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The Reactions of 2-Substituted 4-Chloro-6-(2-hydroxy-1-naphthyl)-1,3,5-triazines with Several Nucleophiles

Shigeo Tsunoda, Yoji Hashida, Shizen Sekiguchi, and Kohji Matsui

Department of Chemistry, Faculty of Engineering, Gunma University, Tenjincho, Kiryu, Gunma 376

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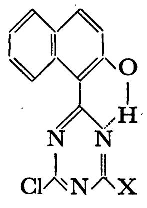
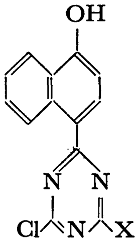
The nucleophilic substitution reactions of 2-methoxy- and 2-diethylamino-4-chloro-6-(2-hydroxy-1-naphthyl)-1,3,5-triazines (**1**) with aniline, diethylamine, sodium azide, and sodium methoxide were carried out and compared with the reactions of the corresponding derivatives of 4-chloro-6-(4-hydroxy-1-naphthyl)-1,3,5-triazine (**2**) and 4-chloro-6-(1-naphthyl)-1,3,5-triazine (**3**). Compound **1** was found to be more reactive than the corresponding (**2**) and (**3**), not only in the reactions of a neutral molecule, but also in those of anionic species. The results of the reactions of neutral species are interpreted in terms of the difference in solvation toward the substrates; however, the loss of coplanarity between the naphthalene and triazine nuclei may be responsible for the high reactivity of Compound **1** in the reactions of anionic species.

It is well known that, in nitrogen heteroaromatic compounds possessing an *O*-hydroxyaryl group in the 2-position, an intramolecular hydrogen-bond formation between the ring nitrogen and the hydroxyl group takes place.1) In these cases, the reactivity of the heteroaromatic compound is expected to be affected more or less by the chelate formation. If the compound has an active halogen atom in the heteroaromatic nucleus, its reactivity towards nucleophiles will be different from that of the corresponding non-chelated compound. However, no such effect of chelation upon the reactivity has yet been revealed. This paper will report on the nucleophilic substitution reactions of 2-substituted 4-chloro-6-(2-hydroxy-1-naththyl)-1,3,5-triazines with some nucleophiles as examples; the experiments were undertaken in order to reveal the effect of chelate formation on the reactivity of nitrogen heteroaromatic compounds.

Results and Discussion

Preparation of Triazine Derivatives. The nucleophilic substitution reactions of 2-methoxy- and 2-diethylamino-4-chloro-6-(2-hydroxy-1-naphthyl)-1,3,5-triazines (**1**) were carried out and compared with the reactions of the corresponding derivatives of 4-chloro-6-(4-hydroxy-1-naphthyl)-1,3,5-triazine (**2**) and 4-chloro-6-(1-naphthyl)-1,3,5-triazine (**3**).


(**1**)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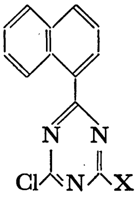

(**3**)

X: $-OCH_3$, $-NEt_2$

Compounds **1** and **2**, containing the methoxy group in the triazine nucleus, were prepared by the Friedel-Crafts reaction of 2,4-dichloro-6-methoxy-1,3,5-triazine with 1- and 2-naphthol in the presence of aluminium chloride, while compounds containing the diethylamino group were obtained by the condensation of cyanuric chloride with 1- and 2-naphthol in the presence of aluminium chloride,2) followed by treatment with diethylamine. (1-Naphthyl)-1,3,5-triazine derivatives (**3**) were obtained by the reaction of cyanuric chloride with 1-naphthylmagnesium bromide, followed by treatment with methanol in combination with sodium carbonate. Table 1 lists the compounds thus obtained.

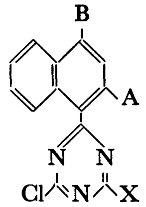
In order to estimate the structural effects upon the reactivity, kinetic measurements of the reactions of Compounds **1**, **2**, and **3** with some nucleophilic reagents were carried out. Diethylamine and aniline were used as the neutral nucleophilic reagents, while sodium azide and sodium methoxide were used as the anionic ones.

