BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN, VOL. 44, 765—771 (1971)

# Mechanism of The Ullmann Condensation Reaction. II.[1,2] Effects of the Medium, the Additives and the Substituents

Tran Dinh Tuong and Mitsuhiko Hida
*Department of Synthetic Chemistry, Faculty of Engineering, The University of Tokyo, Hongo, Tokyo*

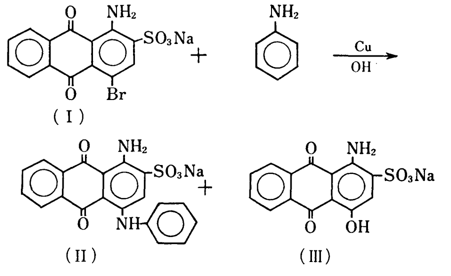
(Received May 12, 1970)

The effects of the medium, the additives, and the oxidation state of the copper catalyst on the rate of the Ullmann condensation reaction of sodium 1-amino-4-bromoanthraquinone-2-sulfonate and aniline in an aqueous buffered solution were investigated. The reaction rate was not affected by the ionic strength but depended very largely on the hydrogen-ion concentration. It was also established that the reaction was retarded by the addition of anions which can coordinate to copper; the retarding effect was in the order: $F^- \ll Cl^- < Br^- < I^- < CN^-$. The inhibiting effects of copper-chelating agents and oxygen were also observed. No marked difference, except a slight increase in initial rate, was observed when cuprous chloride was used as the catalyst instead of cupric sulfate. The effect of the substituents of aniline on the reaction rate can be expressed by Yukuwa-Tsuno's equation, in which the parameters, $\rho$ and $r$, were $-2.20$ and $0.50$ respectively. The experimental results are discussed.

Previous studies[2] of the Ullmann condensation of sodium 1-amino-4-bromoanthraquinone-2-sulfonate (I) and aniline in an aqueous buffered solution, cupric sulfate being used as the catalyst, have shown that the reaction was first order in monomeric aryl halide (I) and first order in amine, while the rate depended hyperbolically on the concentration of cupric sulfate. The reaction was also characterized by a relatively low activation energy (9.14 kcal/mol) and a low frequency factor ($10^6$). These preliminary results, however, are not sufficient for a discussion of the elementary processes of this Ullmann condensation reaction. This paper will describe some supplemental results which, it is believed, will give more insight into the detailed mechanism.

## Results and Discussion

The rate of the reaction (1) was determined under various conditions of the medium. Cupric sulfate was used as the catalyst except when otherwise stated.



(1)

*Effect of The Ionic Strength.* The ionic strength of the reaction system was varied by adding an inorganic salt. Sodium sulfate was chosen for this purpose because of its great solubility in water and because of the poor coordinating ability of the sulfate ion.

As is shown in Fig. 1, through a wide range of ionic strength ($\mu$), no marked influence was observed. In view of this fact, it is unlikely that the rate controlling step, or the equilibria preceding it, involve "true" ionic

---

[1] Presented in Part at the Annual Meetings of The Chemical Society of Japan, March, 1968 (Osaka); April, 1969 (Tokyo), and April, 1970 (Tokyo).

[2] Part I: T. D. Tuong and M. Hida, This Bulletin, **43**, 1763 (1970).

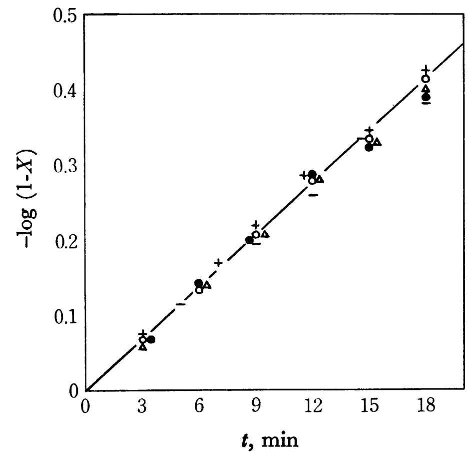


Fig. 1. Effect of ionic strength ($X$: reaction conversion). [I]$=0.31\times10^{-2}$mol/$l$, [$PhNH_2$]$=0.30$ mol/$l$, [$Cu^{2+}$]$=2.50\times10^{-4}$ mol/$l$; pH$=9.94$, $T=70$°C. Experiments in nitrogen. $\mu=0.435$ (○), 0.585 (△), 0.885 (—), 1.035 (+), 1.485 (●).

species. This assumption is partly in agreement with the thermodynamical finding that the frequency factor was quite low. This cannot explained by any mechanism involving collisions between oppositely-charged ions in the rate-determining step.[3,4]

*Effect of the Hydrogen-ion Concentration.* A series of experiments was carried out under various pH conditions (9.37—11.51) which were attained by combining a 0.20M sodium carbonate aqueous solution and a 0.15M borax aqueous solution. The results (Fig. 2) show that no simple relationship exists between the hydrogen-ion concentration and the reaction rate. Because of the absence of the effect of the ionic strength, the behavior observed must be attributed to the action of the hydroxide ion. The presence of an optimum pH can be explained by the assumption that the hydroxide ion acts as both accelerating and retarding species.

