Structure and Reactivity of Heterosubstituted Nitriles. Part XIV.[1] Kinetics and Mechanisms of Cyanogen Bromide Reactions with *N*-Alkylanilines

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The third-order rate constants for formation of *N*-alkyl-*N*-arylcyanamides from cyanogen bromide and *N*-alkyl-*N*-arylamines in the presence of hydroxylic compounds in acetone have been determined. The slow step of the reaction is nucleophilic attack of amine on cyanogen bromide. This probably implies a six-membered ring transition state, as seems proved by a study of electronic and steric effects, entropy and enthalpy of activation, and solvent effects.

In previous Parts a six-membered ring transition state was presumed for the cases of addition of *N*-alkylanilines in the catalysis of phenols and for the addition of phenols in the catalysis of *N*-alkylanilines to aryl cyanates.[1-5] Both reactions have trimolecular kinetics.[1-5] Electronic and steric effects of substituents in the aromatic rings,[4] reaction entropy and enthalpy,[2] and solvent effects [1,5] support this mechanism.

Methanol addition to aryl cyanates [6] was found to be autocatalysed by the reaction product, aryl *C*-methoxyformimidate and the addition can develop through six-membered ring transition states.

In this paper we have studied the reactions of *N*-alkylanilines with cyanogen bromide to find new arguments for this mechanism.

RESULTS AND DISCUSSION

The kinetics of the reaction were followed by conductimetric measurements on the reaction system containing a significant excess of *N*-methylaniline.

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Preliminary investigations of the N-methylaniline reaction with cyanogen bromide showed that in anhydrous acetone the reaction is very slow. Addition of water significantly increases the reaction rates.

TABLE 1

Rate constants for the reaction of cyanogen bromide with N-methylaniline in aqueous acetone

Temp. (°C)	[BrCN]/M	[PhNHMe]/M	$[H_2O]$/M	$10^3k_1/s^{-1}$ *	$10^3k_2/l^2\ mol^{-2}\ s^{-1}$ †	$10^3/l^2\ mol^{-2}\ s^{-1}$ ‡	Average $k_3 \pm p$ §
30	0.0215	0.325	6.24	5.20	16.0	2.56	
	0.0501	0.496	6.21	7.66	15.4	2.48	
	0.0199	0.508	6.04	7.31	14.4	2.38	
	0.0196	0.631	6.03	10.72	17.0	2.82	
	0.0876	0.941	5.86	14.62	15.5	2.64	2.589 ± 0.04
	0.0195	0.425	2.75	3.44	8.10	2.95	
	0.0168	0.448	8.28	9.32	20.8	2.51	
	0.0180	0.459	11.16	12.90	28.2	2.52	
	0.0180	0.472	11.26	13.22	28.1	2.49	
	0.0205	0.462	16.45	19.32	41.9	2.54	
20	0.0204	0.458	5.75	4.32	9.40	1.64	1.643 ± 0.02
	0.0182	0.470	11.28	8.38	17.85	1.58	
	0.0178	0.446	17.15	13.18	29.40	1.71	
10	0.0176	0.458	5.62	2.31	5.04	0.90	0.918 ± 0.01
	0.0179	0.467	5.69	2.23	4.88	0.86	
	0.0202	0.472	11.28	5.12	10.85	0.96	
	0.0232	0.484	17.84	8.19	16.90	0.95	
12	0.0177	0.463	5.69	1.09	2.36	0.415	0.415

* Pseudo-first-order rate constant. † Second-order rate constants $k_2 = k_1/[PhNHMe]$. ‡ Third-order rate constants $k_3 = k_2/[H_2O]$. § $p = 0.67[\Sigma(\bar{X} - X_i)^2/n^2]^{1/2}$.

Table 1 contains the pseudo-first-order rate constants (k_1) for the reaction of N-methylaniline and cyanogen bromide in the presence of various concentrations of V-methylaniline and water in acetone at different temperatures. Figure 1 shows the plot of pseudo-first-order rate constants against the N-methylaniline concentration. A straight line demonstrates first-order kinetics with respect to amine. Second-order rate constants (k_2) are presented in Table 1. Figure 2 shows a plot of second-order rate constants against water concentration. Contrary to all expectation the dependence of second-order rate constants upon the water concentration is also a straight line. This suggests that the reaction is first-order in water and insensitive to changes in solvent polarity. Third-order rate constants (k_3) are also presented in Table 1.

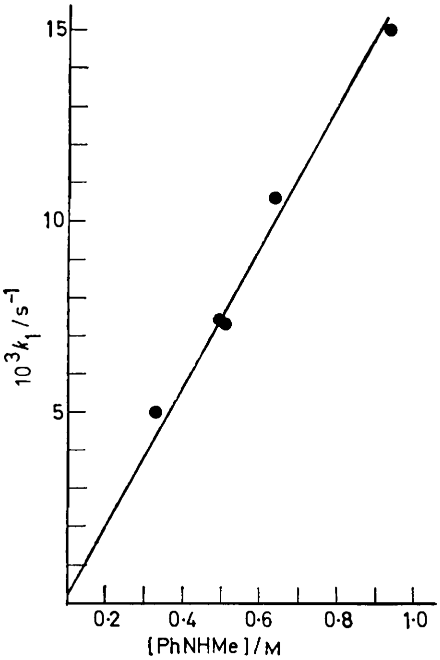

FIGURE 1 Plot of pseudo-first-order rate constants of the cyanogen bromide reaction against the concentration of N-methylaniline at 30°. The rate constants have been corrected for a 6.00M-water

