Mechanism of the Ullmann Condensation Reaction. Part III.[1] Role of the Copper Catalyst

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The Ullmann condensation of sodium 1-amino-4-bromo-9,10-dihydro-9,10-dioxoanthracene-2-sulphonate (I) with nucleophilic reagents in alkaline, aqueous solution has been investigated. When copper(II) sulphate was used as catalyst and aniline as reagent, e.s.r. studies showed that the hydroxide ion and the amine were co-ordinated to a divalent copper species but no evidence indicating the co-ordination of (I) was obtained. The copper(II)-catalysed reaction was accelerated markedly during the earlier stage by the addition of metal reducing agents (Sn^{2+}, Ti^{3+}, and Fe^{2+}). The distribution of the products depended on pH, the relative yield of the phenolic by-product being minimized at high concentrations of hydroxide ion. Anilines were found to enhance the rate of the reaction of (I) with toluene-*p*-sulphonamide. The role of the copper catalyst is discussed and a mechanism is proposed.

Displacement of the halogen from aromatic halides by nucleophiles under the catalytic action of copper salts has been used widely as a synthetic tool since its discovery by Ullmann.[2] The reaction is a powerful method of synthesizing diaryl ethers[3] and diarylamines[4] of research and industrial interest. Its applicability to halogenoanthraquinones was reported by the discoverer[5] and the closely related reaction of halogenoanthraquinones with copper(I) salts has also been mentioned.[6] The practical importance of the Ullmann condensation of halogenoanthraquinones can be readily seen from the fact that it provides several industrial processes in the manufacture of dyestuffs.[7]

On the other hand, little attention has been paid to the mechanism of the reaction. Since Bunnett and Zahler classified the reaction as of unknown mechanism,[8] not much work has been done on the topic. The reaction is still employed in synthesis on a largely empirical basis.

With the purpose of elucidating the mechanism of the reaction, we have carried out an investigation of the Ullmann condensation of sodium 1-amino-4-bromo-9,10-dihydro-9,10-dioxoanthracene-2-sulphonate (I) with aniline in alkaline, aqueous solution.

This reaction was chosen for study partly because of its practical importance[7] and chiefly because it is known to proceed under relatively mild conditions[9] convenient for experimental work. Preliminary investigations

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[1] (*a*) Part I, T. D. Tuong and M. Hida, *Bull. Chem. Soc. Japan*, 1970, **43**, 1763; (*b*) Part II, 1971, **44**, 765.

[2] (*a*) F. Ullmann, *Ber.*, 1903, **36**, 2382; (*b*) F. Ullmann and H. Kipper, *ibid.*, 1905, **38**, 2120; (*c*) F. Ullmann and P. Sponagel, *ibid.*, p. 2211; *Annalen*, 1906, **350**, 85.

[3] H. E. Ungnade, *Chem. Rev.*, 1946, **38**, 407.

[4] R. M. Acheson, 'Acridines,' Interscience, New York, 1956, p. 148.

[5] F. Ullmann, *Ber.*, 1970, **43**, 536; *Annalen*, 1911, **381**, 1.

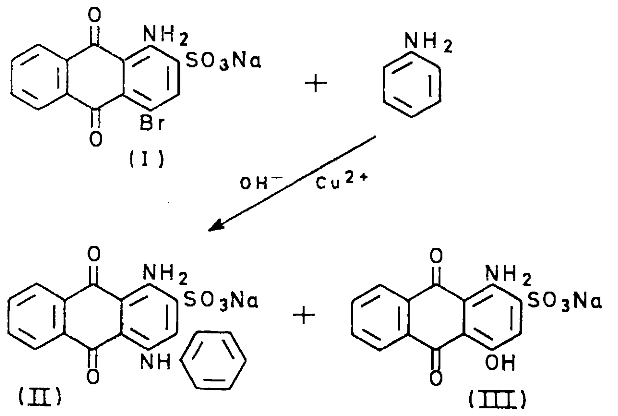
[6] W. B. Hardy and R. B. Fortengaugh, *J. Amer. Chem. Soc.*, 1958, **80**, 1716.

[7] N. N. Woroshzov, 'Grundlagen der Synthese von Zwischenprodukten und Farbstoffen,' Academie Verlag, Berlin, 1966, ch. 7.

[8] J. F. Bunnett and R. E. Zahler, *Chem. Rev.*, 1951, **49**, 273.

[9] T. Maki, *Ann. Rep. Committee Chem. Aromatic Compounds, Japan Soc. Promotion Sci.*, 1951, **4**, 98; 1952, **5**, 162.

showed that when the experimental conditions were appropriately controlled homogeneity could be achieved so that kinetic studies could yield reproducible results.



Although the aryl halide (I) has many functional groups, under our conditions, the expected condensation product was formed almost exclusively.

