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The Ullmann Condensation Reaction of Haloanthraquinone Derivatives with Amines in Aprotic Solvents. II.[1] The Presence of an Induction Period in the Condensation with 2-Aminoethanol

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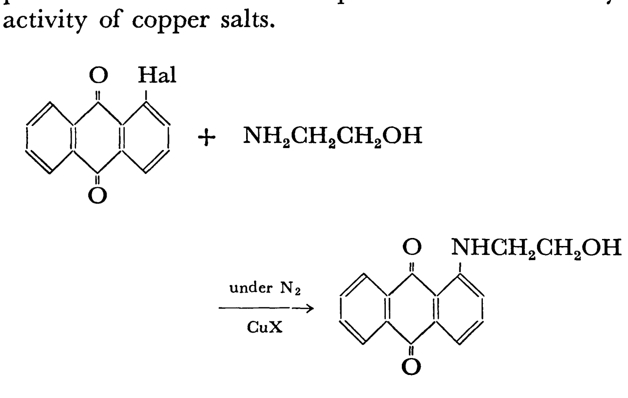
An induction period was present in the Ullmann condensation reactions of 1-bromoanthraquinone(AQBr) with 2-aminoethanol(AE) in the presence of CuBr or CuI in aprotic solvents under a nitrogen atmosphere, while there was no induction period in the reaction systems of 1-iodoanthraquinone(AQI)–AE–CuBr, AQI–AE–CuI, and AQBr–AE–[Cu(CH$_3$CN)$_4$]ClO$_4$. In the condensation system with a copper(I) catalyst, the Cu(I) species was oxidized to the Cu(II) species by means of an electron transfer from Cu(I) to haloanthraquinone as the reaction proceeded. By adding copper(II) bromide, the induction period vanished in the reaction system of AQBr–AE–CuBr. The copper(II) species increased the catalytic activity of the copper(I) species. The formation of the copper(II) species was responsible for the presence of an induction period and played an important role in the Ullmann condensation reaction of haloanthraquinones with amines in the presence of copper(I) salt as a catalyst.

The Ullmann condensation reaction, the nucleophilic substitution of aryl halides by amines or phenols in the presence of copper catalyst, is widely used for the synthesis of diaryl amines or diaryl ethers. Although many studies of the condensation of phenols with aryl bromides have been described, and although aryloxycopper(I) has been proposed as a nucleophile,[2,3] only a few mechanistic studies of the condensation with amines have been reported. We reported previously on the catalysis of copper(II) species in the reaction of sodium 1-amino-4-bromoanthraquinone-2-sulfonate with aniline in an aqueous alkaline solution.[4–7] Kurdyumova investigated the reaction of haloanthraquinones with aromatic and aliphatic amines in the presence of copper salts as catalysts.[8] However, scarcely no systematic studies of the Ullmann condensation reaction of haloanthraquinone derivatives with amines in aprotic solvents have been reported.

In our preceding paper,[1] we discussed the reactivities of haloanthraquinones, amines, and catalysts in the reaction of haloanthraquinones with amines by copper catalysts in aprotic solvents under a nitrogen atmosphere.

In this paper we will report that an induction period is observed under some reaction conditions in the reaction of 1-haloanthraquinones with 2-aminoethanol in the presence of copper(I) halides in aprotic solvents, and we will propose that the formation of the copper(II) species plays an important role in determining the presence of an induction period and the catalytic activity of copper salts.



Results and Discussion

The plot of the yield of the reaction product against the reaction time shows that the copper(I) catalyst is more effective than the copper(II) catalyst, that the catalytic activity of copper(I) salts decreases in this order: CuBr>CuI, and that 1-iodoanthraquinone (AQI) is more reactive than 1-bromoanthraquinone (AQBr) (Fig. 1). An induction period is observed in the condensation systems of AQBr–2-aminoethanol (AE)–CuBr and AQBr–AE–CuI, while an induction period is absent in the condensation systems using AQI. In explaining the presence of an induction period, the following several factors were discussed: the autocatalytic reaction, the halogen-exchange reaction between AQBr and CuI, the depolymerization of the polymeric copper(I) complex to monomeric species, and the formation and catalytic action of the copper(II) species.

