Valorization of Lignin

M2 Watanabe

11/30/2017

1. Introduction
2. Chemical degradation
    2-1. aryl C-O bond cleaverage of lignin
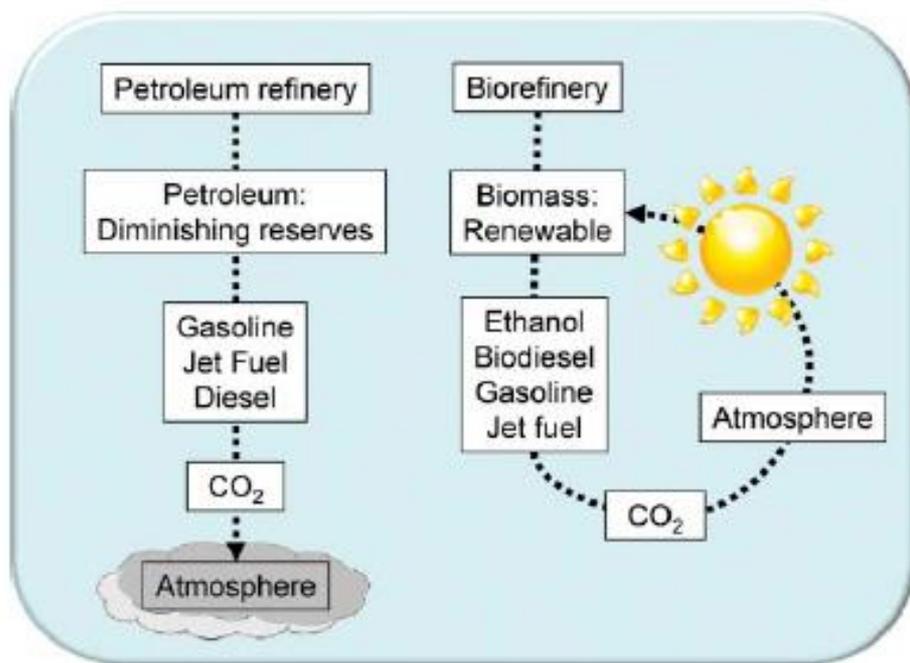   →Hartwig' work
    2-2.   alkyl C-O bond cleaverage of lignin
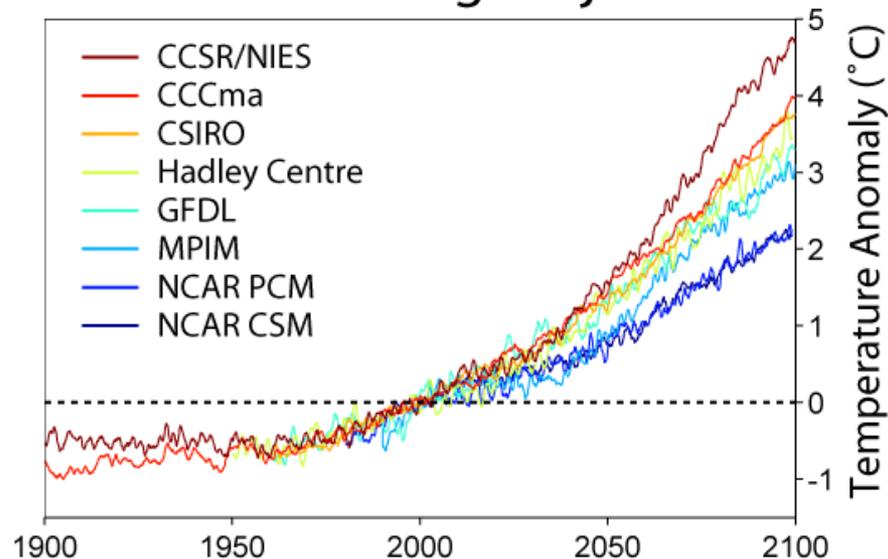3. Problem of lignin separation

Introduction 1

- **Petroleum supplies are finite.**
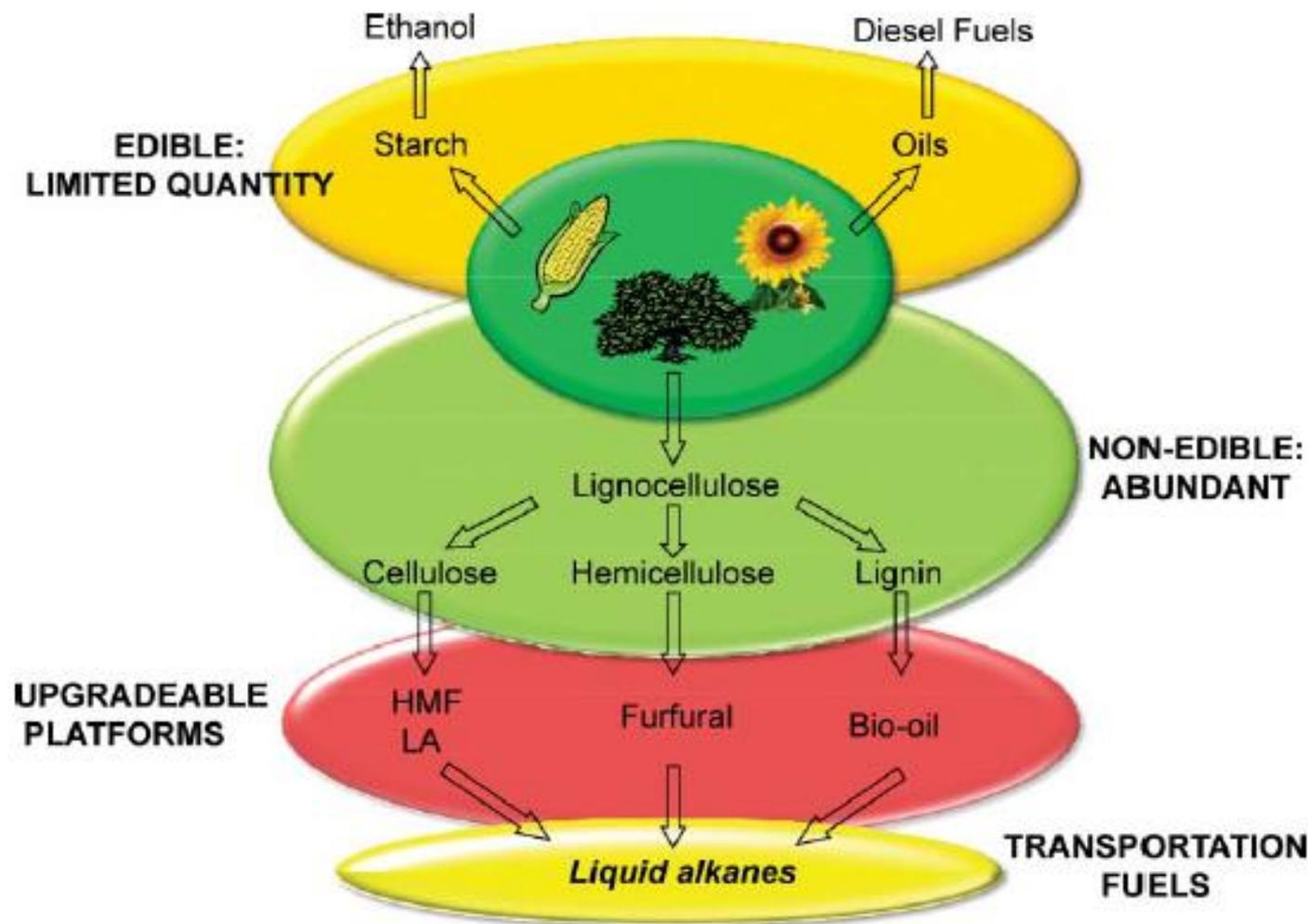- **utilization of biomass mitigates the release of greenhouse gas emissions.**

CO_2 cycles for petroleum- and biomass-derived fuels.
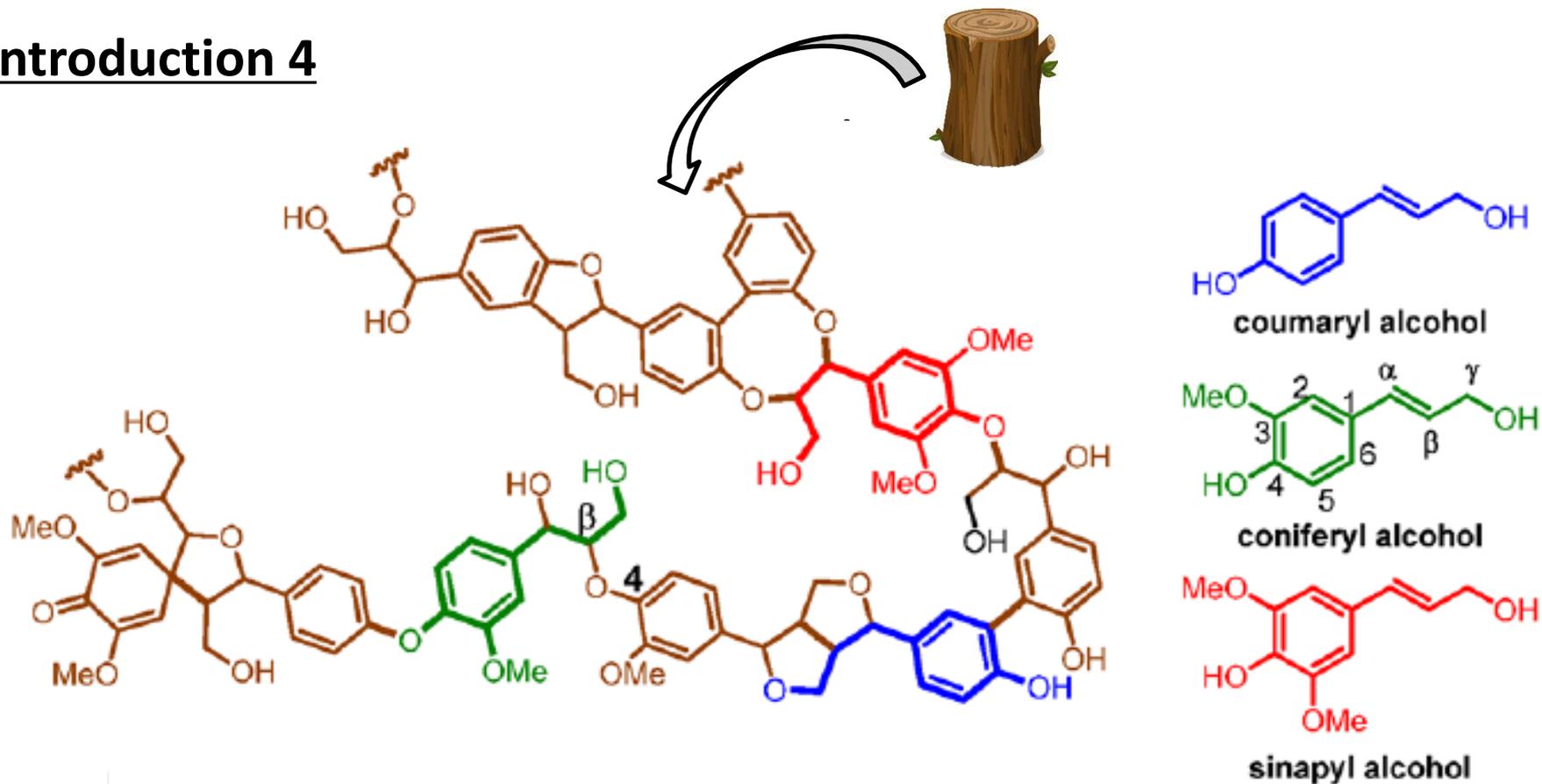

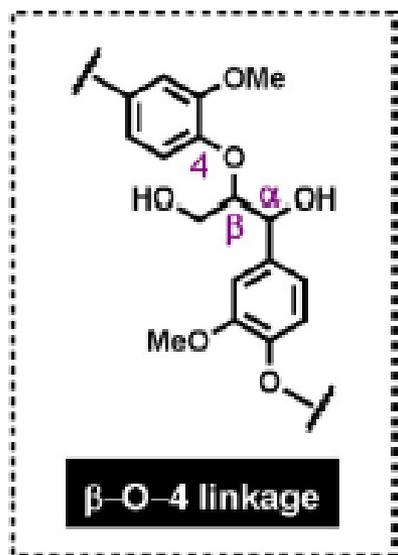（https://ja.wikipedia.org/wiki/地球温暖化）

Introduction 2

- **Lignin utilization is to burn it directly for the production of heat and electricity.**

Introduction 4

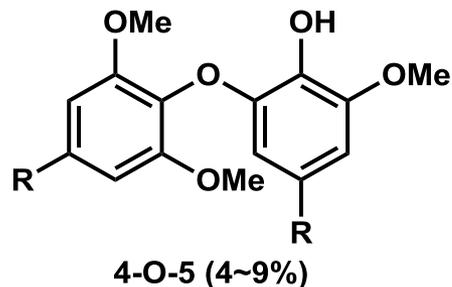- 50% of its components are aromatic hydrocarbons which can be a potentially attractive source of fuels and chemicals
- Research on lignin deconstruction has recently become the center of interest.
- No selective C-O bond cleavage with hydrogen.

