Polymerization by Oxidative Coupling. The Function of Copper in the Oxidation of 2,6-Dimethylphenol

H. Finkbeiner, A. S. Hay, H. S. Blanchard, G. F. Endres

General Electric Research and Development Center, Schenectady, New York 12301

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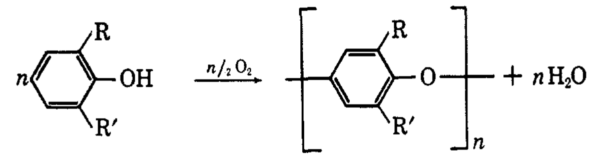
The oxidative coupling of 2,6-xylenol is catalyzed by copper. Two products are possible, poly-2,6-xylenyl oxide and tetramethyldiphenoquinone. The proportion of these products has been studied as a function of type of catalyst employed. An attempt has been made to determine the composition of one of these catalysts.

Oxidative coupling as a synthetic technique has received considerable attention in recent years, particularly in the field of natural products. For examples, Barton and Kirby[2] have coupled N-(3-hydroxy-4-methoxyphenyl)-N-methyl-4-hydroxyphenethylamine to give narwedine using manganese dioxide, Hassell and Lewis[3] used lead dioxide to couple oxidatively geodin hydrate in a partial synthesis of geodoxin, and Davidson and Scott[4a] used manganese dioxide in the synthesis of picrolichenic acid. Among other oxidizing agents, alkaline ferricyanide has been used by Wanzlick[4b] and Scott,[4c] 2,4,6-tri-*t*-butylphenoxy has been used by Cahnmann and Matsuura,[5] and chromium trioxide was employed by Kenner, *et al.*,[6] in coupling various phenols.

In these laboratories our interest has centered on the copper–amine-catalyzed oxidative coupling of 2,6-disubstituted phenols[7] to form either polymeric phenyl ethers or diphenoquinones as shown in eq 1.



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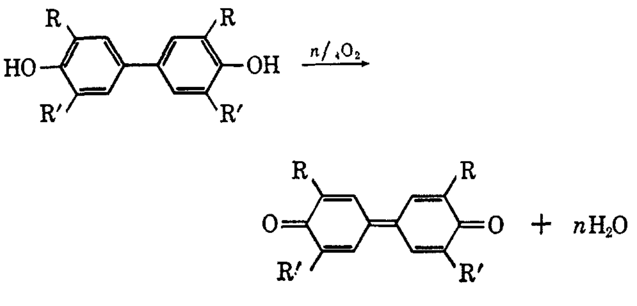

Endres and co-workers[8] have shown that this reaction can be controlled to give either carbon–oxygen or carbon–carbon coupling as the major product. The major variable in control of the course of the reaction appears to be the nitrogen–copper ratio in the catalyst; however, a mechanistic understanding of the course of the copper in the reaction would be a distinct advantage. The first approach in such an understanding was to consider possible analogs with known oxidative systems catalyzed by copper.

As has been pointed out,[8] the copper–amine system has kinetic and mechanistic similarities with the copper oxidases, particularly with tryosinase and ascorbic acid oxidase.[9,10] There is an additional similarity in the case of thyroxine formation. One of the proposed mechanisms for thyroxine formation involves oxidative coupling of two molecules of 3,5-diiodotyrosine to form a phenyl ether bond.[11] Subsequently, Matsuura and Cahnmann showed that model compounds could be coupled in an *in vitro* system in the proposed fashion to form thyroxine analogs.[5] Although it is presently believed that thyroxine formation is catalyzed by an iron-containing peroxidase,[12] the thyroxine enzyme system has not been identified and may be a copper system. The analogy to the carbon–oxygen coupling observed in the case of a 2,6-dimethylphenol oxidation, as discussed by Endres,[8] is obvious.

Recently an *in vivo* system has been used to oxidize 2,6-dimethylphenol.[13] The product of the oxidation was 3,3′,5,5′-tetramethyldiphenoquinone, an example of carbon–carbon coupling. As has been shown, this diphenoquinone is one of the products that can be prepared when 2,6-xylenol is oxidized under the proper conditions by the copper–amine system developed in this laboratory.[8]

Although the use of copper salts as oxidizing agents or oxidation catalysts has included such diverse reactions as the oxidation of carbohydrates to ozones,[14] coupling of acetylenes to diynes[15] or polymeric acetylenes,[16] the oxidation of anilines to azo compounds,[17] and the oxidation of hydrazines to azo compounds,[18] the precise function of copper in these reactions has remained obscure. In the case of the copper oxidases, Kubowitz,[19] as a result of his work on inhibition with

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[1] Presented in part at the 140th National Meeting of the American Chemical Society, Chicago, Ill., Sept. 1961.

[2] D. H. R. Barton and G. W. Kirby, *J. Chem. Soc.*, 806 (1962).

[3] C. H. Hassell and J. R. Lewis, *ibid.*, 2312 (1961).

[4] (a) T. A. Davidson and A. I. Scott, *ibid.*, 4075 (1961); (b) H. W. Wanzlick, *Ber.*, **92**, 3006 (1959); (c) A. I. Scott, *Proc. Chem. Soc.*, 195 (1958).

[5] H. J. Cahnmann and T. Matsuura, *J. Am. Chem. Soc.*, **82**, 2055 (1960).

[6] G. W. Kenner, M. A. Murray, and C. M. B. Taylor, *Tetrahedron Letters*, **No. 1**, 259 (1957).

[7] A. S. Hay, H. S. Blanchard, G. F. Endres, and J. W. Eustance, *J. Am. Chem. Soc.*, **81**, 6335 (1959).

[8] G. F. Endres, A. S. Hay, and J. W. Eustance, *J. Org. Chem.*, **28**, 1300 (1963).

[9] This similarity will be discussed more fully in a forthcoming paper.

[10] J. B. Sumner and K. Myrbäch, "The Enzymes," Academic Press Inc., New York, N. Y., 1951, p. 454; W. D. McElroy and B. Glass, "Copper Metabolism," Johns Hopkins Press, Baltimore, Md., 1950.

[11] T. B. Johnson and L. B. Tewkesbury, Jr., *Proc. Natl. Acad. Sci. U. S.*, **28**, 73 (1942).

