© 1991 The Chemical Society of Japan Bull. Chem. Soc. Jpn., 64, 42—49 (1991) [Vol. 64, No. 1

Aromatic Nucleophilic Substitution of Halobenzenes with Amines under High Pressure

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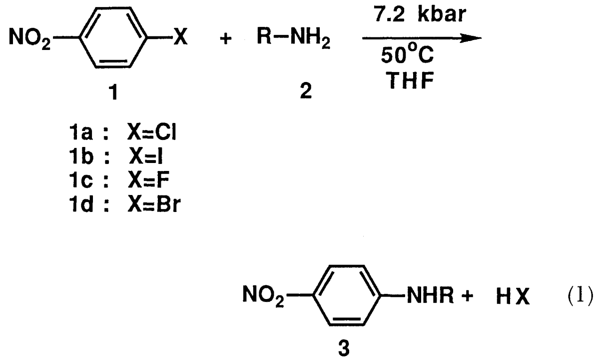
(Received August 15, 1990)

The nucleophilic substitution reactions of aromatic halides having electron-attracting groups on ortho or para position with various primary and secondary amines were accelerated by high pressure to give the corresponding *N*-substituted anilines in high yields. The bulkiness of amines affects its reactivity to lower the yields of the products. Although the secondary amines are usually less reactive than primary amines, cyclic secondary amines such as morpholine, piperidine, and pyrrolidine were found very reactive. 1,4-Diazabicyclo[2.2.2]octane and quinuclidine gave *N*-quaternary ammonium halides in high yields in contrast to the low reactivity of acyclic tertiary amines. Dichloro- and trichloro-nitrobenzenes also react with diethylamine, pyrrolidine, and morpholine to give mono-, di-, and trisubstitution products depending upon the amount of amine and the position of nitro group in these chlorides.

Nucleophilic substitutions of aromatic halides with amines are generally difficult to proceed under ordinary pressure,[1] and are limited to some fluorides or chlorides having a strongly electron-attracting group such as nitro group at ortho or para position. These aromatic nucleophilic substitution ($\mathrm{S_NAr}$) reactions are confirmed to proceed through the Meisenheimer type dipolar intermediate.[2] Because bond formation and charge separation are occurring in the transition state of this reaction, the $\mathrm{S_NAr}$ reaction is expected to be accelerated under high pressure.[3] However, no $\mathrm{S_NAr}$ reaction of aromatic halides with amines had been reported under high pressure from the synthetic point of view,[3] until our preliminary paper was published.[4] Matsumoto and his co-workers reported the high pressure $\mathrm{S_NAr}$ reaction of trifluoromethyl-substituted halobenzenes,[5] halogenopyridines,[6] and halogenothiazoles with amines.[7]

Herein, we describe the $\mathrm{S_NAr}$ reaction of substituted monohalobenzenes with various primary and secondary amines under high pressure. We also report the reaction of dichloro- and trichloro-nitrobenzenes with secondary amines such as diethylamine, pyrrolidine, and morpholine under high pressure in order to test the applicability of this reaction for the preparation of polyamino-substituted nitrobenzenes.

The high pressure reactions were carried out in a Teflon capsule using a Hikari Kouatsu High Pressure Reaction Apparatus.[8] When *p*-nitrochlorobenzene (**1a**) was treated with five molar equivalents of propylamine in a freshly distilled tetrahydrofuran (THF) solution at 50 °C under 7.2 kbar[#] for 20 h, *N*-propyl-*p*-nitroaniline (**3a**) was obtained as yellow crystals in 93% yield along with an almost quantitative amount of propylamine hydrochloride. The products were characterized by the spectroscopic measurement. The reaction did not proceed even at 80 °C under ordinary pressure.



In order to ascertain the acceleration effect on the reaction rate, the yields of the reactions of **1a** with propylamine, morpholine, and pyrrolidine were examined under the variation of pressure in the range of 1/1000—10.0 kbar (Table 1). The reactions of **1a** with propylamine and morpholine are dramatically accelerated at the pressure of 6 kbar. However, 6 kbar is not enough for the completion of these reactions. On the other hand, pyrrolidine is more reactive than these amines and the reaction is completed at 6 kbar.

