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

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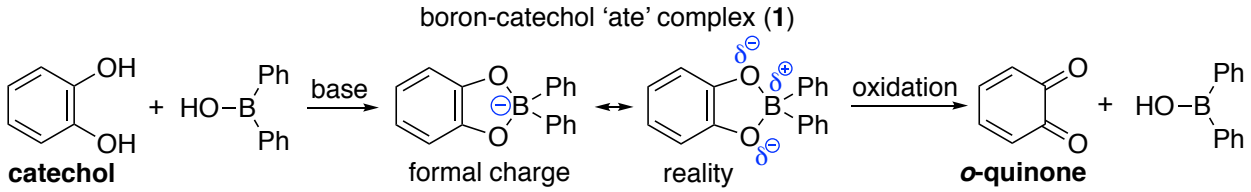
GOAL

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

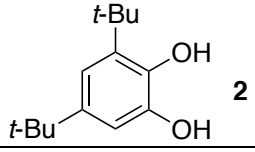
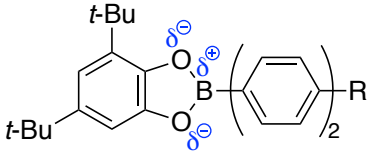
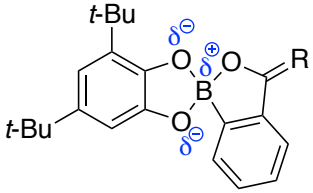
In terms of industrial application, the oxidation of catechol is relatively uncontrolled. We sought to control the oxidation of catechol by using borinic acids to complex catechol (**1**). The negative formal charge of the complex means that oxidation is more facile. Moreover, the oxidation potential 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 reveals 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 initial 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. We are currently investigating how these results might also impact the quantification of neurotransmitters.

Accurate assessment of neurotransmitters is essential to treatment of neurological diseases. Catecholamines such as dopamine, norepinephrine, and epinephrine, are electrochemically active and should theoretically be detectable through monitoring of the oxidation potential of neural fluid. Unfortunately, electrochemical assessment of these catecholamines is difficult due to an overlap in potential and competition with ascorbic acid (Vitamin C) and non-catechol neurotransmitters such as serotonin. To address this current limitation, we will develop a class of reagents based on borinic acids that are designed to selectively bind catecholamines *in situ*. Upon binding, the oxidation potential of the catecholamine is effectively shifted out of the oxidation window associated with ascorbic acid and serotonin. With the complicating effects of ascorbic acid and serotonin removed, quantification of catechol amines can proceed using standard cyclic voltammetry techniques.

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

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.

We anticipate that the students listed above will publish their findings by the end of Fall 2018.