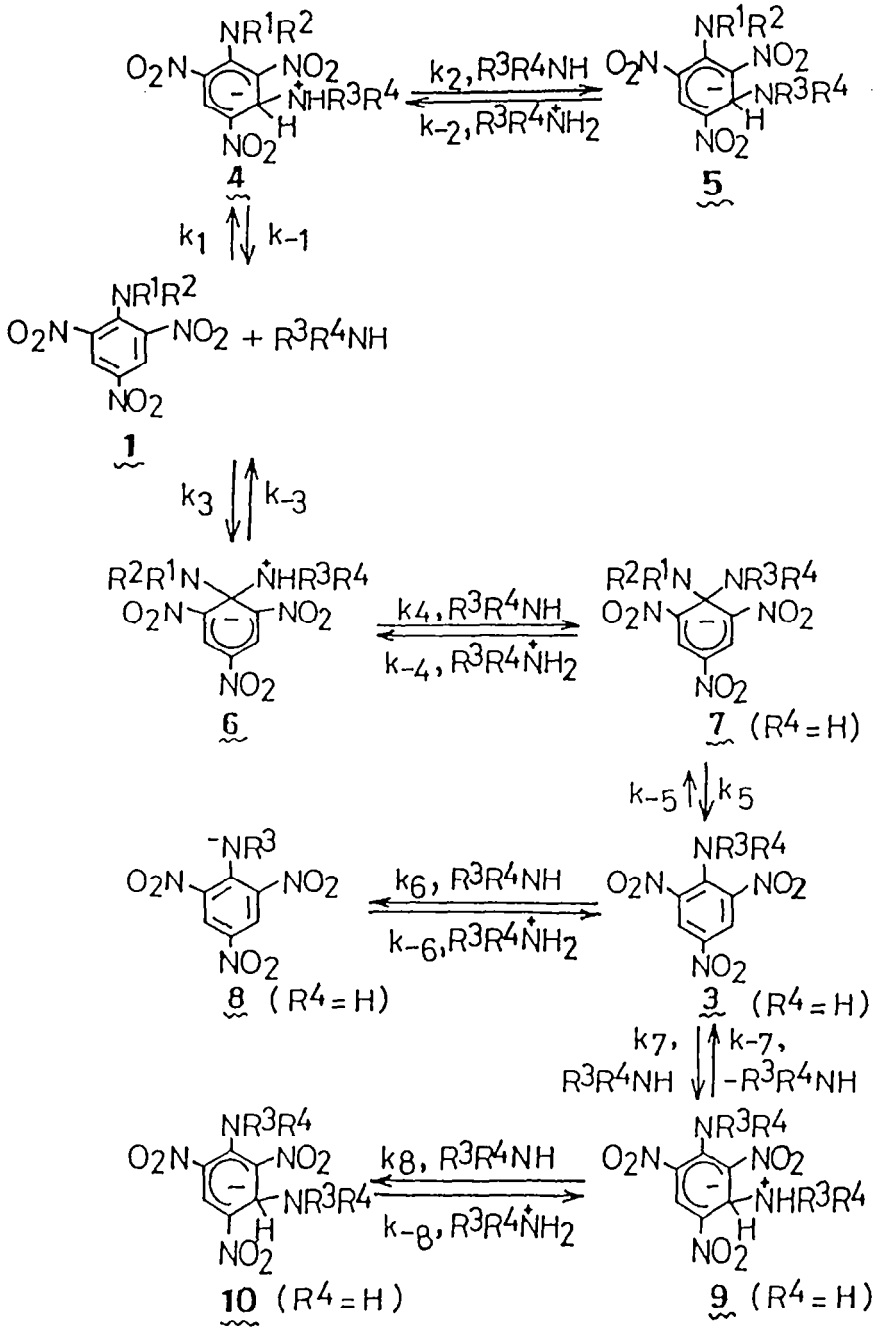
(2) **a**; $R^1 = R^2 = Me$
b; $R^1 = R^2 = -[CH_2]_4-$
c; $R^1 = R^2 = -[CH_2]_5-$

(3) **a**; $R^3 = Me$, $R^4 = H$
b; $R^3 = Et$, $R^4 = H$
c; $R^3 = Pr^i$, $R^4 = H$
d; $R^3 = Bu$, $R^4 = H$
e; $R^3 = Bu^t$, $R^4 = H$
f; $R^3 =$ benzyl, $R^4 = H$
g; $R^3 =$ p-methoxyphenyl, $R^4 = H$
h; $R^3 =$ p-methylphenyl, $R^4 = H$
i; $R^3 =$ phenyl, $R^4 = H$
j; $R^3 =$ p-nitrophenyl, $R^4 = H$
k; $R^3 = Me$, $R^4 = H$

the time-dependent absorption spectra of the reaction of **1a** with excess butylamine in DM at 25 °C to elucidate the reaction path.