It is well known that the ordinary reactions of chloro-1,3,5-triazines with such nucleophilic reagents as amines3) and alkoxides4) take place very readily. The reactions in this paper were also found to take place without any appreciable side reactions by checking the reaction mixtures by tlc after the reactions had been completed; in every case, the substitution product was obtained in an almost quantitative yield, showing that these reactions are well suited to kinetic measurements. Table 2 lists the substitution products thus obtained.

Kinetics of the Reactions of 2-Substituted 4-Chloro-6-(2-hydroxy-1-naphthyl)-1,3,5-triazines with Diethylamine, Aniline, and Sodium Azide. In this study, only the derivatives of α-naphthyl-1,3,5-triazine were investigated, because the effect of the α-naphthyl group upon the reactivity of the chlorine atom is assumed to differ appreciably from that of the β-naphthyl group.5) However, some structural differences which would affect the reactivities of these compounds can be seen between Compounds **1** and **2**. For example, there is a difference in the position of the naphthalene nucleus where the hydroxyl group is attached, and a chelate ring is formed in Compound **1**, but not in the case of Compound **2**.

In 6-substituted 2-aryl-4-chloro-1,3,5-triazines, it is generally considered that the strong electron-donating hydroxyl group in the aryl group lowers the reactivity of the active chlorine atom, not only in the *para* but also in the *ortho* position, by increasing the electron density of the triazine nucleus. Thus, if the chelation were ineffective with regard to the reactivity of the chlorine atom, both 2-hydroxy-1-naphthyl- and 4-hydroxy-1-naphthyl groups would lower the reactivity in a similar manner and the difference in substituent

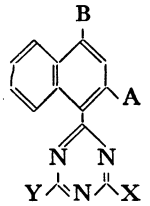
Table 1. Derivatives of 1-naphthyl-1,3,5-triazine



Compound	X	A	B	Mp (°C)	Solvent for recryst.	Anal. (%) Found C	Found H	Found N	Calcd C	Calcd H	Calcd N
1-1	-Cl	-OH	-H	214—215 (215—216)[a]	Dioxane	—	—	—	—	—	—
1-2	-OMe	-OH	-H	168—169	Ligroin	58.64	3.49	14.62	58.44	3.50	14.82
1-3	$-NEt_2$	-OH	-H	104.5—105.5	Ligroin	62.14	5.22	17.07	62.10	5.21	17.03
2-1	-Cl	-H	-OH	239 (decompn)	——[b]	53.71	2.47	14.24	53.45	2.41	14.38
2-2	-OMe	-H	-OH	>300	Dioxane	58.87	3.54	14.71	58.44	3.50	14.82
2-3	$-NEt_2$	-H	-OH	124 (decompn)	——[c]	62.48	5.27	17.15	62.10	5.21	17.03
3-1	-Cl	-H	-H	171—172	Benzene	56.15	2.55	15.20	56.54	2.55	15.21
3-2	-OMe	-H	-H	119—120	Ligroin	62.23	3.70	15.61	61.88	3.70	15.46

a) CIBa, Brit. P., 914798 (1963). b) Purified by column chromatography on silica gel, using a mixture of benzene and acetone (10 : 1 by volume) as the developing solvent. c) Purified by column chromatography on silica gel, using a mixture of benzene and acetone (20 : 1 by volume) as the developing solvent.