Previous studies[1] have revealed several characteristics of the reaction but some problems remained to be solved from the mechanistic point of view. Thus, while e.s.r. measurements proved that when the added catalyst was copper(II) sulphate, it remained mostly in the divalent state in the reaction system, the effects of additives suggested that the truly active species was copper(I). The role of the nucleophile (aniline) and the effect of hydroxide ion were not understood. This paper describes results which give more insight into these points and we propose a mechanism for the reaction.

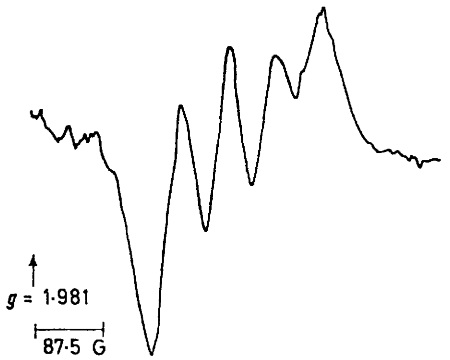


FIGURE 1 E.s.r. spectrum of the Ullmann condensation system $[(I)]_0 = 1{\cdot}25 \times 10^{-2}$M, $[PhNH_2]_0 = 0{\cdot}30$M, $[Cu^{2+}]_0$ $2{\cdot}5 \times 10^{-4}$M, pH = 9·94,[1a] temp. = 20 °C

Complex Formation in the Copper(II) *Catalysed Reaction System.*—E.s.r. measurements were carried out on the Ullmann condensation system of (I) with aniline, copper(II) sulphate being used as catalyst. The spectrum observed at 20 °C is shown in Figure 1.* Under the experimental conditions the reaction system was homogeneous.

While the spectrum of copper(II) sulphate in pure water was a single line, that observed for the alkaline solution of the copper salt had a well resolved hyperfine structure of four lines, undoubtedly resulting from the interaction of the nucleus of the metal ion (for copper, $I = 3/2$) with the unpaired electron. It is well established that a necessary condition for the hyperfine structure of copper(II) complexes to be observable is that the ion must be co-ordinated by strong ligands so that the ligand–ligand relaxation process is minimized.[10-13] In our case, the e.s.r. observation is indicative of the formation of a copper(II) complex containing the hydroxide ion in the co-ordination sphere. Considering the poor solubility of copper(II) hydroxide, the observed spectrum is probably due to a monohydroxo-complex.

The presence of aniline caused a shift of *ca.* 10 G to higher field in the absorption spectrum of the alkaline solution of the copper salt. This suggests that the aromatic amine also formed a co-ordinate bond with the copper(II) ion. It has been reported that aniline is bonded to the divalent copper ion through the lone electron pair (and not through the π-electron system of the benzene nucleus).[14]

In contrast to aniline, the aryl halide (I) did not affect the spectra of the systems (Cu^{2+} + alkaline solution) and (Cu^{2+} + aniline + alkaline solution).

The spectrum of the Ullmann condensation reaction system was not affected by the presence of molecular oxygen and iodide ion (added in the form of sodium iodide). The effect of oxygen and halide ions of decreasing the reaction rate [1b] is thus conceived as resulting from an interaction with the active catalytic species which exists in the system in low concentration and in equilibrium with the copper(II) complex which yields the e.s.r. absorption.

The absorption intensity depended on the quantity of added copper salt and the experimental results can be summarized as follows.

(i) The intensity of the system (Cu^{2+} + pure water) increased linearly with an increase in the concentration of copper(II) sulphate in the range investigated ($1{\cdot}25 \times 10^{-4}$—$1 \times 10^{-2}$M). This observation indicates that an ion–ion interaction is not important as a relaxation process [15] and cannot account for the facts stated below.

(ii) The intensity of the alkaline solutions of Cu^{2+}, (Cu^{2+} + aniline), and of the Ullmann condensation reaction system increased asymptotically with the concentration of added copper salt.

On the other hand, it was found [1a] that the reaction rates at various catalyst concentrations correlated linearly with the signal intensities of the corresponding systems. These facts may be explained by assuming

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* The spectrum observed at 70 °C, at which most of the experiments were carried out, had, as expected, a less well resolved hyperfine structure.

[10] S. Fujiwara and H. Hayashi, *J. Chem. Phys.*, 1965, **43**, 23.

[11] H. M. McConnell, *J. Chem. Phys.*, 1956, **25**, 709.

[12] R. B. Garvey, *J. Phys. Chem.*, 1956, **60**, 71.

[13] H. R. Germann and J. D. Swalen, *J. Chem. Phys.*, 1962, **36**, 3221.

[14] A. V. Heuvelen and L. Goldstein, *J. Phys. Chem.*, 1968, **72**, 481.

