

to the procedure of Frank, Emmick and Johnson<sup>21</sup> afforded a mixture indicated by gas chromatography to be free of the *trans* isomer and consisting of 45% *cis*-piperylene and 55% cyclopentene. In a 100-ml. steel autoclave was placed 14.0 g. of the 45% *cis*-piperylene (93 mmoles) with 40.0 g. of iron pentacarbonyl (204 mmoles). The bomb was then heated for 80 hr. at 150–60°. The reaction mixture was first distilled to remove unreacted materials; then a mixture of iron complexes, b.p. 30–80° (1.2 mm.), was obtained. Fractionation gave 1.5 g. (7.8% yield) of the piperylene complex, b.p. 32–36° (1.2 mm.),  $n_D^{25}$  1.5460, and 1.0 g. of the piperylene dimer complex, b.p. 67–75°,  $n_D^{25}$  1.5340. Gas chromatographic analysis indicated that the unreacted piperylene was entirely the *cis* isomer.

Degradation of the piperylene complex was effected by stirring 1.0 g. with 8.0 g. of ferric chloride dissolved in 20 ml. of 95%

(21) R. L. Frank, *et al.*, *J. Am. Chem. Soc.*, **69**, 2313 (1947).

ethanol with ice cooling. After 1 hr., gas evolution ceased. The mixture was then diluted with water and extracted with 5 ml. of ether. The ether layer was washed with water and dried over sodium sulfate. Gas chromatographic analysis indicated the presence of *trans*-piperylene while none of the *cis* isomer could be detected. Under subjection to the conditions of this degradation, a 4-ml. sample of the 45% *cis*-piperylene remained unchanged.

A 10.0-g. sample of the *cis*-piperylene-cyclopentene mixture was heated at 160° for 70 hr. Gas chromatography of the product from this treatment indicated again the absence of *trans*-piperylene. The original components remained, with minor amounts of higher boiling compounds present.

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## Mechanism of the Ullmann Condensation<sup>1</sup>

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The Ullmann condensation was found to be catalyzed by cuprous copper. It was found to be first order in catalyst, first order in halobenzene, and variable order in potassium phenoxide in the media used. A mechanism is proposed.

Preliminary studies<sup>2</sup> on the Ullmann condensation<sup>3</sup> have led to the conclusion that the reaction is most probably a nucleophilic aromatic substitution involving carbon-halogen bond cleavage in the rate step. To follow up this preliminary work a kinetic study was undertaken and is herein reported.

The specific reaction studied was the formation of phenyl ether from bromobenzene and potassium phenoxide in bis(2-methoxyethyl) ether (diglyme) as solvent in the presence of various copper salts at 100°. The reaction was followed by measuring the disappearance of potassium phenoxide by titration.

Early experiments were carried out in Matheson Coleman and Bell's practical diglyme giving smooth, apparently second-order kinetics. However, when the solvent was purified by distillation from  $\text{LiAlH}_4$  we found the rate of reaction to be greatly diminished. We soon learned that the impure solvent contained an ingredient which acted in some way to enhance catalytic activity. With the aid of gas chromatographic techniques a fraction containing the active ingredient was isolated. The sample was subjected to infrared, n.m.r., and molecular weight analysis. The structure best representing the data is the diester,  $\text{CH}_3\text{OCH}_2\text{COOCH}_2\text{CH}_2\text{OCHO}$ . We did not demonstrate unequivocally that this compound could cause rate enhancement for at this time we discovered that many esters of ethylene glycol and related glycols gave the same rate enhancement.<sup>4</sup> The readily available ethylene diacetate was then used as a standard additive to the reaction media. The function of the ester is not clearly understood,

but it appears to be related to the solubility of the catalyst. In lithium aluminum hydride purified solvent where little or no reaction takes place large amounts of copper are found in the precipitate.