Time-dependent Absorption Spectra of the Reaction of 1-Dimethylamino-2,4,6-trinitrobenze (1a) with Butylamine in DMSO

Just upon addition of butylamine (3.0×10^{-2} M; M means mol·l^{-1}), a DMSO solution c **1a** (2.54×10^{-5} M) turned out red, indicating the presence of some complexes. This colo change corresponds to the change in curve a → b, where curve a is attributed to **1a** and curve b to **5a**[16] (Figure 1). In 4.5 h after addition of butylamine curve b changed to curve d via curve c, which indicates the formation of a mixture of **8** and **10** (R^3 = Bu, R^4 = H) according to the results of Hasegawa,[17] who studied the nucleophilic substitutio of 2,4,6-trinitroanisole with excess butylamine in DMSO in detail. In our present reaction the reaction sequences after the formation of **3d** (R^3 = Bu, R^4 = H) can be expected to be the same as those proposed by Hasegawa.[16-18] The reaction can be considered, therefore, to proceed as shown in Scheme 1, where the key steps are clearly the k_3, k_4, and k_5 ones. As shown in Table 1 later, in the case of nucleophilic seconda amines the reactions generally seem to terminate at the formation of **7** at best except for pyrrolidine.



Scheme 1

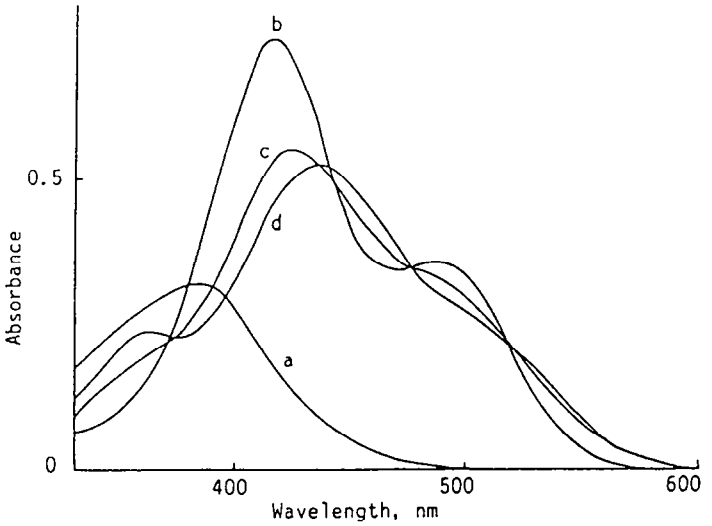


Figure 1. Time-dependent absorption spectra relevant to the reaction of 1-dimethylamino-2,4,6-trinitrobenzene (**1a**, 2.54×10^{-5} M) with butylamine (3.0×10^{-2} M) in DMSO at 25 °C: a **1a**; b just after addition of the amine; c 1 h; d, 4.5 h.

Determination of Substitution Products

Substitution products in the present reactions are listed in Table 1, in the footna of which the reaction conditions were described.

The results are summarized in the following.

i) Among the nucleophilic primary alkylamines studied, methylamine is the most reactive (runs 1, 5, 7-13, 19-37), and generally the substitution with primary n-alkylamines occurs comparatively easily.

ii) The yield decreases with decreasing amount of added amine (Runs 1-6, 14-18, and 56-58). As shown in Scheme 1, the deprotonation (**6** → **7**) and general acid-catalyzed (**7** → **3**) steps are very important in order for the exchange reaction to proceed. If the amount of an amine is decreased, both steps would not sufficiently proceed.

iii) In the case of primary alkylamines, the yield decreases with increasing bulkiness of R^3 group, which can be attributed to the sluggishness at the k_3 (addition), k_4 (proton abstraction), and k_5 steps (Runs 11-13 and 20-22, 24-29, 31-36, 38-40, and 42-44).[19] Moreover, the reduction in yield is larger, as R^3 and R^4 are bulkier (Runs 5, 12, 13, 20, 21, 27, 31, 32, and 34) except for **1d**, where it does not decrease so much (Runs 38-40, see Discussion).

iv) For **1d** and **1e**, interestingly the reduction in yield is very different from each other, which could be ascribed to the conformations of **1d** and **1e**[1] (Runs 38-40 and 42-44, see Discussion).