[15] W. B. Lewis and M. Alei, *J. Chem. Phys.*, 1966, **45**, 4003.

that in the alkaline, aqueous medium polynuclear copper(II) complexes are formed and that these complexes are inactive towards the reaction and also do not give an e.s.r. spectrum. Several workers have reported the formation of polynuclear complexes of the general formula $\mathrm{Cu}_n(\mathrm{OH})^{2+}_{2n-2}$ in aqueous systems.[16-21] The hydroxide ion has been suggested to play the role of a bridge connecting the metal centres. Polynuclear copper(II) complexes are also known to give a very broad line covering thousands of gauss so that they cannot be easily detected by e.s.r.[22]

The dependence of the e.s.r. absorption intensity on pH is illustrated in Figure 2. The presence of a maximum at pH *ca.* 10 was also observed for the pH dependence of the reaction rate [1b] and lends further support to the assumption of formation of polynuclear copper(II) complexes. No linear relationship, however, was observed between the signal intensities and the rates of the reaction at various pH values. This point will be discussed later.

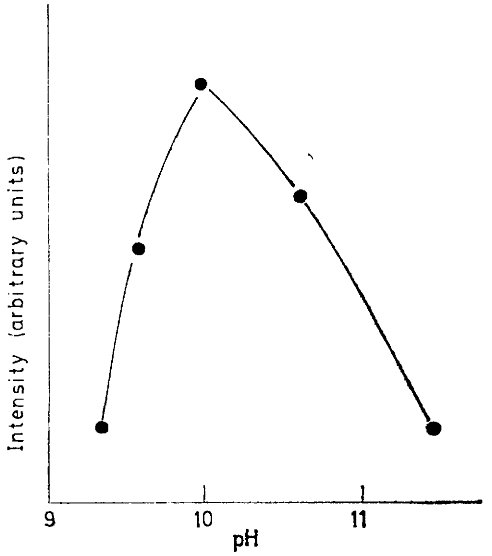
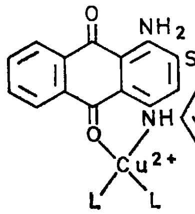


FIGURE 2 Dependence of e.s.r. signal intensity of (I) on pH

The spectrum of the reaction system remained almost unchanged during the reaction, except that, near completion, a small shoulder appeared on the high-field side. The spectrum was then identical with that observed when product (II) was added to an alkaline solution of (Cu^{2+} + aniline). These results showed that product (II) formed a complex with copper(II) ion, and the complex probably has the form (IV).



(IV)

On the other hand, good linear pseudo-first-order plots were obtained for all the reactions of (I) with aniline, including those with conversions >90%. Complexation of the product is thus not expected to exert a noticeable influence on the reaction rate.

Effects of Metal Reducing Agents on the Copper(II) *Catalysed Reaction.*—Several experimental facts reported so far in this series,[1] *e.g.* the decelerating effect of oxygen, halide, and cyanide ions and the specific chelating action of copper(I) ion, strongly suggest that the Ullmann condensation is actually promoted by univalent copper. Direct evidence concerning this point might be expected to be obtained from the use of copper(I) salts as added catalyst but it was found that, in contrast to the cases when copper(II) salts were employed, the systems containing copper(I) salts were heterogeneous.*

We tried to overcome this difficulty by a different method. Instead of using non-soluble copper(I) salts, attempts were made to generate the univalent copper from the dissolved copper(II) catalyst by the use of reducing agents. The effect of the addition of Sn^{2+}, Ti^{3+}, and Fe^{2+} salts on the yields of the reaction catalysed by copper(II) sulphate is shown in Table 1. Independent experiments proved that in the absence of the copper catalyst, the metal reducing agents did not promote the reaction.

TABLE 1 [a,b]

Effect of metal reducing agents on the yields of the copper(II) catalysed reaction of (I) with aniline

Catalyst	$Y_{\mathrm{(II)}}$ [c]	$Y_{\mathrm{(III)}}$ [d]
Cu^{2+}	21·5	0·3
$\mathrm{Cu}^{2+} + \mathrm{Fe}^{2+}$	70·0	1·9
$\mathrm{Cu}^{2+} + \mathrm{Ti}^{3+}$	87·0	0·7
$\mathrm{Cu}^{2+} + \mathrm{Sn}^{2+}$	95·3	1·0

[a] $[(\mathrm{I})]_0 = 1{\cdot}25 \times 10^{-2}\,\mathrm{M}$, $[\mathrm{PhNH_2}]_0 = 0{\cdot}30\,\mathrm{M}$, $[\mathrm{Cu}^{2+}] = [\mathrm{Fe}^{2+}] = [\mathrm{Ti}^{3+}] = [\mathrm{Sn}^{2+}] = 2{\cdot}50 \times 10^{-4}\,\mathrm{M}$; pH = 9·94, temp. = 46 °C; reaction time 30 min. Experiments were carried out under oxygen-free nitrogen. [b] See Experimental section for analytical procedures. [c] Yield of the main product $\{= 100 \times [(\mathrm{II})]/[(\mathrm{I})]_0\}$. [d] Yield of the by-product $\{= 100 \times [(\mathrm{III})]/[(\mathrm{I})]_0\}$