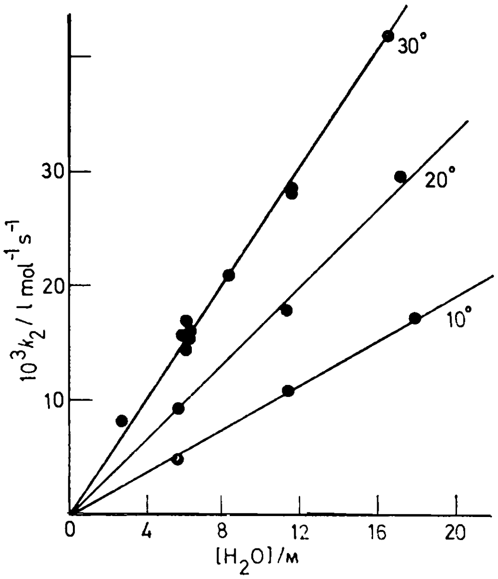

FIGURE 2 Plots of second-order rate constants of the cyanogen bromide reaction with N-methylaniline against the water concentration at 10, 20, and 30°

As both N-methylaniline and water react with cyanogen bromide, it was necessary to identify the reaction product under these kinetic conditions. Therefore we isolated, on one hand, the product and determined its structure by i.r. spectroscopy and, on the other, monitored products as they are being formed, with the help of u.v. spectroscopy. To isolate the product the reaction was carried out over 3 h in acetone–water (90 : 10 v/v) at 30° (BrCN 0.047M; PhNHMe 0.093M). The solvent was evaporated under vacuum and the i.r. spectrum of the remaining oil taken.

TABLE 2

I.r. spectra (cm^{-1}) of the product of cyanogen bromide and *N*-methylaniline, *N*-methylaniline, and *N*-methyl-*N*-phenylcyanamide

	MeNHPh	Product	MePhNCN	
ν(NH)	3 420	3 420		
ν(CH)	3 090	3 090	3 080	ν(CN)
	3 055	3 055	3 050	
	3 020	3 020	3 020	
	2 985	2 990	2 985	
ν(CH_3, as)	2 935	3 935	2 945	ν(CH_3, as)
ν(CH_3, s)	2 882	2 882	2 880	ν(CH_3, s)
		2 225	2 225	ν(C≡N)
		1 725		
		1 710		
Aromatic	1 605	1 600	1 600	Aromatic
	1 500	1 510	1 500	
δ(CH_3, as)	1 475	1 475	1 475	δ(CH_3, as)
Aromatic	1 450	1 450	1 450	Aromatic
δ(CH_3, s)	1 420	1 420		
		1 340	1 340	δ(CH_3, s)
δ(CH)	1 265	1 265		δ(CH)
		1 230	1 230	
	1 160	1 160	1 160	
	1 080	1 080	1 080	
	1 025	1 035	1 035	
		890	890	γ(CH_3)
γ(CH_3)	870	870		
γ(CH)	760	755	760	γ(CH)
Aromatic	695	695	695	Aromatic

Table 2 presents the most significant bands of the product spectrum as well as the bands from a spectrum of *N*-methylaniline and an authentic *N*-methyl-*N*-phenylcyanamide. The product is mainly a mixture of *N*-methyl-*N*-phenylcyanamide and the excess of *N*-methylaniline with a small quantity of a third compound with intense bands at 1 725 and 1 710 cm^{-1}. These bands are due to the hydrolysis product of *N*-methyl-*N*-phenylcyanamide, *N*-methyl-*N*-phenylurea [reaction (1)].

$$\mathrm{PhMeNCN} + \mathrm{H_2O} \longrightarrow \mathrm{PhMeN{-}\underset{\underset{\displaystyle O}{\|}}{C}{-}NH_2} \qquad (1)$$

The hydrolysis products of BrCN, which are CO_2, NH_3, and HBr, cannot be responsible for these two bands.

To follow the products as they are formed, a kinetic run was performed in dioxan–water (90 : 10 v/v at 25 ± 1°) (BrCN 0.045M; PhNHMe 0.090M) and samples diluted with dioxan were analysed with a Unicam SP 8000 spectrophotometer (Figure 3). As can be seen, the intensity of the *N*-methylaniline absorption band at 292 nm gradually diminishes and an absorption band with vibrational structure appears simultaneously at 275 nm. The final intensity of this band becomes practically equal with that of an authentic *N*-methyl-*N*-phenylcyanamide solution of the same concentration as the initial cyanogen bromide.

TABLE 3

Rate constants for the reaction of cyanogen bromide with *N*-methylaniline in acetone (0.2M-water) at 10°

[BrCN]/M	[PhNHMe]/M	10^3k_1/s^{-1}	$10^3k_1''$/s^{-1} *
0.0193	1.13	0.71	0.50
0.0191	2.35	1.92	1.49
0.0189	2.82	2.47	1.95
0.0201	3.54	3.97	3.32

* Corrected for the water content by substracting 0.18 × 10^{-3} [PhNHMe].