The reactions of *p*-nitrochlorobenzene (**1a**) with other primary amines under the high pressure of 7.2—12.0 kbar also gave the corresponding secondary *p*-nitroanilines as shown in Table 2. The yields of the reactions are affected strongly by the bulkiness of amines. For example, isopropylamine gave *N*-isopropyl-*p*-nitroaniline (**3c**) only in 26% yield under the same reaction conditions with those of propylamine, despite the basicity of these amines is almost same (pK_a; 10.63 and 10.53).[9] Similar results were also observed in the reactions of four butylamines (Table 2, Runs d—i). In these cases the order of the yields of **3** is the same as the order of the bulkiness of the butyl groups. *p*-Nitroiodobenzene (**1b**) is less reactive than **1a** (Table 2, Runs b, e, and i) in accordance with the usual $\mathrm{S_NAr}$ reactions of aromatic halides.[10]

Cyclohexylamine gave *N*-cyclohexyl-*p*-nitroaniline (**3k**) in 18% yield similar to the cases of isopropylamine

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[#] 1 kbar=0.1 GPa

Table 1. Pressure Effect on the Yields of the Reaction of *p*-Nitrochlorobenzene (**1a**) with Propylamine, Morpholine, and Pyrrolidine[a)]

Pressure/kbar	Propylamine		Morpholine		Pyrrolidine	
	3a/%	**1a**/%[b)]	**6h**/%	**1a**/%[b)]	**6m**/%	**1a**/%[b)]
1/1000[c)]	0	100	0	100	16.7	81
1.0	0.6	96	0.5	96	43.2	56
2.0	1.7	96	1.4	94	63.5	35
4.0	4.4	94	13.0	81	90.6	5
6.0	28.3	70	36.5	61	100	0
8.0	42.8	53	88.9	10	—	—
10.0	81.1	17	99.7	0	—	—

a) The reactions were carried out in THF solution at 50 °C for 3 h using 1.0 mmol of **1a** and 10.0 mmol of amine. b) Percentage of recovered **1a**. c) Atmospheric pressure.

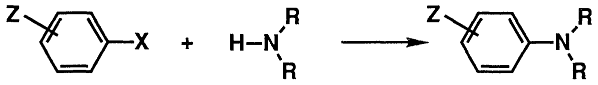
Table 2. Reaction of *p*-Nitrohalobenzenes with Primary Amines under High Pressure[a)]

Run	Halide X	Amine 2	Pressure kbar	Reaction time/h	Product 3	Mp θ_m/°C (lit)	Yield[b)] %
a	Cl	$PrNH_2$	7.2	20	**3a**	68—69 (63.9—71.1)[c)]	93 (0)
b	I	$PrNH_2$	12.0	20	**3a**		28 (0)
c	Cl	*i*-$PrNH_2$	7.2	20	**3c**	68—69 (85.5—85.6)[c)]	26 (0)
d	Cl	$BuNH_2$	7.2	20	**3d**	60—61 (56.2—57.2)[c)]	76 (0)
e	I	$BuNH_2$	8.0	50	**3d**		35 (0)
f	Cl	*i*-$BuNH_2$	7.2	20	**3f**	76—77 (95.9—96.1)[c)]	61 (0)
g	Cl	*s*-$BuNH_2$	7.2	20	**3g**	Oil (40.4)[c)]	13 (0)
h	Cl	*t*-$BuNH_2$	7.2	20	**3h**	Oil	2 (0)
i	I	*t*-$BuNH_2$	12.0	50			0 (0)
j	Cl	*Hex*NH_2	7.2	20	**3j**	67—68	65 (0)
k	Cl	*c*-$C_6H_{11}NH_2$	7.2	20	**3k**	104—105 (100.2—100.5)[c)]	18 (0)
l	Cl	$CH_2{=}CHCH_2NH_2$	7.2	20	**3l**	72—73 (68.2—69.2)[c)]	67 (0)
m	Cl	*p*-$AnisNH_2$	9.0	50	**3m**	158—159 (152.2)[c)]	2 (0)
n	Cl	*p*-$TolNH_2$	9.0	75			0 (0)
o	Cl	$PhNH_2$	9.0	50			0 (0)
p	F	*p*-$AnisNH_2$	9.0	25	**3m**		11 (0)
q	F	*p*-$TolNH_2$	9.0	50	**3q**	145—146 (140—141)[c)]	6 (0)
r	F	$PhNH_2$	9.0	50	**3r**	140—142 (136)[c)]	7 (0)

a) All reactions listed were carried out in THF solution at 50 °C using 1.0 mmol of **1** and 5.0 mmol of amines. b) Yields in parentheses refer to reactions under 1 atm at 80 °C, for 50 h. c) H. Suhr, *Ann. Chem.*, **687**, 175 (1965).