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* When copper (I) chloride was used as the catalyst, the reaction proceeded at almost the same rate to the system catalysed by copper(II) salts.[1b] We explained this result by assuming that the copper(I) salt was converted into copper(II) species and that the reaction took the same course as in the case when copper(II) catalysts were used. Later investigations, however, revealed that the copper(I) catalysed reaction mixture was heterogeneous even with stirring, and contrary to the copper(II) catalysed system, the system promoted by copper(I) chloride did not give an e.s.r. absorption. Furthermore, in the presence of atmospheric oxygen, the rates of the two reactions were different [copper(II) was more effective than the univalent salt as the catalyst]. These facts proved that the reaction was not in the same steady state when copper(I) chloride was used instead of copper(II) sulphate and that the previous assumption is erroneous. The same results were obtained when copper(I) bromide was used in place of the chloride.

[16] C. B. Biedermann, *Arkiv. Kem.*, 1956, **9**, 175.

[17] D. D. Perrin, *J. Chem. Soc.*, 1960, 3185.

[18] H. Ohtaki, *Inorg. Chem.*, 1968, **7**, 1205.

[19] H. Kakihana, T. Amaya, and M. Maeda, *Bull. Chem. Soc. Japan*, 1970, **43**, 4155.

[20] R. C. Courtney, R. L. Gustafson, S. Chaberek, and A. E. Martell, *J. Amer. Chem. Soc.*, 1959, **81**, 519.

[21] R. L. Gustafson and A. E. Martell, *J. Amer. Chem. Soc.*, 1962, **84**, 2309.

[22] M. Mori and S. Fujiwara, *Bull. Chem. Soc. Japan*, 1963, **36**, 1636.

The kinetic profile of the reaction promoted by (Cu^{2+} + Fe^{2+}), shown in Figure 3, proved that the rate was enhanced very markedly during the early stage and in the later phase the reaction proceeded at almost the same rate as the reaction promoted by Cu^{2+} alone. It was also found that the presence of bromide ion (added previously as sodium bromide) at a concentration equal to that of (I), and of Fe^{3+} [added as iron(III) sulphate] at a concentration equal to that of the Fe^{2+} salt, did not alter the kinetic results. The decrease in rate in the later phase is thus not due to formation of bromide ion or Fe^{3+} salt.

These facts suggest that as the result of an interaction of the copper(II) species with Fe^{2+}, an active catalytic species is formed and then consumed. The existence of the interaction was proved by examining the effect of introducing the Fe^{2+} salt on the e.s.r. absorption of the copper(II) catalysed system. While the spectrum of the system promoted by Cu^{2+} did not vary with time, the introduction of the Fe^{2+} salt caused a decrease of the intensity of the absorption spectrum due to Cu^{2+}, and the signal disappeared after *ca.* 5 min. The formation of a precipitate was observed, and e.s.r. measurements proved that it contained Fe^{3+}.

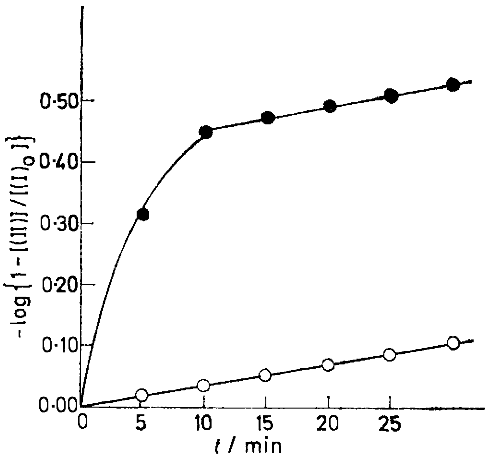
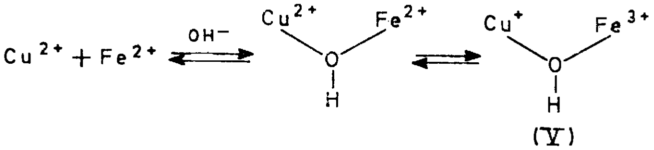


FIGURE 3 Pseudo-first-order plots of the reaction catalysed by copper(II) sulphate (○) and that promoted by copper(II) + iron(II) sulphate (●). For experimental conditions see footnotes to Table 1

The formation of a precipitate and the disappearance of the e.s.r. signal of the alkaline solution of Cu^{2+} and (Cu^{2+} + aniline) were also observed upon addition of iron(II) sulphate. On the other hand, the spectrum of Cu^{2+} in pure water remained unchanged upon addition of the divalent iron salt.*

A plausible explanation for the above observations is that in alkaline solution, an electron transfer process occurred between Cu^{2+} and Fe^{2+} through hydroxide ion acting as a bridge, yielding first a copper(I) species (V) which then collapses irreversibly into insoluble copper(I) species and Fe^{3+} salt. The soluble copper(I) species (V) is thought to be responsible for the acceleration observed in the earlier stage of the reaction, and the reaction in the later phase is promoted by the insoluble copper(I) salt.



