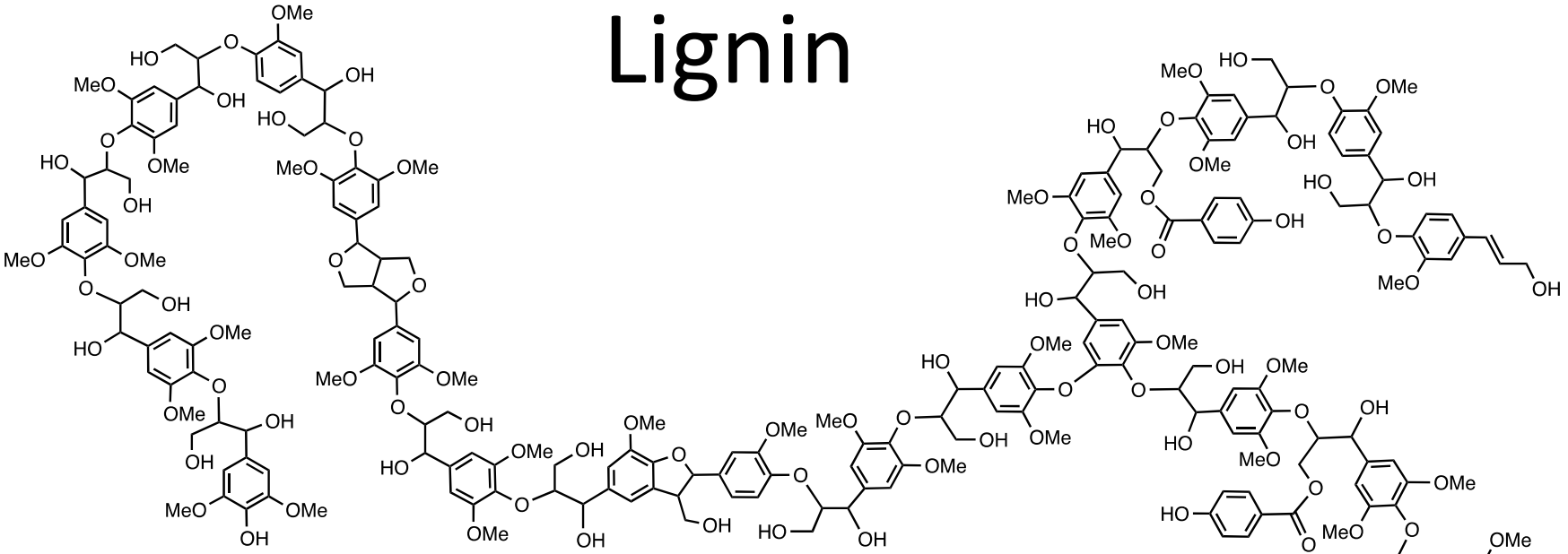
Design of novel nitrogenous base-tethered Co-Schiff base complexes for the selective catalytic cleavage of lignin

Rebecca E. Key and Joseph J. Bozell
Center for Renewable Carbon
The University of Tennessee
November 10, 2016

Lignin



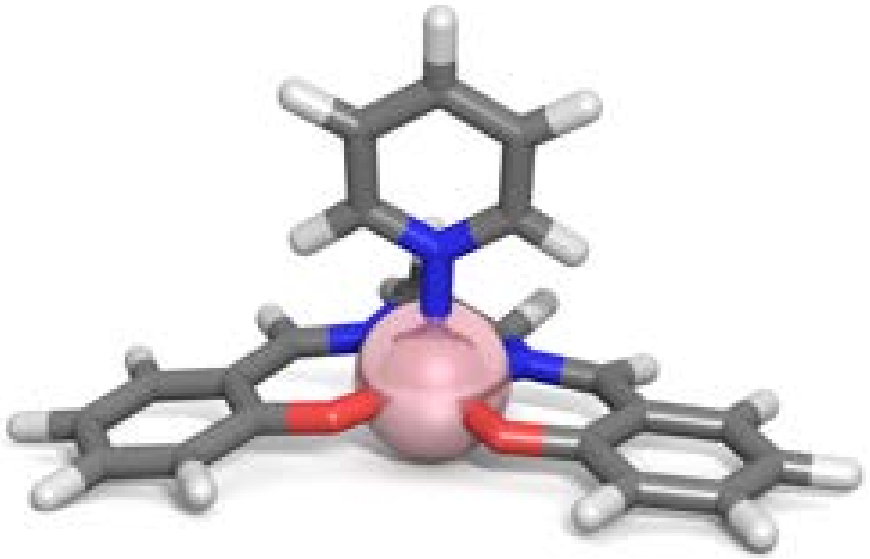
Example of native poplar lignin

- Second most abundant renewable carbon source after cellulose
  - Comprises up to 25% of biomass
- Biorefining processes for isolating lignin introduce drastic changes into the native structure
  - Increase in the number of free phenolic groups

Vanholme, R.; Demedts, B.; Morreel, K.; Ralph, J.; Boerjan, W. *Plant Physiol.* **2010**, *153*, 895.
Bozell, J. J. *Top Curr Chem* **2014**, *353*, 229.
Robert, D. R.; Bardet, M.; Gellerstedt, G.; Lindfors, E. L. *J. Wood Chem. Technol.* **1984**, *4*, 239.

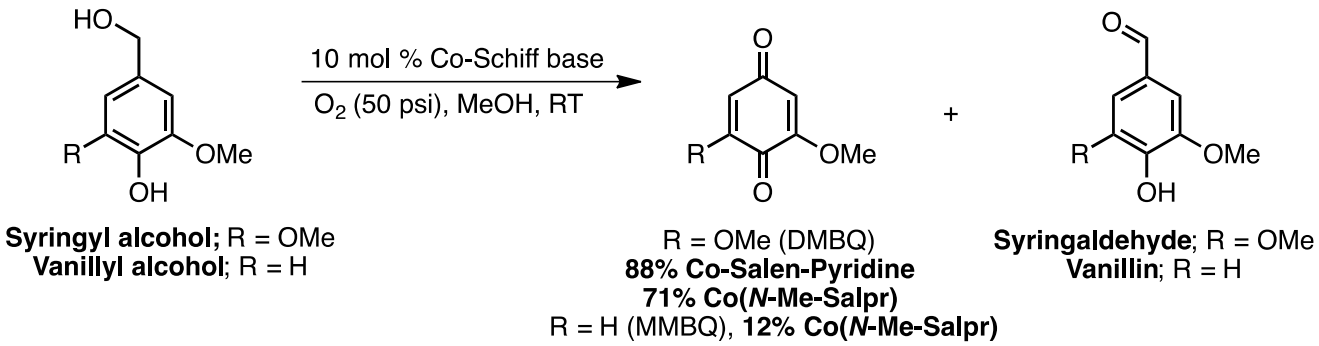
Catalysis of phenolic reactions

- Substituted aromatics in lignin are electron-rich
- Susceptible to phenolic oxidation
- Catalysts that target lignin-like phenol oxidation would be a viable approach for determining applicability of lignin as a chemical feedstock
- Co-Schiff bases catalyze phenolic oxidation under aerobic conditions.