[12] C. R. Harington and R. V. P. Rivers, *Biochem. J.*, **39**, 157 (1945); A. S. Keston, *J. Biol. Chem.*, **153**, 335 (1944).

[13] S. M. Bocks, B. R. Brown, and A. H. Todd, *Proc. Chem. Soc.*, 117 (1962).

[14] J. K. Hamilton and F. Smith, *J. Am. Chem. Soc.*, **74**, 5162 (1952).

[15] A. I. Nogaideli and R. Shvangiradze, *J. Gen. Chem. USSR*, **24**, 1025 (1954); L. Crombie and Nanzoor-i-Khuda, *J. Chem. Soc.*, 2767 (1957).

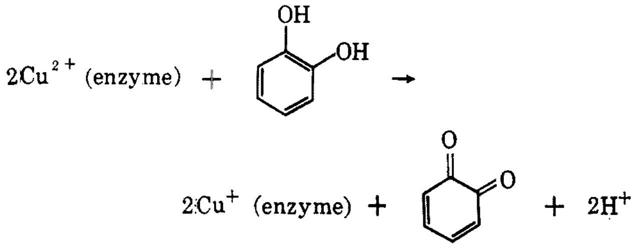
[16] A. S. Hay, *J. Org. Chem.*, **25**, 1275 (1960).

[17] A. P. Terent'ev and Y. D. Mogilyanskii, *Dokl. Akad. Nauk SSSR*, **103**, 91 (1955).

[18] G. Fodor and J. Wein, *J. Chem. Soc.*, 684 (1948).

[19] F. Kubowitz, *Biochem. Z.*, **292**, 221 (1937); **299**, 32 (1939).

carbon monoxide and cyanide ion, has suggested that cupric ion is reduced to cuprous ion which is then reoxidized by molecular oxygen as shown in eq 2.



$$4\mathrm{Cu}^{+}\ (\text{enzyme}) + 4\mathrm{H}^{+} + \mathrm{O}_2 \rightarrow 4\mathrm{Cu}^{2+}\ (\text{enzyme}) + 2\mathrm{H_2O} \quad (2)$$

However, such a scheme has remained largely conjecture owing to the extreme complexity of the enzymatic system, and does not give a description of the species that are coordinated with the copper in its two oxidation states. In a related study, the elegant work of Brackmann and Havinga[20] on the nonenzymatic copper-catalyzed autoxidation of phenol and catechol in an alcohol–morpholine system has demonstrated the large number of steps that are catalyzed by copper in oxidizing phenol to dimorpholino-*o*-quinone. However, a mechanistic understanding of the copper, with respect to the complexes it forms in each of its two oxidation states at successive stages of the reaction, was not obtained.

The enzymatic and nonenzymatic autoxidation of ascorbic acid has probably received more attention with respect to mechanism than any other copper-catalyzed oxidation system. The work of Weissberger and LuValle[21] showed quantitatively that the copper-catalyzed oxidation of ascorbic acid is faster than the uncatalyzed oxidation by a factor of 10^4, that the catalyzed oxidation involved only the ascorbate monoanion, and that the rate was independent of ascorbic acid concentration. Martell and Calvin[22] suggested a detailed mechanism in terms of copper chelates with ascorbic acid to explain the observed facts. A more recent detailed kinetic study by Nord[23] has suggested a somewhat different mode for the reduction of oxygen and the reoxidation of copper; however, the question of the copper coordination compounds involved is not discussed.

The work of Joselow and Dawson[24] on ascorbic acid oxidase has demonstrated that the coordinated ligands associated with the copper are quite important in the physical–chemical behavior of the copper and presumably in the catalytic behavior. Thus, there have been a number of copper-catalyzed oxidations described in the literature, and in some cases the problem of the copper mechanistic path has been considered.

Since it seems likely that, as in the cases discussed above, any detailed understanding of oxidative coupling in the copper–amine-catalyzed system must include an understanding of the path of copper, we have undertaken such a study. This paper reports some of the results of that study.

Results

Oxidation of Copper(I) Chloride.—The general procedure for the oxidative coupling of 2,6-xylenol has been to suspend copper(I) chloride in a solvent and pyridine mixture. The copper(I) chloride was then oxidized with molecular oxygen until oxygen uptake ceased. The stoichiometric requirements of such a reaction are shown in eq 3 for the absence of water and in eq 4 if water is present.

$$4\mathrm{CuCl} + \mathrm{O_2} \xrightarrow{\mathrm{C_6H_6,\ Py}} 2(\mathrm{CuCl_2})\cdot 2\mathrm{CuO}\cdot n\mathrm{Py} \quad (3)$$

$$4\mathrm{CuCl} + \mathrm{O_2} \xrightarrow{\mathrm{C_6H_6,\ Py}} 2(\mathrm{CuCl_2})\cdot 2\mathrm{Cu(OH)_2}\cdot n\mathrm{Py} \quad (4)$$

$$\mathrm{Py} = \text{pyridine}$$

While in water this oxidation has been described by Berthelot[25] and Gröger[26] giving the products shown in eq 5, the oxidation in nonaqueous solvents is more complex. In *o*-dichlorobenzene or benzene, copper(I) chloride is inert toward oxygen, and only in the presence of a coordinating ligand is oxidation observed.

$$6\mathrm{CuCl} + {}^{3}/_{2}\mathrm{O_2} + 3\mathrm{H_2O} \longrightarrow \mathrm{CuCl_2}\cdot 3\mathrm{Cu(OH)_2} + 2\mathrm{CuCl_2} \quad (5)$$

Since it is possible to oxidize copper(I) chloride in a benzene–pyridine mixture, it was of interest to determine the chemical properties of this oxidized material with respect to 2,6-dimethylphenol. As has been pointed out by Endres, *et al.*,[8] at low pyridine to copper ratios in the presence of oxygen this copper compound catalyzes the oxidation of 2,6-dimethylphenol to 3,3′,5,5′-tetramethyldiphenoquinone, and at high nitrogen to copper ratios the product is poly-2,6-dimethyl-1,4-phenylene ether. However, if the analogy to Kubowitz' scheme is valid, these same products should result when an equivalent amount of the copper(II) compound is used in the absence of oxygen. Two experiments were performed with the results shown in Table I. For comparison the results from the use of a catalytic amount of copper are also shown.