(26%) and *s*-butylamine (13%). Aromatic primary amines have lower reactivity than that of the aliphatic amines because of their low basicity. For example, *p*-anisidine gave *p*-nitro-*p′*-methoxydiphenylamine (**3m**) only in 2% yield under the forced reaction conditions (9.0 kbar, 50 h). Aniline and *p*-toluidine gave no substitution product under the same reaction conditions. *p*-Nitrofluorobenzene (**1c**) is more reactive than **1a** and gave substitution products in the reactions with aromatic amines in low yields (Table 2, Runs p—r).

Secondary amines exhibit lower reactivities than the corresponding primary amines as shown in Table 3 (compare Runs c, d, and e in Table 3 with Runs a, c, and d in Table 2, respectively). However, cyclic secondary amines such as morpholine, piperidine, and pyrrolidine indicate extremely higher reactivities (Table 3, Runs h—v) than those of acyclic secondary amines such as diethylamine and diisopropylamine. The difference in reactivities of these high pressure S_NAr reactions seems to be attributed to both basicity and bulkiness of amine.



4 5 6

4a : Z=o-NO_2, X=F
4b : Z=o-NO_2, X=Cl
4c : Z=m-NO_2, X=F
4d : Z=m-NO_2, X=Cl
4e : Z=p-CN, X=Cl
4f : Z=p-Ac, X=Cl

+ HX (2)

Although *o*-nitrochlorobenzene (**4b**) showed high reactivity toward pyrrolidine (Table 3, Run q) as that of *p*-nitrochlorobenzene (**1a**), *m*-nitrochlorobenzene (**4d**) was shown to have much less reactivity (Run t).

Table 3. The S_NAr Reaction of Aromatic Halides with Secondary Amines under High Pressure[a]

Run	Aromatic Z	Halide X	Amine	Pressure	Reaction time/h	Product **6**	Mp	Yield[b]
				kbar			θ_m/°C (lit)	%
a	p-NO$_2$	Cl	Et$_2$NH	7.2	20	**6a**	77—78 (73—74)[c]	39 (0)
b	p-NO$_2$	I	Et$_2$NH	8.0	250	**6a**		49 (0)
c	p-NO$_2$	Cl	Pr$_2$NH	7.2	20	**6c**	62—63 (59)[d]	24 (0)
d	p-NO$_2$	Cl	i-Pr$_2$NH	7.2	50	**6d**		0 (0)
e	p-NO$_2$	Cl	Bu$_2$NH	7.2	20	**6e**	Oil	15 (0)
f	p-NO$_2$	Cl	i-Bu$_2$NH	7.2	20	**6f**		Trace (0)
g	p-NO$_2$	I	i-Bu$_2$NH	12.0	72			0 (0)
h	p-NO$_2$	Cl	Morpholine	6.0	20	**6h**	158—159 (149.5—150.0)[c]	100 (3)
i	p-NO$_2$	I	Morpholine	12.0	50	**6h**		100 (2)
j	p-NO$_2$	Cl	Piperidine	6.0	20	**6j**	108—109 (99.5—100)[c]	100 (22)
k	p-NO$_2$	I	Piperidine	12.0	20	**6j**		100 (4)
l	p-NO$_2$	Cl	N-Methylpiperazine	6.0	20	**6l**	105—106 (108)[e]	96
m	p-NO$_2$	Cl	Pyrrolidine	6.0	20	**6m**	178—179 (167)[c]	100 (92)
n	p-NO$_2$	Br	Pyrrolidine	8.5	20	**6m**		100 (51)
o	p-NO$_2$	I	Pyrrolidine	12.0	20	**6m**		100 (14)
p	o-NO$_2$	F	Pyrrolidine	7.2	20	**6p**	Oil	100
q	o-NO$_2$	Cl	Pyrrolidine	8.5	20	**6p**		100 (85)
r	o-NO$_2$	Cl	Morpholine	6.0	20	**6r**	Oil	100
s	m-NO$_2$	F	Pyrrolidine	9.0	87	**6s**	98—100	98
t	m-NO$_2$	Cl	Pyrrolidine	9.0	50	**6s**		2 (0)
u	p-CN	Cl	Pyrrolidine	6.0	20	**6u**	90—91 (81)[f]	34 (0)
v	p-CH$_3$CO	Cl	Pyrrolidine	7.2	20	**6v**	135—136	18 (0)