Biannic, B.; Bozell, J. J.; Elder, T. *Green Chem.* **2014**, *16*, 3635.
Zombeck, A.; Drago, R. S.; Corden, B. B.; Gaul, J. H. *J. Am. Chem. Soc.* **1981**, *103*, 7580.
Co-salen-pyridine complex designed by Peter Ciesielski, NREL

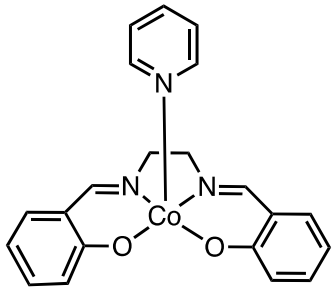
Co-Schiff base catalysis: previous work



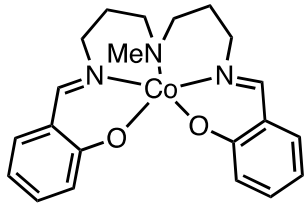
Syringyl alcohol; R = OMe
Vanillyl alcohol; R = H

R = OMe (DMBQ)
88% Co-Salen-Pyridine
71% Co(*N*-Me-Salpr)
R = H (MMBQ), **12% Co(*N*-Me-Salpr)**

Syringaldehyde; R = OMe
Vanillin; R = H



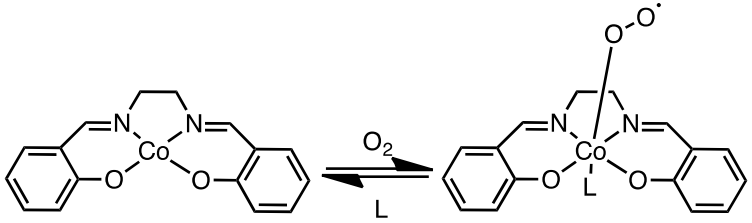
Co-Salen-Pyridine

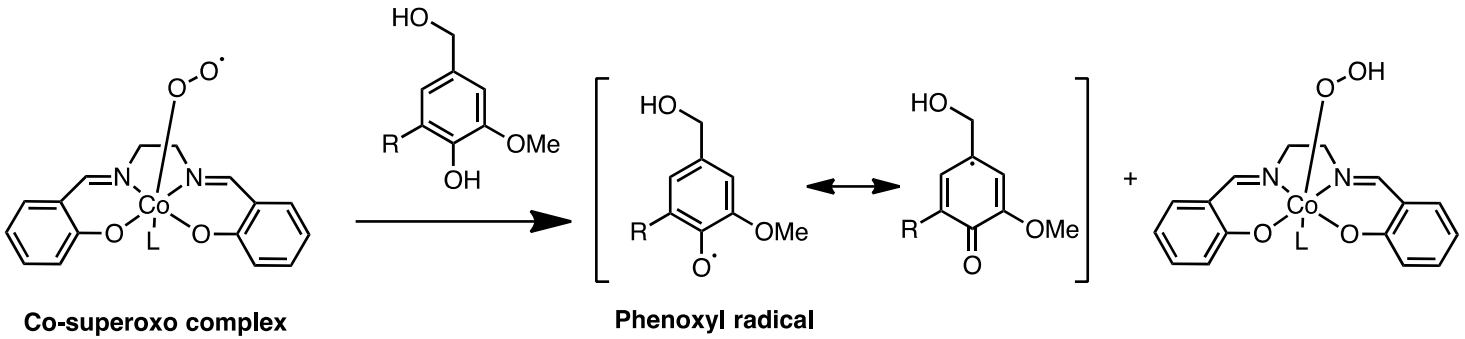


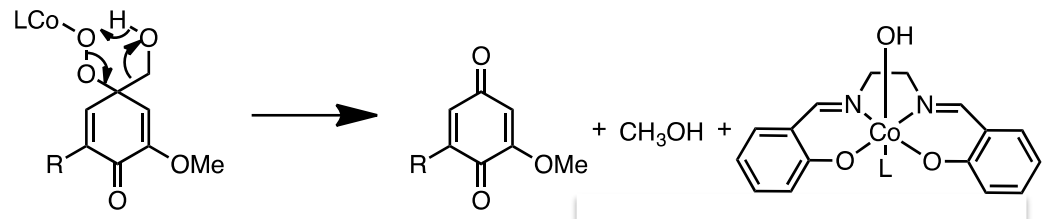
Co(*N*-Me-Salpr)

Bozell, J. J.; Hanes, B. R.; Dimmel, D. R. *J. Org. Chem.* **1995**, *60*, 2398.

Mechanism for Co-Schiff-base-catalyzed phenolic oxidation

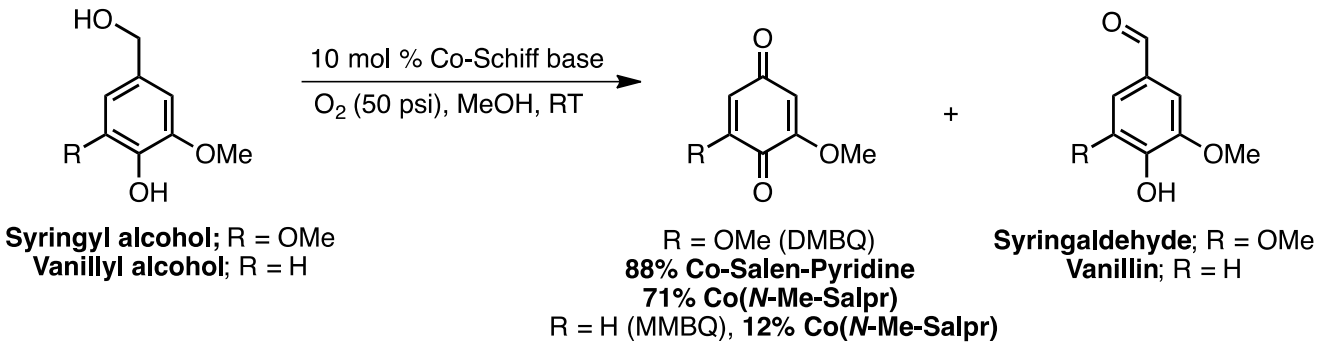






Bozell, J. J.; Hanes, B. R.; Dimmel, D. R. *J. Org. Chem.* **1995**, *60*, 2398.
Nishinaga, A.; Tomita, H. *J. Mol. Catal.* **1980**, *7*, 179.
Zombeck, A.; Drago, R. S.; Corden, B. B.; Baul, J. H. *J. Am. Chem. Soc.* **1981**, *103*, 7580.
Corden, B. B.; Drago, R. S.; Perito, R. P. *J. Am. Chem. Soc.* **1985**, *107*, 2903.

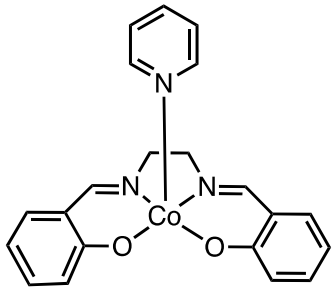
Co-Schiff base catalysis: previous work



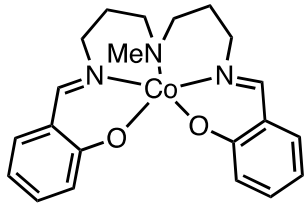
Syringyl alcohol; R = OMe
Vanillyl alcohol; R = H

R = OMe (DMBQ)
88% Co-Salen-Pyridine
71% Co(*N*-Me-Salpr)
R = H (MMBQ), **12% Co(*N*-Me-Salpr)**

Syringaldehyde; R = OMe
Vanillin; R = H



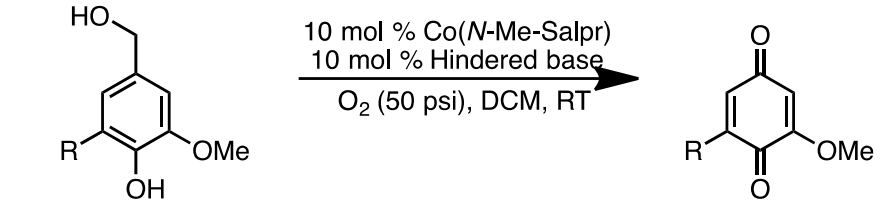
Co-Salen-Pyridine



Co(*N*-Me-Salpr)

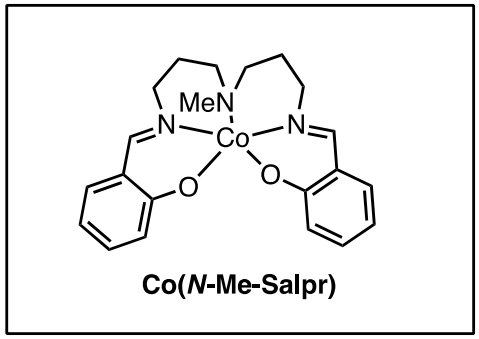
Bozell, J. J.; Hanes, B. R.; Dimmel, D. R. *J. Org. Chem.* **1995**, *60*, 2398.