TABLE I

OXIDATION OF 2,6-DIMETHYLPHENOL[a]

Pyridine/ copper[b]	2,6-Dimethyl- phenol/copper	Poly- phenylene ether, %	Dipheno- quinone, %
1.0	0.48	6.5	58.7
10.0	0.48	74.0	9.3
1.0[c]	40.0	16.4	49.0
10.0[c]	40.0	75.0	10.4

[a] *o*-Dichlorobenzene solvent, 30°, magnesium sulfate (0.2 mole/l) added as a drying agent, 2,6-dimethylphenol 0.2 *M*. [b] Molar ratios. [c] Catalytic conditions, oxygen as the oxidizing agent.

From the data in Table I it can be seen that an equivalent amount of the copper(II) compound is indistinguishable from the catalytic oxidation at least in terms of products and yields. Thus, it seems reasonable that the sole function of oxygen in the catalytic

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(20) W. Brackmann and E. Havinga, *Rec. Trav. Chim.*, **74**, 937, 1021, 1070, 1100, 1107 (1955).

(21) A. Weissberger and J. E. LuValle, *J. Am. Chem. Soc.*, **66**, 700 (1944).

(22) A. E. Martell and M. Calvin, "Chemistry of the Metal Chelate Compounds," Prentice-Hall, Inc., Englewood Cliffs, N. J., 1952, p 390.

(23) H. Nord, *Acta Chem. Scand.*, **9**, 430, 438, 442 (1955).

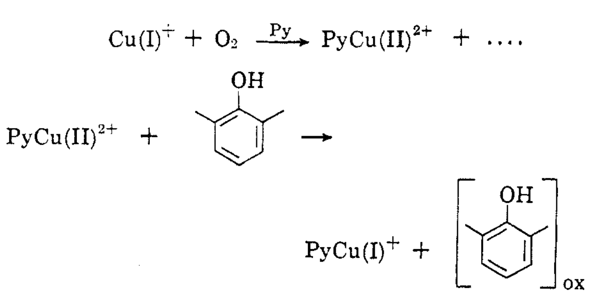
(24) M. Joselow and C. R. Dawson, *Science*, **121**, 300 (1955); *J. Biol. Chem.*, **191**, 11 (1951).

(25) M. Berthelot, *Ann. Chim. Phys.*, [5] **20**, 503 (1880).

(26) M. Gröger, *Z. Anorg. Chem.*, **28**, 154 (1901).

reaction is to reoxidize copper(I) to copper(II) and that the reaction sequence is that shown in eq 6–8.

$$Cu(I)^+ + O_2 \xrightarrow{Py} PyCu(II)^{2+} + \dots \quad (6)$$



(7)

Catalytic

$$PyCu(I)^+ + O_2 \xrightarrow{Py} PyCu(II)^{2+} + \dots \quad (8)$$

Since copper(II) apparently is the true oxidizing agent in the oxidative coupling reaction, it was of interest to determine what limitations, if any, could be placed on the kinds of copper(II) compounds which are catalytically active. A number of simple copper(II) compounds were tried with the results shown in Table II.

TABLE II

CATALYTIC ACTIVITY OF SIMPLE COPPER(II) COMPOUNDS[a]

Compound	Results
CuCl	Theoretical amount of oxygen consumed in ~12 min
$CuCl_2$[b]	No reaction
Py_2CuCl_2	Very slow reaction after several hours
$Cu(OH)_2$	Very slow reaction
$Py_2Cu(OR)_2$[c]	Very slow reaction

[a] Benzene solvent, 30°, pyridine 20 vol %, 2,6-dimethylphenol 0.2 *M*. [b] No pyridine used. [c] R = 2,4,6-trichlorophenyl or 2,6-dichlorophenyl.

The failure of these simple copper(II) compounds to catalyze the oxidative coupling reaction seems to indicate that the oxidation of copper(I) chloride must yield a product which could not be described in the usual terms and instigated an investigation of the autoxidation of copper(I) chloride in nonaqueous systems.

When copper(I) chloride is suspended in either benzene or *o*-dichlorobenzene and stirred under oxygen, no detectable consumption takes place. With the addition of small amounts of pyridine, however, oxidation does begin. A series of experiments was performed to establish the minimum pyridine/copper ratio necessary for complete oxidation of the copper(I) chloride. These experiments were carried out in two different fashions. In one case, the pyridine was all added at one time and the oxygen consumption was measured. This consumption was then plotted as a function of pyridine/copper ratio. In the second case, the pyridine, in solution, was added in small increments and again the oxygen consumption was plotted as a function of the pyridine/copper ratio. The data from these experiments are shown in Figure 1.

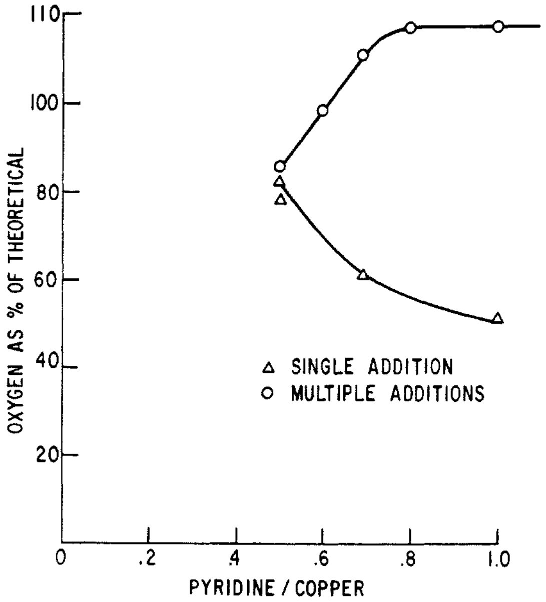


Figure 1.—The oxidation of copper(I) chloride at various pyridine/copper ratios.