(V)

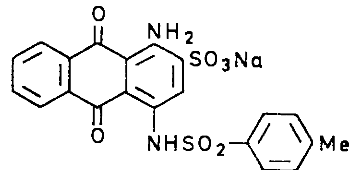
The observations described above support the assumption that even in aqueous media, the Ullmann condensation is promoted by univalent copper. The role of copper(I) as the true catalyst has been suggested by other authors.[23,24]

Role of the Nucleophile.—Expecting to get more insight into the role of the nucleophile, we carried out a series of experiments in which toluene-*p*-sulphonamide was allowed to compete with anilines for the aryl halide (I). This nucleophile was selected for study because it is known to react with (I) at rates appropriate for experimental work,[25] and especially, it has structural features convenient for comparison with the anilines.

The reaction of (I) with toluene-*p*-sulphonamide was complete in *ca.* 3 h to give the expected condensation product (VI) and a trace of the phenol (III).

It was found by t.l.c. that during the first hour the reaction did occur but the rate was very low. During the later phase, the reaction showed autocatalysis which is thought to be due to the action of product (VI). The presence of by-product (III) became recognized only in the later phase when the conversion was >60%. A pseudo-first-order plot of the reaction is shown in Figure 4(a).

p-Toluidine and some other *para*-substituted anilines were then allowed to compete with toluene-*p*-sulphonamide for the aryl halide (I). In all these competitive reactions, it was found that product (VI) was formed almost exclusively; the condensation products of the anilines and the phenol (III) were produced only in negligible amounts. A typical first-order-plot is shown in Figure 4(b). Although the autocatalytic tendency was still observed, deviations from linearity were much suppressed compared with the reaction of (I) with toluene-*p*-sulphonamide in the absence of the anilines. The formation of product (VI) was much enhanced by the amines. The initial rates of the competitive reactions, collected in Table 2, proved that substituents



(VI)

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* The solution of iron(II) sulphate in pure water did not give an e.s.r. signal.

[23] H. Weingarten, *J. Org. Chem.*, 1964, **29**, 977, 3624.

[24] A. L. Williams, R. E. Kinney, and R. F. Bridger, *J. Org. Chem.*, 1964, **32**, 2561.

[25] Y. Hosoda, 'Senryo Kagaku (The Chemistry of Dyes),' Gihodo, Tokyo, 1957, p. 364.

on the aromatic amines accelerated the reaction of (I) with toluene-*p*-sulphonamide in the order p-NO$_2$ < H < *p*-Me < *p*-OMe.

Examination of the e.s.r. spectra of the systems proved that the presence of toluene-*p*-sulphonamide did not cause any change in the spectrum of the alkaline solution of [Cu^{2+} + (I)] but caused a shift of *ca.* 8 G to high field in the spectrum of the system [Cu^{2+} + (I) + aniline] in the same solvent. The same phenomenon was observed for systems not containing (I).

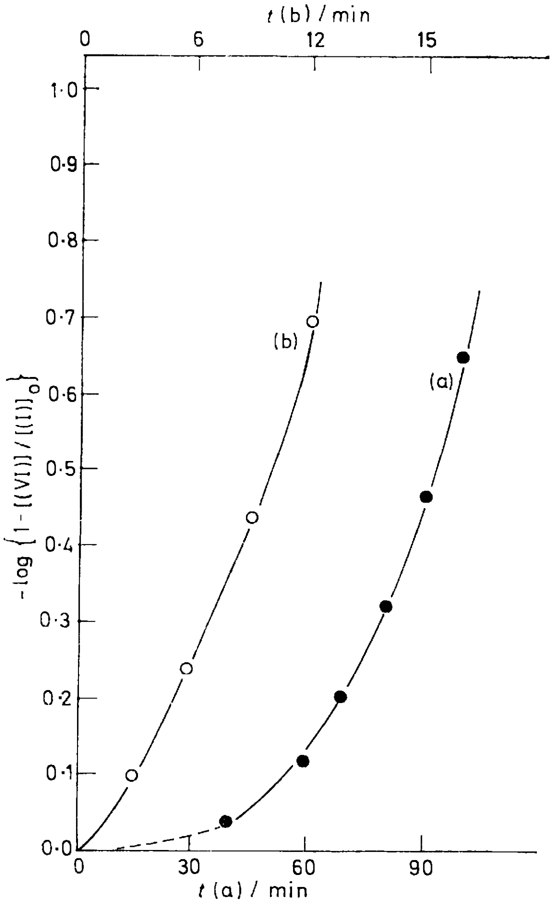

FIGURE 4 Pseudo-first-order plots of the reaction of (I) (0·31 × 10^{-2}M) with toluene-*p*-sulphonamide (7·50 × 10^{-2}M) (a) in the absence of *p*-toluidine and (b) in the presence of *p*-toluidine (7·50 × 10^{-2}M): [Cu^{2+}] = 0·50 × 10^{-2}M, pH = 9·94, temp. = 70 °C, carried out under nitrogen

