Aerobic and biomimetic activation of C-H bonds of phenols catalyzed by copper-amine complexes

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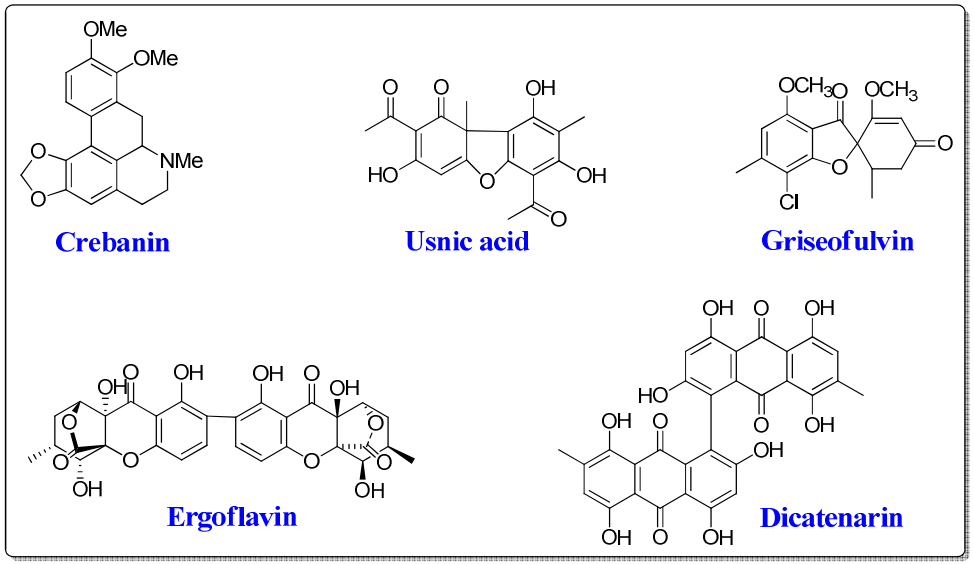
Introduction

Some products formed by oxidative coupling of phenols



Biomimetic phenol couplings studied by D.H.R. Barton and A.R. Battersby since 1950.

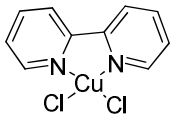
Oxidases (Laccase or Tyrosinase) → Copper-amine model catalysts → CuCl(OH) TMEDA

W. I. Taylor, A. R. Battersby, D. H. R. Barton, T. Cohen, *Festschrift Arthur Stoll.*, Birkhauser, Basel **1957**, 117–143.

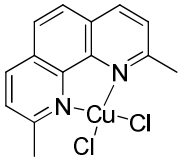
Preparation of the complexes

Copper complexes

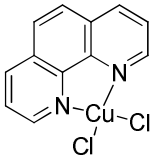
$CuCl_2$



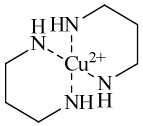
CuCl(phen)



CuCl(neocup)

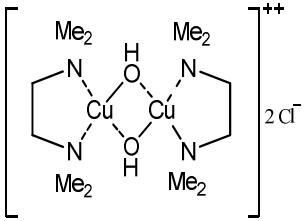


CuCl(bipy)

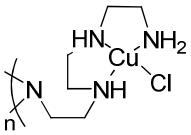


$CuCl_2$- Bis(1,3-propanediamine)

CuCl



$[CuCl(OH)TMEDA]_2$



Cu(I)/PEI

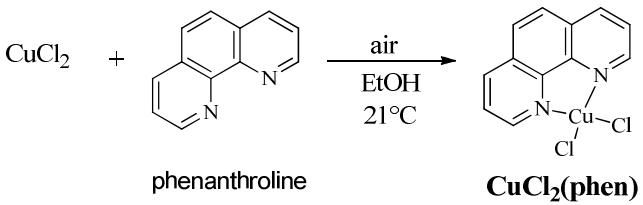
Iron complexe:

$$FeCl_3 + (CH_3)_2NCHO \longrightarrow [Fe(DMF)_3Cl][FeCl_4]$$

Preparation of the complexes

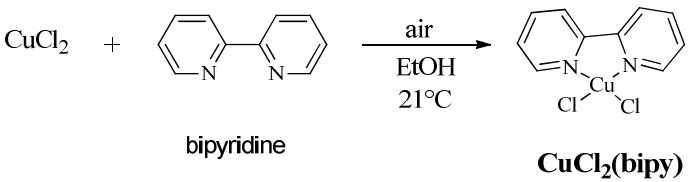
Copper complexes

a) $CuCl_2$



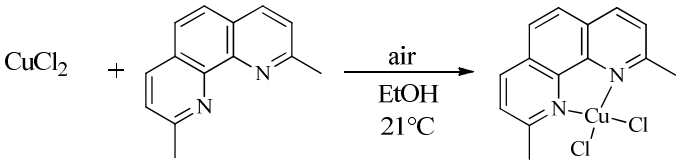
phenanthroline

$CuCl_2$(phen)