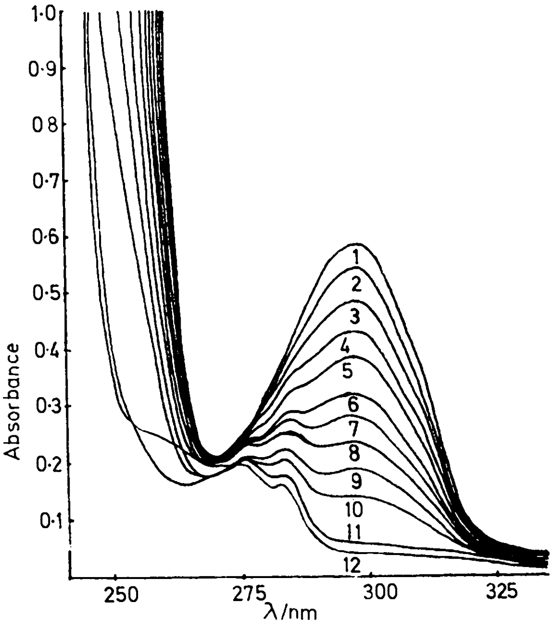

FIGURE 3 U.v. spectra of the samples taken from the reaction mixture [BrCN 0.045M, PhNHMe 0.090M in dioxan–water (90 : 10 v/v); 25 ± 1°] at 0, 3′ 32″, 9′ 30″, 16′ 13″, 22′ 13″, 31′ 35″, 46′ 56″, 66′ 30″, 85′ 11″, and 119′ 37″ (curves 1—10) and the spectrum of a sample taken at the end of the reaction (curve 11). Curve 12 represents the spectrum of a PhNMeCN solution of the initial concentration of 0.045M

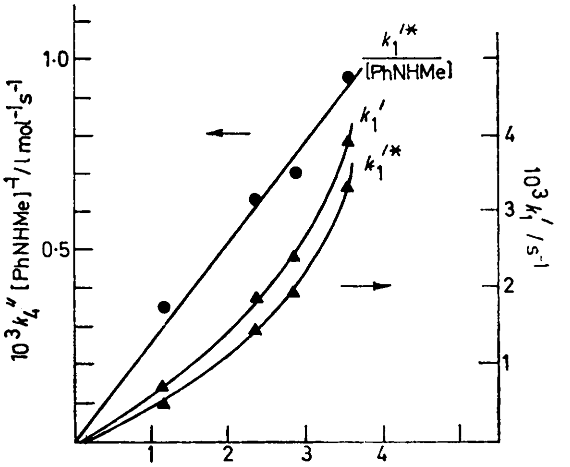

FIGURE 4 Plots of pseudo-first-order rate constants of the cyanogen bromide reaction with *N*-methylaniline corrected or not for water catalysis by high *N*-methylaniline concentration against *N*-methylaniline concentration. Plot of pseudo-first-order rate constants corrected for water catalysis divided by *N*-methylaniline concentration against *N*-methylaniline concentration (10°)

It is well known [7] that cyanogen bromide at high concentrations reacts with secondary amines in the absence of water and kinetic runs have been performed at high *N*-methylaniline concentration (Table 3).

The water content of acetone was determined by i.r. spectroscopy and was found to be 0.2M (*ca.* 0.3%). A correction for this water concentration was made for the rate constants k_1. The rate constants, corrected or not, are not linearly dependent on the amine concentration (Figure 4). Linearity was obtained for a correlation between k_1''/[PhNHMe] and the amine concentration.

This correlation corresponds to equation (2). In this

$$k_1' = k_1[OH_2][PhNHMe] + k_2''[PhNHMe]^2 = 0.92 \times 10^{-3}[H_2O][PhNHMe] + 0.26 \times 10^{-3}[PhNHMe]^2 \quad (2)$$

case, a water molecule was obviously substituted by another molecule of *N*-methylaniline.

The activation enthalpy and entropy computed using the k_3 values from Table 1 are $\Delta H^{\ddagger}$ 9.2 kcal mol^{-1} and $\Delta S^{\ddagger}$ −38.6 cal mol^{-1} K^{-1}. The entropy is similar to the values found for addition to phenyl cyanate of *N*-methylaniline catalysed by phenol (−42.5 cal mol^{-1} K^{-1}),[2] of phenol catalysed by *N*-methylaniline (−43.6 cal mol^{-1} K^{-1}),[2] and of methanol catalysed by phenyl *C*-methoxyformimidate (−38.7 cal mol^{-1} K^{-1}).[6] All these reactions were found to be trimolecular. The highly negative activation entropy supports a high degree of order in the transition state. This order can be due to more enhanced solvation of the transition state than of the initial reactants. Usually such solvation is also responsible for a major solvent effect on the reaction rate but this has not been noticed in our case.[8] Cyclic transition states imply negative activation entropies (−25 to −40 cal mol^{-1} K^{-1}) as has been shown for Diels–Alder [9-12] and 1,3-dipolar additions.[13-15]

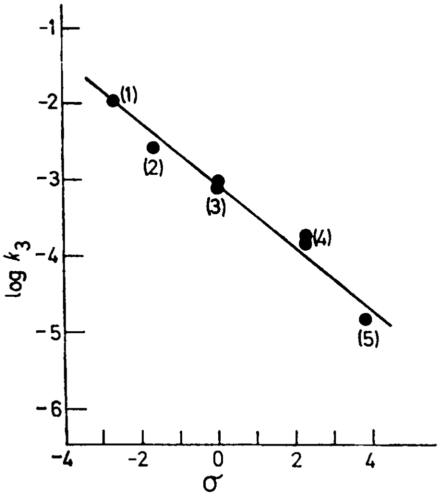

FIGURE 5 Hammett-type plot of rate constants of substituted *N*-methylaniline reaction with cyanogen bromide in acetone–water (90 : 10 v/v; 10°). Numbers as in Table 4