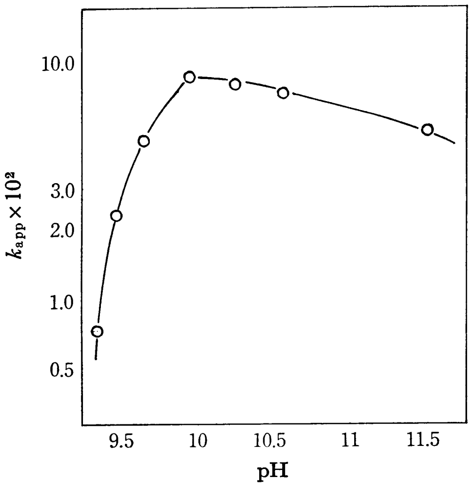


Fig. 2. Semi-logarithmic plots of $k_{app}$ *vs.* pH. [I]$=1.25\times10^{-2}$ mol/$l$, [$PhNH_2$]$=0.30$ mol/$l$, [$Cu^{2+}$]$=2.50\times10^{-4}$mol/$l$; $T=70$°C. Experiments in nitrogen.

In the pH range studied, no product other than that described in Eq. (1) was observed; the main product (II) was predominantly produced, along with a 4-hydroxy compound (III) in almost negligible amounts (0—3%). Therefore, the change in the rate could not be attributed to the formation of by-products.

In an aqueous solution, the amine exists as free and protonated species. The equilibrium:

$$PhNH_2 \overset{H^+}{\rightleftarrows} Ph\overset{+}{N}H_3 \qquad (2)$$

is shifted to the left at a high pH. Since aniline exists as a free base in the pH range used in our experiments, the accelerating effect can be understood by assuming the formation of the $PhNH^-$ which has a greater nucleophilic character and electron-transfer ability to the cupric species than aniline itself. As will be seen later, the process of reducing the divalent metal ion is believed to play an important role in the reaction.

On the other hand, the fact that the rate constant did not vary with the time suggests that the active catalyst is consumed, but then regenerated by a cyclic process. Several results to be described later in this paper suggest that the $Cu^{2+}\rightleftarrows Cu^+$ process is operative. The influence of the alkalinity of the medium on this redox process might be involved. This kind of effect has been observed in several redox equilibria of metal ions in water.[5-7] In our case, it seems reasonable to consider the effect of the pH on the redox potential and to postulate that the coordination to the metal ions of the negative hydroxide ion, $OH^-$, will favor the removal of one electron from the univalent copper ion by electrostatic repulsion. This argument has been used to explain the influence of charged ligands on the equilibrium of the $Fe^{2+}$—$Fe^{3+}$ couple in water.[7] If, in the Ullmann condensation, the univalent copper is responsible for the promotion of the reaction, the coordination of the hydroxide ion will result in a decrease in the cuprous concentration, and, thence, in a deceleration of the rate. It has been reported[8] that the Ullmann condensation of bromobenzene with the disodium salt of resorcinol in pyridine was inhibited by the hydroxide ion (generated from added sodium hydroxide or methoxide). The effect may be partly accounted for by the coordination of the hydroxide ion to the catalyst, although the detailed mechanism of deactivation has not yet been made clear.

Finally, it was suggested that the hyperbolic dependence of the reaction rate on the concentration of the catalyst can be explained by postulating the formation of copper clusters.[2] The hydroxide ion, by its ability to act as bridge between the metal ions, may facilitate the process yielding the inactive polynuclear complexes and decrease the rate.

*Effect of Molecular Oxygen.* When experiments were carried out in air, the reaction rate was markedly

---

[3] A. A. Frost and R. G. Pearson "Kinetics and Mechanism," John Wiley & Sons, 2nd. Ed. (1961), p. 130.

[4] R. P. Bell, *J. Chem. Soc.*, **1943**, 629.

[5] F. Basolo and R. G. Pearson "Mechanisms of Inorganic Reactions," John Wiley & Sons, 2nd. Ed. (1967), p. 474.

[6] B. R. James and R. J. P. Williams, *J. Chem. Soc.*, **1961**, 2007.

