Laccase-generated *o*-quinones in *o*-naphthoquinone synthesis *via* Diels-Alder reaction

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Objectives

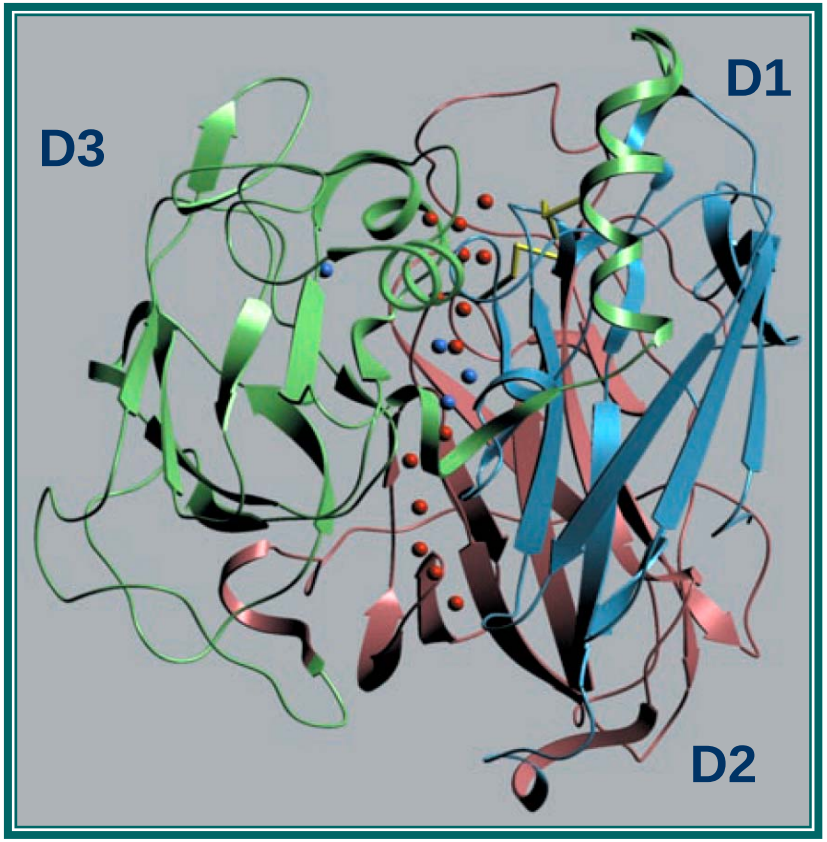
- To find other potential uses of the enzyme laccase in organic synthesis
- Use green chemistry in the synthesis of organic compounds
- Find a reliable mechanism that allows for the synthesis of *o*-naphthoquinones in maximum yield

About the Enzyme Laccase

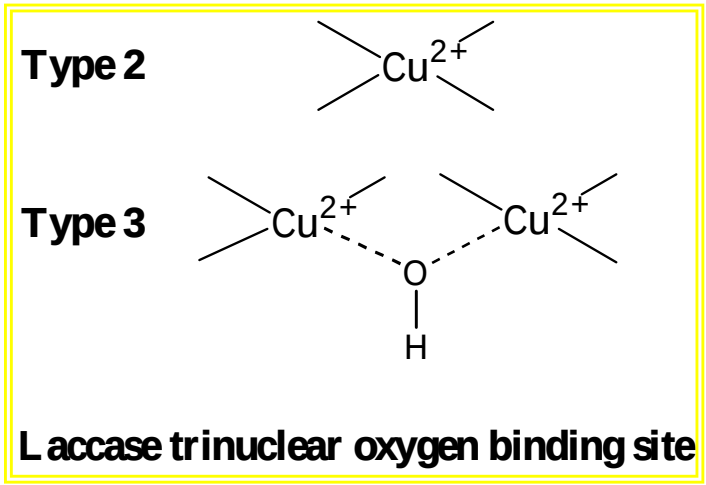
- **It was discovered in 1883 by the Japanese scientist Yoshida**