The most compelling problem of the study involved determining the form of catalytic copper. Literature reports<sup>5</sup> on the subject are meager and inconclusive and we hoped to find a definitive method to distinguish the possibilities. Metallic copper, cuprous oxide, cupric oxide, and cuprous sulfate were inactive as catalysts owing probably to their small solubility in the media. A number of other salts were active including  $\text{CuBr}_2$ ,  $\text{CuCl}_2$ ,  $\text{Cu}(\text{OAc})_2 \cdot \text{H}_2\text{O}$ ,  $\text{CuI}$ ,  $\text{CuBr}$ , and  $\text{CuCl}$ . Furthermore, they were interchangeable as catalysts giving equal rates for equal weights of copper. The reason for the insensitivity of the reaction to the ligands on copper was made clear from a study of the catalyst stoichiometry. If  $\text{CuBr}_2$ , for example, is combined with a solution containing an excess of potassium phenoxide in diglyme 2 equiv. of phenoxide are consumed and 2 equiv. of potassium bromide are precipitated. When  $\text{CuBr}$  is used the changes involve only 1 equiv., suggesting, at least superficially, a simple ligand exchange.

On the other hand, that cuprous and cupric salts should give identical rates was very puzzling. Electron paramagnetic resonance (e.p.r.) and magnetic susceptibility measurements performed on catalytic solutions made from cupric or cuprous salts showed essentially the same result. That is, they both were paramagnetic and gave similar electron paramagnetic signals. These results were interpreted to mean significant amounts of cupric copper were present in the catalytic solutions. However, catalytic solutions prepared under an atmosphere of nitrogen told a rather different story. While the results for cupric salts remained about the same, catalytic solutions prepared from cuprous salts showed a weaker e.p.r. signal and

(1) Presented at the 145th National Meeting of the American Chemical Society, New York, N. Y., Sept., 1963, Abstract, p. 16Q.

(2) H. Weingarten, *J. Org. Chem.*, **29**, 977 (1964).

(3) The Ullmann condensation, the copper-catalyzed reaction of aromatic halides with phenol salts (or anilines) to yield aryl ethers (or aryl amines), should be distinguished from the Ullmann coupling reaction used to form biaryls from aromatic halides. (See A. R. Surry, "Name Reactions in Organic Chemistry," Academic Press, Inc., New York, N. Y., 1954.)

(4) Ethylene carbonate, propylene glycol diacetate, propylene glycol  $\alpha$ -monoacetate, diacetin, and 1,2-diacetoxycyclohexane are also active. Dimethyl adipate, 1,3-diacetoxyp propane, and pinacol diacetate are inactive.

(5) P. W. Weston and H. Adkins, *J. Am. Chem. Soc.*, **50**, 859 (1928); I. Goldberg, *Ber.*, **40**, 4541 (1907).

little or unmeasurable paramagnetism. Also, all reaction rates were increased when measured under 1 atm. of nitrogen. We believe the most reasonable hypothesis explaining the foregoing observations is that a cuprous salt is the true catalytic species and cupric is reduced to cuprous by phenoxide ion giving rise to relatively stable organic radicals of the semiquinone variety, which account for the paramagnetism observed. That this hypothesis was more than reasonable was demonstrated in the following ways: (1) radical absorbers such as 2,6-di-*t*-butyl-4-methylphenol, 2,5-di-*t*-butylhydroquinone, and phenothiazine were added to the catalytic solutions causing great changes in the e.p.r. spectra but causing no change in the reaction rate<sup>6</sup>; (2) a solution prepared by combining CuBr<sub>2</sub> and potassium phenoxide (1 equiv.) in diglyme was poured into water from which a white precipitate was isolated and identified as CuBr by X-ray diffraction.

The determination of the over-all rate law also proved interesting. Initial rate measurements showed the reaction to be first order in bromobenzene (Table I), first order in catalytic copper (Table II), and mixed order (between 0 and 1) in potassium phenoxide.

TABLE I  
BROMOBENZENE ORDER<sup>a</sup>

Time, min.	Reaction variable $x$ , mole/l.	
	[BrC <sub>6</sub> H <sub>5</sub> ] = 0.191 <i>N</i>	[BrC <sub>6</sub> H <sub>5</sub> ] = 0.382 <i>N</i>
0	0.000	0.000
10	0.008	0.016
20	0.016	0.034
30	0.024	0.048
40	0.030	0.063
60	0.045	0.088
80	0.059	0.109

<sup>a</sup> [KOC<sub>6</sub>H<sub>5</sub>] = 0.22 *N*, [Cu] = 0.017 *N*.