[7] Ref. 5, p. 76.

[8] A. L. Williams, R. E. Kinney, and R. F. Bridger, *J. Org. Chem.*, **32**, 2501 (1967).

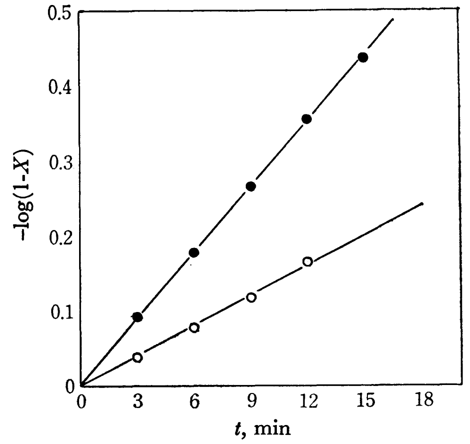


Fig. 3. Effect of oxygen (a): Pseudo-first order plots of the reaction in air (○) and in nitrogen (●). [I] = $1.25 \times 10^{-2}$ mol/*l*, $[PhNH_2]=0.30$ mol/*l*, $[Cu^{2+}] = 1 \times 10^{-2}$mol/*l*; pH=9.94, *T*=70°C.

decreased (to about one third) as compared with that in a nitrogen atmosphere. Figure 3 illustrates a typical case. The results suggest that the copper ion behaves as a catalyst in a lower oxidation state.[9] It has been reported in the literature that oxygen retards the reactions which are believed to be catalyzed by cuprous species (formed from cupric salts added initially), such as the reaction of an aromatic diazonium halide with an aliphatic unsaturated compound to give α-halo-β-phenyl alkanes and alkenes (the Meerwein reaction), the Sandmeyer reaction,[10,11] and the hydrolysis of the diphenyliodonium ion.[12,13] The retardation was interpreted in these cases as resulting from the consumption of the univalent copper by oxygen.

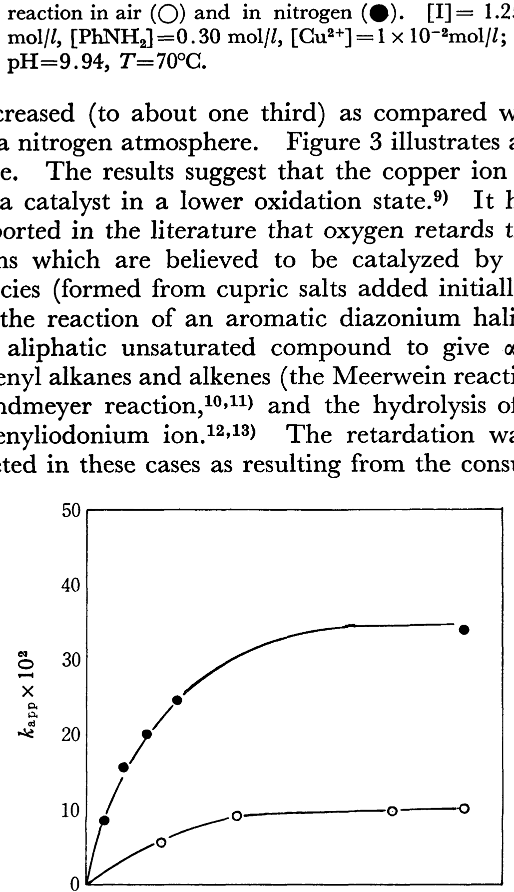


Fig. 4. Effect of oxygen (b): Dependence of the apparent rate constant $k_{app}$ on the initial concentration of cupric catalyst. Experiments in air (○) and in nitrogen (●). [I] $=2.50 \times 10^{-2}$ (○), $1.25 \times 10^{-2}$ (●) mol/*l*, $[PhNH_2]=0.30$ mol/*l*; pH=9.94, *T*=70°C.

An alternative explanation of the inhibiting effect of molecular oxygen may be possible if the reaction is assumed to proceed through a radical (or radicaloid[14]) intermediate which gives the reaction product(s). This point, however, needs further elucidation.

It is noted further that the reaction in the presence of air obeyed the same rate law as the reaction in the case when oxygen was excluded, namely, the reaction was first order in aryl halide (I), and first order in aniline, while the rate increased hyperbolically with the increase in the catalyst concentration (Fig. 4). The effect of oxygen might not be due to the change in the mechanism, but to the decrease in the concentration of the active species.

*Effect of Chelating Compounds.* The addition of chelating compounds to the reaction system was found to yield some suggestive results.

