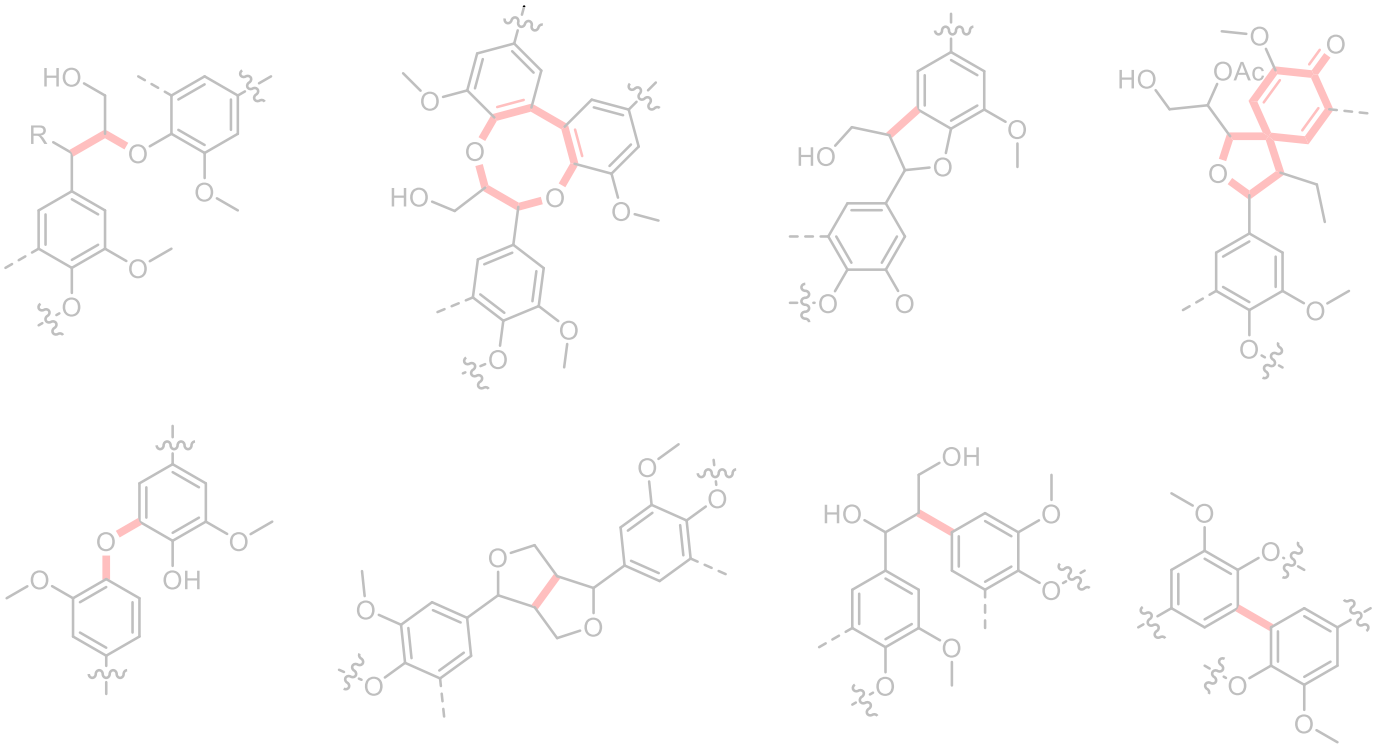
Lignin-Introduction and Valorization

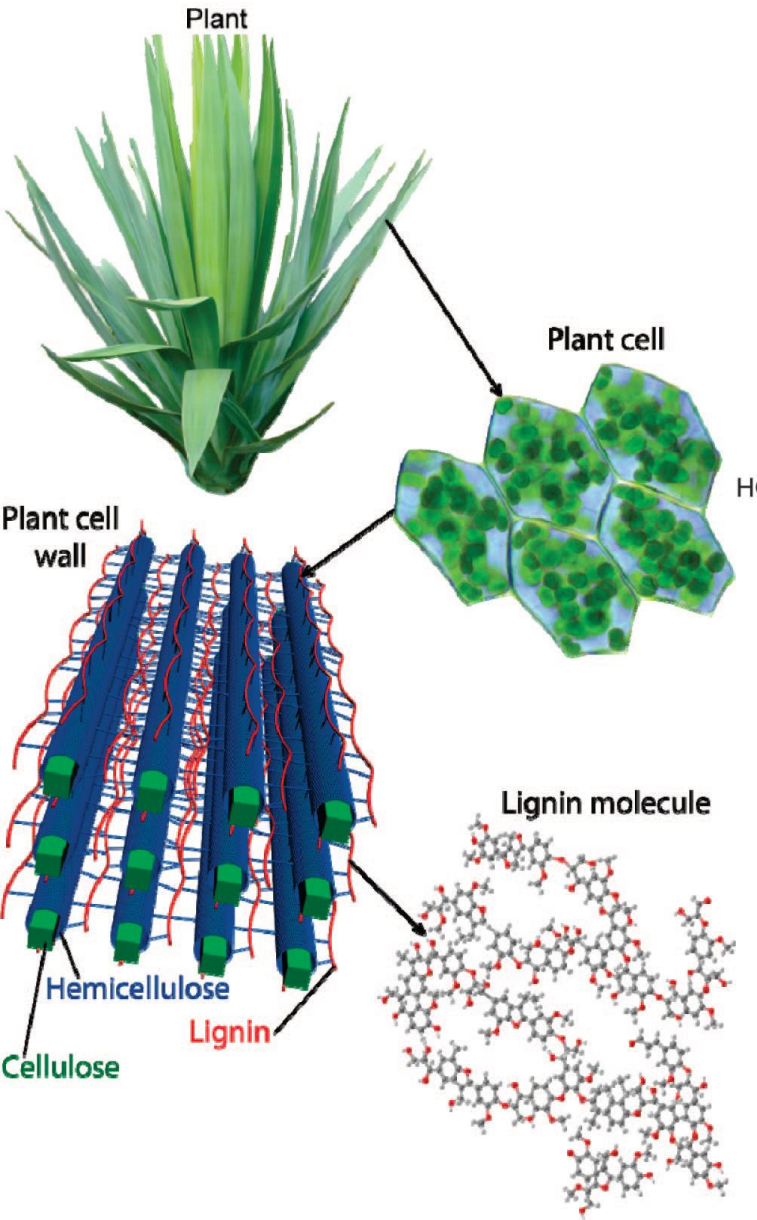


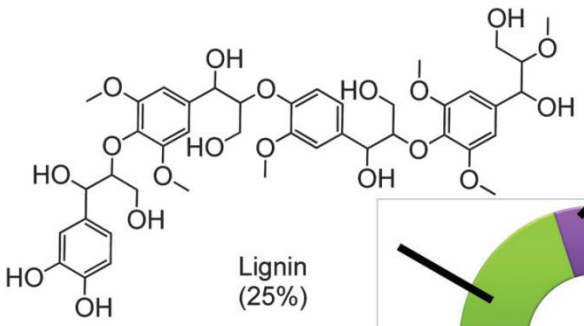
Penghao Chen

Dong Group Seminar

April, 8th, 2015

Introduction

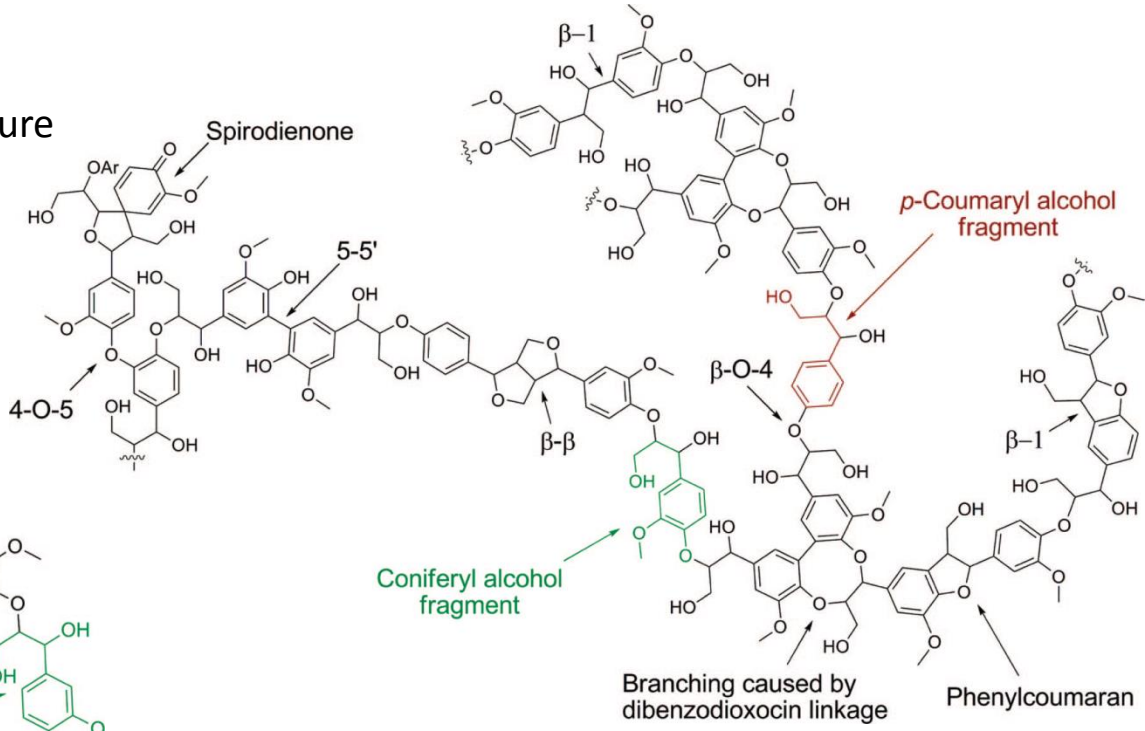




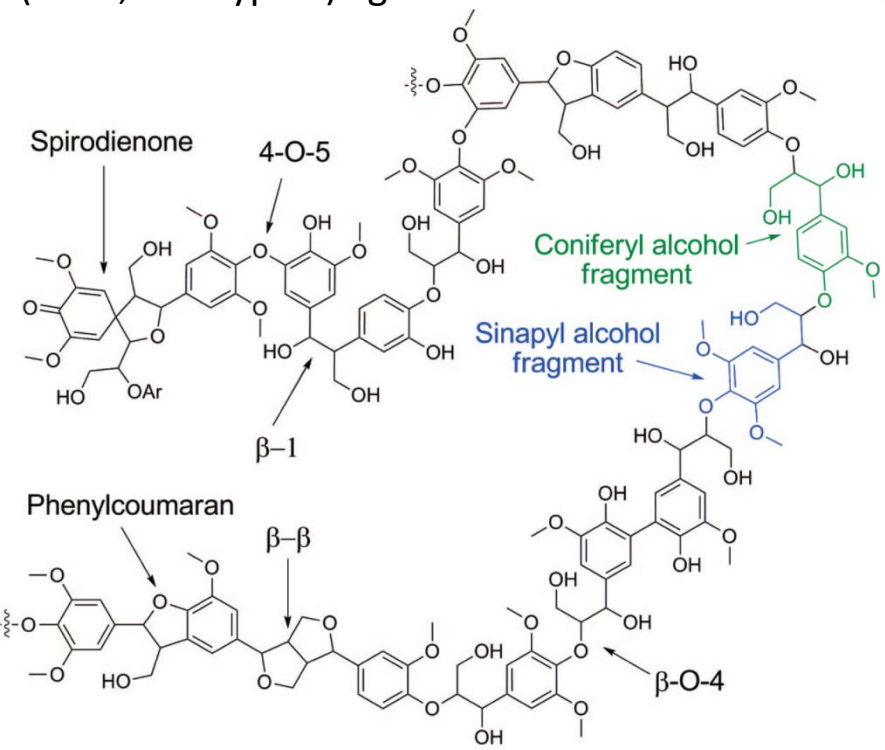
Weckhuysen, *Chem. Rev.* **2010**, *110*, 3552
Luque, *Chem. Soc. Rev.* **2014**, *43*, 7485

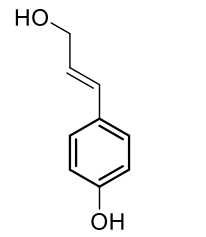
Introduction

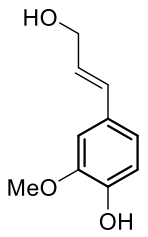
Schematic representation of a softwood (spruce) lignin structure

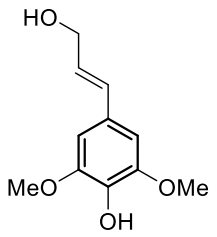


Schematic representation of a Hardwood (birch, eucalyptus) lignin structure



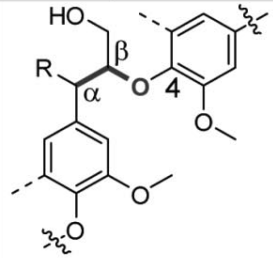
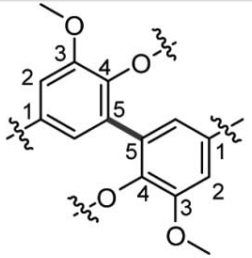
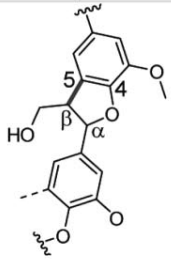
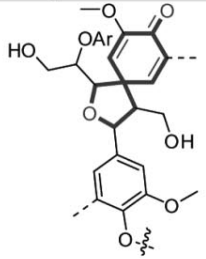
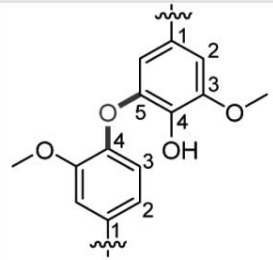
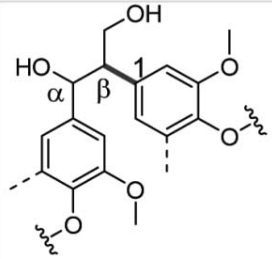
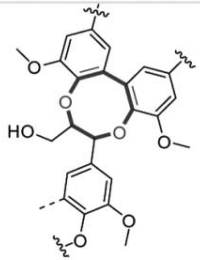
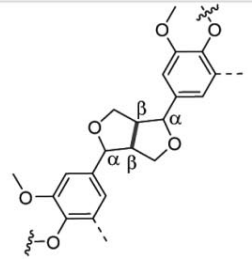




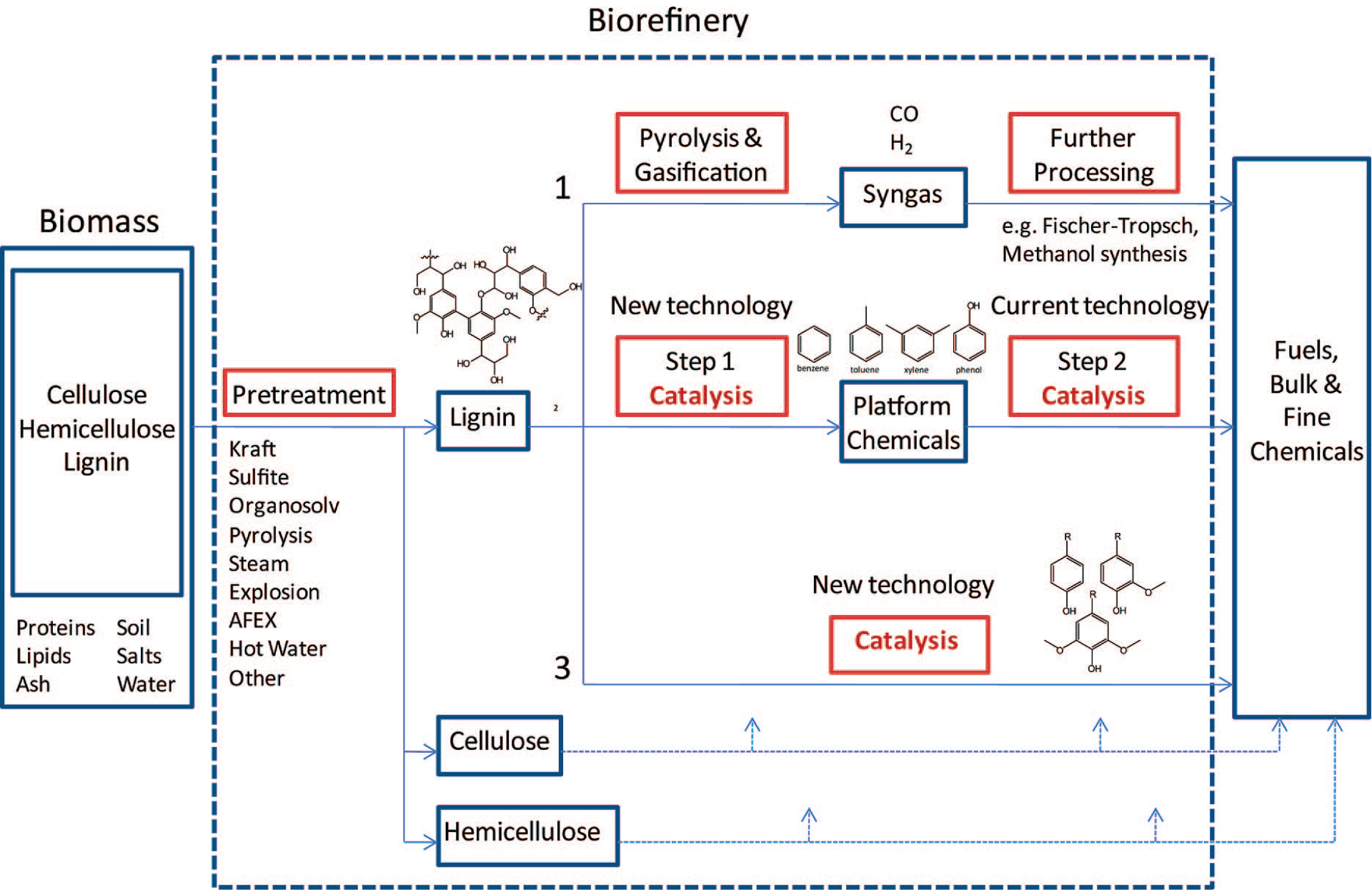


Softwood lignin: about 90%
Hardwood lignin: roughly the same

Introduction

Linkage			β-O-4	5-5	β-5	Spirodienone
						
Abundance	Softwood	Spruce [291,292]	45-50	19-22	9-12	nd
per 100 C9-units		Spruce [293]	nd	22	12	nd
		Spruce [294]	45	24-27	9	nd
		Spruce [27]	45	24-27[a]	9	2
	Hardwood	Birch [291,292]	60	9	6	nd
		Eucalyptus grandis [295]	61	6	3	nd
		Eucalyptus grandis [28]	61	3	3	5
		Paulownia fortunei [26]	62	nd	11	3
Linkage			4-O-5	β-1	Dibenzodioxocin	β-β
						
Abundance	Softwood	Spruce [291,292]	4-7	7-9	nd	2-4
per 100 C9-units		Spruce [293]	nd	2	5	2.5
		Spruce [294]	nd	1	7	2
		Spruce [27]	nd	1	7	6
	Hardwood	Birch [291,292]	6.5	7	nd	3
		Eucalyptus grandis [295]	9	1	<1	3
		Eucalyptus grandis [28]	9	2	nd	3
		Paulownia fortunei [26]	nd	1	2	12

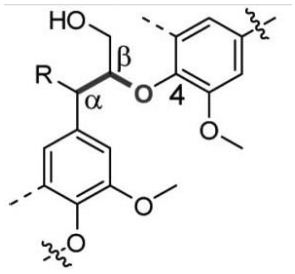
Introduction

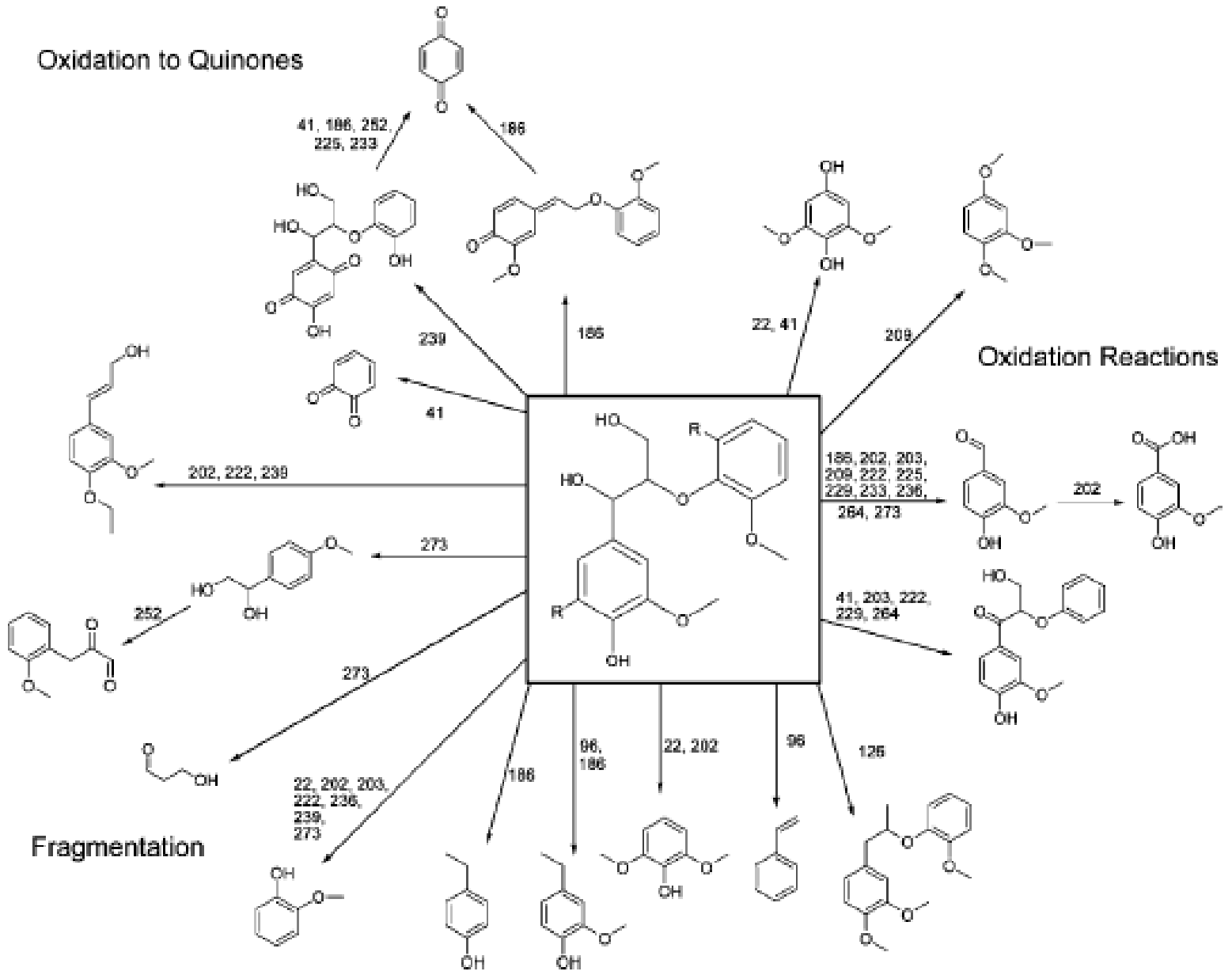


Pretreatment

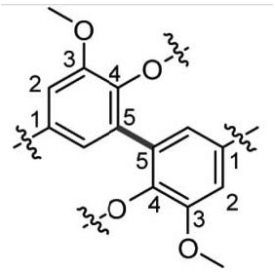
Kraft Process	high pHs, NaOH, Na_2S, 423 - 453 K, by MeadWestvaco, and LignoBoost technology. 5-5’ bond **typically survive and even forming** during kraft pulping process
Lignosulfonate Process	pH between 2 and 12, sulfite with Ca or Mg as counterion, product typically soluble in water or high polar organics and amines, incorporating **sulfonate groups**
Organosolv Process	Treatment of wood or bagasse, crushed to extract juice or sap, forms separate streams of cellulose, hemicelluloses and lignin, usually form derivatives
Many more	Many many many

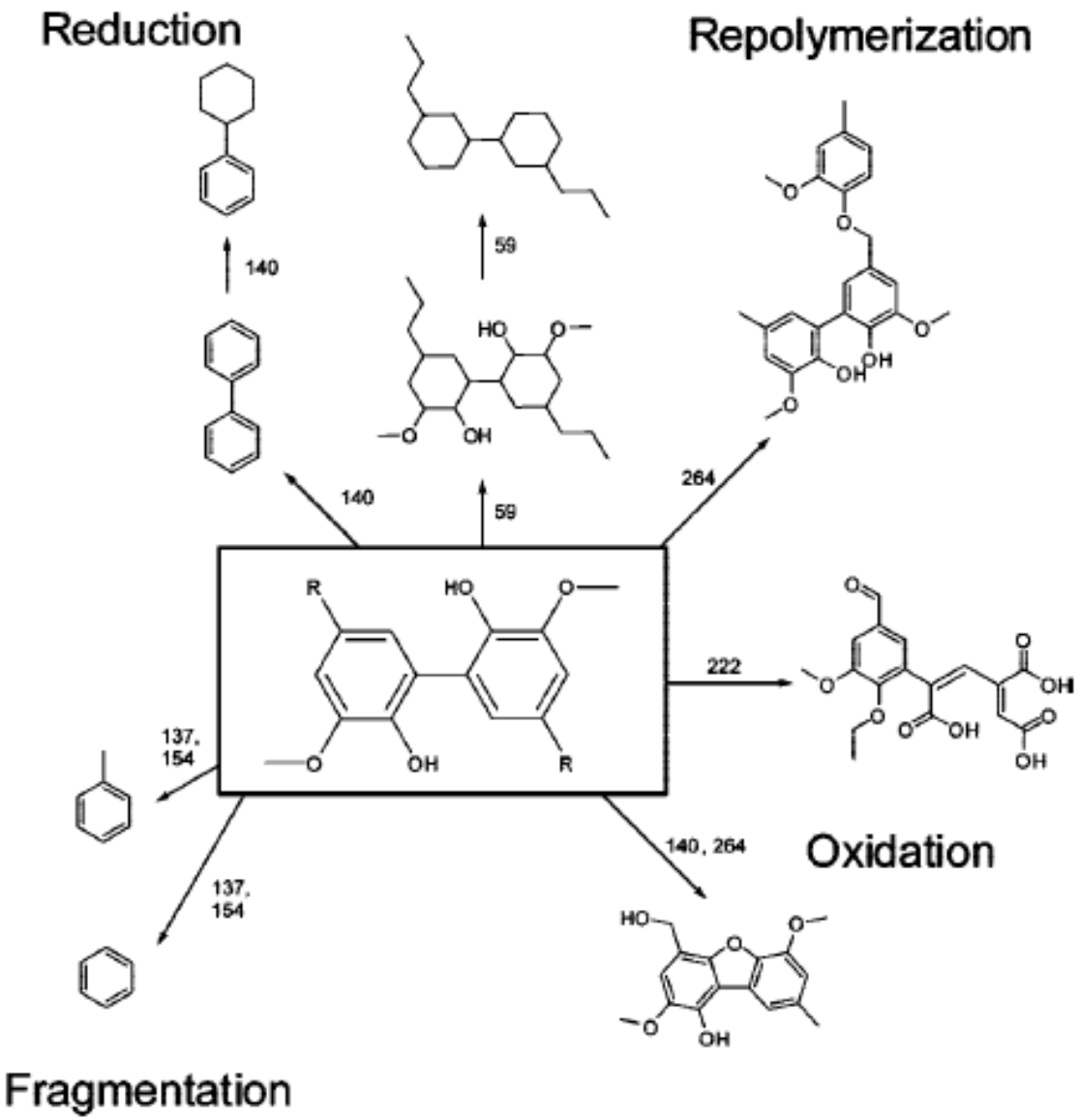
β-O-4 Linkage


HO
β
R
α
O
4
O
O
O

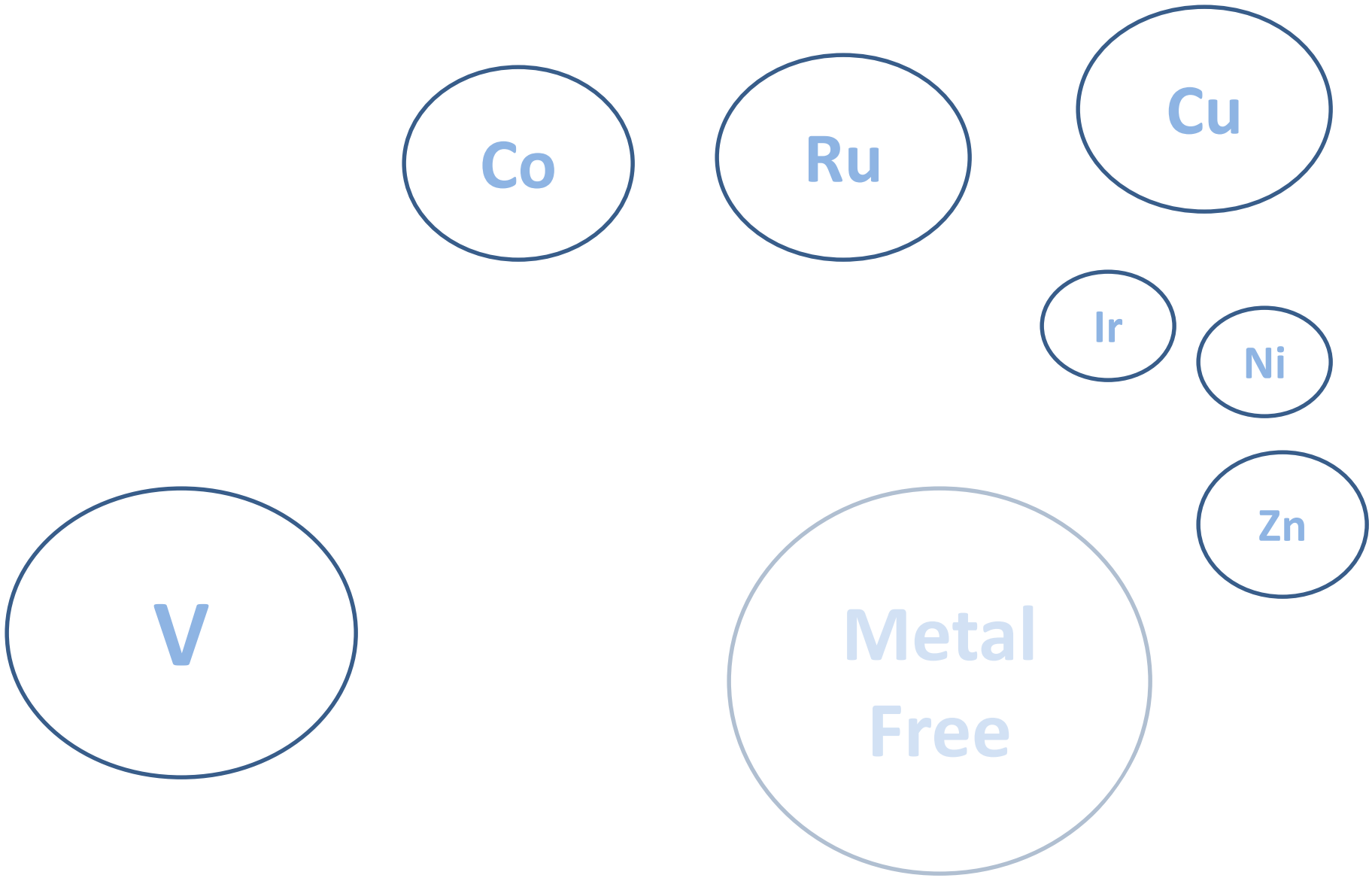

Oxidation to Quinones
41, 186, 252, 225, 233
186
239
41
186
22, 41
209
Oxidation Reactions
202, 222, 239
273
252
273
186, 202, 203, 209, 222, 225, 229, 233, 236, 264, 273
202
41, 203, 222, 229, 264
96, 186
22, 202
96
126
186
22, 202, 203, 222, 236, 239, 273
Fragmentation