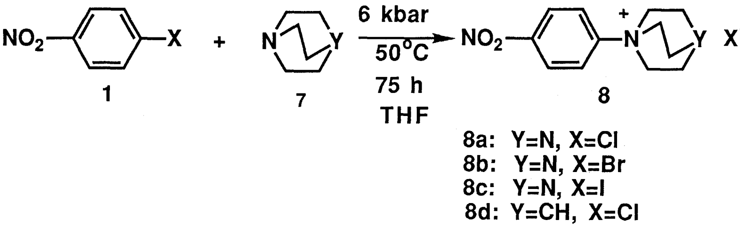
a) All reactions listed were carried out in THF solution at 50 °C using 1.0 mmol of **4** and 5.0 mmol of amine. b) Yields in parentheses refer to reactions under 1 atm at 80 °C, for 50 h. c) E. Matsumura, Y. Tohda, and M. Ariga, *Bull. Chem. Soc. Jpn.*, **55**, 2174 (1982). d) N. Nagornow, *J. Russ. Phys-Chem. Soc.*, **29**, 699. e) L. Loewe, H. Mieth, and H. Suschitzky, *J. Chem. Soc.*, **1963**, 1666. f) S. F. Beach, J. D. Hepworth, J. Sawyer, G. Hallas, R. Marsden, M. M. Mitchell, D. A. Ibbitson, A. M. Jones, and G. T. Neal, *J. Chem. Soc., Perkin Trans. 2*, **1984**, 217.

This indicates that the nitro group increases the reactivity of chloride only at ortho or para position. However, *m*-nitrofluorobenzene (**4c**) is exceptionally reactive toward pyrrolidine (Run s). *p*-Nitrobromobenzene (**1d**) and *p*-nitroiodobenzene (**1b**) reacted with pyrrolidine to give **6m** in high yields (Runs n and o). *p*-Cyanochlorobenzene (**4e**) and *p*-chloroacetophenone (**4f**) gave the corresponding *N*-arylpyrrolidines in moderate yields (Runs u and v). These results indicate that cyano and acetyl groups are not so good substituent as nitro group to promote the reaction, and that 9.0 kbar is not enough to accelerate the SNAr reactions of these chlorides.

In contrast to triethylamine, bicyclic tertiary amines such as 1,4-diazabicyclo[2.2.2]octane (DABCO) and quinuclidine react with *p*-nitrohalobenzenes to give the corresponding quaternary ammonium salts **8**[9] in quantitative yields at 6.0 kbar.

The reaction of 2,3-dichloronitrobenzene (**9**) with diethylamine, pyrrolidine, and morpholine gave ortho substitution product **10** in quantitative yield without affording meta substitution product (Table 4). The structure of **10** was determined by the observation that ^1H NMR signal of aromatic proton H_c changes only a little by the reaction of **9**. This substitution pattern is consistent with the observation that *m*-nitrochlorobenzene has very low reactivity as described above.

Similarly, 2,5-dichloronitrobenzene (**11**) and 3,4-dichloronitrobenzene (**13**) react with these amines at ortho or para position to nitro group, respectively, to



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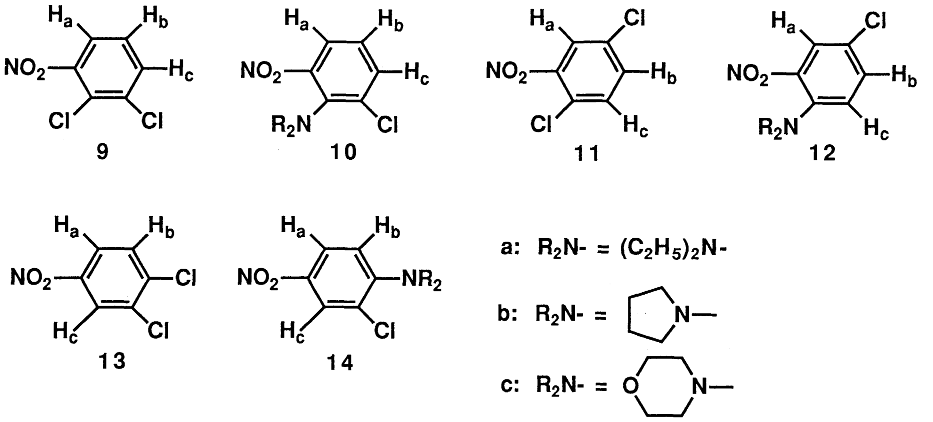

Fig. 1.