- **What are laccases?**
  - They are multi-copper-containing enzymes
  - Widely distributed among plants and can be found in fungi
  - They catalyze the oxidation of various aromatic compounds

Structure of Laccase



Ribbon diagram of laccase showing the two channels leading to the T2/T3 cluster



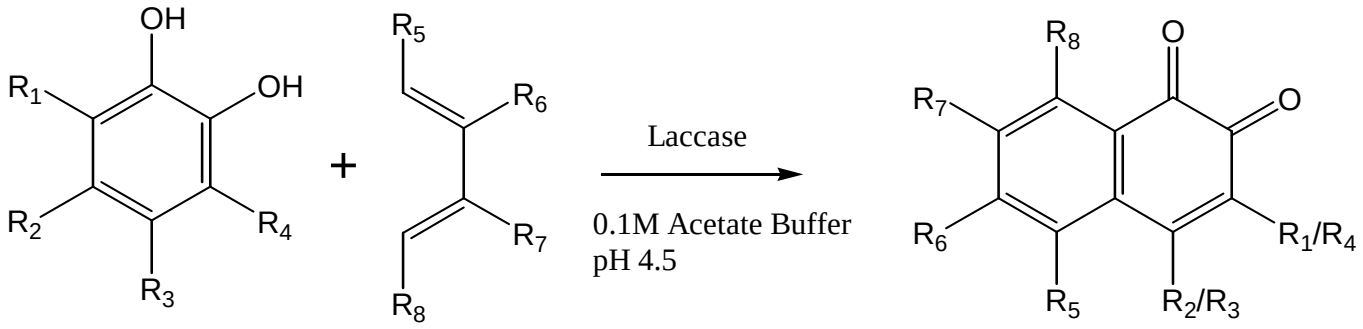
Piontek, K.; Antorini, M.; Choinowski, T. *J. Biol. Chem*. **2002**, *277*, 37663.
Burton, S. G. *Current Organic Chemistry*, **2003**, *7*, 1317.

Reactions in Water

- Benefits:
  - Water is a desirable solvent for reasons of cost, safety, and environmental concerns
  - Ease of product isolation
  - Substantial rate acceleration when insoluble reactants are stirred in aqueous suspension
  - Safety due to high heat capacity and unique redox stability

Experiment

General Reaction Scheme

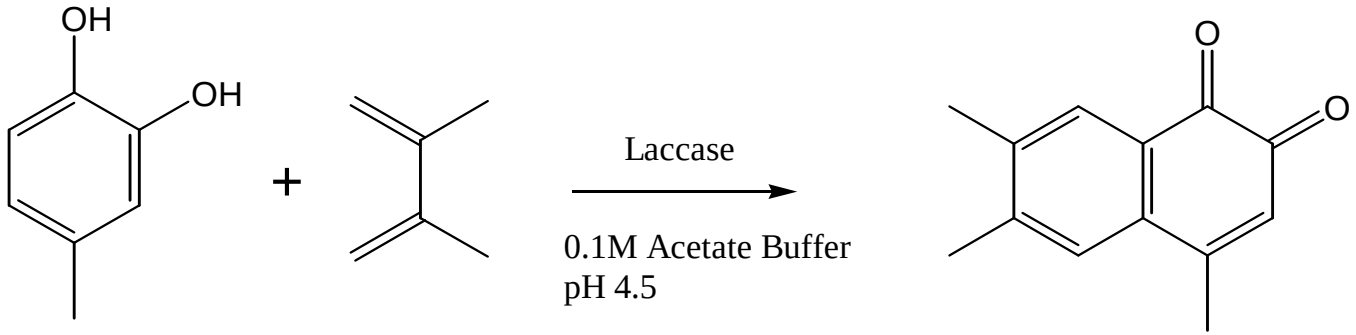


o-naphthoquinone

The following are varied to reach optimal reaction conditions:

- Ratio of diene to dienophile
- Temperature
- Laccase dose

Optimization of Reaction Condition



- Reaction condition with best results:
  - Diene to dienophile ratio of 1:10
  - Reaction remperature of approximately 0-5°C
  - Reaction time of 6 hours