5-5’ linkage

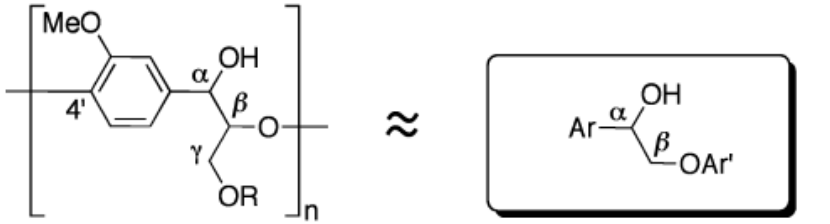



Reduction
Repolymerization
140
59
140
59
264
222
137,
154
137,
154
140, 264
Oxidation
Fragmentation

Valorization

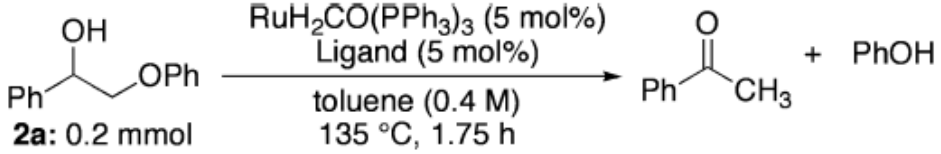


Ruthenium



1: poly(*β*-[O]-4'-glycerolaryl ether) **2:** "*β*-[O]-4'-ethanolaryl ether"

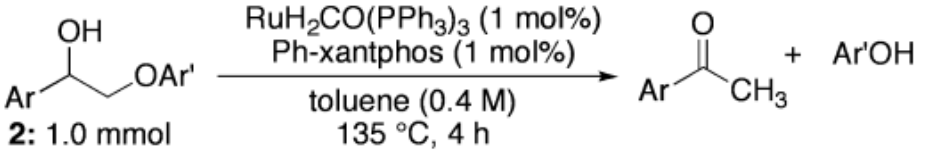
Table 1. Ligand Screening for C–O Bond Cleavage of **2a**

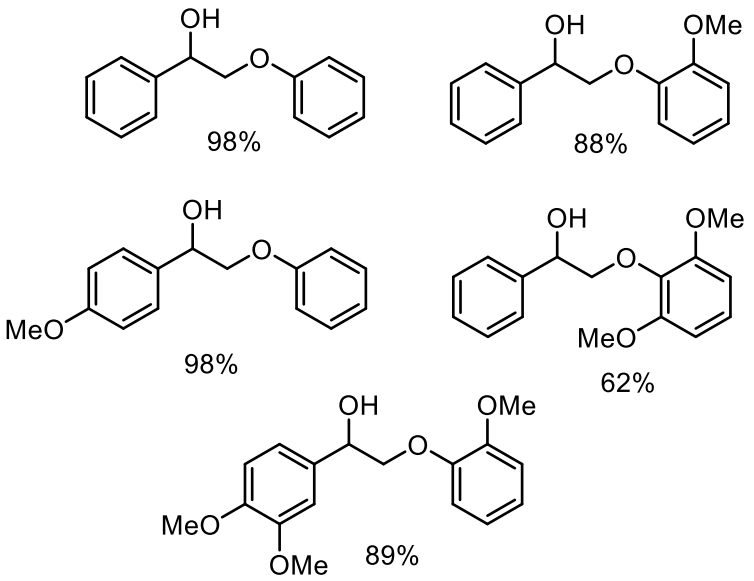


entry[a]	ligand	conv.,[d] (%)	yield (%)[c,d] PhCOMe	yield (%)[c,d] PhOH
1	none	45	5	6
2	PPh_3[b]	39	<1	5
3	PCy_3[b]	27	4	5
4	dppm	11	0	0
5	dppp	32	0	<1
6	dppbz	32	0	0
7	dppf	37	5	6
8	Ph-xantphos	>99	>99	>99

[a] Reactions were run in sealed tubes under nitrogen. [b] 2 equiv relative to Ru. [c] Yields and conversions were determined by GC/MS relative to an internal standard. [d] Average of two duplicate experiments.

Table 2. C–O Bond Cleavage of Various 2-Aryloxy-1-arylethanols



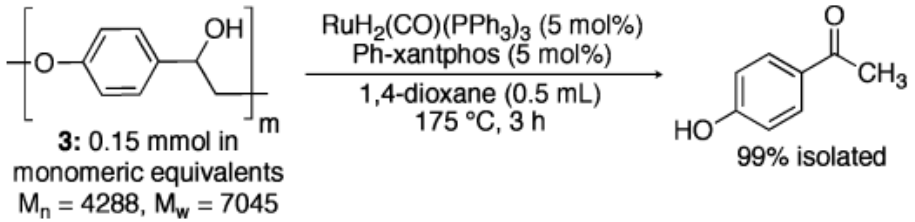


[a] Average isolated yield of the corresponding ketone based on two duplicate experiments.

Bergman and Ellman, *J. Am. Chem. Soc.* **2010**, *132*, 12554

Ruthenium

Scheme 1. Depolymerization of Lignin-Related Polymer



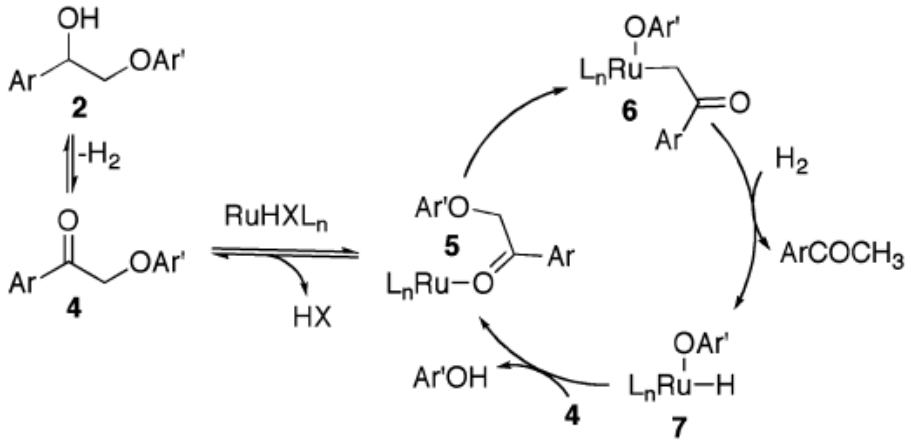
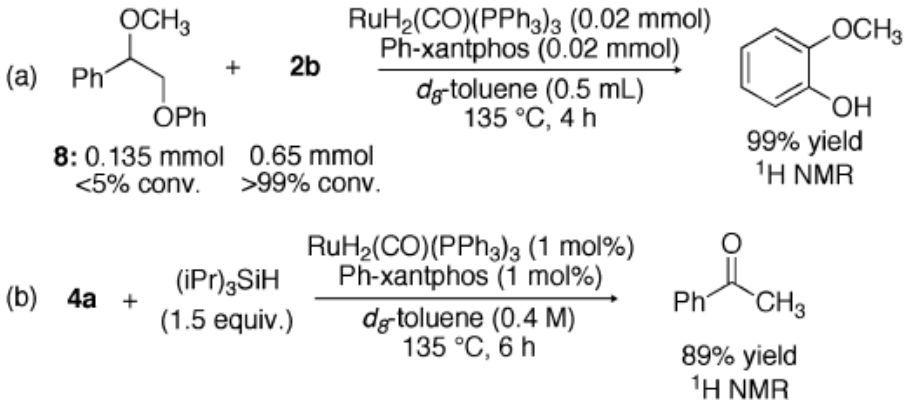
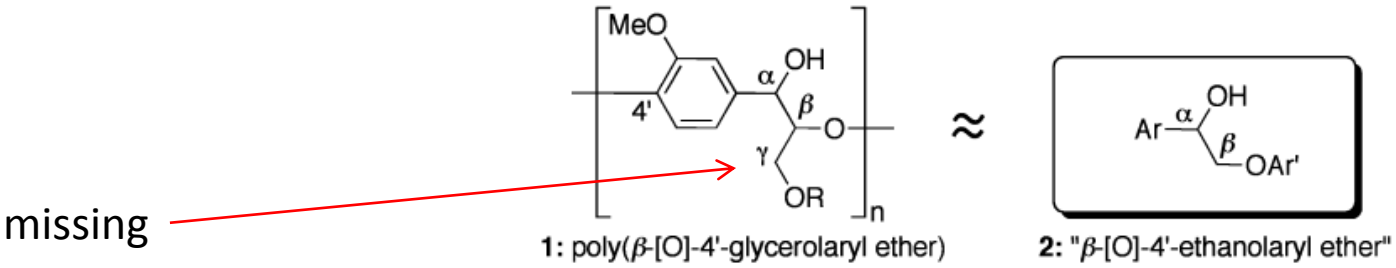


Figure 2. Mechanistic rationale for C–O bond cleavage.

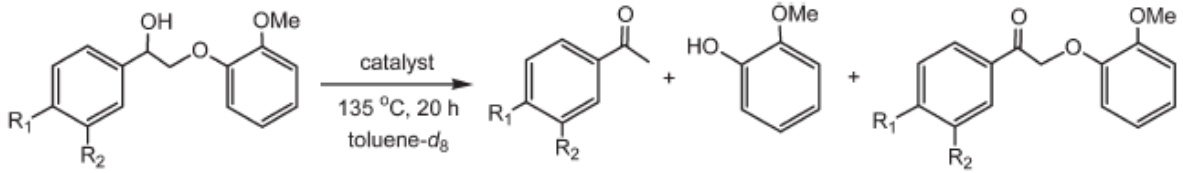
Scheme 2. (a) Blocking Formation of **4a** Prevents C–O Cleavage; (b) Hydrosilylation of **4a** Yields C–O Cleavage





Bergman and Ellman, *J. Am. Chem. Soc.* **2010**, *132*, 12554

Ruthenium



Scheme 3 Catalysed hydrogenolysis of **1–3**.

Table 2 Catalysed hydrogenolysis of **1–3** (see Scheme 3)

Entry	Substrate[a]	Catalyst	Gas[b]	Conversion[c]	**14/15/16**[c]	**17**	**4/5/6**[c]
I	1	[d]	N_2 or Ar	100	97–98	93	0–3
II	2	[d]	N_2	100	91	90	7
III	3	[d]	N_2	100	54	68	21
IV	1	[d]	H_2	91	44[g]	87	0
V	1	[e]	N_2 or Ar	100	95–99	93–97	0–5
VI	2	[e]	N_2	100	77	79	12
VII	3	[e]	N_2	100	63	76	17
VIII	1	[e]	H_2	100	27[h]	95	0
IX	1	[f]	N_2	29	7	10	19

[a] 0.20 M. [b] 1 atm. [c] Average % conversion/yield (by ^{1}H NMR integration) of duplicate experiments. [d] 5 mol% [$Ru(H)_2(CO)(PPh_3)_3$/xantphos]. [e] 5 mol% $Ru(H)_2(CO)(PPh_3)$(xantphos) (**18**). [f] 5 mol% $Ru(H)_2(CO)(PPh_3)_3$. [g] Yield of $PhCH(OH)CH_3$ = 39%. [h] Yield of $PhCH(OH)CH_3$ = 61%.

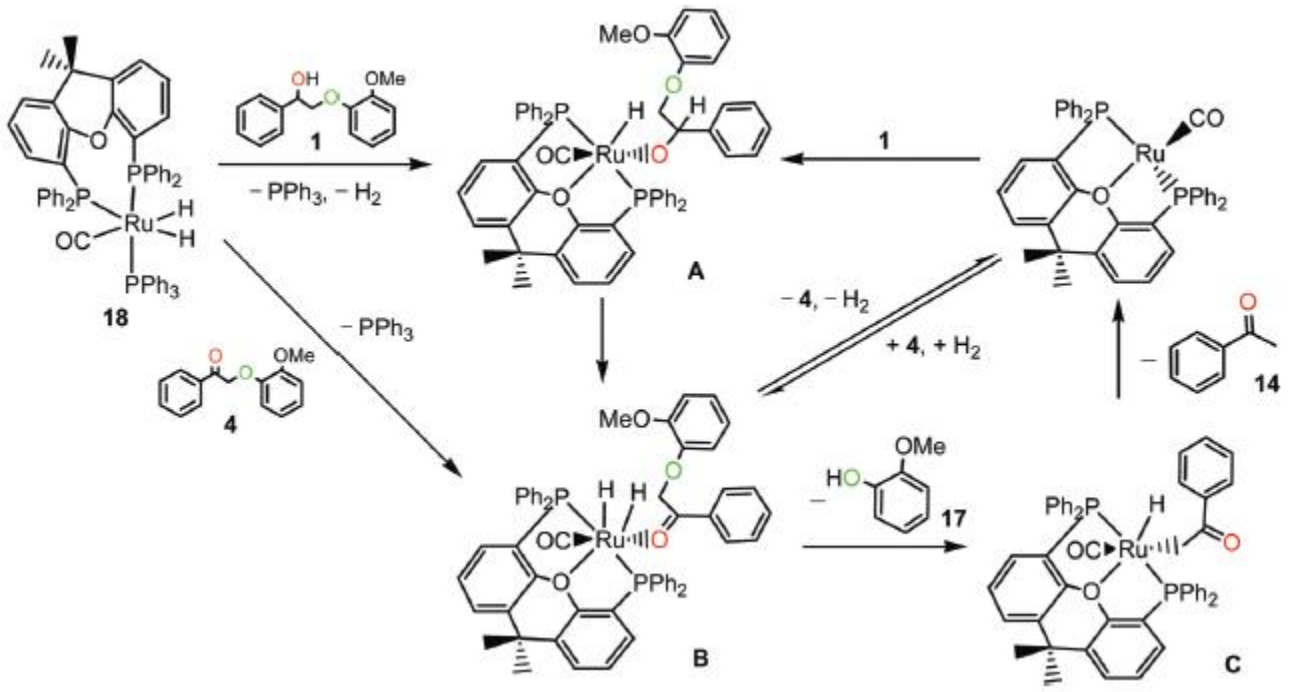
Table 3 Catalysed hydrogenolysis of **4–6** (*cf.* Scheme 3)

Entry	Substrate[a]	Catalyst	Gas[b]	Conversion[c]	**14/15/16**[c]	**17**[c]
I	4	[d,e]	H_2	100	77–85	88–89
II	5	[d,e]	H_2	90–100	79–89	88–99
III	6	[d,e]	H_2	77–91	68–83	75–90
IV	4	[d,e]	N_2	17–23	8–13	15
V	4	[f]	N_2	13	8	13
VI	4	[f]	H_2	63	11[g]	16

[a] 0.20 M. [b] 1 atm. [c] Average % conversion/yield (by ^{1}H NMR integration) of duplicate experiments. [d] 5 mol% [$Ru(H)_2(CO)(PPh_3)_3$/xantphos]. [e] 5 mol% $Ru(H)_2(CO)(PPh_3)$(xantphos) (**18**). [f] 5 mol% $Ru(H)_2(CO)(PPh_3)_3$. [g] Yield of **1** = 47%.

James, *Dalton Trans.*, **2012**, *14*, 11093.

Ruthenium



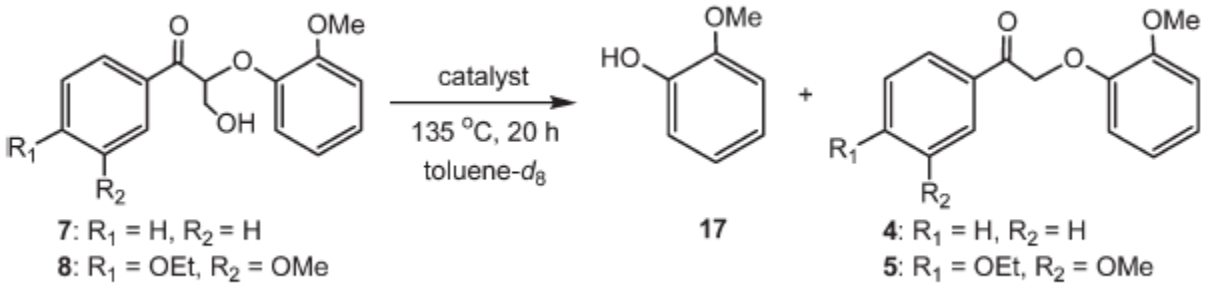
James, *Dalton Trans.*, **2012**, *14*, 11093.

Ruthenium

Table 4 Catalysed reactions of 7 and 8

Entry	Substrate[a]	Catalyst	Gas[b]	Conversion[c]	17[c]	4/5[c]
I	7	[d]	H_2 or Ar	71–81	11–15	17–23
II	8	[d]	H_2 or Ar	68–70	7–8	5–11
III	7	none	H_2 or Ar	9–12	0	3–7
IV	7	[e]	H_2 or Ar	24–32	0	9–13
V	7	[f]	H_2 or Ar	51–59	3–5	16–24

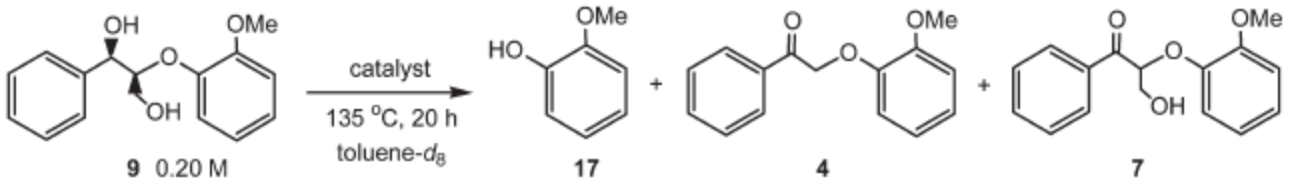
[a] 0.20 M. [b] 1 atm. [c] Average % conversion/yield (by ^{1}H NMR integration) of duplicate experiments. [d] 5 mol% **18**. [e] 5 mol% xantphos. [f] 5 mol% $Ru(H)_2(CO)(PPh_3)_3$.



7: R_1 = H, R_2 = H
8: R_1 = OEt, R_2 = OMe

4: R_1 = H, R_2 = H
5: R_1 = OEt, R_2 = OMe

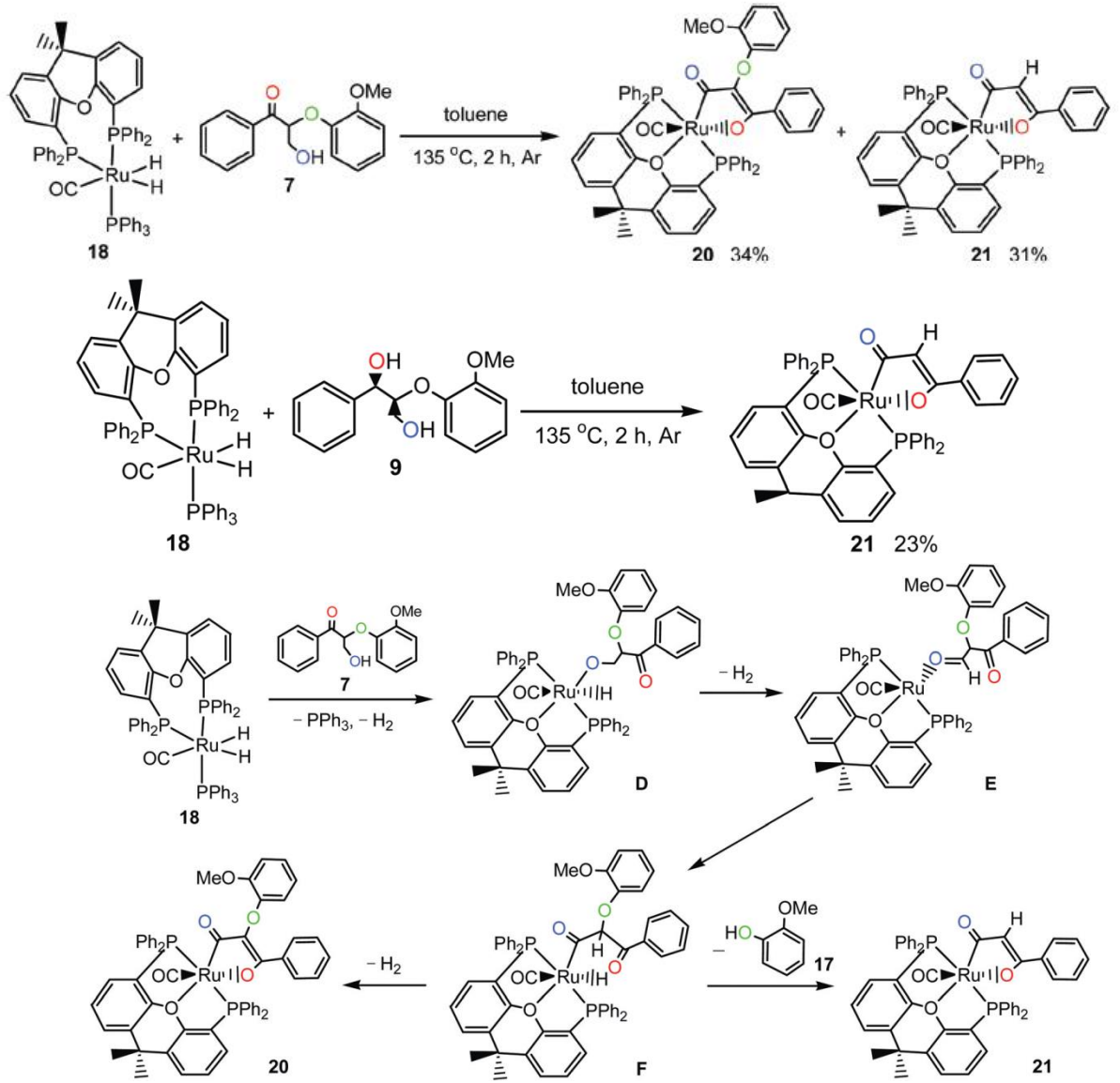
Scheme 5 Catalysed reactions of 7 and 8.



Scheme 6 Catalysed reactions of 9.

James, *Dalton Trans.*, **2012**, *14*, 11093.

Ruthenium

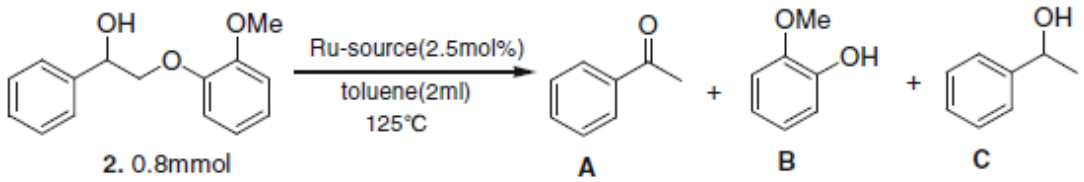


γ-OH poison the catalyst

James, *Dalton Trans.*, **2012**, *14*, 11093.

Ruthenium

Table 1 C–O bond cleavage of 2-(2-methoxyphenoxy)-1-phenylethanol catalyzed by $RuHCl(CO)(PPh_3)_3$ with and without KOH



Entry[a]	Ru-source (2.5 mol%)	KOH (50 mol%)	Cons. (%)[b]	Yield %[b]			Time (h)
				A	B	C	
1	None	Y	60	12	6	10	12
			57	15	9	15	24
			62	13	11	15	36
			70	15	7	16	48
2	$RuHCl(CO)(PPh_3)_3$	Y	50	38	15	0	12
			74	62	39	0	24
			93	80	75	0	36
			95	71	65	0	48
3	$RuHCl(CO)(PPh_3)_3$	N	0	0	0	0	36
4	$Ru(H)_2(CO)(PPh_3)_3$	Y	97	63	16	0	48

[a] Reactions were run in a Schlenk flask under an atmosphere of purified argon equipped with condenser

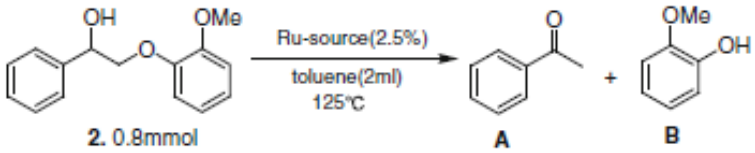
[b] Yields and consumptions were determined by GC relative to an internal standard

In Bergman & Ellman's SI, condition entry 3 also afforded no reactivity

Li, *Catal. Lett.*, **2015**, *144*, 1159.

Ruthenium

Table 4 C–O Bond Cleavage of 2-(2-methoxyphenoxy)-1-phenylethanol catalyzed by other Ru-complex with and without KOH



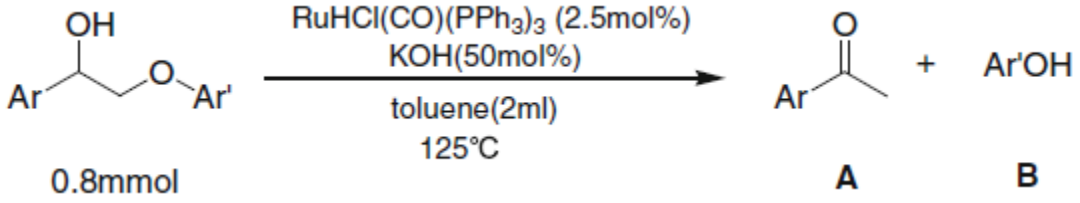
Entry[a]	Ru-source (2.5 mol %)	KOH (50 mol %)	Cons. (%)[b]	Yield %[b]		Time (h)
				A	B	
1	$RuH_2(CO)(PPh_3)_3$	Y	97	63	16	48
		N	30	12	13	48
2	$RuCl_2(PPh_3)_3$	Y	79	57	34	48
		N	26	0	0	48
3	$RuCl_2(COD)$	Y	82	62	24	48
		N	10	0	0	48
4	$Ru(methallyl)_2(COD)$	Y	79	56	26	48
		N	10	2	2	48
5	$RuClCp(PPh_3)_3$	Y	54	24	16	48
		N	8	0	0	48
6	$RuH_2(PPh_3)_4$	Y	56	22	11	48
		N	21	0	3	48
7	$Ru_3(CO_{12})$	Y	56	34	24	48
		N	0	0	0	48

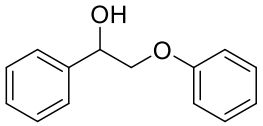
[a] Reactions were run in a Schlenk flask under an atmosphere of purified argon equipped with condenser

[b] Yields and consumptions were determined by GC relative to an internal standard

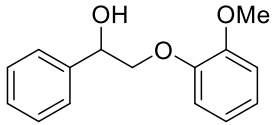
Li, *Catal. Lett.*, **2015**, *144*, 1159.

