

SYNTHETIC UTILITY OF COPPER(I) PHENOXIDE COMPLEXES

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Several sulphur containing organic molecules react with copper(I) phenoxides under extremely mild conditions to give cuprous sulphide and an organic phenoxide. The reaction proceeds through nucleophilic substitution on the coordinated sulphur compound. The nature of the product obtained is governed by the ancillary ligands around copper(I). The high yields of the organic product obtained make these reactions extremely attractive as methods of synthesis for these compounds.

Key Words : Copper(I); Phenoxide Complexes; Thiophilic Reactions

INTRODUCTION

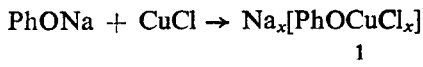
COPPER complexes with phenoxide ligands have received a lot of attention in the recent past, primarily due to their relevance as models for a variety of naturally occurring enzymes which are implicated in oxygen transport ¹(hemocyanin), selective oxidation^{2,3} (tyrosinase and dopamine monooxygenases) and in reduction of oxygen to water⁴ (multicopper "blue" oxidases). Phenoxides have a propensity to bridge copper centres⁵ which is essential for the chemistry of these naturally occurring systems. Thus the reaction of these complexes with oxygen is the subject of many investigations.⁵⁻⁹ However, their reactions with other small molecules remain uninvestigated. It has been shown in the recent past that the reactions of these copper(I) phenoxides with some small molecules could be of great synthetic value.^{10,11} In this paper, some recent modifications in the reactions of copper(I) phenoxide with small molecules other than oxygen are illustrated and how the reaction is very useful for the synthesis of a variety of organic functional groups which are otherwise difficult to synthesise is also shown.

RESULTS AND DISCUSSION

Synthesis of Copper(I) Phenoxides

Synthesis of Copper(I) phenoxides is easily achieved by a metathesis reaction between CuCl and sodium phenoxide¹² in solvents such as acetonitrile or tetrahydrofuran. Under these conditions the sodium chloride does not separate out from copper(I) phenoxide and the yellow solid isolated after the metathesis is apparently a complex salt containing sodium chloride in the crystalline solid incorporated in a polymeric or oligomeric network (*vide infra*). This can be used

for synthetic purposes as a suspension in the solvent in which it is prepared. The copper(I) phenoxide so prepared varies in its reactivity depending on the nature of the ligands present in the solution. It reacts rapidly with sulphur containing organic compounds and lead to easily characterisable and isolated compounds.



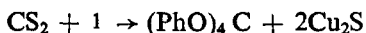
Reactions with Carbon Disulphide

The reaction of 1 with carbondisulphide is extremely fast at room temperature. The canary yellow color of the copper(I) phenoxide darkens and becomes brownish black. This slurry can be worked up to yield orthocarbonates in very high yield (Table I).

TABLE I
Synthesis of orthocarbonates using copper(I) phenoxides

Sustituent on starting phenol	Some relevant data for Tetraphenyl orthocarbononate	
	m.p (°C)	Yield (%)
H	98-9	92
4-Br	142-3	82
4-CH ₃	101	85
3-CH ₃	84-5	33
3,5-(CH ₃) ₂	155-6	64*
4-Bu ^t	254-5	89*
4-CHO	100-1	81
3-CHO	136-7	37
4-COOCH ₃	124-5	64
4-OH	109-10	84
2,4,6-Cl ₃	175-6	15

All compounds gave satisfactory elemental analysis and spectral data.

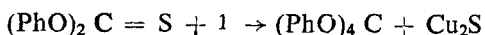
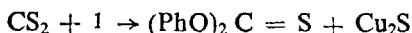


lists the yields of various orthocarbonates that have been synthesised using this method. The ease of formation of the orthocarbonate is dependant on the steric requirements of the aryloxy used and the electronic effects of the substituents. Thus use of *meta* substituted phenols leads to lower yields of the orthocarbonates. This is apparently a steric phenomenon since a variety of functional groups can be present in the *para* position without significantly affecting the yield of the reaction. A systematic increase in the levels of substitution leads to a corresponding decrease in the yields. The reaction of *p-t*-Butyl copper phenoxide however is anomalous and leads to the formation of both orthocarbonate and the thioncarbonate. Catechol forms a spirocyclic compound and attempts to prevent