When the pyridine is added in small amounts, there is a definite break at pyridine/copper ratio of 2/3 and below this ratio oxidation is incomplete. However, when the pyridine is added as one unit, there not only is not a break in the curve but the final oxygen consumption at a pyridine/copper ratio of one is only half of that in the first case. These results can be rationalized if the stoichiometry in eq 9 and 10 is assumed.

$$6CuCl + {}^3/_2O_2 + 4C_5H_5N \longrightarrow 2(C_5H_5N)_2CuCl_2\cdot CuCl_2\cdot 3CuO \quad (9)$$

$$4C_5H_5N + 4CuCl + O_2 \longrightarrow 2(C_5H_5N)_2CuCl_2\cdot Cu_2O \quad (10)$$

The work of Berthelot[25] and Gröger[26] has shown that oxidation of copper(I) chloride in an aqueous system gives products analogous to those shown in eq 9, and, while it might be surprising that a compound like $CuCl_3\cdot 3CuO$ does not coordinate with pyridine, Rooksby and Chinside[27] found that $CuCl_2\cdot 3Cu(OH)_2$ could be formed in aqueous ammonium hydroxide without coordinating any ammonia. In our work it is not clear if the product in eq 9 is a mechanical mixture of basic oxychloride and bispyridine copper(II) chloride or a true complex having a pyridine/copper ratio of 2/3. Precipitation of the copper oxidation product with hexane gives material with a N/Cu ratio of 2/3, but the infrared spectrum shows principally Py_2CuCl_2 absorption bands.

The peculiarities observed when pyridine was added as a single unit seem to be due to the formation of a dark precipitate that did not form when the pyridine was added in small increments. The amount of oxygen absorbed in this case indicates that half of the copper(I) chloride has not been oxidized, presumably forming a mixed copper(I)–copper(II) salt. Mixed copper(I)–copper(II) compounds have been examined by numerous workers. McConnell and Davidson[28] have shown that $CuCl_2\cdot CuCl$ is the principle species in aqueous acid, and the work of Mellor[29] with the arsine derivatives of mixed copper(I)–copper(II) compounds has established the highly insoluble character of the coordination compounds. Mellor also points out that

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[27] H. P. Rooksby and R. C. Chinside, *J. Soc. Chem. Ind.* (London), **53**, 33 (1934).

[28] H. McConnell and N. Davidson, *J. Am. Chem. Soc.*, **72**, 3168 (1950).

[29] D. P. Mellor and D. P. Craig, *J. Proc. Roy. Soc. N. S. Wales*, **75**, 27 (1941); D. P. Mellor, G. J. Burrows, and B. S. Morris, *Nature*, **141**, 414 (1938).

the arsine derivatives are stable in air unlike the ethylenediamine derivative prepared by Harris.[30] By analogy, it seems likely that, when pyridine is added to the copper(I) chloride suspension, the mixed copper(I)-copper(II) compound has sufficient time to form and precipitate, thus removing half of the copper(I) chloride and preventing its oxidation.

The complexities of the products obtained from the autoxidation of copper(I) chloride in benzene or dichlorobenzene prompted us to examine the oxidation in other reaction media. When copper(I) chloride is oxidized in a methanol-pyridine mixture, a deep green crystalline material precipitates. From the infrared spectrum and elemental analysis, the precipitate has the composition, $PyCuOCH_3Cl$ (A). Copper(I) chloride oxidized in methanol in the absence of pyridine gives a pale yellow-green product with the empirical formula, $CuOCH_3Cl$ (B). This latter compound is probably analogous to the CuClOH material described by Maget and co-workers.[31] Both of these compounds, $PyCuClOCH_3$ and $CuClOCH_3$, were at least as active as copper(I) chloride in the oxidation of 2,6-dimethylphenol when used in equivalent amounts based on the copper content. Like the product obtained when copper(I) chloride is oxidized in pyridine/*o*-dichlorobenzene the new compound, $PyCuClOCH_3$, will oxidize 2,6-dimethylphenol to largely poly-2,6-dimethylphenylene ether when used in a system where the pyridine/copper ratio is 10 or greater and to 3,3′,5,5′-tetramethyldiphenoquinone when the pyridine/copper ratio is 1.

The new compounds have been prepared by a number of metathesis reactions in addition to the preparation by oxidation of copper(I) chloride. When copper(II) chloride in methanol solution is treated with 1 equiv of sodium methoxide, the reaction shown in eq 11 takes place. Subsequent reaction of this product

$$CuCl_2 + NaOCH_3 \longrightarrow CuClOCH_3 + NaCl \qquad (11)$$

with pyridine gave $PyCuClOCH_3$ (12). The same

$$CuClOCH_3 + C_5H_5N \longrightarrow C_5H_5NCuClOCH_3 \qquad (12)$$

product was produced when bispyridine copper(II) chloride was treated with 1 equiv of sodium methoxide (13). The reaction of copper(II) methoxide with bis-

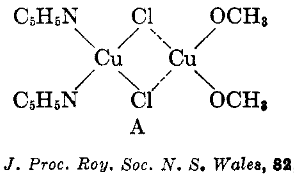
$$(C_5H_5N)_2CuCl_2 + NaOCH_3 \longrightarrow C_5H_5NCuClOCH_3 + C_5H_5N + NaCl \qquad (13)$$

pyridine copper(II) chloride also was shown to produce the same product (14).

$$Cu(OCH_3)_2 + (C_5H_5N)_2CuCl_2 \longrightarrow 2C_5H_5NCuClOCH_3 \qquad (14)$$

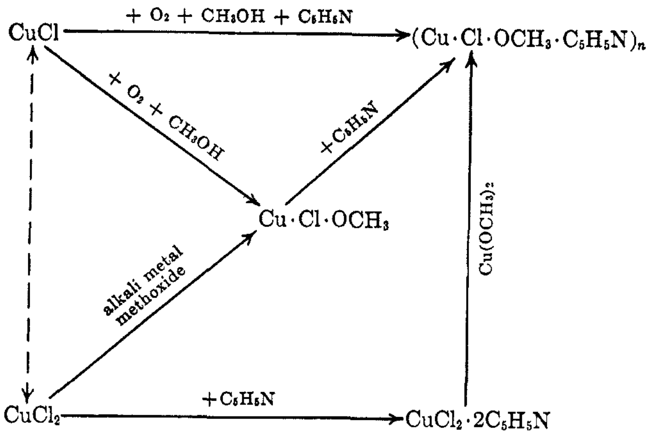
A schematic representation of these inter-relationships is shown in Scheme I.

All attempts to determine the molecular weight of the compound, $PyCuClOCH_3$, have been unsuccessful since the material is either insoluble or reacts with the solvent; however, on the basis of the means of preparation we believe the structure shown (A) is a likely one.