Fedorov, A.; Toutov, A. A.; Swisher, N. A.; Grubbs, R. H. *Chem. Sci.* **2013**, *4*, 1640

Strategy of chemical depolymerization

β–O–4 linkage

45-62%

4-O-5 (4~9%)
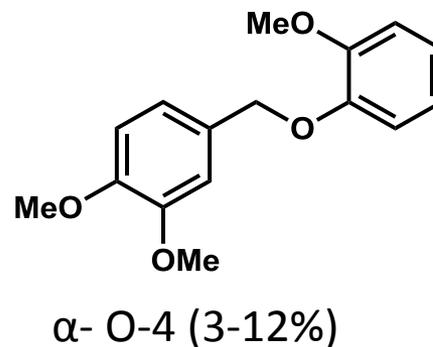
α- O-4 (3-12%)

- **β-O-4motif is the most prevent in native lignin**

aromatic C-O bond

aliphatic C-O bond
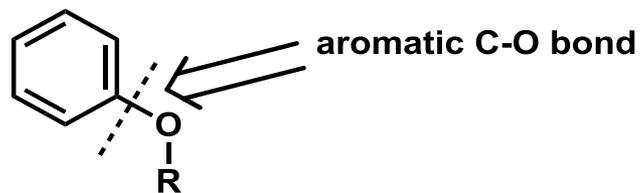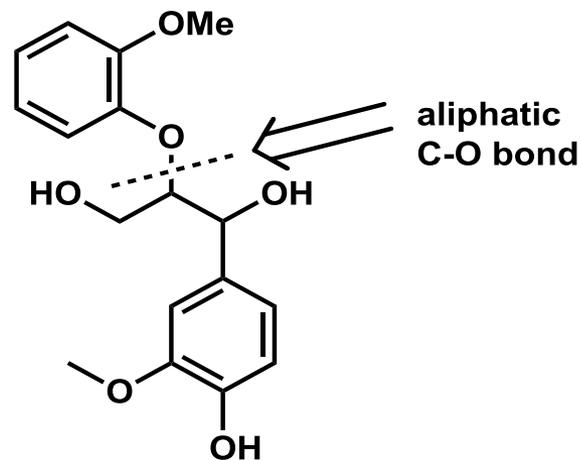
Strategy 1

Strategy 2

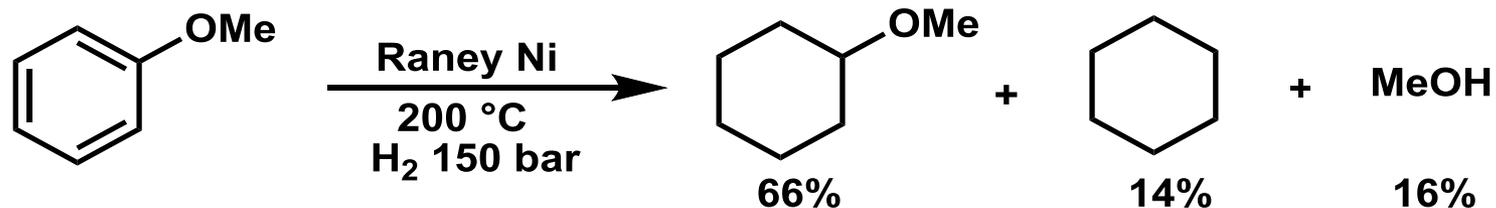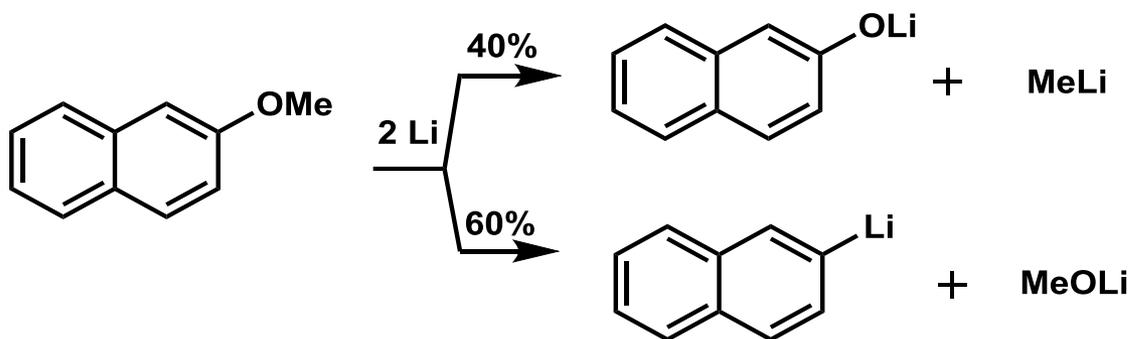# 2-1. aryl C-O bond cleaverage of lignin

→Hartwig' work

Difficulty of selective hydrogenolysis of aromatic C-O bond

E. M. Van Duzee, H. Adkins, *J. Am. Chem. Soc.* **57**, 147 (1935).

- **Cleavage of C-O bond need high temperature and occur with poor selectivity.**
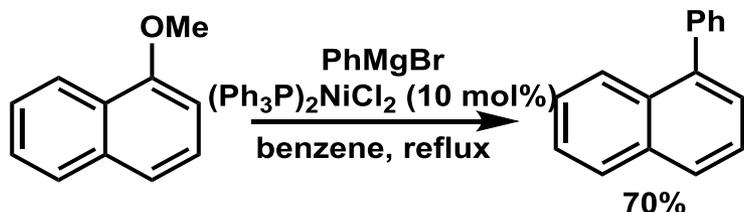

A. Maercker, *Angew. Chem. Int. Ed. Engl.* **26**, 972 (1987).

- **Expensive and difficult to conduct on a large scale.**
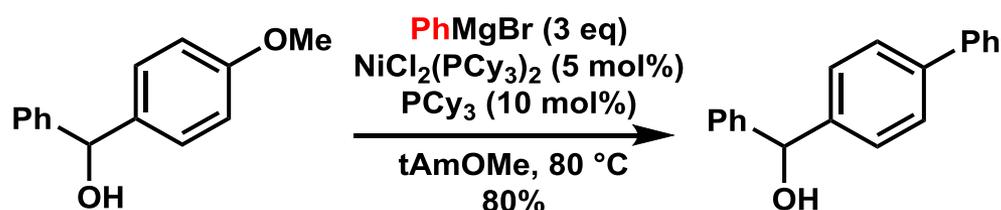
History of aryl C-O cleavage reaction

① **Wenkert's Pioneer work ~unprecedent OMe replacement~**

- Simple phenyl ethers afforded low yields .
- No reaction occurred with ortho substitution (strong steric effect).
- Alkyl Grignard with β-hydrogens.

Wenkert, E.; Michelotti, E. L.; Swindell, C. S. *J. Am. Chem. Soc.***1979**, *101*, 2246

② **Dankwardt extended the scope of this reaction.**

- Better σ donor was favorable.
- Non-π extended conjugation, phenols,
- Alcohols, amines, N-heterocycles

Dankwardt, J. W. *Angew. Chem., Int. Ed*. **2004**, 43, 2428

③ **Chatani and Tobisu extended the scope of ketone and ester.**
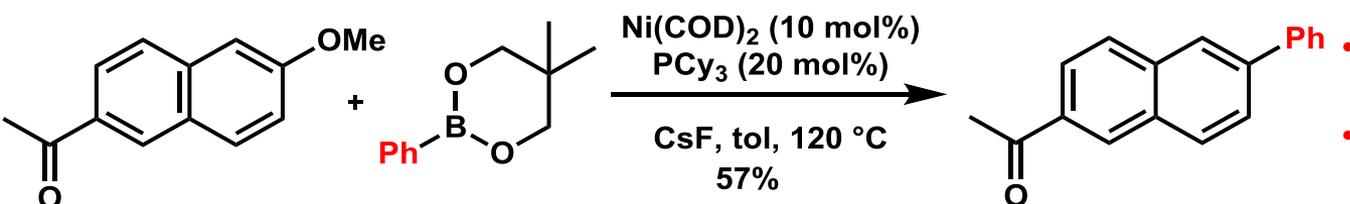
- Tolerance of functional group, such as ketones and esters.
- A base and bulky and electron-rich Phosphine ligand were essential.

Smiasaki, T.; Tobisu, M.; N. Chatani, N. *Angew. Chem. Int. Ed.* **2008**, *47*, 4866

First catalytic reductive cleavage of aryl C-O bond

82 %

78 %

76 %

74 %

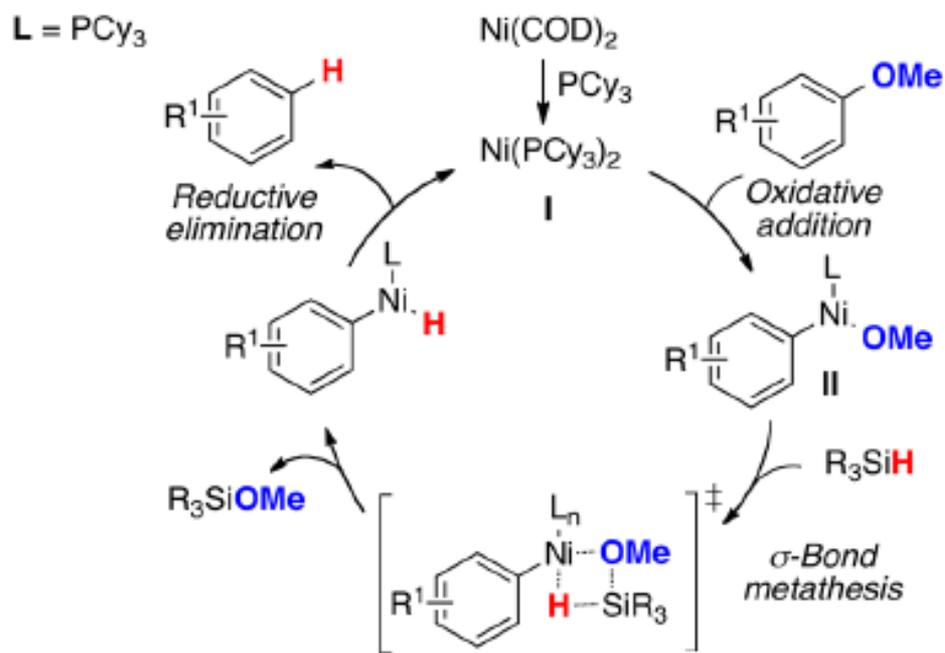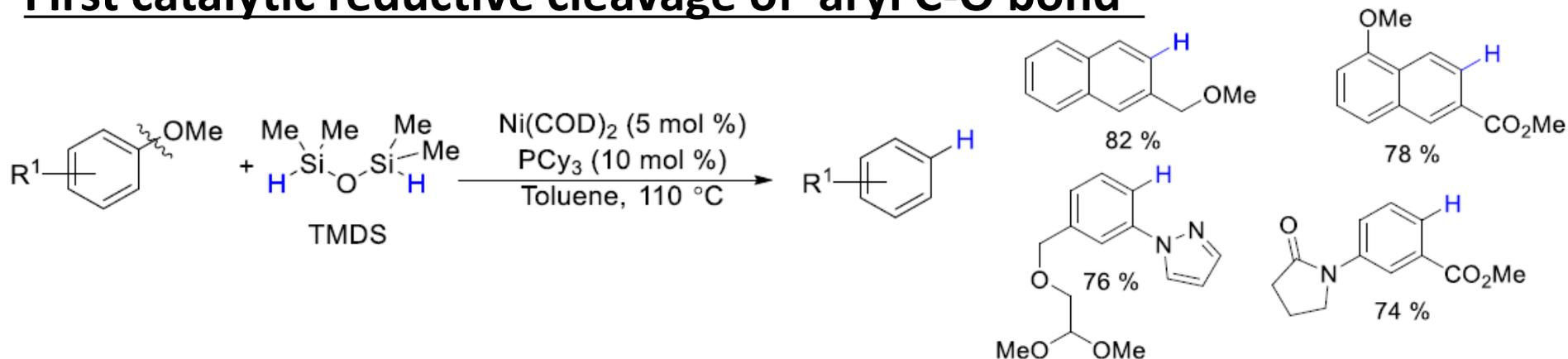

L = PCy$_3$

Reductive elimination

Oxidative addition

σ-Bond metathesis

< isotope labeling experiment>

94% (2a)   93% (2a-D)
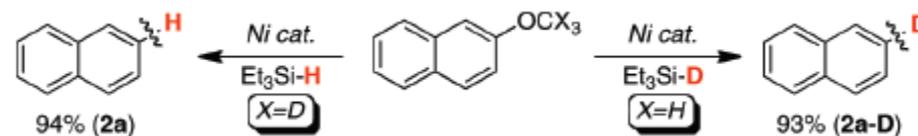
- **An alternative to alkali metal**
- **Ester, amide, acetal, tertiary amine, heterocycle could all be tolerated.**
- **Simple anisole needed ortho-directing group.**

Alvarez-Bercedo, P.; ;Martin, R. *J. Am. Chem. Soc.* **2010**, *132*, 17352

(traces, ~1%)

The yields were based on the amount of PCy$_3$, assuming that only one cyclohexyl group of the phosphine ligand is converted to the hydrocarbons.

