Aromatic Nucleophilic Substitution Reactions of 1-Dialkylamino-2,4-dinitronaphthalenes with Various Amines in Dimethyl Sulphoxide. Part 26.[1]

Shizen Sekiguchi,* Thoru Suzuki, and Masaru Hosokawa
Department of Synthetic Chemistry, Gunma University, Ten-jin cho, Kiryu, Gunma 376, Japan

The dialkylamino group (*e.g.*, dimethyl-, diethyl-, and *N*-methylbutyl-amino, piperidino, and pyrrolidino) of 1-dialkylamino-2,4-dinitronaphthalenes is readily replaced by primary alkylamines in dimethyl sulphoxide. However, substitution does not occur for secondary alkylamines except in the case of pyrrolidine. Aromatic primary amines (*p*-methoxy-, *p*-methyl-, and *p*-nitro-anilines and aniline) are less reactive than aliphatic primary amines, probably owing to their nucleophilicity and bulkiness. Benzylamine is more reactive than aromatic primary amines, but less reactive than aliphatic primary amines. Dependence of substitution on the conformation of nucleophilic amines is discussed.

Although amino groups are not regarded as good leaving groups in activated aromatic substitution reactions (S_NAr),[2,3] we have recently found that the dialkylamino groups, such as dimethyl-, diethyl-, *N*-methylbutyl-amino, piperidino, and pyrrolidino groups, of 1-dialkylamino-2,4-dinitronaphthalene (**1**) are easily replaced by primary amines and pyrrolidine in dimethyl sulphoxide (DMSO).[4]

Interestingly, other nucleophilic secondary amines except for pyrrolidine, *e.g.*, dimethyl-, diethyl-, di-isopropyl-amines, and piperidine, showed only low reactivity. Similar results have been found in the reaction of 1-dimethylamino-2,4-bis(trifluoroacetyl)naphthalene with various amines in acetonitrile.[5] These results are considered to be very interesting in view of base catalysis in S_NAr reactions involving nucleophilic secondary amines.[6–13]

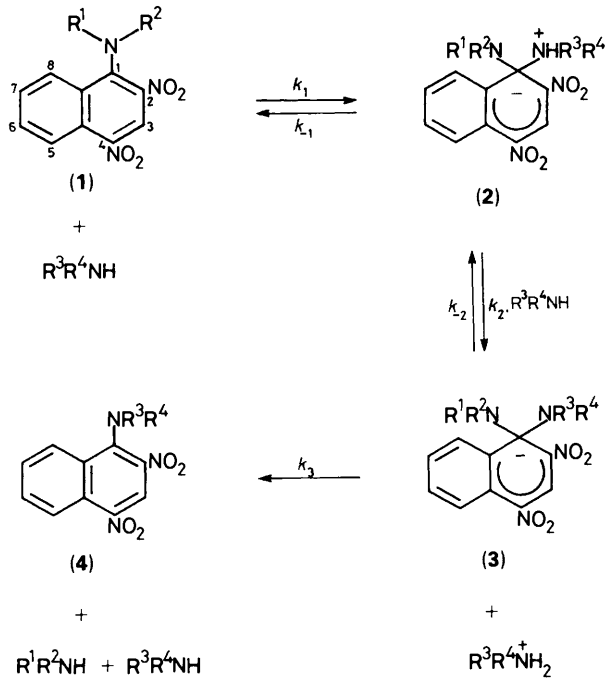
The present reactions proceed as shown in the Scheme.[6–14] Following our previous work,[4] we have extended our studies to the reactions involving aromatic- and aralkyl-amines, and discussed their mechanism in more detail.

Results

General Features.—From our previous work[4] the following summary was obtained in the reactions in the Scheme: (*i*), the dialkyl groups, such as dimethyl-, diethyl-, and *N*-methylbutyl-amino, pyrrolidino, and piperidino ones, are readily replaced by various primary amines (R^3H^4NH, R^4 = H), such as methyl-, ethyl-, and isopropyl-amines; (*ii*), the reaction with methylamine is almost complete in several minutes at 30 °C, and takes place easily, although a dialkyl group is bulky, such as *N*-methylbutyl-amino-, pyrrolidino, and piperidino groups; (*iii*), the yield decreases in the case of isopropylamine, which can be attributed to the steric effect; (*iv*), the reaction with secondary amines, except for with pyrrolidine, is much slower than with primary amines.

The results [(*iii*) and (*iv*)] probably indicate that the steric effects are very important, as well as the basicity of amines (R^3R^4NH) and corresponding amines (R^1R^2NH) to the amino groups at C-1, since both effects would be related to the rates at the k_1, k_2, and k_3 stages (nucleophilic attack, proton transfer, and nucleofuge detachment). We tried an extension of our previous work,[4] paying attention to these factors, and found that the summary described above holds in principle in the present reactions.