A

SCHEME I



The finding that methoxide ion was incorporated in the product when copper(I) chloride was oxidized in methanol prompted an attempt to replace the methoxyl group with other alkoxy or aryloxy groups. The substitution of ethanol or 2-propanol for the methanol gave a glistening brown crystalline material with the empirical formula, $Py_4Cu_4Cl_6O$ (C). While this compound showed some catalytic activity with respect to the oxidation of 2,6-dimethylphenol, it was not so effective as $PyCuClOCH_3$ in terms of rate. Refluxing of $PyCuClOCH_3$ in methanol for prolonged periods also produced C (eq 15). Several easier preparations

$$PyCuClOCH_3 \xrightarrow{\text{reflux}} Py_4Cu_4Cl_6O + \ldots . \qquad (15)$$

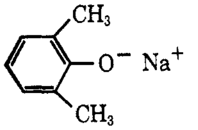
of C are shown in eq 16–18. In every case the products were shown to be identical with the material obtained from the oxidation of copper(I) chloride in 2-propanol by comparison of their infrared spectra and catalytic activity in the 2,6-dimethylphenol oxidation.

$$PyCuClOCH_3 + HCl \longrightarrow Py_4Cu_4Cl_6O + \ldots \qquad (16)$$

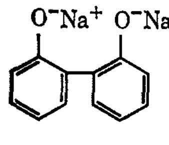
$$Py_2CuCl_2 + CuCl + O_2 \longrightarrow Py_4Cu_4Cl_6O + \ldots \qquad (17)$$

$$Py_2CuCl_2 + CuCl_2 + Cu(OH)_2 \longrightarrow Py_4Cu_4Cl_6O + \ldots \qquad (18)$$

Several attempts were made to replace the methoxide ion in $PyCuClCCH_3$ with aryloxy ions by preparing the alkali metal salt of the appropriate phenol and carrying out a metathesis in methanol solution as in eq 13. In these attempts three different reactions were observed depending on the nature of the substitution in the aromatic ring. If 2,6-dimethylphenolate was used, the net result was oxidation of the phenol (19). 2,2′-Dihydroxydiphenyl gave $PyCuClOCH_3$ (20), and 2,4,6-trichlorophenol produced an analog of Py_2CuCl_2 (21). The last compound,



$$+ Py_2CuCl_2 \xrightarrow{CH_3OH} \text{oxidation products} \qquad (19)$$



$$+ Py_2CuCl_2 \xrightarrow{CH_3OH} PyCuClOCH_3 + \cdots \qquad (20)$$

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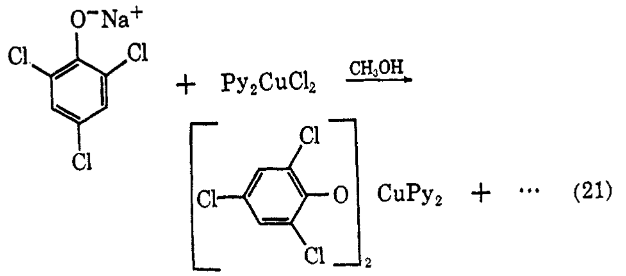
(30) C. M. Harris, *J. Proc. Roy. Soc. N. S. Wales*, **82**, 218 (1949).

(31) W. Feitknecht and K. Maget, *Helv. Chim. Acta*, **32**, 1639 (1949); W. Nowacki and K. Maget, *Experientia*, **8**, 55 (1952).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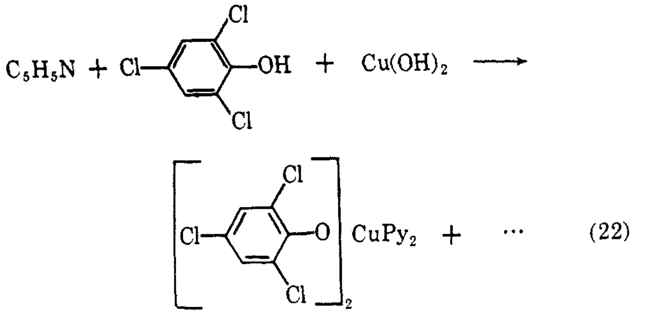
a deep red-black crystalline material, could also be prepared from pyridine, copper(II) hydroxide, and 2,4,6-trichlorophenol (22). Attempts to exchange the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methoxyl group in $PyCuClOCH_3$ for an aryloxy anion led either to no reaction or oxidation of the phenol. In the case of 2,4,6-tri-*t*-butylphenol, the stable tri-*t*-butylphenoxy radical was formed,[32,33] and 2,6-dimethylphenol gave the usual oxidation products.

Endres[8] has previously suggested that the oxidation of copper(I) chloride in the presence of amines produces two different copper compounds which are in equilibrium with each other. These compounds, which were presumed to differ in the number of pyridine molecules associated, were responsible for carbon–carbon coupling and carbon–oxygen coupling. In this connection we have examined the near-infrared absorption region of the compounds formed when copper(I) chloride is oxidized in *o*-dichlorobenzene at various pyridine/copper ratios. The compound, $PyCuClOCH_3$, was also examined in the same region. Figure 2 shows the spectra from 600 to 1100 mμ, at a number of pyridine/copper ratios.

Both $PyCuClOCH_3$ and the copper(I) chloride product from oxidation in *o*-dichlorobenzene showed the double peak with maxima at 750 and 870 mμ at pyridine/copper ratios of 1, which became a single, much less intense peak with a maximum at 740 mμ as the pyridine/copper ratio was increased to 558.

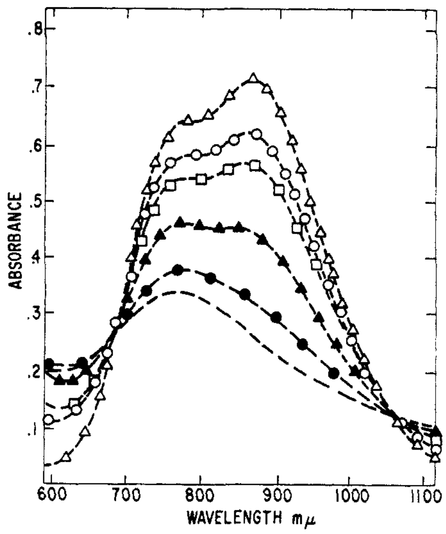


Figure 2.—The spectrum of $PyCuClOCH_3$ as a function of the nitrogen/copper ratio: △, 1; ○, 10; □, 15; ▲, 20; ●, 40; and - - -, 100.