Autocatalytic Reaction. When the catalytic activity of copper salt is increased by the coordination of a condensation product, the reaction rate will increase as the reaction proceeds, and there will be an induction period. If this is the case, the addition of the condensation product [1-(2-hydroxyethylamino)-anthraquinone] will enhance the reaction rate and the induction period will vanish. However, the yield of the condensation product decreased and the induction period did not vanish upon the addition of the condensation product(Fig. 2). This result probably indicates that the catalytic action of the copper(I) species diminishes by means of the coordination of the condensation product. Therefore, autocatalysis does not seem to be responsible for the presence of the induction period.

Halogen-exchange Reaction between 1-Bromoanthraquinone and Copper(I) Iodide. It has been established that the halogen atoms of haloaromatics are replaced by halogens or other groups of copper(I) salts in aprotic solvents.[9–12] In the case of the reaction of 1-bromoanthraquinone with 2-aminoethanol by the CuI catalyst, 1-iodoanthraquinone was indeed produced along

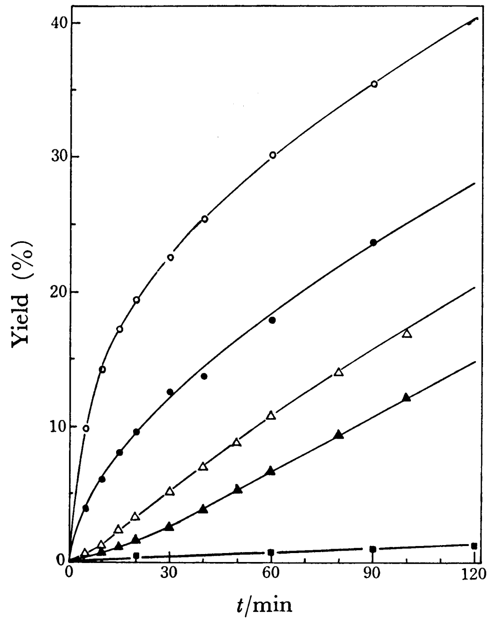


Fig. 1. Plots of the yields of products *vs.* reaction time in the reaction of 1-haloanthraquinone(AQHal) with 2-aminoethanol(AE) by copper salt(CuX) catalyst at 70 °C; $[\mathrm{AQHal}]_0=5.00\times10^{-3}$ mol/l, $[\mathrm{AE}]_0=0.50$ mol/l, $[\mathrm{CuX}]_0=2.00\times10^{-3}$ mol/l, solvent 1,2-dimethoxyethane–methyl cellosolve 4 : 1. ○: AQI–CuBr, ●: AQI–CuI, △: AQBr–CuBr, ▲: AQBr–CuI, ■: AQBr–CuBr$_2$.

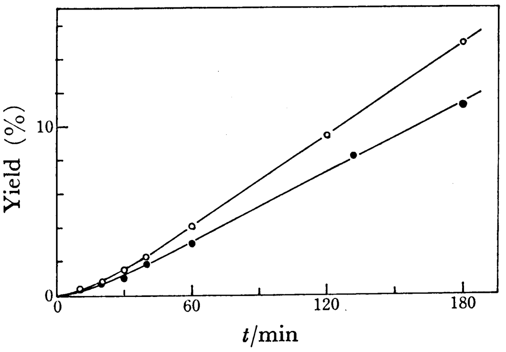


Fig. 2. Effect of the addition of condensation product; $[\mathrm{AQBr}]_0=5.00\times10^{-3}$ mol/l, $[\mathrm{AE}]_0=0.50$ mol/l, $[\mathrm{CuI}]_0=2.00\times10^{-3}$ mol/l, temp 60 °C, solvent THF–ethanol 4 : 1. ○: control, ●: $[\text{1-(2-hydroxyethylamino)anthraquinone}]_0=1.30\times10^{-3}$ mol/l.