TABLE II  
COPPER ORDER<sup>a</sup>

[Cu] × 10 <sup>2</sup> moles/l.	Initial Rate × 10 <sup>2</sup> (moles/l.) min.
0.221	0.28
0.435	0.5
0.852	0.9
1.71	1.7
3.42	3.2

<sup>a</sup> [KOC<sub>6</sub>H<sub>5</sub>] = 0.22 *N*, [BrC<sub>6</sub>H<sub>5</sub>] = 0.38 *N*.

The observed mixed order in potassium phenoxide concentration suggested the mathematical eq. 1. For

$$dx/dt = k_1[a - x] + k_2[a - x][b - x] \quad (1)$$

the over-all rate law, where  $x$  is the reaction variable,  $a$  is the initial concentration of bromobenzene and  $b$  the initial concentration of potassium phenoxide. If this model is correct, a plot of  $(dx/dt)/[a - x]$  vs.  $[b - x]$  should yield a straight line.<sup>7</sup> The plot (Fig. 1), however, shows eq. 1 to be incorrect and reveals the order of potassium phenoxide to be variable, approaching zero at high concentrations of potassium phenoxide and unity at low concentrations.

Three equations were suggested to explain the observed variability in potassium phenoxide order (2-4). Equation 2 suggests an equilibrium, preceding the rate

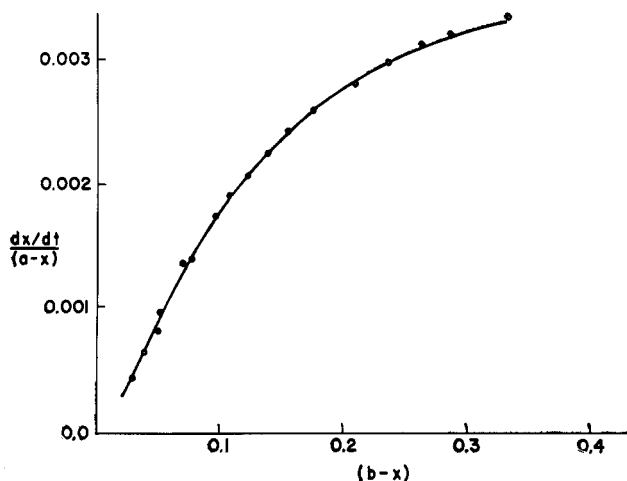


Figure 1.

$$dx/dt = k[a - x] \left( \frac{K[b - x]}{K[b - x] + 1} \right) \quad (2)$$

$$dx/dt = k[a - x] \left( \frac{2[b - x]K + 1 - \sqrt{4[b - x]K + 1}}{2[b - x]K^2} \right) \quad (3)$$

$$dx/dt = k[a - x][b - x]f(\mu). \quad (4)$$

step, between cuprous ion and potassium phenoxide, which is far to the right at high phenoxide concentrations.

Equation 3 taken from work reported by Streitwieser<sup>8</sup> suggests that the potassium phenoxide associates into higher aggregates and only the monomers are reactive. Equation 4 suggests a salt effect caused by the potassium phenoxide itself, which inhibits the reaction at high phenoxide concentrations. (The variable  $\mu$  would be related to ionic strength terms of more polar media.)

Equation 2 was discarded when we observed that *p*-nitrobromobenzene undergoes a similar reaction with potassium phenoxide in diglyme in the absence of copper and is variable order in phenoxide in the same way. In this case no meaningful pre-equilibrium can be written.

The attempts to distinguish between eq. 3 and 4 have so far failed. Colligative and conductometric measurements designed to reveal association of the potassium phenoxide under the conditions of reaction have been inconclusive. Although addition of salts such as KI and NaBr cause retardation only small amounts can be dissolved in the media. Sodium phenoxide, which reacts very slowly with bromobenzene under our conditions, causes marked retardation of the potassium phenoxide reaction. Unfortunately, this can be made consistent with either eq. 3 or 4. We hope to devise experiments to distinguish the possibilities in the near future. Regardless of why the potassium phenoxide order is variable it apparently enters into the reaction in a monomolecular sense.<sup>9</sup>