Table 1. Exchange reactions of 1-dialkylamino-2,4,6-trinitro- (1) or 1-dialkylamino-2,4-dinitrobenzenes (2) with various amines[a]

Run	Substrate	R^1	R^2	R^3	R^4	Reaction temp./°C	Reaction time/h	Yield/%
1[b]	1a	Me	Me	Me	H	30	10 min	72
2[c]	1a	Me	Me	Me	H	30	0.5	21
3[d]	1a	Me	Me	Me	H	30	0.5	56
4	1a	Me	Me	Me	H	30	0.5	89
5[e]	1a	Me	Me	Me	H	30	0.5	95
6	1a	Me	Me	Me	H	30	0.5	96
7	1a	Me	Me	Me	H	30	2	98
8	1a	Me	Me	Me	H	30	10	100
9	1a	Me	Me	Me	H	50	10 min	96
10	1a	Me	Me	Me	H	50	0.5	98
11	1a	Me	Me	Me	H	50	2	100
12	1a	Me	Me	Et	H	50	5	93
13	1a	Me	Me	i-Pr	H	50	5	84
14[b]	1a	Me	Me	n-Bu	H	30	0.5	84
15[c]	1a	Me	Me	n-Bu	H	30	0.5	28
16[d]	1a	Me	Me	n-Bu	H	30	0.5	50
17[e]	1a	Me	Me	n-Bu	H	30	0.5	75
18	1a	Me	Me	n-Bu	H	30	0.5	86
19	1a	Me	Me	n-Bu	H	30	2	97
20	1a	Me	Me	t-Bu	H	30	2	1
21	1a	Me	Me	t-Bu	H	50	5	8
22	1a	Me	Me	t-Bu	H	50	10	11
23	1b	Et	Et	Me	H	30	2	78
24	1b	Et	Et	Me	H	50	2	99
25	1b	Et	Et	Et	H	30	2	43
26	1b	Et	Et	Et	H	50	5	80
27	1b	Et	Et	i-Pr	H	30	2	10
28	1b	Et	Et	i-Pr	H	50	5	53
29	1b	Et	Et	i-Pr	H	50	6.5	62
30	1b	Et	Et	n-Bu	H	30	2	49
31	1c	n-Bu	Me	Me	H	30	2	97
32	1c	n-Bu	Me	Et	H	30	2	86
33	1c	n-Bu	Me	Et	H	30	5	95
34	1c	n-Bu	Me	i-Pr	H	30	2	33
35	1c	n-Bu	Me	i-Pr	H	30	5	61
36	1c	n-Bu	Me	i-Pr	H	50	5	81
37	1c	n-Bu	Me	n-Bu	H	30	2	81
38	1d	$-(CH_2)_4-$		Me	H	30	2	98
39	1d	$-(CH_2)_4-$		Et	H	30	2	94
40	1d	$-(CH_2)_4-$		i-Pr	H	30	2	93
41	1d	$-(CH_2)_4-$		n-Bu	H	30	2	91
42	1e	$-(CH_2)_5-$		Me	H	30	2	94
43	1e	$-(CH_2)_5-$		Et	H	30	2	85
44	1e	$-(CH_2)_5-$		i-Pr	H	30	2	32
45	1e	$-(CH_2)_5-$		i-Pr	H	50	6.5	84
46	1e	$-(CH_2)_5-$		n-Bu	H	30	2	80
47	1a	Me	Me	Et	Et	50	10	0
48	1a	Me	Me	Et	Et	50	24	0
49	1a	Me	Me	n-Bu	Me	50	10	0
50	1a	Me	Me	n-Bu	Me	50	24	0

Table 1. (continued)