with the condensation product (Fig. 3). This result suggests that the bromine atom of 1-bromoanthraquinone is replaced by the iodine atom in the course of the condensation reaction,

$$\mathrm{AQBr} + \mathrm{CuI} \rightarrow \mathrm{AQI} + \mathrm{CuBr}.$$

Since more reactive 1-iodoanthraquinone is produced with the lapse of time, the rate of the condensation reaction will increase as the reaction proceeds, then an induction period will be observed.

If the rate law is supposed to be first-order in both concentrations of the substrate and catalyst,[10] the reaction rate can be written by

$$v = (k_1[\mathrm{CuBr}]+k_1'[\mathrm{CuI}])[\mathrm{AQBr}] + (k_2[\mathrm{CuBr}]+k_2'[\mathrm{CuI}])[\mathrm{AQI}]. \qquad (1)$$

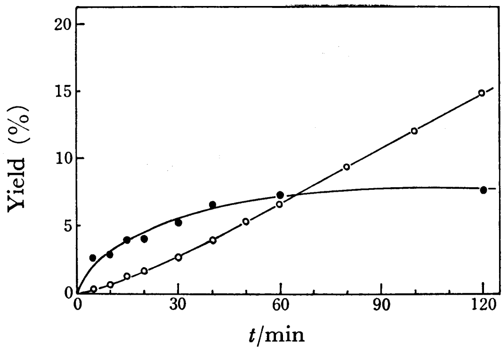


Fig. 3. Reaction of 1-bromoanthraquinone with 2-aminoethanol by CuI catalyst; $[\mathrm{AQBr}]_0=5.00\times10^{-3}$ mol/l, $[\mathrm{AE}]_0=0.50$ mol/l, $[\mathrm{CuI}]_0=2.00\times10^{-3}$ mol/l, temp 70 °C, solvent 1,2-dimethoxyethane–methyl cellosolve 4 : 1.
○: 1-(2-Hydroxyethylamino)anthraquinone,
●: 1-iodoanthraquinone.

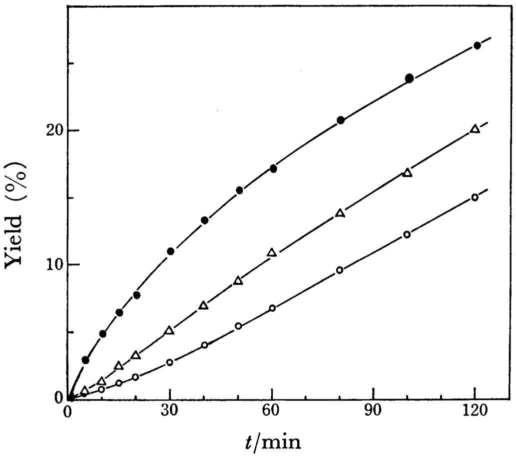
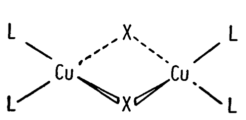


Fig. 4. Effect of anionic ligand of CuX; $[\mathrm{AQBr}]_0=5.00\times10^{-3}$ mol/l, $[\mathrm{AE}]_0=0.50$ mol/l, $[\mathrm{CuX}]_0=2.00\times10^{-3}$ mol/l, temp 70 °C, solvent 1,2-dimethoxyethane–methyl cellosolve 4 : 1. ●: $[\mathrm{Cu(CH_3CN)_4}]\mathrm{ClO_4}$, △: CuBr, ○: CuI.