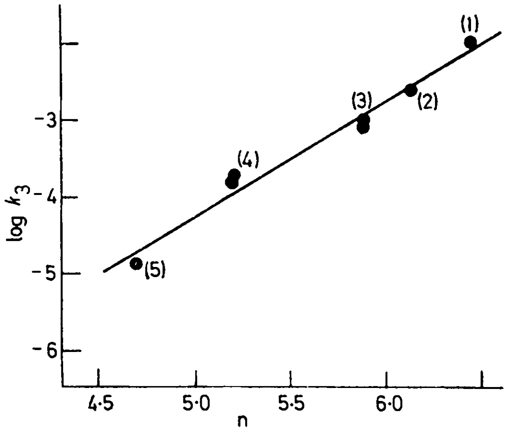

FIGURE 6 Plot of log k_3 against nucleophilicity constants *n* for the reaction of substituted *N*-methylanilines with cyanogen bromide in acetone–water (90 : 10 v/v) at 10°. Numbers as in Table 4

The activation enthalpy is quite small and similar to those for the above mentioned reactions.

Table 4 shows the electronic and steric effects of substituents in the amines upon the rate constants. A good Hammett-type plot (Figure 5) has been obtained for the third-order rate constants corresponding to equation (3). The relatively high ρ value supports nucleophilic

$$\log k_3 = -4.22\sigma - 3.05 \quad (3)$$

attack of *N*-methylaniline on cyanogen bromide as the slow step of the reaction. It is similar to ρ values obtained [16] for reactions of anilines with benzoyl chloride (−2.78 in benzene at 25°), 2,4-dinitrophenyl fluoride (−4.24 in EtOH at 20°), 2,4-dinitrophenyl chloride (−3.98 in EtOH at 25°), and for the reactions of *NN*-dimethylanilines with 2,4,6-trinitroanisole (−2.86 in acetone at 15°) and methyl iodide (−3.30 in acetone at 35°). For the addition of *N*-methylanilines to phenyl cyanate in the catalysis of phenol ρ was −2.64 (in diethyl ketone at 50°)[3].

The logarithms of the third-order rate constants are also proportional to the amine nucleophilicity constants of Pearson [17] (Figure 6) [equation (4)]. This correlation

$$\log k_3 = 1.50n - 11.75 \quad (4)$$

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points out the importance of amine nucleophilicity on the reaction rate. For the addition of *N*-methylanilines to phenyl cyanate in the catalysis of phenol a proportionality coefficient of 0.98 (in diethyl ketone at 50°) [3] was found.

TABLE 4

Rate constants for the reaction of cyanogen bromide with alkylarylamines at 10° in water–acetone (10 : 90 v/v)

No.	Amine	σ [16]	n*	pk_a at 25°	[BrCN]/ M	[ArNHR]/ M	[H_2O]/ M	10^3k_1/ s^{-1} ‡	10^3k_2/ l mol^{-1} s^{-1} §	10^3k_3/ l^2 mol^{-2} s^{-1} ¶
(1)	*p*-Methoxy-*N*-methylaniline	−0.268	6.43	5.80 †	0.0215	0.464	5.64	27.3	59.0	10.65
(2)	*p,N*-Dimethylaniline	−0.170	6.12	5.36 [19]	0.0207	0.460	5.60	6.10	13.3	2.37
(3)	*N*-Methylaniline	0.000	5.87	4.85 [18]	0.0176 0.0179	0.458 0.467	5.62 5.69	2.31 2.23	5.04 4.88	0.90 0.86
(4)	*p*-Chloro-*N*-methylaniline	0.227	5.19	3.90 [20]	0.0208 0.0241	0.460 0.458	5.60 6.05	0.418 0.528	0.91 1.15	0.163 0.191
(5)	*m*-Chloro-*N*-methylaniline	0.373	4.69	3.45 †	0.0215	0.532	5.70	0.0424	0.0795	0.0140
(6)	2,6,*N*-Trimethylaniline			6.12 [21]	0.0246	0.525	5.64	3.74	7.14	1.26
(7)	2,6-Diethyl-*N*-methylaniline				0.0329	0.422	5.60	1.85	4.40	0.785
(8)	*N*-Ethylaniline	0.00		5.12 [19]	0.0203	0.462	5.60	1.45	3.15	0.565
(9)	*p*-Methyl-*N*-ethylaniline	−0.170		5.72 [19]	0.0182	0.531	5.50	5.96	11.2	2.04
(10)	*m*-Methyl-*N*-ethylaniline	−0.069		5.37 †	0.0182	0.531	5.50	2.29	4.32	0.785
(11)	*o*-Methyl-*N*-ethylaniline			4.96 [19]	0.0184	0.533	5.50	0.67	1.26	0.230
(12)	*N*-Butylaniline	0.000		5.12 [21]	0.0188	0.548	5.50	0.96	1.75	0.318
(13)	*N*-Isopropylaniline	0.000		5.77 [21]	0.0179	0.491	5.50	0.64	1.30	0.237
(14)	*N*-Hydroxyethylaniline	0.000		4.06 [22]	0.0183	0.490	5.60	0.105	0.214	0.0382

* Defined by Pearson [17] and determined by us.[3] † Calculated using a Hammett type plot of pK_a against σ. ‡ k_1 = Pseudo-first order rate constant. § k_2 = Second-order rate constant = k_1/[ArNHR]. ¶ k_3 = Third-order rate constant = k_2/[H_2O].

