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Oxidative debromination in a binuclear copper (I) complex

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Abstract: The binuclear copper (I) complex Cu₂(2,6-BPB-1-Br)(BF₄)₂ 1.8CH₃CN (8) undergoes at 20°C with O₂ a rapid oxidative arene debromination.

The design of monooxygenase¹ model systems using well defined binuclear copper (I) complexes allows the study of the binding and reactivity of molecular oxygen at copper centers and has attracted great attention in recent years²,³. Previously we have described unusual arene hydroxylations and demethoxylation (demethylations) of anisole moieties under ambient conditions with O₂ in binuclear Cu(I) complexes containing meta-xylyl bridged ligands⁴.

In order to obtain insight in the mechanism of the arene hydroxylation in binuclear copper complexes the substituent X at carbon C₁ of the aromatic nucleus, which is expected to be most vulnerable to oxygenation, was modified.

Recently Karlin and co-workers reported the first example of an oxidative dehalogenation (i.e. dechlorination) in a related binuclear copper complex⁵.

The ligand 2,6-bis[N-(2-(2-pyridyl)ethyl]iminodiacetyl-1-bromobenzene (2,6-BPB-1-Br) (6) was prepared from 1-bromo-2,6-dimethylbenzene 2 (eq.1).

Selective tetrabromination of 2 was followed by hydrolysis and subsequent condensation of the resulting dialdehyde 4 with two equivalents of 2-(2-pyridyl)ethylamine provided 6 in 54% overall yield⁶.

The tetradeinate ligand 6 reacts with two equivalents of Cu(CH₃CN)₄BF₄(7) in dry THF under an inert nitrogen atmosphere to produce, after it was washed several times with THF, a pure orange binuclear Cu(I) complex [Cu₂(2,6-BPB-1-Br)(BF₄)₂ 1.8 CH₃CN].(8)

Elemental analysis revealed two Cu(I)ions per molecule of 6 and a Cu:N ratio of 1:2.9. This means that both two and presumably three and four coordinated centers are present in 8 due to the binding of one pyridylethyl-imine-bidentate unit by each Cu(I) ion and one or two CH₃CN molecules occupying the vacant coordination sites. The presence of weakly bound CH₃CN is further demonstrated by the decrease of the amount of CH₃CN in the complex by prolonged evacuation. Similar reversible CH₃CN binding i.e. equilibria between two, three and four coordinated complexes depending upon the presence of variable amounts of CH₃CN has been observed for the Cu(I) complexes of ligand 1b⁴ and was reported also for a related case by Karlin and co-workers⁷.

When a solution of the 1-bromo complex 8 in CH₂Cl₂/CH₃OH (40:1) was allowed to react with molecular oxygen at room temperature a rapid colour change from orange to dark green was
observed. Isolation and characterization of the oxidation product after 16 h. showed that dinuclear Cu(II) complex 9 had been formed in about 80% yield. Hydrolysis of the reaction mixture, using aqueous HCl, gave the corresponding phenol (yield 80%) together with unreacted bromodialdehyde 4 (10-20% yield).

Phenoxy-hydroxy bridged complex 9 [Cu2(2,6-BPB-1-O)(OH)(BF₄)₂] was obtained as dark-blue green crystals, identical in all respects with the complexes obtained via arene hydroxylatation of the binuclear Cu(I) complexes of 1b (X = OCH₃) and 1c (X = H). Furthermore 9 and 10 were independently prepared and the structure of the former was determined by X-ray analysis.

Analysis of the reaction mixture for Br⁻ was performed after an aqueous HNO₃ (1N) work up procedure. The separated water layer was titrated with AgNO₃ and indeed Br⁻, up to 57% could be analyzed by potentiometric methods. This accounts for 72% of the theoretical amount of Br⁻. Indications that the debromination is non-selective or that alternative reactions (i.e. disproportionation) occur, were not obtained.

Considering the results of these experiments an overall hydroxylation-debromination at the arene 1-position of 8 has taken place with O₂ under ambient conditions. Although we cannot be sure that Br⁻ is formed directly in this oxygenation reaction, it is most likely that a dicopper (II) peroxo species, initially formed upon binding of O₂ to 8, attacks the C₁ position to form complex 11. Subsequent fragmentation of 11, during which process Br⁻ acts as a leaving group, leads to 9 following a pathway analogous to the oxidative demethoxylation of 10.

Dehalogenation reactions are catalyzed by various enzymes using hydrolytic, reductive or oxidative pathways. However, few enzymes are able to dehalogenate aromatic compounds by an oxidative process. For instance phenylalanine hydroxylase is able to dehalogenate 4-fluorophenylalanine, using oxygen and cofactors, to tyrosine.

It is not too far fetched to suggest that the present system mimics certain aspects of enzymatic dehalogenation. To our knowledge the oxidation described here represents the first example of a copper-dioxygen induced arene-debromination. The mild conditions, room temperature and O₂, should be especially emphasized.

References


6. All new compounds were fully characterized and spectroscopic data and
exact mass and/or elemental analysis were in accordance with the structures shown. Relevant spectroscopic data:

3: m.p. 140.0-141.1°C; $^1$H NMR(CDCl$_3$): $\delta$ 7.54 (m, 1H), 8.13 (d, $J = 8$ Hz, 2H), 10.53 (s, 2H). Analysis calculated for C$_8$H$_5$BrO$_2$: C: 45.07, H: 2.34, Br: 37.56, found: C: 44.87, H: 2.49, Br: 37.49. HRMS calculated for C$_8$H$_5$BrO$_2$: 211.947, found 211.946.

4: $^1$H NMR(CDCl$_3$): $\delta$ 3.15 (t, $J = 7$ Hz, 4H), 4.04 (t, $J = 7$ Hz, 4H), 7.10 (m, 4H), 7.26 (t, $J = 7.8$ Hz, 1H), 7.52 (m, 2H), 7.91 (d, $J = 7.3$ Hz, 2H), 8.50 (d, $J = 5.1$ Hz, 2H), 8.57 (s, 2H). $^{13}$C NMR(CDCl$_3$): $\delta$ 39.19, 60.83, 121.14, 123.52, 126.63, 127.24, 130.51, 135.08, 136.09, 149.12, 159.29, 160.24. HRMS calculated for C$_{22}$H$_{21}$BrN$_4$: 420.095, found: 420.093.


9. Alternatively BrO$^-$ might be formed first, which subsequently decomposes into Br$^-$ and H$_2$O. However, we prefer Br$^-$ elimination in analogy with the oxidative demethoxylation of 1b where OCH$_3$ acts as a leaving group.$^5$