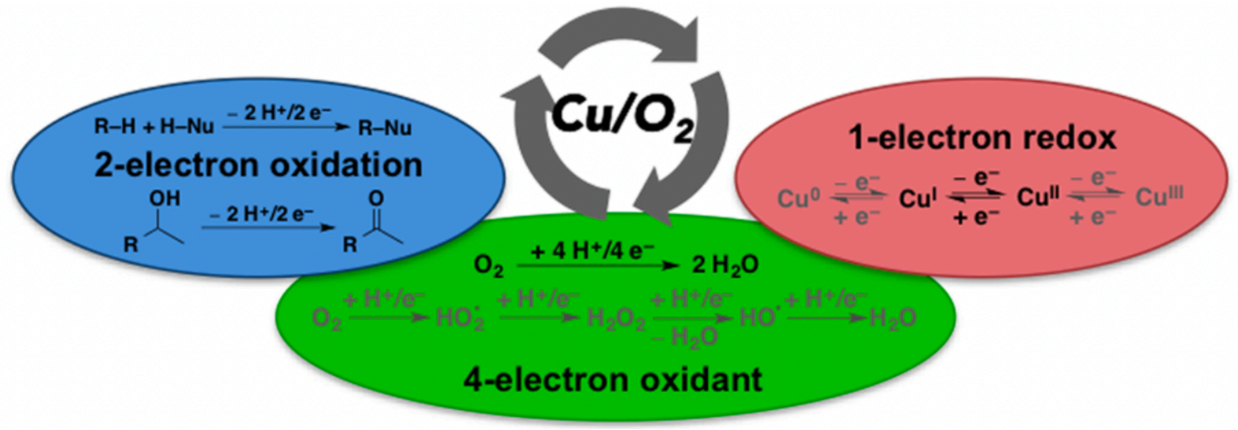
Copper–Catalyzed
Aerobic Oxidative Reaction



2023/10/28 (Sat)
SHUNKI Matsuyama

Contents

1. Introduction

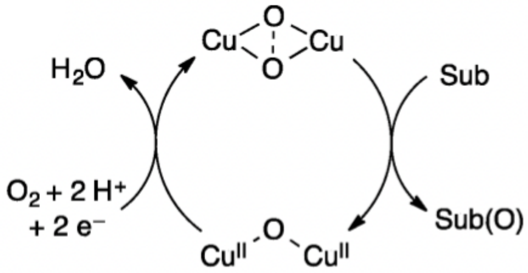
1-1) Aerobic Oxidation

Features

O_2 Low Toxicity Low Cost Natural Abundance

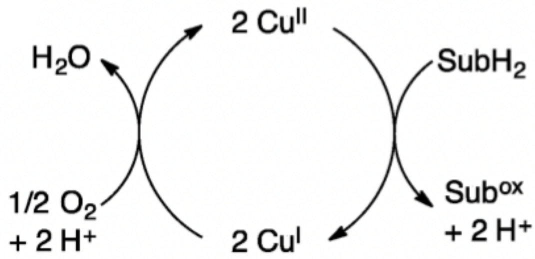
Reaction Types[a]

oxygenase-type



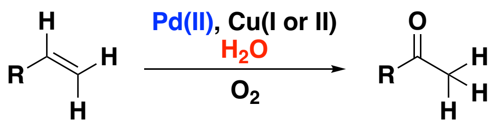
directly incorporate oxygen atoms into the organic molecule