Run	Substrate	R^1	R^2	R^3	R^4	Reaction temp./°C	Reaction time/h	Yield/%
51	1a	Et	Et	Me	Me	50	10	0
52	1a	Et	Et	Me	Me	50	24	0
53	1c	n-Bu	Me	Me	Me	50	10	0
54	1c	n-Bu	Me	Me	Me	50	24	0
55	1a	Me	Me	$-(CH_2)_4-$		30	48	15
56[c]	1a	Me	Me	$-(CH_2)_4-$		50	10	5
57[d]	1a	Me	Me	$-(CH_2)_4-$		50	10	12
58	1a	Me	Me	$-(CH_2)_4-$		50	10	19
59	1a	Me	Me	$-(CH_2)_5-$		50	10	0
60	1a	Me	Me	$-(CH_2)_4-$		50	24	25
61	1a	Me	Me	$-(CH_2)_4-$		50	48	17
62	1b	Et	Et	$-(CH_2)_4-$		50	10	0
63	1b	Et	Et	$-(CH_2)_5-$		50	10	0
64	1b	n-Bu	Me	$-(CH_2)_4-$		50	10	4
65	1b	n-Bu	Me	$-(CH_2)_5-$		50	10	0
66	1d	$-(CH_2)_4-$		Me	Me	50	24	0
67	1d	$-(CH_2)_4-$		$-(CH_2)_5-$		50	10	0
68	1e	$-(CH_2)_4-$		Me	Me	50	24	0
69[f]	1e	$-(CH_2)_5-$		$-(CH_2)_4-$		50	10	6
70[f]	1a	Me	Me	$PhCH_2$	H	30	3 min	56
71[f]	1a	Me	Me	$PhCH_2$	H	30	10 min	40
72[f]	1a	Me	Me	$PhCH_2$	H	30	2	0
73[f]	1a	Me	Me	$PhCH_2$	H	30	10	0
74[f]	1a	Me	Me	$PhCH_2$	H	50	2	0
75[g]	1a	Me	Me	MeOPh	H	30	2	87
76[g]	1a	Me	Me	MeOPh	H	30	5	90
77[h]	1a	Me	Me	MePh	H	50	5	8
78[h]	1a	Me	Me	MePh	H	50	10	16
79[h]	1a	Me	Me	MePh	H	50	24	34
80[i]	1a	Me	Me	Ph	H	50	5	7
81[i]	1a	Me	Me	Ph	H	50	10	11
82[j]	1a	Me	Me	NO_2Ph	H	50	10	0
83[j]	1a	Me	Me	NO_2Ph	H	50	24	0
84	2a	Me	Me	Me	H	50	2	14
85	2b	$-(CH_2)_4-$		Me	H	50	2	39
86	2c	$-(CH_2)_5-$		Me	H	50	2	14

[a] $[1]_0$ or $[2]_0$ 0.5 mmol; $[amine]_0/[1]_0$ or $[2]_0$ 3(molar ratio), unless otherwise noted; solvent(DMSO) 10 ml; as for methyl- and ethylamines, the 40% and 70% aqueous solutions were used, respectively. [b] $[amine]_0/[1]_0$ 0.5 (molar ratio). [c] $[amine]_0/[1]_0$ 1(molar ratio). [d] $[amine]_0/[1]_0$ 2(molar ratio). [e] $[amine]_0/[1]_0$ 10(molar ratio). [f] $PhCH_2$ = benzyl. [g] MeOPh = p-methoxyphenyl. [h] MePh = p-methylphenyl. [i] Ph = phenyl. [j] NO_2Ph = p-nitrophenyl.

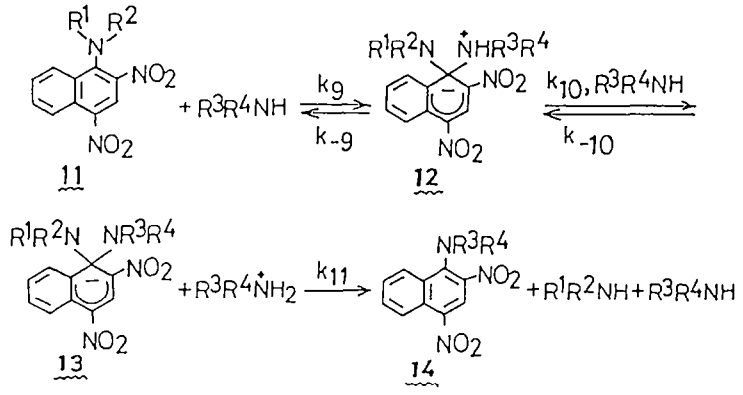
v) The exchange reactions of **1** with secondary amines except for pyrrolidine generally do not occur (Runs 47-69). This tendency involving the specificity of pyrrolidine was also found in the similar reactions of 1-dialkylamino-2,4-dinitronaphthalenes.[1,7,15] It is conspicuously interesting that the replacement with pyrrolidine, although the yields are very low, takes place, but not with piperidine (Runs 55-61).