Reactions with Various Amines.—As DMSO was found to be a better solvent for the present reactions than acetonitrile, ethanol, and benzene,[4] it was used exclusively.



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

(4) R^4 = H
a; R^3 = Me
b; R^3 = Et
c; R^3 = Bu
d; R^3 = Pr^i
e; R^3 = *p*-$NO_2C_6H_4$
f; R^3 = Ph, R^4 = H
g; R^3 = *p*-MeC_6H_4
h; R^3 = *p*-$MeOC_6H_4$
i; R^3 = $PhCH_2$

Scheme.

The results in Table 1 can be summarized in the following way.

(*i*) Although methylamine is most reactive (runs 6, 12, and 16), its reactivity is a little retarded in the reaction with (**1d**) (run 22), which would indicate that 1-piperidino group exerts a steric effect at the k_1 stage.

(*ii*) The reactions of (**1a**) with every primary aliphatic amine proceeds in relatively high yields, whereas the reactions of (**1b–d**) with isopropylamine are retarded probably owing to a steric effect at the k_1 stage (runs 11, 15, and 27).

Table 1. Exchange reactions of 1-dialkylamino-2,4-dinitronaphthalenes (**1**) with various amines.[a]

Run	Substrate	R^1	R^2	R^3	R^4	T/°C	t/h	Yield (%)
1[b]	(**1a**)	Me	Me	Me	H	30	1	97
2[c]	(**1a**)	Me	Me	Me	H	30	1	96
3[d]	(**1a**)	Me	Me	Me	H	30	1	37
4	(**1a**)	Me	Me	Bu	H	30	1	97
5	(**1a**)	Me	Me	Bu	H	30	9	95
6[b]	(**1b**)	Et	Et	Me	H	30	5 min	90
7	(**1b**)	Et	Et	Me	H	30	1	97
8	(**1b**)	Et	Et	Me	H	30	2	98
9	(**1b**)	Et	Et	Me	H	30	5	97
10	(**1b**)	Et	Et	Et	H	30	1	85
11	(**1b**)	Et	Et	Pr^i	H	30	1	61
12	(**1c**)	Bu	Me	Me	H	30	5 min	81
13	(**1c**)	Bu	Me	Me	H	30	1	100
14	(**1c**)	Bu	Me	Et	H	30	1	84
15	(**1c**)	Bu	Me	Pr^i	H	30	1	79
16	(**1e**)	$-[CH_2]_4-$		Me	H	30	5 min	85
17[b]	(**1e**)	$-[CH_2]_4-$		Me	H	30	1	98
18	(**1e**)	$-[CH_2]_4-$		Et	H	30	1	83
19	(**1e**)	$-[CH_2]_4-$		Bu	H	30	1	88
20	(**1e**)	$-[CH_2]_4-$		Bu	H	30	9	94
21	(**1e**)	$-[CH_2]_4-$		Pr^i	H	30	1	85
22	(**1d**)	$-[CH_2]_5-$		Me	H	30	5 min	52
23[b]	(**1d**)	$-[CH_2]_5-$		Me	H	30	1	100
24	(**1d**)	$-[CH_2]_5-$		Et	H	30	1	83
25	(**1d**)	$-[CH_2]_5-$		Bu	H	30	1	83
26	(**1d**)	$-[CH_2]_5-$		Bu	H	30	9	95
27	(**1d**)	$-[CH_2]_5-$		Pr^i	H	30	1	45
28	(**1a**)	Me	Me	$-[CH_2]_4-$		30	1	72
29	(**1a**)	Me	Me	$-[CH_2]_5-$		30	24	12
30[c]	(**1a**)	Me	Me	$-[CH_2]_4-$		30	1	49
31[d]	(**1a**)	Me	Me	$-[CH_2]_4-$		30	1	25
32[b]	(**1a**)	Me	Me	$-[CH_2]_4-$		30	0.5	67
33	(**1a**)	Me	Me	$-[CH_2]_4-$		30	5	72
34	(**1a**)	Me	Me	$-[CH_2]_4-$		50	1	82
35	(**1a**)	Me	Me	$-[CH_2]_4-$		50	10	65
36	(**1b**)	Et	Et	$-[CH_2]_4-$		30	1	1
37	(**1b**)	Et	Et	$-[CH_2]_4-$		50	1	1
38	(**1b**)	Et	Et	$-[CH_2]_4-$		50	10	7.2
39	(**1b**)	Et	Et	$-[CH_2]_4-$		80	10	4
40	(**1c**)	Bu	Me	$-[CH_2]_4-$		30	1	21
41	(**1c**)	Bu	Me	$-[CH_2]_4-$		50	1	27
42	(**1c**)	Bu	Me	$-[CH_2]_4-$		50	10	62
43	(**1c**)	Bu	Me	$-[CH_2]_4-$		80	10	11
44	(**1d**)	$-[CH_2]_5-$		$-[CH_2]_4-$		30	1	12
45	(**1d**)	$-[CH_2]_5-$		$-[CH_2]_4-$		50	1	13
46[b]	(**1d**)	$-[CH_2]_5-$		$-[CH_2]_4-$		50	24	51
47[b]	(**1e**)	$-[CH_2]_4-$		$-[CH_2]_5-$		50	24	6
48[e]	(**1a**)	Me	Me	NO_2Ar	H	50	12	0
49[e]	(**1a**)	Me	Me	NO_2Ar	H	80	21	0
50[f]	(**1a**)	Me	Me	Ar	H	80	21	26
51[g]	(**1a**)	Me	Me	MeAr	H	50	12	14
52[g]	(**1a**)	Me	Me	MeAr	H	80	13	61
53[g]	(**1a**)	Me	Me	MeAr	H	80	21	72
54[h]	(**1a**)	Me	Me	MeAr	H	80	21	78
55	(**1a**)	Me	Me	$ArCh_2$	H	30	2	57
56	(**1a**)	Me	Me	$ArCh_2$	H	30	3	55
57	(**1a**)	Me	Me	$ArCh_2$	H	30	5	33
58	(**1a**)	Me	Me	$ArCh_2$	H	30	10	28
59	(**1a**)	Me	Me	Et	Et	30	24	0.02
60	(**1a**)	Me	Me	Me	Bu	30	24	4.3
61	(**1a**)	Me	Me	Pr^i	Pr^i	30	24	0