Figure 7 shows Brønsted type correlations of rate constants with pK_a values of the *N*-alkyl-*N*-arylamines. Two good straight lines can be plotted. One for *N*-methylanilines [equation (5)] and the other [equation

$$\log k_3 = 1.06\ \mathrm{p}K_a - 8.23 \qquad (5)$$

(6)] for *N*-ethylanilines, including 2-methyl-*N*-ethylaniline (point 11) and other *N*-alkylanilines with a

$$\log k_3 = 1.11\ \mathrm{p}K_a - 9.04 \qquad (6)$$

normal alkyl group (points 12 and 14). The differentiation of the two classes of *N*-alkylanilines reveals a steric effect of the alkyl group which does not seem to be very important as all amines with normal alkyl groups are on the same line. 2,6-Dimethyl-*N*-isopropyl- and 2,6,*N*-trimethyl-anilines show more important steric effects. The steric effects are similar to those found by the addition of *N*-methylanilines to phenyl cyanate.[4]

The interpretation of α values from Brønsted correlations is difficult. It also seems possible that the relative high values, close to 1.00, support the resemblance of the transition state to the product.[23] This means that in the transition states the formation of C–N bond between the carbon atom of cyanogen bromide and the nitrogen atom from the amines is the most rapid step of the reaction.

Table 5 shows the electronic and steric effects of substituents in the hydroxylic compound upon the reaction rate constants. The reaction mechanism does not seem to change if water is substituted by other hydroxylic compounds such as alcohols or phenols. The reaction rate remains third-order, first-order in each of cyanogen bromide, *N*-methylaniline, and hydroxylic compound as Figures 8 and 9 show (see also Table 5).

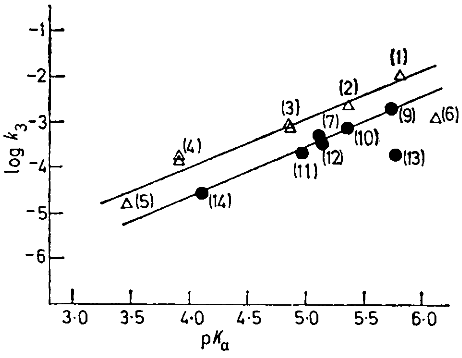

FIGURE 7 Brønsted-type plot of log k against pK_a of alkylarylamines in acetone–water (90 : 10 v/v) at 10°. Numbers as in Table 4

An investigation of the products for the reaction with

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methanol, as for the reaction with water, showed that N-methyl-N-phenylcyanamide was the only product. A kinetic run in dioxan–methanol (90 : 10 v/v at 25 ± 1°) (BrCN 0.0635M; PhNHMe 0.127M) observed by u.v. spectroscopy is shown in Figure 10.

TABLE 5

Rate constants for the reaction of cyanogen bromide with N-methylaniline at 10° in acetone-hydroxylic compound

Hydroxylic compound K_e [a]	E_s [16]	σ^* [16]	[BrCN]/ M	[PhNHMe]/ M	[ROH]/ M	10^3k_1/ s^{-1} [a,b]	10^3k_2/ l mol^{-1} s^{-1} [c]	10^3k_3/ l^2 mol^{-2} s^{-1} [d]	$10^3k_{med} \pm p$
MeOH	0.00	0.00	0.0193	0.322	4.26	0.78	2.42	0.567	0.567 ± 0.01
			0.0125	0.482	4.08	1.03	2.24	0.550	
4.00			0.0181	0.504	4.08	1.13	2.24	0.550	
			0.0173	0.688	4.06	1.45	2.11	0.520	
			0.0184	0.840	4.08	1.77	2.11	0.517	
			0.0184	0.684	2.13	0.97	1.42	0.667	
			0.0185	0.688	6.35	2.58	3.75	0.590	
EtOH	−0.07	−0.10	0.0180	0.683	3.07	1.10	1.61	0.525	0.553 ± 0.01
0.95			0.0182	0.710	4.95	1.98	2.79	0.565	
			0.0184	0.680	6.64	2.56	3.76	0.566	
Pr^{i}OH	−0.47	−0.190	0.0183	0.676	3.08	0.716	1.06	0.345	0.353 ± 0.006
0.08			0.0185	0.684	4.98	1.12	1.66	0.340	
			0.0180	0.685	5.02	1.19	1.74	0.347	
			0.0183	0.665	6.15	1.56	2.35	0.382	
Bu^{t}OH	−1.54	−0.300	0.0179	0.642	1.79	0.41	0.64	0.358	0.342 ± 0.006
<0.2			0.0171	0.640	3.87	0.80	1.25	0.323	
			0.0173	0.645	5.06	1.12	1.74	0.344	
$ClCH_2CH_2OH$	−0.90	+0.385	0.0178	0.676	2.48	0.82	1.21	0.488	0.442 ± 0.013
			0.0180	0.680	4.33	1.23	1.81	0.419	
			0.0185	0.665	5.67	1.58	2.38	0.420	
PhOH			0.0186	0.665	2.33	1.52	2.29	0.982	1.041 ± 0.017
			0.0186	0.687	2.92	2.10	3.06	1.050	
			0.0181	0.686	5.55	2.94	6.05	1.090	

[a] Relative acidity of alcohol in isopropyl alcohol solution.[24] For water $K_e = 1.2$. [b] k_1 = Pseudo-first-order rate constant. [c] k_2 = Second-order rate constant = k_1/[PhNHMe]. [d] k_3 = Third-order rate constant $k_3 = k_2$/[ROH].