vi) Benzylamine is found to have an intermediate reactivity between n-alkylamines and anilines (Runs 70, 71, and 75-81). For benzylamine the longer reaction time reduces the yield, which could result from the side reactions of 1-benzylamino-2,4,6-trinitrobenzene (**3f**), substitution product.

vii) Of aromatic amines, an aniline with p-electron-donating group is comparatively reactive, whereas p-nitroaniline is far much less reactive (Runs 75-83). The k_3 step (addition) seems to be very important for anilines.

viii) Among the reactions of **2** with methylamine, the yield is the highest for **2b**, which could be attributed to the conformation of **2b**[1,15,16] (Runs 84-86, see Discussion).

In the previous study,[1,15] we have reported the nucleophilic substitution reactions of 1-dialkylamino-2,4-dinitronaphthalenes (**11**) with primary and secondary amines in DMSO (Scheme 2), where the replacement of 1-dialkylamino group by primary n-alkylamines or only by pyrrolidine among secondary amines was comparatively fast. Although the overall reaction rate depends on the magnitudes of k_9, k_{-9}, k_{10}, k_{-10}, and k_{11}, the k_{11} step is a key step for the substitution to occur.



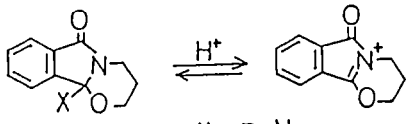
Scheme 2

These results are roughly similar to those obtained in the present reactions, but in the latter the nucleophilicity of pyrrolidine is not so higher than in the reactions of naphthalene derivatives.

DISCUSSION

Reactivity and pK_a

In 1974 Gravitz and Jencks[20] reported the kinetics of the proton-catalyzed breakdo of addition compounds formed from N,O-trimethylenephthalimidium ion and amines in water, and indicated that an amino group with higher pK_a is a better leaving one [equation (2)]



$$X = R_2N \qquad (2)$$

From Table 1 the reactivity order of nucleophilic amines is shown in the following together with their pK_a values (25 °C).[21] These results indicate that the reactivity of

	$MeNH_2$	$EtNH_2$	$BuNH_2$	Pr^iNH_2	$PhCH_2NH_2$	p-MeOPhNH_2	p-MePhNH_2	$PhNH_2$
pK_a	10.62	10.64	10.60	10.63	9.35	5.31	5.08	4.60

	Bu^tNH_2	pyrrolidine	piperidine	Me_2NH	Et_2NH	Bu(Me)NH	p-NO_2PhNH_2
pK_a	11.27	11.12	10.73	10.94	11.00	1.00	

amines does not depend on their pK_a values, which is very different from the proposal of Gravitz and Jencks.[20] It could be expected, therefore, that some steric factor should affect the present exchange reactions. As shown in Scheme 1, the k_5 step is a key step for the replacement to occur, although the reactivity depends on the k_3 and k_4 steps too Of primary n-alkylamines having similar pK_a values, methylamine is the most reactive, which could be attributed to the fast rate at the k_5 step, as will be discussed later. The much lower reactivity of secondary amines except for pyrrolidine could be attributab to the sluggishness at the k_5 step as well as at the k_3 and k_4 steps.[19] The less reactivity of anilines than primary alkylamines would result mainly from the slower rate owing to their low nucleophilicity, at the k_3 step.

Structure of the Transition State at the k_5 Step

As described in the introduction, only pyrrolidine can replace 1-dialkylamino group in the reactions of 1-dialkylamino-2,4-dinitronaphthalenes with secondary amines.[1,14,15] Accordingly, in order to elucidate the higher nucleophilicity of pyrrolidine, we propose the following transition state (T.S.) from NMR and absorption spectral evidence[14,15] and structural analyses by X-ray[1] (Figure 2A). For T.S. at the k_{11} step (R^3R^4NH = pyrrolidine, Scheme 2), the unshared electron pair on pyrrolidino nitrogen is antiperiplanar to the C(1)-N[dialkylamino(nucleofuge) nitrogen] bond with respect to the C(1)-N(pyrrolidin nitrogen) bond, which helps the dialkylamino group to leave, giving **14**$^{\pm}$ (R^3R^4N = pyrrolidine). Such a conjugation in **14**$^{\pm}$, therefore, would play an important part. By the structural analyses by X-ray (part 28),[1] it was found that the C(1)-N(pyrrolidino nitrogen) bond length is 1.313 Å, which is almost equal to the $>C{=}N-$ bond one, and the