Ruthenium

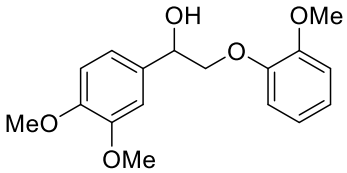




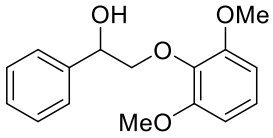
A: 86%, **B**: 84%



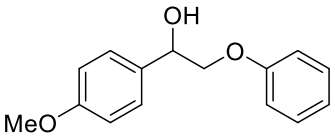
A: 80%, **B**: 75%



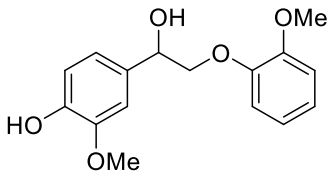
A: 66%, **B**: 45%



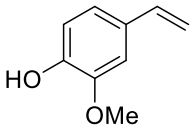
A: 30%, **B**: 4%



A: 80%, **B**: 77%



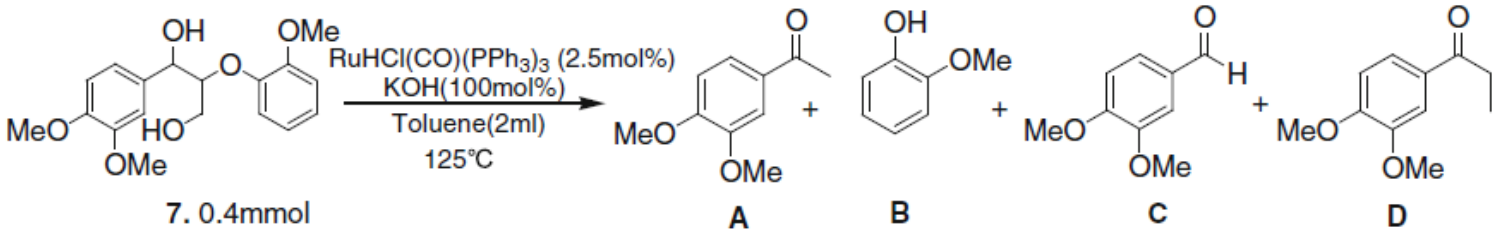
A: 0%, **B**: 14%



Li, *Catal. Lett.*, **2015**, *144*, 1159.

Ruthenium

Table 3 C–O bond cleavage of 2-(2-methoxyphenoxy)-1-(3,4-dimethoxy)phenyl-1,3-propanediol



7. 0.4mmol

A B C D

Ru-source (2.5 mol %)	Cons. (%)[b]	Yield %[b]				Time (h)
		A	B	C	D	
$RuHCl(CO)(PPh_3)_3$[a]	95	4	18	5	N[c]	12
	94	6	26	7	N[c]	24
	89	6	26	8	N[c]	36
	91	4	53	11	N[c]	48

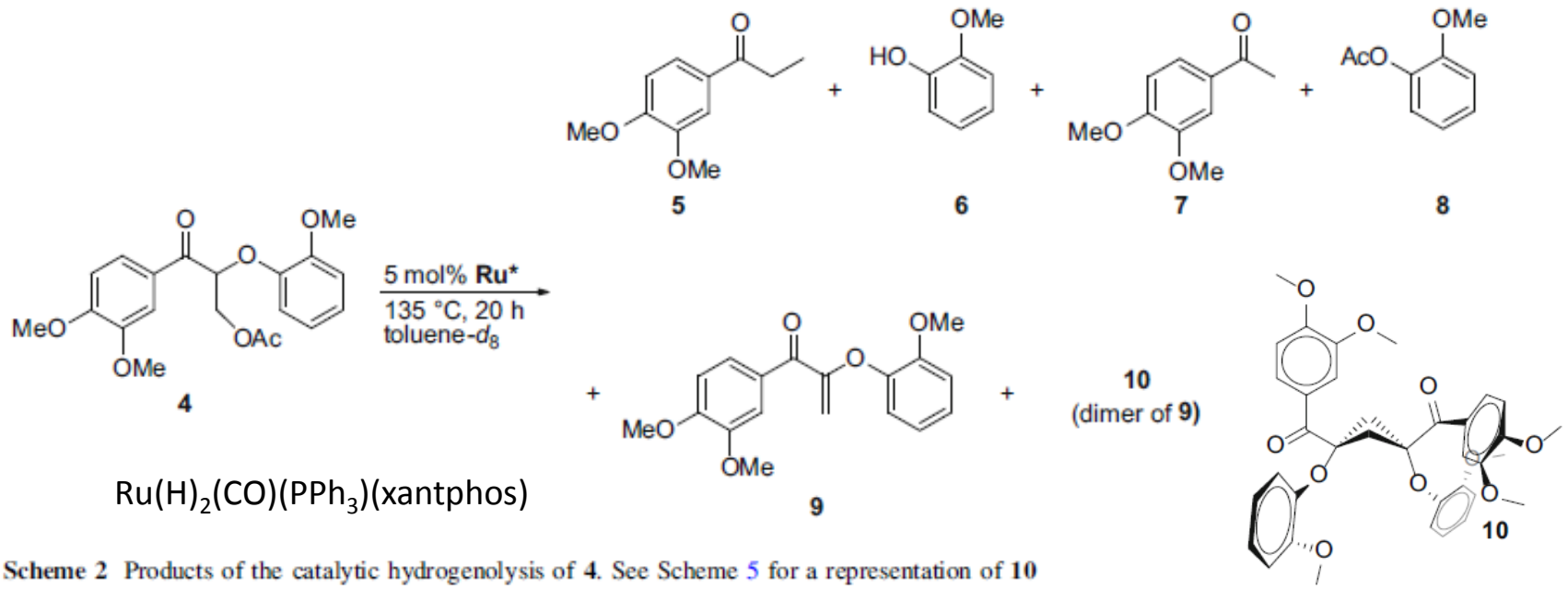
[a] Reactions were run in a Schlenk flask under an atmosphere of purified argon equipped with condenser

[b] Yields and consumptions were determined by GC relative to an internal standard

[c] Minor and not quantitated

Li, *Catal. Lett.*, **2015**, *144*, 1159.

Ruthenium



$Ru(H)_2(CO)(PPh_3)$(xantphos)

Scheme 2 Products of the catalytic hydrogenolysis of **4**. See Scheme 5 for a representation of **10**

Table 1 Catalytic hydrogenolysis of **4** (Scheme 2) and 9 (Scheme 5) after 20 h

Entry	Substrate[a]	Catalyst	Gas[b]	Consumpn.[c]	5[c]	6[c]	7[c]	8[c]	9[c]	10[c]
I	**4**	**Ru***	Ar	100	9	20	25	24	17	≤39[d]
II	**4**	**Ru***	H_2	100	27	42	19	18	9	≤31[d]
III	**9**	**Ru***	Ar	85	8	13	0	0	–	72
IV	**9**	**Ru***	H_2	86	15	23	0	0	–	≤63[d]
V	**9**	None	Ar	81	0	<2	0	0	–	75
VI	**9**	None	H_2	82	0	<2	0	0	–	77

[a] 0.20 M

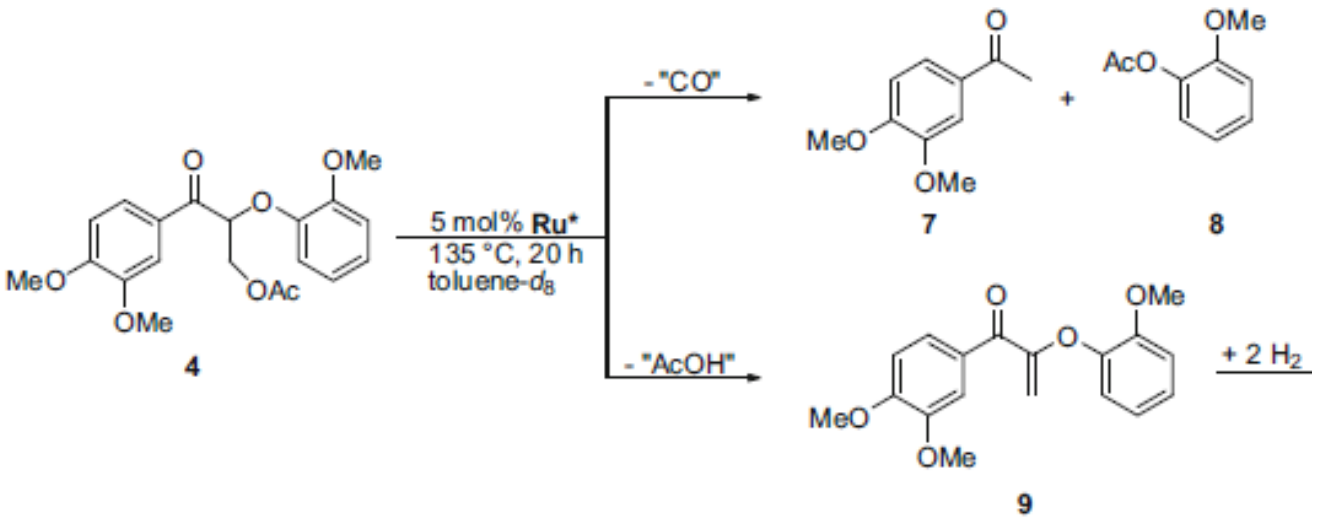
[b] 1 atm

[c] Average consumption and yield (average of duplicate experiments) determined by ^{1}H NMR integration

[d] Overlapping signals prevent determination of yield; the upper limit is given, based on mass balance

James, *Catal. Lett.*, **2015**, *145*, 511.

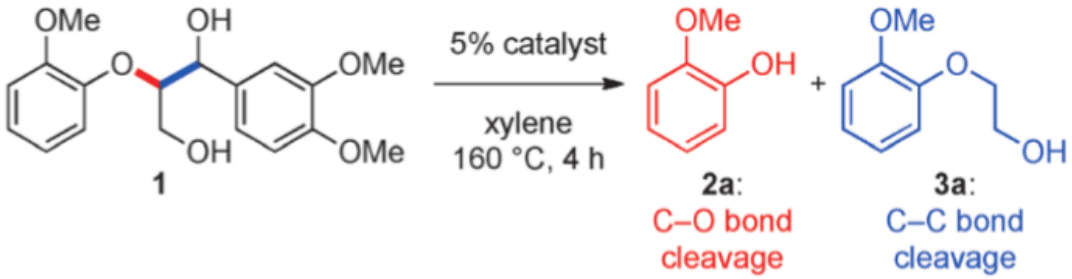
Ruthenium



James, *Catal. Lett.*, **2015**, *145*, 511.

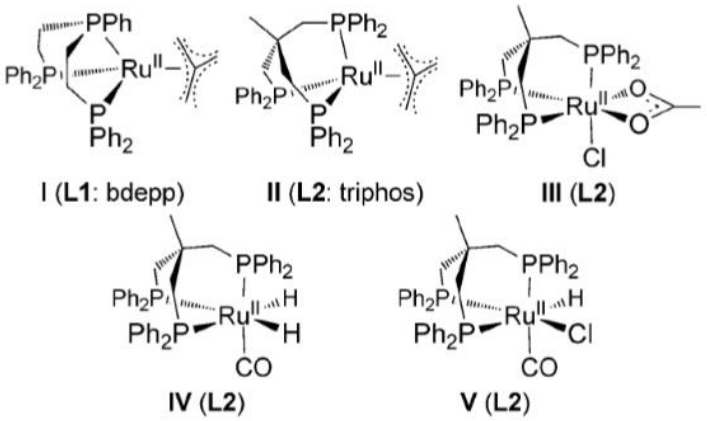
Ruthenium

Table 1: C–O and C–C bond cleavage of **1**.[a,b]



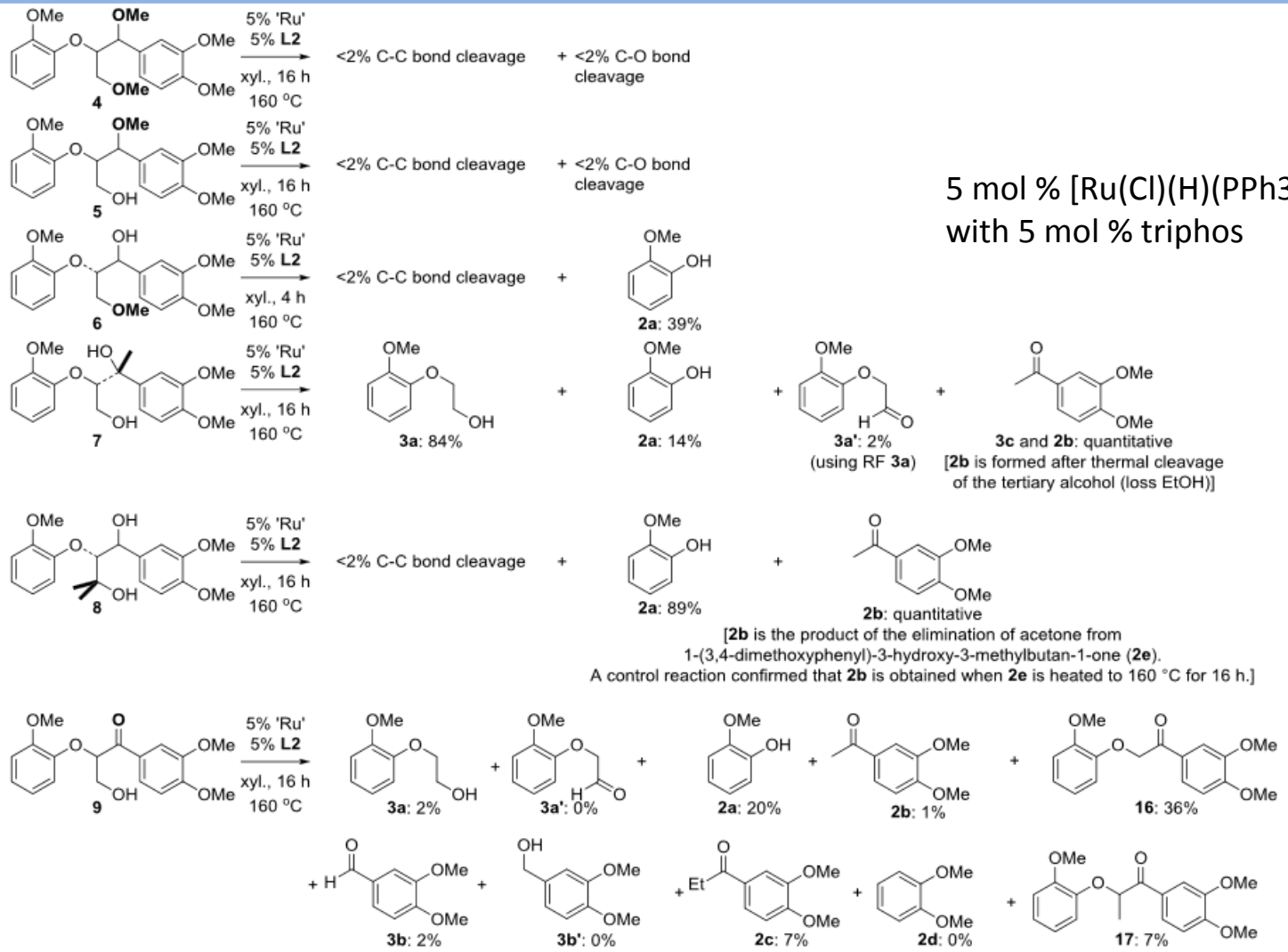
Entry	Precursor	Yield of **2a** [%][c]	Yield of **3a** [%][c]
1	**I**	28	4
2	**II**	14	21
3	**III**	5	24
4	**IV**	26	15
5	**V**	4	66

[a] Only the products containing the phenolic ring are shown. For a complete list of products from the reactions, see the Supporting Information. [b] Reaction conditions: **1** (0.1 mmol), *ortho*-xylene (0.5 mL). [c] The yield was determined by GC with dodecane as an internal standard.



Klankermayer, *Angew. Chem. Int. Ed.* **2015**, *54*, XXX

Ruthenium



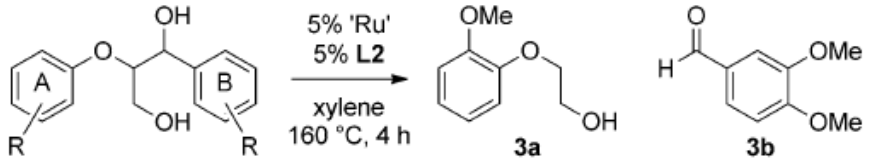
5 mol % [Ru(Cl)(H)(PPh3)]
with 5 mol % triphos

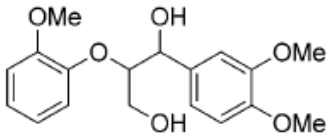
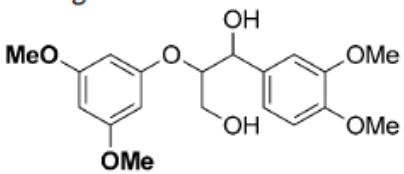
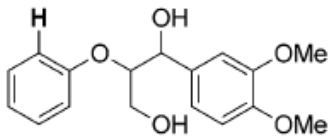
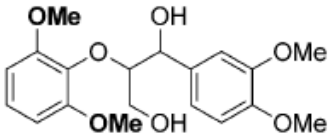
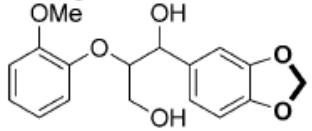
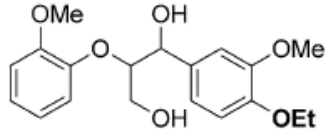
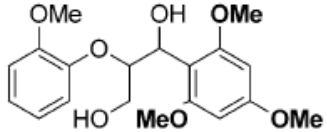
Scheme 2. Reactivity of [Ru(Cl)(H)(PPh_3)$_3$]/Triphos towards analogues of substrate **1**. The dotted bonds denote the bonds that will be broken. Reaction conditions: [Ru(Cl)(H)(PPh_3)$_3$] (5 mol%), substrate (0.1 mmol), *ortho*-xylene (0.5 mL); cat/**L** mixture was preheated for 2 h at 140 °C.

Klankermayer, *Angew. Chem. Int. Ed.* **2015**, *54*, XXX

Ruthenium

Table 3: Reactivity of [Ru(Cl)(H)(PPh_3)$_3$]/triphos towards substrates with various aryl substitution patterns.[a,b]



Entry	Substrate		Yield of **3a** [%][c]	Yield of **3b** [%][c]
1		**1**	77	75
variation of fragment A:				
2		**10**	–	86
3		**11**	–	63
4		**12**	–	26
variation of fragment B:				
5		**13**	94	–
6		**14**	75	–
7		**15**	14	–

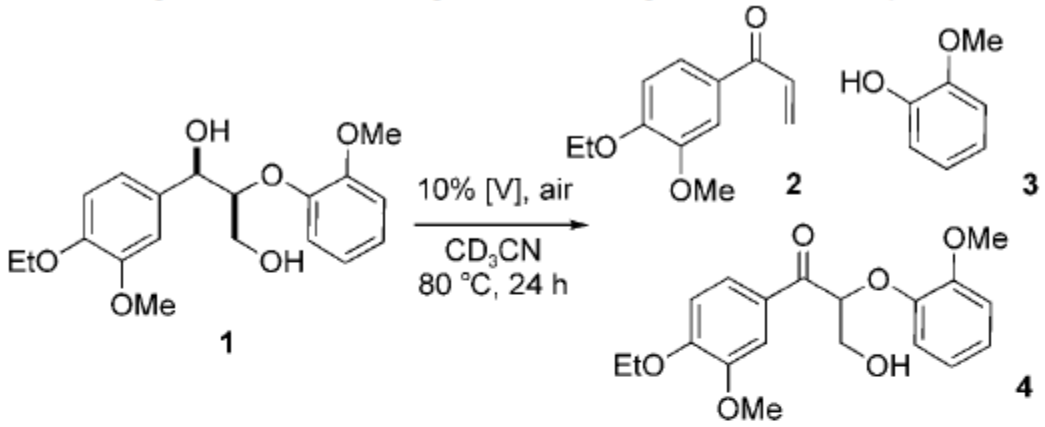
[a] For a complete list of products from the reactions, see the Supporting Information. [b] Reaction conditions: [Ru(Cl)(H)(PPh_3)$_3$] (5 mol%), substrate (0.1 mmol), *ortho*-xylene (0.5 mL); the catalyst/**L** mixture was preheated for 2 h at 140°C. [c] The yield of fragment **3a** or **3b** was determined by GC with dodecane as an internal standard.

5 mol % [Ru(Cl)(H)(PPh3)]
with 5 mol % triphos

Klankermayer, *Angew. Chem. Int. Ed.* **2015**, *54*, XXX

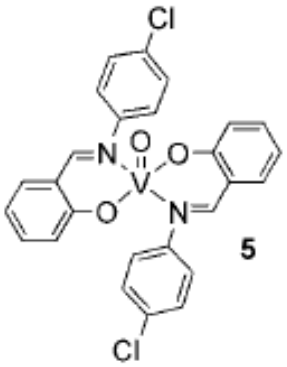
Vanadium

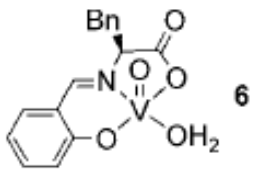
Table 1: Ligand effects on degradation of lignin model compound **1**.[a]

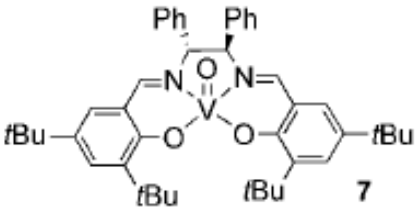


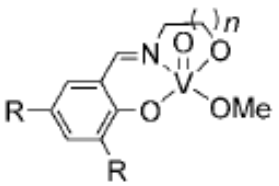
Entry	Vanadium catalyst	Conversion [%]	**2** [%]	**3** [%]	**4** [%]
1	none	0	–	–	–
2	$VOSO_4 \cdot xH_2O$	34	2	2	6
3	$VO(acac)_2$	79	13	22	31
4	$VO(OiPr)_3$	82	5	11	45
5	**5**	86	6	6	59
6	**6**	66	13	14	41
7	**7**	55	3	–	37
8	**8**	>95	61	45	27
9	**9**	86	70	62	8
10	**10**	95	65	50	18
11	**11**	>95	82	57	7

[a] Conversion and yields were determined by ^{1}H NMR spectroscopy versus an internal standard.







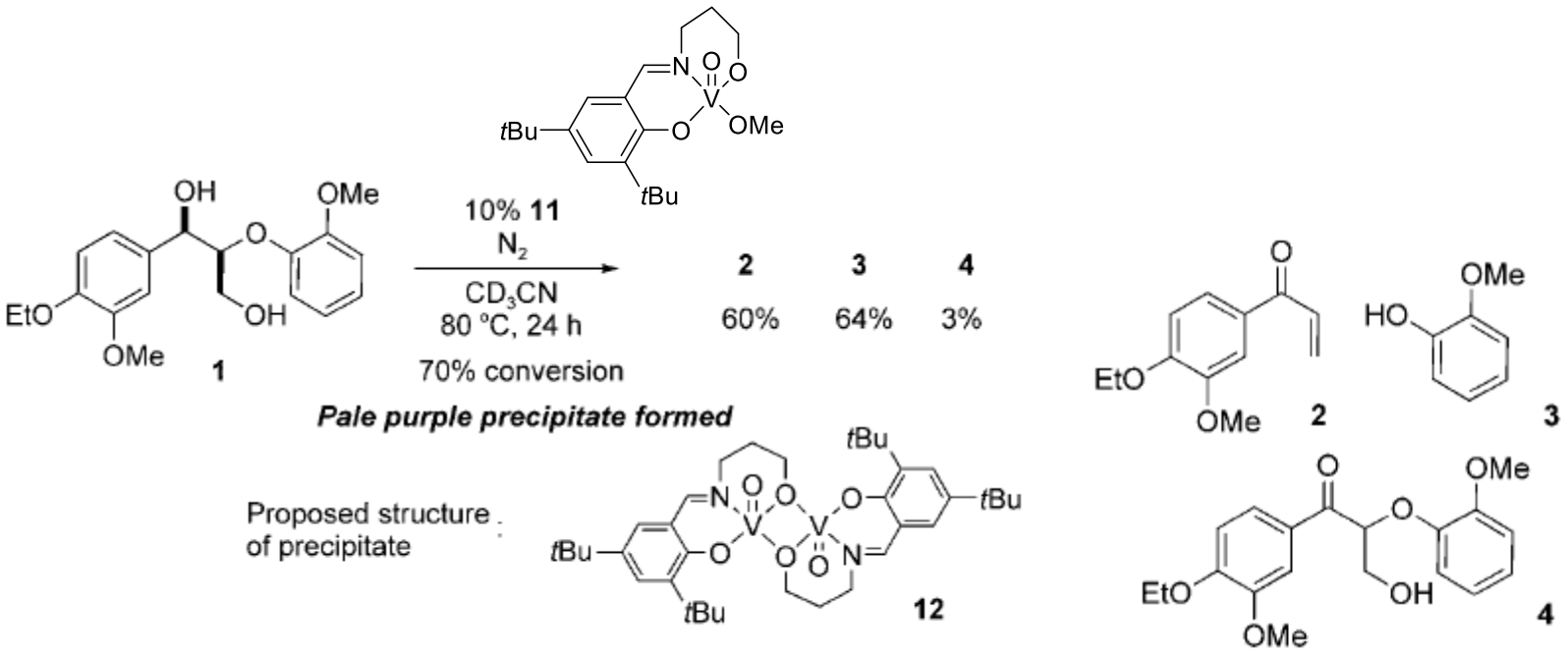


R= H *n*=1 **8**
2 **9**
R= *t*Bu 1 **10**
2 **11**

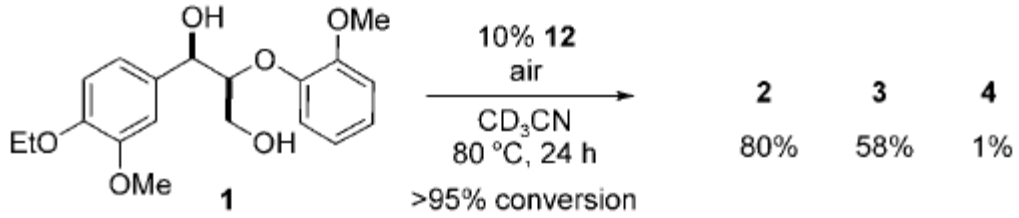
Toste, *Angew. Chem. Int. Ed.* **2010**, *49*, 3791

Toste, *ACS Catal.* **2013**, *3*, 1369

Vanadium



Scheme 1. Degradation of **1** under anaerobic conditions.

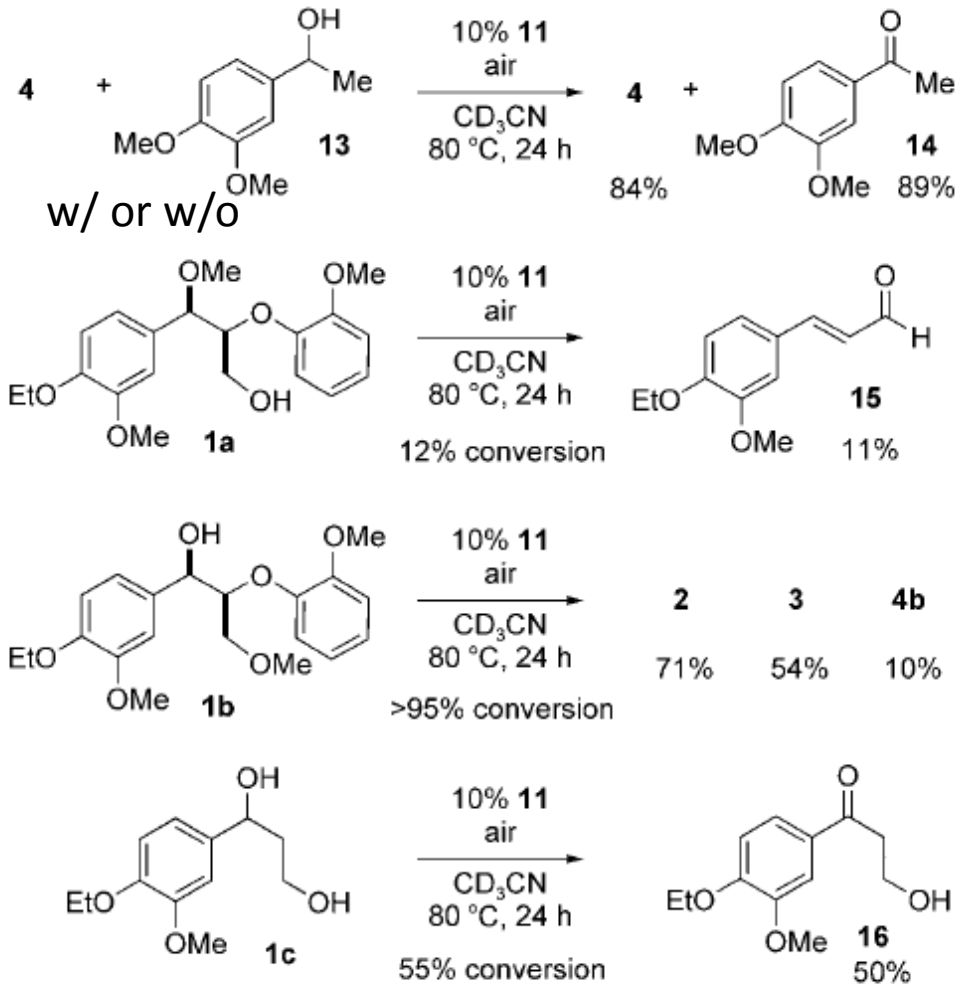


Scheme 2. Recovery of the reactivity of V^{IV} complex **12** under aerobic conditions.