These results suggest that the accelerating effect of the anilines on the condensation of (I) with toluene-*p*-sulphonamide results from their ability to attract the amide into the co-ordination sphere of Cu^{2+}, as proved by e.s.r. measurements,* and to reduce the copper(II) to the active univalent state. The anilines may also affect the reactivity of toluene-*p*-sulphonamide through some kind of ligand effect. It has been reported by Bacon [26] that the reaction of aryl halides with copper(I) salts was sensitive to solvent. The yield of the reaction of 2-acetylamino-3-bromoanthraquinone with copper(I) chloride giving the chloroanthraquinone was found to be much better in α-picoline than in chlorobenzene.[6] Ito and Watanabe have investigated the effect of bases with a co-ordinating capacity towards copper(I) ion in the Rosenmund–von Braun reaction and found that the reactivity of aryl halides depended on the structures of the added bases.[27]

TABLE 2 [a]

Initial rates v_0 [b] of the reaction of (I) (0·31 × 10^{-2}M) with toluene-*p*-sulphonamide (7·50 × 10^{-2}M) in the presence of *para*-substituted anilines (7·50 × 10^{-2}M)

Substituent	$10^4 v_0$/mol l^{-1} min^{-1}
p-NO$_2$	[c]
p-Cl	0·35
H	0·57
p-Me	2·90
p-OMe	14·60

[a] [Cu^{2+}] = 0·50 × 10^{-2}M; pH = 9·94; temp. = 70 °C. Experiments were carried out under nitrogen. [b] d[(VI)]/dt at t = 0. [c] Too slow to measure. The first-order-plots were almost identical with Figure 4(a).

Effect of pH on the Distribution of Products.—The effect of the pH of the medium on the rate of the reaction of (I) with aniline is complicated,[1b] suggesting that hydroxide ion may assume more than one role.

The reaction was found always to be accompanied by the formation of the phenol (III) although the yield of this by-product was invariably small (<2%). Compound (III) was also formed on treating the aryl halide (I) with copper(II) sulphate in alkaline solution.†

Expecting to get more information on the role of hydroxide ion, we investigated the effect of pH on the distribution of products, and found that the ratio of the yield of the main product (II) to that of the phenol (III) increased with an increase in concentration of hydroxide ion (Table 3). We found earlier [1a] that the rate associated with the postulated monomeric copper(II) species, k_1 (= dk_{app}/d[Cu^{2+}]$_0$ at infinitely dilute concentration of added catalyst, k_{app} being the apparent rate constant), increased regularly

TABLE 3 [a, b]

Effect of pH on the distribution of products

pH	$Y_{(II)}$ [c]	$Y_{(III)}$ [d]	$Y_{(II)}/Y_{(III)}$
9·37	11·0	1·5	7·3
9·87	30·9	1·6	19·6
9·94	35·6	1·6	21·8
10·57	54·4	1·2	47·3

[a] [(I)]$_0$ = 1·25 × 10^{-2}M; [PhNH$_2$]$_0$ = 0·30M; reaction time 30 min.; temp. = 70 °C. [b] See Experimental section for analytical procedures. [c] Yield of (II) {= 100[(II)]/[(I)]$_0$}. [d] Yield of (III) {= 100[(III)]/[(I)}$_0$.

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* We cannot explain the effect of aniline on the co-ordinating capacity of toluene-*p*-sulphonamide. No evidence on their interaction was obtained from an investigation of their electronic spectra in alkaline solution.

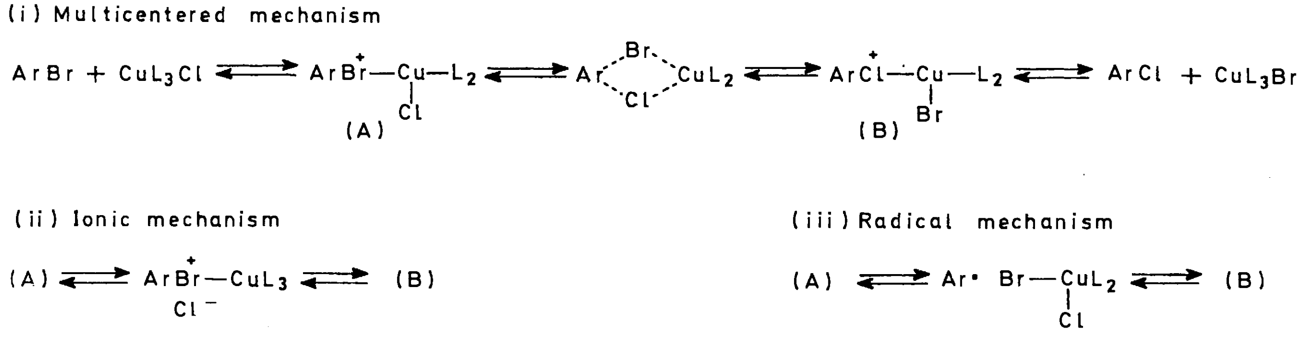
† Attempts were made to synthesize the phenol (III) by treating the aryl halide with the alkaline solution, but it was found that even when reaction was allowed to proceed as long as 72 h, the yield was only 60%. This result, however, proves that the poor yield of (III) in the reaction of (I) with aniline is the result of a kinetically, but not thermodynamically, controlled process.