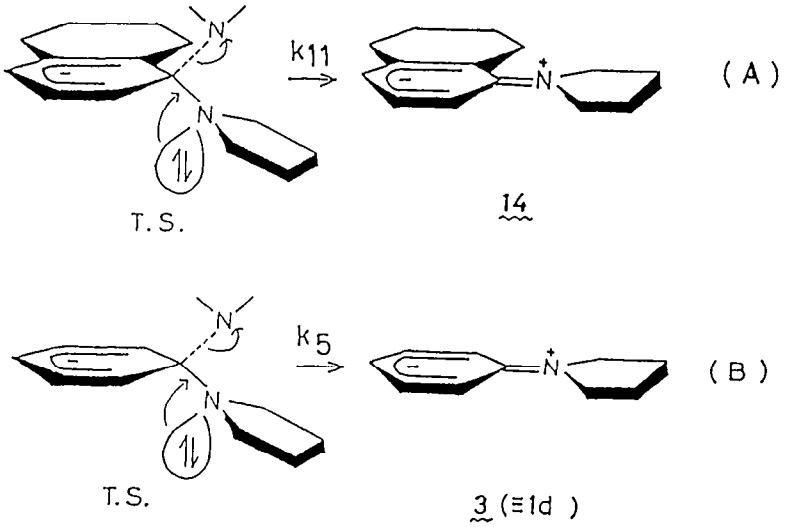


Figure 2. Transition state at the k_{11} and k_5 steps (all NO_2 groups omitted for simplicity).

plane of 2-nitro group is deviated upward by 26° and the plane involving N(pyrrolidino), C(2') and C(5') of the pyrrolidino ring, C(1), C(2), and C(8a) downward by 28°, according to the repulsion between 2-nitro and α-CH_2 groups. These lines of evidence would support the validity of the process in Figure 2A. This conjugation would cause the stabilization of T.S., giving more 14 for pyrrolidine than for other secondary amines.[15] These reasoning could be applied to the cases for 1 (Figure 2B). In the present reactions, only pyrrolidine can replace 1-dialkylamino group of 1, for which the similar transformation of T.S. to 3 (k_5 step) to that for the naphthalene derivatives (11) could hold. In the present case (Figure 2B), the steric effect of 2- and 6-nitro groups seems to affect the release of a nucleofuge more greatly than that of 2-nitro group and peri-hydrogen of 13. In this transformation the planes of 2- and 6-nitro groups would, to some extent, deviate from the benzene ring. Consequently, although the considerable coplanarity as shown in $14^{\pm}$ does not exist in 3 (≡ 1d), there should be some extent of conjugation in 1d at the expense of the coplanarity of 2- and 6-nitro groups.

Greater facility of substitution with primary alkylamines, except for t-butylamine, would be due to the ease of assuming the conformation of T.S. (Figure 2B). In spite of the expectation that pyrrolidine would react faster than p-methoxyaniline from a consideration of their pK_a values, parallel to nucleophilicity, the greater reactivity for p-methoxyaniline (runs 75 and 76) than for pyrrolidine (run 55) depends on the difference between the kinds of amines (primary or secondary), that is, the facility to assume the antiperiplanar conformation in T.S..

The yield did not so much decrease in the reactions of 1d with primary amines, even when the bulkiness of nucleophilic amine increased (Runs 38-40), whereas it sharply did

in the reactions of **1e** (Runs 42-44). In the former the pyrrolidino group would exert less steric hindrance against an approaching amine, owing to the specific structure of **1d** (Figure 2B). It would be anticipated that in **1e** the piperidino group should be not coplanar to the benzene ring, exerting larger steric hindrance. This tendency is seen i the cases of **2**.

In conclusion, it was found that in the release of the amino group from 1,1-diamino-substituted anionic σ complexes, such as **13** and **7**, the steroelectronic configuration of each amino group plays an important part rather than its pK_a value.[22]

EXPERIMENTAL

^1H NMR spectra were operated on a Varian A-60D spectrometer with tetramethylsilane as an internal reference. All the melting points were uncorrected.