Co-Schiff base catalysis: addition of a hindered base

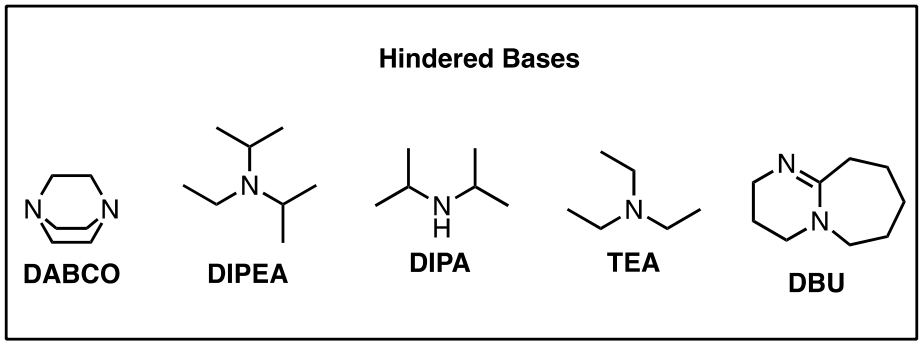


Vanillyl alcohol; R = H

R = H (MMBQ)



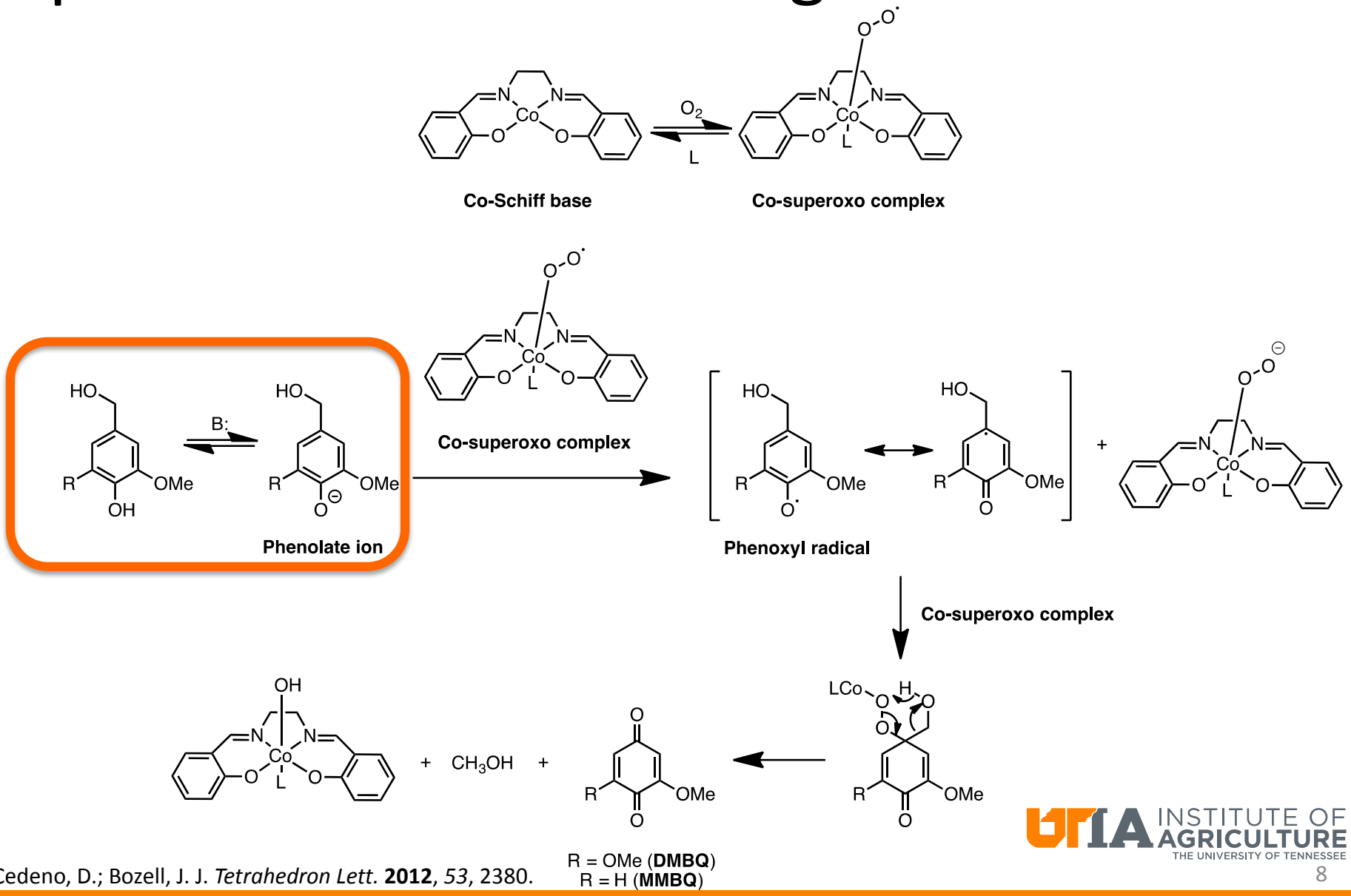
Co(*N*-Me-Salpr)



Hindered Base	Conjugate Acid pK_a	Yield MMBQ (%)
None	N/A	21
DABCO	8.19	21
DIPEA	10.98	55
DIPA	10.76	51
TEA	10.60	52
DBU	13.28	0

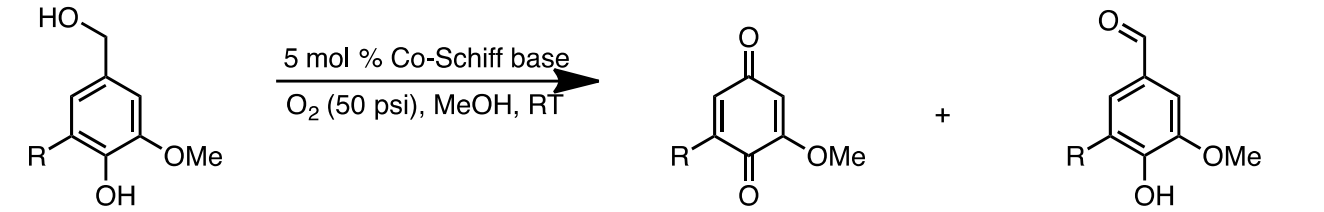
Cedeno, D.; Bozell, J. J. *Tetrahedron Lett.* **2012**, *53*, 2380.

Mechanism for Co-Schiff-base-catalyzed phenolic oxidation using a hindered base



Cedeno, D.; Bozell, J. J. *Tetrahedron Lett.* **2012**, *53*, 2380.