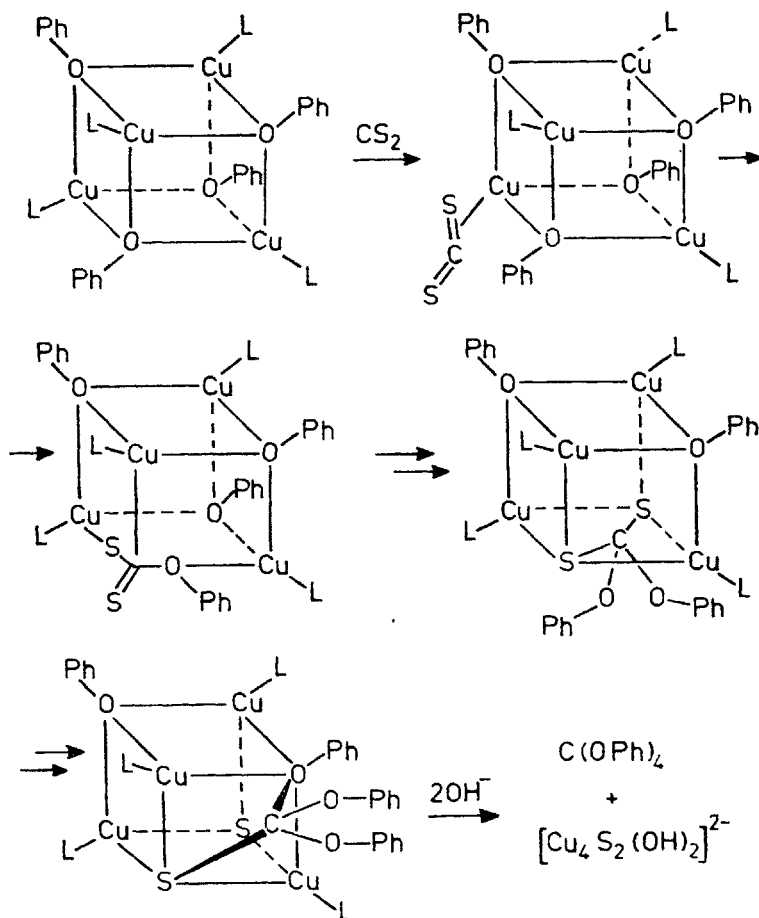
cyclisation by the use of stoichiometric amounts of copper(I) are not successful. The use of electron withdrawing substituents on the phenyl group leads to lower yields also. This is reflected in the yields obtained when *p*-CHO *p*-COOMe groups are present in the starting phenols. The most severe limitation of this method is revealed when *p*-cyano phenol, *p*-amino phenol and *p*-nitro phenols are reacted; these do not yield the orthocarbonate. The reason for this is presumably the result of co-ordination of these groups with the copper(I), leading to a different structure for the copper phenoxide which is unfavourable for reaction.

It is instructive to compare the above reaction with the reaction of Copper(I) phenoxide with carbontetrachloride which also leads to the formation of orthocarbonates.¹³ This reaction proceeds with much poorer yields and leads to the formation of orthoformates in the presence of moisture in the reaction medium. The mechanism of these two reactions are very different. Copper(I) phenoxide reacts with CCl₄ to generate radicals¹⁴ and hence in the presence of substituents on the ring which react with free radicals, the reaction fails to occur and leads to side products.

However, the reaction with carbondisulphide is not affected by the presence of groups susceptible to radical attack. The presence of moisture lowers the yield of the product but does not result in the formation of orthoformates. Hence, these reactions seem to proceed through an initial nucleophilic attack on the carbondisulphide by the coordinated phenoxide. If this nucleophilic substitution occurs in stages it would be possible



to isolate thioncarbonates in the presence of excess carbondisulphide. Attempts to stop the reaction at this stage by the use of excess CS₂ failed. Furthermore, the addition of thioncarbonates to copper(I) phenoxide does not lead to aryl orthocarbonates. This clearly indicates that thioncarbonates are not formed in this reaction and are definitely not intermediates in the reaction sequence. These results can be nicely accommodated if one assumes that the nucleophilic addition is occurring on a cluster or a polymeric network as shown in Scheme 1. Successive additions of the phenoxide ligand occur in the cluster framework in rapid succession. The use of a sterically hindered phenoxide reduces the rate of subsequent additions such that it is possible to isolate thioncarbonates as in the case of Cu(I) 3,5-dimethylphenoxide. The use of electron withdrawing groups also lead to lower yields due to the reduced nucleophilicity of the coordinated phenoxide, however the products are formed in these cases since the cluster is formed. However, in the case of cyano and amino groups the extra coordination sites on the phenoxide leads to different structures of the copper phenoxide, such structures either have no vacant sites for the initial coordination of the carbondisulphide and thus addition products are not formed or the structures are unsuitable for the nucleophilic substitutions to occur. However, *p*-nitro group is



SCHEME 1 A tentative mechanism for the reaction of copper(I) phenoxide and CS_2

apparently too electron withdrawing to promote a nucleophilic substitution. Thus this is a convenient method for the synthesis of a variety of arylorthocarbonates in a one step procedure and without using phosgene.

