Mechanism of the Cyanide Ion-catalysed Cleavage of Benzils by Amines in Aqueous Dioxan

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Kinetics and product distributions of the cyanide ion-catalysed reaction of benzils with ammonia or amines, to give benzaldehydes (or benzaldimines) and benzamides, have been studied. The rate of reaction of benzil with ammonia in aqueous dioxan is expressed as $v = k_{obs}$ [Benzil][CN$^-$][NH$_3$]. The rates depend on the aliphatic amine, decreasing in the order MeNH$_2$ > EtNH$_2$ > Bu^{n}NH$_2$ > NH$_3$ > Pr^{i}NH$_2$ > Bu^{t}NH$_2$. The rate constants for substituted benzils fit the Hammett relationship with $\Sigma\sigma$, giving a ρ value of 2.70. Addition of ammonium chloride or potassium hydroxide decreases the rate. The reactivity order of amines for this reaction differs from that for the reaction with benzoyl chloride. Ammonolysis of α-cyanobenzyl benzoate in basic aqueous dioxan is much slower than cyanide ion-catalysed ammonolysis of benzil. These results suggest a mechanism involving reversible addition of cyanide ion and amine to the two carbonyl groups of benzil, followed by protonation and cleavage of the C–C bond assisted by electron withdrawal by the cyano-group and by electron release by the oxyanion or the hydroxy-group. The ratio of products (Ar^{1}CHO : Ar^{2}CHO) from the reaction of unsymmetrical benzils (Ar^{1}COCOAr^2) varies with the substituents in benzil and amine.

THE reaction of benzil with ammonium cyanide undergoes C–C bond cleavage to yield mandelonitrile and benzamide,[1] which is quite different from the reaction of most monocarbonyl compounds with ammonium cyanide to give Strecker aminonitriles.[2] In analogous cleavage reactions of benzil with cyanide ion in alcohol solution, a mechanism involving a rate-determining formation of α-benzoyloxy-α-cyanobenzyl carbanion has been proposed on the basis of second-order kinetics which are independent of alcohol concentrations.[3] The formation of the carbanion was confirmed by trapping experiments in aprotic solvents.[4,5] However, the mechanism for the reaction of benzil with cyanide ion and ammonia is obscure and no kinetic study has been done. We carried out product and kinetic studies of cyanide ion-catalysed reactions of some benzils with ammonia or amines in aqueous dioxans, where the product distribution from unsymmetrical benzils, the dependence of the rates on ammonia, the structural effects of benzil and amines on the rate, and the possibility of the intermediacy of α-cyanobenzyl benzoate were examined.

RESULTS

The reaction products were identified and estimated by means of g.l.c. The results are summarised in Table 1. The reaction of benzil with ammonia in the presence of 10 mole % KCN or NaCN gave nearly equivalent amounts of benzaldehyde (70%) and benzamide (70%), while the reaction of benzil with primary amines instead of ammonia yielded *N*-benzylidenealkylamines and *N*-alkylbenzamides together with a small amount of benzaldehyde.

N-Benzylidenealkylamine is the condensation product of the resulting benzaldehyde and unchanged amine. Since only 0.1 mol. equiv. KCN is sufficient for complete reaction, KCN is a true catalyst. However, the reaction of benzil with 0.1 mol. equiv. KCN to give benzoic acid and benzaldehyde stopped at *ca.* 10% conversion when no KOH was added, as benzoic acid makes KCN ineffective.[3] The

TABLE 1

Typical examples of the KCN (0.1 mmol)-catalysed reaction of some benzils (1 mmol) with amines (7 mmol) or water (110 mmol) in aqueous dioxan (67% v/v)

Run	Substrate	Reagent	Product	Yield [a] (%)
1	Benzil	Ammonia	Benzaldehyde	71
			Benzamide	71
2	Benzil	Ethylamine	Benzaldehyde	32
			N-Benzylidene(ethyl)-amine	63
			N-Ethylbenzamide	96
3	Benzil	Water	Benzaldehyde	9
			Potassium benzoate	
			Unchanged benzil	89
4	Benzil	Water [b]	Benzaldehyde	84
			Potassium benzoate	65 [c]
5	*p*-Methoxy-benzil	Ammonia	Benzaldehyde	50
			p-Anisamide	45
			p-Anisaldehyde	24
			Benzamide	24
6	*p*-Chloro-*p*′-methoxy-benzil	Ammonia	*p*-Chlorobenzaldehyde	61
			p-Anisamide	41
			p-Anisaldehyde	27
			p-Chlorobenzamide	26
7	*p*-Chloro-*p*′-methoxy-benzil	Ethylamine	*N*-*p*-Chlorobenzylidene-(ethyl)amine	46
			N-Ethyl-*p*-anisamide	42
			N-*p*-Methoxybenzilidene-(ethyl)amine	10 [d]
			N-Ethyl-*p*-chloro-benzamide	24
8	*p*-Methoxy-benzil	Ethylamine	*N*-Benzylidene(ethyl)-amine	43 [d]
			N-*p*-Methoxybenzylidene-(ethyl)amine	18 [d]
			N-Ethylbenzamide	
			N-Ethyl-*p*-anisamide	

[a] Determined by means of g.l.c. and based on benzil. [b] In the presence of KOH (2.8 mmol). [c] Converted into methyl ester by refluxing with H$_2$SO$_4$–MeOH. [d] Includes a small amount of the corresponding aldehyde.