[a] $[(1)]_0$ 0.5 mmol; $[amine]_0/[(1)]_0$ 3 (molar ratio), unless otherwise noted; solvent DMSO (10 cm^3); as for methyl- and ethyl-amines, 40 and 70% aqueous solutions were used. [b] See ref. (4). [c] $[amine]_0/[(1)]_0$ 2. [d] $[amine]_0/[(1)]_0$ 1. [e] NO_2Ar = *p*-nitrophenyl. [f] Ar = phenyl. [g] MeAr = *p*-tolyl. [h] MeOAr = *p*-methoxyphenyl. [i] $ArCH_2$ = benzyl.

(*iii*) The amount of a nucleophilic amine affects the yield (runs 1–3, 28, 30, and 31), which shows the validity of the reaction sequence in Scheme 1 (see Discussion).

(*iv*) Although pyrrolidine was found to be most reactive among secondary amines,[4] it is lower in reactivity than primary amines (runs 1–28, 30–46, and 59–61). Conspicuously, pyrro-

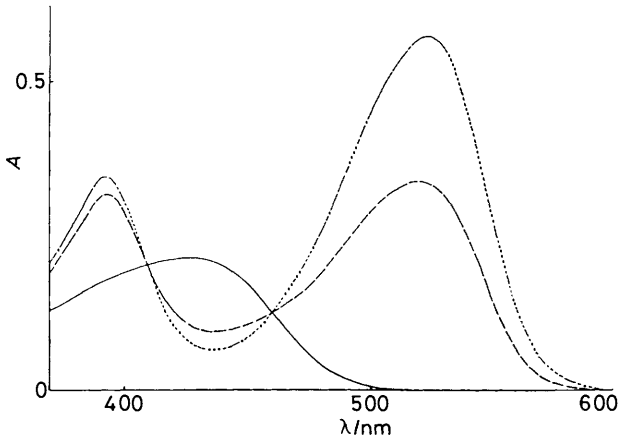


Figure 1. Time-dependent absorption spectroscopic change relevant to the reaction of 1-dimethylamino-2,4-dinitronaphthalene [(**1a**), 2.5 × 10^{-5} mol dm^{-3}] with butylamine (2.5 × 10^{-2} mol dm^{-3}) at 30 °C in DMSO: —— (**1a**); — — just after mixing; - - - - after 15 min.

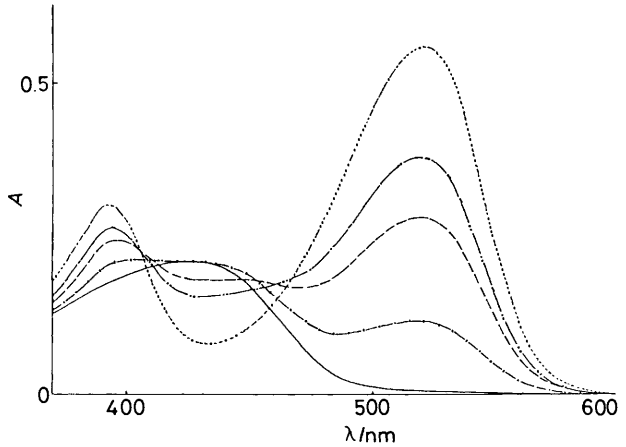


Figure 2. Time-dependent absorption spectroscopic change relevant to the reaction of 1-dimethylamino-2,4-dinitronaphthalene [(**1a**), 2.5 × 10^{-5} mol dm^{-3}] with pyrrolidine (2.5 × 10^{-2} mol dm^{-3}) at 30 °C in DMSO: —— (**1a**); — · — just after mixing; — — after 3; — · · — 5; - - - - and 24 h.

