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Gelling, O.J.; Feringa, Bernard

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Oxidative debromination in a binuclear copper (I) complex

O.J. Gelling and Ben L. Feringa*, Department of Organic Chemistry,
University of Groningen, Nijenborgh 16, 9747 AG Groningen, The Netherlands
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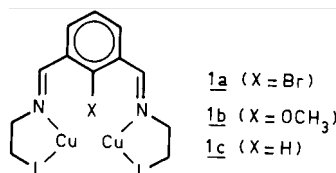
Abstract: The binuclear copper (I) complex $\text{Cu}_2(2,6\text{-BPB-1-Br})(\text{BF}_4)_2 \cdot 1.8\text{CH}_3\text{CN}$ (**8**) undergoes at 20°C with O_2 a rapid oxidative arene debromination.

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 years^{2,3}. Previously we have described unusual arene hydroxylations and demethoxylations (demethylations) of anisole moieties under ambient conditions with O_2 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 **1** the substituent X at carbon C₁ of the aromatic nucleus, which is expected to be most vulnerable to oxygenation, was modified.

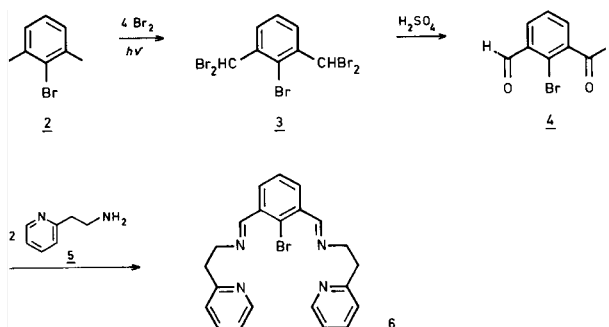
We now report the results of an unprecedented O_2 induced oxidative arene debromination in a binuclear Copper (I) complex (**8**).

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)formimidoyl-1-bromobenzene (2,6-BPB-1-Br)](**6**) was prepared from 1-bromo-2,6-dimethylbenzene **2** (eq.1).

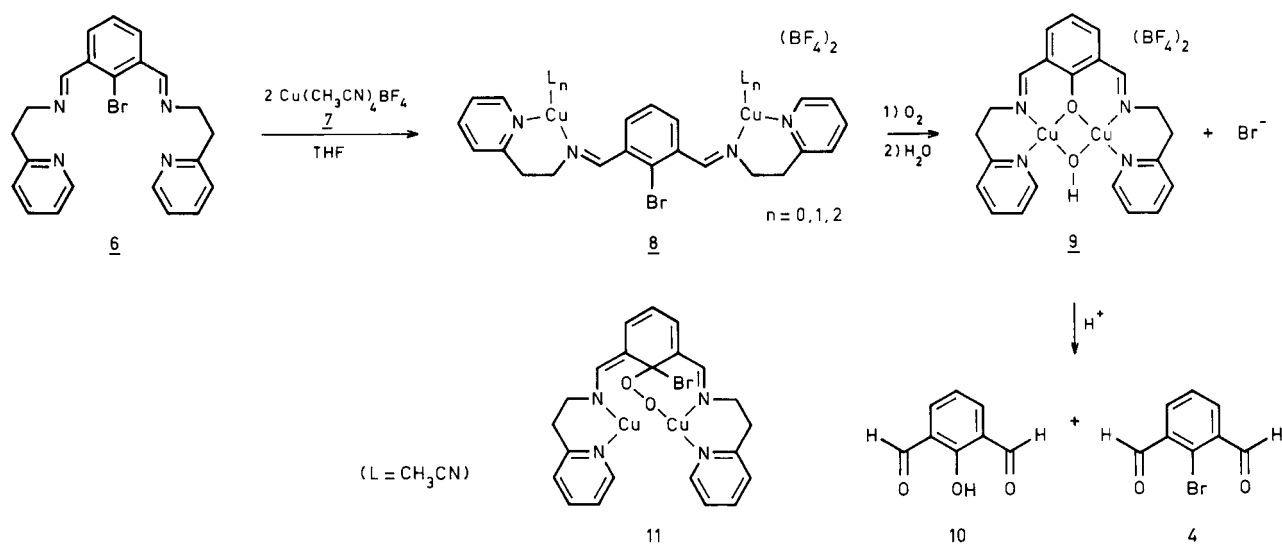
Selective tetrabromination of **2** was followed by hydrolysis and subsequent condensation of the resulting dialdehyde **4** with two equivalents of 2-(2-pyridyl)ethylamine provided **6** in 54% overall yield⁶.