Table 4. Reaction of Dichloronitrobenzenes with Secondary Amines,[a] and ^1H NMR Data of the Reaction Products

Halide	R_2NH	Product	Yield %	^1H NMR/δ						
				H_a	H_b	H_c	NCH_2	CH_3	CH_2	OCH_2
9	Diethylamine	**10a**	98	7.47(dd)	7.10(t)	7.39(dd)	3.12	1.03	—	—
9	Pyrrolidine	**10b**	100	7.47(d)	7.01(t)	7.45(d)	3.24	—	1.94	—
9	Morpholine	**10c**	100	7.53(dd)	7.11(t)	7.46(dd)	3.07	—	—	3.77
				(7.70(d)	7.36(dd)	7.70(d))[b]				
11	Diethylamine	**12a**	98	7.61(d)	7.34(dd)	7.06(d)	3.14	1.11	—	—
11	Pyrrolidine	**12b**	97	7.64(d)	7.22(dd)	6.79(d)	3.16	—	1.97	—
11	Morpholine	**12c**	100	7.74(d)	7.43(dd)	7.09(d)	3.03	—	—	3.82
				(7.87(d)	7.50(dd)	7.43(d))[b]				
13	Diethylamine	**14a**	91	7.96(dd)	6.97(d)	8.12(d)	3.35	1.11	—	—
13	Pyrrolidine	**14b**	98	7.82(dd)	6.54(d)	8.01(d)	3.61	—	1.97	—
13	Morpholine	**14c**	98	8.05(dd)	7.03(d)	8.16(d)	3.21	—	—	3.88
				(8.07(dd)	7.61(d)	8.33(d))[b]				

a) The reactions were carried out in the following conditions; 6 kbar, 50 °C, 20 h, in THF. b) The values in the parentheses are the chemical shift of starting dichloronitrobenzenes.