lidine is much more reactive, however, than piperidine (see Discussion).[4,8–13] Pyrrolidine is comparatively fast to react with (**1a**) (runs 28 and 30–35), and to a lesser extent with (**1c**) (runs 40–43), but very slow to react with (**1b**) (runs 36–39), from which it is found that the presence of, at least, one methyl group in the dialkylamino substituent of (**1**) affects the yield considerably.

(*v*) Aromatic primary amines are generally less reactive than aliphatic primary amines and pyrrolidine (runs 48–54), probably owing to their nucleophilicity and bulkiness, where the substituent effect seems to be conspicuous. In the case of *p*-methoxyaniline, the high yield was obtained, depending on high reaction temperature and prolonged reaction time, which would indicate its higher nucleophilicity at the k_1 stage than other aromatic amines.

(*vi*) Benzylamine is more reactive than aromatic primary amines (runs 48–54 and 55–58), but less reactive than aliphatic primary ones, which would support the summary in (*v*).

In general high reaction temperature and long reaction time seems to produce tarry products.

Time-dependent Absorption and ^1H N.M.R. Spectra of Reaction Systems.—The time-dependent absorption spectra of the reactions of (**1a**) with butylamine and pyrrolidine were measured in DMSO. In the former reaction the transformation of (**1a**) to (**4c**) (R^3 = Bu; R^4 = H) was found to be fast, compared with the pyrrolidine system (Figures 1 and 2), where the double maximum absorption (393 and 524 nm) is due to the amide ion $(\mathbf{4c})^-$ formed by fast proton abstraction from (**4c**) by butylamine.

On the other hand, in the latter reaction the transformation of (**1a**) to (**4**) [R^3R^4N = pyrrolidino, identical with (**1e**)] was found to be slower as shown in Figure 2, where the double maxima absorption would be due to two different (**3**) (R^1 = R^2 = Me and R^3R^4N = pyrrolidino; and R^1R^2N = R^3R^4N = pyrrolidino), the latter being formed from (**4**) (R^3R^4N = pyrrolidino) and excess pyrrolidine, since in the preliminary experiment it was confirmed that the reaction of (**4**) [R^3R^4N = pyrrolidino] with pyrrolidine is almost complete in *ca.* 1 h under the same conditions as shown in Figure 2. The time-dependent increase in absorbance, therefore, would stem from the formation of two foregoing complexes (**3**), and, thus, did not yield two isosbestic points near 410 and 460 nm.

As mentioned in paragraph (*iii*) above, pyrrolidine is particular in reactivity among secondary amines, which appears to be inexplicable especially since they have similar nucleophilicitics as expected from their pK_a values. Bunnett *et al.*,[12] have speculated that such difference in reactivity between pyrrolidine and piperidine should stem from their conformations.

In order to elucidate its origin, the time-dependent ^1H n.m.r. spectra for the reaction of (**1a**) with pyrrolidine was measured, see Figure 3.

The signal pattern [Figure 3(*a*)], due to the aromatic protons of (**1a**) is similar to those of (**1b–d**) as shown in Table 2, in which the singlet at δ 8.67 and multiplets centred at δ *ca.* 8.53 and 7.87 are attributed to 3-H, 5,8-H, and 6-, 7-H (Scheme 1).[14–16] These patterns are distinctly different from those of (**1e**) and (**4b–d**) (see below). The pattern of Figure 3*b* was obtained at the fast sweep rate (20 cps) just after (**1a**) and pyrrolidine (4 equiv) in [$^2H_6$]DMSO were mixed, so peak resolution was a little incomplete. Although both patterns [Figure 1(*a*) and 1(*b*)] are similar to each other, the small new singlet at δ 9.05 (Figure 3*b*) could be attributed to 3-H of (**4**) (R^3R^4N = pyrrolidino), *i.e.*, (**1e**) which shows that the product is a mixture of (**1a** and **e**). The pattern [Figure 3(*c*)] was observed [at the usual sweep rate (2 Hz) just after the spectrum was recorded (Figure 3*b*)], in which the singlet at δ 9.05, finely split doublets at δ 8.77 and 8.47, and finely split quintet at 7.78 can be attributed to 3-H, 8-H, 5-H, and 6-, 7-H of (**1e**). In this pattern,* 5-H and 8-H signals are clearly separated, 6-H and 7-H signals overlap and appear in a quintet characteristic throughout (**4a–d**) and very different from the signal patterns of (**1a–d**). The pattern [Figure 3(*c*)] changed to the pattern of [Figure 3(*d*)] in 12 h, in which the new singlet appeared at δ 9.35, and its strength increased to the expense of the singlet at δ 9.05 with time. This new singlet could be attributed to 3-H of (**3**) (R^1R^2N = R^3R^4N = pyrrolidino) compared with the pattern [Figure 3(*e*)], which was obtained in 14 days after addition of pyrrolidine (4 equiv) to (**1e**) in [$^2H_6$]DMSO.[15–17] The pattern [Figure 3(*d*)] indicates that the