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[1] H. D. Dakin and C. R. Harington, *J. Biol. Chem.*, 1923, **55**, 487.

[2] D. T. Mowry, *Chem. Rev.*, 1948, **42**, 236.

[3] H. Kwart and M. M. Baevsky, *J. Amer. Chem. Soc.*, 1958, **80**, 580.

[4] J. P. Kuebrich and R. L. Schowen, *J. Amer. Chem. Soc.*, 1971, **93**, 1220.

[5] W. G. Reardon, J. E. Wilson, and J. C. Trisler, *J. Org. Chem.*, 1974, **39**, 1596.

stoicheiometry of the reaction is given in equations (1)—(3).

$$\mathrm{PhCOCOPh + RNH_2 \xrightarrow{KCN} PhCHO + PhCONHR} \qquad (1)$$

$$\mathrm{PhCHO + RNH_2 \longrightarrow PhC{=}NR + H_2O} \qquad (2)$$

$$\mathrm{PhCOCOPh + KOH \xrightarrow{KCN} PhCHO + PhCO_2K} \qquad (3)$$

The reaction with unsymmetrical benzils gave four products (Table 1, runs 5 and 6), that is, heterolysis of the central C–C bond occurs in two ways (a) and (b) as shown in equation (4). If Ar^1 has a more electron-withdrawing group than Ar^2, path (a) is generally more predominant, as seen in Table 2. That is, major products are benzaldehydes derived from a benzoyl group with a more electron-withdrawing group (Ar^1) and benzamides derived from a benzoyl system with a less electron-withdrawing group (Ar^2) except for the reaction with *p*-chlorobenzil, which gave a less amount of *p*-chlorobenzaldehyde than that of unsubstituted benzaldehyde. Therefore, the aldehyde component in the products decreases in the order H > *p*-Cl > *p*-MeO > *p*-Me_2N. The order is not strictly the same as the rate-decreasing one: *p*-Cl > H > *p*-MeO > *p*-Me_2N (see Table 5).

TABLE 2

Effect of substituents on cleavage ratio of unsymmetrical benzils by ammonia [a]

$R^1C_6H_4COCOC_6H_4R^2$		Product ratio [b]
R^1	R^2	$R^1C_6H_4CHO : R^2C_6H_4CHO$
p-Cl	H	0.95 ± 0.05
p-Cl	*p*-OMe	2.6 ± 0.3
H	*p*-OMe	2.6 ± 0.3
p-Cl	*p*-NMe_2	1.6 ± 0.1
H	*p*-NMe_2	3.4 ± 1.4

[a] See equation (4; R = H). [b] Average value of 2—3 runs.

$$\mathrm{Ar^1COCOAr^2 + RNH_2}\left\{\begin{array}{ll}\xrightarrow{\text{KCN}} \mathrm{Ar^1CHO\ (and\ Ar^1CH{=}NR) + Ar^2CONHR} & \text{(a)}\\ \longrightarrow \mathrm{Ar^1CONHR + Ar^2CHO\ (and\ ArC^2H{=}NR)} & \text{(b)}\end{array}\right. \qquad (4)$$

Kinetics.—The reaction in aqueous dioxan (80 and 67%) at 23° was followed by spectrophotometry of decreasing benzil concentration. The initial concentrations used were 0.01—0.02M-benzil, 0.001—0.02M-NaCN, and 0.23—0.92M-ammonia. The rate of reaction can be expressed as $v = k_{obs}[\text{Benzil}][NH_3][CN^-]$. The kinetic data for the reaction of benzil with cyanide ion and ammonia in aqueous dioxan are shown in Table 3, where the third-order rate coefficients are satisfactorily constant. A slight decrease (*ca.* 30%) in the third-order rate constants with an increase in concentration of ammonia from 0.23M is probably due to the change of solvent acidity (pH), since the addition of unreactive triethylamine resulted in a decrease of the rate. As shown in Table 4, the rate constants decrease on addition of ammonium chloride and also KOH. This is essentially the effect of medium acidity, though it is partly due to a salt effect, since a slight decrease of the rate constants (35%) was observed on addition of NaBr (0.25M). There is a broad maximum between 11 and 13 in plots of log k_{obs} against pH, as shown in Figure 1.