N-Methyl-N-phenylcyanamide absorption at 277 nm is practically equal to that of an authentic N-methyl-N-phenylcyanimide solution with concentration that of initial cyanogen bromide (0.0635M).

The third-order rate constants do not depend so much on the electronic or steric effects of the hydroxylic compounds. The reaction rates decrease along the series HOH > MeOH ~ EtOH > Pr^{i}OH ~ Bu^{t}OH, and generally speaking steric hindrance is more efficient than the electronic effect of the substituent. An increase of hydroxylic compound acidity also increases its catalytic effect (see for example PhOH, HOH, MeOH, $ClCH_2CH_2$-OH, and Pr^{i}OH). A Brønsted type correlation does not seem to be possible with the relative acidity constants of the alcohols.

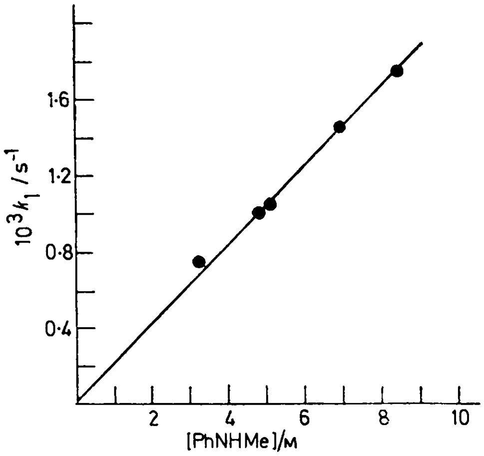

FIGURE 8 Plot of pseudo-first-order rate constants of the cyanogen bromide reaction against the concentration of N-methylaniline at 10° in acetone–methanol. The rate constants have been corrected for 4.08M-methanol

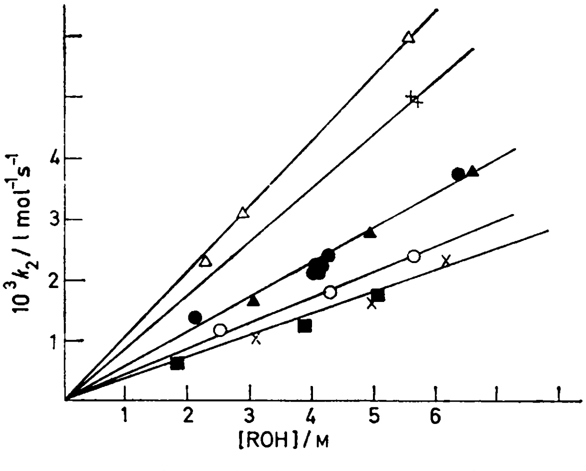

FIGURE 9 Plots of second-order rate constants of the cyanogen bromide reaction with N-methylaniline against the hydroxylic compounds concentration (+, H_2O; ●, MeOH; ▲, EtOH; ×, Pr^{i}OH; ○, $ClCH_2CH_2OH$; ■, Bu^{t}OH; △, PhOH) at 10°

As the polarity of the acetone–water, –alcohol, and –phenol mixtures are quite different, it is evident that the reaction is not sensitive to solvent effects at all. The absence of the solvent polarity influences on the reaction rate is usually characteristic of reactions of neutral molecules which imply a non-polar or cyclic transition

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[24] J. Hine and M. Hine, *J. Amer. Chem. Soc.*, 1952, **74**, 5266.

state.[8] In our case the reactants are polar and a non-polar transition state is not possible and thus it seems that a cyclic transition state is responsible for the lack of solvent effect.

The absence of solvent polarity effects on the reaction rate was used as a criterion for cyclic transition states for Diels–Alder reactions,[25,26] decarboxylation of β-keto-acids,[27,28] and for 1,3-dipolar cycloadditions.[14,29-31]

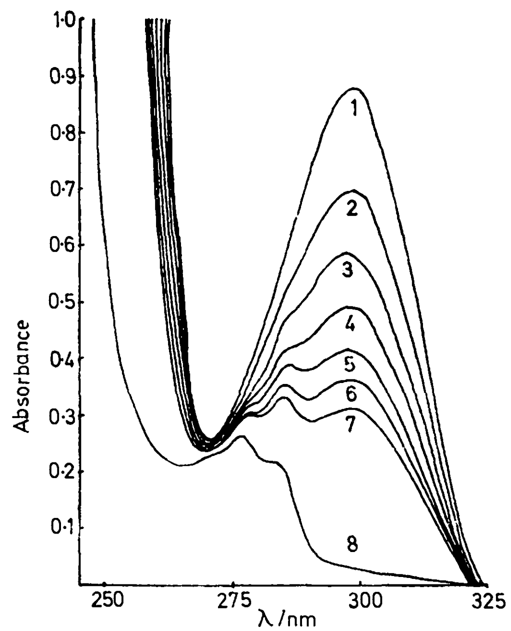
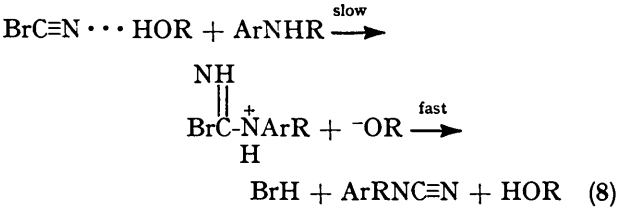