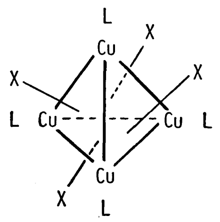
The values of k_1/k_1', k_2/k_1', and k_2'/k_1', estimated from the initial rate of each, were 2.4, 45.4, and 17.2 respectively. AQI was formed in a yield of about 7% after 60 min (Fig. 3). Since the resulting AQI is consumed in the reaction with 2-aminoethanol, the concentration of the resulting CuBr may be supposed to be higher than that of the observed AQI. Consequently, the rate after 60 min was estimated to be larger than the initial rate by a factor of more than 2.7. On the other hand, Fig. 3 shows that the rate after 60 min rises to about two times the initial rate. These values may indicate some effects of the halogen exchange on the reaction rate. However, it cannot be considered as the main reason for the presence of the induction period even in the reaction of AQBr with 2-aminoethanol caused by the CuI catalyst, for the induction period was also present in the condensation system of AQBr–AE–CuBr and it could not result from an increase in the rate by the halogen-exchange reaction.

Consequently, the presence of the induction period cannot be understood on the basis only of the halogen-exchange mechanism.

Depolymerization of the Polymeric Copper(I) Complex to Monomeric Species. As is shown in Fig. 4, the induction period was observed in the reaction systems of AQBr–AE–CuBr and AQBr–AE–CuI, while it was not present in the system of AQBr–AE–tetrakis(acetonitrile)copper(I) perchlorate ($[Cu(CH_3CN)_4]ClO_4$). Copper perchlorate complexes are known to be present as monomeric species in solution because the perchlorate ligand cannot act as a bridging group between copper(I) species.[13–14] The structures of copper(I) halide–amine complexes were proposed to be the halogen-bridged dimer(A)[15–17] or the tetramer(B)[15,16,18] on the basis of the cryoscopic data on solution and an X-ray examination of the crystalline state.

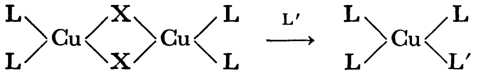


(A)
L=RNH_2, R_2NH.
X=Cl, Br, I.



(B)
L=RNH_2; X=Cl, Br, I.
L=R_2NH; X=Cl.

The $[Cu(CH_3CN)_4]ClO_4$ catalyst, which did not exhibit the induction period, was more effective catalyst than CuBr and CuI, which did exhibit the induction period(Fig. 4). These facts seem to indicate that the monomeric copper(I) species is a rather more effective catalyst than the polymeric one in the Ullmann condensation and that the induction period may be ascribed to the change from the polymeric copper(I) species to the active monomeric species. The polymeric copper(I) species will be depolymerized by the coordination of amine as follows:



X=Halogen; L=Halogen, Amine, AQBr; L′=Amine.

As is shown in Fig. 5, the induction period was shortened with the increase in the concentration of amine, and it was not observed at a high concentration of amine. This result seems to support the above consideration. The Cu(I)–amine solution was allowed to stand for a long time, either at room temperature or at 70 °C, and then the solution was added to a solution containing 1-bromoanthraquinone. If the induction period was caused by the depolymerization of the polymeric copper(I) species in the course of the reaction, the induction period would vanish under the above condition, but no change of the induction period was observed. This finding may enable us to exclude the idea that the change in copper(I) species from a polymeric complex to a monomeric one was responsible for the presence of the induction period.

Formation and Catalytic Action of the Copper(II) Species. Figure 6 shows that the plots of $-\log(1-x)$ against the time, where x denotes the yield of the reaction product, are independent of the initial concentration of AQBr. This result suggests that the reaction rate is first-order in the concentration of AQBr. Since the concentration of amine used in a large excess may reasonably be supposed to be kept constant, the presence of the induction period is considered to reflect the change in the catalytic activity. We reported previously that the copper(I) species was oxidized to the copper(II) species by means of an electron transfer from copper(I) to haloanthraquinone as the reaction proceeded, but the reaction rate did not decrease in accordance with the formation of the copper(II) species, which was less active than the copper(I) species.[1] Figures 4 and 7 suggest that the induction period is observed in the case of the slow formation of the copper(II) species. As has been mentioned above, the induction period was absent at high concentrations of amine. The ESR spectra of the reaction system indicated that the formation of copper(II) species increased with the increase in the concentration of amine. The ESR spectra showed also that the formation of the copper(II) species in the reaction of 1-iodoanthraquinone with 2-aminoethanol was much faster than that in the reaction using 1-bromoanthraquinone. The reaction with 1-iodoanthraquinone did not reveal any induction period, but the