The effect of substituents is shown in Table 5. Plots of log k_{obs} against the sum of Hammett σ constants gave a straight line with a slope (ρ) of 2.70 (Figure 2). The ρ value is smaller than the reported value of 3.45 for cyanide ion-catalysed alcoholysis.[3]

TABLE 3

Rate constants for cyanide ion-catalysed ammonolysis of benzil in aqueous dioxan (80% v/v) at 23 ± 0.5°

[Benzil]/ M	$[NH_3]_0$/ M	$[NaCN]_0$/ M	10^2k_{app}[a]/ s^{-1}	k_{obs}[b]/ $l^2\ mol^{-2}\ s^{-1}$
0.02	0.23	0.005	0.97	8.5
0.02	0.46	0.005	1.57	6.9
0.02	0.46	0.005	1.52	6.6
0.02	0.92	0.005	2.63	5.8
0.02	0.23	0.01	2.21	9.6
0.02	0.23	0.02	3.94	8.6
0.01	0.23	0.01	2.16	9.3
0.01	0.46	0.002 5	1.06	9.2
0.01	0.46	0.005	2.10	9.1
0.01	0.46	0.007 5	2.98	8.6
0.01	0.46	0.01	3.82	8.3
0.01	0.46	0.001 5	4.85	7.1
0.01	0.46	0.015	5.18	7.5
0.01	0.46	0.02	7.9	8.6
0.01	0.69	0.01	4.66	6.8
				Av. 8.0 ± 1.0

[a] Apparent first-order rate constant k_{app} in $v = k_{app}[\text{Benzil}]$. [b] Third-order rate constant k_{obs} in $k_{obs} = k_{app}/[NH_3]_0[NaCN]_0$.

The rates of cyanide-catalysed reactions of benzil with aliphatic amines decreased in the order $MeNH_2 > EtNH_2 > Bu^nNH_2 \sim NH_3 > Pr^iNH_2 > Bu^tNH_2$ when the concentration of NaCN used was only one tenth of benzil; hence the rates did not follow third-order kinetics (Figure 3). The reactivity order of amines depended on their size and basicity, suggesting that they act as nucleophiles but not simple bases.

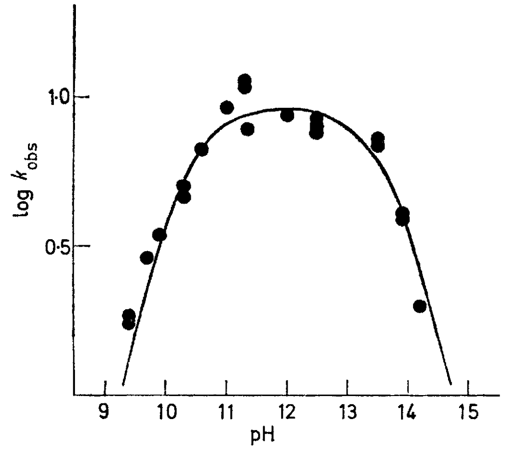

FIGURE 1 Plots of log k_{obs} *versus* pH for the cyanide ion (0.01M) catalysed ammonolysis of benzil in aqueous dioxan at 23°

Relative reactivities of amines for the cyanide ion-catalysed reaction of benzil and those for the reaction of benzoyl chloride * were evaluated from competitive reactions (Table 6). Reactivities toward benzil varied over 30-fold, while those toward benzoyl chloride varied only by a factor of 4. Moreover, the order of relative reactivity toward PhCOCl, $PhCH_2NH_2 > PhCH_2CH_2NH_2 > MeNH_2 > EtNH_2 > Pr^iNH_2$, is not parallel with that toward PhCOCOPh, $MeNH_2 > EtNH_2 > PhCH_2CH_2NH_2 > PhCH_2NH_2 > Pr^iNH_2$. The results suggest that the rate-determining step for the reaction of benzil is not a nucleo-

TABLE 4

Effect of added salts and base on the cyanide ion-catalysed ammonolysis of benzil in aqueous dioxan (67% v/v) at 23 ± 0.5°; $[NH_3]_0 = 0.46$M; $[NaCN]_0 = 0.01$M; $[Benzil]_0 = 0.01$M

$[NH_4Cl]$/M	[NaBr]/M	[KOH]/M	pH	k_{obs}/$l^2 mol^{-2} s^{-1}$
0	0	0	12.5	8.4
0	0	0		7.6
0	0	0		8.0
0	0	0		8.2
0	0	0		8.2
0.001	0	0	12	8.8
0.005	0	0	11.3	11.1
0.005	0	0		11.2
0.005	0	0		11.4
0.005	0	0		7.8
0.012 5	0	0	11	9.2
0.031	0	0	10.6	6.7
0.05	0	0	10.2	4.7
0.05	0	0		5.1
0.05	0	0		5.0
0.125	0	0	9.9	3.5
0.20	0	0	9.7	2.9
0.35	0	0	9.4	1.85
0.35	0	0		1.76
0	0.05	0		7.5
0	0.05	0		7.4
0	0.25	0		5.2
0	0.25	0		5.3
0	0.25	0		5.3
0.001	0.249	0		5.9
0.005	0.245	0		8.2
0.01	0.24	0		8.9
0.025	0.225	0		7.6
0.05	0.20	0		5.9
0.10	0.15	0		4.7
0.25	0	0		2.0
0	0	0.002	13.5	7.0
0	0	0.002		7.2
0	0	0.005	(13.9) [a]	4.1
0	0	0.005		3.9
0	0	0.01	(14.2) [a]	2.0
0	0	0.01		2.0

[a] Calculated using the equation $pH = pK_w + \log[OH^-]$, where pK_w was assumed to be 16.2 from the pH reading of 13.5 of a 0.002M-KOH solution.