oxidase-type

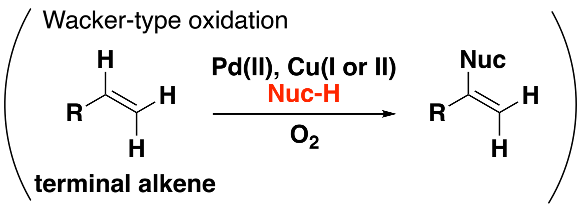


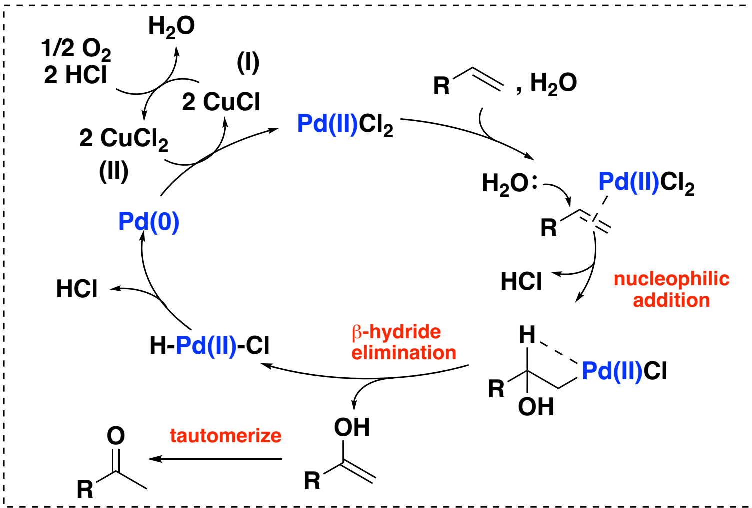
couple diverse oxidation reactions to the reduction of O2 to water or hydrogen peroxide

Wacker Oxidation[b]

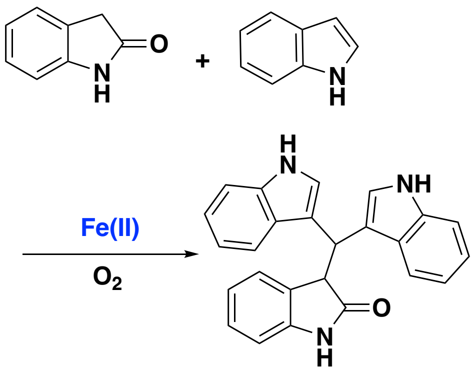


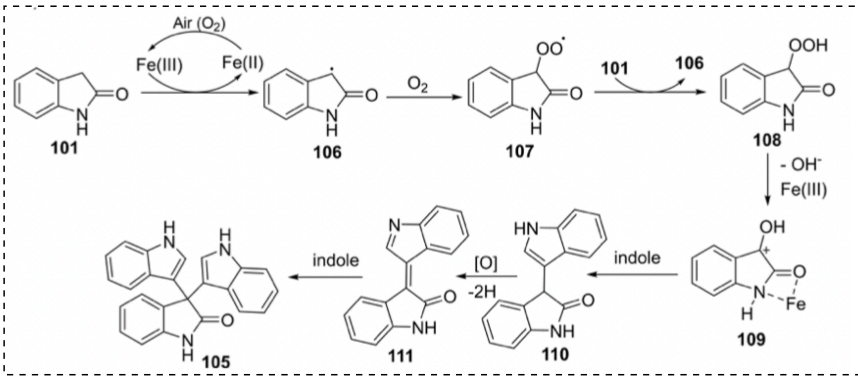
terminal alkene





Aerobic Oxidative Alkylation with Fe Catalysis[c]





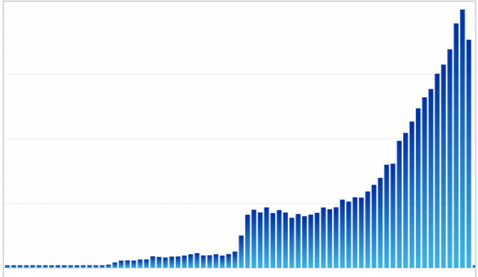
(a) Hayaishi, O. et al. *J. Am. Chem. Soc.* **1955**, 77, 5450-5451.
(b) Smidt, J.; Sieber, R. *Angew. Chem.* **1959**, 1, 176.
(c) Xu, D-Z. at al. *Angew. Chem.* **2020**, *132*, 3904–3908.