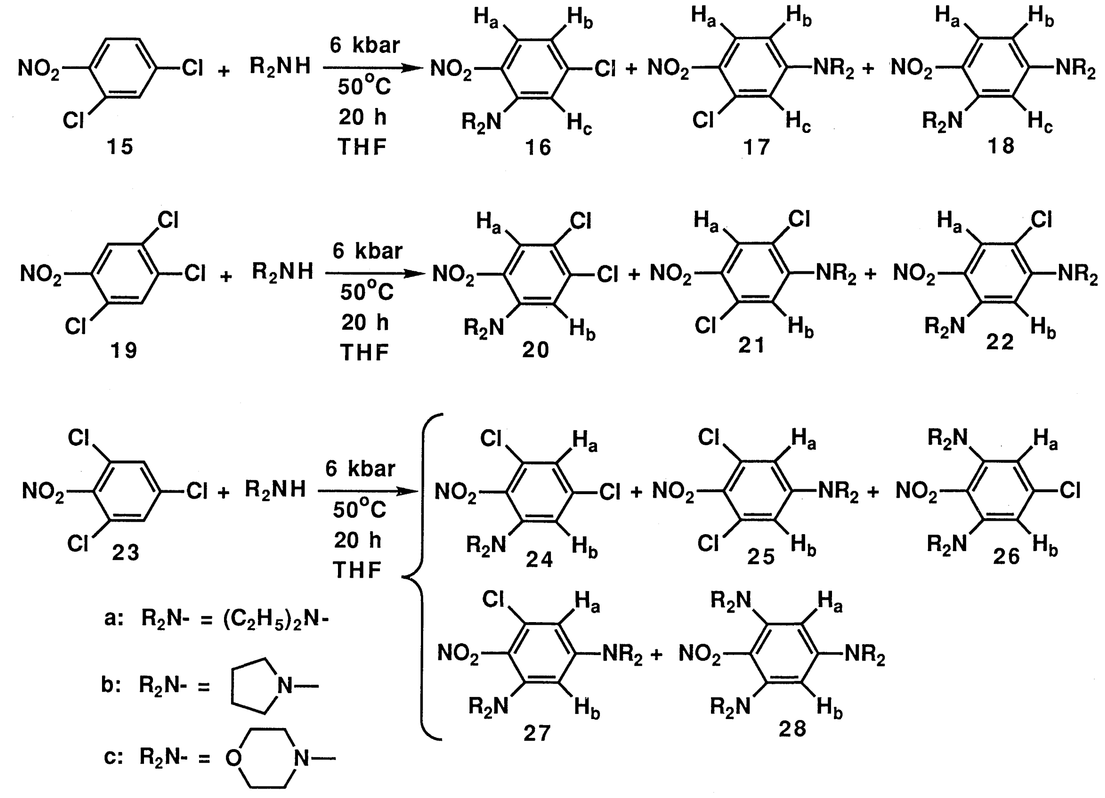

Fig. 2.

give a single product **12** and **14** in quantitative yields (Table 4). The structure of the products was based on the NMR spectra. For example, the fact that only ortho substitution takes place in the reactions of **11**, was concluded by the observation that this reaction caused the largest chemical shift change for H_c in the aromatic protons of **11** (Table 4). These three dichloronitrobezenes were found to be more reactive than monochloronitrobenzenes, and then no difference in the reactivity of amines was observed in these reactions.

2,4-Dichloronitrobenzene (**15**) has ortho and para chlorine atoms which are both reactive. The reactions of **15** gave a mixture of ortho substitution product **16**, para substitution product **17**, and disubstitution product **18**. Yields of these three types of products depend on the reactivity and the amount of the amine used. When five molar equivalents of amine was used, diethylamine gave ortho-mono substitution product in high yield along with a small amount of **18**. On the other hand, pyrrolidine and morpholine gave the disubstitution product **18** as a major product together with a small amount of ortho-mono substitution product **16**. In these cases, isolation of para-mono substitution product was unsuccessful (Table 5). In the case of 1.1 molar equivalent of pyrrolidine or morpholine was used, ortho-mono substitution products became predominant together with a small amount of para-mono and disubstitution products. These results may be explained by the assumption that the para-mono substitution products **17** are more reactive than ortho-mono product **16** in the second substitution. Diethylamine is less reactive than pyrrolidine or morpholine in this second step.

Table 5. Reaction of 2,4-Dichloronitrobenzene (**15**) with Secondary Amines[a)]

Amine	Amount of amine[b)]	Yield/%		
		16	**17**	**18**
Diethylamine	5.0	90	0	10
Pyrrolidine	5.0	15	0	85
Pyrrolidine	1.1	89	3	2
Morpholine	5.0	36	0	61
Morpholine	1.1	86	2	11

a) The reactions were carried out under the following conditions; 6 kbar, 50 °C, 20 h, in THF. b) Amount of amine was shown in molar equivalent.

In the reactions of 2,4,5-trichloronitrobenzene (**19**), no substitution was observed at meta position and the reaction proceeded in a manner similar to that of 2,4-dichloronitrobenzene (Table 6-1). In these cases, yields of disubstitution products **22** were higher than the case of **15** and even diethylamine gave **22a** as the major product. This means that **19** is more reactive than **15** due to the effect of 5-chlorine atom. When 1.2 molar equivalent of morpholine was used in the presence of triethylamine to trap hydrogen chloride generated, ortho-mono and disubstitution products were obtained without yielding para-mono product. This is explained by the assumption that the ortho position of para-mono product **21** is more reactive than the para

Table 6. Reaction of Trichloronitrobenzenes with Secondary Amines[a)]

(1) Reaction of 2,4,5-Trichloronitrobenzene (**19**)

Amine	Amount of amine[b)]	Yield/%		
		20	**21**	**22**
Diethylamine	5.0	37	0	59
Pyrrolidine	5.0	0	0	100
Morpholine	5.0	0	0	94
Morpholine	1.2	53	0	34

(2) Reaction of 2,4,6-Trichloronitrobenzene (**23**)

Amine	Amount of amine[b)]	Yield/%				
		24	**25**	**26**	**27**	**28**
Diethylamine	5.0	0	91	0	0	0
Pyrrolidine	5.0	0	0	0	5	93
Pyrrolidine	1.1	0	85	8	2	0
Morpholine	5.0	0	0	80	6	1
Morpholine	1.1	87	3	8	2	0

a) The reactions were carried out under the following conditions; 6 kbar, 50 °C, 20 h, in THF. b) Amount of amine was shown in molar equivalent.