TABLE 5

Rate constants for substituted benzils [a]

$R^1C_6H_4COCOC_6H_4R^2$ R^1	R^2	Substituent constant	k_{obs}/ [b] $l^2 mol^{-1} s^{-1}$
p-Cl	H	0.23	18.0 ± 2.8
H	H	0	8.2 ± 0.2
p-Cl	*p*-OMe	−0.04	3.9 ± 0.1
H	*p*-OMe	−0.27	0.79 ± 0.05
p-Cl	*p*-NMe_2	−0.60	0.16 ± 0.01
H	*p*-NMe_2	−0.83	0.027 ± 0.001

[a] In 80% v/v aqueous dioxan at 23°; $[NH_3]_0 = 0.46$M; $[NaCN]_0 = 0.01$M; $[NH_4Cl] = 0.005$M. [b] Third-order rate constant. ± Denotes average deviations of 2—3 runs.

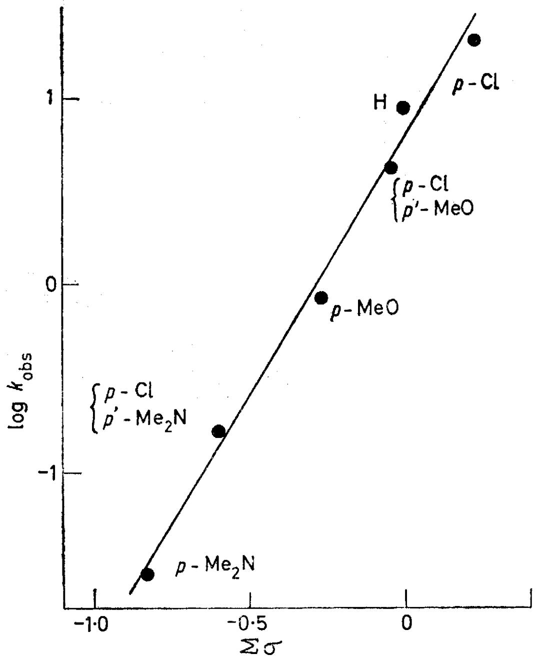

FIGURE 2 Hammett plot for the cyanide ion (0.01M)-catalysed ammonolysis of substituted benzils in aqueous dioxan (80% v/v) containing NH_4Cl (0.005M) at 23°: ρ = +2.70 (*r* 0.996)

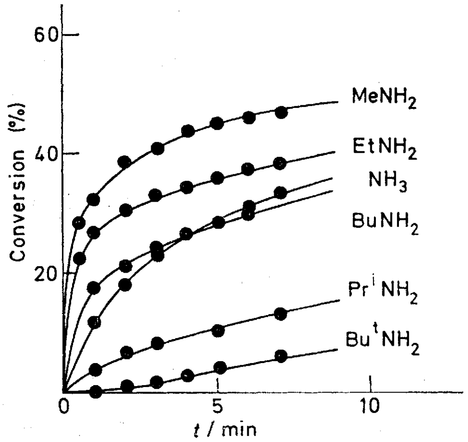

FIGURE 3 Cyanide ion (0.001M) catalysed reaction of benzil (0.001M) with amines (0.5M) in aqueous dioxan (67% v/v) at 15°

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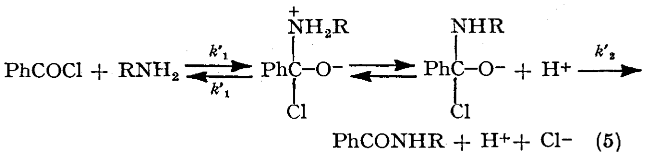
* Though a synchronous or addition–elimination mechanism is postulated for the reaction of benzoyl chloride with amines,[6] Bender and Jones [7] have presented evidence for the stepwise mechanism. It is plausible that the reaction with strongly nucleophilic amines under basic conditions should proceed *via* rate-determining attack of amine on the carbonyl carbon, since chloride ion is a better leaving group than amine or its conjugate base ($k'_2 \gg k'_{-1}$).[7]



$$PhCOCl + RNH_2 \underset{k'_{-1}}{\overset{k'_1}{\rightleftharpoons}} PhC(\overset{+}{N}H_2R)(Cl){-}O^- \rightleftharpoons PhC(NHR)(Cl){-}O^- + H^+ \xrightarrow{k'_2} PhCONHR + H^+ + Cl^- \quad (5)$$

[6] A. Kivinen, ' The Chemistry of Acyl Halides,' ed. S. Patai, Interscience, London, 1972, ch. 6.

[7] M. L. Bender and J. M. Jones, *J. Org. Chem.*, 1962, **27**, 3771.

philic attack of amine on the carbonyl carbon as for the reaction of benzoyl chloride.

Comparison of Rates with Benzil and with α-Cyanobenzyl Benzoate.—To test the possibility that cyanide ion-catalysed ammonolysis proceeds *via* α-cyanobenzyl benzoate or its carbanion, the rates of reaction of α-cyanobenzyl benzoate in aqueous dioxan were compared with those of benzil. Figure 4 shows the reaction of α-cyanobenzyl benzoate (0.1M) with NaOH (0.03M)–NH_3 (0.46M) and Figure 5 shows the reaction of benzil (0.1M) with NaCN (0.023M)–NH_3 (0.46M). Apparently, ammonolysis of benzil was much more rapid than that of α-cyanobenzyl benzoate in spite of higher concentration of base for the latter reaction. In the α-cyanobenzyl benzoate reaction (Figure 4), there was a difference between the yields of benzaldehyde and benzamide which corresponds to benzoic acid formation resulting from attack of hydroxide ion. Analogous results were also obtained in that the benzil (0.2M)–KCN (0.03M)–NH_3 (2.8M) reaction was much more rapid than the α-cyanobenzyl benzoate (0.20M)–KCN (0.03M)–NH_3 (2.8M) reaction.