* Chemical shifts for (**1e**) are a little different from previous ones.[4] The authors recommend that the new values should be used. The results of ^1H n.m.r. spectra (Figure 3) indicate the rapid conversion of (**1a**) to (**1e**) without the observation of (**3**) (R^1 = R^2 = Me and R^3R^4N = pyrrolidino), whereas those of visible spectra (Figure 2) indicate the presence of both (**3**) (R^1 = R^2 = Me and R^3R^4N = pyrrolidino) and (**3**) (R^1R^2N = R^3R^4N = pyrrolidino), *i.e.*, the slow conversion. This discrepancy is caused by the concentration effect; for instance, in the reaction of (**1a**) with pyrrolidine under the same conditions as those of run 28 except for the use of DMSO (50 cm^3) the yield decreased to 21%. This tendency was observed in the other reactions. The author (S. S.) expresses appreciation to the referee for indicating this point.

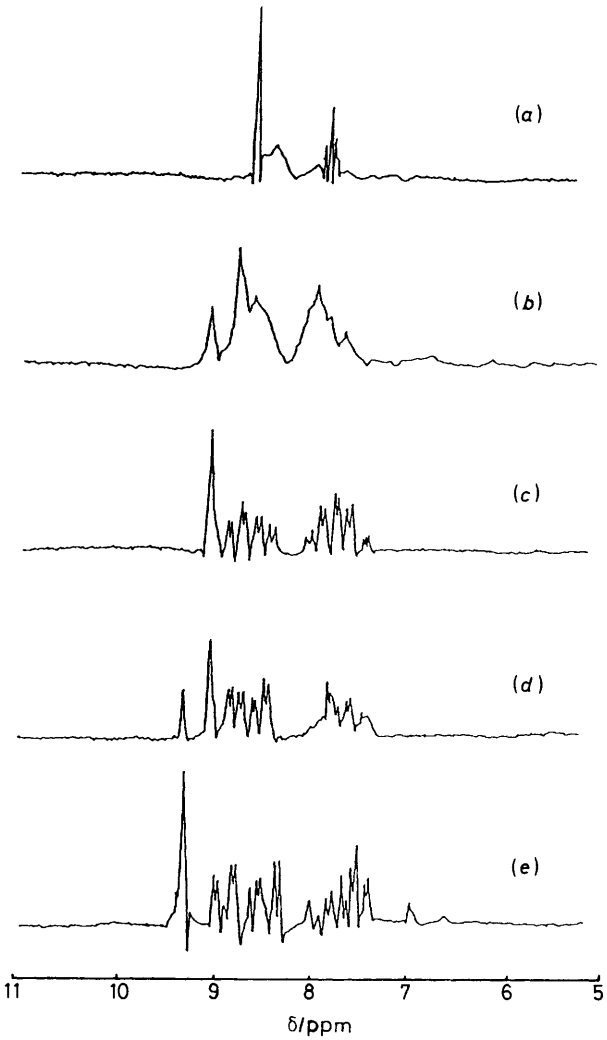
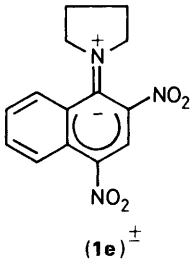


Figure 3. Time-dependent ^{1}H n.m.r. spectroscopic change relevant to the reaction of 1-dimethylamino-2,4-dinitronaphthalene (**1a**) with pyrrolidine (4 equiv) in [$^3H_6$]DMSO: (*a*) (**1a**); (*b*) at the fast sweep rate (20 cps) after mixing; (*c*) just after taking the spectrum (*b*); (*d*) 12 h after mixing; (*e*) 14 days after mixing 1-pyrrolidino-2,4-dinitronaphthalene (**1e**) with pyrrolidine (4 equiv) in [$^3H_6$]DMSO.

(**4**) (R^3R^4N = pyrrolidino) formed reacts further with excess pyrrolidine to give (**3**) (R^1R^2N = R^3R^4N = pyrrolidino). By comparison with the patterns of Figure 3*a*, *c*, and *e* it was found that the 3-H signal of (**1e**) shifts a little more downfield than those of (**1a–d**) and its 5-H, 8-H, and 6-, 7-H signals are similar in shape to those of (**3**) (R^1R^2N = R^3R^4N = pyrrolidino) rather than those of (**1a–d**). As a result, contribution by the



(**1e**)$^{\pm}$

canonical structure (**1e**)$^{\pm}$ to the stability of (**1e**) would be larger than with (**1a–d**),[12,13] which would correspond to the higher reactivity of (**1e**), see Discussion.

