Copper(I) and Copper(II) mediated Two-electron Oxidations of Benzylic Alcohols and Diaryl Acetic Acids by Trimethylamine *N*-Oxide

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A novel ligand oxidation of Cu^I and Cu^{II} benzylic alcoholates and diaryl acetic carboxylates to carbonyl compounds by trimethylamine *N*-oxide gives support to the existence of cupryl ($-Cu^{III}=O$) intermediates, previously postulated in the reaction of Cu^I derivatives with dioxygen.

Tertiary amine *N*-oxides are known to transfer their oxygen atom to iron(II),[1] iron(III),[2] manganese(III),[3] vanadium(IV),[4] chromium(III),[5] and molybdenum(IV)[4] porphyrins or other complexes P, to provide high-valence reactive compounds [equation (1)]. To our knowledge, the only previous report of a copper(I)–amine oxide interaction describes an intramolecular diphenol oxidative coupling used in alkaloid synthesis.[6]

$$\text{P–M}^{n} + \text{R}_3\text{NO} \rightarrow \text{P–M}^{n+2}\text{=O} + \text{R}_3\text{N} \qquad (\text{M} = \text{Fe,Mn,V,Cr,Mo}) \qquad (1)$$

This Communication deals with the oxidation of Cu^I and Cu^{II} primary and secondary benzylic alcoholates and diaryl acetic carboxylates by trimethylamine *N*-oxide (TMAO) to carbonyl compounds; alcoholates present two-electron dehydrogenation and carboxylates undergo four-electron (2 successive two-electron) oxidative decarboxylation.

Each reaction (Scheme 1), carried out in dry acetonitrile at 60 °C, under anaerobic conditions, for 24 h, has been established to be a very slow process at room temperature, indicating that Cu^I and Cu^{II} salts are less reactive towards amine oxides than the aforementioned metal salts.

Copper(I) (**A1a,A1b**) and copper(II) (**A3a**) alcoholates are prepared *in situ* from the sodium alcoholates by metathesis with, respectively, Cu^ICl (as previously reported[7]) and $Cu^{II}Cl_2$. With such strong Cu^I and Cu^{II} chelating ligands as saligenols (**B**) no previous stoicheiometric formation of copper salts is needed; for instance (**B1d**), Cu^ICl (1 equiv.), and trimethylamine *N*-oxide (TMAO; 4 equiv.) afford 4,6-di-t-butyl salicylaldehyde in quantitative yield. Copper(I) carboxylates (**C1e**) and (**C1f**) are prepared *in situ* either by reaction of acids with copper(I) oxide (0.5 equiv.) in acetonitrile or by metathesis of sodium carboxylates with Cu^ICl in the same solvent. Copper(II) diphenylacetate (**C4e**) is classically prepared by its sodium salt reaction with $CuSO_4$ in water. As shown in Table 1, Cu^I salts efficiently and selectively react with TMAO; transformations are quantitative or nearly so, and by-products are not detected, in contrast with Cu^{II} alcoholates which do not react at all (**A3a,A4a**) and saligenol (**B3d**) which affords carbonyl compound in moderate yield together with a significant quantity of unidentified by-products.

Table 1. Oxidation[a,b] of Cu^I and Cu^{II} salts by TMAO.[c]

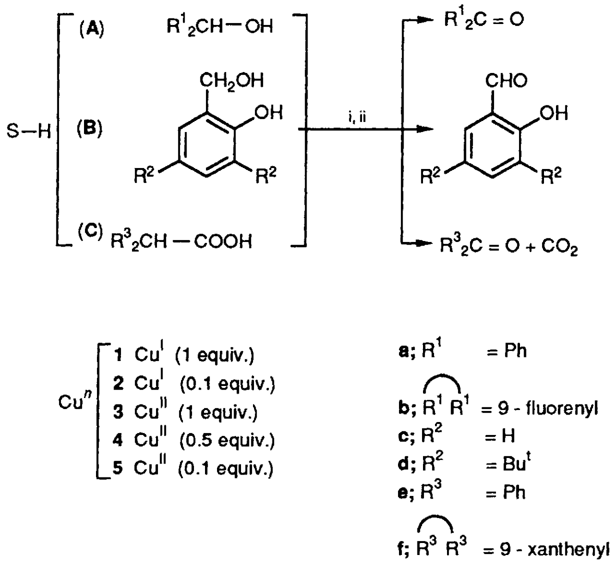
		Carbonyl compounds	
S–H	Procedure	Conversion[d]/%	Yield[d]/%
Alcohols	**A1a**	38	100
	A1b	84	96
	A3a	0	0
	A4a	0	0
Saligenols	**B1c**	58	96
	B1d	100	100
	B2d	70	80
	B3d	100	40
	B5d	33	96
Acids	**C1e**	72	98
	C1f	94	94
	C4e	63	98

[a] Copper salt (1 mmol substrate, 0.1—1 mmol Cu^n), excess TMAO (4 mmol) in dry MeCN (40 cm^3), 60 °C, 24 h, N_2 atmosphere. [b] In preliminary experiments each copper derivative is obviously shown to be stable under the experimental conditions, without TMAO. [c] Obtained from $TMAO{\cdot}2H_2O$ by azeotropic distillation of its toluene solution. [d] Pure isolated (preparative TLC) products.