TABLE 6

Relative reactivities of amines toward benzil (in the presence of KCN) and benzoyl chloride (in the presence of KOH)

Amine	pK_a	Taft E_s	Relative reactivity [a] toward PhCOCl	Relative reactivity [a] toward PhCOCOPh	Ratio of relative reactivity
Methylamine	10.6	0.0	1.00	1.00	1
Ethylamine	10.6	−0.07	0.81	0.17	5
Butylamine	10.6	−0.36		0.12	
Phenethylamine	10.6		1.6	0.063	25
Ammonia	9.3			0.062	
Benzylamine	9.4	−0.38	2.3	0.044	50
Isopropylamine	10.6	−0.47	0.53	0.035	15

[a] Relative to methylamine. The ratio was determined by g.l.c. analysis of competitive reaction products (benzamides).

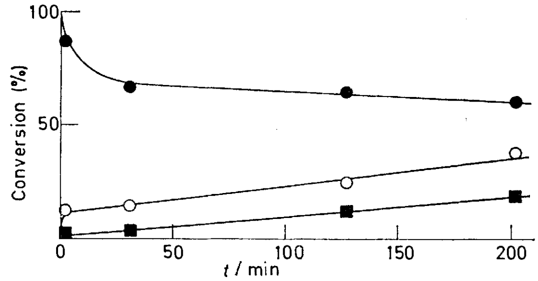
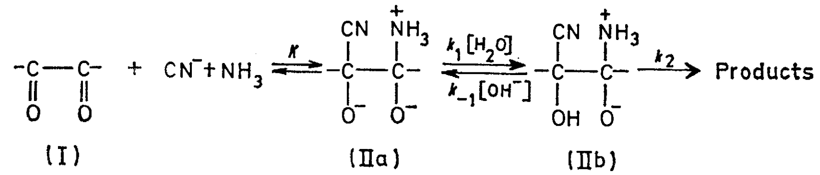


FIGURE 4 Ammonolysis of α-cyanobenzyl benzoate (0.1M) in aqueous dioxan (80% v/v) containing NaOH (0.03M) and NH_3 (0.46M): ●, RhC(CN)HOCOPh; ○, PhCHO; ■, $PhCONH_2$



SCHEME 1

pK_a *Determinations.*—The pK_a values for HCN and NH_4^+ were determined by half-neutralisation or pH measurements of conjugate acid–base system in aqueous dioxan (67%) at 25° to be 10.2 and 9.2, respectively. HCN and NH_4^+ have almost the same pK_a values in water (*ca.* 9.2), but the change of the solvent from water to aqueous dioxan gives different pK_a values. This is probably due to the solvent effect on the dissociation of ionic and neutral acids.

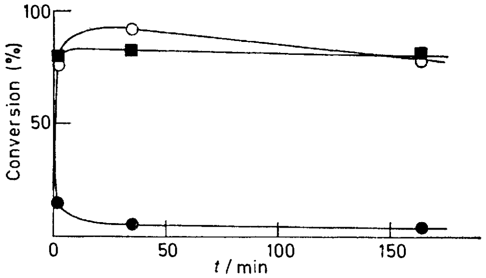


FIGURE 5 Ammonolysis of benzil (0.1M) in aqueous dioxan (80% v/v) containing NaCN (0.023M) and NH_3 (0.46M): ●, PhCOCOPh; ○, PhCHO; ■, $PhCONH_2$

DISCUSSION

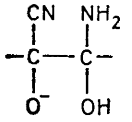
The results are summarised as follows. (i) The rate is $v = k_{obs}[Benzil][CN^-][NH_3]$. (ii) The pH–rate profile has a broad maximum between pH 11 and 13. (iii) The rates with amines instead of ammonia depend on the concentrations of amine. (iv) The reactivity of amines for the reaction differs from that toward benzoyl chloride which is a model compound for nucleophilic attack on a carbonyl group. (v) The rate constants with substituted benzils fit the Hammett correlation with $\Sigma\sigma$, giving a ρ value of $+2.70$. (vi) The reaction with unsymmetrical benzils ($Ar^1COCOAr^2$), in which Ar^1 is a more electron-withdrawing aryl group than Ar^2, gives more Ar^1CHO and Ar^2CONH_2 than Ar^2CHO and Ar^1CONH_2 except for *p*-chlorobenzil. (vii) The rate of ammonolysis of α-cyanobenzyl benzoate in basic aqueous dioxan is lower than that of cyanide ion-catalysed ammonolysis of benzil.