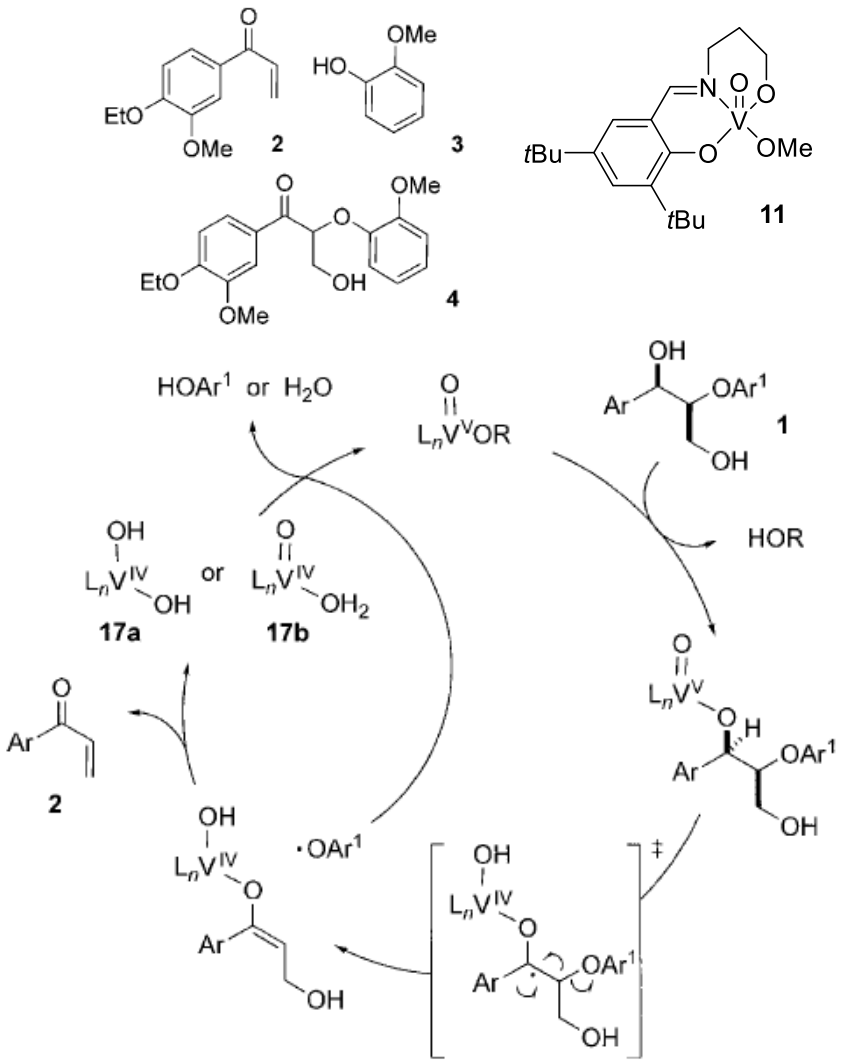
Toste, *Angew. Chem. Int. Ed.* **2010**, *49*, 3791

Toste, *ACS Catal.* **2013**, *3*, 1369

Vanadium



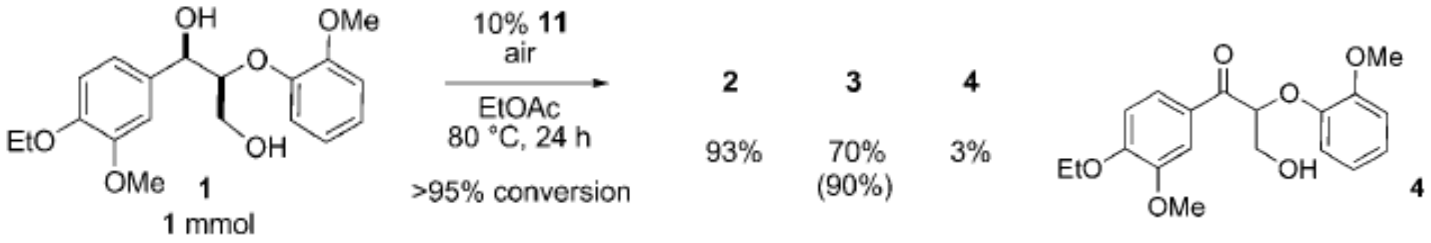
Scheme 3. Reactivity study of analogues of 1.



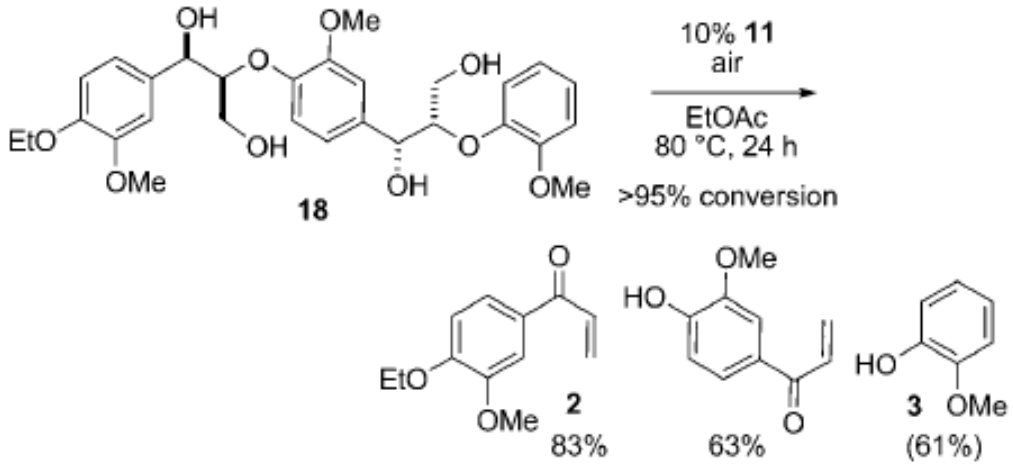
Toste, *Angew. Chem. Int. Ed.* **2010**, *49*, 3791

Toste, *ACS Catal.* **2013**, *3*, 1369

Vanadium



Scheme 5. Conversion of 1 on 1 mmol scale in a solvent without nitrogen atoms.

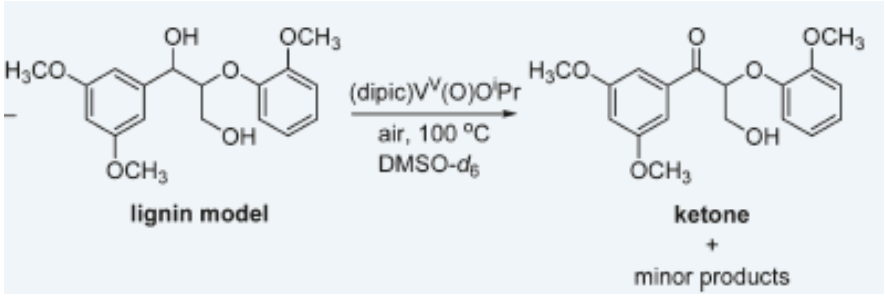


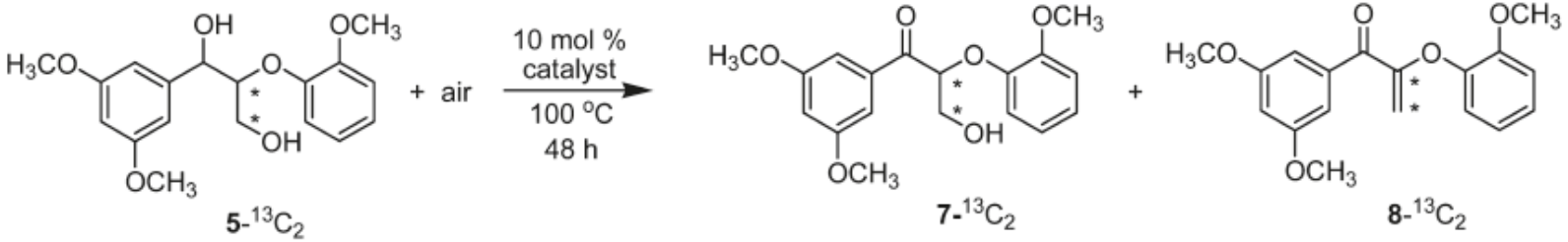
Scheme 6. Conversion of trimeric lignin model compound 18.

Toste, *Angew. Chem. Int. Ed.* **2010**, *49*, 3791

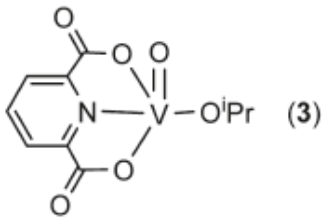
Toste, *ACS Catal.* **2013**, *3*, 1369

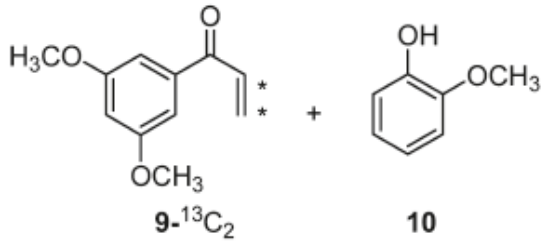
Vanadium



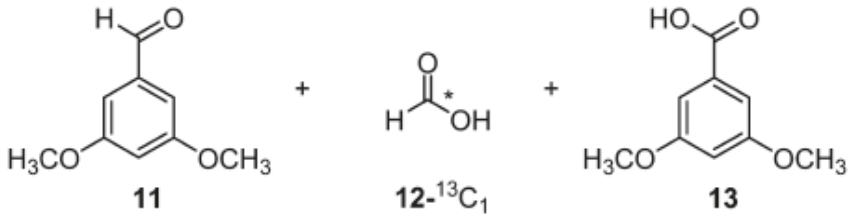


catalyst = $V^{V}(O)(O^{i}Pr)_3$ (**6**)





unable to quantify by ^{1}H NMR

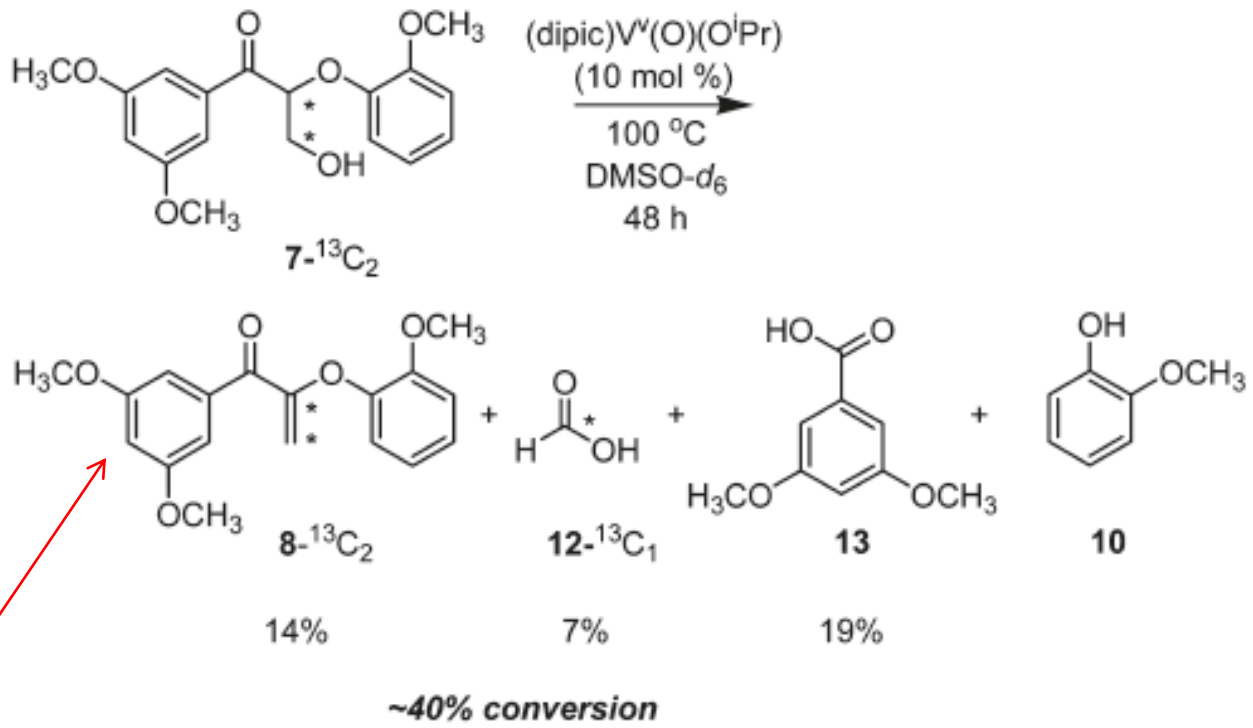


entry	catalyst	solvent	% conv.	7	8	9	11	12	13
1	6	DMSO-d_6	~75%	39		16	7	7	12
2	3	DMSO-d_6	>95%	65	5	14	2	4	11
3	3	pyr-d_5	~85%	27	14	29	4	<1	6

Baker, Gordan, Thorn, *Inorg. Chem.* **2010**, *49*, 5611

Hanson, *ACS Catal.* **2011**, *1*, 794

Vanadium

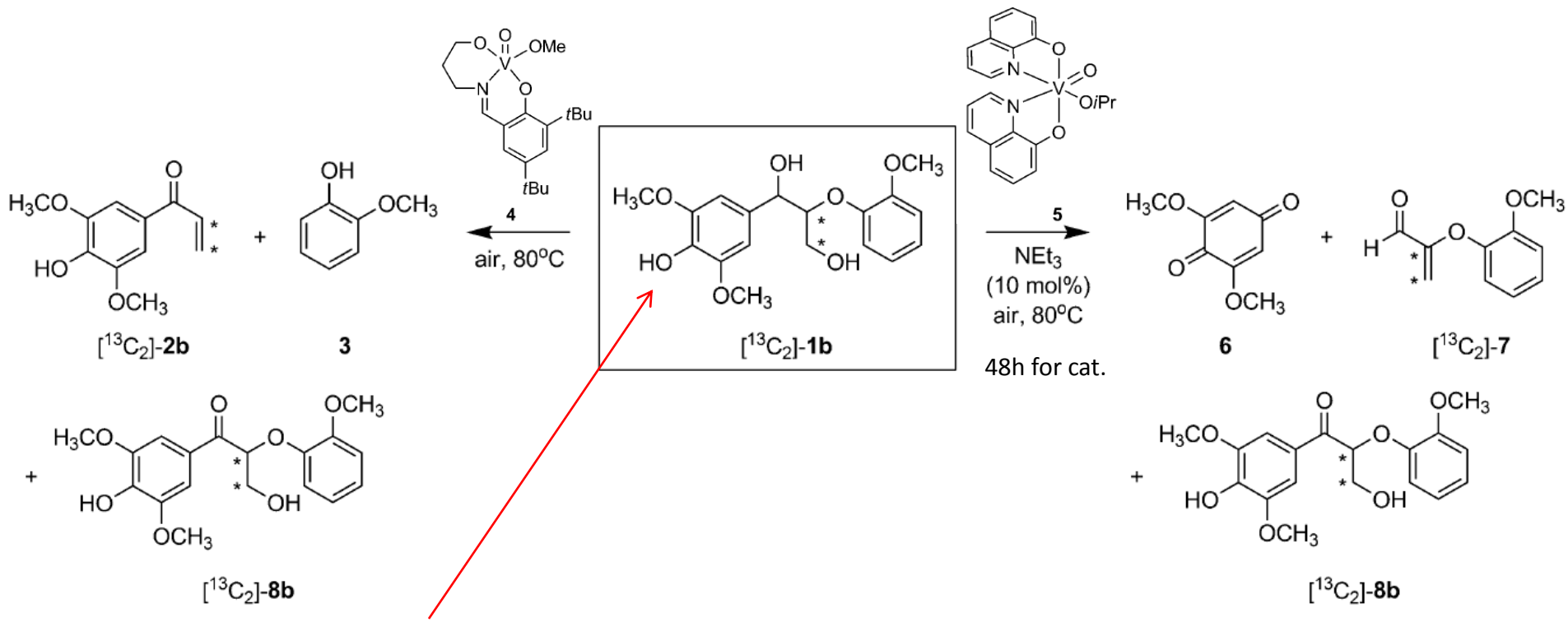


nonphenolic

Baker, Gordan, Thorn, *Inorg. Chem.* **2010**, *49*, 5611

Hanson, *ACS Catal.* **2011**, *1*, 794

Vanadium



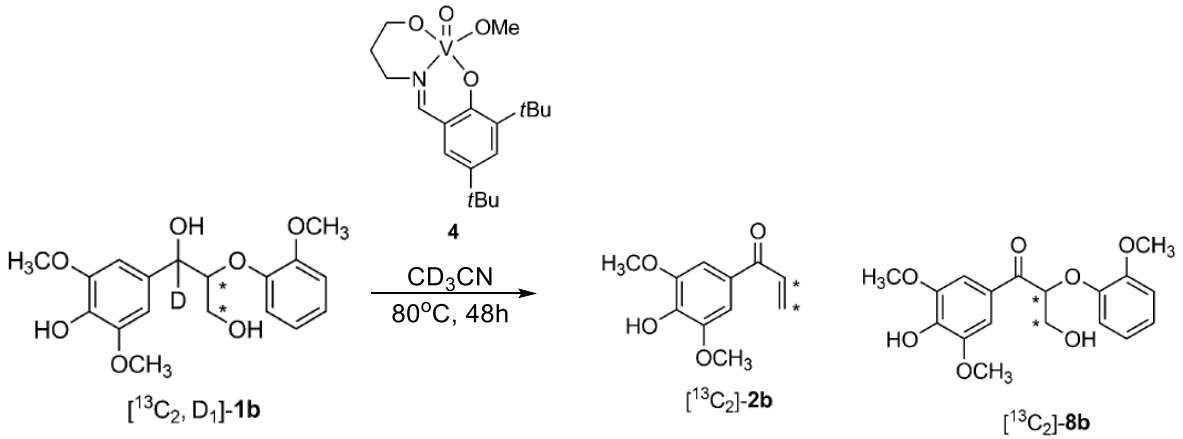
phenolic

1 *equiv* **4** in CD_3CN at 80°C for 48h, 28%, 43%
1 *equiv* **4** in pyridine at 80°C for 48h, 30%, 41%
10 mol % **4** in pyridine at 80°C for 48h, 32%, 44%

1 *equiv* **5** in pyridine at 80°C, 40%, 38%, 20%
10 mol % **5** in pyridine at 80°C for 48h, 30%, 34%, 27%
10 mol % **5** in EA at 80°C for 48h, 44%, 45%, 14%
10 mol % **5** in 2-MeTHF at 80°C for 48h, 26%, 45%, 11%

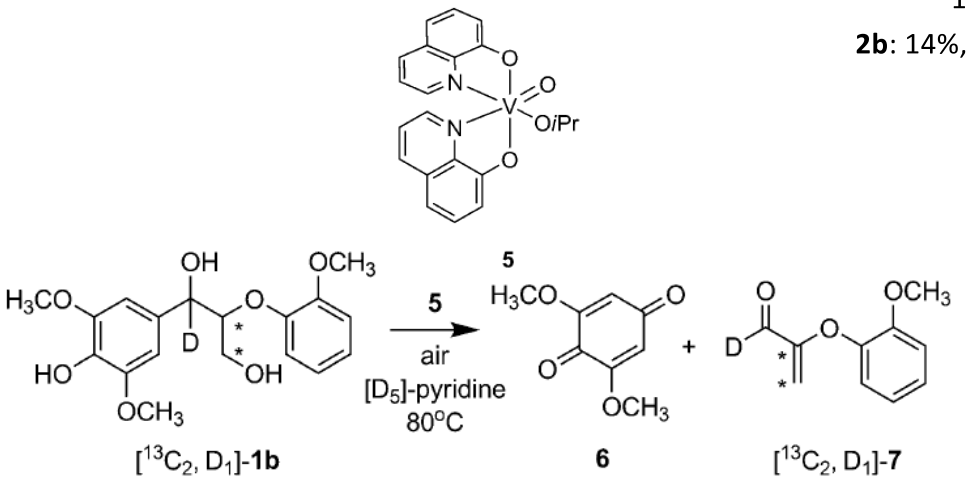
Hanson, *Angew. Chem. Int. Ed.* **2012**, *51*, 3410

Vanadium



1 *equiv* **4**, 56%. 83% for [^{13}C]-**1b**

2b: 14%, **8b**: 35%. **2b**:28%, **8b**:43% for [^{13}C]-**1b**

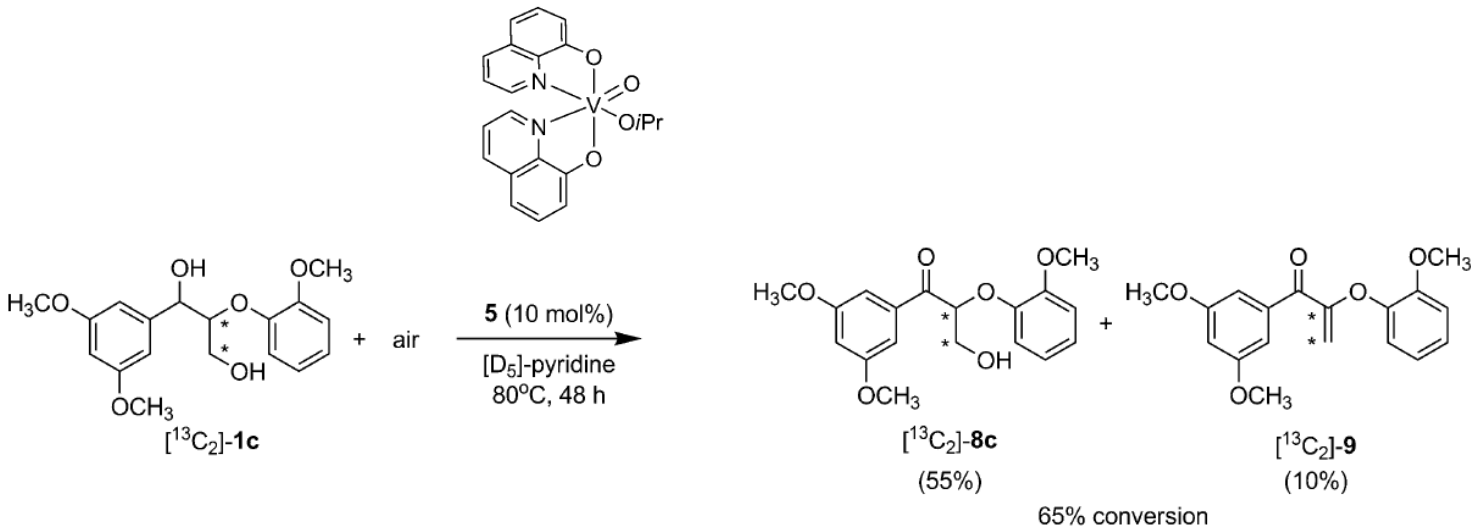


1 *equiv* **5**, **6**: 54%, **7**: 57%, **8b**: barely no.

6:40%, **7**:38%, **8b**: 20% for [^{13}C]-**1b**

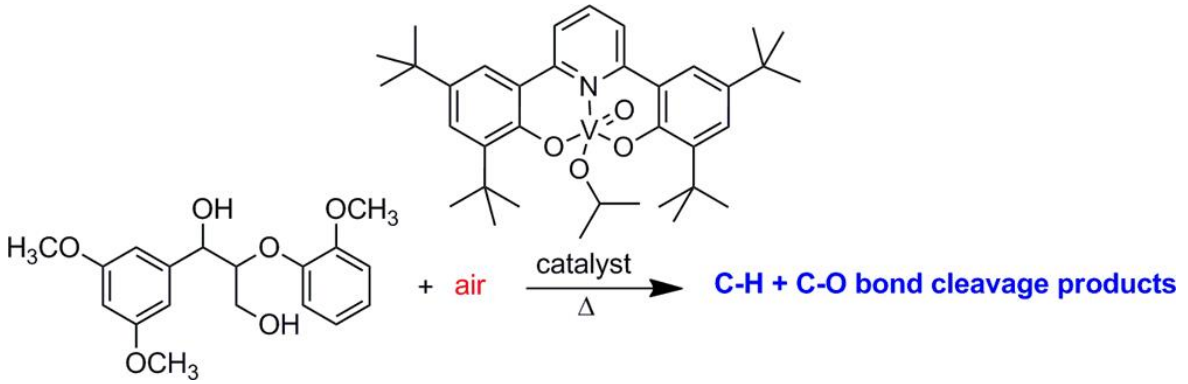
Hanson, *Angew. Chem. Int. Ed.* **2012**, *51*, 3410

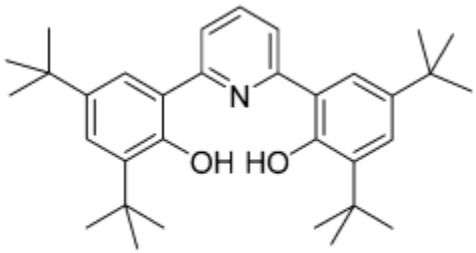
Vanadium



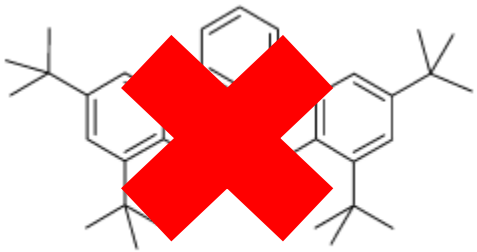
Hanson, *Angew. Chem. Int. Ed.* **2012**, *51*, 3410

Vanadium

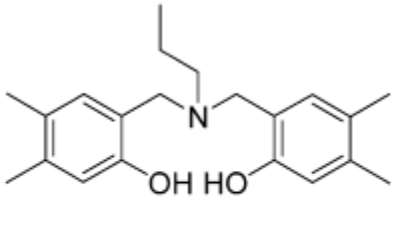




H_2BPP



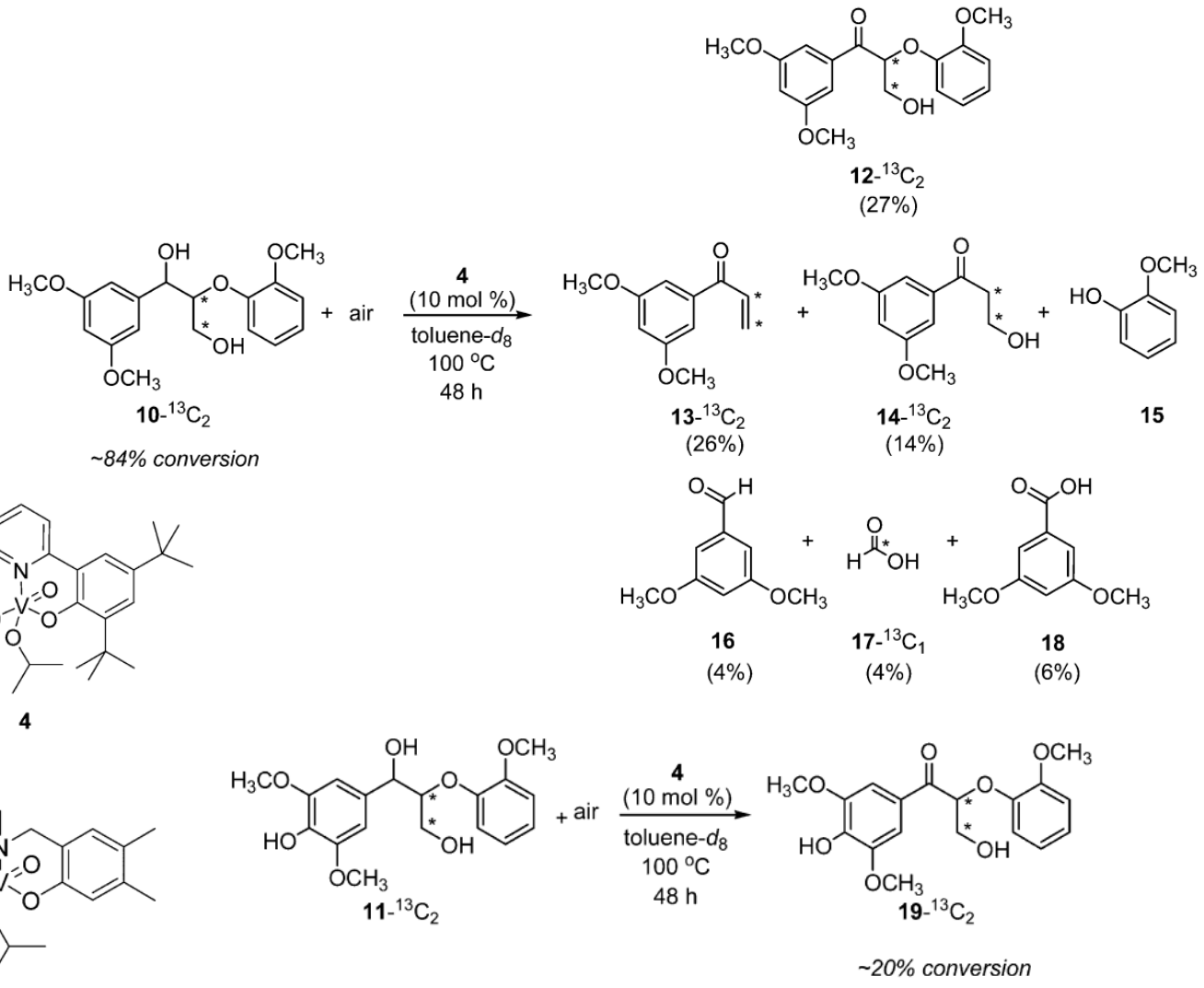
H_2BPB



H_2BPA

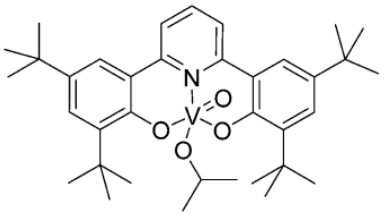
Hanson, *Inorg. Chem.* **2012**, *51*, 7354