Second-generation Co-Schiff base catalysts

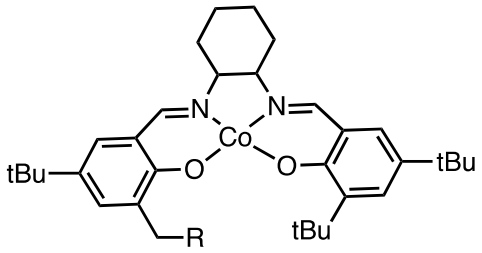


Syringyl Alcohol
R = OMe

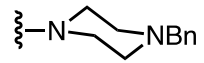
2,6-DMBQ; R = OMe

Syringaldehyde; R = OMe

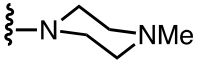
Cat.	Loading (mol %)	Reaction Time (h)	Yield 2,6-DMBQ (%)	Yield SyCHO (%)	SyOH Recovery (%)
1, NBn	**5**	**1**	**74**	**19**	**0**
2, NH	5	5	61	25	trace
3, NMe	5	16	54	0	40
4, NPh	5	2	65	22	trace
5, Pip	5	16	75	19	0



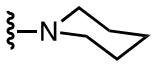
1-5

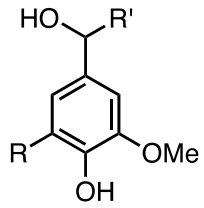
1: R = 

2: R = 

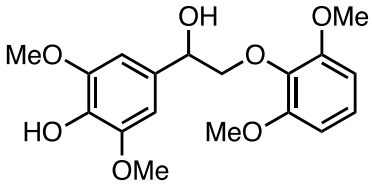
3: R = 

4: R = 

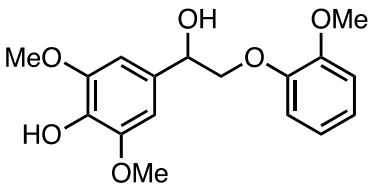
5: R = 



Vanillyl Alcohol
R = R' = H
83% MMBQ



***S,S*-Dimeric Model**
81% 2,6-DMBQ

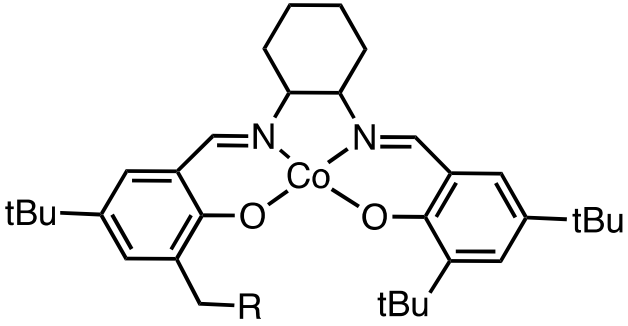


***S,G*-Dimeric Model**
86% 2,6-DMBQ

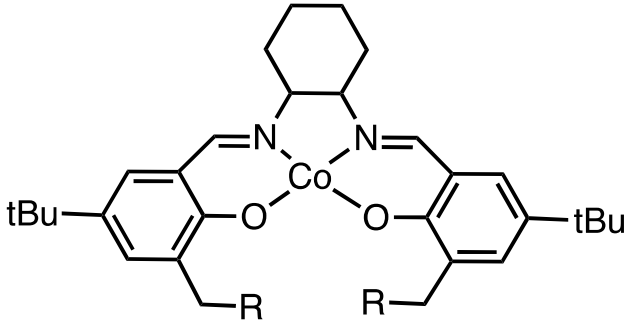
Biannic, B.; Bozell, J. J. *Org. Lett.* **2013**, *15,* 2730.

ALTERNATIVE NITROGENOUS COBALT-SCHIFF BASE CATALYSTS: EXPANDING THE SCOPE OF BULKY, NITROGENEOUS BASE SUBSTITUENTS

Arylpiperazine-tethered Co-Schiff base catalysts: expanding the scope



1-6



7-10

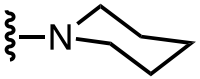
Previously Synthesized Catalysts

1,6: R = 

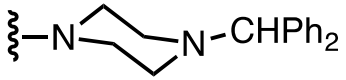
2: R = 

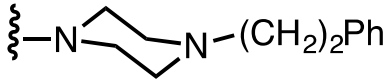
3: R = 

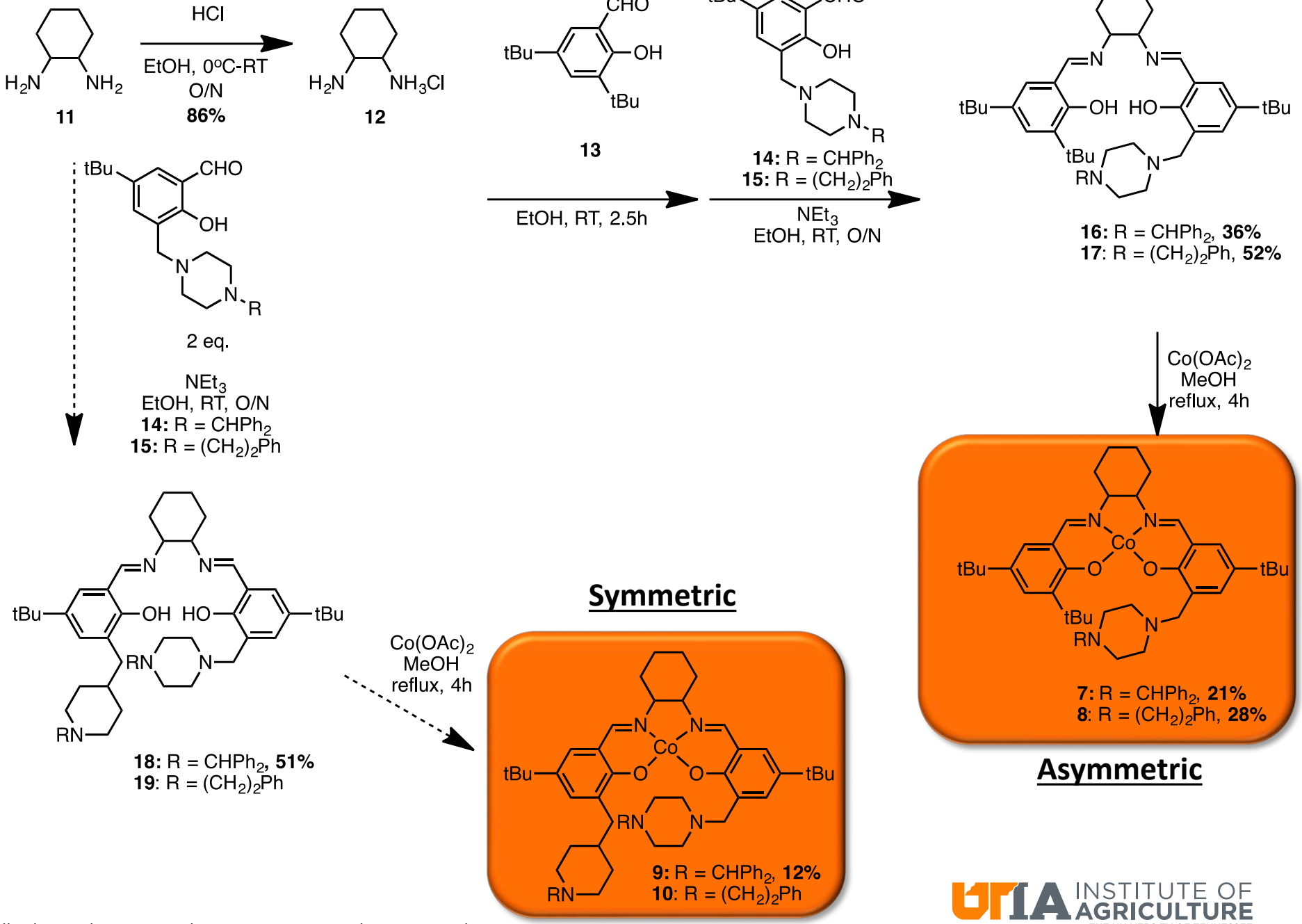
4: R = 

5: R = 

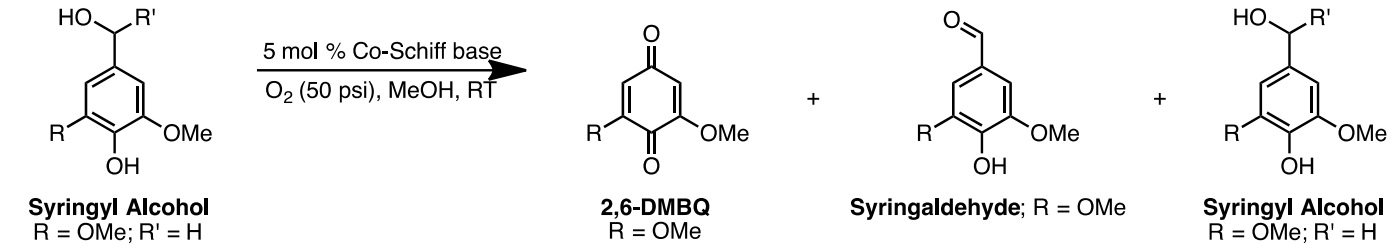
New Catalysts

7,9: R = 

8,10: R = 



Holbach, M.; Zheng, Z.; Burd, C.; Jones, C. W.; Weck, M. *J. Org. Chem.* **2006**, *71*, 2903.
Biannic, B.; Bozell, J. J. *Org. Lett.* **2013**, *15*, 2730.