FIGURE 10 U.v. spectra of the samples taken from the reaction mixture (BrCN 0.0635M, PhNHMe 0.127M), in dioxan–methanol (90 : 10 v/v; 25 ± 1°) at 0, 10, 20, 36, 58, 83, and 135 min (curves 1—7) and the spectrum of a sample taken at the end of reaction (curve 8)

The reaction mechanism necessarily implies the participation of a hydroxy-compound molecule in a pre-equilibrium or in the rate-determining step of the cyanogen bromide–*N*-alkylaniline reaction. This is completely analogous to the case of phenol participation in *N*-methylaniline addition to aryl cyanates.[2,3] There are two possibilities for the participation of the hydroxy-compound in a pre-equilibrium which can facilitate *N*-alkylaniline nucleophilic attack on cyanogen bromide. Thus the hydroxylic compound can associate with cyanogen bromide before nucleophilic attack of the amine [reactions (7) and (8)]. Complete transfer of the proton from alcohol or water to cyanogen bromide is unlikely because of the low acidity of the former and the small basicity of the latter (pK_a at 25° 11.7)[25] but association by a proton has been proved by i.r. spectroscopy.[32,33]

The mechanism in (7) and (8) in our opinion cannot account for the relatively small influence of the hydroxylic

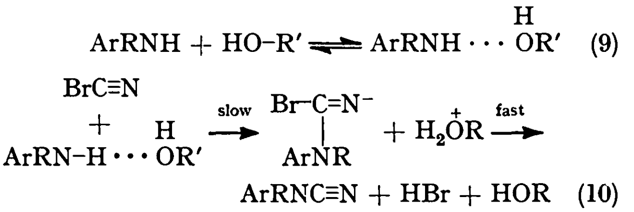
$$\mathrm{BrC{\equiv}N + HOR \rightleftharpoons BrC{\equiv}N\cdots HOR} \qquad (7)$$



$$\mathrm{BrC{\equiv}N\cdots HOR + ArNHR \xrightarrow{slow} \overset{NH}{\overset{\|}{BrC}}\text{-}\underset{H}{\overset{+}{N}}ArR + {}^{-}OR \xrightarrow{fast} BrH + ArRNC{\equiv}N + HOR} \qquad (8)$$

compound acidity upon the reaction rate. The ratio k_3(MeOH) : k_3(PhOH) is only 0.55 and if the hydroxylic compound is substituted by another molecule of *N*-methylaniline the ratio k_3(MeOH) : k_3(HNMePh) becomes 2.46 although phenol is much more acid than methanol and this one much more acid than *N*-methylaniline. It cannot also account for the insensitivity to solvent effects.

The second possibility is a proton association pre-equilibrium between *N*-alkylaniline and hydroxylic compound (9). The complex effects nucleophilic attack on cyanogen bromide in the slow step (10). This second

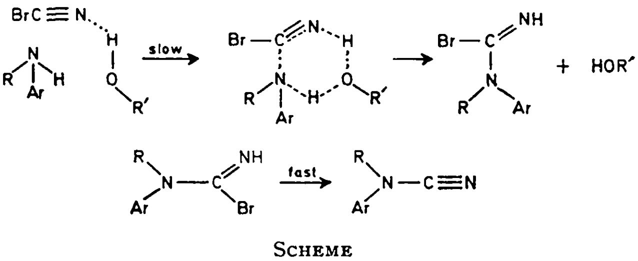


$$\mathrm{ArRNH + HO\text{-}R' \rightleftharpoons ArRNH\cdots \overset{H}{O}R'} \qquad (9)$$

$$\mathrm{BrC{\equiv}N + ArRN\text{-}H\cdots\overset{H}{O}R' \xrightarrow{slow} \begin{matrix}Br\text{-}C{=}N^{-}\\ |\\ ArNR\end{matrix} + H_2\overset{+}{O}R \xrightarrow{fast} ArRNC{\equiv}N + HBr + HOR} \qquad (10)$$

mechanism is evidently not supported by the increase of catalytic activity in parallel with the acidity of hydroxylic compound and not its basicity as can be expected. The best mechanism we can suggest is an *N*-alkylaniline nucleophilic attack on the cyanogen bromide–hydroxylic compound complex.

This attack is the slow step of the reaction and through



SCHEME

a cyclic transition state forms *N*-aryl-*N*-alkylcarbamimidoyl bromide (Scheme). The intermediate loses an HBr molecule in a very fast reaction. This second

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[25] H. Kaufmann and A. Wassermann, *J. Chem. Soc.*, 1939, 870.

[26] G. Göster and E. Pfeil, *Chem. Ber.*, 1968, **101**, 4248.

[27] F. H. Westheimer and W. A. Jones, *Ber.*, 1941, **63**, 3283.