44%   7%
products of the C-P bond cleavage in PCy$_3$
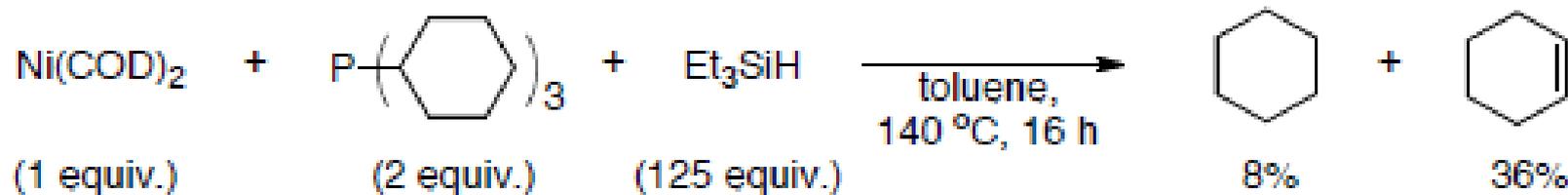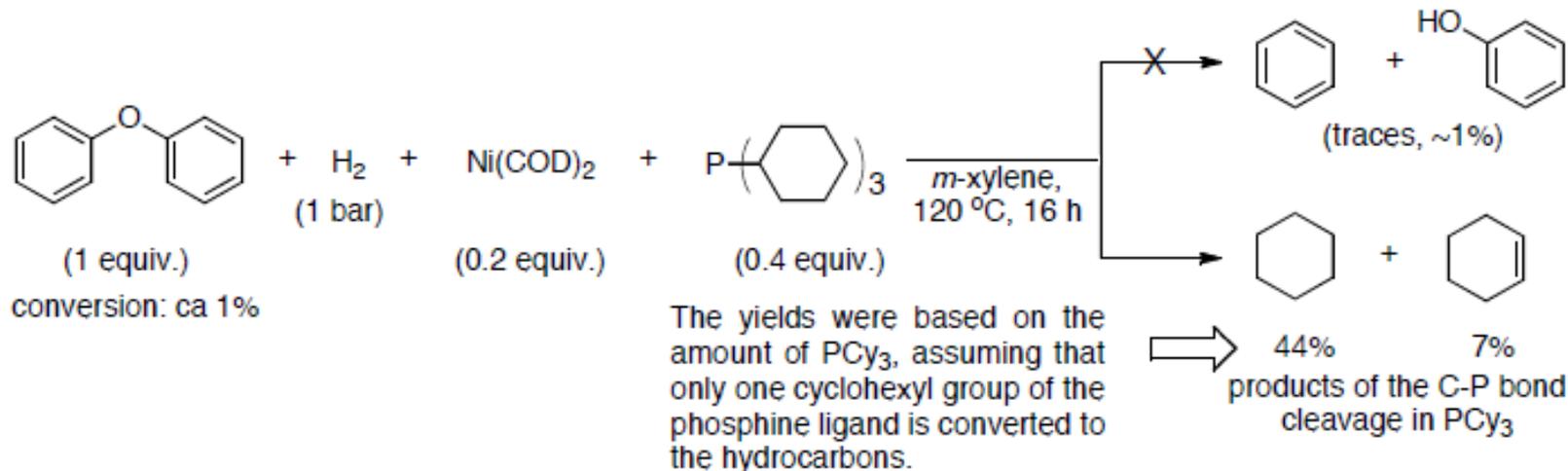
Harsh condition lead to reduction of catalyst itself.
More tight ligand was necessary.

Sergeev, A. G.; Hartwig, J. F. *Science* **2011**, 332, 439–443
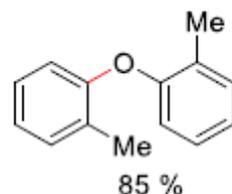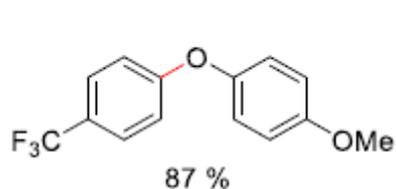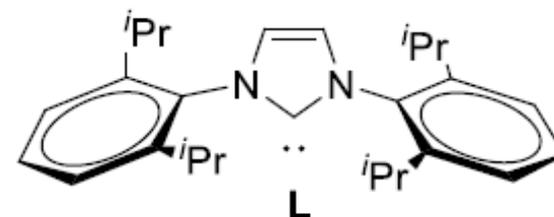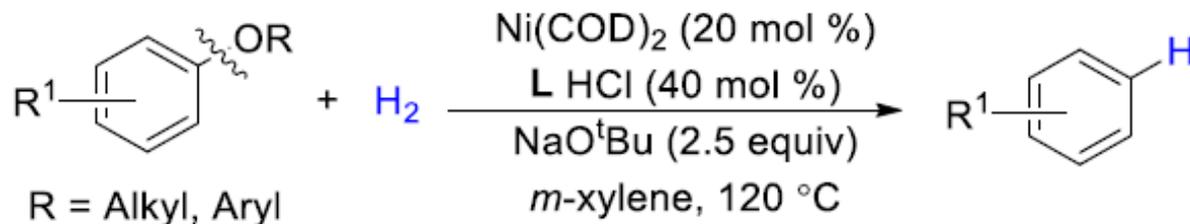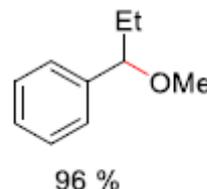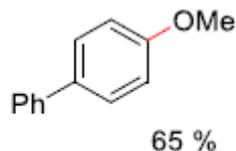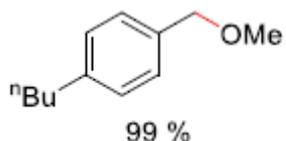
- **Excess base is needed for desired reactivity.**

- **AlMe3 is needed to activate C-O(alkyl)**

- **relative reactivity was found to be Ar−OAr > Ar−OMe > ArCH2−OMe**

Sergeev, A. G.; Hartwig, J. F. *Science* **2011**, 332, 439–443
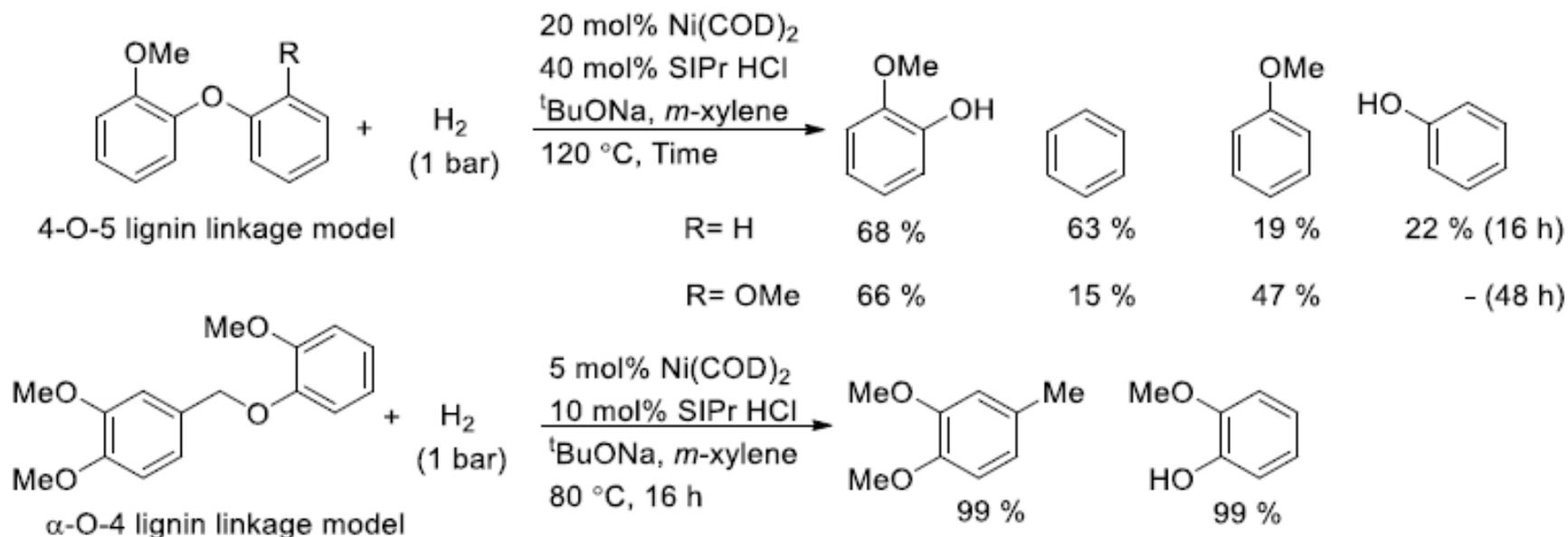
Hartwig validated the synthetic utility on depolymerization of lignin model.

but the catalyst loading and temperature for the current reaction are too high for the reaction to be applicable on a large scale

these reported molecular catalysts are sensitive to large concentrations of water, which is costly to separate from raw biomass.

Sergeev, A. G.; Hartwig, J. F. *Science* **2011**, 332, 439–443

Mechanism of Ni-NHC Catalyzed Hydrogenolysis of Aryl Ethers

Agapie and coworkers

20 % Ni(COD)$_2$
40 % SIPrHCl
H$_2$ (1atm)
NaO^{t}Bu, *m*-xylene
120°C

R = D
R = (CH$_2$)$_4$CH$_3$

X = 90% D
X = 90% D

Since the mechanism above does not require H2 for the conversion of aryl ether to arene, the catalytic trials were also performed in the absence of H2; <5% conversion was observed.

Mechanism consistent with labeling studies

Mechanism NOT consistent with labeling studies

Inactive Ni catalyst

Cornella, J; Zarate, C.; Martin, R. *J. Am. Chem. Soc.* 2013. **135**. 1997
Kelley, P.; Lin, S.; Edouard, G.; Day, M. W.; Agapie, T. *J. Am. Chem. Soc.* 2012, **134**, 5480–5483

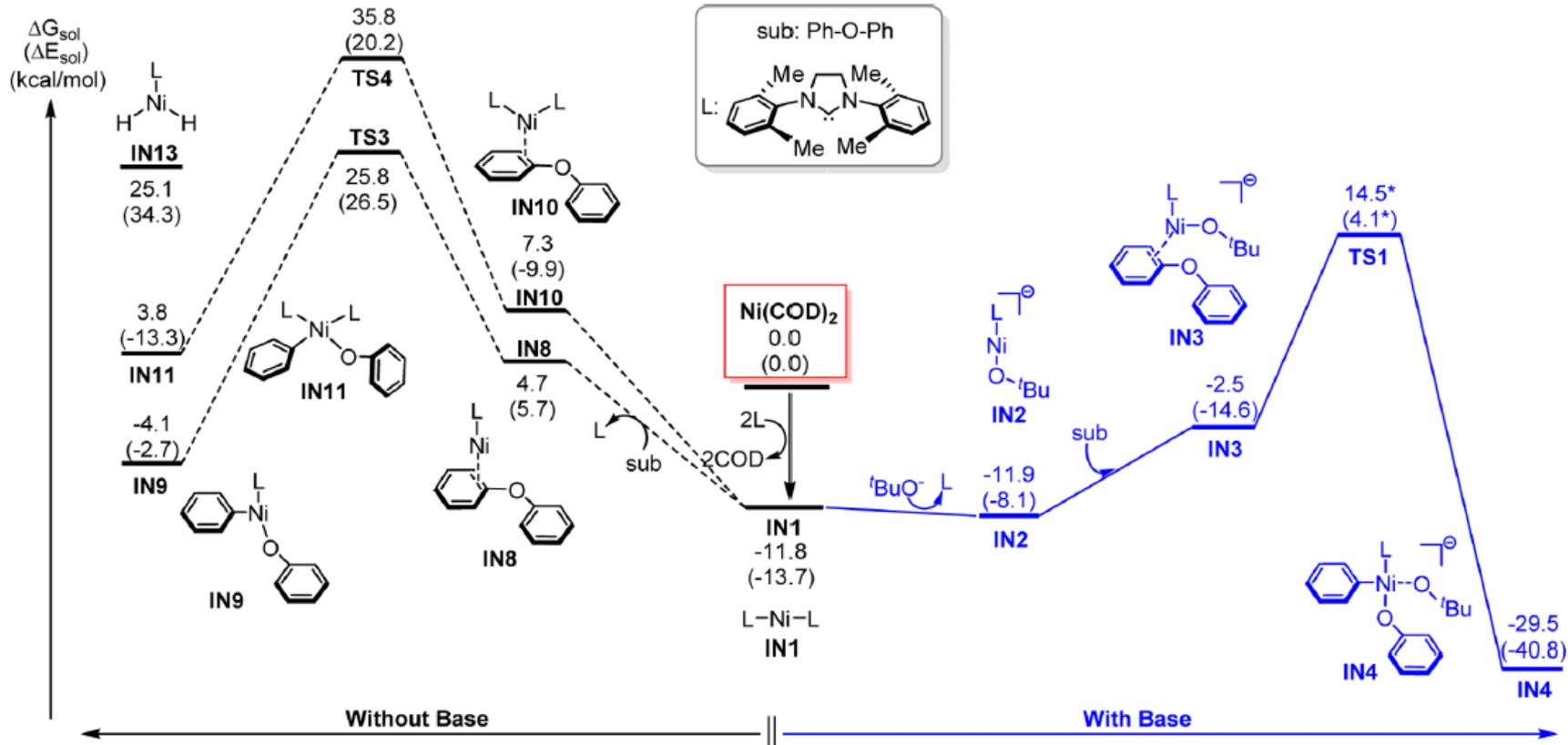# Mechanism of Ni-NHC Catalyzed Hydrogenolysis of Aryl Ethers 3

gure 1. Computed free (electronic) energy profiles of the rate-determining oxidative-addition steps with and without the base in the solution. The erisk indicates that the reader should see the text and ref 24a for a discussion of this estimated value. The small ligand (NHC) is used.

rate-determining oxidative addition of the C–O bond takes place to afford a new and stable [NiII(NHCpr)(Ot Bu) (Ph)(OPh)]– intermediate

Liping Xu[†], Lung Wa Chung[*‡], and Yun-Dong Wu ACS Catal. 2016, 6, 483–493

delocalize the more negative charge on the oxygen atom and reduce electronic repulsion between the filled Ni d orbital and the filled O lone pair.
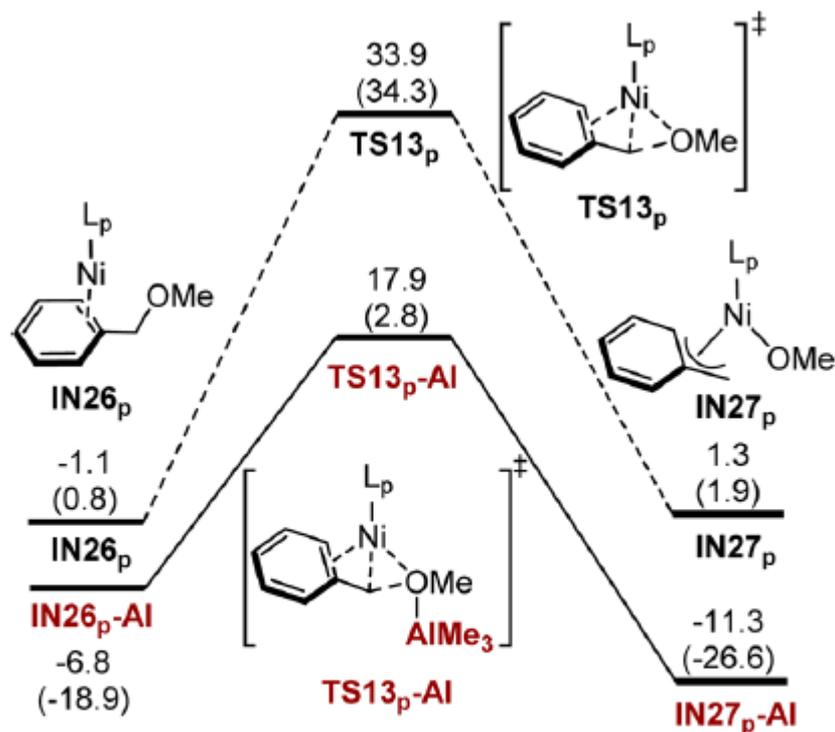
Figure 7. Computed free (electronic) energy profiles for hydrogenolysis of benzyl ethers in the absence and presence of $AlMe_3$. The real ligand (NHC_{pr}) is used.