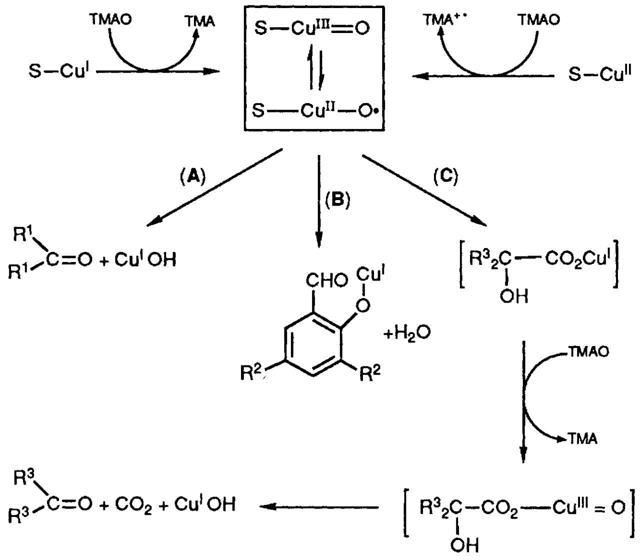
In previous studies concerning oxidations of phenols[8] (tyrosine-like *o*-hydroxylation), alcohols[7,9] (dehydrogenation), and carboxylic acids[10] (oxidative decarboxylation) by Cu^I–dioxygen systems in acetonitrile, we have postulated that the homolytic cleavage of an early formed μ-peroxodicopper(II) intermediate affords reactive oxocopper(III) species (cupryl $S-Cu^{III}=O$, S being here alcoholate or carboxylate ligand), see equation (2).

$$2\ \text{S–Cu}^{\text{I}} + \text{O}_2 \rightarrow [\text{S–Cu}^{\text{II}}\text{–O–O–Cu}^{\text{II}}\text{–S}] \rightarrow 2\ [\text{S–Cu}^{\text{III}}\text{=O} \rightleftharpoons \text{S–Cu}^{\text{II}}\text{–O}^{\bullet}] \rightarrow \text{products} \qquad (2)$$

The TMAO/S-$Cu^{I\ \mathrm{or}\ II}$ interaction seems to provide an 'amine oxide shunt' to the S-Cu^I/O_2 system. Thus in TMAO reactions with Cu^I or Cu^{II} alcoholates or carboxylates, the same corresponding products are always formed suggesting that both reaction types may proceed by the same two-electron oxidant cupryl intermediates (Scheme 2) we have already discussed in previous papers.[8—10]



Scheme 1. *Reagents and conditions*: i, Cu^n, MeCN; ii, $\overset{-}{O}\overset{+}{N}Me_3$ (4 equiv.), 60 °C.



Scheme 2

Further chemical evidence is given by the isolation of minor amounts (2%) of the intermediate α-hydroxy acid (benzilic acid), trapped as its Cu^{II} salt and found in the recovered acid fraction from (**C4e**) oxidation runs, to be compared with the same observation in the corresponding Cu^{I} carboxylate reaction with dioxygen.[10]

In each reaction (Scheme 2) Cu^{I} is formed or reactivated, suggesting a catalytic ability in these systems, whenever the basicity of medium is strong enough (due to trimethylamine appearance) to allow copper–alcohol (or acid) linkage. Thus, in di-t-butyl saligenol catalytic oxidations (**B2d**) and (**B5d**), turnover numbers of 7.0 and 3.3 are measured with respect to $Cu^{I}Cl$ and $Cu^{II}Cl_2$ under the same conditions.

Further interest in these catalytic systems is given by their high yields and selectivities, in particular $Cu^{II}Cl_2$-catalysed oxidation (**B5d**) is a considerable improvement on the stoicheiometric reaction (**B3d**). We are currently investigating these mechanisms in more detail, particularly the behaviour of the postulated aminium radical $TMA^{+\bullet}$ in Cu(II)–TMAO mediated oxidations. Together with the following Communication,[11] this preliminary report describes the first example of a copper(II) salt oxidation by an amine *N*-oxide.

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