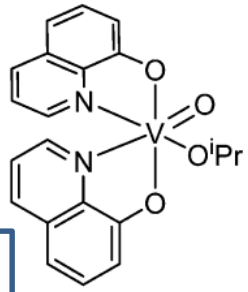
Vanadium



Hanson, *Inorg. Chem.* **2012**, *51*, 7354

Vanadium

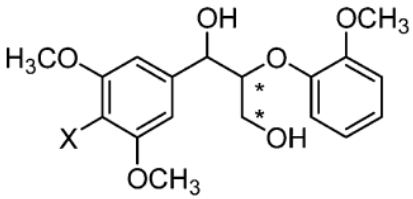




4

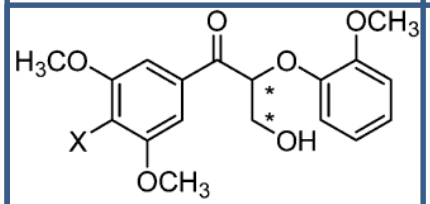
3

substrates:

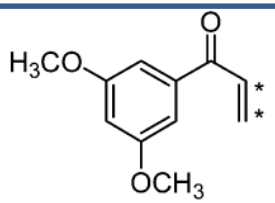


X = H (**10**-$^{13}C_2$)
= OH (**11**-$^{13}C_2$)

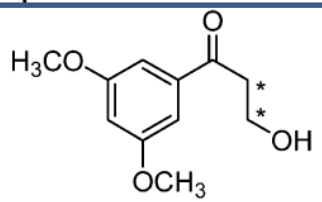
products:



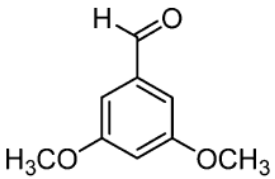
X = H (**12**-$^{13}C_2$)
= OH (**19**-$^{13}C_2$)



13-$^{13}C_2$



14-$^{13}C_2$



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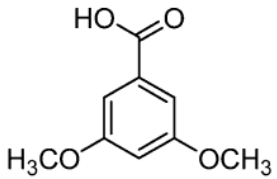

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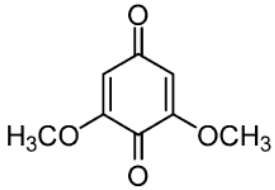

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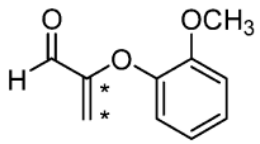


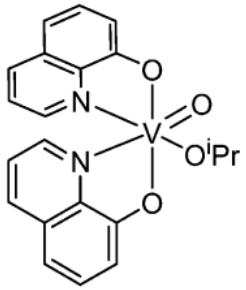
21-$^{13}C_2$

				percent yield							
entry	substrate	catalyst	% conv.	12	13	14	16	18	19	20	21
1	**10**-$^{13}C_2$	**3**[a]	65	55	0	0	0	0			
2	**10**-$^{13}C_2$	**4**[b]	84	27	26	14	4	6			
3	**11**-$^{13}C_2$	**3**[a]	100						27	30	34
4	**11**-$^{13}C_2$	**4**[b]	20						19	trace	trace

[a]Conditions: 10 mol % catalyst, pyridine-d_5, 80 °C, 48 h. [b]Conditions: 10 mol % catalyst, toluene-d_8, 100 °C, 48 h.

Hanson, *Inorg. Chem.* **2012**, *51*, 7354

Vanadium



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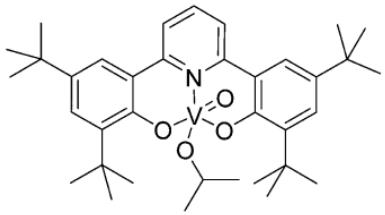

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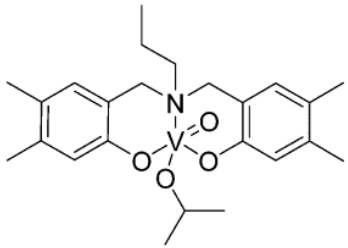
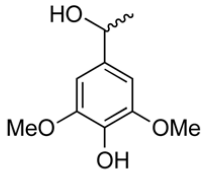


5

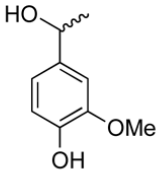
nonphenolic	phenolic
benzylic oxidation	C_α-C_β cleavage and benzylic oxidation
C_β-O cleavage and benzylic oxidation	benzylic oxidation
decompose	decompose

Hanson, *Inorg. Chem.* **2012**, *51*, 7354

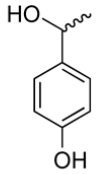
Cobalt



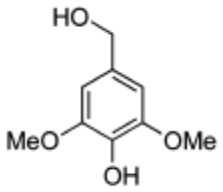
Subunits: **1** - syringyl (S)



2 - guaiacyl (G)



3 - p-hydroxyphenyl (H)



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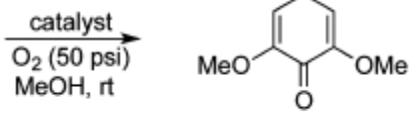
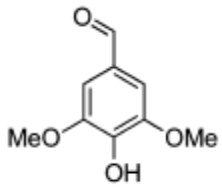
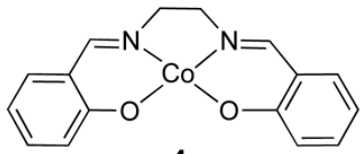


6

+



12

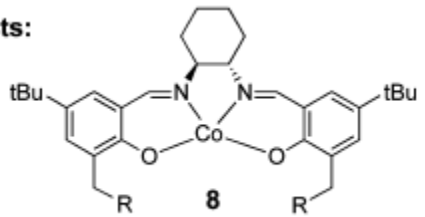


4

entry	catalyst (mol %)	additive (mol %)[c]	*t* (h)	**6** (%)[a]	**12** (%)	**10** (%)
1[b]	–	–	16	0	7	93
2	**4**(10)	pyr (100)	16	82	<5	0
3	**8a** (10)	DBZP (15)	16	50	5	28
4	**8a** (10)	pyr (100)	16	79	10	traces
5	**8b** (5)	–	16	39	32	6
6	**9a** (10)	–	16	67	20	traces
7	**9a** (5)	–	5	61	25	traces
8[b]	**9a** (2)	–	3	34	31	35
9[b]	**9a** (10)	pyr (100)	16	11	29	60
10	**9b** (5)	–	16	54	0	40
11	**9c** (5)	–	1	74	19	0
12	**9c** (2)	–	16	69	30	0
13	**9d** (5)	–	2	65	22	traces
14	**9e** (5)	–	16	75	19	0
15	**9f** (5)	–	16	46	0	44

[a] Yields are given for isolated material unless otherwise specified. [b] Yields determined by ^{1}H NMR analysis. [c] Mol % based on substrate; pyr = pyridine, DBZP = dibenzylpiperazine.

Catalysts:



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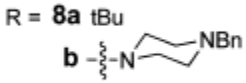

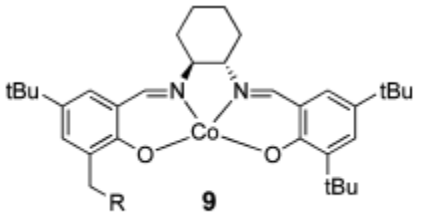

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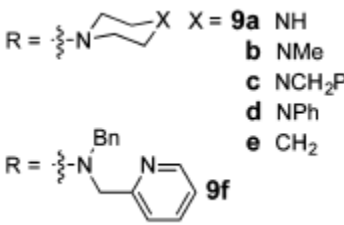
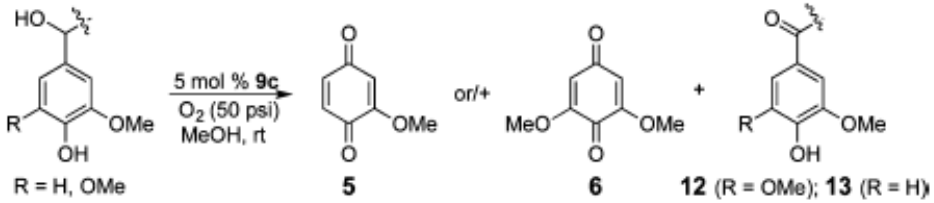
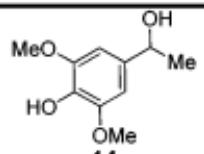
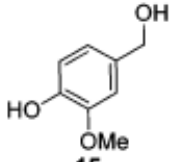
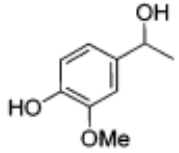
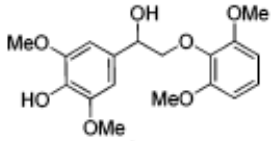
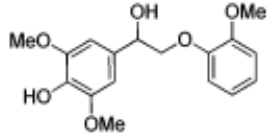
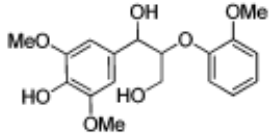
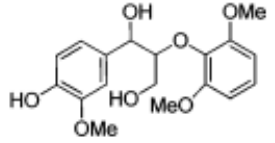


Bozell, *Org. Lett*. **2013**, *15*, 2730

Cobalt

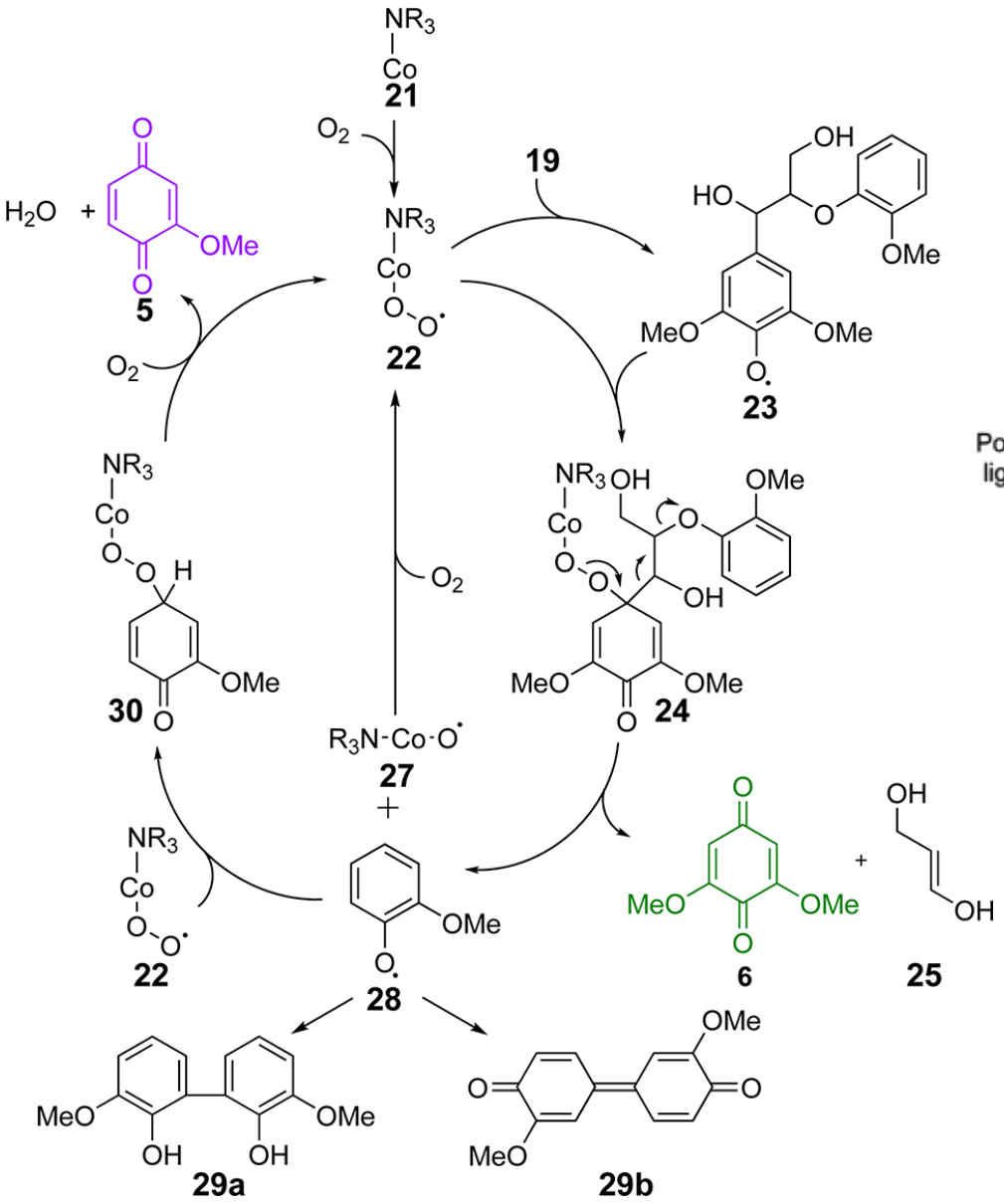


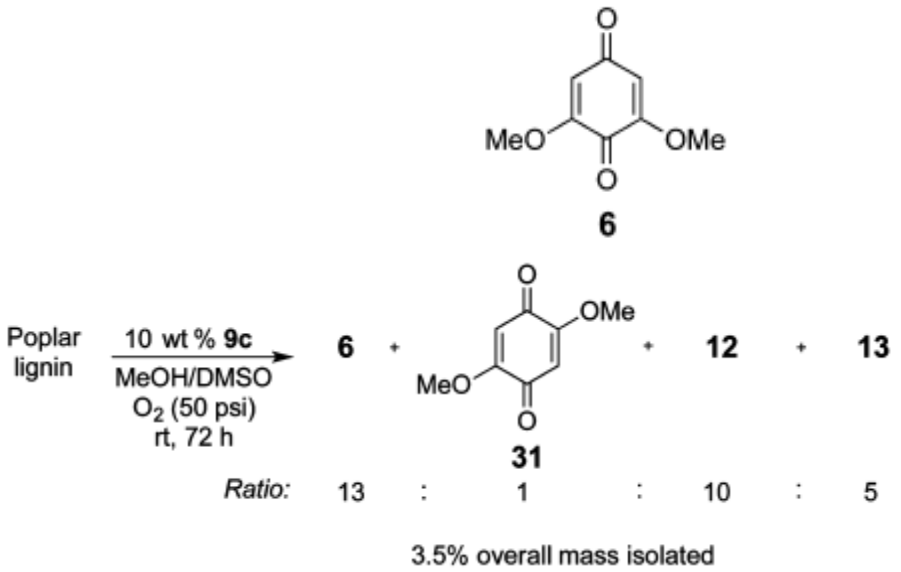
entry	substrate	*t*(h)	**5** (%)[a]	**6** (%)	**12/13** (%)
1	 **14**	16	-	72	11
2	 **15**	16	83	-	-
3[b]		24	51	-	22
4[c]	 **17**	16	-	81	traces
5	 **18**	16	17	86	traces
6[b]	 **19**	48	21	64	traces
7[b]	 **20**	48	0[d]	10	0[e]

[a] Yields are given for isolated material. [b] 10 mol % of catalyst used. [c] Yields relative to 2 equiv of product formed. [d] 14% 2,5-DMBQ isolated.[19] [e] 30% aldehydes.[20]

Bozell, *Org. Lett*. **2013**, *15*, 2730

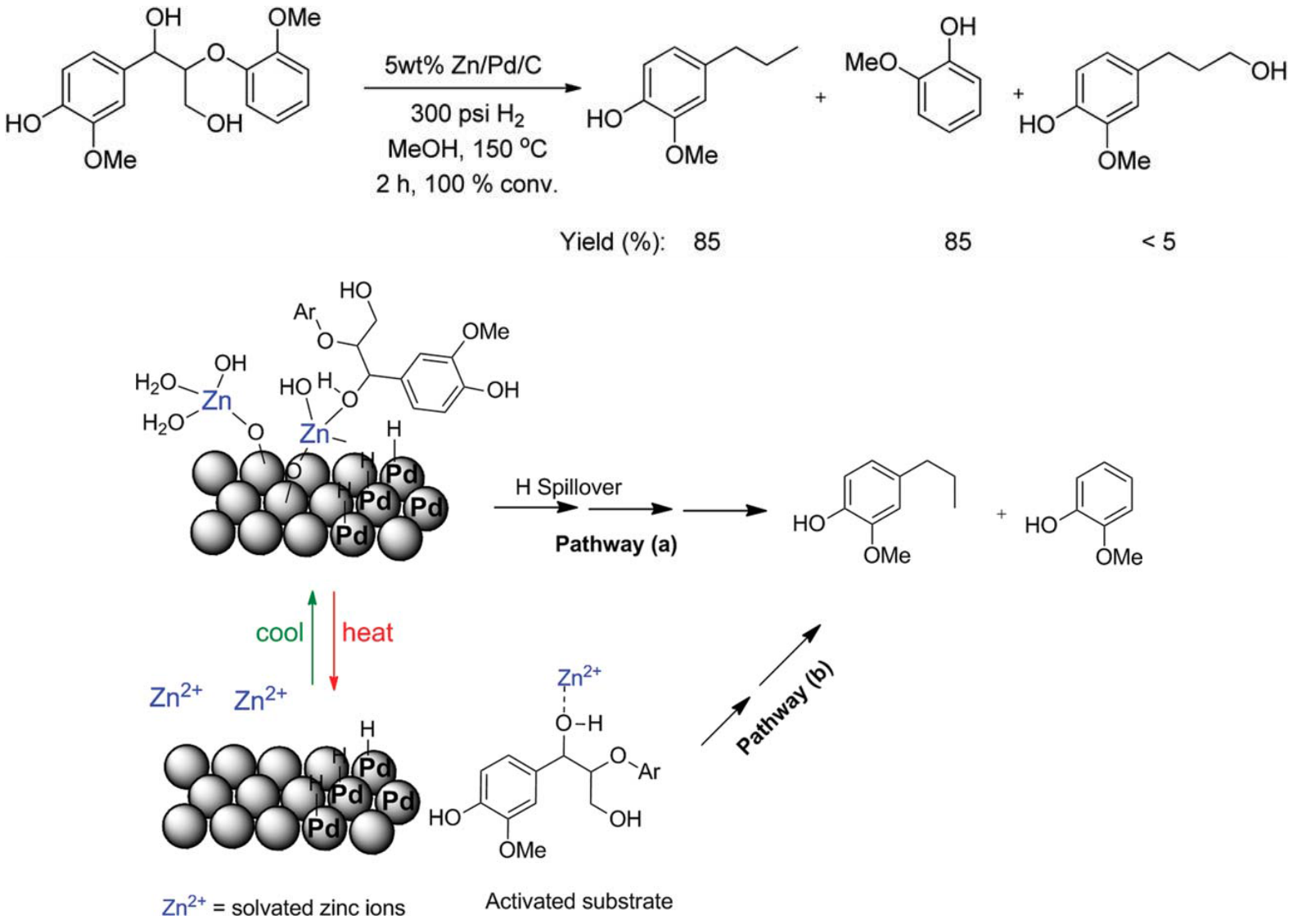
Cobalt





Bozell, *Org. Lett*. **2013**, *15*, 2730

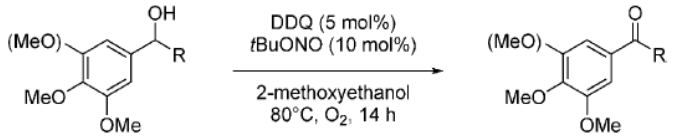
Zinc



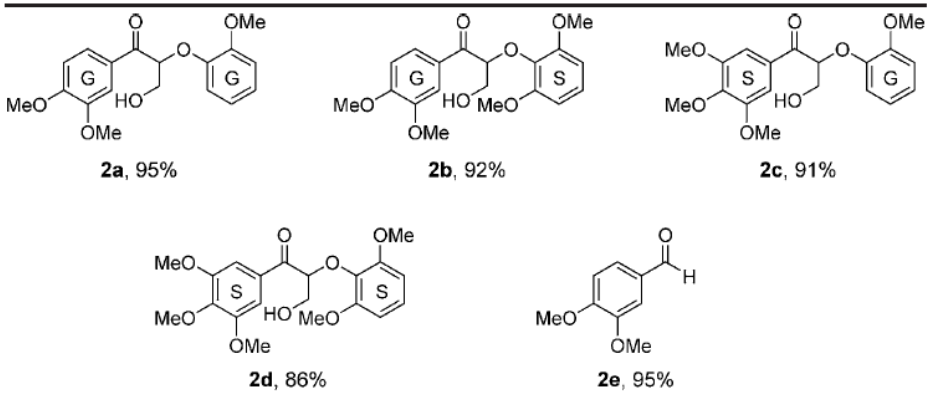
Abu-Omar, *Chem. Sci.* **2013**, *4*, 806

Zinc

Table 1: Selective catalytic benzylic oxidation of lignin β-O-4 models.



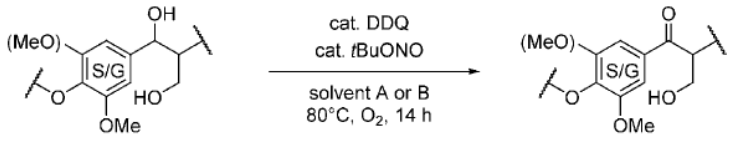
1a–e **2a–e**



2a, 95% **2b**, 92% **2c**, 91%

2d, 86% **2e**, 95%

Table 2: Selective catalytic benzylic oxidation of a lignin β-O-4 model polymer.



3 S:G = 1:1 **4**

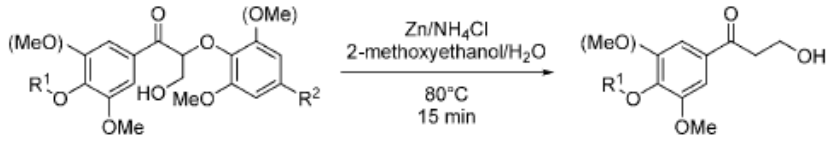
Entry	DDQ [mol%]	*t*BuONO [mol%]	Solvent system[a]	Conversion [%][b] total	G	S
1	5	10	A	50	64	35
2	10	10	A	74	83	64
3	5	10	B	69	81	57
4	10	10	B	91	100	82
5	15	15	B	97	100	94
6	20	20	B	99	100	98

[a] A = 2-methoxyethanol, B = 2-methoxyethanol/1,2-dimethoxyethane (2:3). [b] Conversions were determined by comparison of the integrals of the aromatic cross-peaks characteristic of oxidized and unoxidized structures in the 2D HSQC NMR. Error analysis indicated the standard deviation for these measurements was less than 0.05. See the Supporting Information for more information.

Westwood, *Angew. Chem. Int. Ed.* **2015**, *54*, 258

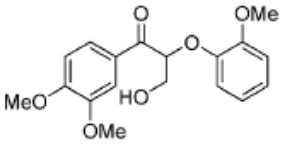
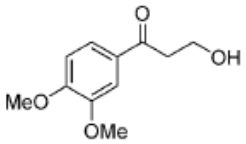
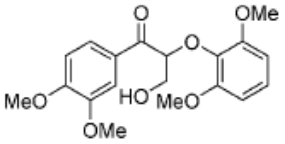
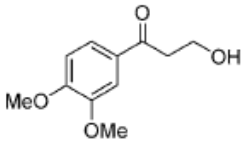
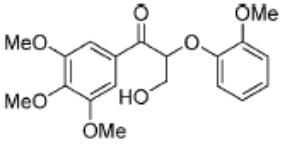
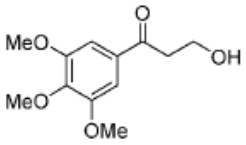
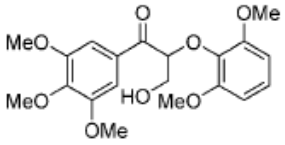
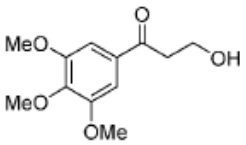
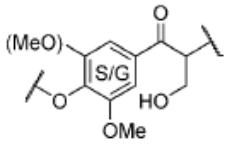
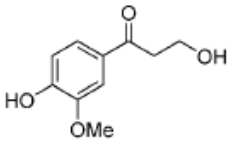
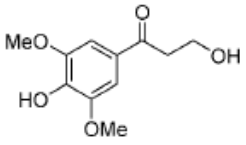
Zinc

Table 3: C–O bond cleavage of oxidized β-O-4 model compounds **2a–d** and **4**.

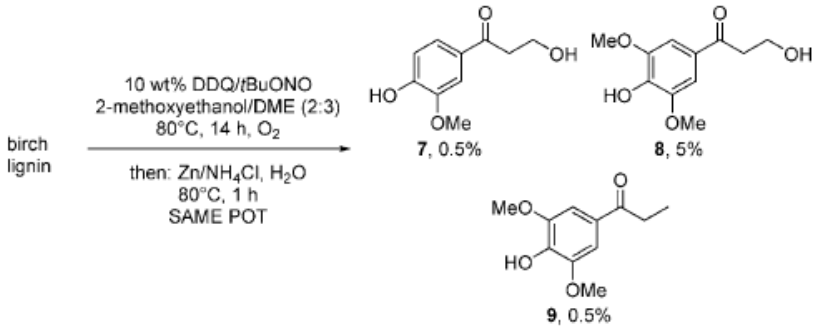


R^1 = Me or polymer chain
R^2 = H or polymer chain

R^1 = Me or H

Substrate	Product	Yield[a] [%]
 **2a**	 **5**	88 (92)[b]
 **2b**	 **5**	84
 **2c**	 **6**	81
 **2d**	 **6**	90
 **4**	 **7**	27
	 **8**	23

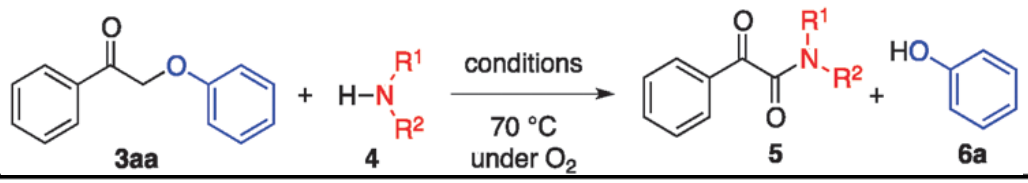
[a] Yields of isolated products. [b] Yield of the isolated product from a one-pot reaction.[16]



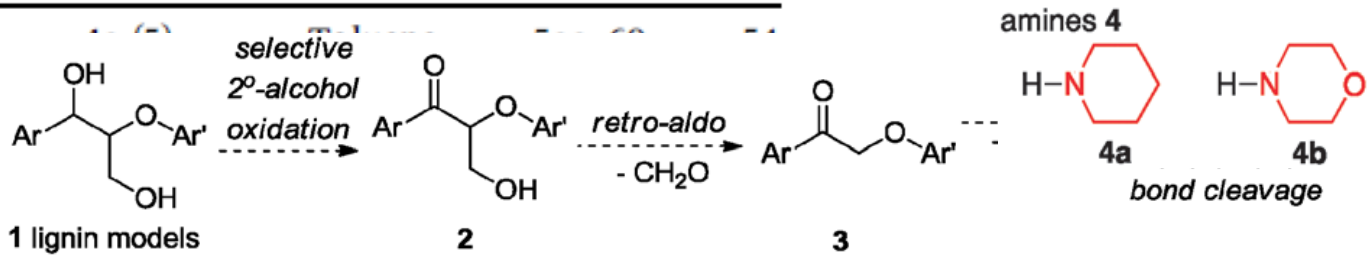
Scheme 3. Depolymerization of lignin to phenolic monomers. DME = 1,2-dimethoxyethane.