In view of the observed third-order kinetics, $v = k_{obs}[Benzil][NH_3][CN^-]$, the nucleophilic reagent NH_3 participates in the rate-determining step. The mechanism in Scheme 1, which involves the formation of a tetrahedral intermediate (IIa) followed by the partially rate-determining transfer of a proton (k_1) and then by the cleavage of the C–C bond (k_2), is consistent with observations (i)—(vii).

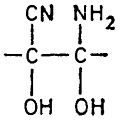
Steady-state approximation leads to the rate expression (6). Here, K_{HCN}, $K_{NH_4^+}$, and K_w denote ioniz-

$$k_{obs} = \frac{KK_{HCN}}{K_{HCN} + [H^+]} \frac{k_1[H_2O][H^+]}{k_{-1}K_w/k_2 + [H^+]} \qquad (6)$$

ation constants of HCN and NH_4^+, and ionic product of water, respectively, and k_{obs} is the third-order rate constant in $v = k_{obs}[\text{Benzil}][CN^-][NH_3]$. The values of pK_{HCN}, $pK_{HCN_4^+}$, and pK_w in aqueous dioxan (67% v/v) are 10.2, 9.2, and 16.2, respectively. Since $[NH_3]$ was kept constant irrespective of pH as shown in Table 4, the term $K_{NH_4^+}/(K_{NH_4^+} + [H^+])$ for the fraction of free ammonia is not required for expression (6). The mechanism satisfies the observed kinetics and shows the dependence of the rate on ammonia [observations (i) and (iii)]. In view of observation (iv), the rate-determining step is not attack of ammonia on the carbonyl group but a composite of the proton transfer (k_1 and k_{-1}) and the cleavage of the C–C bond (k_2). Introduction of an electron-attracting group into benzil increases not only K but also k_2 [observation (v)], since a partial negative charge appears at the carbon atoms in the transition state of k_2. The pH–rate profile is shown in Figure 1, where the observed points lie close to the theoretical line calculated from equation (6) with $K_{HCN} = 10^{-10.2}$ mol l^{-1}, $K_w = 10^{-16.2}$ mol^2 l^{-2}, $k_{-1}/k_2 = 10^{2.4}$ mol l^{-1}, and $k_1K = 0.5$ l^3 mol^{-3} s^{-1} [observation (ii)]. If the value of k_{-1} is taken as 10^{10} l mol^{-1} s^{-1} for diffusion-controlled proton transfer step from (IIb) to OH^-, the values of k_1, k_2, and K can be estimated to be 3×10^2 l mol^{-1} s^{-1}, 4×10^7 s^{-1}, and 2×10^{-3} l^2 mol^{-2}, respectively, by employing the following relationship: $\log k_1 = \log k_{-1} + pK_a(\text{IIb}) - pK_a(H_2O)$. Since $[H^+]$ is quite low under these alkaline conditions, the proton transfer (IIa) $\longrightarrow$ (IIb) with the rate proportional to $k_1[H_2O]$ involving a weaker acid H_2O (pK_a in water 15.7) and the conjugate base of the stronger acid (IIa) (pK_a in water *ca.* 8.2 ‡) may be partially rate determining. Another process having $k_1[H^+]$, k_{-1}, and $k_2[OH^-]$ instead of $k_1[H_2O]$, $k_{-1}[OH^-]$, and k_2 in equation (6) is less plausible because it requires an improbably large value of $10^{14.8}$ for k_1K. The alternative pathway *via* (IIc and d) instead of (IIa and b) is also consistent with the observations [pK_a of (IId) in water *ca.* 8.6 ‡]. They are indistinguishable at present, but (IIb) seems more likely to produce heterolysis of the C(CN)–C(O^-) bond because of electron release by the oxyanion.[15,16] Introduction of an electron-withdrawing group into the mandelonitrile portion of intermediates (IIb or d) increases the rate (k_2), which is compatible with observation (vii).


$-\overset{CN}{\underset{O^-}{C}}-\overset{NH_2}{\underset{OH}{C}}-$

(IIc)


$-\overset{CN}{\underset{OH}{C}}-\overset{NH_2}{\underset{OH}{C}}-$

(IId)

Other conceivable mechanisms described in Scheme 2 are inconsistent with our results.

The mechanism in equation (7), which involves a partially rate-determining addition step instead of the proton transfer step in Scheme 1, is compatible with all the observations except (iv). The rate expression with $K_{HCN} = 10^{-10.2}$ l mol^{-1}, $k_1 = 10$ l^2 mol^{-2} s^{-1}, and $k_{-1}K_a/k_2 = 10^{-13.8}$ mol l^{-1} agrees with the pH–rate profile. However, it seems to be less probable in terms of observation (iv), since it involves a partially rate-determining nucleophilic attack k_1.

The mechanism in equation (8) is inconsistent with the pH–rate profile [observation (ii)], since the values of pK_{HCN} and $pK_{NH_4^+}$ are 10.2 and 9.2 in aqueous dioxan, respectively, and the concentration of NH_3 was kept constant in our experiments (Table 4), the term for the fraction of free ammonia $K_{NH_4^+}/(K_{NH_4^+} + [H^+])$ being unnecessary. For the same reasons the mechanism in equation (11) is inadequate.