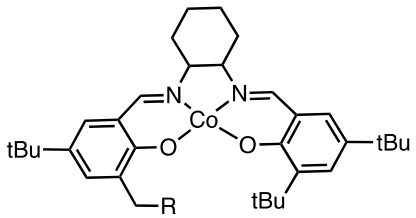


Syringyl Alcohol
R = OMe; R' = H

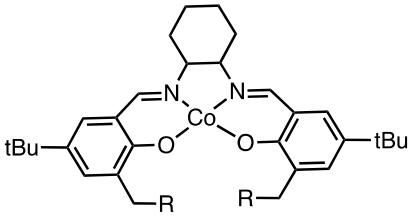
2,6-DMBQ
R = OMe

Syringaldehyde; R = OMe

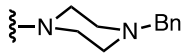
Syringyl Alcohol
R = OMe; R' = H



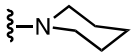
1, 4-5, 7-8

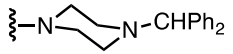


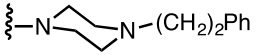
6, 9-10

1,6: R = 

4: R = 

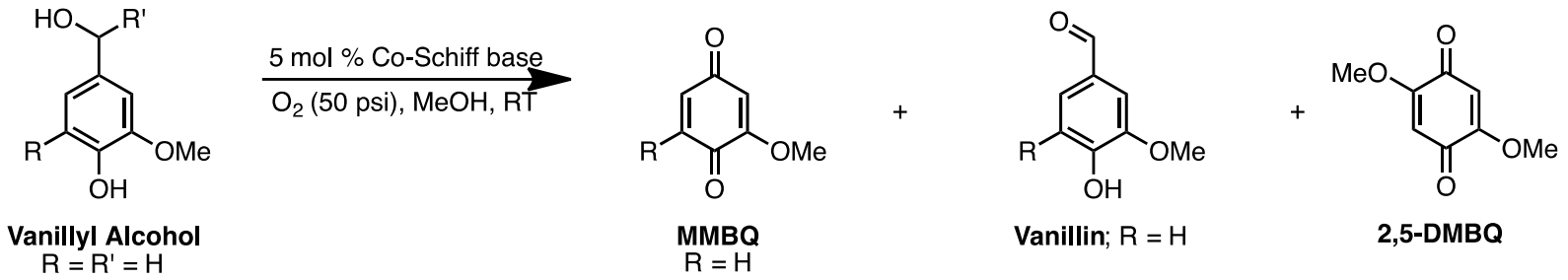
5: R = 

7,9: R = 

8, 10: R = 

Catalyst.	Time (h)	2,6-DMBQ (%)	SyCHO (%)	SyOH (%)
1*, *asymm*-NBn	1	74	19	
1, *asymm*-NBn	18	71	4	-
4*, *asymm*-NPh	2	65	22	
5*, *asymm*-Piperidine	16	75	19	
6, *symm*-Bn	21.5	76	11	-
7-*asymm*-diPhMe	18	74	9	-
8, *asymm*-Phenethyl	18	65	9	-
10, *symm*-diPhMe	18	67	9	-

*Biannic, B.; Bozell, J. J. *Org. Lett.* **2013**, *15,* 2730.

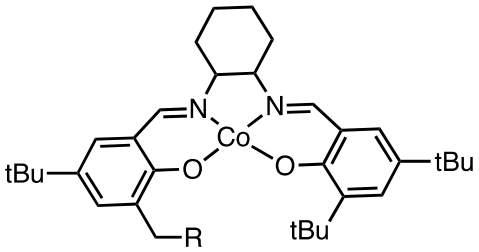


Vanillyl Alcohol
R = R' = H

MMBQ
R = H

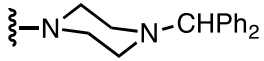
Vanillin; R = H

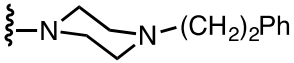
2,5-DMBQ



1, 7-8

1: R = 

7: R = 

8: R = 

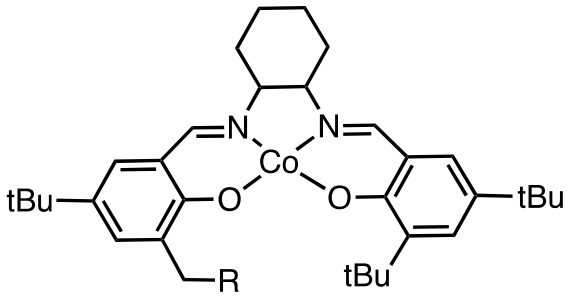
Catalyst	Time (h)	MMBQ (%)	2,5-DMBQ (%)	Vanillin (%)	VaOH (%)
1*, *asymm*-NBn	16	83	NR	NR	NR
7-*asymm*-diPhMe	18	34	5	-	21
8, *asymm*-Phenethyl	17 (DCM)	38	-	-	33

*Biannic, B.; Bozell, J. J. *Org. Lett.* **2013**, *15,* 2730.

INSTITUTE OF AGRICULTURE
THE UNIVERSITY OF TENNESSEE

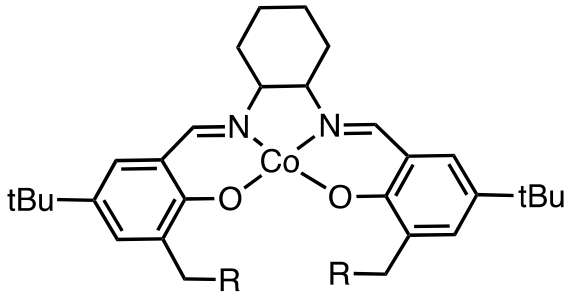
Summary: Ar-piperazine-tethered-Co-salen-catalyzed S and G unit oxidations

- S Models
  - Catalysts **7-9**: **Comparable yield of 2,6-DMBQ** relative to lead catalyst **1**
  - Catalyst **10**: Activity TBD



1, 7-8

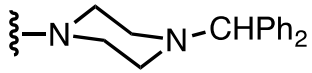
- G Models
  - Catalysts **7-8**: **Low yield of MMBQ** relative to lead catalyst **1**
  - Catalyst **6, 9-10**: Activity TBD
  - Are increases in side chain bulk altering the steric environment between the catalytically active species and substrate?
    - **Computational analyses: TBD**