Table 2. Derivatives of 1-naphthyl-1,3,5-triazine



X	Y	A	B	Mp (°C)	Solvent for recryst.	Anal. (%) Found C	Found H	Found N	Calcd C	Calcd H	Calcd N
-OMe	$-NHC_6H_5$	-OH	-H	200—201	Ligroin	69.50	4.68	16.20	69.75	4.68	16.27
-OMe	$-NHC_6H_5$	-H	-OH	194—195	Benzene	70.10	4.74	16.28	69.75	4.68	16.27
$-NEt_2$	$-NEt_2$	-OH	-H	126—127	Ligroin	69.08	7.34	19.47	69.01	7.45	19.16
$-NEt_2$	$-NEt_2$	-H	-OH	118—119	Benzene	69.07	7.55	19.36	69.01	7.45	19.16
$-NEt_2$	$-N_3$	-OH	-H	93—94	Ligroin	60.89	5.25	28.95	60.88	5.11	29.24
$-NEt_2$	$-N_3$	-H	-OH	102—103	Benzene-Petroleum ether	60.78	5.47	28.88	60.88	5.11	29.24
-OMe	$-N_3$	-OH	-H	163—164	Benzene	57.25	3.44	28.45	57.14	3.43	28.56
-OMe	$-N_3$	-H	-OH	198—199	Benzene	57.24	3.44	28.62	57.14	3.43	28.56
-OMe	$-N_3$	-H	-H	98—99	Ligroin	60.75	3.64	30.87	60.42	3.62	30.20
-OMe	-OMe	-OH	-H	146—147	Ligroin	63.73	4.35	—	63.59	4.63	—
-OMe	-OMe	-H	-OH	203.5—204.5	Benzene	63.48	4.45	—	63.59	4.63	—
$-NEt_2$	-OMe	-OH	-H	87—88	Ligroin	66.86	6.30	17.21	66.65	6.22	17.27
$-NEt_2$	-OMe	-H	-OH	137—138	Benzene	66.50	6.22	17.29	66.65	6.22	17.27

Table 3. Rate constants for the nucleophilic reactions of 2-substituted 4-chloro-6-(hydroxy-1-naphthyl)-1,3,5-triazines

Compound	k_2 ($l\cdot mol^{-1}\cdot s^{-1}$)
With aniline at 35 °C	
1-2	4.28×10^{-3}
2-2	2.28×10^{-5}
With diethylamine at 20 °C	
1-3	2.36×10^{-2}
2-3	2.12×10^{-4}

effect between the two groups would not be large. However, as is apparent from Tables 3 and 4, the hydroxyl group was found to affect the reactivity of chloro-triazinyl-naphthalene in very different manners depending upon its position in the naphthalene nucleus. As compared with the case of Compound **3**, it is apparent that the hydroxyl group in the *para* position lowered the reactivity, as was to be anticipated. The hydroxyl group in the *ortho* position, on the contrary, raised the reactivity in spite of its powerful electron-donating character; in every case, the reactivity varied in the following order:

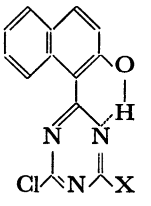
Compound **1** > **3** > **2**

Therefore, it may be reasonable to assume that the high reactivity of *O*-hydroxy compounds is mainly ascribable to the presence of the chelate ring in these compounds.

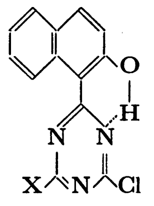
The hydroxyl group of these compounds can dissociate into anions whose reactivities should be different from those of the neutral species. Therefore, it may be necessary to ascertain the actual species in the above reactions. As the absorption spectra of these compounds are different from those of their anions, the dissociation can be checked spectrophotometrically to determine that Compounds **1** and **2** react practically like the neutral molecule in every case under the present reaction conditions.

The activation by the intramolecular hydrogen bond seems in this case to be a phenomenon similar to the acid catalysis in the reactions of chloro-triazines.[6]

However, from the activation parameters for the reactions with sodium azide, it is clear that the high reactivity of Compound **1** does not depend on the energy of activation, but results mainly from the difference in the entropy of activation. Thus, even if the chelation raised the reactivity by reducing the electron density of the triazine nucleus in a manner similar to the acid catalysis, this would not be the major reason for the high reactivity of the *O*-hydroxy compound; the assumption may also be supported by the fact that the differences in rate constant were rather larger in the cases of the derivatives containing the methoxyl group than in those of the derivatives having the diethylamino group, in spite of the fact that the order of the stability of chelation is known to be **1-2**<**1-4**.[7] In these derivatives, the two types of chelate-ring formation shown below are possible. Although it is obscure at present which is the true chemical species in the actual reactions under the present experimental conditions, the results can be reasonably explained as follows.



(**1**)′



(**1**)″

In these cases, a difference in solvation between two compounds is assumed to be responsible for the difference in reactivity.

In the initial state of the reaction (in the reaction with sodium azide, a mixture of dioxane and water was used as the solvent), the hydroxyl group and the ring nitrogen atoms of the substrates would be the principal centers for solvation. Thus, in the case of Compound **1** the solvation may be hindered by the chelate formation, because by the chelate formation the two centers for solvation should partially negate each others abilities to solvate.