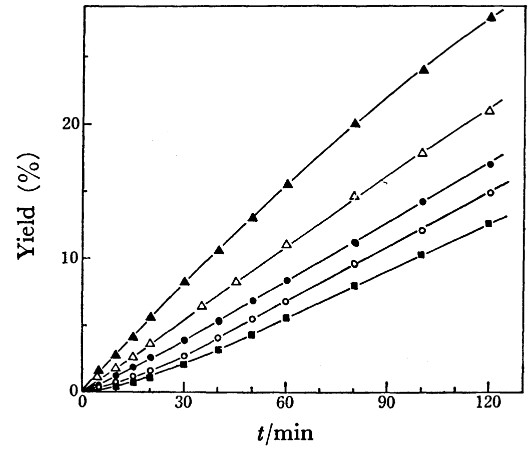


Fig. 5. Effect of the concentration of 2-aminoethanol; $[AQBr]_0=5.00\times10^{-3}$ mol/l, $[CuI]_0=2.00\times10^{-3}$ mol/l, temp 70 °C, solvent 1,2-dimethoxyethane–methyl cellosolve 4 : 1. $[AE]_0$; ▲: 2.00, △: 1.50, ●: 1.00, ○: 0.50, ■: 0.25 mol/l.

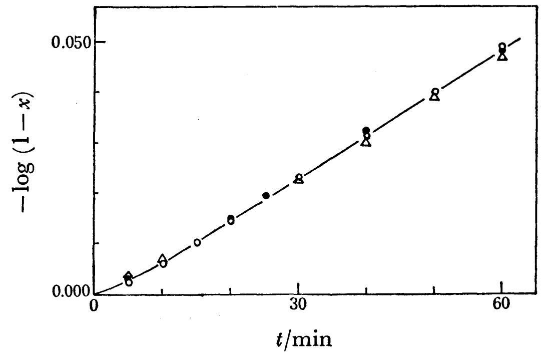


Fig. 6. Effect of the concentration of 1-bromoanthraquinone; $[AE]_0=0.50$ mol/l, $[CuBr]_0=2.00\times10^{-3}$ mol/l, temp 70 °C, solvent 1,2-dimethoxyethane–methyl cellosolve 4 : 1. $[AQBr]_0$; ●: 7.00×10^{-3}, ○: 5.00×10^{-3}, △: 3.00×10^{-3} mol/l.

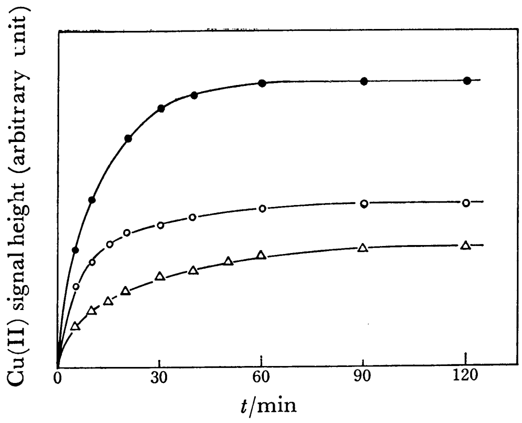


Fig. 7. Time dependence of Cu(II) signal height; $[AQBr]_0=5.00\times10^{-3}$ mol/l, $[AE]_0=0.50$ mol/l, $[CuX]_0=2.00\times10^{-3}$ mol/l, temp 70 °C, solvent 1,2-dimethoxyethane–methyl cellosolve 4 : 1. ●: $[Cu(CH_3CN)_4]ClO_4$, ○: CuBr, △: CuI.

