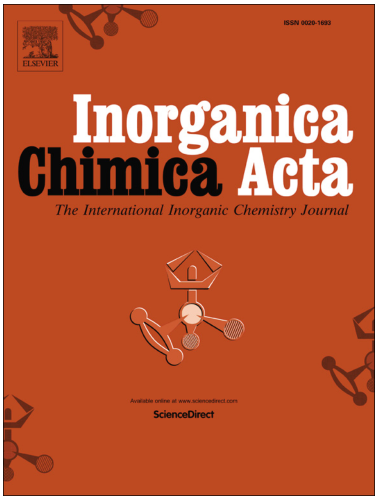

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PII: S0020-1693(17)31021-6
DOI: http://dx.doi.org/10.1016/j.ica.2017.08.009
Reference: ICA 17803

To appear in: *Inorganica Chimica Acta*

Received Date: 29 June 2017
Accepted Date: 3 August 2017

Please cite this article as: K.V.N. Esguerra, Y. Fall, J-P. Lumb, Catalytic Aerobic Oxidation of Halogenated Phenols, *Inorganica Chimica Acta* (2017), doi: http://dx.doi.org/10.1016/j.ica.2017.08.009

# Catalytic Aerobic Oxidation of Halogenated Phenols

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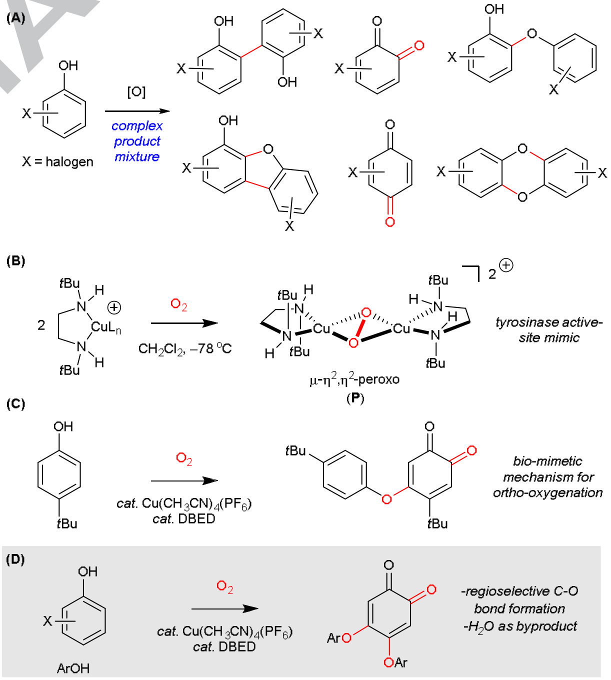
*Keywords: halophenol oxidation, oxygenation, tyrosinase, aerobic oxidation, dehydrogenative coupling.*

**ABSTRACT:** Phenol pollutants such as halophenols and guaiacol derivatives are produced as byproducts of many industrial processes. Aerobic oxidations for their degradation in the context of effluent treatment or environmental remediation often lack selectivity. This work describes a copper (Cu)-catalyzed approach that converts three equivalents of halogenated phenols into a single *ortho*-quinone, at the expense of reducing dioxygen ($O_2$) to water ($H_2O$).

## Introduction

Halophenols are compounds of great environmental concern due to their toxicity, mutagenicity, and carcinogenicity.[1-3] These compounds are widely used as disinfectants, preservatives, and are common byproducts of the paper bleaching industry.[4] They are generally resistant to biodegradation, and often difficult to remove from the environment.[5] Current strategies for the oxidation of halophenols in the context of environmental remediation include photochemical, chemical and enzymatic methods, but each carry their own set of limitations.[5] For instance, photochemical methods can require elaborate instruments,[6-8] and oxidation reactions can produce toxic byproducts such as biphenyls, dibenzo-*p*-dioxins, benzofurans and phenoxyphenols, which can carry acutely negative toxicological profiles (Scheme 1A).[9,8] A wide variety of bacteria and fungi that over-expresses phenol oxidases,[10-12] particularly tyrosinase,[13] have also been explored for their biocatalytic activity to degrade chlorophenols. However, these enzymes can be limited to a narrow range of conditions, and they denature at elevated temperatures.[14]

Transition metal complexes that mimic metalloenzymes can present certain alternatives. In the particular case of the enzyme tyrosinase, several bio-inspired complexes have been shown to selectively oxygenate phenols to *ortho*-quinones.[15,16] Mimicking the active site of this enzyme has been the focus of numerous bio-inorganic studies that aim to determine the mechanism of $O_2$ activation and substrate oxygenation.[17] Recently, our group has investigated a tyrosinase mimic composed of *N, N'*-di-*tert*-butyl-ethylene diamine (DBED) and $Cu(CH_3CN)_4(PF_6)$ (abbreviated $CuPF_6$) (Scheme 1B).[18-20] Stack and co-workers have previously demonstrated that the mixture of DBED and Cu(I) self-assemble to the dinuclear $\mu$-$\eta^2$: $\eta^2$peroxo (**P**) upon exposure to $O_2$.[21,22] Building upon this study, our group has demonstrated the involvement of **P** in the catalytic aerobic *ortho*-oxygenation / oxidative coupling of simple phenols (Scheme 1C).[20] For the current study, we report the unexpected formation of a 4,5-di-substituted *ortho*-quinone from three equivalents of a halophenol (Scheme 1D). To our knowledge, this transformation has not been observed previously for tyrosinase mimics. It extends our previous work to a catalytic aerobic oxidation of persistent phenol pollutants, which could provide a greener and practical approach for their oxidative degradation.



**Scheme 1. (A) Oxidation of halogenated phenols. (B) Tyrosinase mimicry with DBED. (C) Catalytic aerobic *ortho*-oxygenation with DBED/Cu(I). (D) Work described herein.**

## Results and Discussion

Our previously optimized conditions for the catalytic aerobic *ortho*-oxygenation of phenols consists of 4 mol% $CuPF_6$, 5 mol% DBED and $O_2$ (2 atm) in $CH_2Cl_2$ (0.1 M) for 4h at room temperature.[19] Applying these conditions to the oxidation of 4-chlorophenol (**1**) affords a 57% isolated