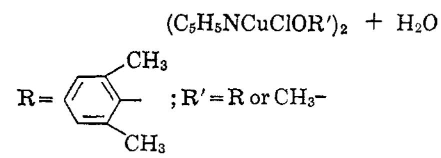
The work of Bjerrum and Nielsen[34] on copper(II)–pyridine complexes in water showed that, as more pyridine is coordinated with copper, the absorption maximum shifts to shorter wavelengths and becomes more intense. This has led to the conclusion that the two peaks observed at a pyridine/copper ratio of 1 represent two compounds, one of which probably is present at low concentration. Addition of more pyridine causes the formation of more of this material at the expense of the major component, causing a shift to a shorter wavelength. These spectra seem to confirm the existence of two different complexes in the 2,6-dimethylphenol oxidation system.

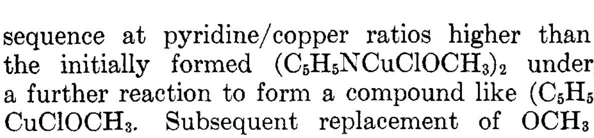
With the evidence available, the role of copper in the oxidation of 2,6-dimethylphenol can be represented as involving first the oxidation of copper(I) chloride to $C_5H_5NCuOCH_3Cl$ or the analogous OH compound. At a pyridine/copper ratio of 1 this compound then undergoes a metathesis with 2,6-dimethylphenol. The copper compound is then reduced and a molecule of 3,3′,5,5′-tetramethyl-4,4′-dihydroxydiphenyl is formed. Subsequent oxidation of the dihydroxydiphenyl by either oxygen or copper(II) leads to tetramethyldiphenoquinone. Oxidation of the copper(I) species by oxygen forms the starting $C_5H_5NCuClOR'$. These steps are shown in eq 23–27. In the reaction sequence at pyridine/copper ratios higher than 10, the initially formed $(C_5H_5NCuClOCH_3)_2$ undergoes a further reaction to form a compound like $(C_5H_5N)_2CuClOCH_3$. Subsequent replacement of OCH_3 (or OH) by 2,6-dimethylphenoxide and reduction of the

$$4CuCl + O_2 + 4CH_3OH + 4C_5H_5N \longrightarrow 2(C_5H_5NCuClOCH_3)_2 + 2H_2O \quad (23)$$

$$(C_5H_5NCuClOCH_3)_2 + ROH \longrightarrow (C_5H_5NCuClOR)_2 + 2CH_3OH \quad (24)$$

$(C_5H_5CuClOR)_2 \longrightarrow$


(25)


(26)

$$4C_5H_5NCuCl + 4R'OH + O_2 \longrightarrow (C_5H_5NCuClOR')_2 + H_2O \quad (27)$$

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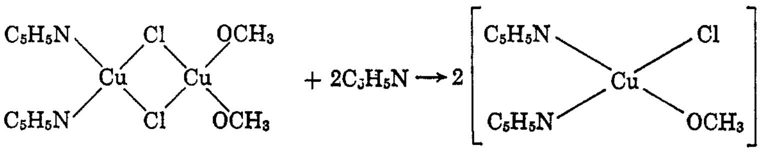
[32] C. D. Cook and R. C. Woodworth, *J. Am. Chem. Soc.*, **75**, 6242 (1953).

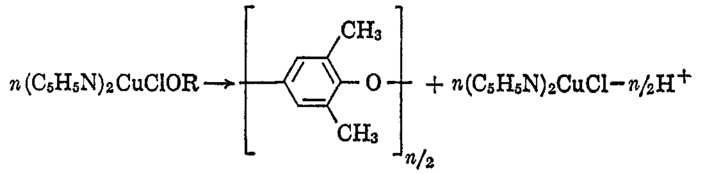
[33] The implications of this result will be discussed more fully in a forthcoming paper.

[34] J. Bjerrum and E. J. Nielsen, *Acta Chem. Scand.*, **2**, 297 (1948).



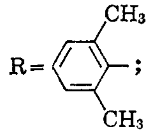
(28)

$$(C_5H_5N)_2CuClOCH_3 + ROH \rightarrow (C_5H_5N)_2CuClOR + CH_3OH \qquad (29)$$



(30)

$$4(C_5H_5N)_2CuCl + O_2 + 4HOR' \rightarrow (C_5H_5N)_2CuClOR' + 2H_2O \qquad (31)$$



; R′ = R or CH_3–

copper(II) to copper(I) with concurrent oxidation of the phenoxide to phenylene ether form the next two steps. Finally, the copper(I) compound is reoxidized to $(C_5H_5N)_2CuClOR'$ as shown in eq 28–31 above.

In those cases where copper(I) chloride is oxidized in the absence of methanol, the methoxyl group shown in eq 28–31 would be replaced by hydroxide or oxide. Thus, the oxidation of 2,6-dimethylphenol is catalyzed by copper–pyridine coordination compounds in which the anions associated with the copper are not identical. One of these anions apparently can be hydroxide, oxide, or alkoxide. The first step of the oxidation presumably is the replacement of the hydroxide or alkoxide by the 2,6-dimethylphenol anion and the subsequent steps determined by the pyridine/copper ratio.

Experimental Section

Materials.—Copper(I) chloride was prepared by the method of Stathis.[35] Other copper salts were reagent grade materials and used without further purification. Solvents were purified by standard techniques. The various phenols were recrystallized before use, usually from *n*-hexane.

Oxidation of Copper(I) Chloride in *o*-Dichlorobenzene.—A suspension of 0.200-g (0.002 mole) of copper(I) chloride in 30 ml of *o*-dichlorobenzene was thermostated at 30.0° in a self-contained gas-absorption apparatus. Pyridine (0.158 g in 10 ml of *o*-dichlorobenzene) was added to the suspension from a 10-ml, pressure-equalized dropping funnel. The oxygen consumption at 1.0 atm was measured after equilibrium had been reached. This usually required a few minutes.

In the experiments where pyridine was added in small increments, the pyridine–*o*-dichlorobenzene solution was added in approximately 0.1-ml (1.58×10^{-3} g of pyridine) additions spaced to approximately equilibrium conditions. The additions were continued until the desired pyridine/copper ratio was achieved, and an oxygen consumption reading was taken. The additions were then resumed until the next ratio was attained. In the single addition experiments, the required pyridine was added in one unit. Each pyridine/copper ratio required a separate experiment in this case. The data for these experiments is shown in Table III.