In the transition state, a negative charge poured into the triazine nucleus from the reagent (N_3^-) would spread over the three ring nitrogen atoms, and the solvation would increase with an increase in the electron density of the triazine nucleus. However, in the transition state of Compound **1** the chelation would become stronger; thus, the increase in solvation in this case would be inferior to that of the case of Compound **2**.

Table 4. Rate constants for the reactions of 2-substituted 4-chloro-6-(1-naphthyl)-1,3,5-triazines with sodium azide

Compound	k_2 ($l\cdot mol^{-1}\cdot s^{-1}$)			Activation parameters	
	35 °C	45 °C	55 °C	ΔE kcal/mol	$\Delta S^{\neq}$ cal/deg·mol (35 °C)
1-3	0.85×10^{-4}	1.77×10^{-4}	4.70×10^{-4}	16.7	−25.3
2-3	1.39×10^{-5}	2.26×10^{-5}	5.59×10^{-5}	13.5	−39.1

Compound	k_2 ($l\cdot mol^{-1}\cdot s^{-1}$)				Activation parameters	
	15 °C	25 °C	35 °C	45 °C	ΔE kcal/mol	$\Delta S^{\neq}$ cal/deg·mol (25 °C)
1-2	1.29×10^{-2}	2.77×10^{-2}	7.03×10^{-2}	——	15.3	−15.7
2-2	——	0.77×10^{-3}	1.94×10^{-3}	4.20×10^{-3}	15.4	−23.1
3-2	——	4.38×10^{-3}	9.15×10^{-3}	2.05×10^{-2}	14.5	−22.5

In other words, although Compound **2** would solvate water more strongly than Compound **1** during the full course of the reaction, the difference in solvation degree between the two would be larger in the transition state than in the initial one.

Thus, in spite of the advantage in the energy of activation, Compound **2** was less reactive because of the disadvantage in the entropy term, as can be seen by comparing the reactions of **1–3** and **2–3**. A similar relation is also seen in the reactions of **1–2** and **2–2**.

Kinetics of the Reactions with Sodium Methoxide. The reactions of Compounds **1** and **2** with sodium methoxide were carried out in a mixture of methanol and acetone (1 : 1, by volume); the rate constants for the reactions are listed in Table 5.

Table 5. Rate constants for the reactions of 2-substituted 4-chloro-6-(hydroxy-1-naphthyl)-1,3,5-triazines with sodium methoxide

Compound	k_2 ($l\cdot mol^{-1}\cdot s^{-1}$) at 20 °C	Compound	k_2 ($l\cdot mol^{-1}\cdot s^{-1}$) at 30 °C
1-2	2.03	**1-3**	4.85×10^{-3}
2-2	4.55×10^{-2}	**2-3**	4.46×10^{-4}

In these reactions, Compound **1** was again found to be more reactive than **2**. In the reactions with sodium methoxide, the substrates are assumed to dissociate into their anions. In fact, most of the substrates were found to react practically as their anions, as can be seen in Table 6.[8] It is obvious from Table 6 that the rate constants of the two compounds are of an anionic species, regardless of the substituent in the triazine nucleus. However, in the case of Compound **1–3** about 3% of the substrate was found to remain as an undissociate form in the solution. Thus, the rate constant of Compound **1–2** was practically that of the anionic species; however, when the substituent is $-NEt_2$ the rate constant probably results from the reactions of anionic and neutral substrates. Therefore, the apparent rate constant may vary with the concentration of sodium methoxide. In fact, when the apparent rate constants were plotted against the concentration of sodium methoxide, a curve converging to a constant value with an increase in the concentration of the base was obtained, as is shown in Fig. 1.

Table 6. Ratios of anion to neutral molecule of 2-substituted 4-chloro-6-(hydroxy-1-naphthyl)-1,3,5-triazines in methanol

Compound	C^-/C	Compound	C^-/C
1-3	32	**1-2**	120
2-3	1000	**2-2**	3900

C^-: Concentration of ionized molecule.
C: Concentration of non-ionized molecule.