Table 7. ^{1}H NMR Data of the Reaction Products[a)]

Product	H_a	H_b	H_c	NCH_2	CH_3	CH_2	OCH_2
16a	7.59(d)	6.80(dd)	7.04(d)	3.15	1.11	—	—
16b	7.63(d)	6.61(dd)	6.84(d)	3.19	—	1.98	—
16c	7.74(d)	6.77(dd)	7.05(d)	3.04	—	—	3.83
17b	8.03(d)	6.35(dd)	6.49(d)	3.36	—	2.06	—
17c	7.98(d)	6.67(dd)	6.81(d)	3.31	—	—	3.83
18a	7.94(d)	6.10(dd)	6.13(d)	3.17 3.39	1.11 1.21	—	—
18b	7.81(d)	5.93(dd)	5.68(d)	3.20 3.31	—	1.93 2.00	—
18c	7.98(d)	6.43(dd)	6.31(d)	3.05 3.32	—	—	3.83
20a	7.75(s)	7.14(s)	—	3.15	1.13	—	—
20c	7.89(s)	7.17(s)	—	3.03	—	—	3.81
22a	7.86(s)	6.54(s)	—	3.14 3.24	1.11 1.13	—	—
22b	7.87(s)	5.94(s)	—	3.19 3.54	—	1.97	—
22c	7.98(s)	6.53(s)	—	3.04 3.16	—	—	3.83 3.87
24c	7.18(d)	7.06(d)	—	2.93	—	—	3.70
25a	7.08(s)	—	—	3.05	1.04	—	—
25b	6.66(s)	—	—	3.25	—	1.98	—
25c	6.78(s)	—	—	3.30	—	—	3.90
26b	6.24(s)	—	—	3.20	—	1.90	—
26c	6.95(s)	—	—	2.93	—	—	3.72
27b	5.97(d)	5.60(d)	—	3.22 3.27	—	1.93 2.00	—
27c	6.58(d)	6.44(d)	—	2.97 3.21	—	—	3.76 3.85
28b	5.12(s)	—	—	3.33 3.40	—	1.93 1.97	—
28c	6.36(s)	—	—	2.94 3.17	—	—	3.74 3.83

a) Chemical shifts were shown in δ.

position of **20**, and that **21** produced by the first substitution of **19** was consumed completely in the second substitution.

Product ratio of the reaction of 2,4,6-trichloronitrobenzene (**23**) is affected by the amine used. When five molar equivalents of amine was used, diethylamine gave para-mono substitution product **25a** as a sole product. Pyrrolidine gave trisubstitution product **28b**, and morpholine gave ortho-ortho disubstitution product **26c** as major products (Table 6-2). These results suggest that the order of reactivity of amines in this reaction is as follows; pyrrolidine>morpholine>diethylamine.

The reaction with 1.1 molar equivalent of amine gave mono substitution product as a major product. Pyrrolidine yielded para-mono product **25b** which was confirmed by the singlet signal of aromatic proton observed at 6.66 in its ^{1}H NMR spectrum. On the other hand, morpholine gave ortho-mono product **24c** which has two doublet signals of aromatic protons at 7.06 and 7.18. The difference in the behavior of these two amines may be attributed mainly to the bulkiness of amines.

Experimental

Melting points were measured with a Yanagimoto Melting Point Apparatus and not corrected. IR spectra were recorded on a Perkin-Elmer model 983. ^{1}H NMR spectra were measured on a Varian EM-390 in a $CDCl_3$ solution using TMS as an internal standard.

Materials. All aromatic halides were purified by recrystallization or distillation of commercial compounds just before use. THF and amines were purified by distillation under an atmosphere of nitrogen after appropriate drying procedure.