Oxidation of Copper(I) Chloride in Methanol. A. Without Pyridine.—A reaction mixture containing 0.5 g (0.0051 mole) of copper(I) chloride in 50 ml of dry methanol was stirred at 30.0° under oxygen in the absorption apparatus described above. After 16 hr, a total of 36.4 cc of oxygen had been absorbed. The pale yellow-green solid was filtered off, dried, and weighed: yield 0.62 g (94.5%).

TABLE III

OXIDATION OF COPPER(I) CHLORIDE IN *o*-DICHLOROBENZENE

Pyridine/ copper	Oxygen consumption,[a] moles of $O_2 \times 4$/moles of Cu	
	Successive additions	Single addition
0.05	...	0.04
0.50	0.833	0.820, 0.784
0.60	0.991	...
0.67	1.06	0.602
0.80	1.09	...
1.00	1.09	0.528

[a] Calculations based on $4Cu^+ + O_2 \rightarrow 4Cu^{2+} + 2O^{2-}$. Calcd $4O_2/Cu = 1.0$.

Anal. Calcd for CH_3ClCuO: Cu, 48.85. Found: Cu, 48.8.

B. With Pyridine.—The above experiment was repeated except that 2.0 ml of pyridine was added before the reaction mixture was oxidized. After 16 hr, a total of 38.8 cc. of oxygen was absorbed. The deep green crystalline solid was filtered off, washed several times with 20-ml portions of methanol, and dried: yield 1.0 g (95.5%).

Anal. Calcd for $C_6H_8ClCuNO$: C, 34.45; H, 3.85; Cl, 16.95; Cu, 30.38; N, 6.69. Found: C, 33.6; H, 3.7; Cu, 17.3; Cu, 30.3; N, 6.6.

Oxidation of 2,6-Dimethylphenol. A. Equivalent Amount of $(C_5H_5NCuClOCH_3)_2$.—To 40 ml of an *o*-dichlorobenzene solution of 2,6-dimethylphenol (0.977 g) was added, under nitrogen, in small portions, 3.5 g of $(C_5H_5NCuClOCH_3)_2$ at such a rate as to keep the temperature of the reaction mixture at 30.0°. Previously 1.0 g of magnesium sulfate had been suspended in the reaction mixture to absorb water. After 3 hr the reaction mixture was poured into 100 ml of 1% hydrochloric acid. The three-phase system was filtered, and 0.573 g of 3,3′,5,5′-tetramethyldiphenoquinone (mp 215°) was obtained. The *o*-dichlorobenzene layer was separated from the water and poured into 160 ml of methanol containing 2 ml of concentrated hydrochloric acid. This gave 0.062 g of white 2,6-dimethylphenol polymer.

The experiment was repeated except that 12 ml of pyridine was substituted for an equal volume of *o*-dichlorobenzene. After work-up, a 0.090-g yield of tetramethyldiphenoquinone and a 0.722-g yield of 2,6-dimethylphenol polymer were obtained.

B. Catalytic amount of $(C_5H_5NCuClOCH_3)_2$.—To a solution of 0.977 g (0.008 mole) of 2,6-dimethylphenol in 40 ml of *o*-dichlorobenzene was added 1.0 g of magnesium sulfate and 0.042 g of $(C_5H_5NCuClOCH_3)_2$. The reaction mixture was agitated under oxygen at 30°. After 4 hr 97.4 cc. (0.00396 mole) of oxygen had been absorbed. The reaction mixture was filtered, and 0.478 g of 3,3′,5,5′-tetramethyldiphenoquinone was obtained. The *o*-dichlorobenzene was poured into a mixture of 150 ml of methanol and 2.0 ml of concentrated hydrochloric acid. Filtration gave 0.160 g of 2,6-dimethylphenol polymer.

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[35] E. C. Stathis, *Chem. Ind.* (London), 633 (1958).

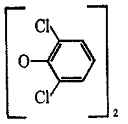
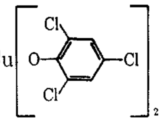
When the above experiment was repeated, except that 0.158 g of pyridine was added to the reaction mixture before oxidation, oxygen absorption was complete (98.5 cc, 0.00399 mole) after 25 min. The reaction yielded 0.101 g of tetramethyldiphenoquinone and 0.731 g of 2,6-dimethylphenol polymer.

Oxidation of 2,5-Dimethylphenol with Other Copper Compounds.—A general procedure was adopted for screening other copper compounds as possible catalysts. These compounds were evaluated on the basis of the amount of time required to absorb half of the theoretical oxygen, $t_{1/2}$, compared with the time required when $(C_5H_5NCuClOCH_3)_2$ is the catalyst.

To a mixture of 9 ml of pyridine and 31 ml of benzene was added 0.732 g (0.006 mole) of 2,6-dimethylphenol and enough of the appropriate copper compound to give a copper content of 0.003 g. The data for these experiments are shown in Table IV.

TABLE IV

OXIDATION OF 2,6-DIMETHYLPHENOL USING VARIOUS COPPER COMPOUNDS AS CATALYSTS

Catalyst	Wt. of catalyst used, mg	$t_{1/2}$, min
$(C_5H_5NCuClOCH_3)_2$	10.0	28
$CuCl_2$[a]	6.5	>300
$Cu(OH)_2$	4.6	>300
Py_2CuCl_2	13.8	240
Py_2Cu 	25.9	195
Py_2Cu 	29.1	110

[a] No pyridine was used in this case.

Preparation of $C_5H_5NCuClOCH_3$ by Metathesis. A.—A solution of 0.54 g of sodium methoxide in 10 ml of anhydrous methanol was added to a solution of 1.345 g of copper(II) chloride in 50 ml of anhydrous methanol. The pale yellow-green precipitate was filtered off and dried. From the empirical formula and infrared spectrum this material was identical with compound $CuClOCH_3$ described above.

B.—This reaction was then repeated and, without filtering off the precipitate, 2.0 g (0.025 mole) of pyridine was added to the suspension and the reaction mixture was stirred for 2 hr at room temperature. The deep green crystalline solid was identical with $C_5H_5NCuClOCH_3Cl$ formed by the oxidation of copper(I) chloride in methanol–pyridine as described above.