Reactions in the presence of Ancillary Ligands

As mentioned earlier the most studied reaction of copper(I) phenoxide is its reaction with oxygen in the presence of nitrogen donors.⁵⁻⁷ The structures of these complexes have been ascertained, in several cases through single crystal X-ray structure determinations. Understandably, the blocking of two of the coordination sites in the copper(I) complex leads to a dimeric structure⁷ as shown in Fig. 1. We have found that the reactivity of the copper(I) phenoxide synthesised as detailed earlier can be modified by addition of two equivalents of a nitrogen

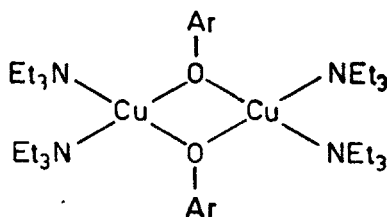


FIG 1 Structure of copper(I) phenoxide complexes in the presence of nitrogen bases

base such as triethyl amine or tetramethylethylenediamine. The reaction can also be run in pyridine as a solvent. Under these conditions the reaction of carbondisulphide with copper(I) phenoxide does not lead to the formation of orthocarbonates but leads to the formation of thioncarbonates in excellent yield. Table II lists the thioncarbonates synthesised using this reaction. Several interesting observations can be made from this table. Notably

TABLE II

Synthesis of thioncarbonates using copper (I) phenoxides

Substituent on starting Phenol	Some relevant data for Thioncarbonates	
	m.p (°C)	Yield (%)
H	105-6	40 ^a
H	"	95 ^b
4-Br	175-6	98
4-OCH ₃	162-3	88 ^c
4-OCH ₃	"	66 ^d
5-OC ₁₂ H ₂₅	100-1	42
3-CHO	127-8	74
4-CHO	139-40	96
4-Bu ^f	157-8	76
4-CN	210-2	70
4-C ₆ H ₅	262-3	85
3,5-CH ₃	160-1	71
1-Naphthol ^e	127-8	73
2-Naphthol ^e	217-9	71

All compounds gave satisfactory elemental analysis and spectral data

Melting points are uncorrected

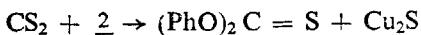
a. Pyridine as a solvent and Triethylamine as a ligand

b. Tri-*n*-Butyl Phoshine as a ligand

c. TMEDA as a ligand

d. Triethylamine as a ligand

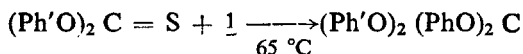
e. Starting phenol



the restrictions that applied to the synthesis of orthocarbonates both steric and electronic do not seem to apply to this synthesis. This is the result of two factors. In the presence of these nitrogen donors the structure of the complex that is formed is presumably similar to those of the known copper (I) phenoxide complexes,⁷ this would indeed lead to substitution of one sulphur with two phenoxides forming thioncarbonates. The reactivity of the thioncarbonate with this copper (I) phenoxide complex is however much less compared to the reactivity of CS₂, thus leading to exclusive formation of thioncarbonates. This has been confirmed by the reaction of thioncarbonates with copper (I) phenoxide complexes. The second factor that leads to different reactivity is the presence of nitrogen donors in the coordination sphere of the copper (I) which increases the nucleophilicity of the coordinated phenoxide. This increased nucleophilicity is reflected in the increased yields of thioncarbonates formed from Cu(I) phenoxides with *p*-CHO and *p*-COOMe. That the increased nucleophilicity is vital to the formation of thioncarbonates is borne out by the reaction in the presence of triarylphosphines. These would lead to the same general structure for copper (I) phenoxide but reduced nucleophilicity of the phenoxide. Under more rigorous conditions the product formed by insertion of the phenoxide into the coordinated carbondisulphide is isolated.¹⁵ Further insertions do not take place and no thioncarbonates are observed. The use of more electron-donating trialkylphosphines however reverses this trend and leads to the formation of thioncarbonates. Furthermore, the *p*-CN group which completely prevented the formation of orthocarbonates, leads to the formation of thioncarbonates in excellent yields. This is because the Cu(I) centre prefers coordination through the tertiary amines which are excellent ligands to coordinate to Cu(I). However, *p*-nitrophenoxide could not be used to make the corresponding thioncarbonate. Apparently, even the increased nucleophilicity of the corresponding copper phenoxide is insufficient to effect the reaction. The parent thioncarbonate, however, could not be synthesised except when pyridine was used as a solvent and triethylamine used as a ligand. Under all other conditions this reaction leads to the formation of orthocarbonate. Another anomaly is the reaction of the *p*-*t*-butylphenoxide which leads to the formation of the corresponding orthocarbonate. The reason for these are not obvious.