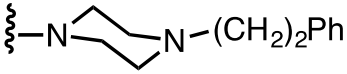
6, 9-10

1, 6: R =

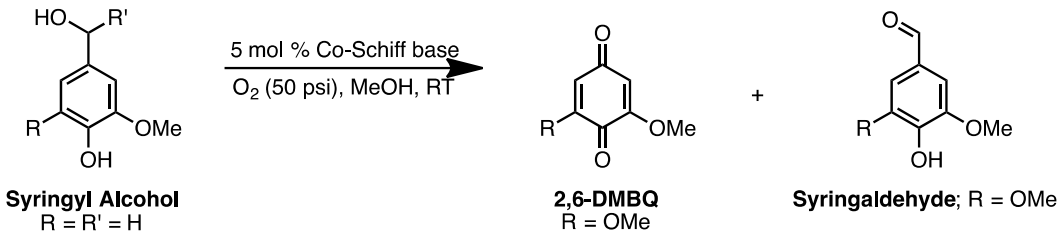
7, 9: R =



8, 10: R =



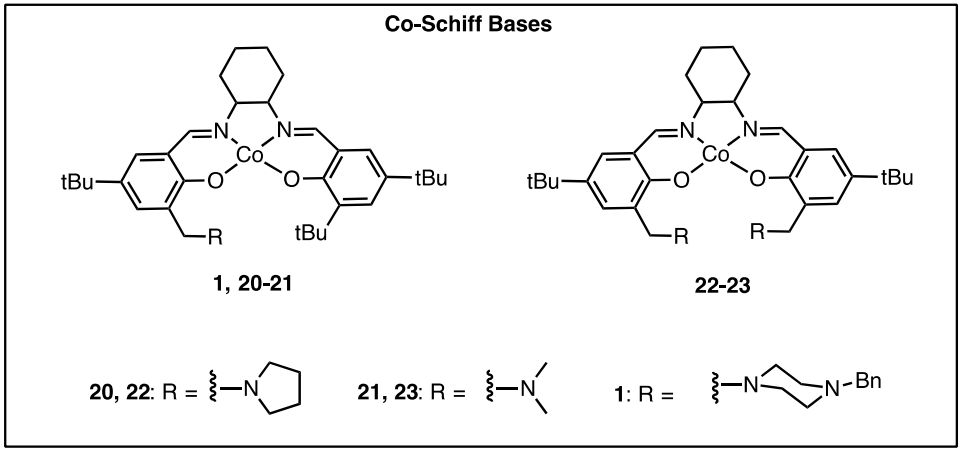
INSTITUTE OF AGRICULTURE
THE UNIVERSITY OF TENNESSEE



Syringyl Alcohol
R = R' = H

2,6-DMBQ
R = OMe

Syringaldehyde; R = OMe

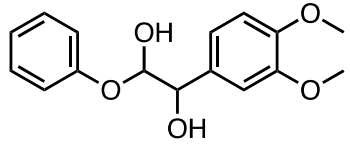


Catalyst	Time (h)	2,6-DMBQ (%)	SyCHO (%)	SyOH (%)
20, *asymm*-Pyrrolidine	18.5	19	49	-
21, *asymm*-Dimethylamine	18.5	47	20	-
1, *asymm*-NBn	**18**	**71**	**4**	**-**
22, *symm*-Pyrrolidine	18.5	24	26	21
23, *symm*-Dimethylamine	18	48	11	-

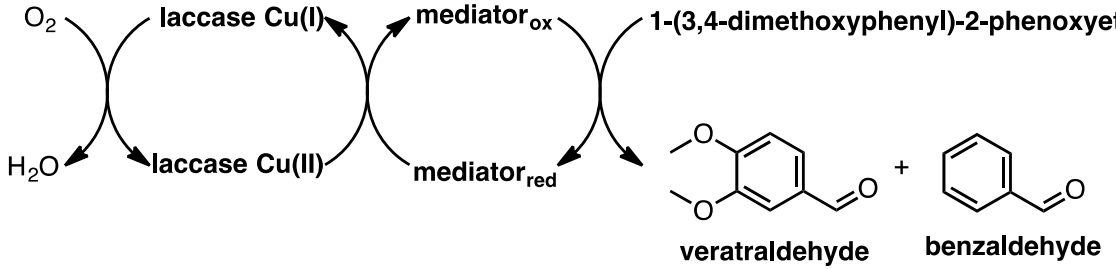
COPPER-SCHIFF BASE CATALYSIS

Laccase

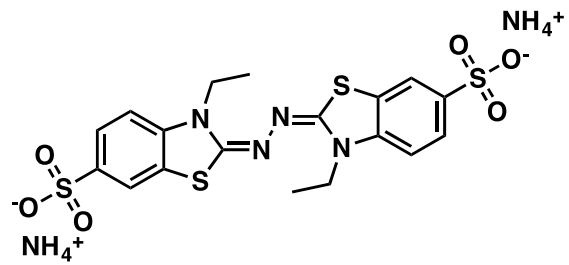
- Cu-containing oxidase
  - Deconstructs lignin and lignin models



1-(3,4-dimethoxyphenyl)-2-phenoxyethane-1,2-diol



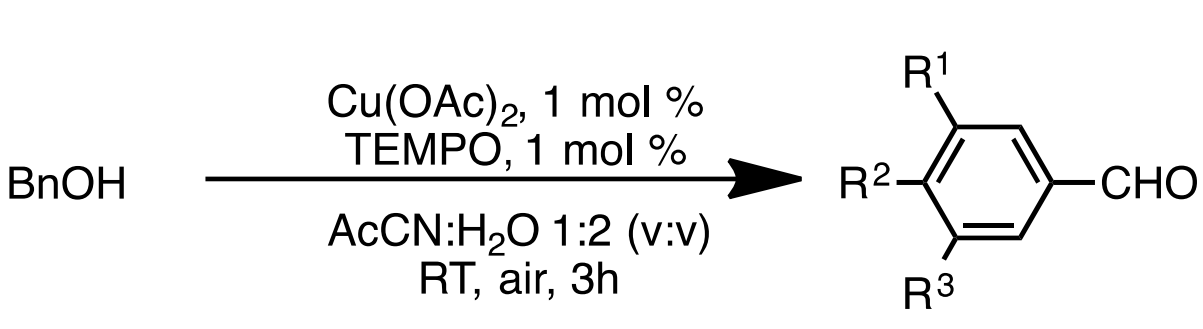
veratraldehyde benzaldehyde

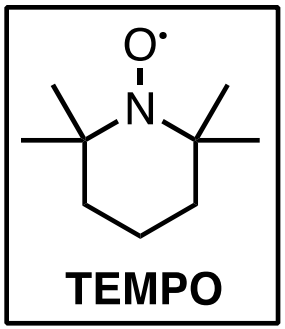


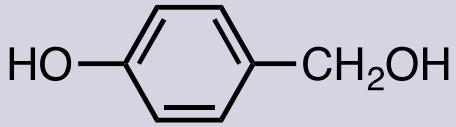
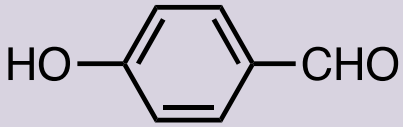
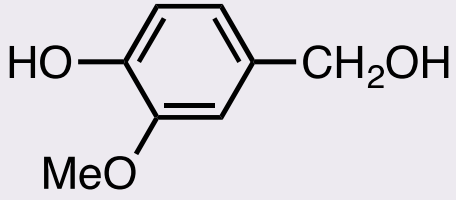
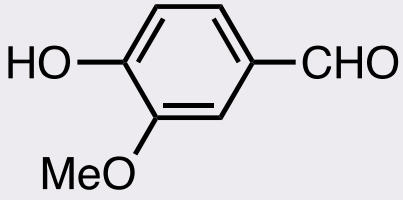
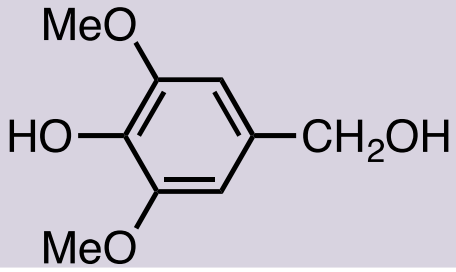
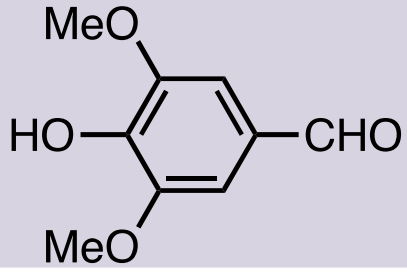
Mediator: Diammonium 2,2,Ä≤-azino-bis(3-ethylbenzothiazoline-6-sulfonate) (ABTS)

Tadesse, M. A.; D'Aggibale, A. D.; Galli, C.; Gentili, P.; Sergi, F. *Org. Biomol. Chem.* **2008**, *6*, 868.
Morozova, O. V.; Shumakovich, G. P.; Schleev, S. V.; Yaropolov, Y. I. *Appl. Biochem. Microbiol.* **2007**, *43*, 523.