The results indicate that the anion is less reactive than the neutral substrate, and that the converged value (about 2.9×10^{-3} l/mol·s) in the high-base-concentration region is the true rate constant of the anionic species. Thus, in the reaction of anionic species, Compound **1** was also more reactive than the corresponding Compound **2**; it may be of interest that Compound **1** is more reactive even in the absence of an intramolecular hydrogen bond.

Table 7. Effect of concentration of $NaOCH_3$ on apparent rate constant of compound **1-3**

[$NaOCH_3$] (mol/l)	k_2' ($l\cdot mol^{-1}\cdot s^{-1}$) at 30 °C
18.67×10^{-2}	2.90×10^{-3}
14.58×10^{-2}	3.14×10^{-3}
9.65×10^{-2}	4.07×10^{-3}
9.14×10^{-2}	4.85×10^{-3}
7.18×10^{-2}	6.04×10^{-3}
4.96×10^{-2}	1.08×10^{-2}

[Substrate] : 2×10^{-2} mol/l.

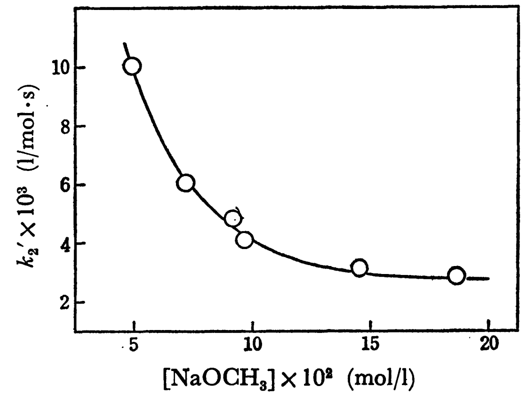
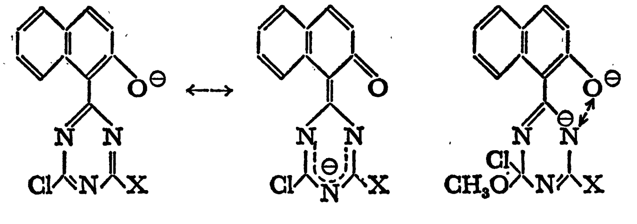


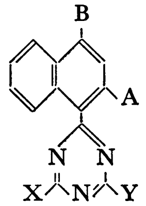
Fig. 1. Dependence of apparent rate constants of Compound **1-3** on concentration of sodium methoxide.

In the case of Compound **1**, one of the ring nitrogen atoms and one of the naphthoxide oxygen atom are assumed to be located very close to each other. Therefore, in the transition state there should be a repulsion between two atoms of same kinds of negative charge, leading to a loss of coplanarity between the naphthalene and triazine nuclei.



In the reaction of anionic species, the negative charge poured into the triazine nucleus from the naphthoxide anion should lower the reactivity of the substrate, regardless of the type of compound. However, in the case of Compound **1**, this lowering of reactivity should be prevented in some degree by the loss of copolanarity between the aromatic rings. Thus, Compound **1** would be more reactive than Compound **2** even in the reaction with sodium methoxide. As a whole, in the reactions with nucleophiles, Compound **1** was more reactive than the corresponding Compound **2**, regardless of the nucleophile used. The chelation

TABLE 8. $\mathrm{p}K_a$ VALUES OF (HYDROXY-1-NAPHTHYL)-1,3,5-TRIAZINES IN METHANOL AT 20 °C



X	Y	A	B	$\mathrm{p}K_a'$ [a]	Indicator[c]	Buffer
-OMe	-Cl	-OH	-H	13.2[b]	——	——
-OMe	-OMe	-OH	-H	14.0	Thymol Blue	SBA
$-NEt_2$	-Cl	-OH	-H	14.2	Thymol Blue	SBA
$-NEt_2$	$-NEt_2$	-OH	-H	16.2	*O-t*-Butylphenol	$NaOCH_3$
-OMe	-Cl	-H	-OH	11.7	Bromocresol Purple	SBA+SBE
-OMe	-OMe	-H	-OH	12.4	Bromothymol Blue	SBA+SBE
$-NEt_2$	-Cl	-H	-OH	12.7	Bromothymol Blue	SBA+SBE
$-NEt_2$	$-NEt_2$	-H	-OH	13.6	Phenol Red	SBA+SBE