General Procedure of the S_NAr Reaction of Aromatic Halides with Primary or Secondary Amines under High Pressure. A THF solution (5 cm^3) of aromatic halide (1.0 mmol) and amine (5.0 mmol) was pressurized in Teflon capsule under the cited reaction conditions using Hikari Kouatsu High Pressure Apparatus.[3] After the removal of solvent under reduced pressure the residue was suspended in benzene, and amine hydrohalide was removed by filtration on glass filter and the solid was washed several times with benzene (10 cm^3). The combined benzene solution was separated by medium pressure column chromatography (silica gel, benzene). Products were characterized by IR and ^{1}H NMR spectra. The characteristic ^{1}H NMR data were listed in Tables 4 and 7. In their IR spectra, absorptions of aromatic NO_2 were observed in the regions of 1480—1520 and 1330—1350 cm^{-1}, and the aromatic absorption near 1600 cm^{-1} was very strong. The results of elemental analysis were shown in Table 8. The reactions with 1.1—1.2 molar equivalent of amines were carried out using 1.0 cm^3 (ca. 7.2 mmol) of triethylamine and treated in the same way.

The Reactions of *p*-Nitrohalobenzenes with DABCO or Quinuclidine under High Pressure. The reaction was carried out in the similar manner under the following reaction conditions; 6.0 kbar, 50 °C, 75 h, in THF. After the reaction was over, the yellow crystals that precipitated in the Teflon capsule were collected by filtration and washed with benzene several times, and dried. The melting points of the salts were higher than 300 °C. The elemental analyses of these products did not give correct results for salts **8**[11] because purification of the salts was difficult due to the low solubility in usual organic solvents.

Table 8. Melting Points and Results of Elemental Analysis of the Products[a)]

Product	Mp θ_m/°C	Found/% C	Found/% H	Found/% N	Calcd/% C	Calcd/% H	Calcd/% N	Molecular formula
3j	b)	64.86	8.23	12.53	64.84	8.16	12.60	$C_{12}H_{18}N_2O_2$
10b	76—77	53.05	4.91	12.36	52.99	4.89	12.36	$C_{10}H_{11}N_2O_2Cl$
10c	100—101[c)]							
12c	50—51[c)]							
14b	101—103	53.05	4.90	12.34	52.99	4.89	12.36	$C_{10}H_{11}N_2O_2Cl$
14c	135—136[c)]							
16b	86—87	52.99	4.89	12.33	52.99	4.89	12.36	$C_{10}H_{11}N_2O_2Cl$
16c	75—76[c)]							
18b	140—141	64.55	7.37	16.09	64.35	7.33	16.08	$C_{14}H_{19}N_3O_2$
18c	175—176	57.42	6.55	14.21	57.33	6.53	14.33	$C_{14}H_{19}N_3O_4$
22b	160—161	57.11	6.15	14.21	56.88	6.13	14.21	$C_{14}H_{18}N_3O_2Cl$
22c	183—185	51.52	5.61	12.75	51.30	5.54	12.82	$C_{14}H_{18}N_3O_4Cl$
24c	160—161	43.47	3.66	10.11	43.34	3.64	10.11	$C_{10}H_{10}N_2O_3Cl_2$
25b	87—88	46.24	3.90	10.67	46.00	3.86	10.73	$C_{10}H_{10}N_2O_2Cl_2$
25c	143—144	43.34	3.64	10.06	43.34	3.64	10.11	$C_{10}H_{10}N_2O_3Cl_2$
26b	183—184	56.85	6.22	14.11	56.85	6.13	14.21	$C_{14}H_{18}N_3O_2Cl$
26c	137—139	51.53	5.62	12.73	51.30	5.54	12.82	$C_{14}H_{18}N_3O_4Cl$
27b	169—170	56.95	6.16	14.31	56.85	6.13	14.21	$C_{14}H_{18}N_3O_2Cl$
28b	144—145	65.70	7.99	16.75	65.43	7.93	16.96	$C_{18}H_{26}N_4O_2$
28c	234—236	57.40	6.95	14.60	57.13	6.93	14.80	$C_{18}H_{26}N_4O_5$

a) Other products omitted in this Table did not give correct analytical results because of difficulty in purification due to low yields or low melting point of the products. b) Listed in Table 2. c) Melting points reported in literature: **10c** 97 °C; **12c** 45—46 °C; **14c** 130 °C; **16c** 70—71 °C; M. D. Nair and R. Adams, *J. Am. Chem. Soc.*, **83**, 3518 (1961).

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11) Although the correct elemental analyses were not obtained, the authors tentatively propose the structure of these salts as **8**.