Liping Xu[†], **Lung Wa Chung**[*‡], **and Yun-Dong Wu** ACS Catal. 2016, 6, 483−493
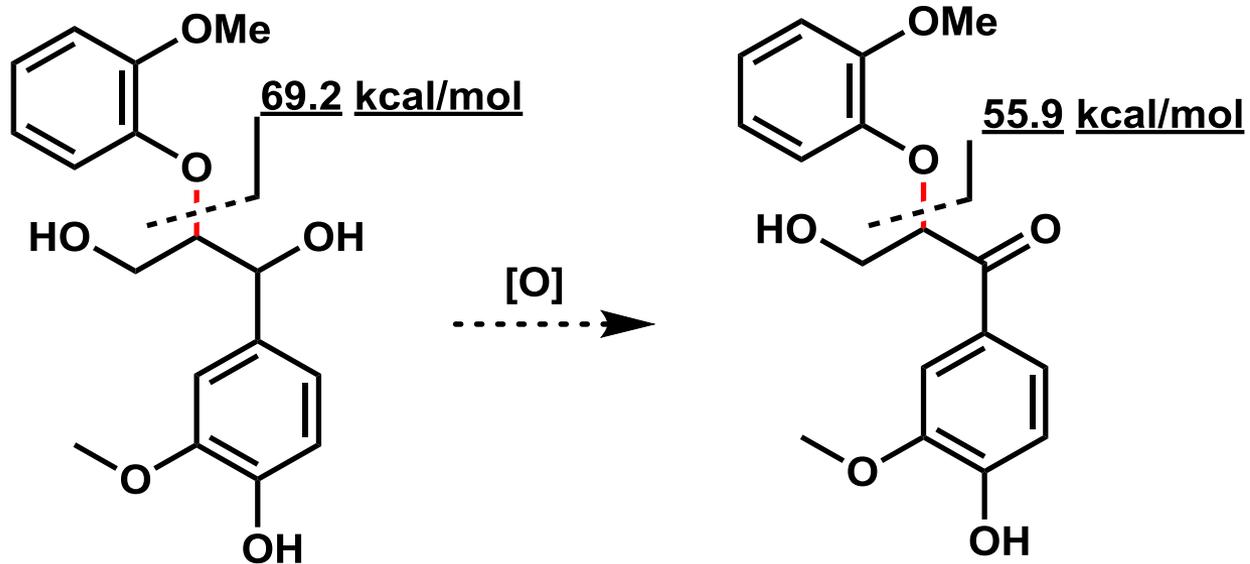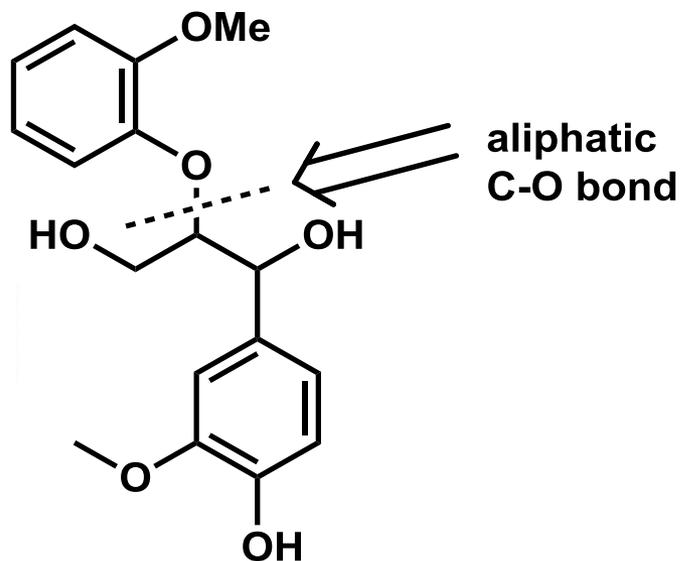
Summary 1

- **In the field of cleavage of aryl ether, Ni is very promising.**

- **Hartwig achieved selective cleavage of aromatic C-O bonds using metal and the cheap, mild, and atom-economical reductant hydrogen .**

- **but the catalyst loading and temperature for the current reaction are too high for the reaction to be applicable on a large scale**

2-2. alkyl C-O bond cleaverage of lignin
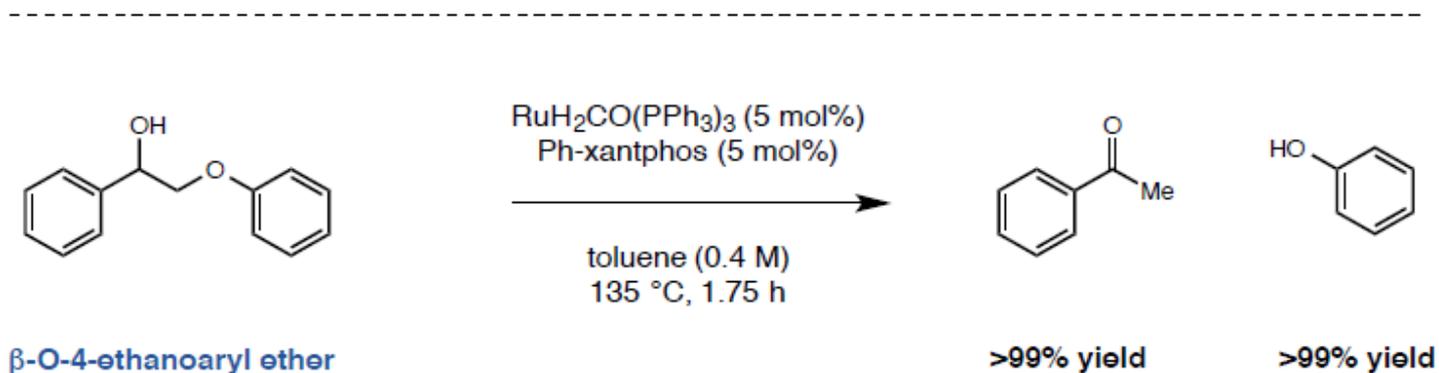
→Stahl's work

Strategy 2

β–O–4 linkage

45-62%

aliphatic C-O bond

69.2 kcal/mol

[O]

55.9 kcal/mol

Ellman and Bergman Lignin C-O bond cleavage with Ru

RuH₂CO(PPh₃)₃ (5 mol%)
Ph-xantphos (5 mol%)

toluene (0.4 M)
135 °C, 1.75 h

β-O-4-ethanoaryl ether

>99% yield   >99% yield
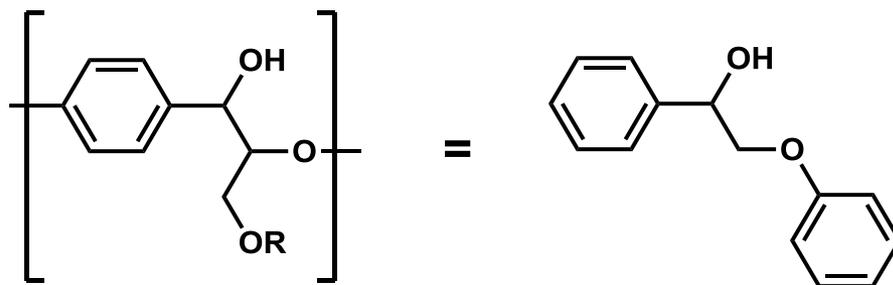
RuH2(CO)(PPh3)3 is known to be competent for both Dehydrogenation and C-O activation chemistry and was chosen as the starting point for catalyst development.

Ellman and Bergman Lignin C-O bond cleavage with Ru 2

3: 0.15 mmol in monomeric equivalents

RuH₂(CO)(PPh₃)₃ (5 mol%)
Ph-xantphos (5 mol%)
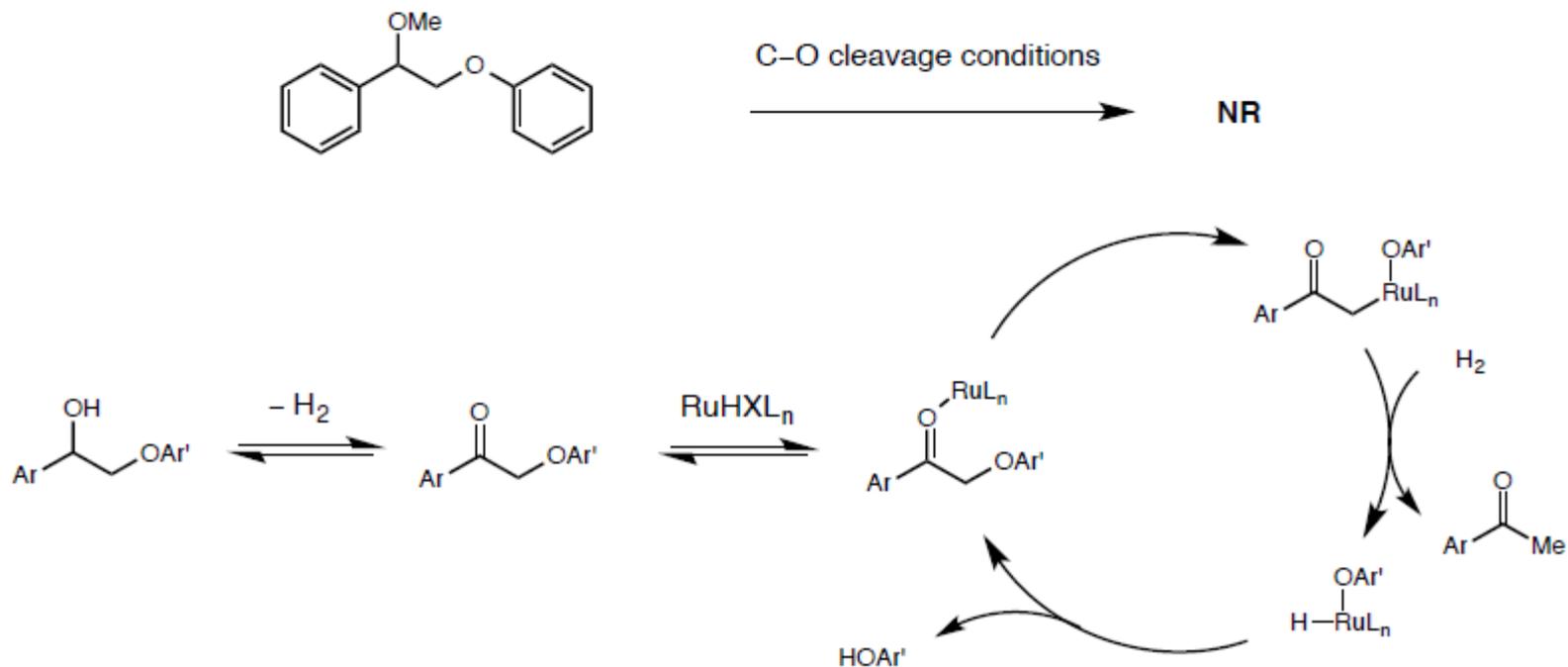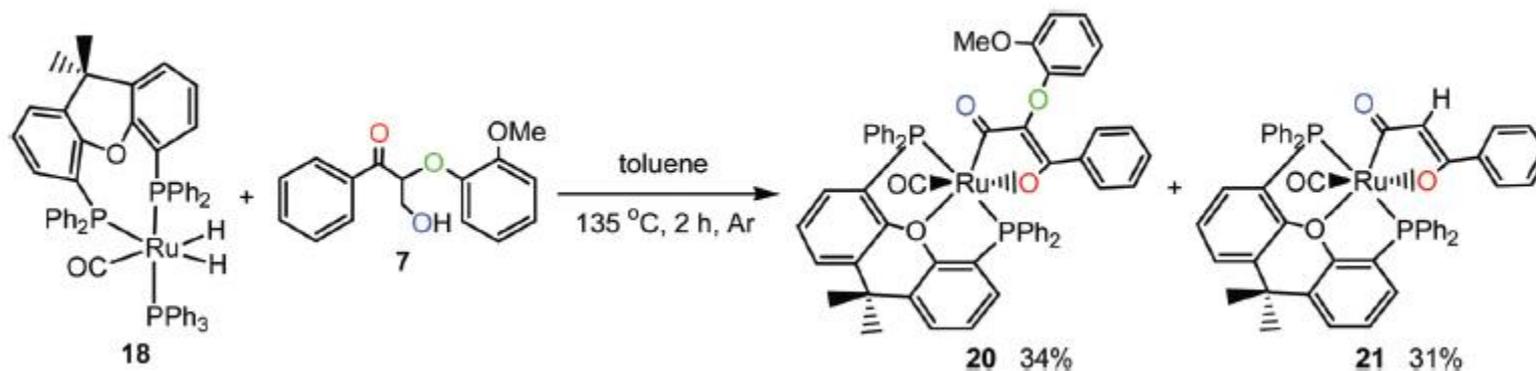1,4-dioxane (0.5 mL)
175 °C, 3 h