Cu Catalysts: Benzyl Alcohol Oxidation

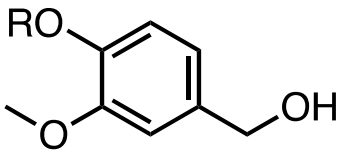




BnOH	Aldehyde	Yield (%)
		88
		90
		90

Jiang, J.-A.; Du, J.-L.; Wang, Z.-G.; Zhang, Z.-N.; Xu, X.; Zheng, G.-L.; Yi, Y-F. *Tetrahedron Lett.* **2014**, *55*, 1677.

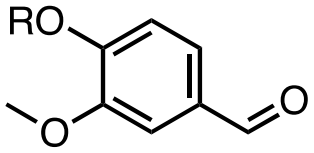
Water-Soluble Metallo-Schiff Bases



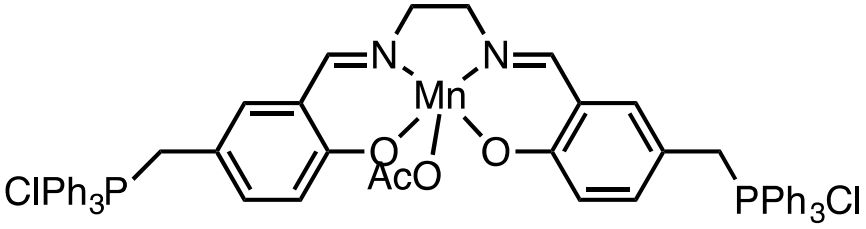
Vanillyl Alcohol, R = H
Veratryl Alcohol, R = Me

5 mol % Mn-Schiff Base

MeOH: Buffer (1:1), pH = 10
H_2O_2 (30% solution)
RT, O/N
70% yield



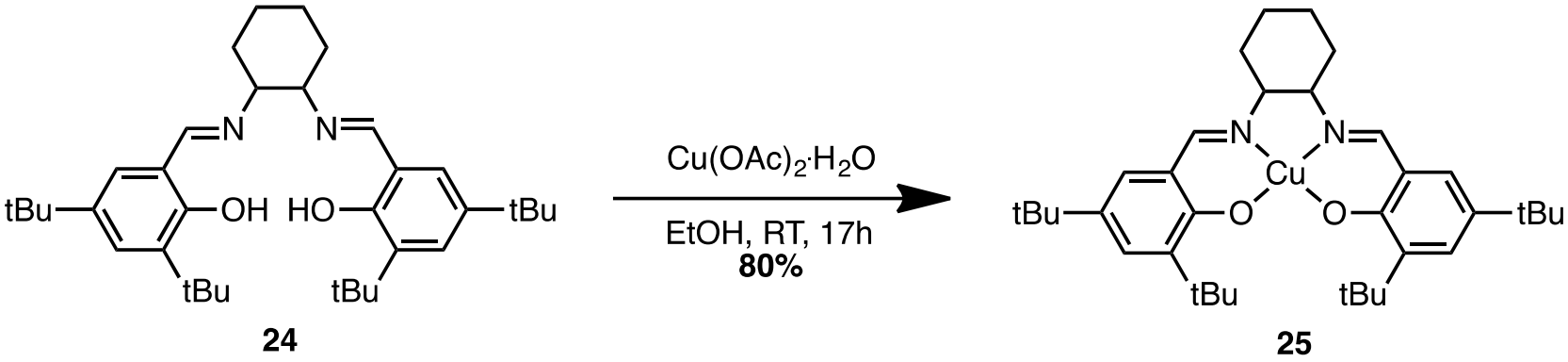
Vanillin, R = H
3,4-dimethoxybenzaldehyde, R = Me



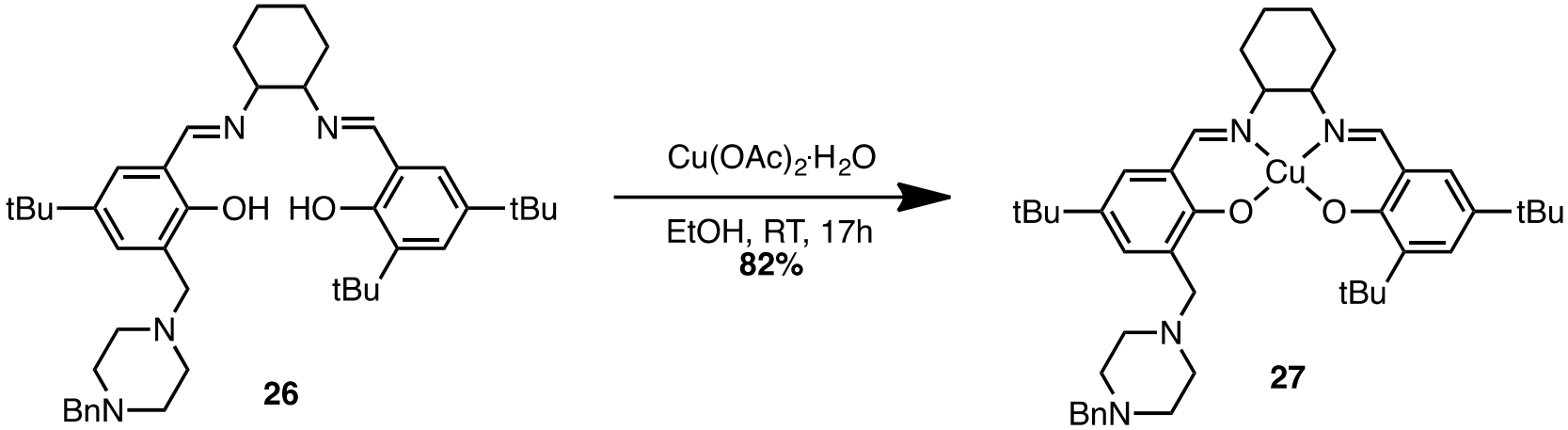
Mn-Schiff Base

Haikarainen, A.; Sipila, J.; Pietikainen, P.; Pajunen, A.; Mutikainen, I. *Bioorg. Med. Chem.* **2001**, *9*, 1633.