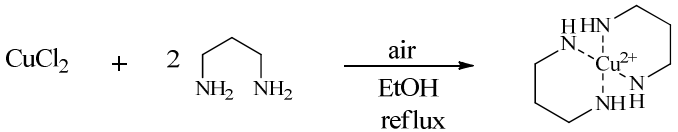
bipyridine

$CuCl_2$(bipy)



dimehylphenanthroline

$CuCl_2$(neocup)



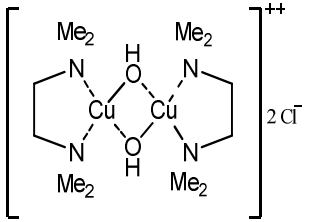
$CuCl_2$-bis(1,3-propanediamine

Preparation of the complexes

Copper complexes

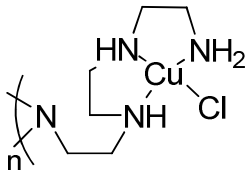
b) CuCl

$$2\ CuCl + 2\ TMEDA \xrightarrow[7h,\ 20°C]{O_2,\ CH_3OH} [CuCl(OH)TMEDA]_2$$



$[CuCl(OH)TMEDA]_2$

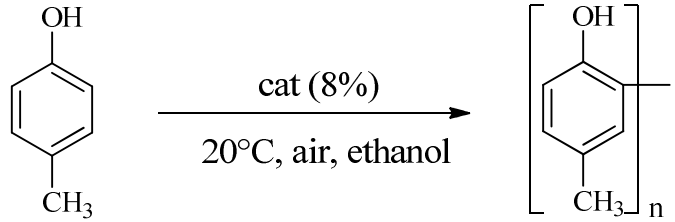
$$CuCl + PEI \xrightarrow[4h,\ 20°C]{air,\ C_2H_5OH} Cu(I)/PEI$$



Cu(I)/PEI

Oxidative coupling of the phenol

para-cresol



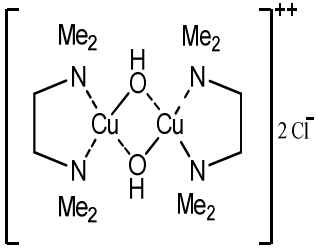
(n=2)

(n= 3, 4, 5)

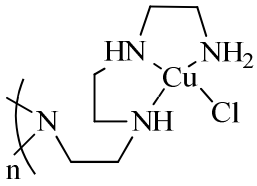
Oxidation conditions:

Phenol/Cu (100/8)
Phenol/Fe (100/8)
Room temperature(20°C),
EtOH, 120h.

Complexe	Rdt (%)
CuCl(OH).TMEDA	**71**
Cu(I)/PEI	31
CuCl(phen)	17
CuCl(neocup)	39
CuCl(bipy)	9
$CuCl_2$- Bis(1,3-propanediamine)	41
$[Fe(DMF)_3Cl][FeCl_4]$	63



$[CuCl(OH)TMEDA]_2$



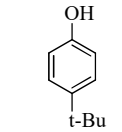
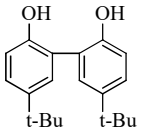
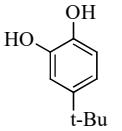
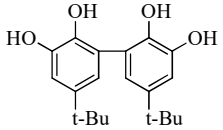
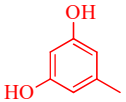
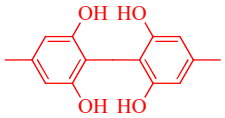
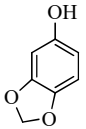
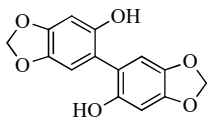
Cu(I)/PEI

S. E. Allen, R. R. Walvoord, R. Padilla-Salinas, M. C. Kozlowski, **Aerobic Copper-Catalyzed Organic Reactions**, *Chem. Rev*. **2013**, 113, 6234–6458 ; doi :10.1021/cr300527g