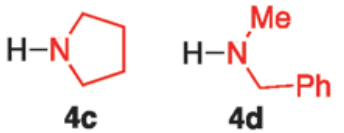
Westwood, *Angew. Chem. Int. Ed.* **2015**, *54*, 258

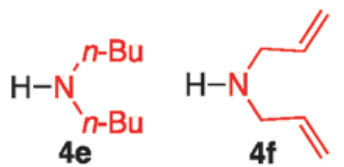
Copper



Entry	Catalyst (10 mol%)	Amine 4 (equiv.)	Solvents	Yield[b] (%) 5	6a
1	CuCl				
2	CuBr				
3	CuI				
4[c]	CuI				
5	CuI				
6	CuI				
7	CuI	4a (5)	MeCN	5aa: 81	65
8	CuI	4a (5)	DMF	5aa: 67	60
9	CuI	4a (5)	DMSO	5aa: 71	59
10	CuI	4a (5)	MeOH	5aa: 9	0
11	$FeCl_3$	4a (5)	Toluene	5aa: 21	12
12	$RuCl_3$	4a (5)	Toluene	5aa: 29	14
13	CuI	4b (5)	Toluene	5ab: 79	66
14	CuI	4c (5)	Toluene	5ac: 73	69
15	CuI	4d (5)	Toluene	5ad: 63	57
16	CuI	4e (5)	Toluene	5ae: 62	55
17	CuI	4f (5)	Toluene	5af: 56	56



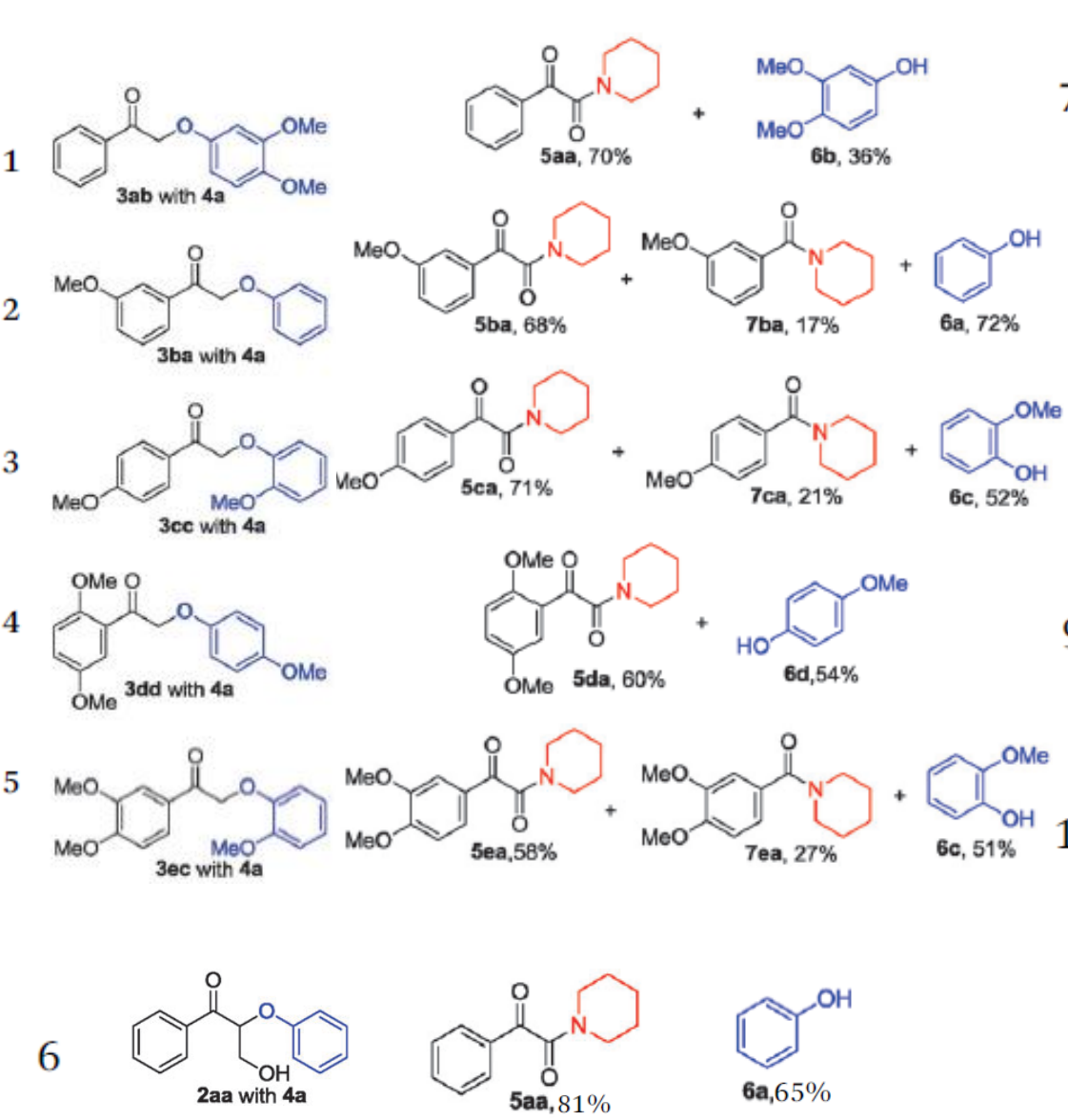




[a] Unless otherwise noted, the reactions were carried out using 2-phenoxyacetophenone (3aa) (0.1 mmol), amine 4 (0.5 mmol), and catalyst (10 mol%) in solvents (0.25 M, 0.4 mL) at 70 °C for 8 h under an oxygen atmosphere (1 atm). [b] Isolated yields. [c] The reaction was performed under an air atmosphere (0.21 atom of O_2).

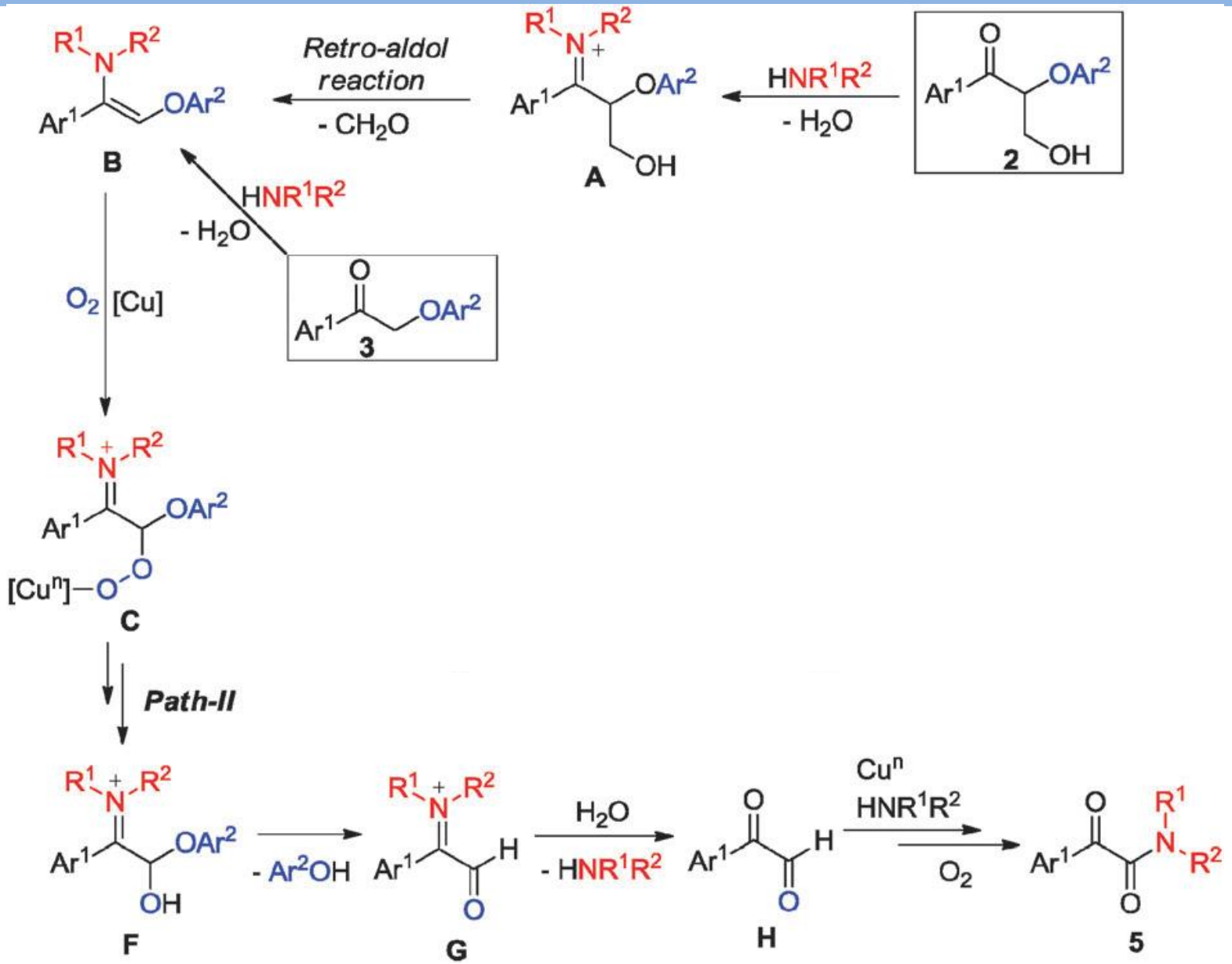
Loh, *Chem. Commun.* **2013**, *49*, 11439

Copper



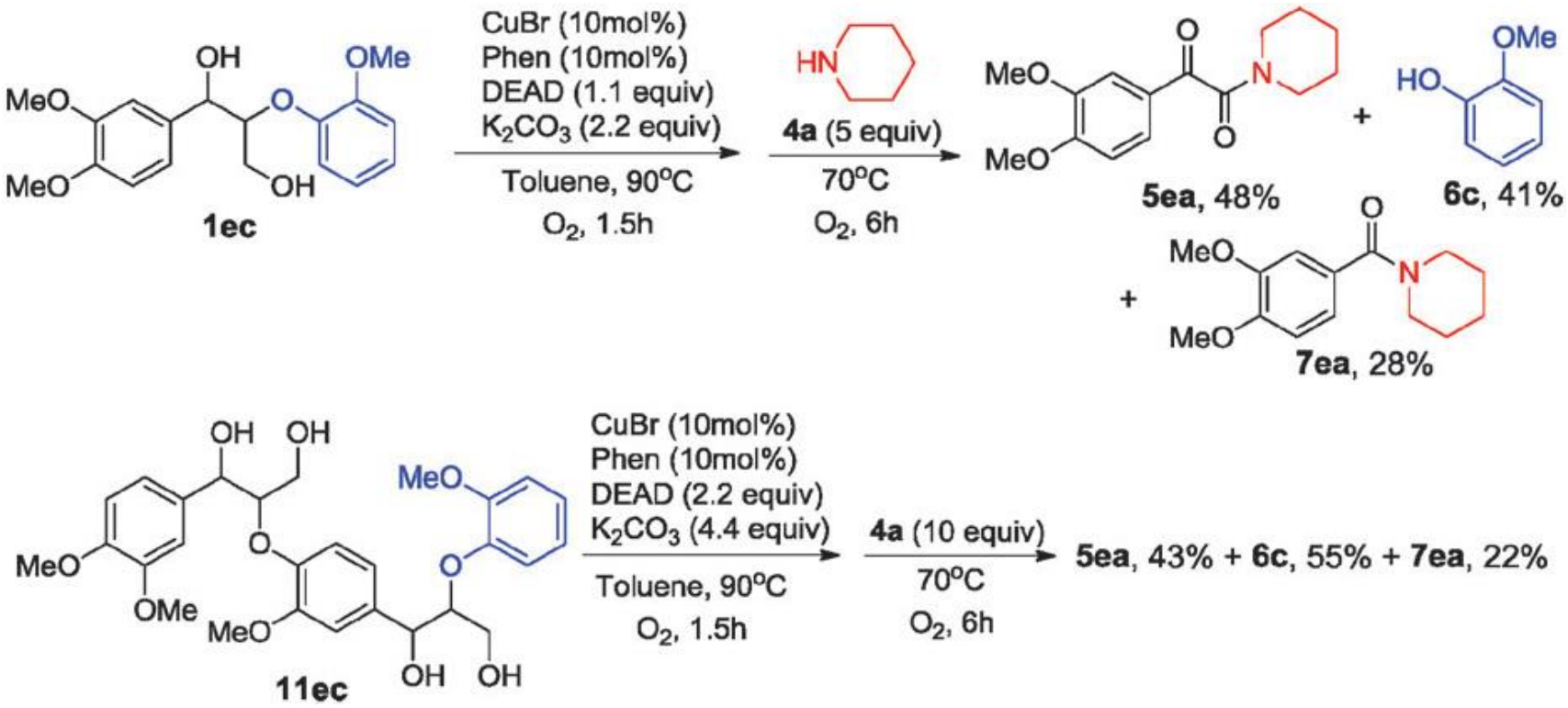
Loh, *Chem. Commun.* **2013**, *49*, 11439

Copper



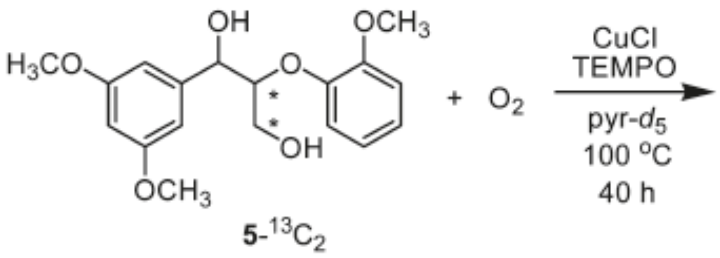
Loh, *Chem. Commun.* **2013**, *49*, 11439

Copper

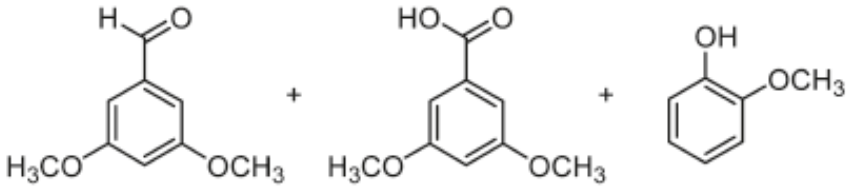


Loh, *Chem. Commun.* **2013**, *49*, 11439

Copper



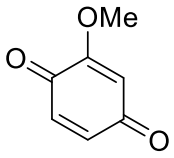
~89% conversion

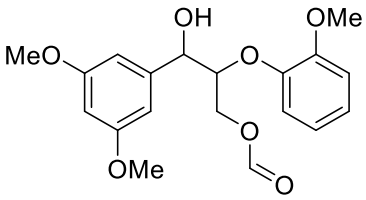


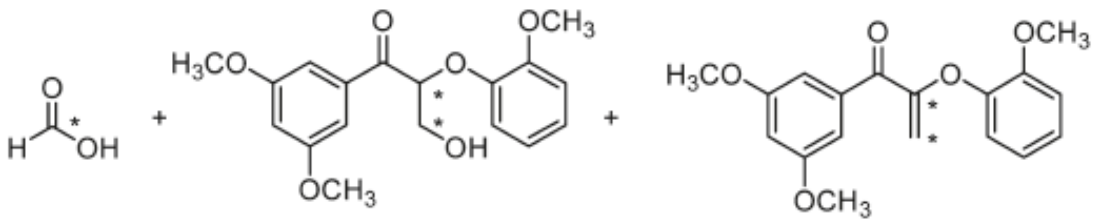
11 43%

13 13%

10 7%







12-$^{13}C_1$ 7%

7-$^{13}C_2$ 1%

8-$^{13}C_2$ 2%

7 could only afford **8** under the reaction condition

Hanson, *ACS Catal.* **2011**, *1*, 794

Baker, *Adv. Synth. Catal.* **2014**, *356*, 3563

Copper

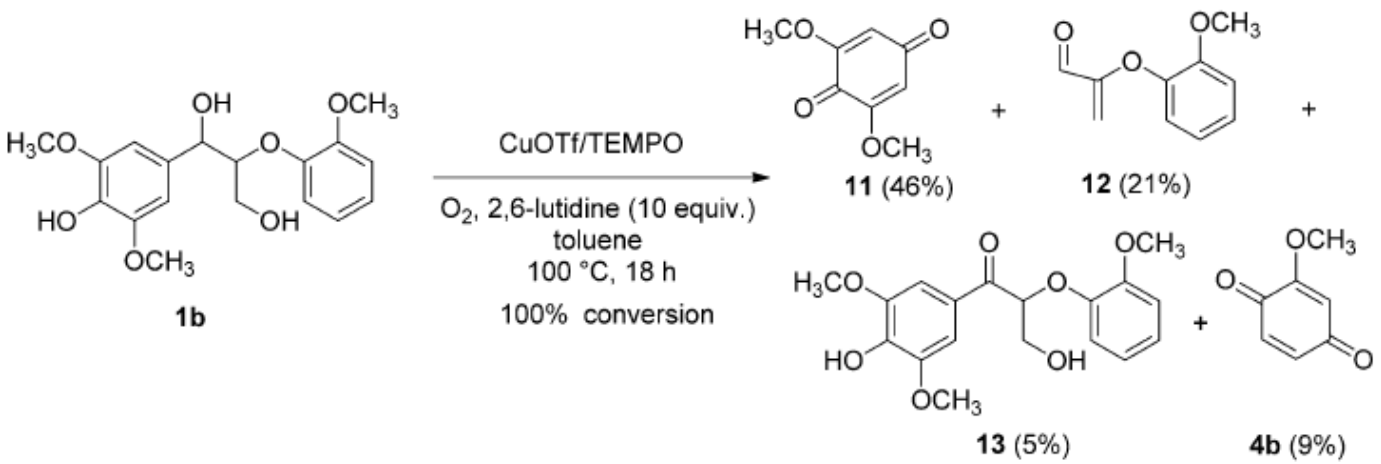


Figure 4. Aerobic oxidation of **1b** mediated by stoichiometric Cu(OTf)/2,6-lutidine/TEMPO.

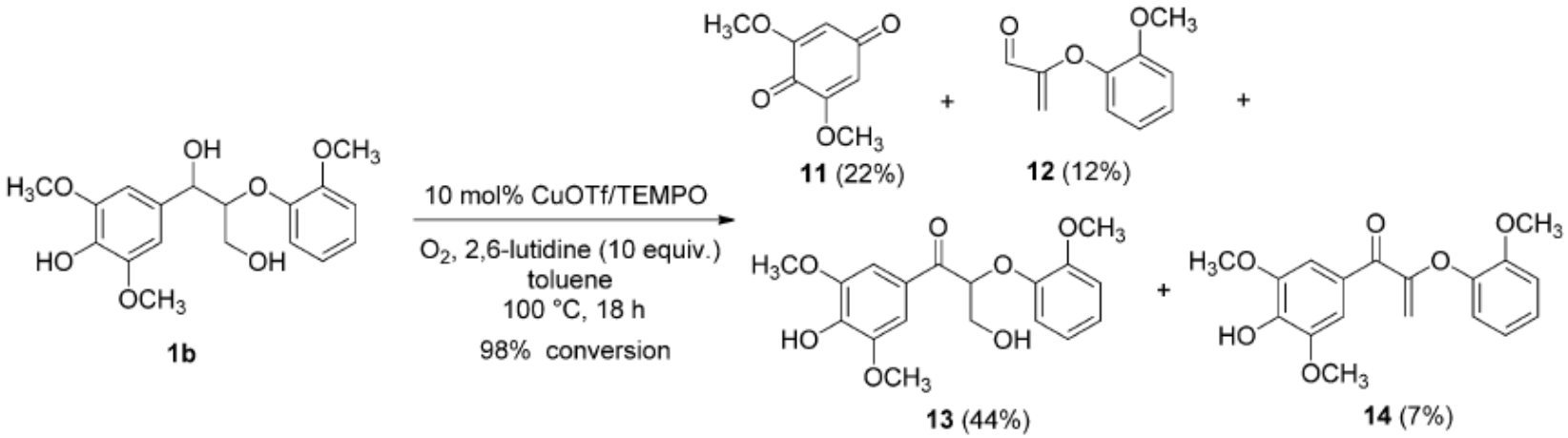
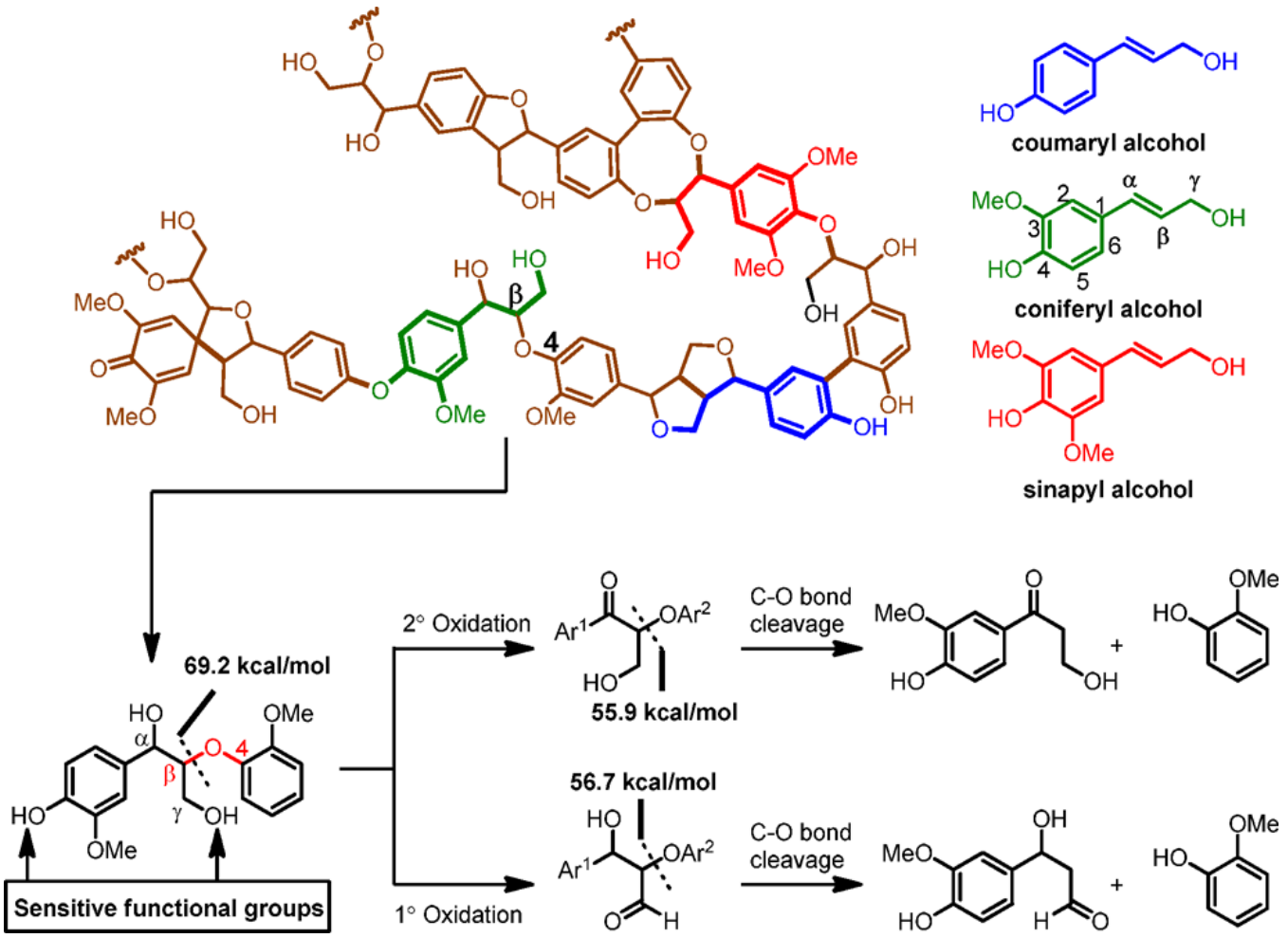


Figure 5. Copper complex-catalyzed aerobic oxidation of **1b**.

Hanson, *ACS Catal.* **2011**, *1*, 794

Baker, *Adv. Synth. Catal.* **2014**, *356*, 3563

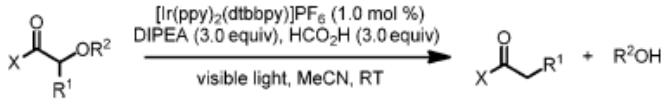
Iridium

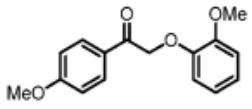
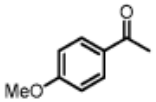
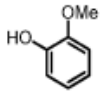
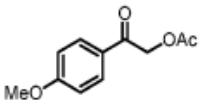
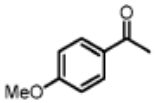
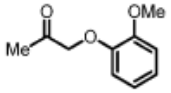
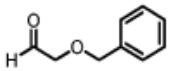
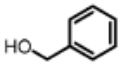
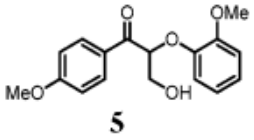
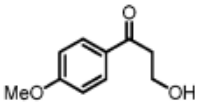
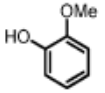
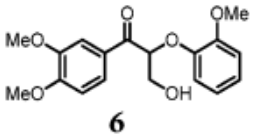
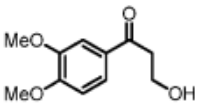
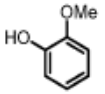
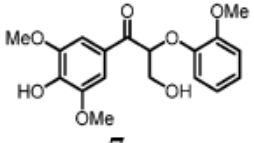
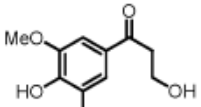
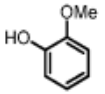
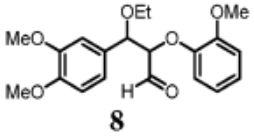
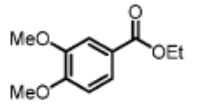
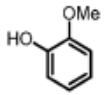


Stephenson, *J. Am. Chem. Soc.* **2014**, *136*, 1218

Iridium

Table 1. Substrate Scope of Visible-Light-Mediated C_α–O Bond Cleavage



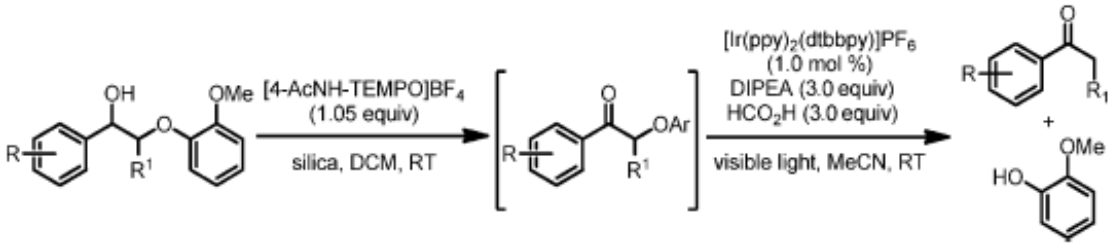
entry	substrate	time (h)	products[a]	
1	 1	12	 88%	 89%
2	 2	4	 77%	 Not isolated
3	 3	24	No reaction	
4	 4	12	 Not isolated	 83%
5	 5	15	 85%	 88%
6	 6	18	 85%	 76%
7	 7	48	 90%	 95%
8	 8	24	 30%	 70%

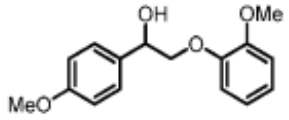
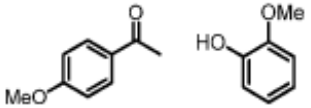
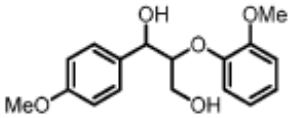
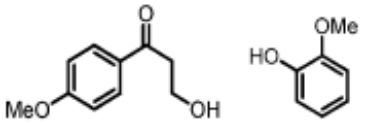
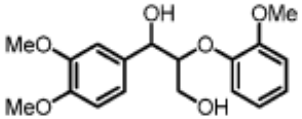
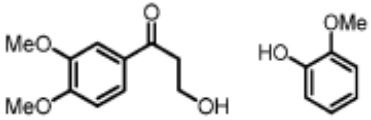
[a]Yields of products isolated via column chromatography and based on an average of two runs.