C.—The pyridine complex of copper(II) chloride was prepared by adding 10 ml of pyridine to a solution of 6.75 g of copper(I) chloride in 300 ml of methanol. The fine blue crystalline precipitate that formed on cooling was shown to contain 22.0% copper. Bispyridine copper(II) chloride, $(C_5H_5N)_2CuCl_2$, requires 21.75% copper. A solution of 1.8 g of this complex dissolved in 20 ml of methanol was combined with 5.0 ml of 1.21 *N* sodium methoxide in anhydrous methanol. A deep green crystalline precipitate formed whose infrared spectrum was identical with the product, $(C_5H_5NCuClOCH_3)_2$, formed from the oxidation of copper(I) chloride as described above.

D.—To 1.8 g of bispyridine copper(II) chloride in 25 ml of methanol was added 0.8 g of copper(II) methoxide. This suspension was stirred for 18 hr at room temperature. The deep green product was identical with $(C_5H_5NCuClOCH_3)_2$.

Reaction of Bispyridine Copper(II) Chloride with Sodium Phenoxides. A.—To a solution of 2.92 g of Py_2CuCl_2 in 50 ml of methanol was added 1.44 g of sodium 2,6-dimethylphenoxide. The system was stirred under nitrogen for 2 hr, during which time the color changed from deep blue to red-orange and small amounts of 3,3′,5,5′-tetramethyldiphenoquinone separated. A white crystalline precipitate formed which appeared to be copper(I) chloride, and the addition of 2 ml of concentrated hydrochloric acid produced first a haziness and then precipitated a small amount of polymer.

B.—Replacement of the sodium salt of 2,6-dimethylphenol in the above experiment with 2.30 g of the sodium salt of 2,2′-dihydroxydiphenyl gave a green precipitate (1.89 g) which from its infrared spectrum was shown to be $C_5H_5NCuClOCH_3$.

C.—To 2.92 g of bispyridine copper(II) chloride in 50 ml of methanol was added 2.2 g of sodium 2,4,6-trichlorophenoxide. The reaction mixture immediately turned black and, after standing overnight at 0°, deposited 1.8 g of glistening black crystals, mp 124–125° dec.

Anal. Calcd for $C_{22}H_{14}Cl_6CuN_2O_2$: C, 42.99; H, 2.30; Cl, 34.61; Cu, 10.34; 2,4,6-trichlorophenol content, 64.25. Found: C, 43.2; H, 2.3; Cl, 34.9; Cu, 10.5; 2,4,6-trichlorophenol content, 65.0.

When 4.4 g of the sodium salt of 2,4,6-trichlorophenol was used, the yield of copper complex increased to 3.1 g.

The compound, $(C_5H_5N)_2Cu(OC_6H_2Cl_3)_2$, was also prepared by adding 1.0 g of copper(II) hydroxide to a solution of 4.0 g of 2,4,6-trichlorophenol in 100 ml of methanol. This mixture was heated to reflux, filtered, and cooled to room temperature. Then 5.0 ml of pyridine was added and the reaction mixture was placed in the refrigerator overnight: yield 1.21 g (20%). The product was recrystallized from isooctane: mp 124–126° dec.

Preparation of $(C_5H_5N)Cu_4Cl_6O$. A. By Oxidation of Copper(I) Chloride in Isopropyl Alcohol.—To a suspension of 0.99 g (0.01 mole) of copper(I) chloride in 50 ml of dry isopropyl alcohol was added 2.0 ml of pyridine and the reaction mixture was stirred under oxygen for 18 hr. The brown crystalline solid was filtered off. A yield of 1.3 g was obtained.

Anal. Calcd for $C_{20}H_{20}Cl_6Cu_4N_4O$: C, 30.05; H, 2.52; Cl, 26.61; Cu, 31.79; N, 7.01; O, 2.00. Found: C, 30.8; H, 2.4; Cl, 26.5; Cu, 31.1; N, 7.3; O, 3.2.

B. Decomposition of $(C_5H_5NCuClOCH_3)_2$.—A methanol suspension of $(C_5H_5NCuClOCH_3)_2$ was refluxed for 2 hr during which time the green solid disappeared and the solution deposited glistening tan or brown platelets whose infrared spectrum was identical with that described in part A.

C. Reaction of $(C_5H_5NCuClOCH_3)_2$ with Hydrogen Chloride.—The compound, $(C_5H_5NCuClOCH_3)_2$, 1.0 g, was suspended in methanol. To this suspension was added 25 ml of 0.1 *N* hydrogen chloride in methanol. After a few minutes the green compound turned tan. The reaction was allowed to stir for 15 min, and then filtered; the solid was washed with methanol and dried.

D. Preparation from Copper(II) Chloride, Copper(I) Chloride, and Oxygen.—A solution of 0.5 g of anhydrous copper(II) chloride in 40 ml of methanol was prepared under nitrogen. To this solution was added 0.370 g of copper(I) chloride followed by 0.6 ml of pyridine. As soon as the pyridine was added, a purple solid precipitated. Oxygen was then added to the reaction, and a brown solid formed, which was filtered off and dried. The infrared spectrum was identical with that of the compound in part A.

E. Preparation from Bispyridine Copper(II) Chloride, Copper(II) Chloride, and Copper(II) Hydroxide.—A suspension of 2.92 g of bispyridine copper(II) chloride, 0.67 g of copper(II) chloride, and 0.5 g of copper(II) hydroxide in 60 ml of methanol was refluxed for 10 min, by which time the solids had become a brown crystalline solid identical with the one described above.

Examination of Copper Chloride Oxidation Products in the Near-Infrared. A.—Copper(I) chloride (0.020 g) was suspended in 30 ml of *o*-dichlorobenzene, pyridine (0.058 g) was added, and the system was stirred under oxygen for 30 min. The sample was then made up to 40-ml total volume and the spectrum from 600 to 1100 mμ was determined, using the Cary Model 14 spectrophotometer. Other samples at different pyridine/copper ratio were prepared in an identical fashion except that the amount of pyridine was changed.

B.—A solution of 0.042 g of $(C_5H_5NCuClOCH_3)_2$ was prepared in 40 ml of *o*-dichlorobenzene and the spectrum was determined. Other ligand ratios were obtained by replacing part of the *o*-dichlorobenzene with pyridine.

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