Reactions with Thioncarbonates

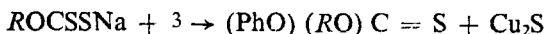
Although thioncarbonates do not react with 1 or 2 at room temperature a reaction does take place at elevated temperatures leading to the substitution of the thiono functionality with phenoxo groups. This allows one to synthesise mixed orthocarbonates as shown below.



The yields in these reactions are consistently good and hence serve as excellent substitutes for the synthetic routes available for preparing such orthocarbonates.

Reaction with Xanthates

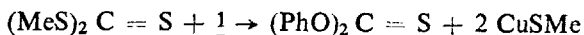
Since xanthates have two different sulphur-containing functional groups a selectivity might be expected. Based on the above results a very easy replacement of the S- group would be expected and this is indeed the case as can be seen from the reactions described below. However, it is seen from the stoichiometry of these reactions that only one phenoxide is necessary per xanthate molecule although two coppers are required to effect the transformation. Hence, in order to optimise the use of phenoxide, a complex 3 was prepared from a solution of CuCl and 0.5 equivalents of the appropriate phenoxide ligand using the same procedure used to prepare the complex 1. This would presumably have the structure shown in Fig. 2.



Reaction of 3 with sodium xanthate led to formation of mixed thioncarbonates in excellent yields.

Reaction with Dithioesters and Trithiocarbonates

Since xanthates lead to such a facile reaction, the reactions of dithioesters and trithiocarbonates were also tested with copper phenoxides. These also showed a facile exchange of the SMe and OPh groups in the presence of copper (I).

*Reaction with Thiones*

In the reactions mentioned above, the reactivity of C = S has always been lower than the reactivity of C-S with copper (I) phenoxide. Although in the case of CS₂ there is a very facile reaction with copper (I) phenoxide. A plausible explanation for this observation could be the presence of electron withdrawing O-R groups on the C = S functionality. In order to test this possibility the reactions of 1 with thiones were attempted. Although a brown intermediate complex was formed, work up of these solutions resulted in the formation of ketones and recovery of the corresponding phenols. Hence, the same reaction was attempted in the absence of phenols and in the presence of CuCl and NaOH. This also resulted in the formation of ketones. Table III lists the yields obtained

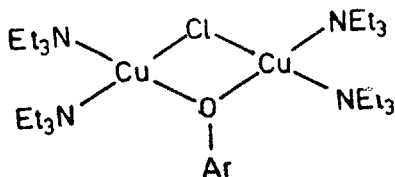


FIG 2 Structure of copper(I) phenoxide complexes designed for reaction with xanthates

TABLE III
Thione to ketone conversion using thiophilicity of Cu(I)

Substrate	Time (mts)	Temp. (°C)	Yield (%)
Thiocoumarin	15	25	100
Thiocomphor	30	25	85
4,4'-Dimethyl Thiobenzophenone	10	25	100
Michler's Thione	720	80	85
Xanthione	15	25	100
Thioxanthione	15	25	100
1,4-Thiobenzoylbenzene*	30	25	100
1-Methel-2-thio-pyridone	20	25	96

*Two equivalents of CuCl were used.

on carrying out the reaction with a variety of thiones. Interestingly trithiocarbonates could not be converted to the corresponding ketone. In all cases, a stable complex of CuCl was formed on addition of the thiones. Thiones which had a higher oxidation potential such as Michler's thione were difficult to oxidise whereas the reaction was instantaneous with others. Hence, this turns out to be an excellent method for the conversion of thiones to ketones under rather mild conditions.

CONCLUSION

The transformations developed here have very good synthetic potential. Many of these molecules could not be synthesised by the available procedures or were available with difficulty by the use of phosgene. It is possible to think of a variety of transformations that can be carried out using copper (I) phenoxide complexes. We have illustrated here a few with sulphur-containing organic molecules. In all these reactions there is a transformation that leads to the net conversion of a Cu-O bond to a Cu-S bond. Due to the soft nature of Cu(I) it prefers a softer S to a hard O. Hence, these reactions might be termed as thiophilic reactions of Cu(I). It would be interesting to compare these reactions with the reactions of the naturally occurring enzymes with sulphur-containing organic molecules. These might very well throw light on the biological activity of sulphur-containing organic molecules.

ACKNOWLEDGEMENT

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