SBA = Sodium barbiturate. SBE = Sodium benzoate.

a) $\mathrm{p}K_a'$ denotes the ionization constant of (hydroxy-1-naphthyl)-1,3,5-triazine in methanol. b) Calculated using a linear relation between $\mathrm{p}K_a'$ and $\sum\sigma_m$ values of two substituents in the 1,3,5-triazine nucleus [Y. Ohto, Y. Hashida, S. Sekiguchi, and K. Matsui, *Bull. Chem. Soc. Japan*, **47**, 1301 (1974)], because the compound was found to be too unstable to measure an accurate $\mathrm{p}K_a'$ value in an alkaline solution; in this calculation the substituent constant of $-NMe_2$ was substituted for that of $-NEt_2$. c) Indicator employed for the measurement of $\mathrm{p}K_a'$ of triazines as the primary standard.

in Compound **1** surely plays an important role in the high reactivity; however, it has become apparent that the function of chelation is not a mere lowering of the electron density of the triazine nucleus.

Experimental

All melting points are uncorrected.

Materials. *2,4-Dichloro-6-(2-hydroxy-1-naphthyl)-1,3,5-triazine (**1-1**)*: Compound **1-1** was prepared by the reaction of cyanuric chloride with 2-naphthol in the presence of aluminium chloride in benzene.[2]

*2,4-Dichloro-6-(4-hydroxy-1-naphthyl)-1,3,5-triazine (**2-1**)*: A solution of 40.6 g (0.22 mol) of cyanuric chloride and 32.1 g (0.22 mol) of 1-naphthol in 350 ml of benzene was added, drop by drop, into a mixture of 30.7 g (0.23 mol) of aluminium chloride in 200 ml of benzene at room temperature. After stirring for 2 h under reflux, the mixture was poured into 1 l of ice water containing 200 ml of a concd hydrochloric acid solution. The precipitate thus formed was filtered, dried, and purified by column chromatography on silica gel using a mixture of benzene and acetone (10 : 1 by volume) to give an analytical sample. Mp 239 °C (decompn.). This product gave 2,4-dimethoxy(4-hydroxy-1-naphtnyl)-1,3,5-triazine (mp 204—205 °C)[2] upon treatment with an excess of sodium methoxide in methanol.

*2-Diethylamino-4-chloro-6-(2-hydroxy-1-naphthyl)-1,3,5-triazine (**1-3**) and 2-Diethylamino-4-chloro-6-(4-hydroxy-1-naphthyl)-1,3,5-triazine (**2-3**)*: A typical preparation is shown in the case of Compound **1-3**. A solution of 7.5 g (0.1 mol) of diethylamine in 100 ml of acetone was added, drop by drop, into a solution of 14.6 g (0.05 mol) of Compound **1-1** in 250 ml of acetone at 0 °C. After stirring for 3 h at 0—5 °C, the reaction mixture was poured into 1 l of ice water. The precipitate was then filtered and dried to give a crude product in an almost quantitative yield. The recrystallization of the product from ligroin gave an analytical sample of Compound **1-3**. Mp 104.5—105.5 °C.

*2-Methoxy-4-chloro-6-(2-hydroxy-1-naphthyl)-1,3,5-triazine (**1-2**) and 2-Methoxy-4-chloro-6-(4-hydroxy-1-naphthyl)-1,3,5-triazine (**2-2**)*: A typical preparation is shown in the case of Compound **1-2**. A solution of 10.5 g (0.073 mol) of 2-naphthol in 200 ml of benzene was added, drop by drop, into a mixture of 13.1 g (0.073 mol) of 2,4-dichloro-6-methoxy-1,3,5-triazine and 9.7 g (0.073 mol) of aluminium chloride at room temperature. After stirring at 40—50 °C for 8 h, the mixture was poured into ice water containing hydrochloric acid as has been described above. The precipitate thus formed was filtered and washed with dilute hydrochloric acid, with cold water, and then with a small amount of acetone to give a crude product in a yield of 80%. The recrystallization of the product from ligroin gave an analytical sample. Mp 168—169 °C.