Oxidative coupling of the phenol

➢ Oxidation of phenols in the presence of $[CuCl(OH)(TMEDA)]_2$

ortho-ortho coupling

Reagent	Product	Yield(%)
		63
		67
		**80**
		48

Substrate: the para position is blocked or difficult to access

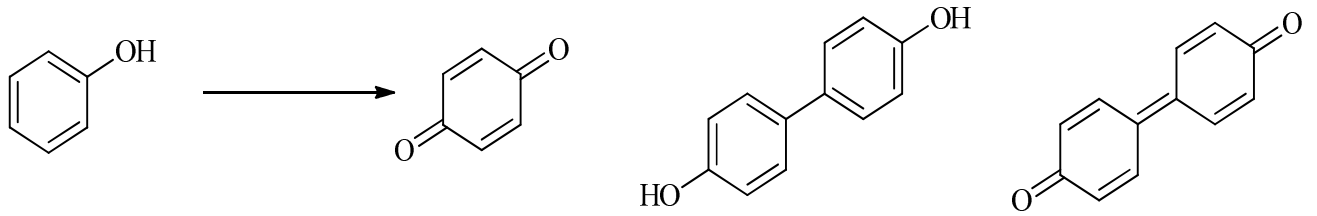
Couplage ortho-ortho coupling

Oxidation conditions:

- ➢ Phenol/Cu (100/8)
- ➢ 21°C
- ➢ EtOH
- ➢ 96h.

Oxidative coupling of the phenol

- **Oxidation of the phenols in presence of $[CuCl(OH)(TMEDA)]_2$**
  - **Para-para** coupling

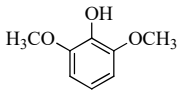
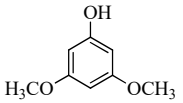
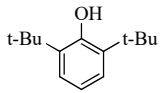
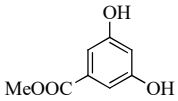
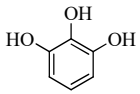


Quinone Bisphenol Diphenoquinone

Oxidative para-para coupling of phenols

➢ Oxidation of phenol in the presence of CuCl(OH)(TMEDA)

para-para coupling

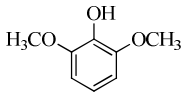
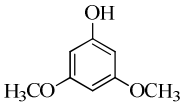
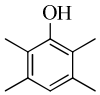
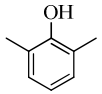
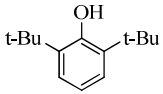
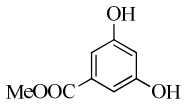
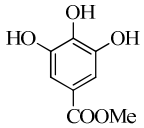
Reagent	Yield(%) Quinone	Yield(%)Bisphenol	Yield(%) Diphenoquinone
	0	0	53
	**16**	**75**	**0**
	0	15	41
	0	0	**87**
	0	0	**99**
	0	0	0
	0	0	0

Oxidation conditions

- Phenol / Cu (100 / 8)
- Room temperature 21°C
- EtOH
- 96 h.

Oxidative para-para coupling of phenols

➢ Oxidation of phenols in the présence of Cu(I)/PEI

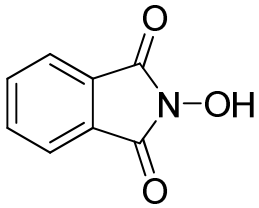
Reagent	Yield (%) Quinone	Yield(%)Bisphenol	Yield (%) Diphenoquinone
	0	0	53
	**16**	**75**	**0**
	0	15	41
	0	0	**87**
	0	0	**99**
	0	0	0
	0	0	0

Oxidation conditions:

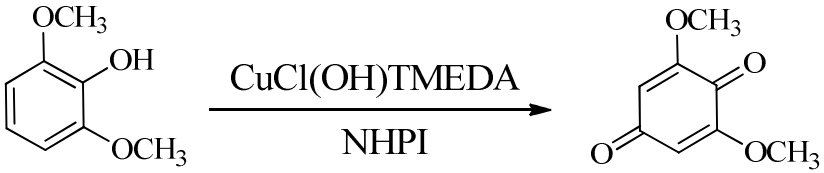
- Phenol / Cu (100 / 3.75) (1.5mL)
- Room temperature
- EtOH
- 120 h.

Oxidation of phenols

- **Oxidation of phenols in the presence of NHPI: formation of quinone**



NHPI = *N*-hydroxyphthalimide



Solvent	Temperature (°C)	Yield (%)
EtOH	21	16
EtOH	70	27
CH_3CN	21	32
CH_3CN	**70**	**92**

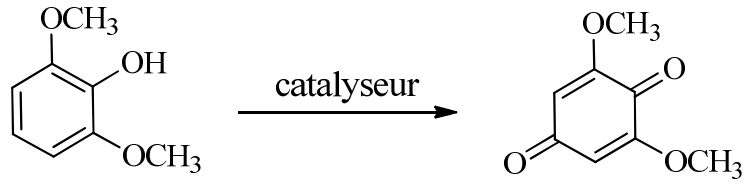
Oxidation conditions:

- Phenol/Cu/NHPI (100/8/10)
- 96 h.