Discussion

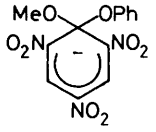
Reaction Mechanism and Leaving-group Abilities of Amines.— We have confirmed in the preliminary kinetic experiment that the present reactions, such as the reactions of (**1e**) with pyrrolidine and butylamine, follow the mechanism of Scheme 1 which involves no spontaneous step, *i.e.*, direct transformation of (**2**) to (**4**).[18] This mechanism is proposed in the reaction of trinitrobenzene with pyrrolidine, piperidine, or mono- and di-alkylamine.[8–10,13] In this mechanism, reactivity at the k_3 stage is very important, as well as at the k_1 and k_2 stages. The fact that the departure of either of the two amino groups from (**3**) (R^1R^2N or R^3R^4N group) is faster is of considerable chemical and biochemical importance.[17,19]

Although much work has so far centred on the leaving group departure from 1,1-dialkoxy- or 1-alkoxy-1-amino-disubstituted Meisenheimer complexes,[6,7,15] we believe that the present amine–amine exchange reaction is of great use in the elucidation of the mechanism for leaving from the complexes, because the pK_a values of the amines (R^1R^2NH and R^3R^4NH) can be altered freely.

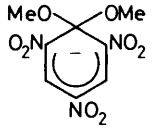
In the reaction of (**1a**) with primary amines the yield does not depend on the amine except for isopropylamine (runs 1, 4, and 5; as for ethyl- and isopropyl-amine, see runs 3–5 of Table 1 of the previous paper[4]), although their pK_a values are almost the same ($MeNH_2$ 10.62, $EtNH_2$ 10.64, Pr^iNH_2 10.63, and $BuNH_2$ 10.60 in water at 25 °C). Reduction in yield in the case of isopropylamine was observed with each substrate (**1**), being especially high for (**1d**) which may be due to its lower reactivity at the k_1 step (runs 11, 15, 21, and 27). These results would indicate the importance of a steric factor.

It is interesting that in the reactions of (**1**) with primary amines the amino group department from (**3**) is always a nucleofuge, *i.e.*, a secondary amino group, although pK_a of nucleophilic amines is a little lower than that of the corresponding secondary amines (Me_2NH 10.73, Et_2NH 10.94, pyrrolidine 11.27, and piperidine 11.12 in water at 25 °C).*

On the other hand, as Bernasconi and Muller[20] showed, that phenoxide ion departure from (**5**) is *ca.* 10^7 times faster than methoxide ion departure from (**6**), and suggested that in the alkoxyl or aryloxyl group departure from complexes or intermediates, an RO group of lower pK_a generally leaves faster.[19]



(**5**)



(**6**)

This is not the case, however, with the present reactions. The leaving tendency from (**3**) in the present reactions is believed to depend on the conformation of amino groups attached, see below.

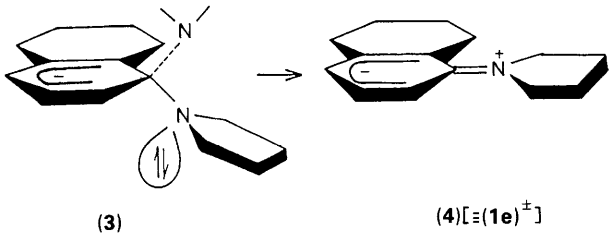
The Large Difference in Reactivity between Pyrrolidine and Piperidine.—As shown in Table 1 (runs 28–35 and 59–61), pyrrolidine is higher in reactivity than other secondary amines. In the time-dependent absorption spectra of the reaction of (**1e**) (2.5×10^{-5} mol dm^{-3}) with piperidine (0.25 mol dm^{-3}) in DMSO at 30 °C (corresponding to run 47) (not shown), the double maxima absorption (394 and 523 nm), similar in shape to that in Figure 2 (15 min after mixing) was obtained in *ca.* 24 h, when the reaction went essentially to completion. Further, two

* Although the pK_a value of *N*-methylbutylamine is not known, it is expected to be a little larger than those of primary alkylamines on consideration of the pK_a values of $BuNH_2$ (10.60) and Bu_2NH (11.25) in water at 25 °C.

Table 2. Aromatic and amino proton chemical shifts of mono- and di-alkylamino-2,4-dinitronaphthalenes in [$^3H_6$]DMSO.