99% isolated

<Mechanism study>

C–O cleavage conditions → NR

Jason M. Nichols, Lee M. Bishop, Robert G. Bergman,* and Jonathan A. Ellman*J. AM. CHEM. SOC. 2010, **132**, 12554–12555
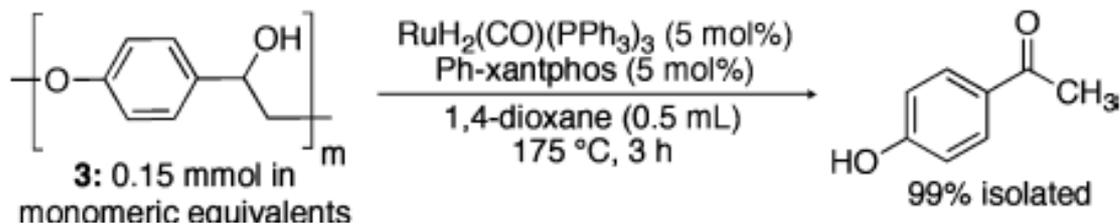
This method can not be applied to real β-O-4 linkage

2 - 6%   3 - 4%   2 - 5%

20 34%   21 31%

Adam Wu, Brian O. Patrick, Enoch Chung and Brian R. James*, *Dalton Trans.*, **2012**, 41, 11093–11106
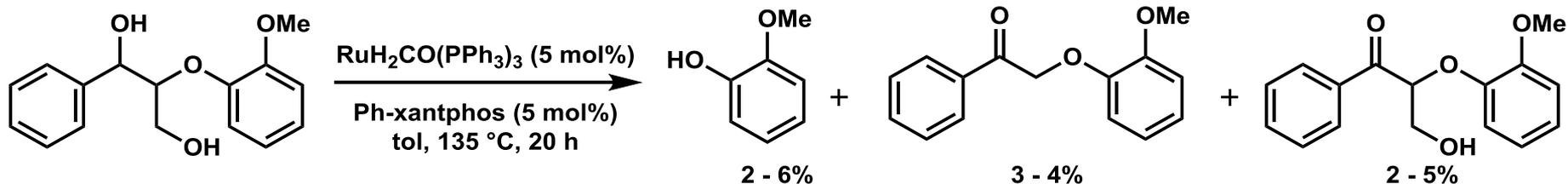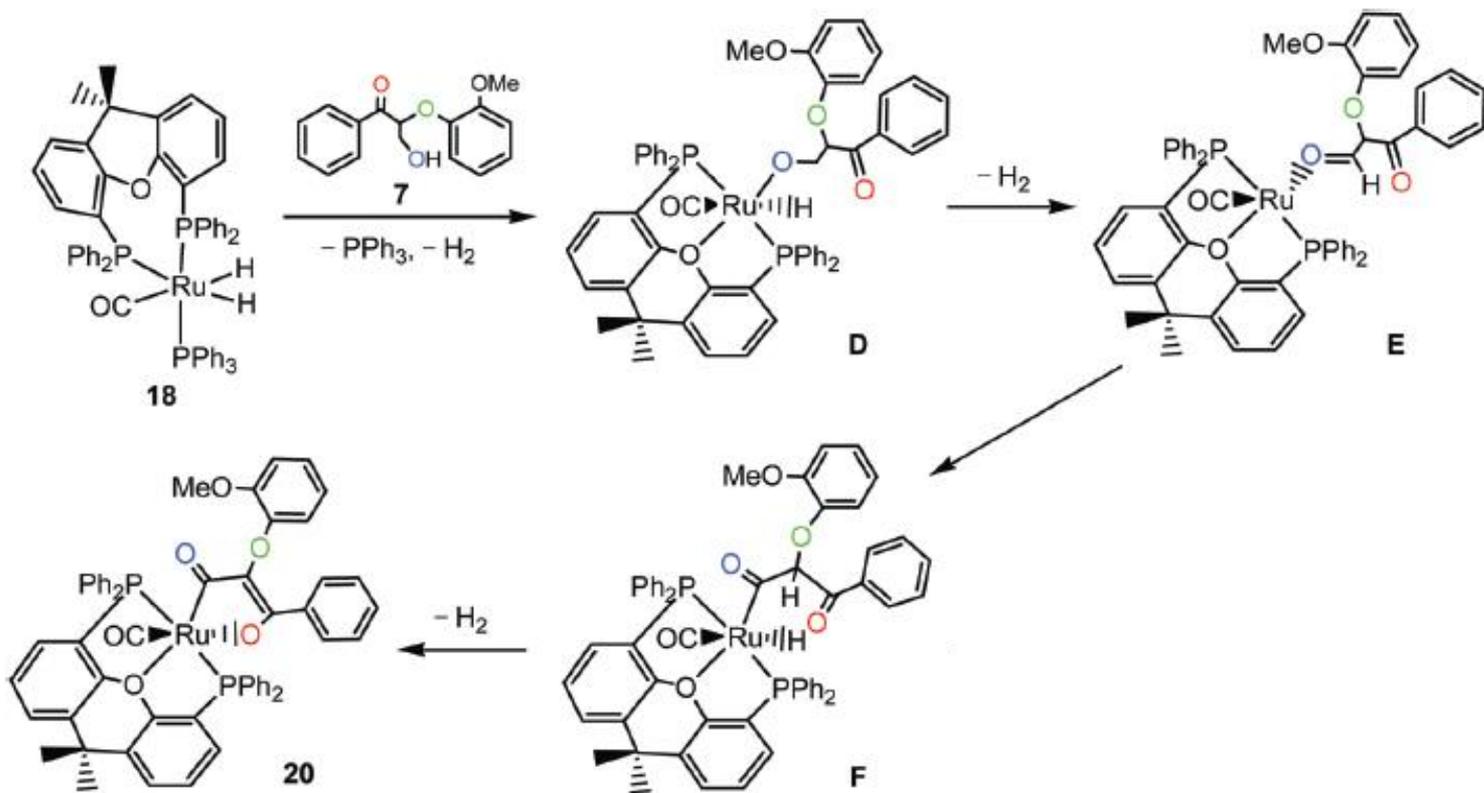
Scheme 9 Proposed mechanism for formation of 20 and 21 from reaction of 7 with 18.

Adam Wu, Brian O. Patrick, Enoch Chung and Brian R. James*, *Dalton Trans*., **2012**, 41, 11093–11106
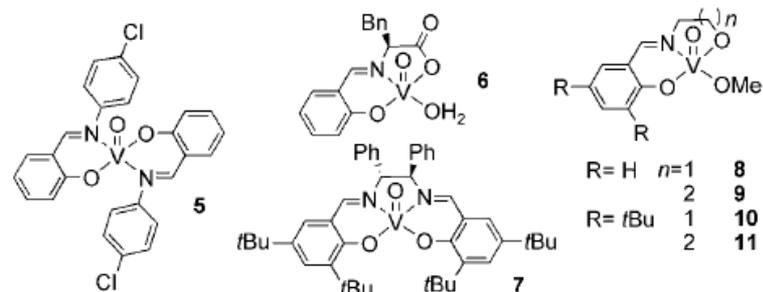
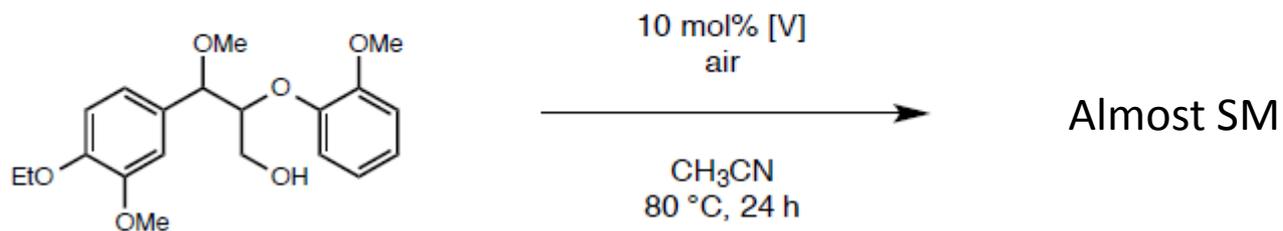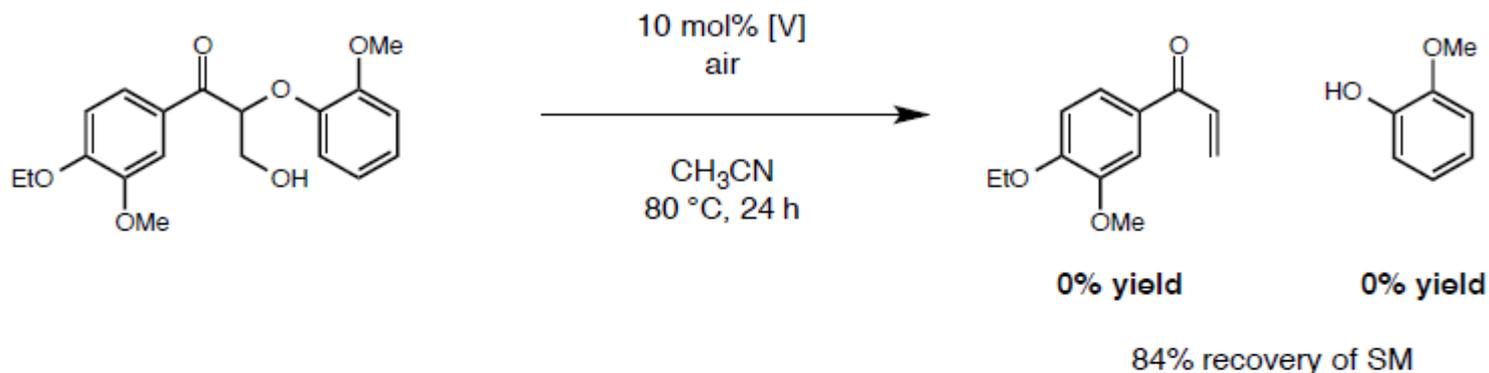# Toste's Lignin C-O bond cleavage with Vanadium
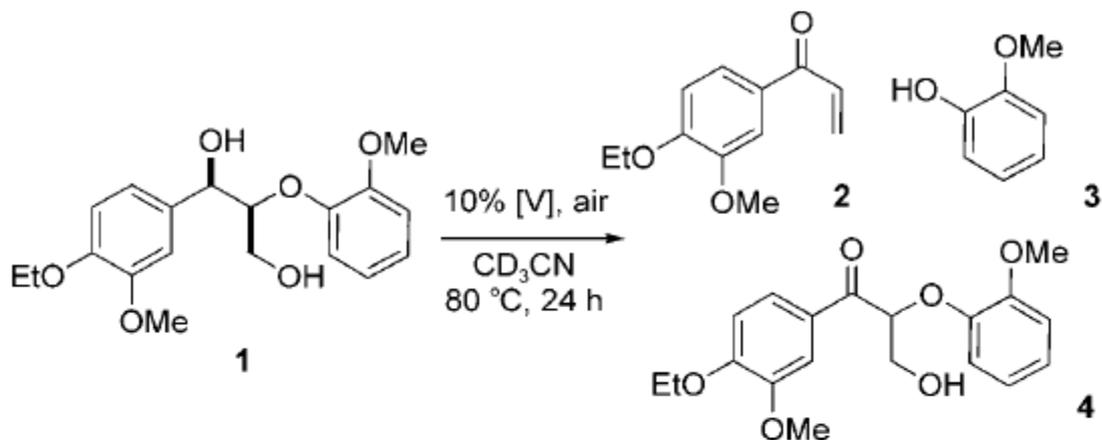
O$_2$ is needed because under N$_2$ condition, catalyst 11 precipitated to become 12
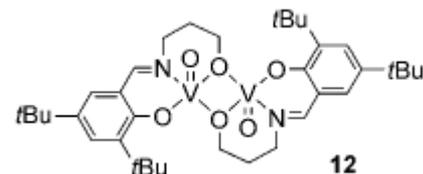
Entry	Vanadium catalyst	Conversion [%]	2 [%]	3 [%]	4 [%]
1	none	0	–	–	–
2	VOSO$_4$·xH$_2$O	34	2	2	6
3	VO(acac)$_2$	79	13	22	31
4	VO(OiPr)$_3$	82	5	11	45
5	5	86	6	6	59
6	6	66	13	14	41
7	7	55	3	–	37
8	8	>95	61	45	27
9	9	86	70	62	8
10	10	95	65	50	18
11	11	>95	82	57	7