The tetradentate ligand **6** reacts with two equivalents of $\text{Cu}(\text{CH}_3\text{CN})_4\text{BF}_4$ (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 $[\text{Cu}_2(2,6\text{-BPB-1-Br})(\text{BF}_4)_2 \cdot 1.8\text{CH}_3\text{CN}]$ (**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 CH_3CN molecules occupying the vacant coordination sites. The presence of weakly bound CH_3CN is further demonstrated by the decrease of the amount of CH_3CN in the complex by prolonged evacuation. Similar reversible CH_3CN binding i.e. equilibria between two, three and four coordinated complexes depending upon the presence of variable amounts of CH_3CN has been observed for the Cu(I) complexes of ligand **1b**⁴ and was reported also for a related case by Karlin and co-workers⁷.

When a solution of the 1-bromo complex **8** in $\text{CH}_2\text{Cl}_2/\text{CH}_3\text{OH}$ (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 bromobenzaldehyde **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 hydroxylation 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 analysis⁴.

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)⁵ 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^{8,9} 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 **1b**⁴.

Dehalogenation reactions are catalyzed by various enzymes using hydrolytic, reductive or oxidative pathways⁸. 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 tyrosine¹⁰.

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.

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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; ^1H NMR(CDCl_3): δ 7.54 (m, 1H), 8.13 (d, $J = 8$ Hz, 2H), 10.53 (s, 2H). Analysis calculated for $\text{C}_8\text{H}_5\text{BrO}_2$: C: 45.07, H: 2.34, Br: 37.56, found C: 44.87, H: 2.49, Br: 37.49. HRMS calculated for $\text{C}_8\text{H}_5\text{BrO}_2$: 211.947, found 211.946.

4: ^1H NMR(CDCl_3): δ 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): δ 39.19, 60.83, 121.14, 123.52, 126.63, 127.24, 130.51, 135.08, 136.09, 149.12, 159.29, 160.24. H R M S calculated for $\text{C}_{22}\text{H}_{21}\text{BrN}_4$: 420.095, found: 420.093.

Cu_2 (2,6-BPB-1-Br) $(\text{BF}_4)_2$ $(\text{CH}_3\text{CN})_{1.8}$. (**8**) Analysis calcd. for $\text{C}_{25.6}\text{H}_{26.4}\text{B}_2\text{BrCu}_2\text{F}_8\text{N}_{5.8}$: C 38.63, H: 3.34, Br: 10.03, Cu: 15.96, N: 10.21, found C: 37.72, H: 3.45, Br: 9.91, Cu: 16.10, N: 10.10.

Cu_2 (2,6-BPB-1-O)(OH) $(\text{BF}_4)_2$. (**9**)

Analysis calcd. for $\text{C}_{22}\text{H}_{22}\text{B}_2\text{Cu}_2\text{F}_8\text{N}_4\text{O}_2$: C: 39.14, H: 3.28, Cu: 18.82, F: 22.51, N: 8.30, found: C: 39.12, H: 3.41, Cu: 18.65, F: 22.00, N: 8.56. IR(KBr): 1575, 1640, 3500 cm^{-1} .

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9. Alternatively BrO^- might be formed first, which subsequently decomposes into Br^- and H_2O . However, we prefer Br^- elimination in analogy with the oxidative demethoxylation of **1b** where OCH_3 acts as a leaving group⁵.
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