[26] R. G. R. Bacon and H. A. O. Hill, *J. Chem. Soc.*, 1964, 1097, 1108, 1112.

[27] T. Ito and K. Watanabe, *Bull. Chem. Soc. Japan*, 1968, **41**, 419.

with pH. These results suggest that hydroxide ion, besides affecting the formation of polynuclear copper(II) complexes,* also enhances the condensation of (I) with aniline. Since under our experimental conditions, free aniline does not dissociate into its conjugate base, the effect of hydroxide ion is probably to deprotonate the ligand aniline and to favour the reduction of the copper(II) species. Kinoshita has proposed a mechanism for the reduction of copper(II) by aniline and pointed out the role of Lewis bases in the process.[28]

Mechanism.—Although divalent copper salts were used in our studies, several results reported so far in this series suggest that the metal ion possesses catalytic activity only after being reduced to the copper(I) state. The mechanism of the reaction of copper(I) salts with aromatic halides have been proposed by Bacon and Hill.[26] These authors suggested three alternative ways of bond breaking in the intermediate formed as the result of co-ordination of, for example, aryl bromide to copper(I) chloride to give aryl chloride (Scheme 1).



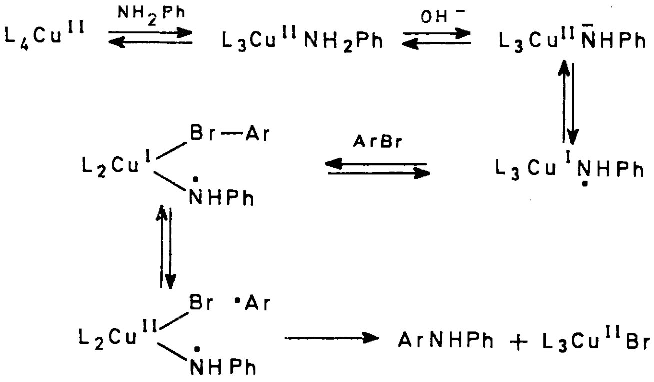
SCHEME 1

This theory, which is similar to an earlier idea of Stephens and Castro,[29] is supported by several workers.[27,30-33] Although application of these ideas does not completely explain our results, we propose them as a framework, but with modifications which we feel explain our experimental facts.

In our experiments, the copper(II) catalyst was added in small quantities relative to the aryl halide (I) and the e.s.r. signal due to copper(II) species remained almost unchanged during the reaction. We also verified that copper(I) bromide was not oxidized to the divalent state in the alkaline solution of [(I) + aniline].† These observations suggest that the added copper(II) salt is regenerated by a cyclic process. Thus, in our case the multicentred and ionic mechanisms do not operate. The radical mechanism seems more probable since it involves a step leading to the formation of divalent copper as the result of the oxidation of the copper(I) species by the bromine radical. Scheme 2 is proposed for the copper(II) catalysed reaction of the aryl halide (I) (denoted as ArBr) with aniline in alkaline, aqueous solution.

It is relevant that use of copper(II) bromide instead of sulphate as the catalyst did not alter the rate of the reaction.[1b]

The aryl radical is assumed to be in the solvent shell and to react rapidly with the aniline radical. This assumption is necessary to explain the absence of biaryl in the product mixtures, as in some other copper-promoted reactions.[34]



SCHEME 2 L = Various ligands

When the reaction was conducted at low temperature (46 °C), using a relatively high-concentration of copper(II) catalyst (25×10^{-4}M), in addition to products (II) and (III), another coloured compound was detected by t.l.c. This compound was formed in an extremely small amount so that we could not determine it quantitatively, but, by comparing colours and R_F values, the compound was probably the debrominated product (VII) of the aryl halide (I). Compound (VII) was also formed, and in larger quantities, in the reaction of (I) with aniline under the catalytic action of (Cu^{2+} + Fe^{2+}), when the metal ions were used in relatively

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* See earlier on the effect of pH on the e.s.r. absorption intensity of the reaction system.

† See footnote on p. 678.