Substrate	3-H	5-H[a]	8-H[a]	6-H[b]	7-H[b]	NH
(**1a**) $R^1 = R^2 = Me$	8.67 (s)	8.53 (m)	8.53 (m)	7.87 (m)	7.87 (m)	—
(**1b**) $R^1 = R^2 = Et$	8.73 (s)	8.53 (m)	8.53 (m)	7.93 (m)	7.93 (m)	—
(**1c**) $R^1 = Bu$, $R^2 = Me$	8.73 (s)	8.53 (m)	8.53 (m)	7.95 (m)	7.95 (m)	—
(**1d**) $R^1R^2 = -[CH_2]_5-$	8.67 (s)	8.50 (m)	8.50 (m)	7.90 (m)	7.90 (m)	—
(**1e**) $R^1R^2 = -[CH_2]_4-$	9.05 (s)	8.77 (d–d)	8.47 (d–d)	7.78 (q)	7.70 (q)	—
(**4a**) $R^3 = Me$	9.03 (s)	8.68 (d–d)	8.95 (d–d)	7.93 (q)	7.93 (q)	9.60 (br s)
(**4b**) $R^3 = Et$	8.97 (s)	8.62 (d–d)	8.96 (d–d)	7.87 (q)	7.87 (q)	9.28 (br s)
(**4c**) $R^3 = Bu$	8.87 (s)	8.62 (m)	8.62 (m)	7.84 (q)	7.84 (q)	9.35 (br t)
(**4d**) $R^3 = Pr^i$	8.97 (s)	8.53 (d–d)	8.83 (d–d)	7.90 (q)	7.90 (q)	8.97 (br s)
(**4e**) $R^3 = p\text{-}NO_2C_6H_4$	9.03 (s)	8.60 (t)	8.70 (t)	8.19 (m)	8.19 (m)	10.27 (s)
(**4f**) $R^3 = Ph$	8.87 (s)	8.62 (t)	8.75 (t)	7.84 (q)	7.84 (q)	10.18 (s)
(**4g**) $R^3 = p\text{-}MeC_6H_4$	8.87 (s)	8.53 (t)	8.67 (t)	7.84 (q)	7.84 (q)	10.19 (s)
(**4h**) $R^3 = p\text{-}MeOC_6H_4$	8.88 (s)	8.76 (t)	8.88 (t)	7.85 (q)	7.85 (q)	10.28 (s)
(**4i**) $R^3 = PhCH_2$	8.94 (s)	8.70 (d)	8.70 (d)	7.87 (q)	7.87 (q)	9.80 (br t)

[a] The sign (d–d) indicates that the heads of two peaks of a doublet are finely doubly split [Figure 1(*c*)]. The signs (m, t, and d) mean that each doublet overlaps to give a multiplet, a triplet, or a doublet. In this doublet each peak is broad. [b] The signs (m and q) mean that 6-H and 7-H peaks overlap to give a multiplet or a quartet, each peak of which is finely doubly split [Figure 1(*a*) and (*c*)].



(**3**) (**4**)[≡(**1e**)$^{\pm}$]

Figure 4. Transition state at the k_3 stage: 2- and 4-nitro groups omitted for simplicity.

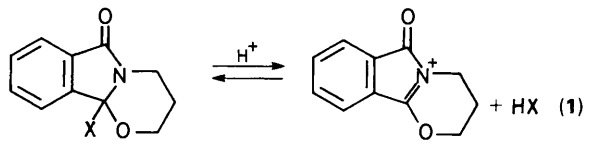
isosbestic points in this case appeared at 410 and 460 nm from the beginning, indicating the transformation of (**1e**) to (**3**) (R^1R^2N = pyrrolidino, R^3R^4N = piperidino). The reaction is considered to terminate with the formation of (**3**), where the exchange reaction giving (**4**) (R^3R^4N = piperidino), identical with (**1d**), would scarcely take place. On the other hand, in the time-dependent spectra of the reaction of (**1d**) (2.5×10^{-5} mol dm^{-3}) with pyrrolidine (2.5×10^{-2} mol dm^{-3}) in DMSO at 30 °C (corresponding to the reaction of run 46) (not shown), the double maxima absorption (392 and 523 nm) was obtained in *ca.* 7 h (not shown), when the reaction was almost complete. In this case, however, two isosbestic points did not appear (Figure 2), because the time-dependent increase in absorbance at 392 and 523 nm is probably due to contribution from the formation of two complexes (**3**) (R^1R^2N = piperidino and R^3R^4N = pyrrolidino for one; $R^1R^2N = R^3R^4N$ = pyrrolidino for the other). The latter complex would be formed from the reaction of (**4**) [R^3R^4N = piperidino, identical with (**1e**)], a substitution product, with excess pyrrolidine.