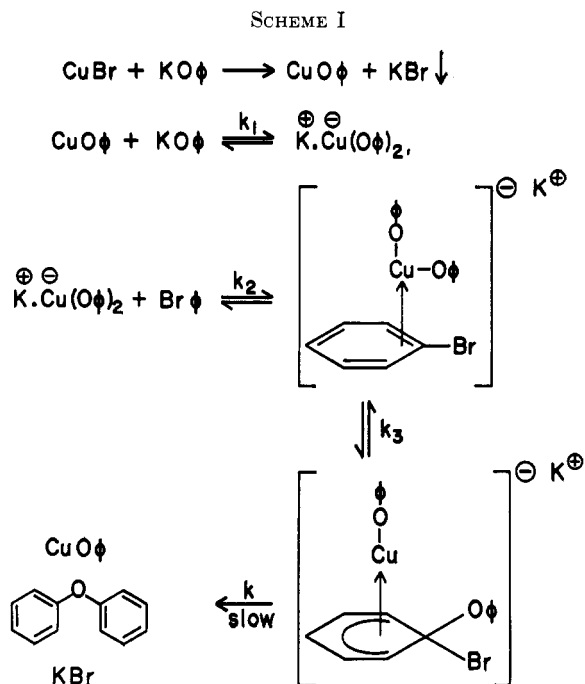
The mechanism proposed in Scheme I was constructed with these ideas in mind. First, cuprous copper in some form is the catalytic species and we feel this is adequately established. Second, the reaction is assumed to be a nucleophilic aromatic substitution based

(8) A. Streitwieser, Jr., D. E. Van Sickle, and W. C. Langworthy, *ibid.* **84**, 244 (1962).

(6) This result provides strong evidence against a free-radical chain mechanism and any mechanism involving free phenoxide radical.

(7) W. C. Young and L. J. Andrews, *J. Am. Chem. Soc.*, **66**, 421 (1944).

(9) At low potassium phenoxide concentrations where the retardation appears to be unimportant, a second-order rate constant can be calculated (0.101 mole<sup>-1</sup> sec.<sup>-1</sup>).



on the observation<sup>2</sup> that the pattern of reactivity of various halo aromatics in the Ullmann condensation parallels closely the pattern observed in other known nucleophilic aromatic substitutions.<sup>10</sup> Third, the carbon-halogen bond cleavage is assumed to be involved in the rate step based on the observation<sup>2</sup> that the reactivity pattern of the halogens parallels the pattern observed for reactions known to involve carbon-halogen cleavage in the rate step. Finally, we propose the catalytic influence of the copper to arise through interaction of the catalytic species with the  $\pi$ -electrons of the aromatic system rather than with those of the leaving halogen atom. This proposal is attractive for several reasons. Cuprous ion-benzene complexes with related structures have recently been reported by Turner and Amma.<sup>11</sup> Also, the transition metal-halo aromatic complex, chlorobenzene-chromium tricarbonyl, has been shown to be very reactive toward nucleophilic replacement of the halogen.<sup>12</sup> Lastly, if we accept the idea that the reaction is basically a nucleophilic aromatic substitution the most likely function of the catalyst is to lower the activation energy required to go from reagents to a Wheland type intermediate.<sup>10</sup> This conceivably can be done through interactions between catalytic species and the aromatic  $\pi$ -system but not by interactions with the halogen atom. Furthermore, catalysis by way of interaction with the halogen atom would be inconsistent with a rate step involving carbon-halogen bond cleavage.

### Experimental

**Stoichiometry of the Catalyst Formation.**—In a 25-ml. volumetric flask were combined 1.32 g. (0.01 mole) of  $\text{KOC}_6\text{H}_5$ , 0.447 g. (0.002 mole) of  $\text{CuBr}_2$ , and 25 ml. of diglyme. The resulting

(10) J. F. Bunnett and R. E. Zahler, *Chem. Rev.*, **49**, 273 (1951).

(11) R. W. Turner and E. L. Amma, *J. Am. Chem. Soc.*, **85**, 4046 (1963).

(12) B. Nichols and M. C. Whitting, *J. Chem. Soc.*, 551 (1959).

mixture was kept in a 100° bath for 10 min. and cooled; a 1-ml. aliquot was titrated against 0.1 N  $\text{H}_2\text{SO}_4$  using cresol red indicator. The  $\text{KOC}_6\text{H}_5$  consumed was 1.8 equiv. The remaining mixture was filtered and the precipitate was washed with fresh solvent, and dried yielding 0.418 g. of  $\text{KBr}$  (88%). The  $\text{KBr}$  was identified by X-ray diffraction.