Stephenson, *J. Am. Chem. Soc.* **2014**, *136*, 1218

Iridium

Table 2. Two-Step Degradation of Lignin Model Systems

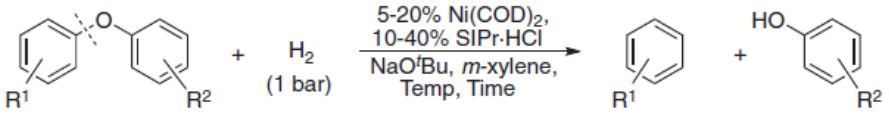


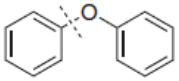
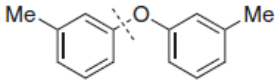
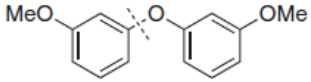
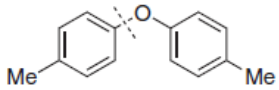
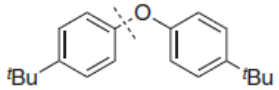
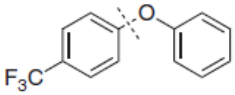
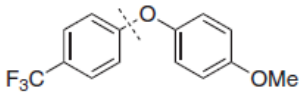
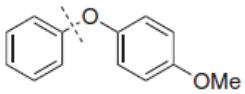
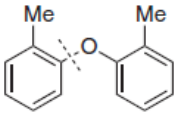
substrate	oxid. time (h)	red. time (h)	products[a]
 **9**	15	16	 85% 83%
 **10**	18	20	 81% 80%
 **11**	15	14	 84% 93%

[a]Yields of products isolated via column chromatography and based on an average of two runs.

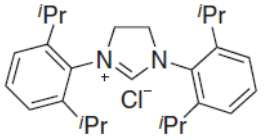
Stephenson, *J. Am. Chem. Soc.* **2014**, *136*, 1218

Nickle



Entry	Diaryl ether	Ni, mol%	T, °C	Time, h	Conversion, %	Arene, %	Phenol, %
1		20	120	16	100	99	99
2		10	120	32	87	82	87
3		5	120	32	59	59	54
4		20	120	16	100	96	99
5		20	120	16	94	88*	86†
6		20	120	48	100	97	99
7		20	120	48	74	72	73
8		10	100	16	100	87§	99
9		10	100	16	100	87‖	92
10		20	120	16	100	88¶	80#
11		20	120	32	85	85	85

*Anisole (65%) and benzene (23%). †3-Methoxyphenol (83%) and phenol (3%). ‡Trifluoromethylbenzene (64%) and toluene (23%); benzene (4%) as a side product. §Trifluoromethylbenzene (68%) and toluene (19%). ‖Anisole (4%) as a side product. ¶Phenol (17%) as a side product.

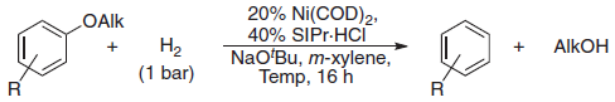


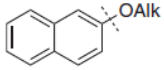
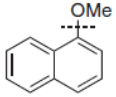
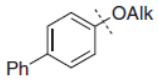
SIPr·HCl

Hartwig, *Science*, **2011**, *332*, 439

Nickle

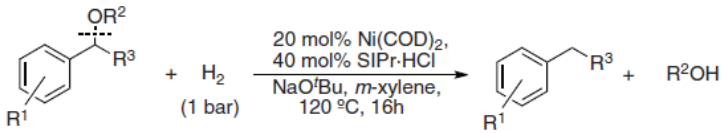
Table 2. Hydrogenolysis of alkyl aryl ethers.

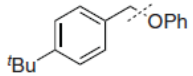
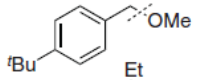
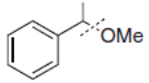


Entry	Alkyl Aryl Ether		T, °C	Time, h	Additive (1 equiv.)	Conversion, %	Arene, %	AlkOH, %
1		Alk = ^{n}Hexyl	120	16	-	100	95	98
2		Alk = Methyl	120	16	-	89	89	nq*
3		Alk = Methyl	80	16	$AlMe_3$	100	98	nq
4			120	16	-	72	72	nq
5			100	16	$AlMe_3$	100	99	nq
6		Alk = ^{n}Hexyl	120	32	-	85	85	85
7		Alk = Methyl	120	32	-	60	59	nq
8		Alk = Methyl	100	32	$AlMe_3$	65	65	nq

*nq, not quantified.

Table 3. Hydrogenolysis of benzyl ethers.



Entry	Alkyl Benzyl Ether	Ni, mol%	Additive (1 equiv.)	Conversion, %	Arene, %	R^2OH, %
1		10	-	100	99	93
2		20	-	1	0	0
3		20	$AlMe_3$	100	99	nq*
4		20	-	0	0	0
5		20	$AlMe_3$	100†	96	nq

*nq, not quantified. †32 hours.

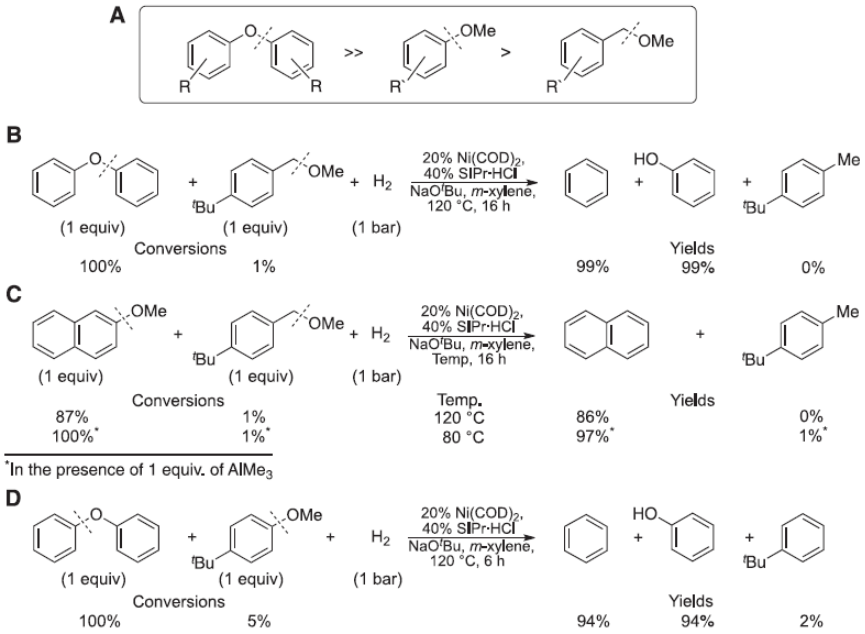


Fig. 2. (**A**) Relative reactivity of aryl and benzyl ethers toward hydrogenolysis of C-O bonds catalyzed by $Ni(COD)_2$ and SIPr. Selective hydrogenolysis of (**B**) diphenyl ether in the presence of 4-*tert*-butylbenzyl methyl ether; (**C**) 2-methoxynaphthalene in the presence of 4-*tert*-butylbenzyl methyl ether; and (**D**) diphenyl ether in the presence of 4-*tert*-butylanisole.

Hartwig, *Science*, **2011**, *332*, 439

Nickle

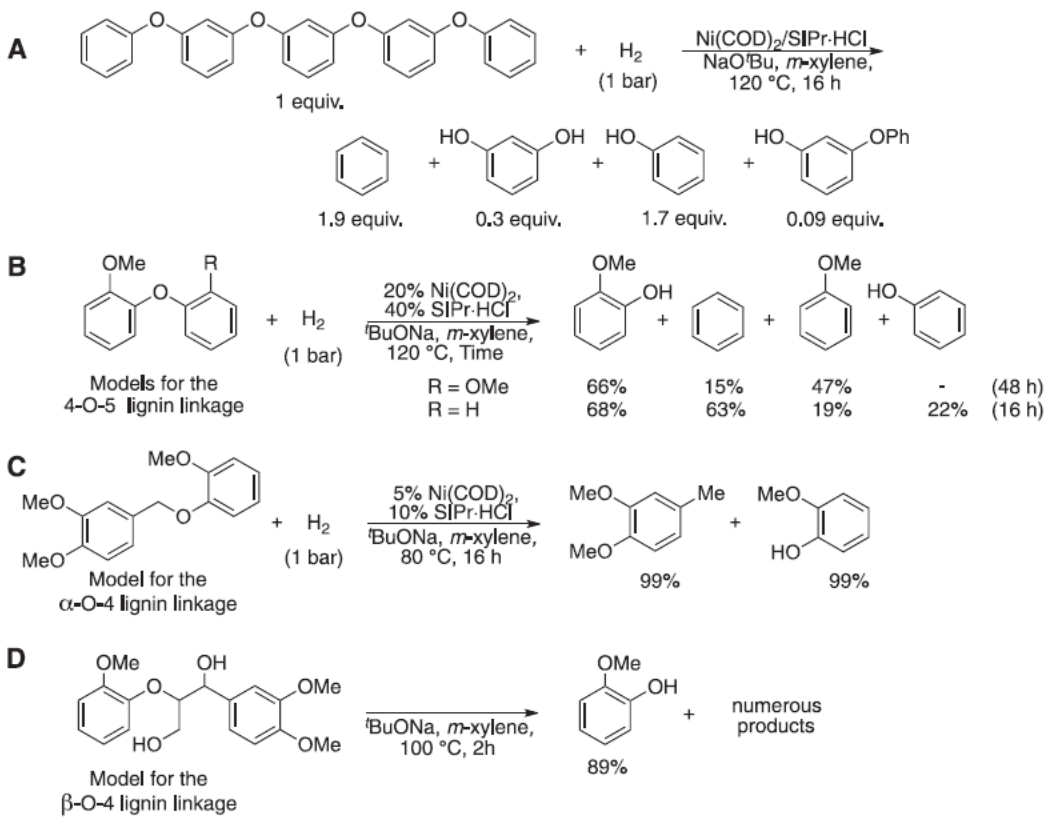
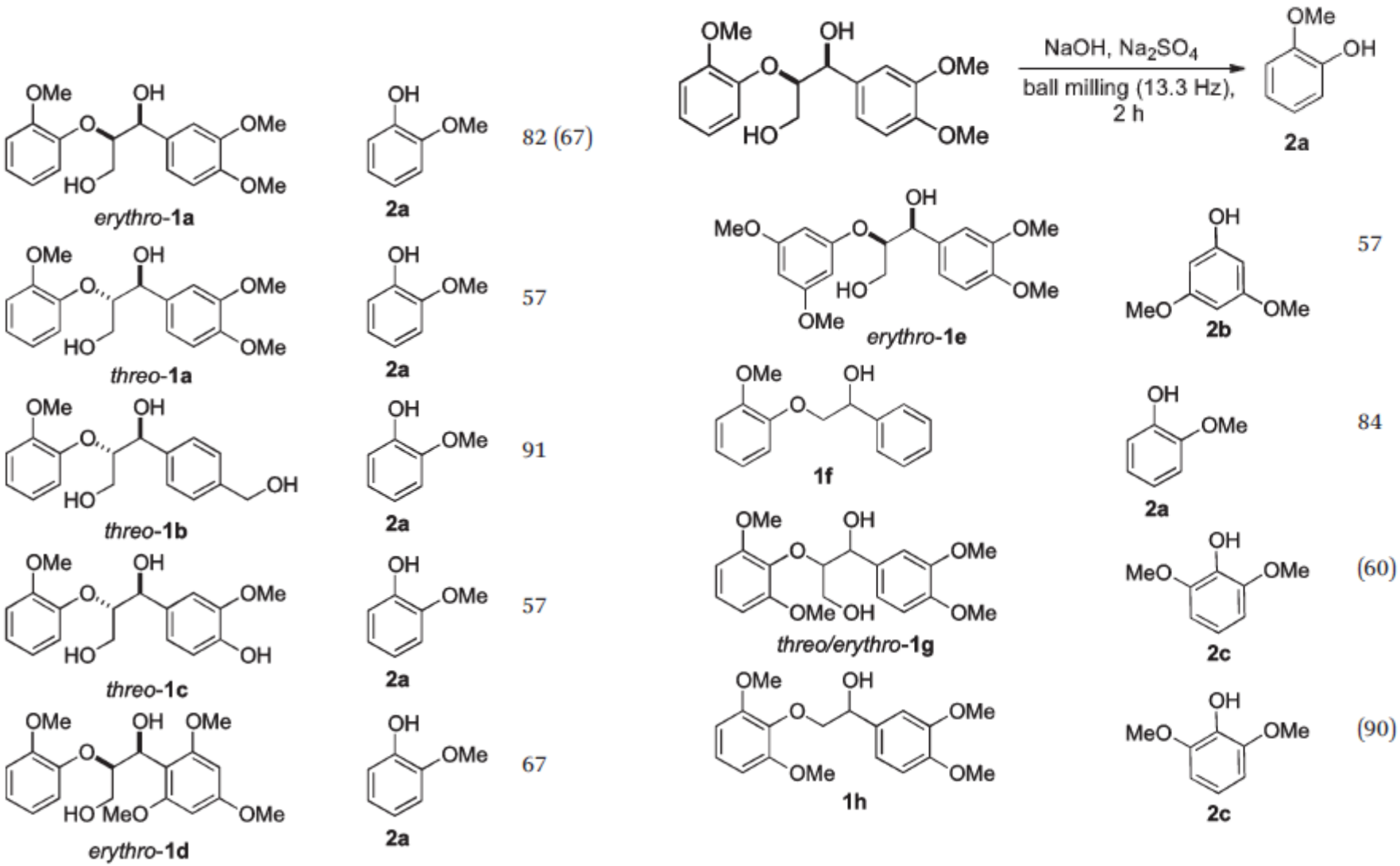


Fig. 3. Hydrogenolysis of (**A**) bis(*m*-phenoxyphenyl)benzene. (**B**) A model of the 4-O-5 linkage in lignin. (**C**) A model of the α–O-4 linkage in lignin. (**D**) A model of the β–O-4 linkage in lignin.

Hartwig, *Science*, **2011**, *332*, 439

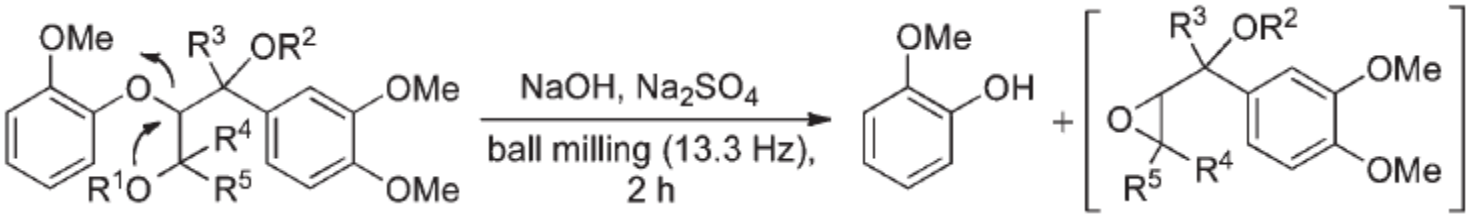
Metal-Free



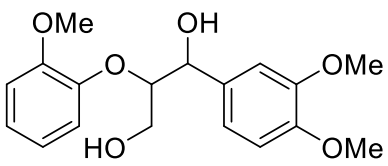
[a] Use of 0.2 mmol of 1, 3.5 equiv. of NaOH, 1 g of Na_2SO_4, 30 balls, 720 min, 13.3 Hz. [b] Determined by GC using 4-methoxyphenol as an internal standard. The values given in parentheses refer to the amount of isolated phenol obtained from reactions performed on a 0.8 mmol scale.

Bolm, *Green Chem.* **2013**, *15*, 160

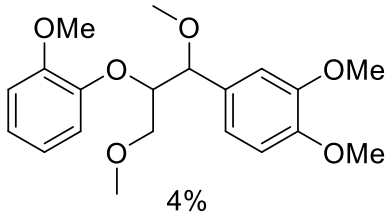
Metal-Free



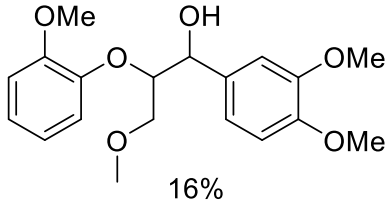
Mechanochemical degradation



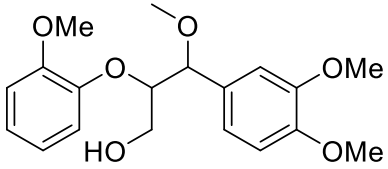
62%



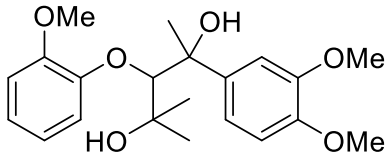
4%



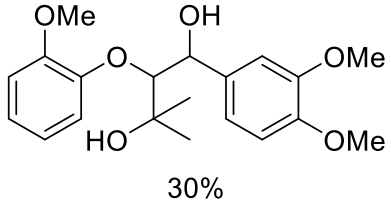
16%



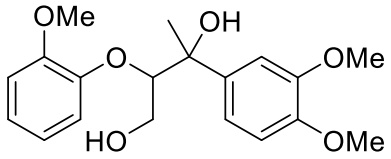
50%



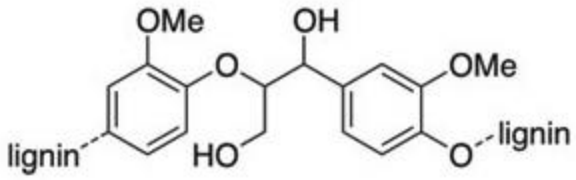
15%



30%



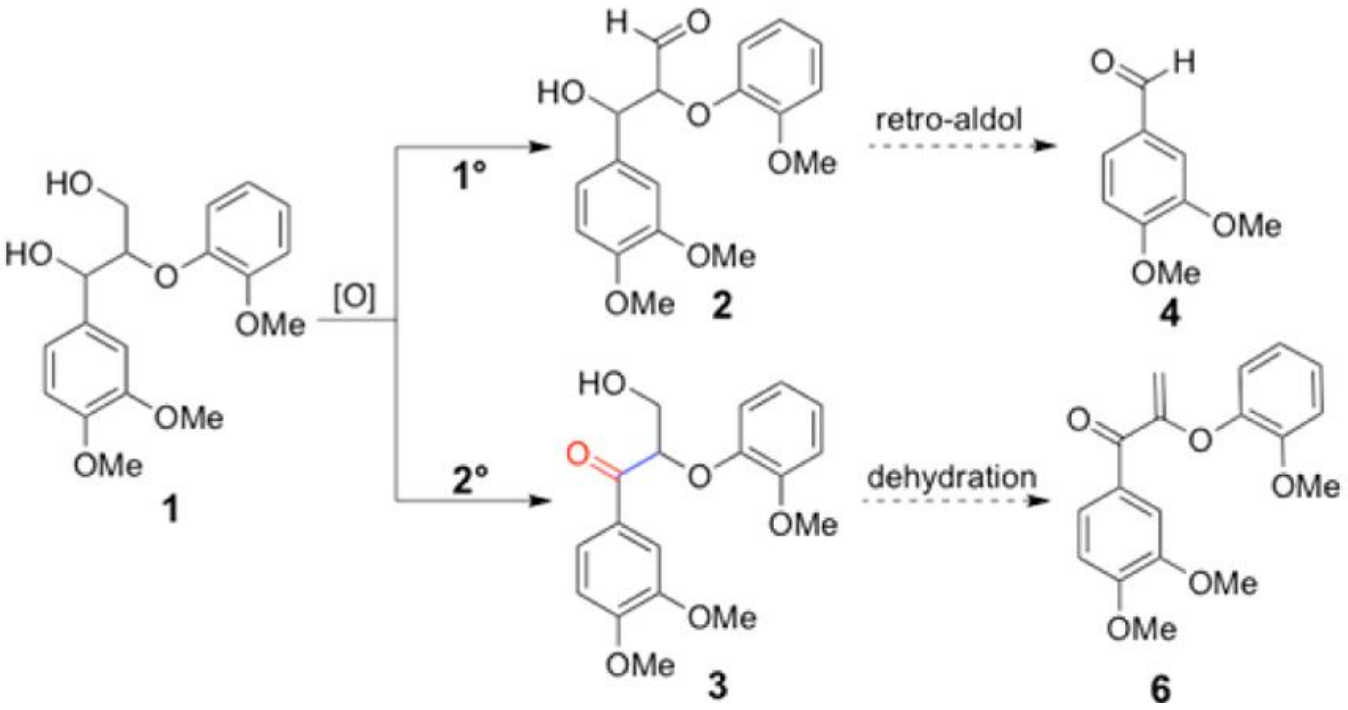
56%



76% of β-O-4 was cleaved

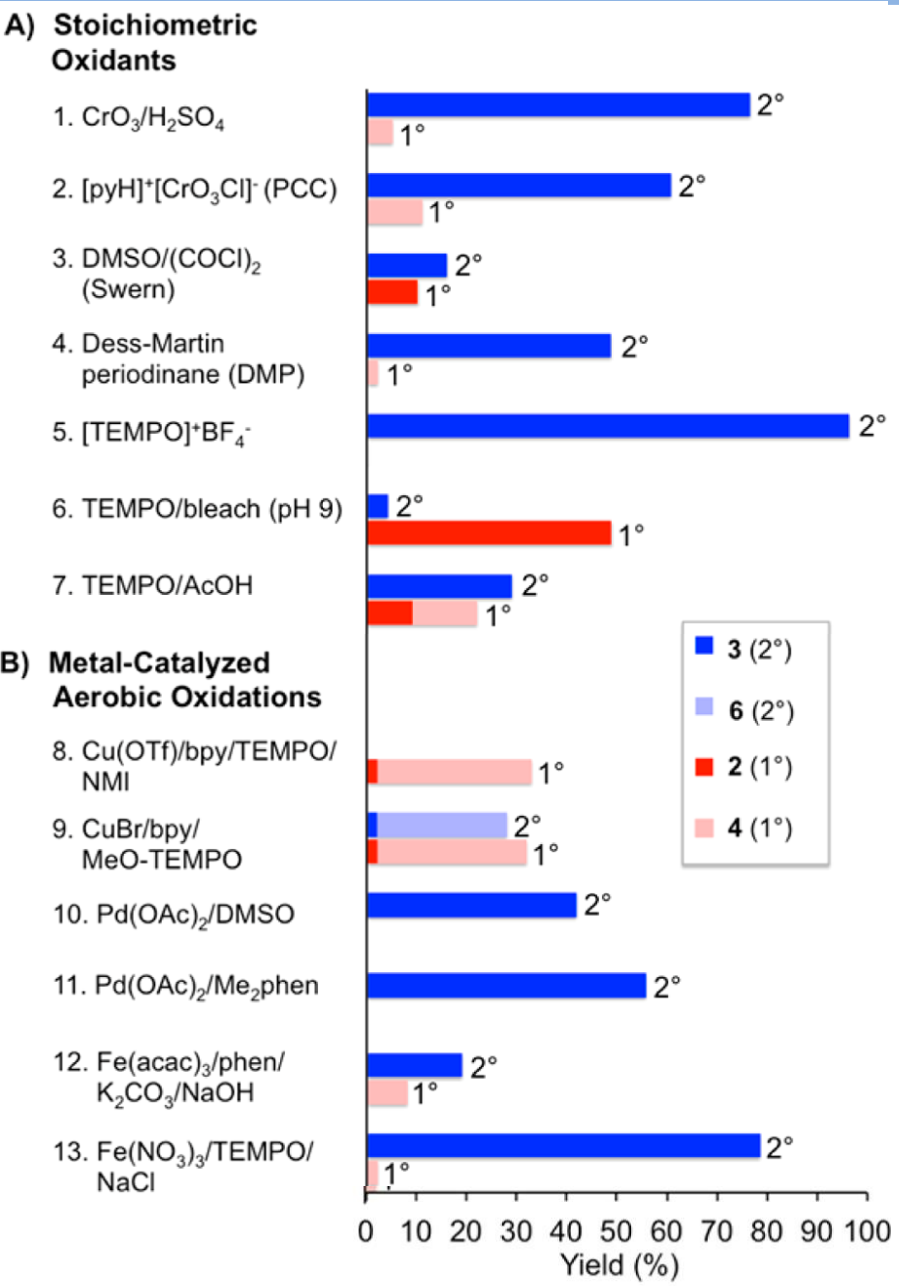
Bolm, *Green Chem.* **2013**, *15*, 160

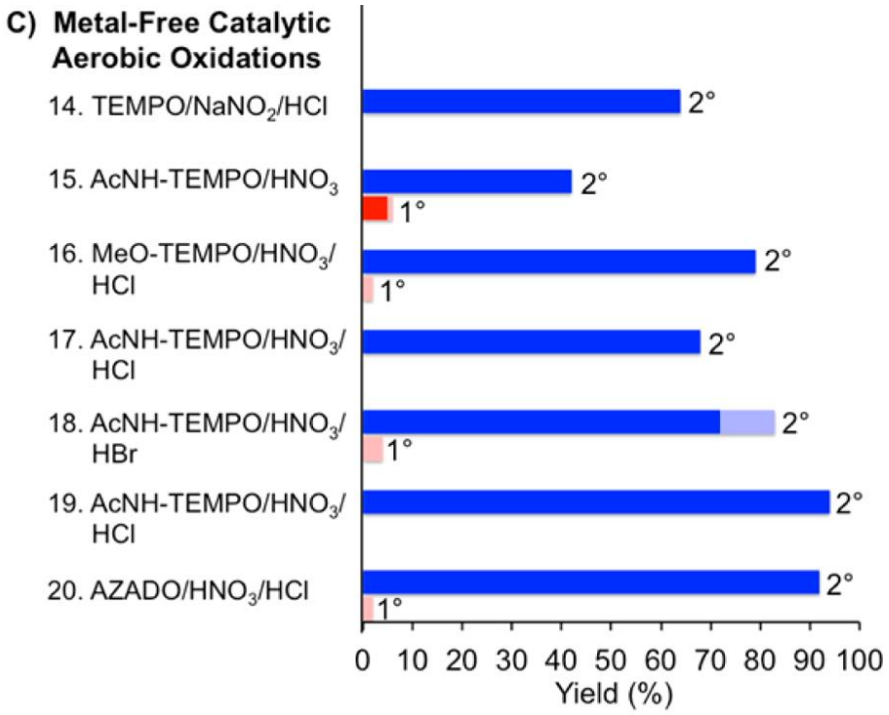
Metal-Free

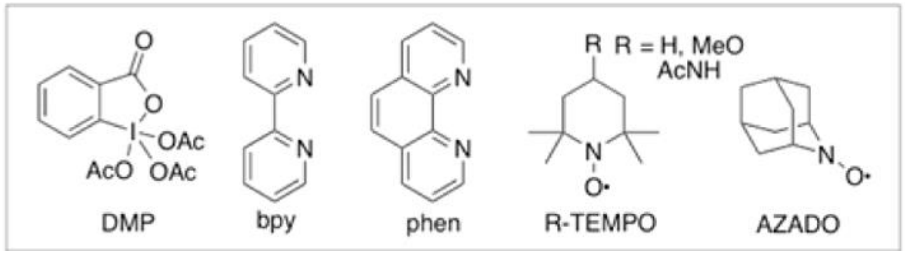


Stahl, *J. Am. Chem. Soc.* **2013**, *135*, 6415

Metal-Free

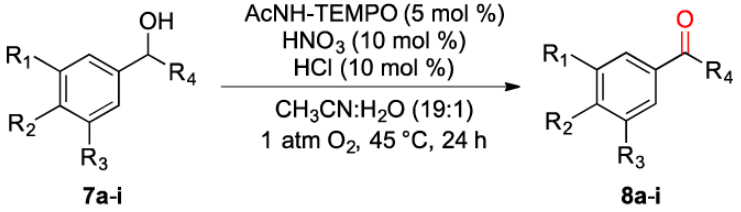




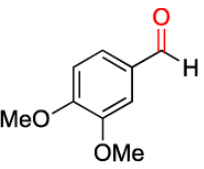


Stahl, *J. Am. Chem. Soc.* **2013**, *135*, 6415

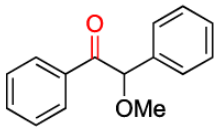
Metal-Free



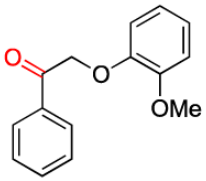
7a-i **8a-i**



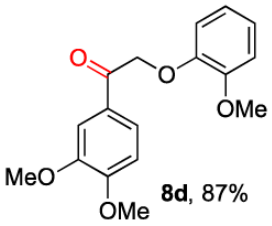
8a, 92%
(10 g scale: 94%)



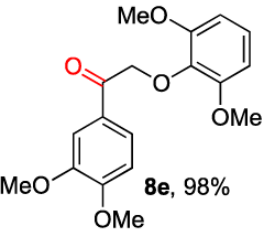
8b, 87%[b]



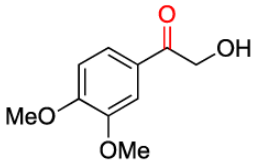
8c, 82%[c]



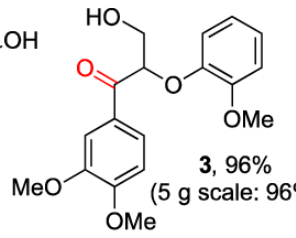
8d, 87%



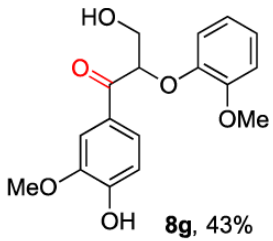
8e, 98%



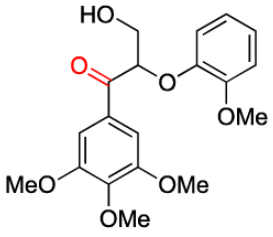
8f, 77%
(7% dicarbonyl)