All the compounds were prepared in the similar way. The typical procedure was described of 1-dimethylamino-2,4,6-trinitrobenzene (**1a**): the DMSO 50 ml solution containing dimethylamine and 2,4,6-trinitrochlorobenzene (TCB)([amine]/[TCB] = 10 mole ratio, with TCB [*ca.* 5 g] used) was stirred for 3 h at 30 (or 50 for **2**) °C, poured, neutralized with dilute aqueous H_2SO_4, and filtered. The residue was crystallized from methanol in a 76% yield: m.p. 137-137.5 °C; λ_{max} 384 nm (ε 14800); NMR (DMSO-d_6) δ = 2.93 (6H, s, N-CH_3), 8.97 (2H, s, H^3 and H^5 [the figures 3 and 5 indicate the positional number of the benzene ring; see 1 in equation (1)]).

1-Diethylamino-2,4,6-trinitrobenzene (1b)
Yield 48%; m.p. 161.5-162 °C; λ_{max} 396 nm (ε 11000); NMR (DMSO-d_6) δ = 1.10 (6H, t, β-CH_3), 3.13 (4H, q, α-CH_2), 8.90 (2H, s, H^3, and H^5).

1-(N-Methyl)butylamino-2,4,6-trinitrobenzene (1c)
Yield 77%; m.p. 110-111 °C; λ_{max} 389 nm (ε 12700); NMR (DMSO-d_6) δ = 0.83 (3H, t, δ-CH_3), 1.24 (2H, s, γ-CH_2), 1.55 (2H, qui, β-CH_2), 2.86 (2H, t, α-CH_2), 3.03 (2H, s, N-CH_3), 8.85 (2H, s, H^3 and H^5).

1-Pyrrolidino-2,4,6-trinitrobenzene (1d)
Yield 48%; m.p. 189.5-191 °C; λ_{max} 370 nm (ε 20000); NMR (DMSO-d_6) δ = 1.93 (4H, m, β-CH_2), 3.28 (4H, m, α-CH_2), 8.83 (2H, s, H^3 and H^5).

1-Piperidino-2,4,6-trinitrobenzene (1e)
Yield 61%; m.p. 104.5-105.5 °C; λ_{max} 394 nm (ε 11200); NMR (DMSO-d_6) δ = 1.50 (6H, m, β,γ-CH_2), 3.05 (4H, m, α-CH_2), 8.85 (2H, s, H^3 and H^5).

1-Dimethylamino-2,4-dinitrobenzene (2a)
Yield 92%; m.p. 75.5-76.5 °C; λ_{max} 386 nm (ε 22200); NMR (DMSO-d_6) δ = 3.00 (6H, s, N-CH_3), 7.27 (1H, d, H^6), 8.23 (1H, d, H^5), 8.60 (1H, s, H^3).

1-Pyrrolidino-2,4-dinitrobenzene (2b)
Yield 89%; m.p. 101.5-102.5 °C; λ_{max} 387 nm (ε 21500); NMR (DMSO-d_6) δ = 1.93 (4H, m, β-CH_2), 3.30 (4H, m, α-CH_2), 7.23 (1H, d, H^6), 8.33 (1H, d, H^5), 8.70 (1H, s, H^3).

1-Piperidino-2,4-dinitrobenzene (2c)
Yield 87%; m.p. 91.5–92.5 °C; λ_{max} 393 nm (ε 17100); NMR (DMSO-d_6) δ = 1.60 (6H, m, β,γ-CH_2), 3.30 (4H, m, α-CH_2), 7.40 (1H, d, H_6), 8.27 (1H, d, H^5), 8.62 (1H, s, H^3).

1-Methylamino-2,4,6-trinitrobenzene (3a)
Yield 57%; m.p. 110–110.5 °C; λ_{max} 352 nm (ε 15100); NMR (DMSO-d_6) δ = 2.83 (3H, s, N-CH_3), 8.98 (2H, s, H^3 and H^5), 9.30 (1H, br s, N-H).

1-Ethylamino-2,4,6-trinitrobenzene (3b)
Yield 34%; m.p. 83.5–84 °C; λ_{max} 353 nm (ε 14900); NMR (DMSO-d_6) δ = 1.23 (3H, t, β-CH_3), 3.11 (2H, q, α-CH_2), 8.83 (1H, br s, N-H), 8.99 (2H, s, H^3 and H^5).

1-Isopropylamino-2,4,6-trinitrobenzene (3c)
Yield 60%; m.p. 107.5–108 °C; λ_{max} 352 nm (ε 14900); NMR (DMSO-d_6) δ = 1.25 (6H, d, β-CH_3), 3.51 (1H, m, α-CH), 8.63 (1H, br s, N-H), 9.07 (2H, s, H^3 and H^5).