Cuprous bromide (0.287 g., 0.002 mole) was treated as above consuming 0.9 equiv. of  $\text{KOC}_6\text{H}_5$  and yielding 0.233 g. of  $\text{KBr}$  (98%).

**Potassium Phenate Reduction of  $\text{CuBr}_2$ .**—To a 25-ml. volumetric flask, containing 0.5017 g. (0.00224 mole) of  $\text{CuBr}_2$  and 0.3044 g. (0.0023 mole) of  $\text{KOC}_6\text{H}_5$ , was added 25 ml. of diglyme. The mixture was shaken for 10 min., filtered under nitrogen, and poured into water kept slightly acid with  $\text{HCl}$ . The white precipitate which formed was collected by centrifugation, washed with acetone, and dried, yielding 0.2 g. (62%) of  $\text{CuBr}$  identified by X-ray diffraction.

**Typical Kinetic Measurement.**—In a 25-ml. volumetric flask 0.0058 mole of  $\text{KOC}_6\text{H}_5$  was combined with 0.000224 mole of  $\text{CuBr}$ . The flask was then flushed gently with nitrogen, stoppered, and placed in a nitrogen atmosphere drybox. To a 50-ml. flask were added about 0.2 g. of ethylene diacetate and 0.01 mole of bromobenzene. This flask also was gently flushed with nitrogen, stoppered, and placed in a nitrogen atmosphere dry box. In the drybox diglyme solvent was added to the bromobenzene solution and this solution was then added to the volumetric flask. The volume was brought to 25 ml. with diglyme. A T-tube adaptor made with a female and male joints was placed in the volumetric flask in place of a stopper to permit the system to be kept under a constant nitrogen pressure. The flask was then placed in a constant-temperature bath ( $100 \pm 0.1^\circ$ ) and equilibrated for 10 min. The zero point aliquot was then emptied into 5 ml. of aqueous ethanol 50:50 and titrated against 0.1 N  $\text{H}_2\text{SO}_4$  using cresol red as indicator. Aliquots were taken at 5–50-min. intervals as required.

**Purification of Solvent.**—Approximately 1 l. of diglyme (Matheson Coleman and Bell practical) was placed in a 2-l., round-bottom flask. Two to five grams of  $\text{LiAlH}_4$  were then gradually added until reaction subsided. The diglyme was then distilled from the flask under a slight nitrogen pressure. The distillate was then distilled through an 18-in. Vigreux column (boiling point of cut taken, 160–160.5°) also under a slight nitrogen pressure. The solvent was then stored under nitrogen in the dark.

**Electron Paramagnetic Resonance.**—The e.p.r. spectra were obtained using a standard Varian U-4500 100Kc spectrometer at a resonant frequency of 9500 Mc. Microwave power and sweep modulation field levels were adjusted for maximum sample response. Semiquantitative results were obtained by maintaining constant instrument settings for each run. Day-to-day instrumental response changes were checked using a prepared standard and normalizing.

**Magnetic Susceptibility Measurements.**—The classical Gouy method was used. The equipment consisted of a standard 4-in. magnet (Varian Model V4004), power supply (Varian Model V2300A), and current regulator (Varian Model V2301A). The balance was an Ainsworth semimicro type TCX No. 23720. A compensation vessel made of 0.5-in.-i.d. precision bore ( $\pm 0.0002$  in.) Pyrex tubing was used.

**Preparation of Potassium Phenoxide.**—To a 1-l., four-neck flask equipped with azeotrope head, stirring motor, thermometer, and gas inlet tube was added 64 g. (0.97 mole) of  $\text{KOH}$ , 94 g. (1 mole) of phenol, and 400 ml. of toluene. The mixture was refluxed under a small stream of nitrogen until all of the water was removed. The potassium phenoxide precipitate was collected by filtration in a nitrogen atmosphere drybox, washed with toluene, and dried in a vacuum oven at 70° for 2 days. The yields generally were quantitative. The purity of the potassium phenoxide was established by neutral equivalent against 0.1 N  $\text{H}_2\text{SO}_4$  to a cresol red endpoint. The salt was considered acceptable when this analysis indicated purity of 98% or better.<sup>13</sup> Sodium phenoxide was prepared in the same way.

(13) Water did not interfere with the reaction rates when present to less than 0.2% of the total solution.