Best conditions for formation of p-quinone
70°C in acetonitrile

Oxidation of phenols

➢ Oxidation of phenols in the presence of NHPI

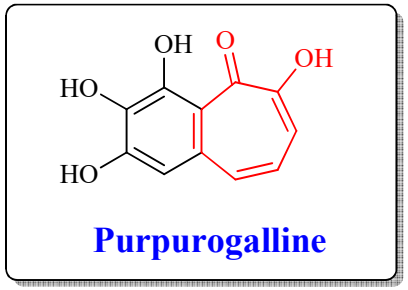


Catalyst	Yield (%)
CuCl(OH)TMEDA	**92**
Cu(I)/PEI	0
$CuCl_2$(neocup)	0
$[Fe(DMF)_3Cl][FeCl_4]$	0

Oxidation conditions :

- Phenol/Cu/NHPI (100/8/10)
- Phenol/Fe/NHPI (100/8/10)
- 70°C
- CH_3CN
- 96 h

Synthesis of purpurogallin from pyrogallol



Purpurogalline

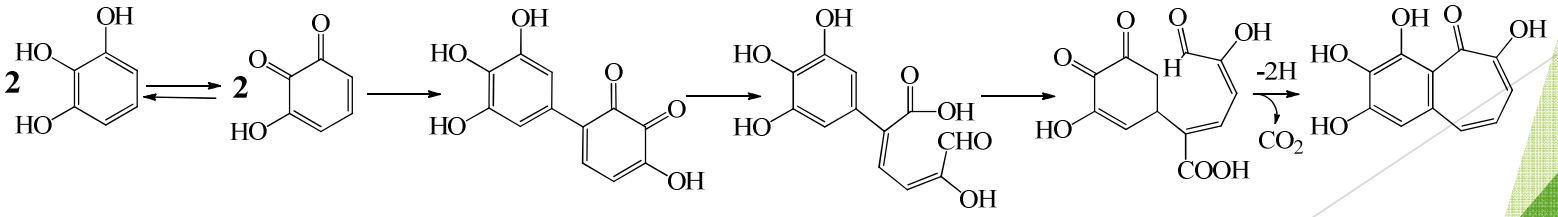
Purpurogallin:

- ✓ naturel red dye
- ✓ tropolone

Synthesis of purpurogallin by oxidation :

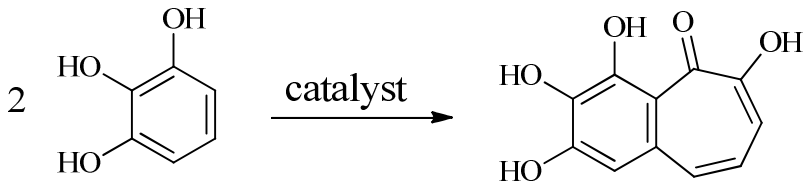
- ✓ Stoichiometric oxidation (KIO_3)
- ✓ Oxidases : laccase, tyrosinase, peroxidase

Mechanism according to Haworth



Synthesis of purpurogallin from pyrogallol

- **Synthesis of Purpurogallin by aerobic oxidation like Laccase**



Catalyst	Solvent	T (°C)	Yield(%)
CuCl(OH)TMEDA[a]	EtOH	20	43
Cu(I)/PEI[b]	EtOH	20	0
CuCl(OH)TMEDA / NHPI[c]	CH_3CN	70	0

Conditions :

[a] Phenol/Cu (100/8), 20°C, EtOH, 96h

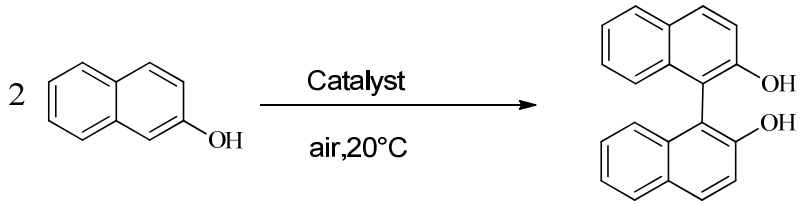
[b] Phenol/Cu(I)/(100/3.75) (1.5 mL), 20°C, EtOH, 96h

[c] Phenol/Cu/NHPI (100/8/10), 70°C, CH_3CN, 96 h

S. Dib ; D. Villemin; A. Hamhami; B. Mostefa-Kara; N. Bar; M. Dekhici ; N. Cheikh, **On the green catalytic synthesis of Purpurogallin**, *Rev. Roum. Chim.*,**2020**, 65(12), 1153-1157, **doi: 10.33224/rrch.2020.65.12.1.**