[28] C. G. Swain, R. F. W. Bader, R. M. Esteve, and R. N. Griffin, *Chem. Ber.*, 1961, **83**, 1951.

[29] (*a*) R. Huisgen, H. Stangl, H. S. Sturm, and H. Wagenhofer, *Chem. Ber.*, 1971, **73**, 170; (*b*) R. Huisgen, L. Möbius, G. Müller, H. Stangl, G. Szeimies, and J. H. Vernon, *ibid.*, 1965, **98**, 3992; (*c*) R. Huisgen, G. Szeimies, and L. Möbius, *ibid.*, 1967, **100**, 2494.

[30] A. Ledwith and D. Parry, *J. Chem. Soc.* (*C*), 1966, 1408.

[31] P. K. Kadaba, *Tetrahedron*, 1966, **22**, 2453.

[32] D. Martin, W. Brause, and R. Radeglia, *J. prakt. Chem.*, 1970, **312**, 797.

[33] A. Allerhand and P. V. Schleyer, *J. Amer. Chem. Soc.*, 1963, **85**, 866.

reaction is similar to the loss of HCl from N-arylcarbamoyl chloride which we have shown to be very fast.[34]

This mechanism accounts for all our data. Thus the importance of the nucleophilicity of the alkylarylamines implies its attack on the cyanogen bromide in the slow step of the reaction. In a cyclic transition state both the acidity of the proton and the nucleophilicity of the oxygen atom should play a prominent part so that the electronic effects of the organic radical are compensated. The large negative entropy as well as the small enthalpy of activation are justified by the high degree of order of the transition state and the simultaneous breaking and building up of bonds. The cyclic transition state explains the unexpectedly small steric effects of organic radicals in amine and hydroxylic compounds. The relative rigidity of the six-membered ring removes steric interference. The absence of solvent effects is also explained.

EXPERIMENTAL

Cyanogen bromide was prepared from sodium cyanide and bromide and purified by distillation.[7] *N*-Methyl-, *N*-ethyl-, and 2-, 3-, and 4-methyl-*N*-ethyl-aniline were commercial samples purified by vacuum distillation, 4-methoxy-*N*-methyl-, 4,*N*-dimethyl-, 3-chloro-*N*-methyl-, 4-chloro-*N*-methyl-, 2,6,*N*-trimethyl-, and 2,6-diethyl-*N*-methyl-aniline were obtained from the respective anilines as previously described.[3,4] *N*-butyl-, *N*-isopropyl-, and *N*-hydroxymethyl-aniline were prepared by the *N*-*p*-tolylsulphonylaniline sodium salt reaction with the corresponding alkyl bromide.[35]

Acetone was dried over potassium carbonate and distilled. The water content was determined by i.r. spectroscopy [$\nu_{max.}$ 3 580 cm^{-1} (OH)]. The alcohols (commercial) were refluxed for 24 h over CaO and distilled. Dioxan (commercial sample) was dried over sodium and distilled. Methylphenylcyanamide was obtained from cyanogen bromide and *NN*-dimethylaniline.[7]

A UR-10 Carl Zeiss Jena i.r. spectrophotometer and a Unicam SP 8000 u.v.–visible spectrophotometer were employed.

Kinetic procedures were as before.[36] The pseudo-first-order rate constants were calculated from conductivities and were constant to 90—95% conversion. A typical example for rate constant determination is in Table 6.

TABLE 6

Rate constants for a run with 0.178M-cyanogen bromide, 0.446M-*N*-methylaniline, and 17.15M-water at 20°. $\Lambda_\infty = 700$ μohm^{-1}, $\Lambda_0 = 5$ ohm^{-1}. The average constant is $5.73 \times 2.303 \times 10^{-3} = 13.18 \times 10^{-3}$ s^{-1}

t/s	$10^6\Lambda_t$/ohm^{-1}	$\log \frac{\Lambda_\infty - \Lambda_0}{\Lambda_\infty - \Lambda_t}$	$\frac{10^3}{t} \log \frac{\Lambda_\infty - \Lambda_0}{\Lambda_\infty - \Lambda_t} / \mathrm{s}^{-1}$
13.0	100	0.064	4.92
17.0	140	0.094	5.54
20.0	170	0.118	5.90
24.0	200	0.143	5.96
28.6	230	0.170	5.94
38.8	250	0.189	5.95
36.7	280	0.218	5.94
40.0	300	0.240	5.94
44.6	320	0.262	5.88
49.0	340	0.285	5.82
53.6	360	0.311	5.80
58.6	380	0.336	5.74
64.0	400	0.365	5.70
70.0	420	0.395	5.65
81.7	460	0.462	5.71
95.8	500	0.542	5.66
115.1	550	0.666	5.79
133.5	575	0.746	5.60
155.5	600	0.842	5.42
175.5	625	0.967	5.52
209.5	650 *	1.253	5.98

* 95% Conversion.

The apparent activation parameters were calculated as usual from the coefficients of the Arrhenius equation at 300°.

[4/1171 *Received*, 17*th June*, 1974]

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[35] Houben-Weyl, 'Methoden der Organischen Chemie,' vol. XI/1, 'Stickstoffverbindungen II,' ed. E. Müller, Georg Thieme, Stuttgart, 1957, p. 99.

[36] G. Ostrogovich, C. Csunderlik, and R. Bacaloglu, *J. Chem. Soc.* (*B*), 1971, 18.