The apparent rate constants, $k_{app}$,[2] of the reaction in the presence of 8-hydroxyquinoline-5-sulfonic acid (HQS) are summarized in Table 1.[15]

The tendency of the reaction rate to decrease with an increase in the concentration of the chelating agent can reasonably be understood if the added agent is assumed to form thermodynamically stable and unreactive (or less active) complexes. HQS is known to coordinate to cupric copper ($\beta_1=11.9$, $\beta_2=21.9$ at 25°C).[16]

In order to understand quantitatively the behavior of the chelating agent in the reaction system, we attempted calculations on the assumption that HQS forms an inactive complex:

$$Cu^{2+} + HQS \overset{K_1}{\rightleftarrows} Cu^{2+}\cdot HQS \qquad (3)$$

From ESR measurements,[2] the catalyst was found to exist mostly in the divalent form. The concentration of cupric copper not bonding to HQS was denoted as $c_1$, the concentration of HQS not bonding to the metal ion, as $L$, the equilibrium constant of (3), as $K_1$, the total concentration of HQS, as $l_0$, and that of

Table 1. Effects of HQS on the reaction rate[a)]

| No. | R=[HQS]/ $[Cu^{2+}]$ | $k_{app} \times 10^2$ *l*·mol/min | $k_R$[b)] |
|---|---|---|---|
| 1 | 0.00 | 17.66 | 1.000 |
| 2 | 0.21 | 14.20 | 0.804 |
| 3 | 0.41 | 10.11 | 0.570 |
| 4 | 0.82 | 7.13 | 0.413 |
| 5 | 1.22 | 5.14 | 0.291 |
| 6 | 1.85 | 3.08 | 0.174 |
| 7 | 0.00 | 8.46 | 1.000 |
| 8 | 0.50 | 5.85 | 0.690 |
| 9 | 0.90 | 3.14 | 0.370 |

a) $[I]_0=0.31 \times 10^{-2}$ mol/*l* (Nos. 1—6), $1.25 \times 10^{-2}$ mol/*l* (Nos. 7—9); $[PhNH_2]_0=0.30$ mol/*l*; $[Cu^{2+}]_0=2.50 \times 10^{-4}$ mol/*l*; pH=9.94, T=70°C.
Experiments in nitrogen.

b) Relative rate constant (see the text).

---

[9] Zero valent copper has been proved to be inactive in the absence of oxygen.[8] See also P. W. Weston and H. Adkins, *J. Amer. Chem. Soc.*, **50**, 859 (1928).

[10] J. K. Kochi, *ibid.*, **77**, 5090 (1955); **78**, 1228 (1956); **79**, 2942 (1957).

[11] S. C. Dickerman, K. Weiss, and A. K. Ingberman, *ibid.*, **80**, 1904 (1958).

[12] M. C. Caserio, D. L. Glusker, and J. D. Roberts, *ibid.*, **81**, 336 (1959).

[13] F. M. Beringer, E. M. Gindler, M. Rapoport, and R. J. Taylor, *ibid.*, **81**, 351 (1959).

[14] O. Vogl and C. S. Rondestedt, Jr., *ibid.*, **77**, 3067 (1955).

[15] The authors are indebted to Mr. H. Inoue of our laboratory for having carried out the experiments Nos. 7, 8, and 9 of Table 1.

[16] C. F. Richard, R. F. Gustafson, and A. E. Martell, *J. Amer. Chem. Soc.*, **81**, 1033 (1959).

the catalyst, as $c_0$. We have:

$$c_1(1+K_1L) = c_0 \tag{4}$$

The mass balance of the chelating agent is represented as:

$$L + K_1c_1L = l_0 \tag{5}$$

or:

$$L = l_0/(1+K_1c_1) = \frac{l_0/c_0}{(1/c_0)+(K_1c_1/c_0)} \tag{6}$$

By combining Eqs. (4) and (6), Eq. (7) is obtained:

$$c_1/c_0 = \left(1+K_1\frac{l_0/c_0}{(1/c_0)+(K_1c_1/c_0)}\right)^{-1} \tag{7}$$

Denoting the $c_1/c_0$ and $l_0/c_0$ ratios as $x$ and $R$ respectively, Eq. (7) can be rewritten as:

$$x = \left(1+K_1\frac{R}{(1/c_0)+(K_1x)}\right)^{-1} \tag{8}$$

or:

$$x^2 + ((1/K_1c_0)-1+R)x - 1/K_1c_0 = 0 \tag{9}$$

By solving this equation, $x$ is obtained as a function of $R$:

$$x = \frac{1}{2}[\sqrt{((1/K_1c_0)-1+R)^2+4/K_1c_0} - (1/K_1c_0-1+R)] \tag{10}$$

We postulate further that the apparent rate constant is proportional to the concentration of cupric copper[17] not bonding to HQS, and that the complex $Cu^{2+}\cdot$HQS is inactive; therefore:

$$x = c_1/c_0 = k_R \tag{11}$$

where $k_R$ is the relative rate constant.