Cu-Schiff Base Catalysts

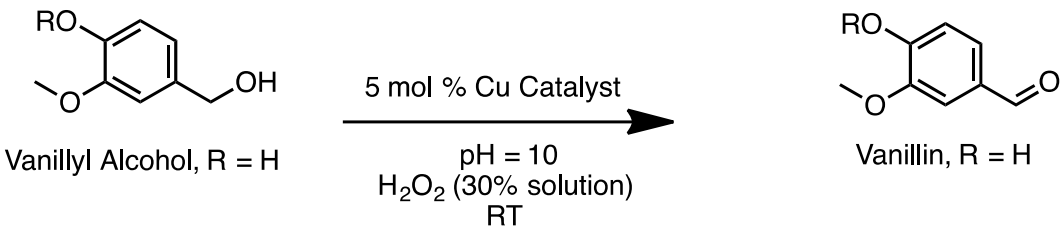


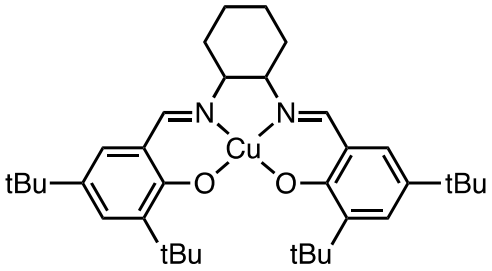
24 **25**



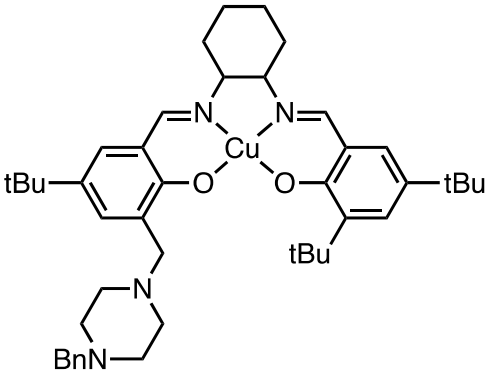
26 **27**

Kannan, M; Punniyamurthy, T.; *Tetrahedron: Asymmetry* **2014**, *125*, 1331.





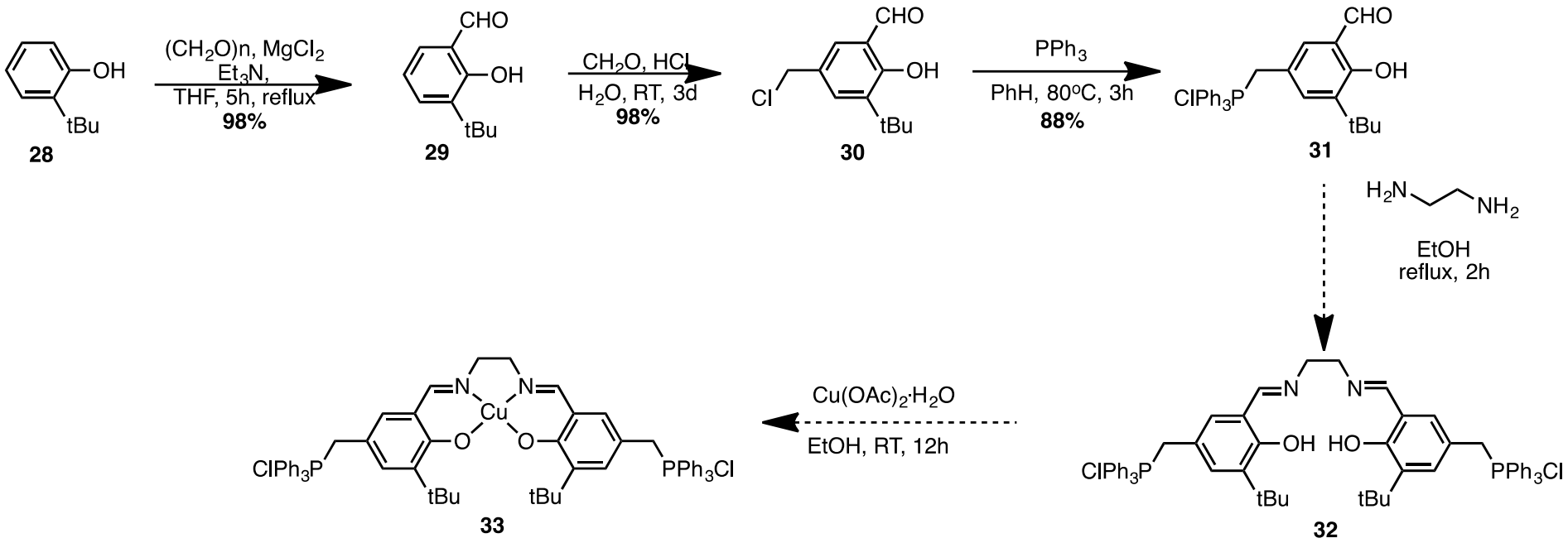
Cu-Salen
25



Bn-Piperazine-Tethered-Cu-Salen
27

Catalyst	Solvent	Time (h)	MMBQ (%)	2,5-DMBQ (%)	Vanillin (%)	VaOH (%)
Cu-Salen 25	MeOH: H_2O (1:1)	23	-	-	-	88
Cu-Salen 25	MeOH: DCM (1:1)	90	-	-	-	64
Cu-Salen 25	iPrOH	42	-	-	-	>99
Cu-Salen 25	DCM	18	-	-	3	20

Water-soluble Cu-Schiff base



WO2008/132474 A1

Haikarainen, A.; Sipilc, J.; Pietikainen, P.; Pajunen, A.; Mutikainen, I. *J. Chem. Soc. Dalton Trans.*, **2001**, 991.

Minutolo, F.; Pini, D>; Petri, A.; Salvadori, P. *Tetrahedron: Asymmetry*, **1996**, *7*, 2293.

Overall summary of studies

- Activity regarding phenolic oxidation of lignin models is being examined
- Synthesis and characterization of homogeneous (symmetric and asymmetric) metallo-Schiff base catalysts are ongoing
- Active catalysts will be tested for ability to deconstruct lignin
- Expand the library of nitrogeneous base-tethered Co-Schiff base and novel metallo-Schiff base catalysts for phenolic oxidation
  - New methodology for the conversion of biorefinery lignin
    - Streamline biorefinery operation
    - Offer new catalytic routes to biobased chemicals and fuels from renewable carbon sources

Acknowledgements

- Professor Joseph Bozell
- Bozell Group
- UT Biological and Small Molecule Mass Spectrometry Core (BSMMC)
- Center for Direct Catalytic Conversion of Biomass to Biofuels (C3Bio)
  - Director: Professor Maureen McCann, Purdue University
  - DOE, Basic Energy Sciences
    - DE-SC0000997

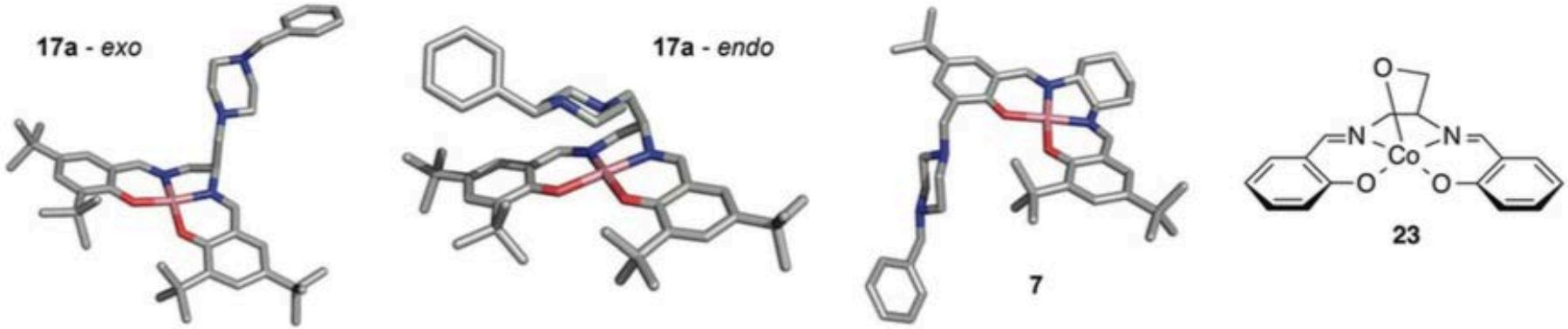


Fig. 3 Low energy conformations of complexes **17a** (*exo* and *endo*) and **7** (hydrogens omitted for clarity).

Biannic, B.; Bozell, J. J.; Elder, T. *Green Chem.* **2014**, *16*, 3635.