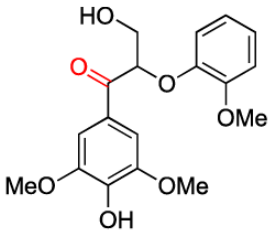
3, 96%
(5 g scale: 96%)



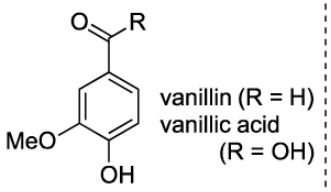
8g, 43%
(74% total, incl. 16% vanillin and 15% vanillic acid)

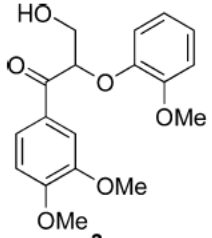


8h, 87%

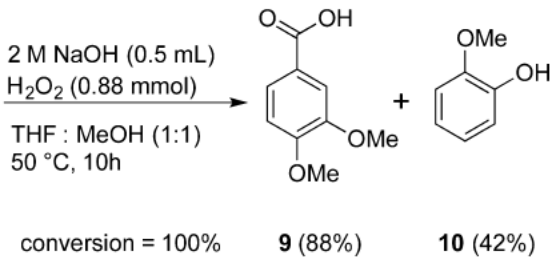


8i, 91% (at 60 °C)





3

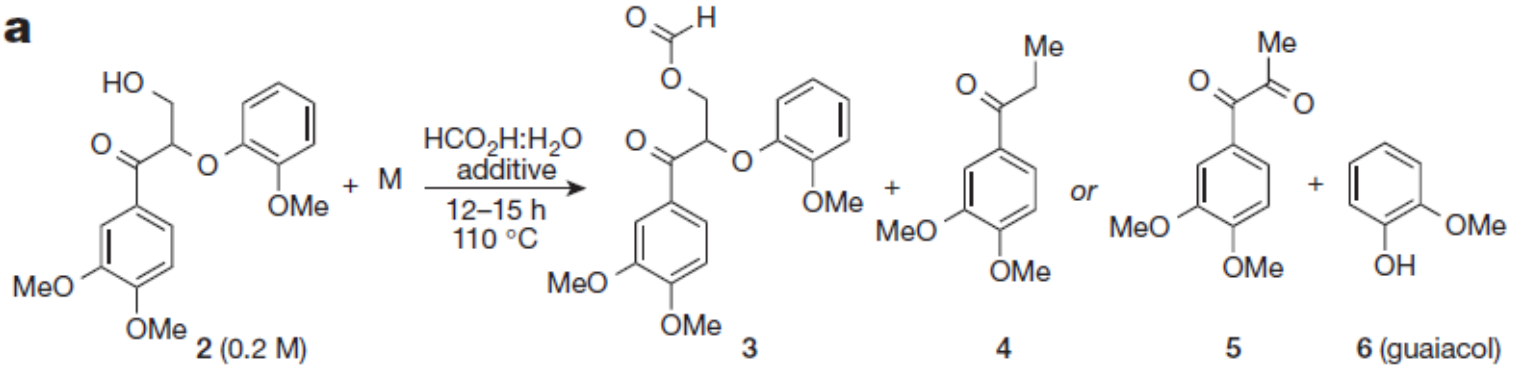


conversion = 100% **9** (88%) **10** (42%)

Stahl, *J. Am. Chem. Soc.* **2013**, *135*, 6415

Metal-Free

a

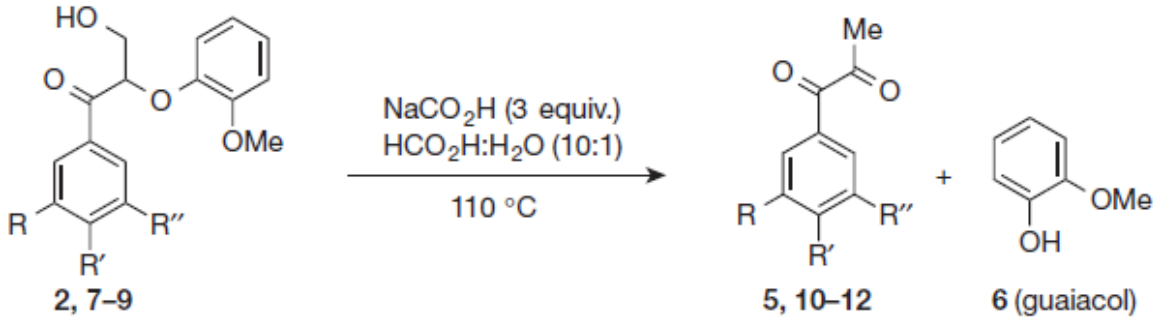


Entry	M (2 equiv.)	Additive	3 (%)	4:5 (%)	6 (%)
1	Zn	–	6	76:0	69
2	Al	–	49	0:39	36
3	Mg	–	51	0:45	24
4	Fe	–	49	0:31	24
5	Mn	–	19	0:74	63
6	–	–	18	0:77	64
7	–	**HCO_2Na (3 equiv.)**	**0**	**0:96**	**87**

Stahl, *Nature*, **2014**, *515*, 249

Metal-Free

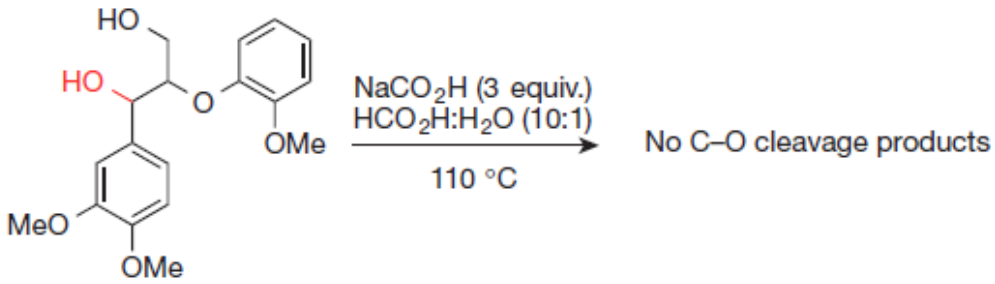
b



2, 7–9 **5, 10–12** **6** (guaiacol)

Lignin^{ox} model compound		Product: NMR yield (isolated yield)	
2: R = R′ = OMe, R″ = H	Non-phenolic model	**5**: 96% (92%)	**6**: 87% (81%)
7: R = R″ = H, R′ = OH	*p*-Hydroxyphenyl unit (H)	**10**: 93% (89%)	**6**: 82% (73%)
8: R = OMe, R′ = OH, R″ = H	Guaiacyl unit (G)	**11**: 92% (90%)	**6**: 89% (84%)
9: R = R″ = OMe, R′ = OH	Syringyl unit (S)	**12**: 93% (91%)	**6**: 90% (88%)

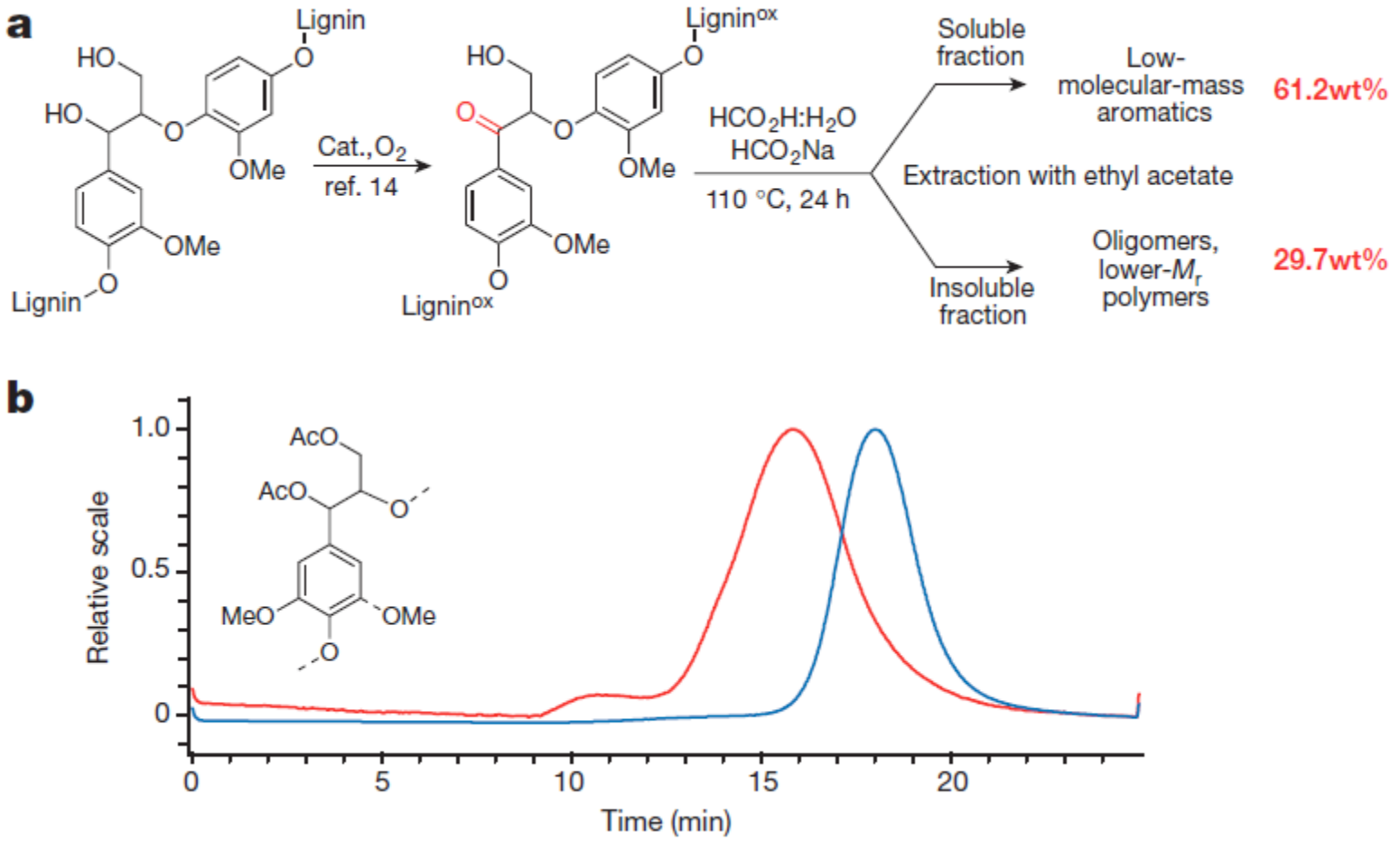
c



Non-oxidized lignin model (**1**)

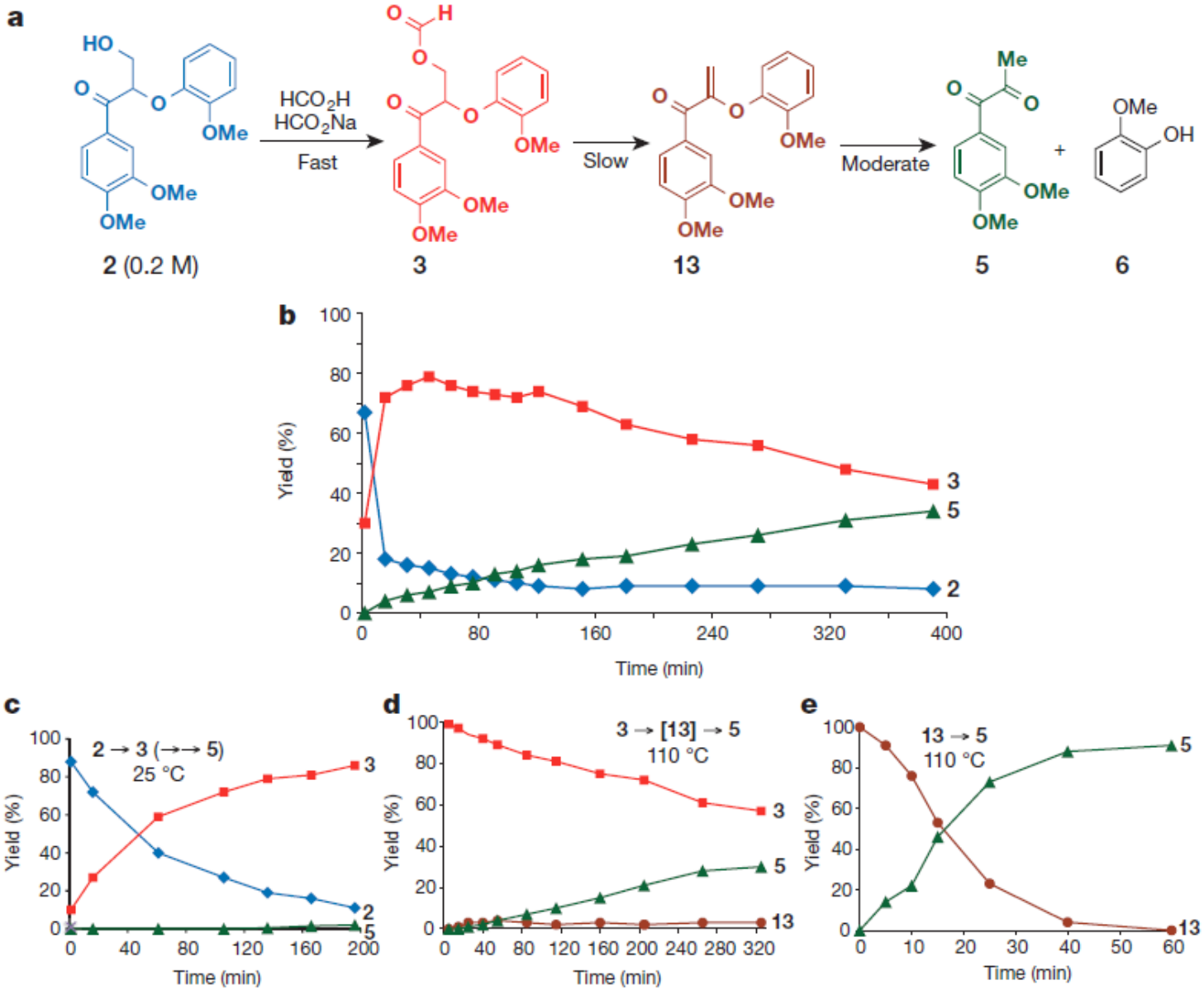
Stahl, *Nature*, **2014**, *515*, 249

Metal-Free



Stahl, *Nature*, **2014**, *515*, 249

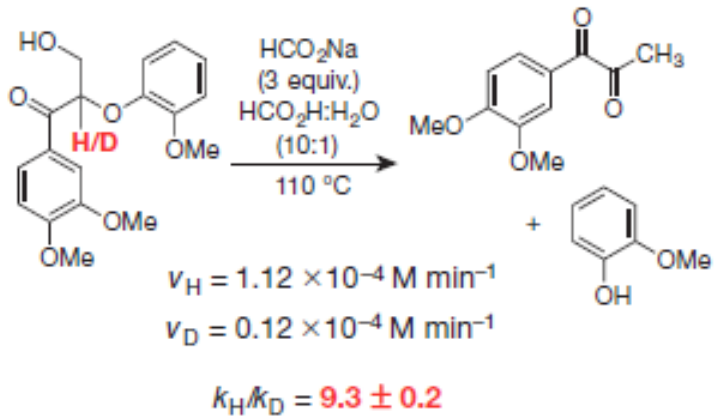
Metal-Free



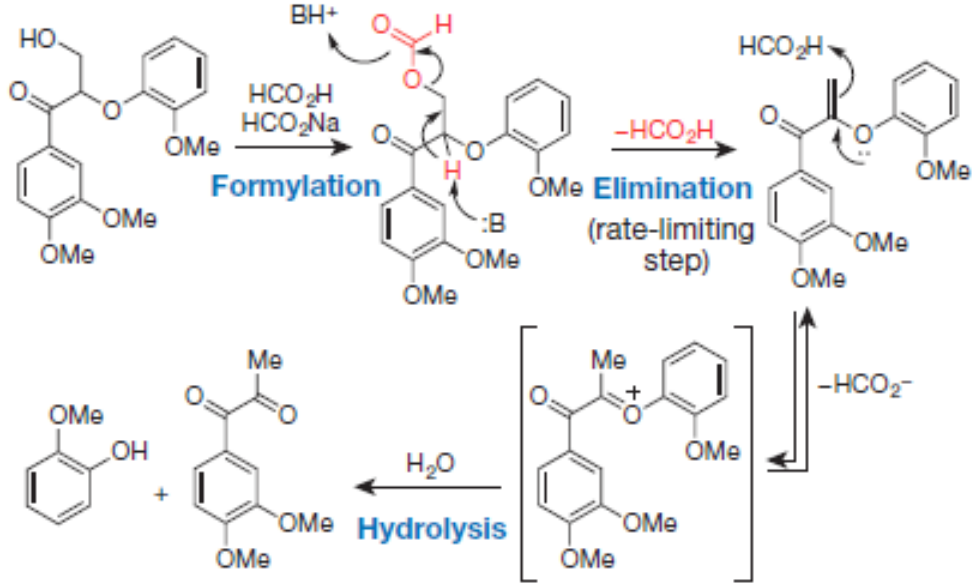
Stahl, *Nature*, **2014**, *515*, 249

Metal-Free

f



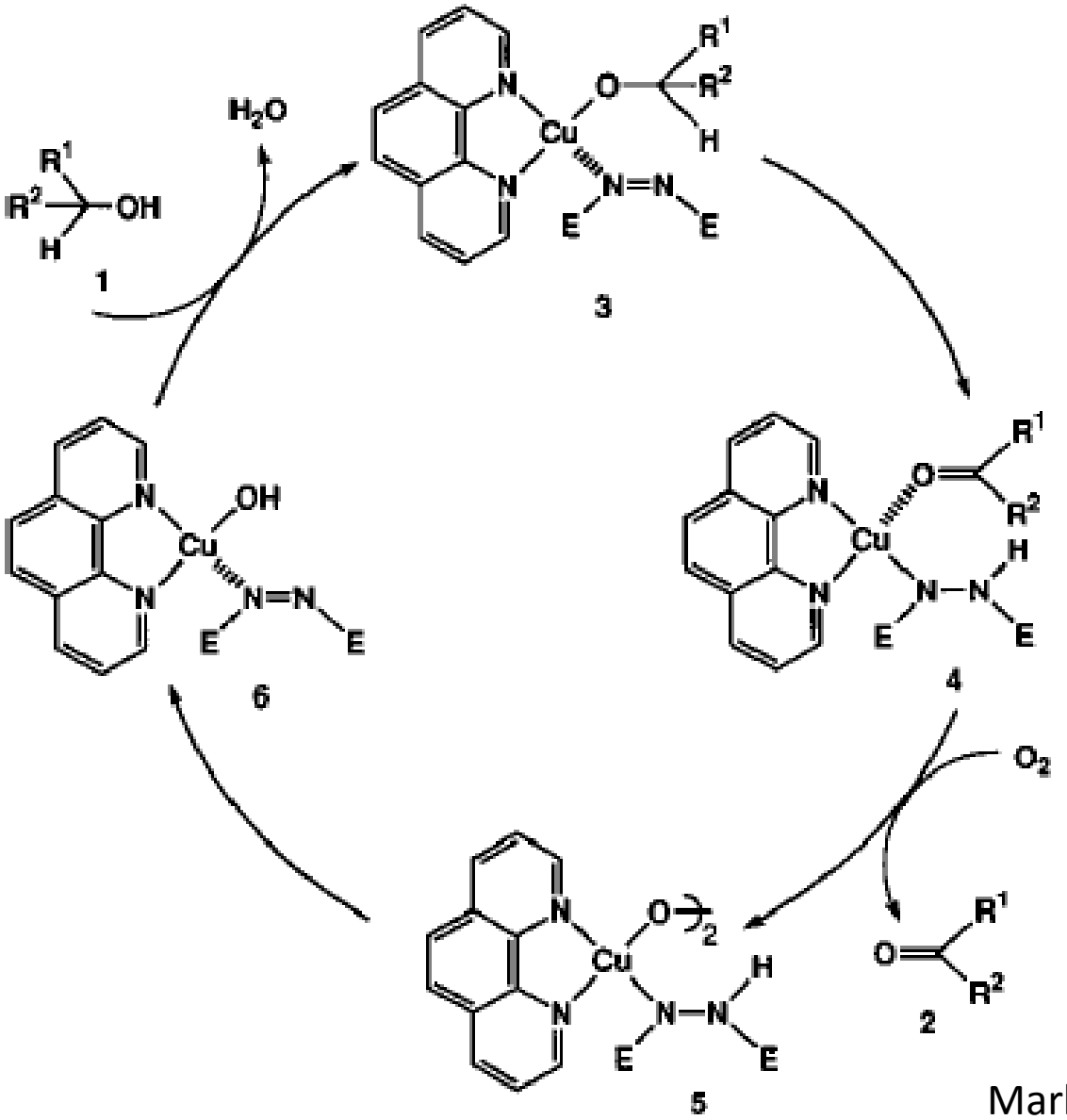
g



Stahl, *Nature*, **2014**, *515*, 249

Acknowledge

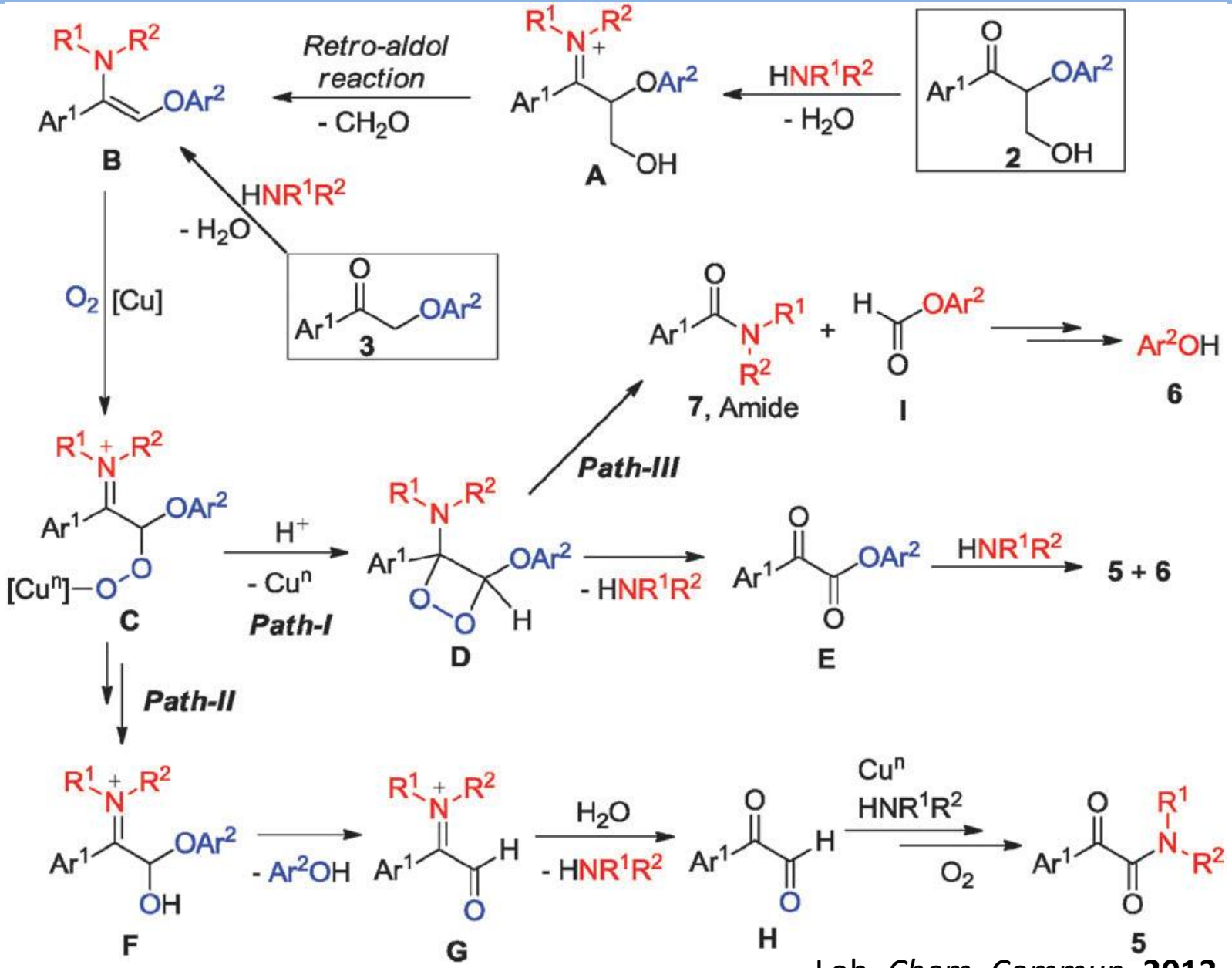
Answer Key



Markó, *Science*, **1996**, *274*, 2044

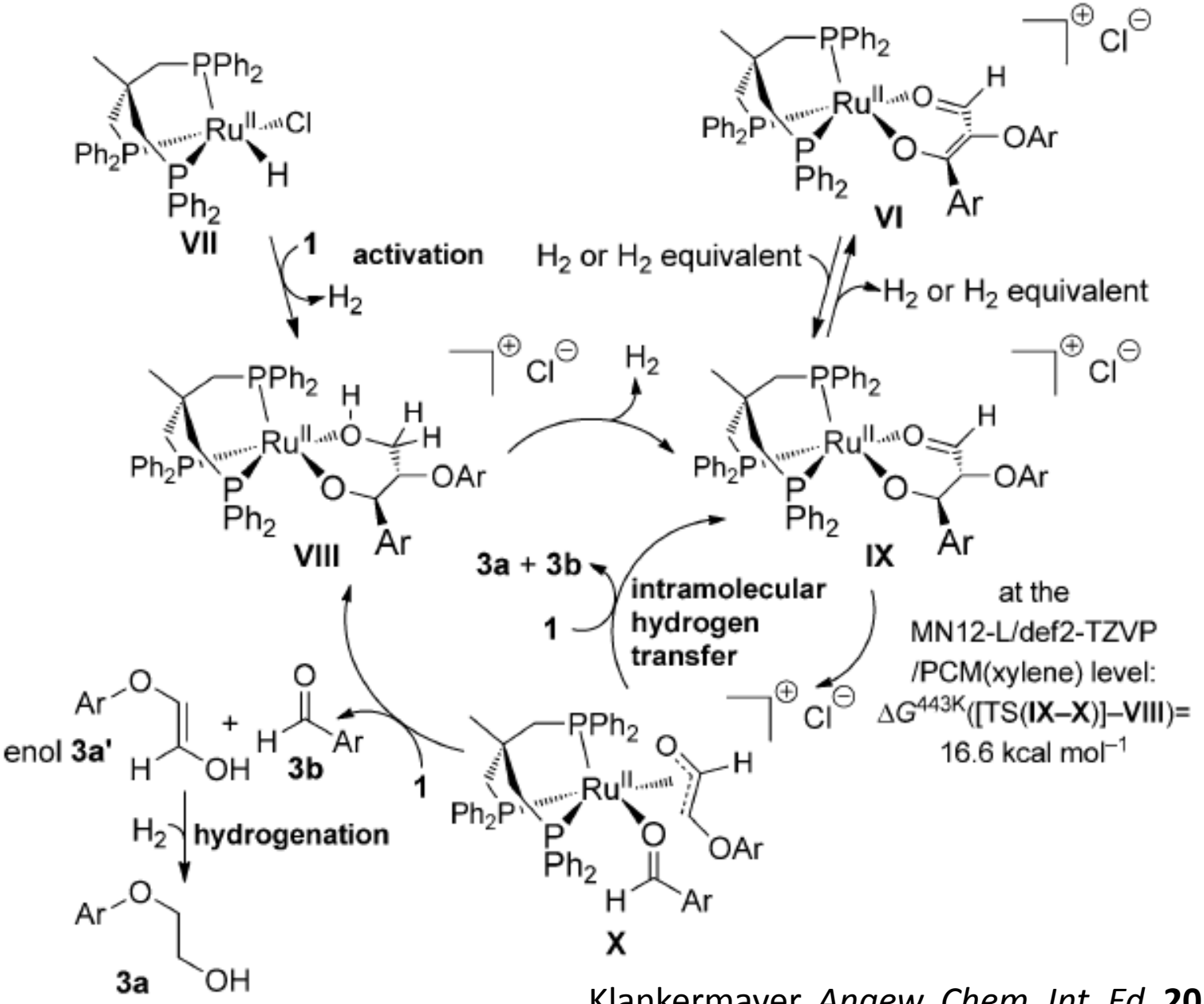
Markó, *Angew. Chem. Int. Ed.* **1997**, *36*, 2208

Answer Key



Loh, *Chem. Commun.* **2013**, *49*, 11439

Answer Key



Klankermayer, *Angew. Chem. Int. Ed.* **2015**, *54*, XXX