Proposed Reaction Pathway

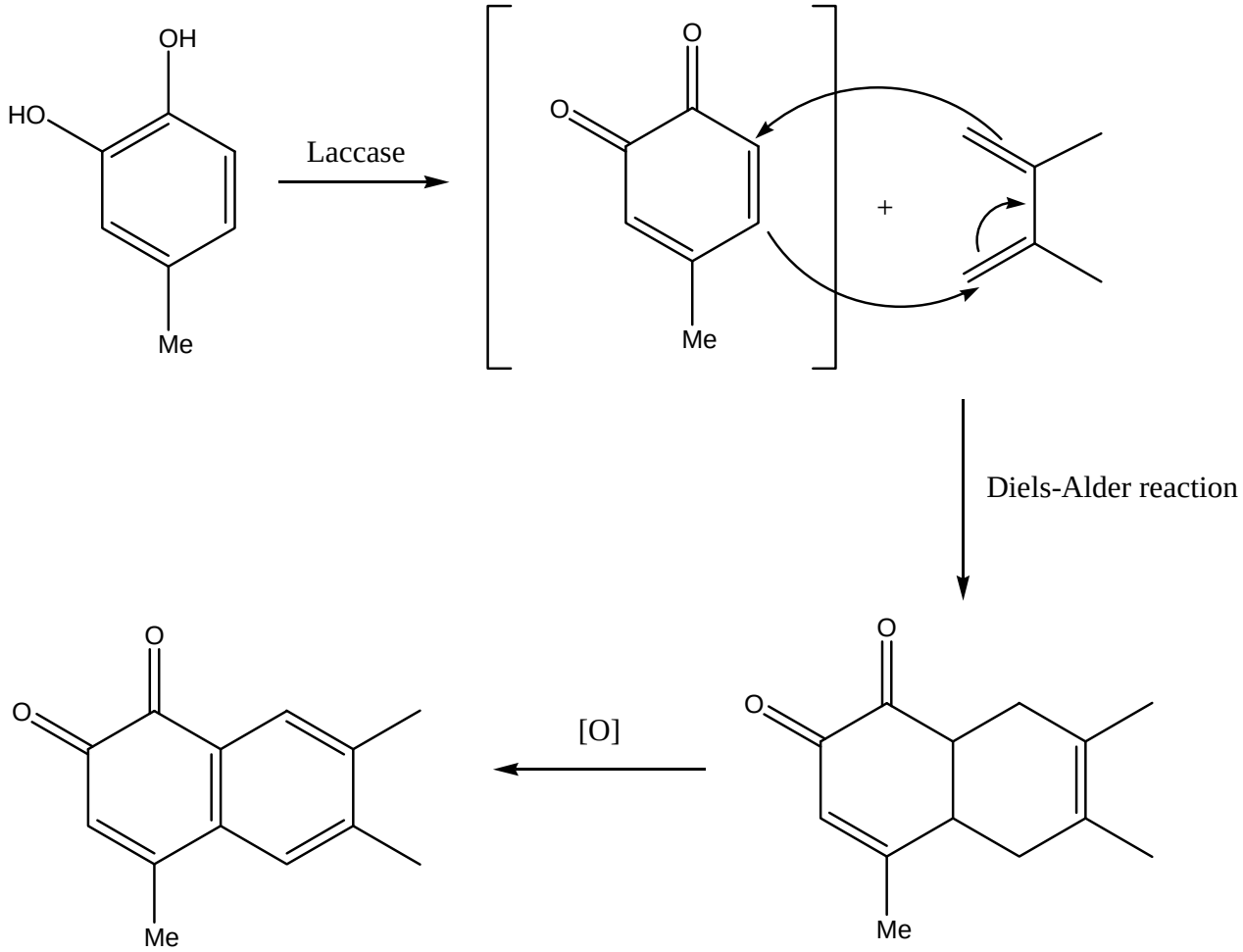


Table 1: reaction of 4-methylcatechol with a variety of dienes

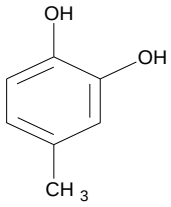
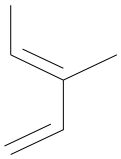
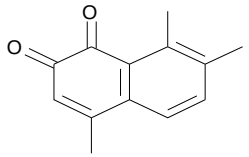
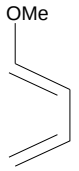
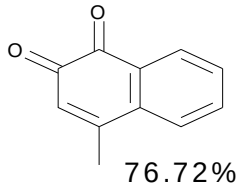
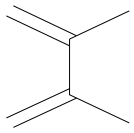
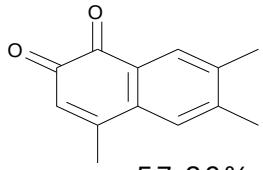
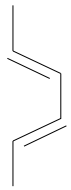
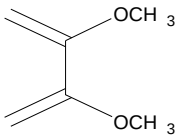
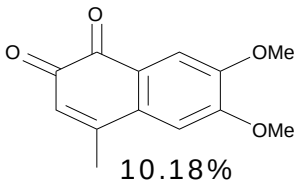
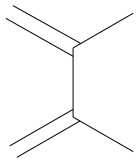
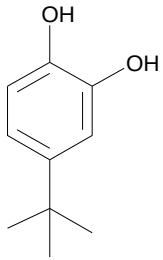
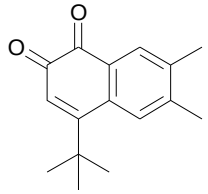
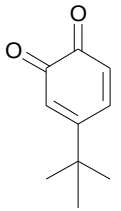
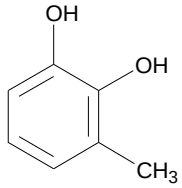
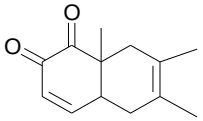
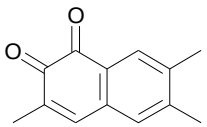
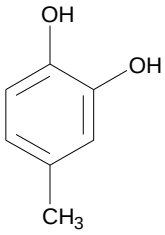
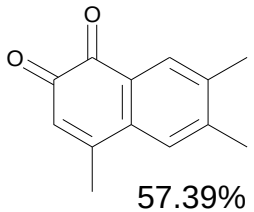
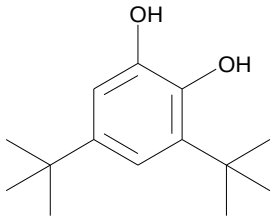