Sunghee Son and F. Dean Toste*. *Angew. Chem. Int. Ed*. 2010, **49**, 3791–3794

Toste's Lignin C-O bond cleavage with Vanadium 2

Sunghee Son and F. Dean Toste*. *Angew. Chem. Int. Ed.* 2010, **49**, 3791 –3794
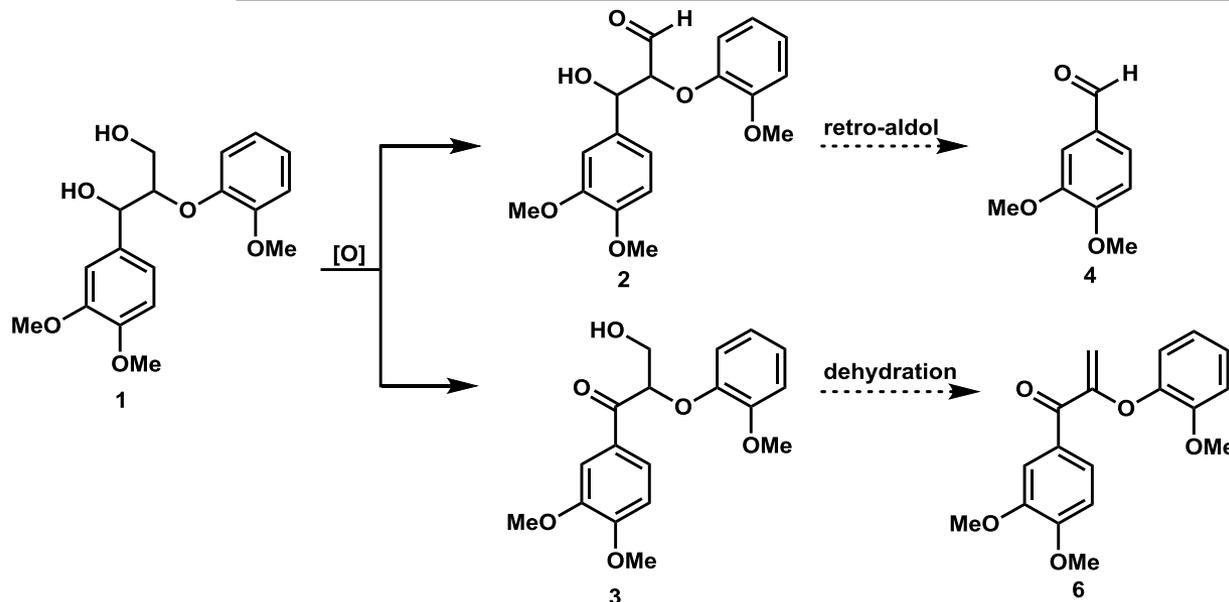
Toste's Lignin C-O bond cleavage with Vanadium 3
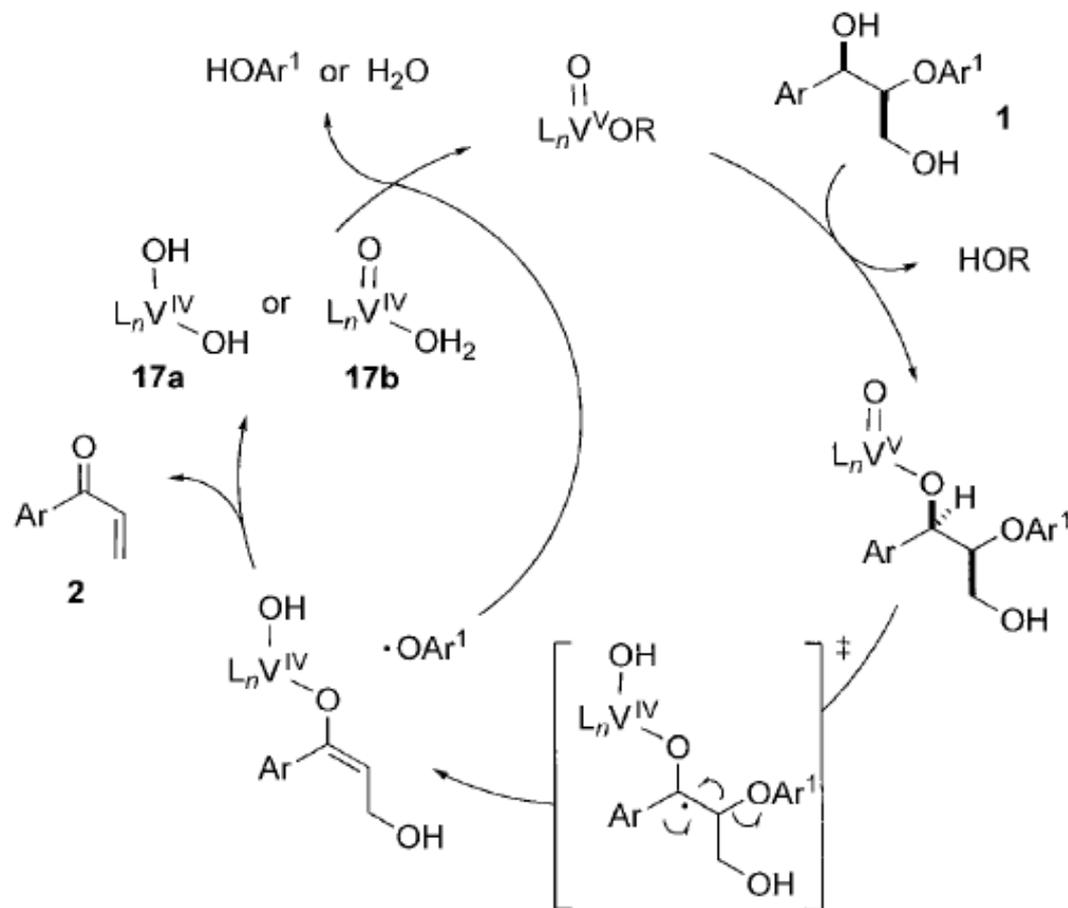
Scheme 4. Plausible mechanism for vanadium-catalyzed non-oxidative cleavage of **1**.

Sunghee Son and F. Dean Toste*. *Angew. Chem. Int. Ed*. 2010, **49**, 3791 –3794
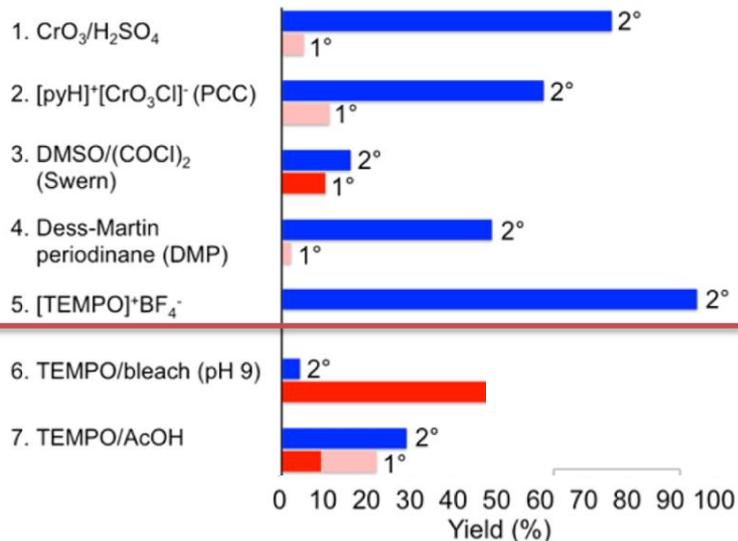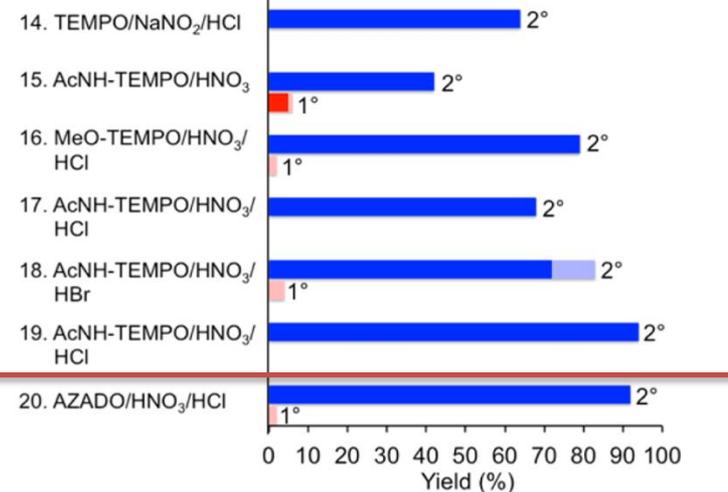
Stahl's Chemoselective aerobic alcohol oxidation in lignin

Scheme 1. Simplified Proposed Catalytic Cycle for the Metal-Free Aerobic Oxidation of Alcohols
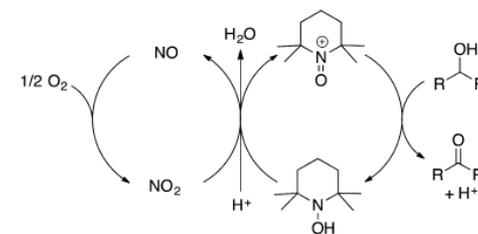
A) Stoichiometric Oxidants

1. CrO$_3$/H$_2$SO$_4$
2. [pyH]$^+$[CrO$_3$Cl]$^-$ (PCC)
3. DMSO/(COCl)$_2$ (Swern)
4. Dess-Martin periodinane (DMP)
5. [TEMPO]$^+$BF$_4^-$
6. TEMPO/bleach (pH 9)
7. TEMPO/AcOH

C) Metal-Free Catalytic Aerobic Oxidations

14. TEMPO/NaNO$_2$/HCl
15. AcNH-TEMPO/HNO$_3$
16. MeO-TEMPO/HNO$_3$/HCl
17. AcNH-TEMPO/HNO$_3$/HCl
18. AcNH-TEMPO/HNO$_3$/HBr
19. AcNH-TEMPO/HNO$_3$/HCl
20. AZADO/HNO$_3$/HCl

Alireza Rahimi,† Ali Azarpira,‡ Hoon Kim,‡ John Ralph,‡ and Shannon S. Stahl*
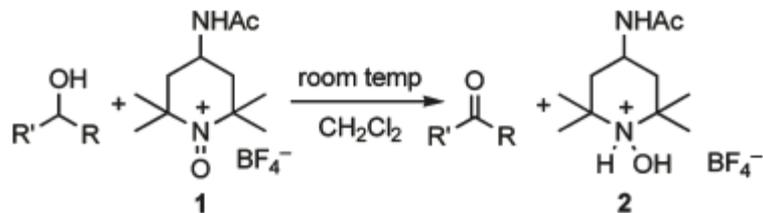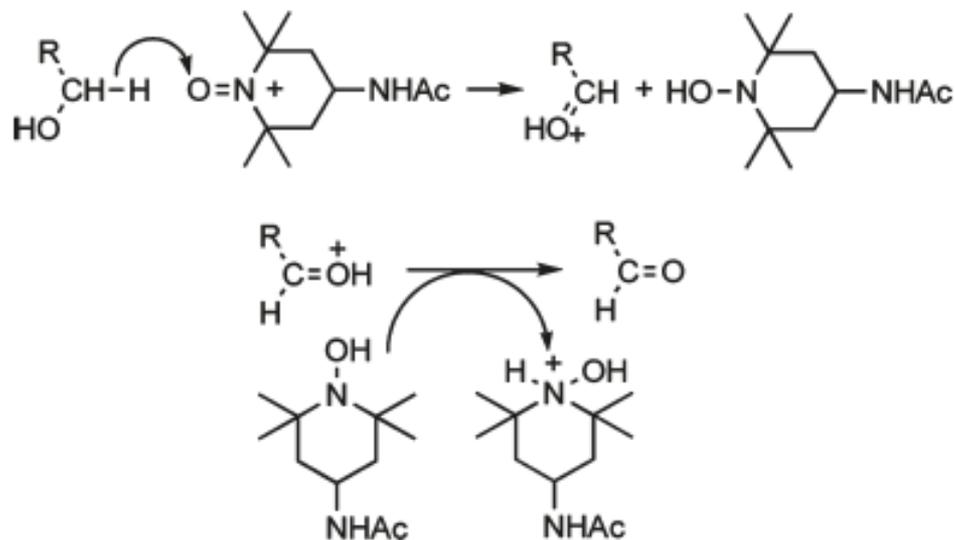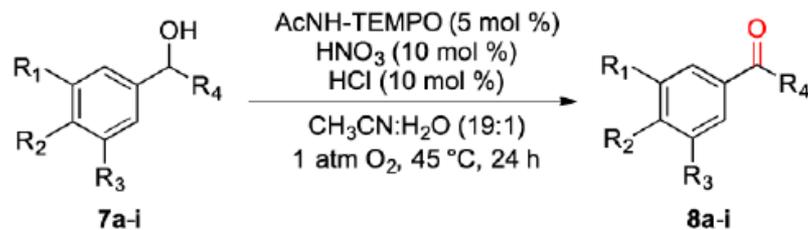
Scheme 1

Table 1. Relative Rates of Oxidation of Primary Alcohols to the Corresponding Aldehydes by **1** in CH_2Cl_2 (Scheme 1)

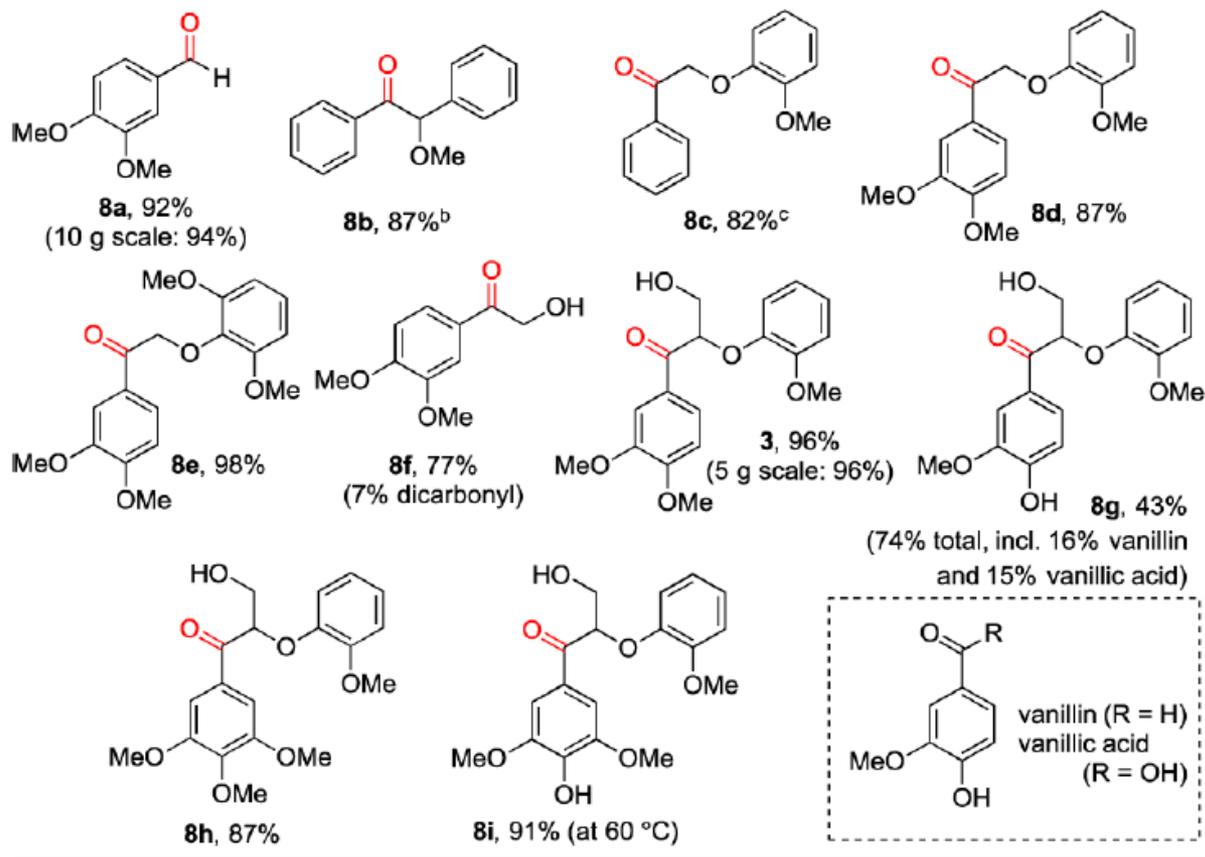| entry	alcohol	rel oxidn rate
1		1.0
2		5.8
3		0.09
4		0.77
5		0.76
6		6.4
7[a]		0.11
8[a]		0.08
9		0.04
10[a]		0.01