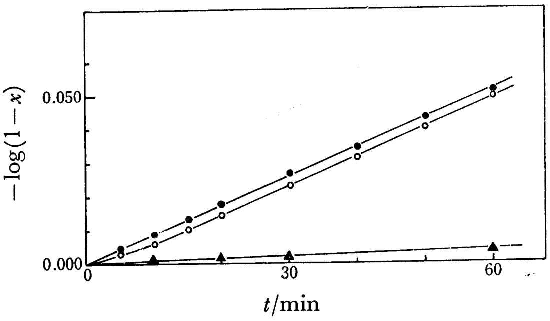


Fig. 8. Pseudo-first order plots of the condensation catalyzed by CuBr, $CuBr_2$, or CuBr+$CuBr_2$; $[AQBr]_0=5.00\times10^{-3}$ mol/l, $[AE]_0=0.50$ mol/l, temp 70 °C, solvent 1,2-dimethoxyethane–methyl cellosolve 4 : 1. ●: $[CuBr]_0=1.70\times10^{-3}+[CuBr_2]_0=0.30\times10^{-3}$ mol/l, ○: $[CuBr]_0=2.00\times10^{-3}$ mol/l, ▲: $[CuBr_2]_0=2.00\times10^{-3}$ mol/l.

reaction using 1-bromoanthraquinone revealed a marked induction period(Fig. 1).

Thus, the formation of the copper(II) species seems to be related to the presence of the induction period. If this is the case, the induction period will vanish upon the addition of copper(II) bromide to copper(I) bromide. The experimental results fit in with this expectation(Fig. 8). Although the yield of the condensation product was strikingly low when the $CuBr_2$ catalyst was used, it is noteworthy that the copper(II) species increased the catalytic activity of the copper(I) species.

All of the results support the idea that the formation of copper(II) species is closely correlated with the induction period. Thus, the presence of an induction period can be understood to be due to the effect of the formation of the copper(II) species on the catalytic activity of the copper(I) species.

Further detailed studies are in progress to elucidate the formation and role of the copper(II) species.

Experimental

Materials. The 1-bromoanthraquinone, 1-(2-hydroxyethylamino)anthraquinone, and copper(I) halides were prepared as has been reported previously.[1)] The 1-iodoanthraquinone was prepared by the reaction of anthraquinone-1-diazonium salt and potassium iodide and purified by column chromatography on silica gel (using benzene as the developing solvent), followed by recrystallization from acetic acid: mp 205.3—205.5 °C (cor) (lit, mp 204—205 °C[19)]) (Found: C, 50.32; H, 1.94%). Copper(II) bromide was purified by washing with ethyl acetate and anhydrous ethanol and then dried *in vacuo.* Tetrakis(acetonitrile)copper(I) perchlorate was prepared as has been described in the literature,[20)] recrystallized several times from acetonitrile, and dried under a nitrogen atmosphere. The 2-aminoethanol was purified by the method described previously.[1)] All the solvents were dried by the usual methods, distilled, and stored under a nitrogen atmosphere.

Kinetic Measurements. The kinetic measurements were conducted by the method described in the previous paper.[1)] The 1-iodoanthraquinone formed by the halogen-exchange reaction was analyzed as follows: sample(0.5 ml) were withdrawn and diluted in ethanol. The solution was analyzed by the use of a Shimadzu Du Pont LC-1 high-speed liquid chromatograph(column: Zorbax ODS; eluent: methanol-water 67 : 33), with 1-amino-2-bromoanthraquinone as the internal standard.

ESR Measurement. The ESR spectra were measured at 70 °C by means of a JEOL-PE-3X ESR spectrometer. A single sample tube was used throughout the measurement, and the conditions of the ESR spectrometer were kept constant as far as possible.

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