By combining Eqs. (10) and (11), we obtain:

$$k_R = \frac{1}{2}[\sqrt{((1/K_1c_0)-1+R)^2+4/K_1c_0} - ((1/K_1c_0)-1+R)] \tag{12}$$

By substituting the numerical values of $k_R$ and $R$ corresponding to Experiment No. 6 in Table 1 into Eq. (9), the value of $k_1$ was determined to be $1.85\times 10^4$. The values of $k_R$ as calculated from Eq. (12), were plotted against the observed values. The results (Fig. 5) show the validity of the assumptions made above and can be reasonably understood by the assumption that the ligands, such as aniline,[18] with great coordinating power towards the cupric ion, prevent the entering of a second molecule of HQS into the coordination sphere of the metal. Further, the relatively small value of $K_1$, compared with the stability constant in water at 25°C, is not unreasonable if we consider the presence of the ligands stronger than water and the higher temperature at which the experiments were carried out.

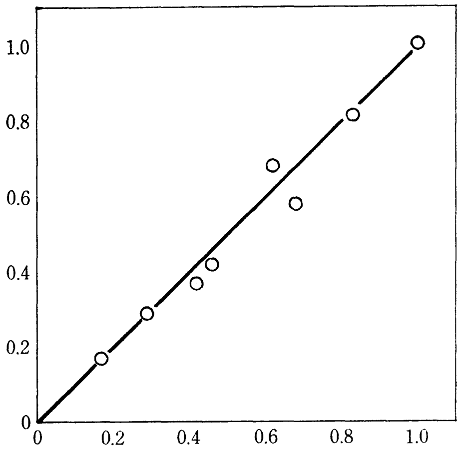


Fig. 5. Effect of the addition of HQS: Plots of $k_R$ (observed) *vs.* ${}_Rk$ (calculated).

The inhibiting effect of the chelating agents can be interpreted by the assumption that at least three sites of coordination are required for the reaction to be promoted, or that the complexing metal ion is prevented from changing into the univalent state.

Retarding or inhibiting effects were also observed when other chelating agents, such as 2,2′-bipyridyl, 2,2′-biquinolyl, and 2,9-dimethyl-1,10-phenanthroline, were introduced into the reaction system. The effects of these additives are shown in Fig. 6.

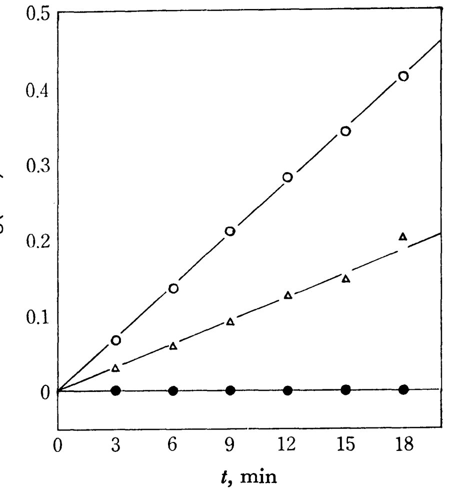


Fig. 6. Effect of chelating compounds (che). [I]$=0.31\times10^{-2}$ mol/*l*, [PhNH$_2$]$=0.30$ mol/*l*, [che]$=5.00\times10^{-4}$ mol/*l*, [Cu$^{2+}$] $=2.50\times10^{-4}$ mol/*l*; pH=9.94, $T$=70°C.
Experiments in nitrogen.
Control (○), che: cuproin (△), neocuproin, 2,2-dipyridyl (●)

When the mole ratio of the chelating agent to that of the catalyst was 2 : 1, 2,2′-bipyridyl and 2,9-dimethyl-1,10-phenanthroline completely inhibited the reaction, but 2,2′-biquinolyl did so incompletely. The inferiority of the latter in effecting inhibition is presumably due to its poor solubility in the aqueous solution. It was observed that the agent was partly left undissolved and that it floated on the surface of the reaction mixture.

---

[17] Although the rate depended hyperbolically on the initial concentration of the catalyst,[2] linearity between the rate and the concentration of the catalyst could be assumed in the dilute region of the cupric copper.