1. Introduction

1-2) Copper Catalysis

29
Cu
copper
63.546

Electron confiduration: [Ar] $3d^{10}$ $4s^1$
Period numver: 4 Group number: 11
Group name: transition metal



reports about Cu and molecular oxygen (1950-2023)

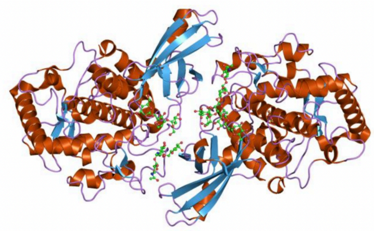
Superiority (compared to other 4d, 5d metal)

Low cost Low toxicity High occurrence in the earth's crust

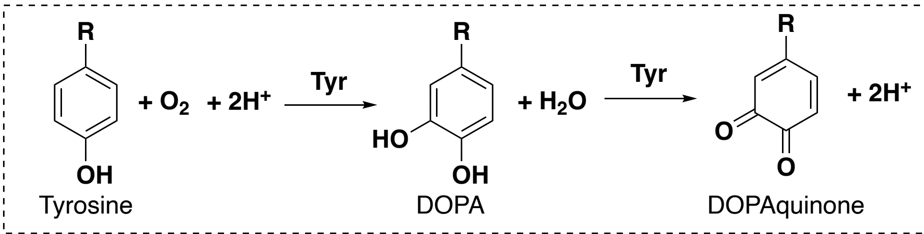
Features

Cu(0), Cu(I), Cu(II), Cu(III) Lewis acid interactions π-coordination

Copper-Containing Enzymes(1)

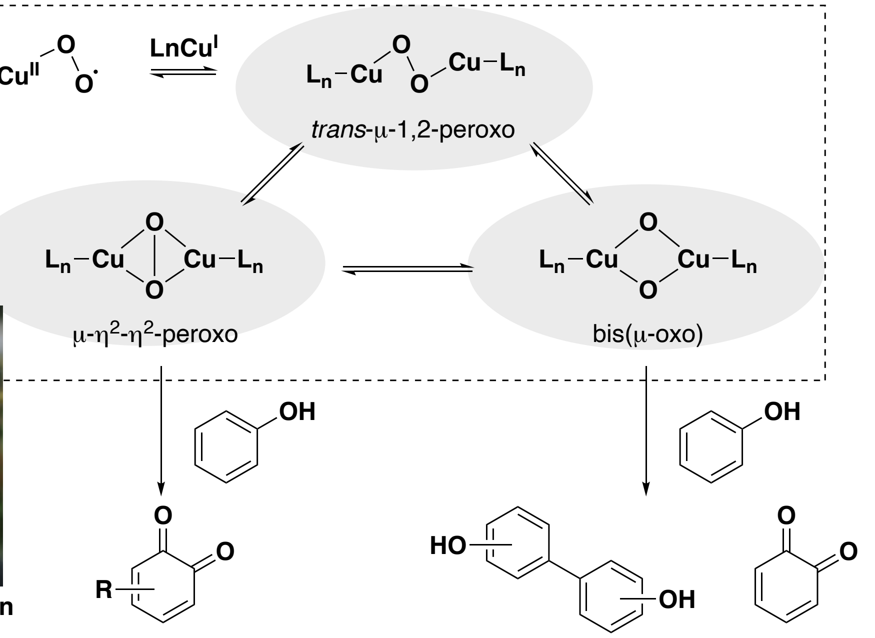


Tyrosinase

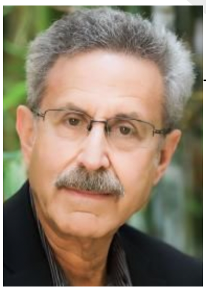


Diverse Biochemical Processes
Melanin production, protection from pathogens, hydrocarbon metabolism, etc.

1-3) Cu_2-O_2 Complex(2)



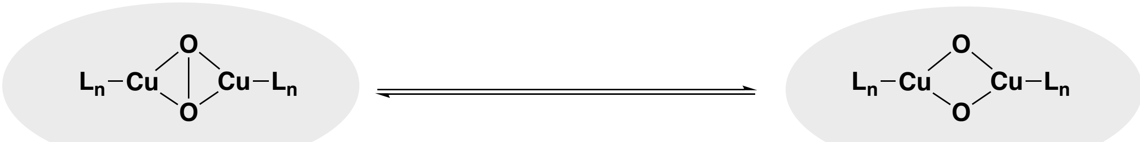
William B. Tolman (1961-)



Edward I. Solomon (1946-)

1) Fujieda, N.; Ito, S. *J. Jpn. Biochem. Soc.* **2021**, 93, 4, 521-525.
2) (a)*Chem. Rev.* **2004**, 104, 2, 1047–1076. (b)Ch*em. Rev.* **2014**, 114, 7, 3659–3853.