Although pyrrolidine seems to be more reactive at the k_1 step than piperidine in the reactions of 1,3,5-trinitrobenzene[8,10] or 1-ethoxy-2,4-dinitronaphthalene[12] with these cyclic amines, it is clear that the large difference in reactivity between the two amines in both reactions (runs 46–47) would arise from the reactivity at the k_3 stage. From the result in Figure 3(*c*), the transition state at the k_3 step in the reaction of (**1d**) with pyrrolidine could assume the following configuration (Figure 4). For substituted cyclopentane there are two conformations, *i.e.*, one of C_2 symmetry and the other of C_s symmetry,[21] and C_2 symmetry is likely to be predominant for pyrrolidine,[22,23] although a pyrrolidine ring is shown as a plane for the sake of simplicity in Figure 4.

For (**3**), the unshared electron pair on pyrrolidino nitrogen is antiperiplanar to the C(1)–N [piperidino (nucleofuge) nitrogen] bond with respect to the C(1)–N (pyrrolidino nitrogen) bond, which helps the piperidino group to leave, giving (**1e**)$^{\pm}$. By considering the greater stability of (**1e**) as is shown in Figure 3(*c*) and in its m.p. (Experimental), a transition state such as (**3**) would be deemed energetically favourable. At present, however, the degree of steric interference between 2-NO_2 group and α-CH_2 group of the pyrrolidino ring, when this ring is co-planar with the naphthalene ring in (**1e**)$^{\pm}$ is unclear.

The results in Table 1 and Figure 1, indicate that the exchange reactions with primary amines are very fast in most cases which stems from their preference for antiperiplanar geometry in the transition state at the k_3 stage to the secondary amine system.

Although it is said that amino groups are replaced in S_NAr reactions with comparative difficulty,[2,3] Gravitz and Jencks[24] directly compared the rate constants for expulsion of amines with those for expulsion of alkoxide ions for a given basicity in the acid-catalysed breakdown of amine addition compounds formed from *N,O*-trimethylenephthalimidium ion, which suggests that for a given basicity the amines are better leaving groups by a factor of *ca.* 10^5, [equation (1)].



X = RO or R_2N

In conclusion, however, we would like to suggest that in the detachment of an amino group from anionic σ complexes conformation of nucleophilic amines should be taken into account as well as their pK_a values.

Experimental

GPR grade DMSO was dried by being refluxed over calcium hydride, fractionally distilled under reduced pressure, and protected from moisture. The primary and secondary amines were AnalaR grade reagents used as supplied.

1-Amino-2,4-dinitronaphthalenes were prepared as follows: the solution containing weighed amounts of an amine and 1-chloro-2,4-dinitronaphthalene (CDN) ([amine]/[CDN] mole ratio = 10, with CDN [*ca.* 5 g] used) in DMSO (50 cm^3) was stirred for 3 h at 30 (or 50 °C), poured, neutralized with dilute aqueous H_2SO_4, and filtered. The residue was recrystallized from methanol except for pyrrolidine and methylamine (acetic acid used): (**1a**), m.p. 87.0–87.5 °C, λ_{max} 419 nm; (**1b**), m.p. 87.5–88.5 °C, λ_{max} 430 nm (ε 15 000); (**1c**), m.p. 66.0–67.0 °C, λ_{max} 425 nm (ε 7 400); (**1d**), m.p. 136–136.5 °C, λ_{max} 416 nm (ε 8 000); (**1e**), m.p. 201.5–202.0 °C, λ_{max} 438 nm (ε 21 000); (**4a**), m.p. 161–161.5 °C, λ_{max} 411 nm (ε 17 000); (**4b**), m.p. 163–163.5 °C, λ_{max} 410 nm (ε 17 000); (**4c**), m.p. 91.5–92 °C, λ_{max} 410 nm (ε 17 100); (**4d**), m.p. 151.5–152 °C, λ_{max} 410 nm (ε 15 600); (**4e**), m.p. 214.5–215 °C, λ_{max} 366 nm (ε 15 100); (**4f**), m.p. 181–181.5 °C, λ_{max} 434 nm (ε 17 200); (**4g**), m.p. 199.5–200 °C, λ_{max} 435 nm (ε 13 400); (**4h**), m.p. 200.5–201 °C, λ_{max} 435 nm (ε 13 900); (**4i**), m.p. 137.5–138 °C, λ_{max} 408 nm (ε 16 400). In the elemental analysis of C, H, and N, the observed values agreed with the calculated ones within ±0.2%.

The typical procedure for determination of the reaction products was described in the reaction of (**1a**) with methylamine: the solution containing (**1a**) (5 mmol, 1.306 g) and methylamine (3 equiv, 40% solution) was stirred at the prescribed temperature for the prescribed time, poured into water (200 cm^3), acidified with HCl (3 equiv, relative to methylamine), extracted with benzene (3 × 200 cm^3), and dried ($MgSO_4$). After the mixture was filtered, the benzene layer was subjected to HSLP [Shimazu LC-6A, silica gel; hexane–propanol-2-ol (20:1 v/v for runs 1–49 and 54–61 and 100:1 v/v for runs 50–53)].

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