[18] It was observed that cupric copper formed a precipitate with aniline in an aqueous solution. See also: P. Spacu, V. Voicu, and I. Pascaru, *J. Chim. Phys.*, **60**, 368 (1963); I. S. Ahuja, D. H. Brown, R. H. Nuttall, and D. W. A. Snarp, *J. Inorg. Nucl. Chem.*, **27**, 1105 (1965); M. S. Barvinok, I. S. Bukhareva, and Yu. S. Varshavskii, *Zh. Neorg. Khim.*, **10**, 1799 (1965); *Chem. Abstr.*, **64**, 167 (1966).

2,2'-Biquinolyl(cuproin)[19] and 2,9-dimethyl-1,10-phenanthroline(neocuproin)[20] are known as specific chelating agents of cuprous copper and not of cupric species. This specific chelating ability has been used to detect the existence of cuprous copper and, in some cases, to prove its catalytic capacity, especially in systems where the metal is believed to exist in various oxidation states. Thus, the evidence for the presence of $Cu^+$ intermediate in the cupric-ion-catalyzed oxidation of ascorbic acid[21] or in the solvolysis of diaryliodonium salts in the presence of $Cu^{2+}$ [12] has been afforded by the use of these specific cuprous-ion complexing reagents.

The inhibition of the reaction by cuproin and neocuproin mentioned above likely suggests that the catalyst, initially added as cupric sulfate, is partly reduced to the cuprous state.

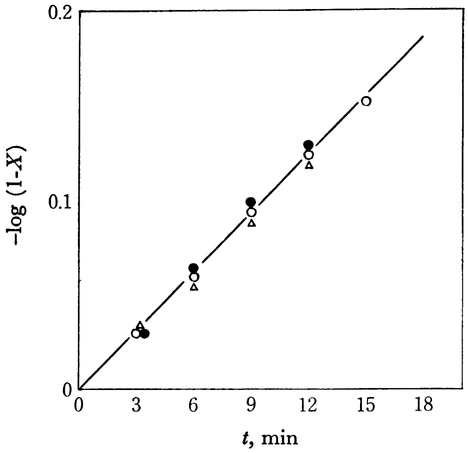


Fig. 7. Effect of anions (a). $[I]=1.25\times10^{-2}$ mol/*l*, $[PhNH_2]=0.30$ mol/*l*, $[Cu^{2+}]=2.50\times10^{-4}$ mol/*l*; pH=9.94, *T*=70°C.
Experiments in nitrogen.
Catalyst: $CuSO_4$ (○), $CuCl_2$ (●) $CuBr_2$ (△)

*Effect of Anions.* It was found (Fig. 7) that cupric sulfate, cupric chloride and cupric bromide, when used at equal molar concentrations, all catalyzed the reaction at the same rate. This result can be interpreted by assuming that the anion associated with the cupric ion was readily replaced by other ligands existing in the system.

The situation, however, was different when the anion was added in sufficiently large amounts. Several anions ($F^-$, $Cl^-$, $Br^-$, $I^-$, $CN^-$) were introduced in the form of their sodium salts. Their effects are illustrated in Fig. 8, where the pseudo-first order plots of the reaction are represented.

The results show that the fluoride did not exert any marked influence on the reaction, but the other anions decreased the rate. Since the absence of the effect of the ionic strength was confirmed, as has been mentioned above, the retarding effect must be ascribed to the action of the added anions.

Figure 8 reveals that the anions inhibit the reaction in this order: $F^- \ll Cl^- < Br^- < I^- < CN^-$. It is well known that both cuprous and cupric copper can form complexes with halides and cyanide, but the reverse order of stability of the complexes has been observed for the two oxidation states.[22] Thus, while the $F^- < Cl^- < Br^- < I^- < CN^-$ order has been reported for the cupric ion, the univalent copper ion forms complexes with the opposite sequence of stabilities: $CN^- < I^- < Br^- < Cl^- < F^-$ (In fact, complex formation from $Cu^+$ and $F^-$ has not yet been established). The available thermodynamic data[23] also suggest that in an aqueous solution, the cupric complexes with halide and cyanide ions are far more unstable than the corresponding complexes of cuprous copper.

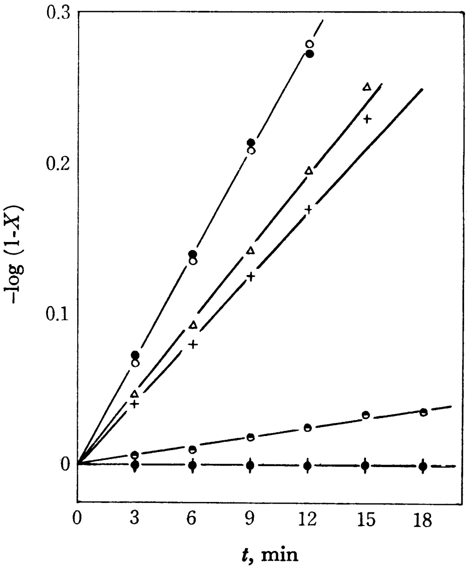


Fig. 8. Effect of anions (b). $[I]=1.25\times10^{-2}$ mol/*l*, $[PhNH_2]=0.30$ mol/*l*, $[NaX]=0.20$ mol/*l*, $[Cu^{2+}]=2.50\times10^{-4}$ mol/*l*; pH=9.94, *T*=70°C.
Experiments in nitrogen.
Control (○); X:F (●), Cl (△), Br (+), I (⊖), CN (⧫)