*2,4-Dichloro-6-(1-naphthyl)-1,3,5-triazine (**3-1**) and 2-Methoxy-4-chloro-6-(1-naphthyl)-1,3,5-triazine (**2-3**)*: A solution of 36.9 g (0.2 mol) of cyanuric chloride in 300 ml of dry ether was added all at once into a mixture of Grignard reagent prepared from 41.4 g (0.2 mol) of 1-bromonaphthalene and 5.0 g (0.2 mol) of magnesium in 200 ml of dry ether. After the mixture had been stirred overnight at room temperature, the precipitate was filtered and washed with cold dilute hydrochloric acid and then with water to give a crude product of Compound **3-1** in a 55% yield.

A solution obtained by dissolving 1.2 g (0.05 mol) of sodium in 150 ml of methanol was added, drop by drop, into a solution of 13.8 g (0.05 mol) of Compound **3-1** in a mixture of 450 ml of dioxane and 200 ml of methanol at 0 °C. After stirring for 3 h, the solution was poured into 1.5 l of ice water. The precipitate was filtered and dried to give Compound **3-2** in an almost quantitative yield.

Kinetic Measurements. Runs were carried out with an excess of the nucleophile (the substrate and the nucleophile were used in a molar ratio of about 1 : 5; the initial concentration of the former was about 0.02 mol/l). In the reaction with aniline, acetone was used as the solvent; the reaction in aliquot portions was stopped by dilution with cold acetone (−20 °C), followed by a titration of the hydrochloric acid with a standard acetone solution of triethylamine, using Neutral Red as the indicator.

In the reaction with diethylamine (solvent : acetone), the reaction in aliquote portions was stopped by pouring in an excess of an acetone solution of hydrochloric acid of a known concentration; the reagent consumed was estimated by back-titration with a standard acetone solution of triethylamine, using Neutral Red as the indicator.

In the reaction with sodium azide (solvent: a mixture of dioxane and water in a ratio of 4 : 1 by volume), reaction in aliquot portions was stopped by pouring in a mixture of carbon tetrachloride and water; the chloride in the water layer was estimated by titration with silver nitrate by the Volhard method in the presence of a small amount of nitrobenzene.[9)]

In the reaction with sodium methoxide (solvent: a mixture of acetone and methanol in a ratio of 6 : 4 by volume), reaction in aliquot portions was stopped by pouring in an excess of a hydrochloric acid solution of a known concentration, followed by back-titration with a standard sodium hydroxide solution, using Methyl Red as the indicator. For the reactions with aniline and diethylamine, the rate constants were calculated from Eq. (1):

$$k_2t = 2.303/b-2a\cdot\log a(b-2x)/b(a-x) \qquad (1)$$

where *a* and *b* are the initial concentrations of the substrate and the nucleophile respectively, and where *x* is the concentration of the product at time *t*. On the other hand, in the cases of sodium azide and sodium methoxide Eq. (2) was used:

$$k_2t = 2.303/b-a\cdot\log a(b-x)/b(a-x) \qquad (2)$$

However, in the reactions of Compounds **1** and **2** with sodium methoxide, the rate constants were calculated using *b-a* as the initial concentration of nucleophile, because equimolar proportions of the substrate and the nucleophile should combine to form an anion of the substrate prior to the substitution reaction.

The mean values of not less than four separately determined values of k_2, which agreed within 5%, were taken as the rate constants for these reactions; they are listed in Tables 3, 4, 5, and 7.

pK$_a$ *Measurements.* The pK_a values of naphthol derivatives in methanol were determined by the indicator method using Eq. (3);[10)] the ratio of the acidic to the basic form of an indicator and naphthol derivatives was determined spectrophotometrically:

$$\mathrm{p}K_a' = \mathrm{p}K_I + \log C_{Ib}\times C_{Na}/C_{Ia}\times C_{Nb} \qquad (3)$$

where pK_a'=pK_a value of naphthol derivative, pK_I=the pK_a value of an indicator; C_{Ia} and C_{Ib} are the concentrations of the acidic and basic forms of an indicator respectively, and C_{Na} and C_{Nb} are the concentrations of the acidic and dissociated forms of the naphthol derivative respectively. The results obtained are summarized in Table 8.

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