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Transformation of catechol through modulation of boron 'ate' complex reactivity

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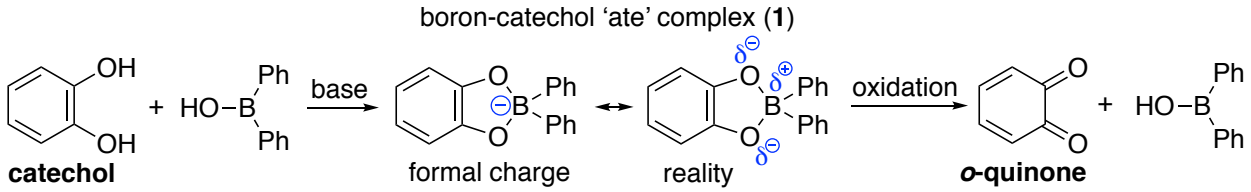
GOAL

Catechol is a petrochemical feedstock that serves as the base molecule for a variety of higher-value products across a multitude of industries. The oxidation of catechol to *o*-quinone, however, is currently of limited synthetic utility. We address these limitations by employing borinic acids designed to tune and control the oxidation potential of catechol.

RESEARCH DESIGN

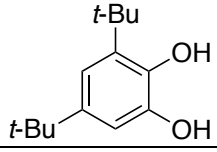
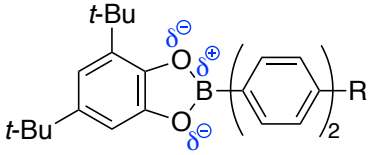
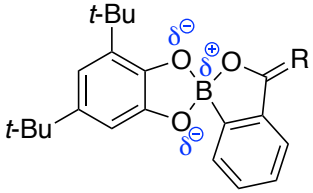
In terms of industrial application, the oxidation of catechol is relatively uncontrolled. We sought to control the oxidation of catechol by using borinic acids to complex catechol (**1**). The negative formal charge of the complex means that oxidation is more facile. Moreover, the oxidation potential of the complex can be tuned by modifying the substituents on the borinic acid to alter the electron density within the complex.



RESULTS

The oxidation potential of the complexes was measured using cyclic voltammetry. The 3,5-di-tertbutyl-catechol (**2**) was used as a stable and reversible electrochemical model of catechol. The experiment was conducted by adding borinic acid to a solution of **2** in acetonitrile (with tetrabutylammonium hexafluoride as electrolyte). The results of these experiments are shown in Table 1.

Table 1: Oxidation potentials of complexes (**1**)

Entry		R	Oxidation Potential (V)
1	 **2**		+.91
2		H	-.01
3		OMe	-.04
4		*t*-Bu	-.05
5		F	+.06
6		-H, -H	+.12
7		=O	+.39

Overall, the data reveal that borinic acid 'ate' complexes with catechol display more facile oxidation (lower oxidation potential) relative to catechol alone. In general, it would appear that the identity of R in aryl borinic acids (entries 2-5) does not lead to pronounced differences between each complex. Alternatively, placing another electronegative atom onto the sp^3 boron atom leads to a greater variability in oxidation potential as evinced by entries 6 and 7.

IMPACT OF RESERACH
Our results indicate that the oxidation potential of catechol can be tuned over a range of potentials through reversible covalent complexation with borinic acids and related derivatives. These results confirm the central hypothesis of our proposal and were recently published: Zachary M. Robole, Kira L. Rahn, Bryan J. Lampkin, Robbyn K. Anand, Brett VanVeller *Journal of Organic Chemistry* **2019**, *84*, 2346-2350.

These findings could impact the quantification of neurotransmitters concentrations using electrochemical analysis.

Support from this grant also impacted the work of two other studies that were recently published.

Sean R. Norris, Caroline C. Warner, Bryan J. Lampkin, Paige Bouc, Brett VanVeller *Organic Letters* **2019**, *21*, 3817-3821
A new class of push−pull dyes based on the reactive isobenzofuran core have been synthesized. The new dyes have a smaller HOMO−LUMO gap than a related class of dyes based on benzofurazan and allow for isolation of structural factors that contribute to environmental sensitivity. Experimental and theoretical evidence implicate different photophysical processes are responsible for a reversal of emissive behavior that is observed between isobenzofuran and benzofurazan analogues.

Luis A. Camacho, III, Bryan J. Lampkin, Brett VanVeller *Organic Letters* **2019**, *21*, 7015-7018
Thioamides are useful biophysical probes for the study of peptide structure and folding. The α-C stereochemistry of thioamide amino acids, however, is easily epimerized during solid-phase peptide synthesis (SPPS), which limits the sequence space that is available to thioamide incorporation. This work demonstrates that the α-C stereochemistry of thioamides can be reversibly protected in a manner that is compatible with the standard methodology of SPPS to enable the facile implementation of thioamide probes.

IMPACT ON PI'S CAREER
Funds from the ACS PRF have been essential to establishing several physical organic research projects in my group. We have been successful in acquiring the following grant support.

2019 National Science Foundation CAREER Award
2018 Cottrell Scholars Award, Research Corporation for Science Advancement
2018 Pfizer Global ASPIRE Research Award in TTR Amyloidosis

IMPACT ON STUDENTS
Funds from the ACS PRF have supported the research of two graduate students (Bryan Lampkin and Yen Nguyen). Additionally, funds supported an undergraduate student (Zach Robole) who was able to present his work on this project at the 2018 Reaction Mechanisms Conference in Vancouver, BC and who, as an undergraduate student, was the first author on the *JOC* paper discussed above.