These facts might be interpreted as indicating that cuprous copper is responsible for the promotion of the reaction, and that the retarding effect of the halide and

Table 2. Retarding effects of the $Cl^-$ and $Br^-$ anions[a]

| No. | $[X^-]$, mol/*l*[b] | $k_R$ |
|---|---|---|
| 1 | 0.00 | 1.000 |
| 2 | 0.10 | 0.805 |
| 3 | 0.20 | 0.625 |
| 4 | 0.40 | 0.500 |
| 5 | 0.60 | 0.415 |
| 6 | 0.10 | 0.785 |
| 7 | 0.20 | 0.607 |
| 8 | 0.30 | 0.430 |
| 9 | 0.40 | 0.286 |

a) $[I]_0=0.31\times10^{-2}$ mol/*l*, $[PhNH_2]_0=0.30$ mol/*l*, $[Cu^{2+}]_0=2.50\times10^{-4}$ mol/*l*; pH=9.94, *T*=70°C.
Experiments in nitrogen.
b) $X^-=Cl^-$ (Nos. 1—5), $Br^-$ (Nos. 6—9)

---

19) J. Hoste, *Anal. Chim. Acta*, **4**, 23 (1950).

20) W. H. McCurdy and G. F. Smith, *Analyst* (London), **77**, 846 (1952).

21) R. Flitman and E. Frieden, *J. Amer. Chem. Soc.*, **79**, 5198 (1958).

22) S. Ahrland, J. Chatt, and N.R. Davies, *Quart. Rev.* (London), **12**, 265 (1958).

23) "Stability Constants," *Chem. Soc.* (London), Special Pub., No. 17 (1964).

cyanide ions might be described as resulting from the competition between the added anions and the reactants for the metal ion.

The retarding effect of the anions was increasingly pronounced as their concentration increased. The relative rate constants are tabulated in Table 2.

Attempts to derive the quantitative relations between the relative rate constant and the concentration of the anion were, however, unsuccesful, presumably because of the complexities of the manner of action of the anions. Thus, besides their ability of competing with the reactants for the catalyst, the anions might facilitate the formation of polynuclear clusters postulated earlier[2] by bridging. This point is expected to be clarified by further studies.

*Catalytic Activity of Cuprous Cloride.* The data obtained by investigating the effects of molecular oxygen, cuproin and neocuproin, and added anions suggest that even when the catalyst is introduced as cupric salts, the univalent metal ion might be formed in the reaction system and that this species might play an important role in promoting the reaction. In order to obtain more direct evidence concerning this point, cuprous chloride was used as the catalyst.

The experiments showed that the initial rate was somewhat larger than that of the reaction catalyzed by cupric sulfate, but the steady state was rapidly established (within less than three minutes), and at this steady stage, the rate was found to be almost the same as in the case when cupric copper was used (Table 3).

These results can be explained on the assumptions that cuprous chloride was rapidly converted to cupric species and that the reaction took the same course as when cupric salt was used. The comparatively large rate during the early stage of the reaction might be due to the unconverted univalent copper salt. The reaction during this stage might take place on the surface of the solid catalyst.

Neocuproin exhibited the same inhibiting effect as in the experiments using cupric salt when added in a sufficiently large amount as compared with the concentration of the catalyst, but the reaction did occur (No. 6, Table 3) when the neocuproin: catalyst mole ratio was 1 : 1. This fact can be easily understood if we remember that two molecules of neocuproin can coordinate to one metal ion.[20]

TABLE 3. COMPARISON OF THE ACTIVITY OF CUPROUS CHLORIDE AND CUPRIC SULFATE[a)]

| No. | $[Cu^+]_0$ $\times 10^3$ mol/$l$ | $[Cu^{2+}]_0$ $\times 10^3$ mol/$l$ | [Che][b)] $\times 10^3$ mol/$l$ | $k_{app} \times 10^2$ $l\cdot$mol/min |
|---|---|---|---|---|
| 1 | 2.00 | 0.00 | 0.00 | 32.30 |
| 2 | 0.00 | 2.00 | 0.00 | 36.40 |
| 3 | 1.00 | 0.00 | 0.00 | 26.90 |
| 4 | 0.00 | 1.00 | 0.00 | 28.00 |
| 5 | 1.00 | 0.00 | 2.00 | 0.00 |
| 6 | 2.00 | 0.00 | 2.00 | 33.80 |

a) $[I]_0 = 1 \times 10^{-2}$ mol/$l$, $[PhNH_2]_0 = 0.30$ mol/$l$; pH=9.94, $T$=70°C (Nos. 1—4), 90°C (Nos. 5 and 6). Experiments in nitrogen.

b) Neocuproin.