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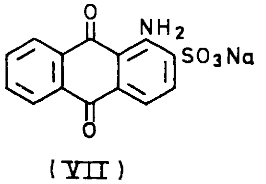
large concentrations. The yields of the products of these reactions are shown in Table 4. It was also verified that (VII) was not formed on treating the alkaline solution of [(I) + aniline] with Fe^{2+} or Fe^{3+} salts. Product (VII) probably results from the reaction of the aryl radical with free aniline existing in the solution. Copper-promoted hydrogen transfer from aromatic donors to halides has been investigated,[35] and the possibility of hydrogen transfer proceeding by homolytic mechanisms has been discussed.

TABLE 4 [a,b]

Formation of the debrominated compound (VII)

T/°C	$10^4[Cu^{2+}]$/ M	$10^4[Fe^{2+}]$/ M	$Y_{(II)}$ [c]	$Y_{(III)}$ [d]	$Y_{(VII)}$ [e]
46	12·5	12·5	87·6	1·1	1·1
70	12·5	12·5	93·4	3·0	1·5
46	25·0	25·0	94·1	1·0	2·0
70	25·0	25·0	95·1	2·5	2·5

[a] $[(I)]_0 = 1·25 \times 10^{-2}$M, $[PhNH_2]_0 = 0·30$M; pH = 9·94, reaction time 30 min. Experiments were carried out under nitrogen. [b] See Experimental section for analytical procedures. [c–e] Yields of the compounds (II), (III), and (VII) respectively, based on the reactant (I).



(VII)

EXPERIMENTAL

Materials.—The condensation products of the reaction of the sodium salt (I) with *para*-substituted anilines and with toluene-*p*-sulphonamide were purified by steam distillation, repeated salting-out using sodium acetate, and recrystallization from ethanol–water (1 : 1 v/v). The purity was verified by paper chromatography, visible spectra, and elemental analyses of the compounds and their salts formed with *p*-toluidine and *S*-benzylthiuronium chloride.[36] The product of (I) with toluene-*p*-sulphonamide gave sodium 1,4-diamino-9,10-dihydro-9,10-dioxoanthracene-2-sulphonate on treatment with concentrated sulphuric acid followed by neutralization by sodium hydroxide. Sodium 1-amino-9,10-dihydro-9,10-dioxoanthracene-2-sulphonate (Nihon Kayaku) was used after purifying by recrystallization from EtOH–H_2O (1 : 1 v/v). The purity was verified as before. Metal salts were reagent grade (Tokyo Kasei) and used without further purification.

E.s.r. Measurements.—E.s.r. spectra were obtained with a Japan Optics model JES-BS-X spectrometer modulated at 100 kHz. The solutions were examined at 20 and 70 °C. To minimize dialectric losses, thin quartz tubes (diameter 0·75 mm) were used. *g* Values and field shifts were calculated by comparison with an Mn^{2+} marker.

Kinetics.—The method was described previously.[1a] In investigations of the effect of metal reducing agents, an aqueous solution of [copper(II) sulphate + metal reducing agent] was introduced after the solution had been brought to the reaction temperature.

Quantitative analyses were carried out by spectrometric measurements using a Spectronic 20 spectrometer (Shimadzu). In all cases, the by-products were neglected because of their low yields, and the absorbances at the maxima of the spectra of reactant (I) and the main product were used [$\lambda_{max.}$ (I) 485 nm; $\lambda_{max.}$ (VI) 522 nm]. The initial rates (Table 2) were calculated from the [Product] *vs.* time curves, using Newton's interpolation formulae.

Quantitative Determination of By-product (III) *and Debrominated Compound* (VII).—The amounts of by-product (III) and the debrominated compound (VII) formed in the reactions were too small to be determined by the above method which involved measurements of the optical densities of more than two components in small portions (0·05 ml) of the reaction solution (50 ml). Another method, described below, was used to obtain data on the effect of pH on the distribution of the products, on the influences of the metal reducing agents, and on the formation of the debrominated compound.

After allowing the reaction to proceed for *x* (usually 30) min, a mixture of cold pyridine (20 ml) and water (30 ml) was added to the solution. Preliminary experiments showed that the reaction did not continue after quenching. The organic solvent was used because compound (II) was found to have low solubility in cold water. The whole solution was then developed on large (40 × 20 cm) filter papers, using Bu^nOH–EtOH–0·5N-ammonia (6 : 2 : 3 v/v) in the dark to avoid the photoamination of (I) by ammonia[37] for 24 h. For the filter paper (Toyo Roshi No. 52) and the developing solvent used, the R_F values of the compounds were (I) 0·72, (II) 0·78, (III) 0·55, and (VII) 0·59. The coloured bands were cut off, and the compounds were extracted independently with pure water. The extracts were then diluted or concentrated to appropriate volumes and subjected to spectrometric measurement. The calibration curves were constructed using the compounds synthesized as described earlier. The Beer–Lambert law was obeyed in the ranges investigated. Quantities of products could be determined with errors <2%, as proved by the analyses of mixtures of known concentrations of the components by the same procedure.

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