The third mechanism, in equation (9), would be compatible with the kinetics and the pH–rate profile if k_{-1}/k_2 were $10^{-13.8}$. However, this assumption is unacceptable. The comparison of the rate expression (9) with the observed rate constants leads to 10 l^2 mol^{-2} s^{-1} for k_1 and the maximum value for k_2 can be assumed to be 10^{10} l mol^{-1} s^{-1}, *i.e.* it is a diffusion-controlled rate constant. From these values, k_1/k_{-1} ($=K_1$) is estimated to be over 10^5 mol^2 l^{-2}, which is much too large for the equilibrium addition of CN^- and NH_3 to the carbonyl groups of benzil.

The fourth mechanism [equation (10)] leads to a wrong rate expression with regard to the order in ammonia. Both pathways in equations (10) and (11) are inconsistent with observation (vii).

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‡ These pK values of alcohols (IIb and d) can be roughly estimated to 8.2 and 8.6, respectively, employing the empirical equation[8] $pK_a(RCH_2OH) = -1.316\ \sigma^* + 15.74$. Here, the substituent R and the σ^* values used are as follows: α-Ph, 0.60 ($=0.215 \times 2.8$); α-CN, 3.64 ($=1.30 \times 2.8$); α-NH_2, 1.12 ($=0.40 \times 2.8$); β-OH, 0.555;[9] β-Ph, 0.215;[9] β-CN, 1.30;[9] β-NH_3^+ (= β-NMe_3^+), 1.90; β-NH_2, 0.40; β-O^-, −0.62. The unavailable $\sigma^*(CH_2NH_2)$ is assumed to be 0.40 which is slightly smaller than $\sigma^*(CH_2OH)$,[10] based on the acidity constants (K_e) in isopropyl alcohol (7.7 for 2-aminoethanol, 8.0 for 2-methoxyethanol, 11 for 2-phenoxyethanol, and 43 for ethylene glycol), and $\sigma^*(CH_2O^-)$ is based on the Branch–Calvin induction constant I_{O^-}, $(-12.4 + 4)/2.8$[2] $= -1.06$ pK unit[11] and the ρ value of −1.72 for pK_a (RCO_2H).[9] However, these pK_a values would be somewhat larger in 67% aqueous dioxan than those estimated above, since the dielectric constant of solvent decreases from water (80) to 70% aqueous dioxan (*ca.* 17) and the transfer of H_2O, AcOH, and PhOH from water to *ca.* 67% aqueous dioxan results in an increase of pK_a by 2.7, 2.0, and 2.9 units, respectively,[12,13] but the difference ($pK_{HA} - pK_{H_2O}$) in aqueous dioxan would be close to that in water. Analogous $\rho\sigma^*$ correlations for the pK_a values of alcohols have been observed, where ρ values are −1.364[10] and −1.40.[14]

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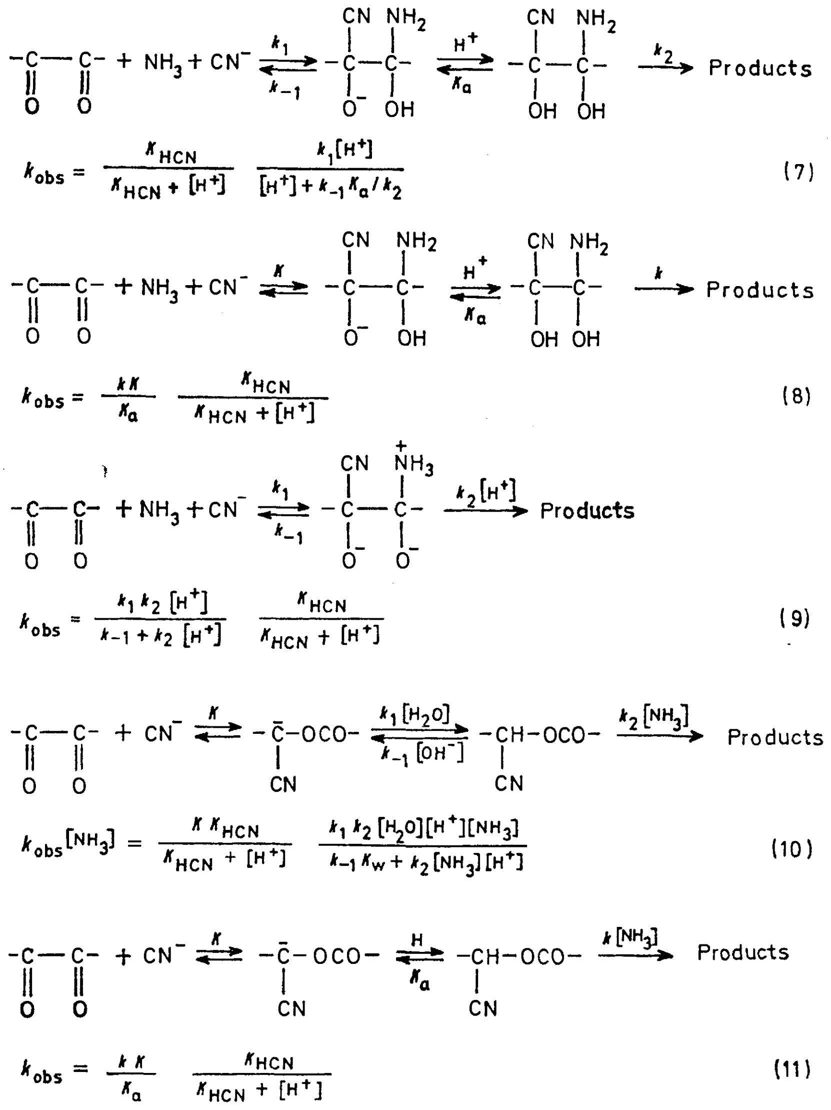