Although no decisive conclusions as to the activity of cuprous species could be deduced from the above results alone, we have noted that the addition of reducing agents to the system catalyzed by cupric salts enhanced the reaction rate markedly.[2] Detailed results will be reported in a subsequent paper of this series.

*Substituent Effect.* Six substituted anilines were allowed to react with (I). The reaction rates corresponding to *p*-anisidine, *p*-toluidine, aniline, and *p*-chloroaniline were found to fit Yukawa-Tsuno's equation[24]:

$$\log (k_X/k_H) = \rho(\sigma + r\cdot\Delta\bar{\sigma}_{R^+}) \qquad (13)$$

in which the reaction parameter, $\rho$, was found to be $-2.20$, $r$, to be 0.50. $\Delta\bar{\sigma}_{R^+}$ is the difference between the Brown-Okamoto substituent coefficient[25] and the Hammett coefficient.[26] The relation is represented in Fig. 9.

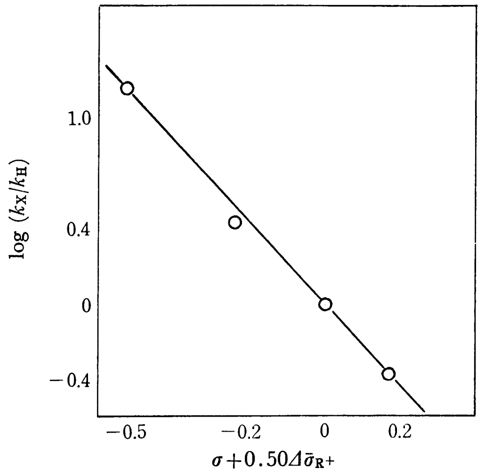


Fig. 9. Substituent effect.

Under the experimental conditions of this work, the reaction rates of *p*-nitroaniline and *p*-aminobenzoic acid with I were too slow to measure.

It has been reported that the yield of the Ullmann condensation reaction of 2-chloro-5-methoxybenzoic acid and anilines increased with an increase in the basicity of the amines[27] but no quantitative correlation has been established.

The basicities of anilines were known to be well correlated by the "normal" Hammett equation,[28] at least when the *para* substituents are not strongly electron-withdrawing. Furthermore, Chapman and Parker have reported that the Hammett relationship was useful in correlating the reactivities of substituted anilines towards activated aryl halides in the absence of a catalytic agent.[29]

The results observed in the Ullmann condensation of I with anilines show that, in the presence of a copper

---

[24] Y. Tsuno, T. Ibata, and Y. Yukawa, This Bulletin, **32**, 960, 965, 971 (1959).

[25] H. C. Brown and Y. Okamoto, *J. Amer. Chem. Soc.*, **79**, 1913 (1957); **80**, 4979 (1958).

[26] Taken from H. H. Jaffe, *Chem. Rev.*, **53**, 191 (1953).

[27] W. G. Dauben, *J. Amer. Chem. Soc.*, **70**, 2420 (1948).

[28] A. I. Biggs and R. A. Robinson, *J. Chem. Soc.*, **1961**, 388.

[29] N. B. Chapman and R. E. Parker, *ibid.*, **1951**, 3301.

catalyst, the mesomeric effect of the substituents on the reaction center (nitrogen atom) was considerably emphasized. More work must be done in this connection.

## Experimental

The experimental technique was described in Part I.[2] The additives were introduced into the reaction system prior to the catalyst.

8-Hydroxyquinoline-5-sulfonic acid, 2,2′-dipyridyl, cuproin, and neocuproin of a guaranteed grade were used without further purification.

Cuprous chloride was prepared by reducing a (cupric sulfate+sodium chloride) system with anhydrous sodium sulfite.[30] Found: Cu, 64.13% (Calcd for CuCl: Cu, 64.18%). This catalyst was added as powder.

This research was supported financially in part by the Asahi Glass Foundation for the Contribution to Industrial Technology.

---

[30] W. C. Ferrelius, "Inorganic Syntheses," Vol. 2, p. 1.