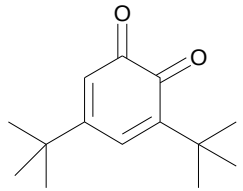
catechol	diene	temperature (^{o}C)	time (hours)	ratio	%yield
		ice—RT	24	1:10	 33.48%
		ice—RT	24	1:10	 76.72%
		ice—RT	24	1:10	 57.39%
		ice—RT	24	1:10	No product formed
		ice—RT	24	1:10	 10.18%

Table 2: reaction of 2,3-dimethyl-1,2-butadiene with a variety of dienophiles

diene	catechol	temperature (^{o}C)	time (hrs)	ratio	%yield
		**A** ice→RT **B** ice→RT	24 96	1:10 1:15	 **A** 6.86% **B** 13.73  **A** 47.73% **B** 15.10
	ice→RT	5	1:10	 6.57%  10.05%
	ice→RT	24	1:10	 57.39%
	ice→RT	24	1:10	 97% only quinone no product formation

Conclusion

- This method is effective in the synthesis of *o*-napthoquinones
- The use of the enzyme laccase as an oxidizing agent and water solvent is both safe and environment-friendly
- The percent yield of the reaction depends on multiple factors

Acknowledgements

And

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My mentor Suteera Witayakran

And to all REU Supervisors