Scheme 2

Stahl's Chemoselective aerobic alcohol oxidation in lignin 2
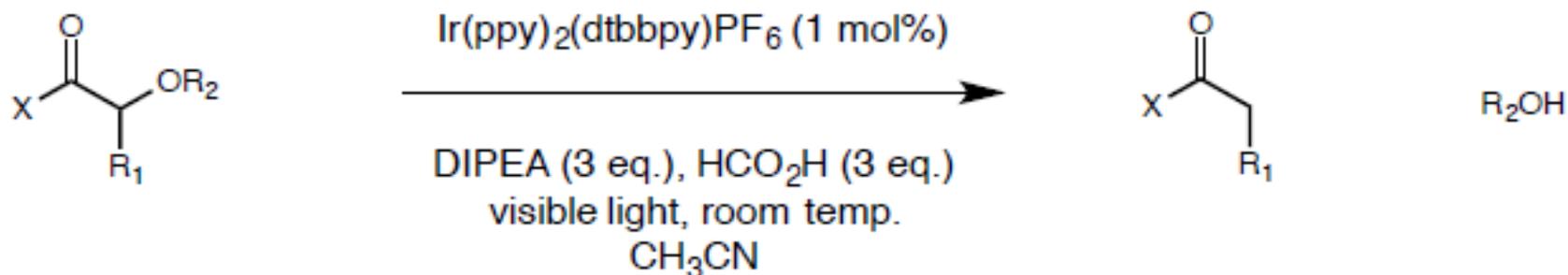

- **Electron rich substrates afforded higher yields.**

- **Phenol did not disturb this reaction.**

- **this oxidation method also exhibits good reactivity and similar chemoselectivity with real lignin**

Alireza Rahimi,† Ali Azarpira,‡ Hoon Kim,‡ John Ralph,‡ and Shannon S. Stahl*

Stephenson's photoredox strategy for lignin degradation.

John D. Nguyen,‡ Bryan S. Matsuura,‡ and Corey R. J. Stephenson. *J. Am. Chem. Soc.* 2014, **136,** 1218−1221

Stephenson's photoredox strategy for lignin degradation 2

Stahl's Depolymerization of oxidized lignin (Redox-neutral cleavage)
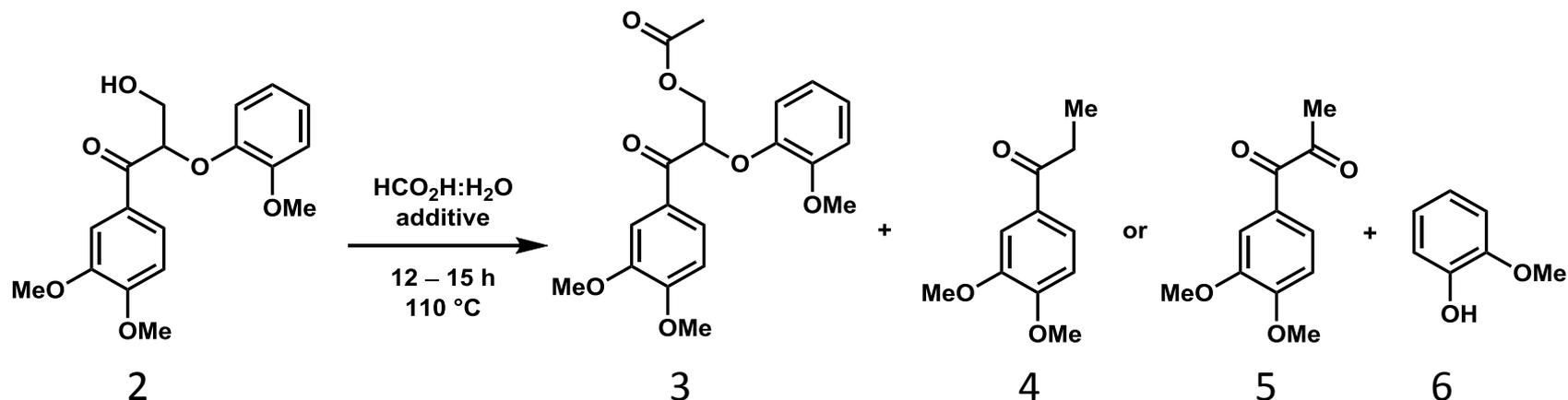
Entry	M (2 equiv.)	Additive	3 (%)	4:5 (%)	6 (%)
1	Zn	–	6	76:0	69
2	Al	–	49	0:39	36
3	Mg	–	51	0:45	24
4	Fe	–	49	0:31	24
5	Mn	–	19	0:74	63
6	–	–	18	0:77	64
7	–	HCO₂Na (3 equiv.)	0	0:96	87

Absence of a reducing metal showed good result.
Even better yields with 3eq NaCO$_2$H.

Alireza Rahimi1 , Arne Ulbrich1 , Joshua J. Coon1,2 & Shannon S. Stahl, *Nature,* **515** , 249 (2014)

Depolymerization of oxidized lignin (Redox-neutral cleavage) 2

Cat., O₂ → **HCO₂H:H₂O HCO₂Na** — **110 °C. 24 h**

soluble fraction → low molecular-mass aromatics **61.2wt%**

extraction with AcOEt

Insoluble fraction → **29.7%**

29.7wt% 29.5wt%

■ Syringyl
■ Guaiacyl
■ p-Hydroxyphenyl
■ Dimers and trimers
■ Polymeric material

9.0wt%

4.4wt%   18.3wt%

S:G:H = 1.6:1.0:0.24

R = C(O)Me (13.1%)
H   (8.5%)
OH   (7.9%)

Syringyl

R = C(O)Me (6.7%)
H   (3.5%)
OH   (2.9%)

Guaniacyl

R = OH   (4.0%)
C(O)Me (0.1%)
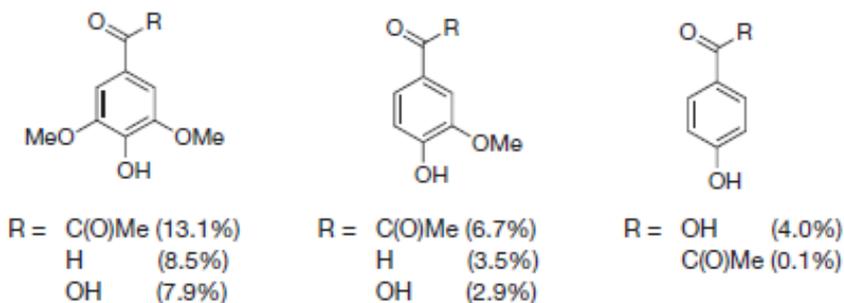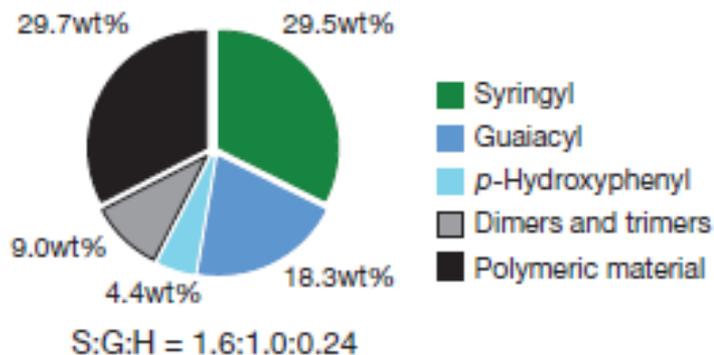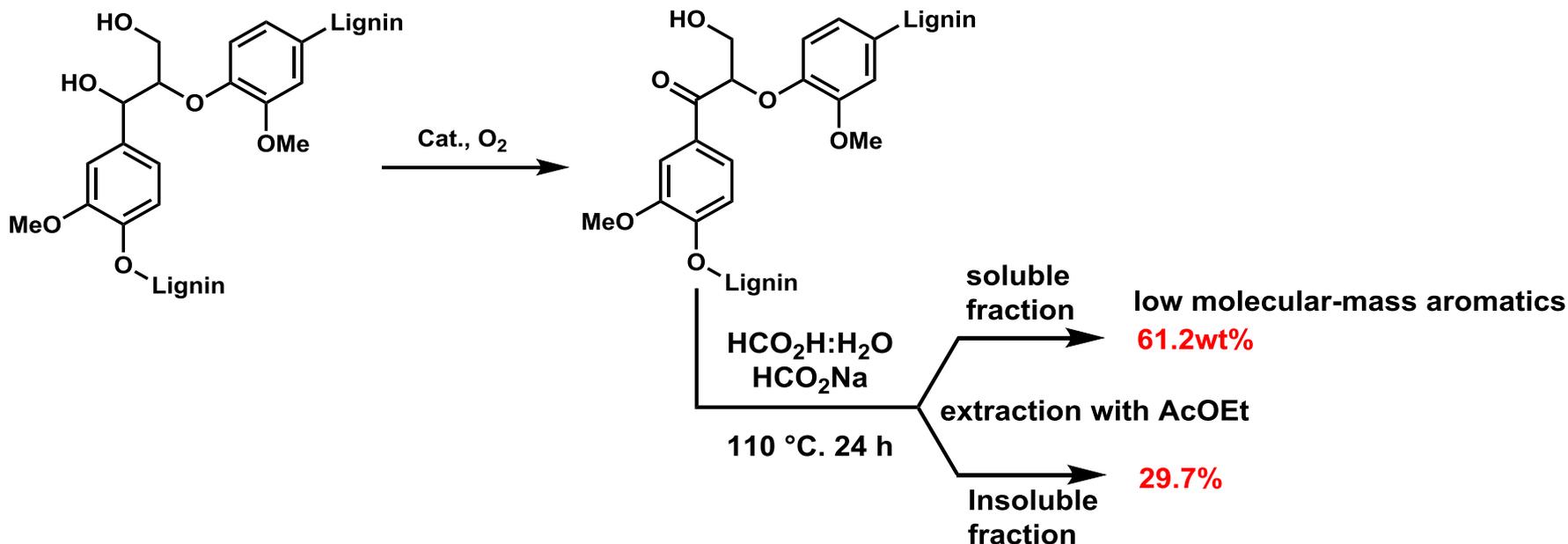
- **Unoxidized lignin in the reaction resulted in only 7.2wt% yield.**