1-Butylamino-2,4,6-trinitrobenzene (3d)
Yield 60%; m.p. 80.5–81.5 °C; λ_{max} 352 nm (ε 15400); NMR (DMSO-d_6) δ = 0.87 (3H, t, δ-CH_3), 1.54 (4H, m, β,γ-CH_2), 3.11 (2H, m, α-CH_2), 8.91 (1H, m, N-H), 9.13 (2H, s, H^3 and H^5).

1-t-Butylamino-2,4,6-trinitrobenzene (3e)
Yield 40%; m.p. 94–95 °C; λ_{max} 362 nm (ε 11600); NMR (DMSO-d_6) δ = 1.28 (9H, s, CH_3), 7.62 (1H, s, N-H), 8.91 (2H, s, H^3 and H^5).

1-Benzylamino-2,4,6-trinitrobenzene (3f)
Yield 63%; m.p. 142–142.5 °C; λ_{max} 351 nm (ε 15800); NMR (DMSO-d_6) δ = 4.48 (2H, d, N-CH_2), 7.46 (5H, s, benzyl phenyl proton), 9.19 (2H, s, H^3 and H^5), 9.47 (1H, br s, N-H).

1-(p-Methoxy)phenylamino-2,4,6-trinitrobenzene (3g)
Yield 59% (recrystallized from ethanol); m.p. 171.5–172 °C; λ_{max} 401 nm (ε 13000); NMR (DMSO-d_6) δ = 3.81 (3H, s, OCH_3), 6.96 (2H, d, p-methoxyphenyl $H^{3'}$ and $H^{5'}$), 7.26 (2H, d, p-methoxyphenyl $H^{2'}$ and $H^{6'}$), 9.05 (2H, s, H^3 and H^5), 10.13 (1H, s, N-H).

1-(p-Methyl)phenylamino-2,4,6-trinitrobenzene (3h)
Yield 25% (recrystallized from propanol); m.p. 165–166.5 °C; λ_{max} 394 nm (ε 14000); NMR (DMSO-d_6) δ = 2.29 (3H, s, p-CH_3), 6.49 (2H, d, p-methylphenyl $H^{3'}$ and $H^{5'}$), 7.00 (2H, d, p-methylphenyl $H^{2'}$ and $H^{6'}$), 9.02 (2H, s, H^3 and H^5), 10.26 (1H, m, N-H).

1-Phenylamino-2,4,6-trinitrobenzene (3i)
Yield 54%; m.p. 179–180 °C; λ_{max} 389 nm (ε 13800); NMR (DMSO-d_6) δ = 7.32 (5H, m, phenyl protons), 9.07 (2H, s, H^3 and H^5), 10.19 (1H, s, N-H).

1-(p-Nitro)phenylamino-2,4,6-trinitrobenzene (3j)
Yield 43% (recrystallized from propanol); m.p. 226–227 °C; λ_{max} 407 nm (ε 17700); NMR (DMSO-d_6) δ = 7.30 (2H, d, p-nitrophenyl $H^{3'}$ and $H^{5'}$, 8.23 (2H, d, p-nitrophenyl $H^{2'}$ and $H^{6'}$), 9.13 (2H, s, H^3 and H^5), 10.38 (1H, s, N-H).

1-Methylamino-2,4-dinitrobenzene (3k).

Yield 70%; m.p. 173.5-174.5 °C; λ_{max} 363 (ε 17700), 420 nm (sh, ε 7200); NMR (DMSO-d_6) δ = 3.06 (3H, d, N-CH_3), 7.14 (1H, d, H^6), 8.30 (1H, finely doubly-split d, H^5), 8.85 (1H, finely split d, H^3), 8.92 (1H, br s, N-H).

The results of elementary analyses of all the compounds were within the experimer error.

Preparation and Determination of Substitution Products

The typical procedure for the determination of substitution products was describe in the reaction of **1a** with methylamine; a DMSO solution containing **1a** (5 mmol, 1.28 g) and methylamine (3 equiv, 40% solution) was stirred at the prescribed temperature for the prescribed time (Table 1), poured into water (200 mL), acidified with HCl (3 equiv relative to methylamine), extracted with benzene (3 × 200 mL), and dried over $MgSO_4$. After the mixture was filtered, the benzene layer was subjected to HPLC [Shimazu LC-6A silica gel; hexane-2-propanol (20:1 v/v)].

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