$$k_{obs} = \frac{K_{HCN}}{K_{HCN} + [H^+]} \; \frac{k_1[H^+]}{[H^+] + k_{-1}K_a/k_2} \qquad (7)$$

$$k_{obs} = \frac{kK}{K_a} \; \frac{K_{HCN}}{K_{HCN} + [H^+]} \qquad (8)$$

$$k_{obs} = \frac{k_1 k_2 [H^+]}{k_{-1} + k_2 [H^+]} \; \frac{K_{HCN}}{K_{HCN} + [H^+]} \qquad (9)$$

$$k_{obs}[NH_3] = \frac{K K_{HCN}}{K_{HCN} + [H^+]} \; \frac{k_1 k_2 [H_2O][H^+][NH_3]}{k_{-1}K_w + k_2[NH_3][H^+]} \qquad (10)$$

$$k_{obs} = \frac{kK}{K_a} \; \frac{K_{HCN}}{K_{HCN} + [H^+]} \qquad (11)$$

SCHEME 2

EXPERIMENTAL

Materials.—Benzils were prepared by the oxidation of the appropriate benzoins or deoxybenzoins.[17-25] M.p.s of benzils are as follows: benzil, 94—95°; *p*-methoxybenzil, 56—58°; *p*-chlorobenzil, 75—75.5°; *p*-chloro-*p*′-methoxybenzil, 128—130°; *p*-dimethylaminobenzil, 162—162.5°; *p*-chloro-*p*′-dimethylaminobenzil, 145°. α-Cyanobenzyl benzoate was prepared by the reaction of benzaldehyde, KCN, and benzoyl chloride, m.p. 59.5—60°.[26] All m.p.s are identical with those in the literature. Amines used were of commercial guaranteed grade.

Products.—A mixture of unsymmetrical benzil (0.5—1.0 mmol), and KCN or NaCN (0.1 mmol) in 67% v/v aqueous dioxan (5 ml) was kept at *ca.* 25°. To this solution, anisole (0.05—0.1 ml) was added as an internal standard and the contents, aldehydes or imines and occasionally benzamides, were determined by g.l.c. Relative reactivities of amines were estimated by the relative amounts of amides produced from the competitive reaction of a pair of amines (each 5—10 mmol) with benzil (0.5—1.0 mmol) and KCN (0.1 mmol). The reaction with benzoyl chloride was carried out in the presence of KOH and the relative amounts of amides were determined by g.l.c.

Kinetic Procedure.—The reaction in a thermostatted photocell was started on addition of NaCN solution (0.025—0.2 ml, 0.15M) to a temperature-equilibrated solution (2.975—2.8 ml) containing benzil (*ca.* 10^{-2}M) and ammonia (*ca.* 0.5M) in aqueous dioxan (67 or 80%). The decrease in extinction (E_t) of benzil at 370 or 430 nm was monitored 20 s after mixing. Plots of log E_t against time gave fairly good

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straight lines at higher concentrations of NaCN (>0.01M). Apparent first-order rate constants (k_{app}) were calculated from the slope of the plots. Division of k_{app} by the concentrations of NaCN and ammonia leads to the third-order rate constants (k_{obs}). However, at lower concentrations of NaCN ([NaCN] $<$ [Benzil]$_0$), especially at $<1/10$ molar ratio, the apparent rate coefficients decreased as the reaction proceeded (Figure 3). This is probably due to the effect of the benzaldehyde produced and benzoic acid, which is reported to reduce the effective concentration of cyanide ion.[5]

pH Measurement.—The pH of 67% aqueous dioxan containing the same components as the kinetic solutions except for benzil was measured on a Hitachi–Horiba glass electrode pH meter M-4. pH Values >14 were calculated using the equation $\text{pH} = \text{p}K_w + \log [\text{OH}^-]$, where p$K_w$ was determined to be 16.2 from the pH reading of 13.5 for 2×10^{-3}M-KOH solution.

pK_a *Determinations.*—The pK_a values for HCN and NH_4^+ in aqueous dioxan (67% v/v) at 25° were determined by half-neutralisation or by employing the equation $\text{p}K_a = \text{pH} + \log ([\text{HA}]/[\text{A}^-])$. Half neutralisation of *ca.* 0.3M-NH_3 in aqueous dioxan with 0.4N-HCl in aqueous dioxan and the pH determination of NH_3–NH_4^+ solutions with the $[NH_4^+]:[NH_3]$ ratio varying from 1 to 0.11 gave an average value of 9.2 for $\text{p}K_{NH_4^+}$. Half-neutralisation of 0.4N-NaCN solution with 0.4N-HCl solution gave an average value of 10.2 for $\text{p}K_{\text{HCN}}$.

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