Alireza Rahimi1 , Arne Ulbrich1 , Joshua J. Coon1,2 & Shannon S. Stahl, *Nature,* **515** , 249 (2014)
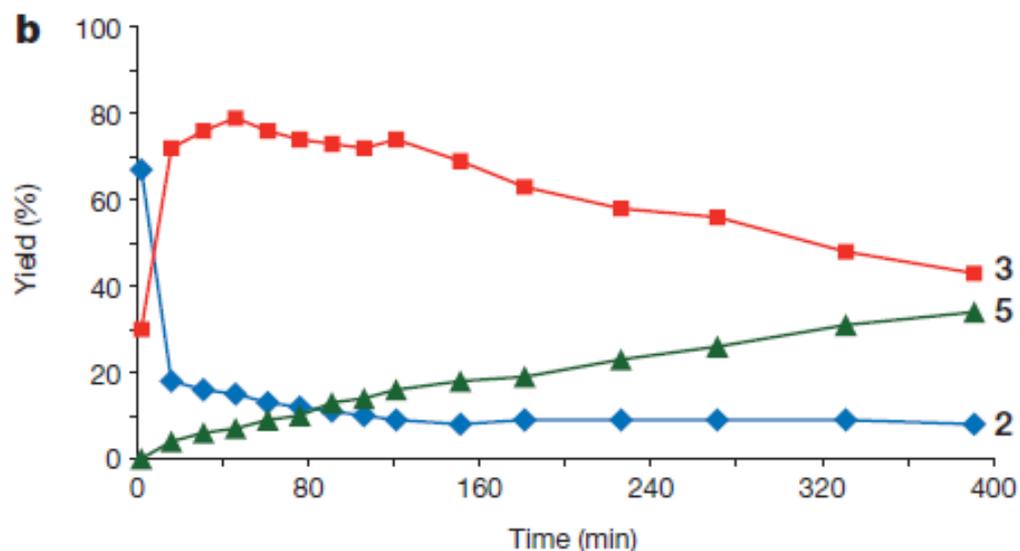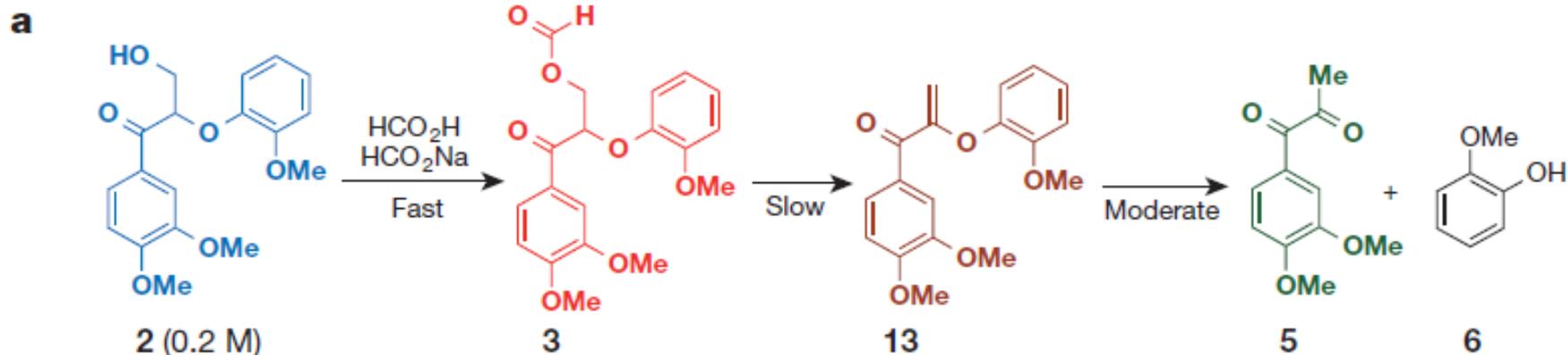
- $K_H/K_D = 9.3 \pm 0.2$
- **Oxidation may be attributed to E2 elimination reaction.**
- **This mechanism accounts for the effect of buffered reaction medium.**
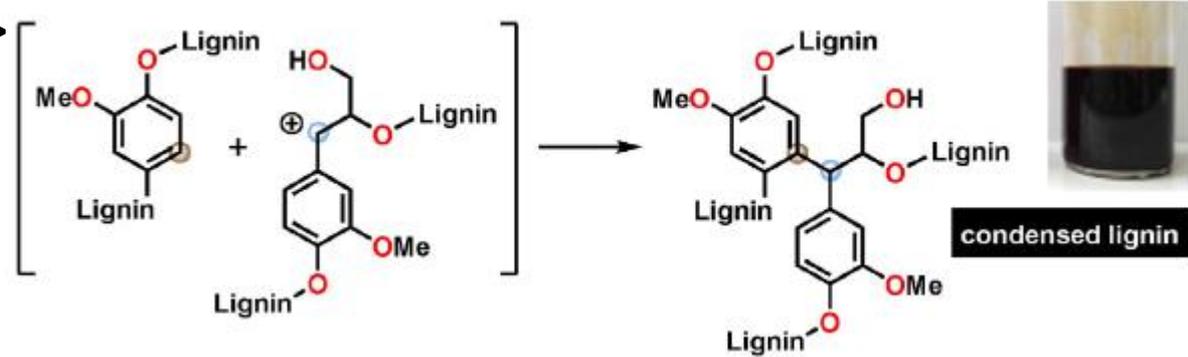
Problem of lignin separation

problem during biomass pretreatment processes

Lignin (25%)

Ash, others (~5%)

Hemicellulose (30%)

acid → soluble → cellulose, hemicellulose

acid → insoluble → Lignin
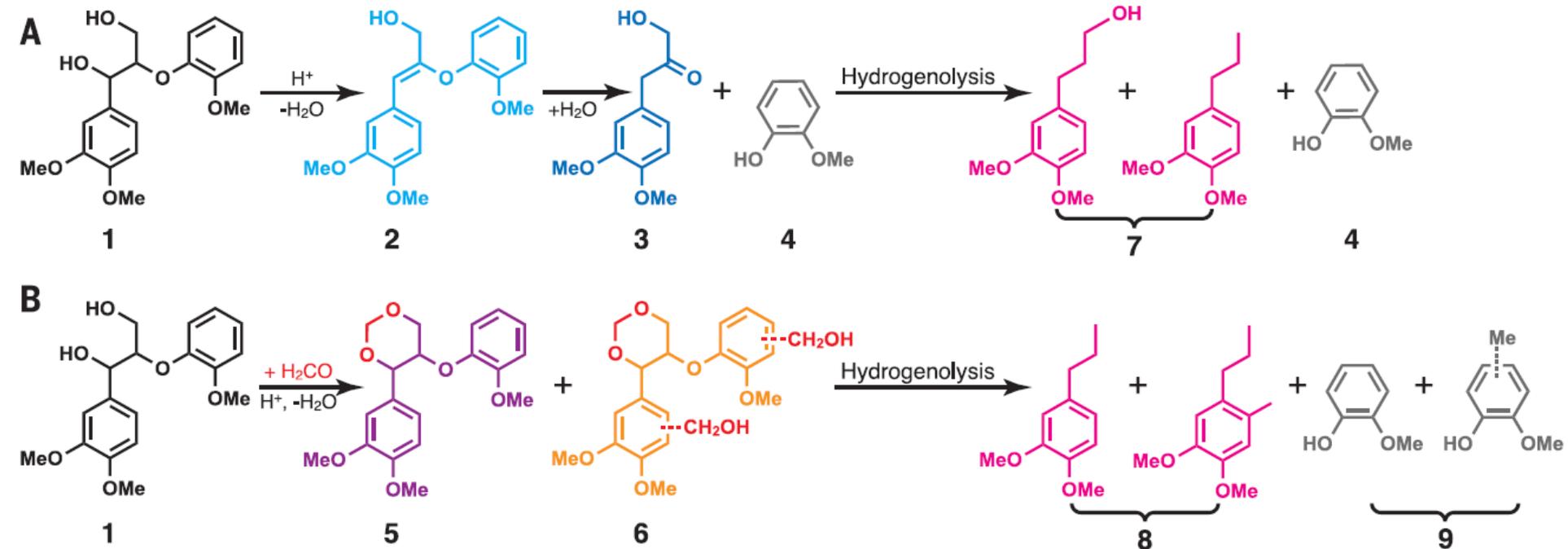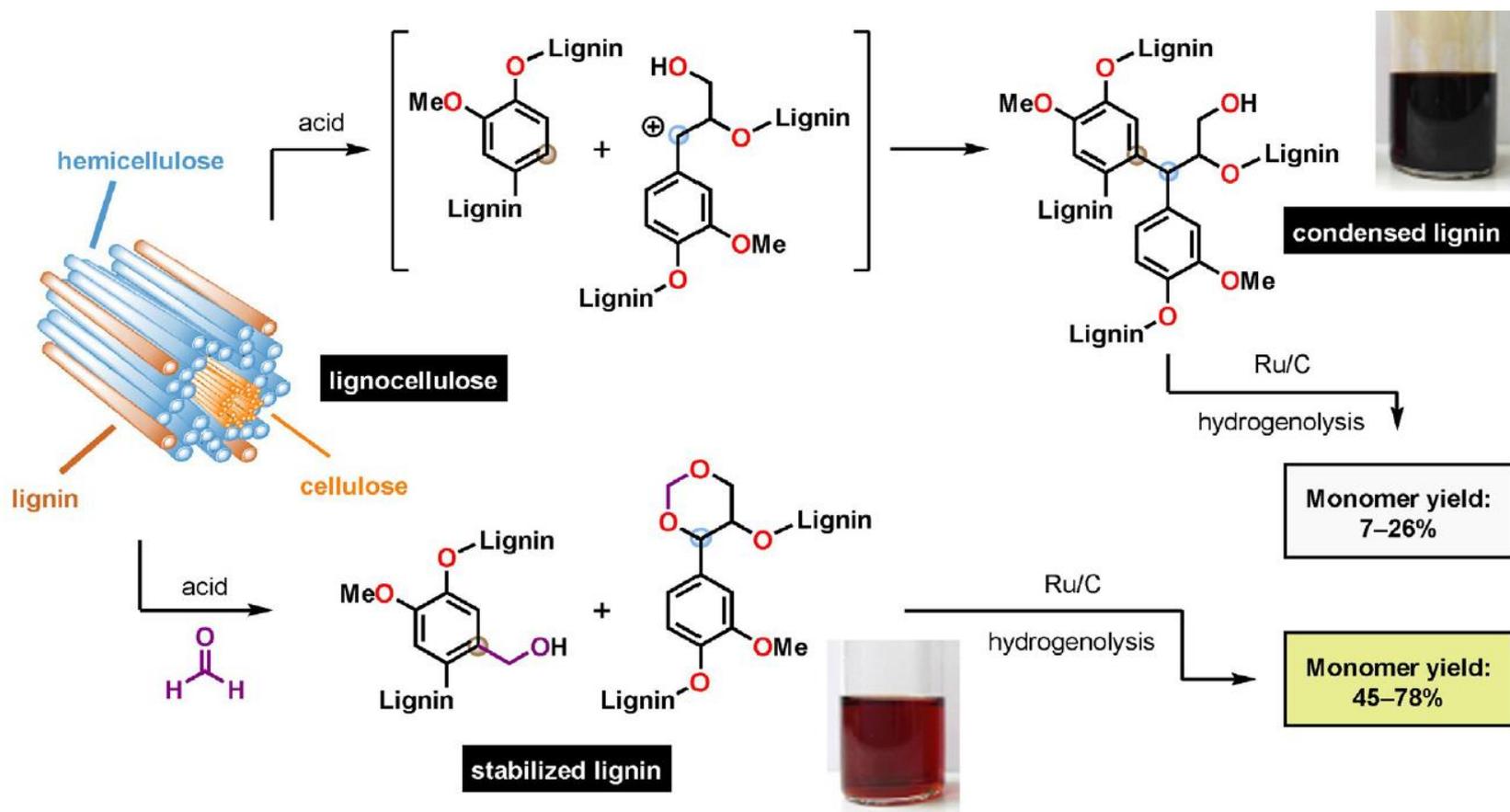
Cellulose (40%)

<interunit C-C bond>

condensed lignin
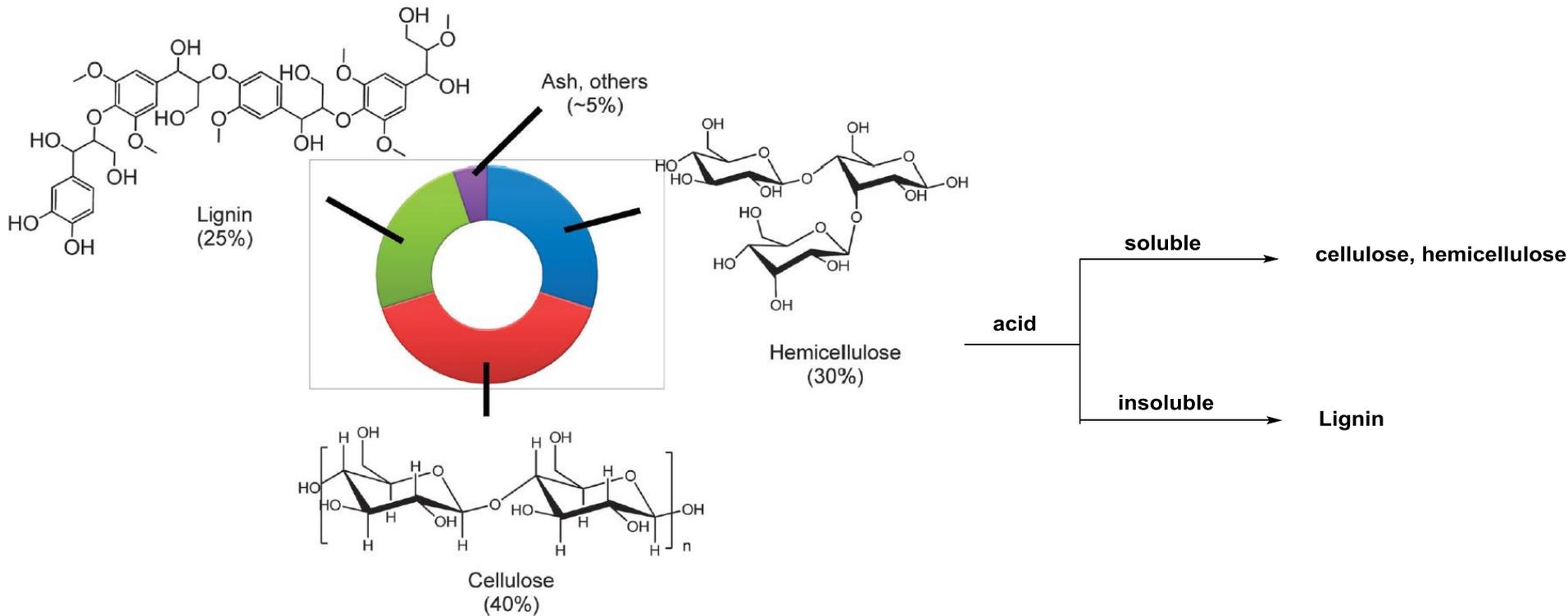
Interunit C-C bond formed through lignin extraction inhibit lignin depolymerization.

Formaldehyde inhibit interunit C-C bond .

L. Shuai, M. Talebi Amiri, Y. M. Questell-Santiago, F. H8roguel, Y. Li, H. Kim, R. Meilan, C. Chapple, J. Ralph, J. S. Luterbacher, *Science* 2016, **354**, 329– 333

Formaldehyde inhibit interunit C-C bond 2 .

L. Shuai, M. Talebi Amiri, Y. M. Questell-Santiago, F. H8roguel, Y. Li, H. Kim, R. Meilan, C. Chapple, J Ralph, J. S. Luterbacher, *Science* 2016, **354**, 329– 333

Summary

- **Lignin deporymerization method have developed rapidly for ten years.**
- **Hartwig developed reductive C(sp2)-O bond cleavage.**
- **Stahl method showed highest monomer yield from real lignin from**
- **Main problem now is how to separate lignin from lignocelloce.**