Oxidation of 2-naphthols and analogues

➢ Oxydation of 2-naphthols

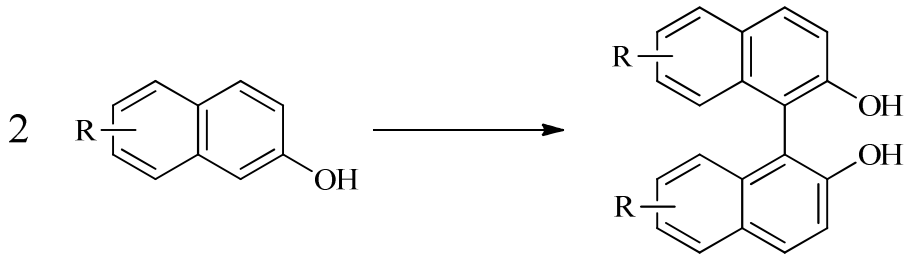


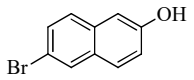
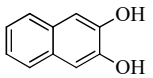
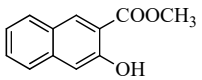
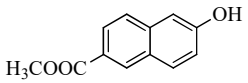
Catalyst	Solvent	T (°C)	Yield (%)
CuCl(OH)TMEDA[a]	**EtOH**	**21**	**86**
CuCl(OH)TMEDA / NHPI[b]	CH_3CN	70	43
Cu(I)/PEI[c]	EtOH	21	77
$CuCl_2$(phen)[a]	EtOH	21	29
$CuCl_2$(neocup) [a]	EtOH	21	31
$CuCl_2$(bipy) [a]	EtOH	21	traces
$CuCl_2$-Bis(1,3-propanediamine) [a]	EtOH	21	71
$[Fe(DMF)_3Cl][FeCl_4]$ [a]	EtOH	21	55

Oxidative conditions:
[a] naphthol/catalyst (100/8), 96h.
[b] naphthol/catalyst (/NHPI (100/8/10), 96 h.
[c] naphthol/catalyst ((100/3.75) (1.5 mL), 96h.

Oxydation des 2-naphtols et analogues

➢ Oxidation of naphthols



Reagent	[CuCl(OH)TMEDA]$_2$[a]		[CuCl(OH)TMEDA]$_2$/NHPI][b]	
	t (h)	Yield (%)	t (h)	Yield (%)
	96	80	96	43
	96	67	96	0
	24	85	96	31
	24	**99**	96	**49**

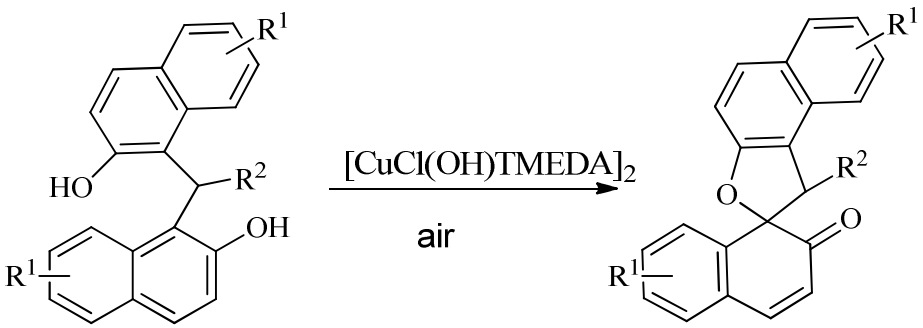
Conditions :

[a] naphthol/Cu (100/8), 21°C, EtOH,

[b]naphthol/Cu/NHPI (100/8/10), 70°C, CH_3CN,

Oxidation of methylenebinaphthols andt benzylidenebinaphthols

➢ Oxidation of methylenebinaphthols and benzylidenebinaphthols



Oxidative conditions:

- Phenol/Cu (100/8)
- Air
- Room temperature(21°C)
- Solvent
- Time (48 h)

- Creation of C-O bond
- Desaromatisation
- Green conditions

M. Dekhici ; S. Plihon, N. Bar ; D.Villemin ; H. Elsiblani ; N. Cheikh, **Aerobic Copper Catalytic Oxidation of Methylene and Arylidenebisnaphthols: A Green and Efficient Synthesis of Spironaphthalenones** , *ChemistrySelect* , **2019**, 4, 705 - 708 ; **doi: 10.1002/slct.201803153**