1. Introduction



μ-η²-η²-peroxo bis(μ-oxo)

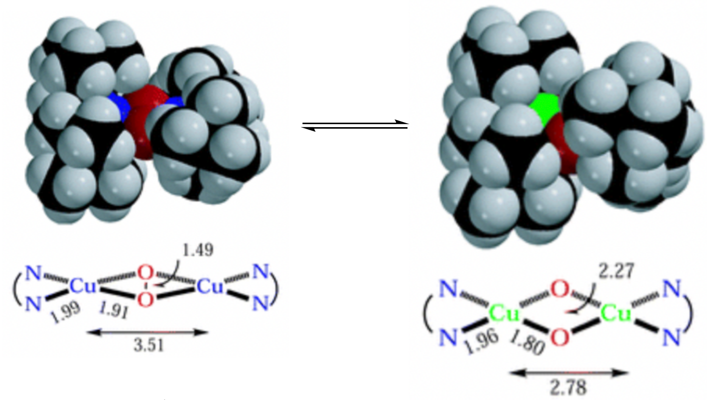
influenced by

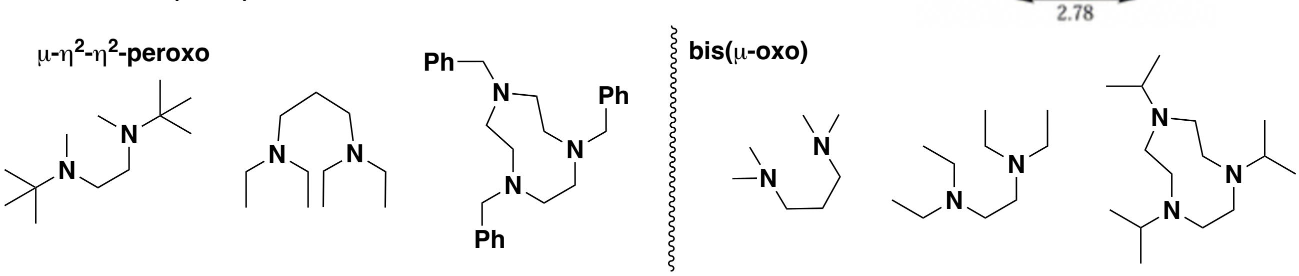
the steric and electronics effects of the ligands,
the counter-ion on copper,
solvent, temperature

Ligand Steric Effects[(a)]

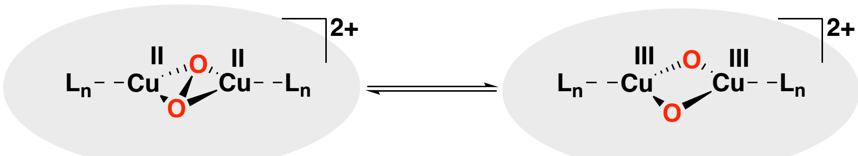
T. Daniel P. Stack
(1959-)

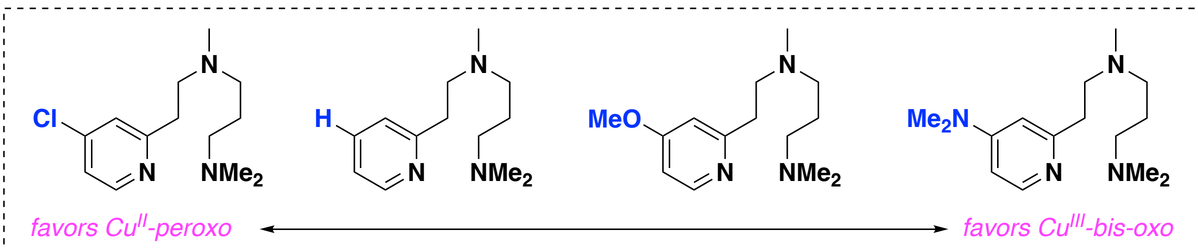
μ-η^2-η^2-peroxo bis(μ-oxo)





Ligand Electronic Effects[(b)]

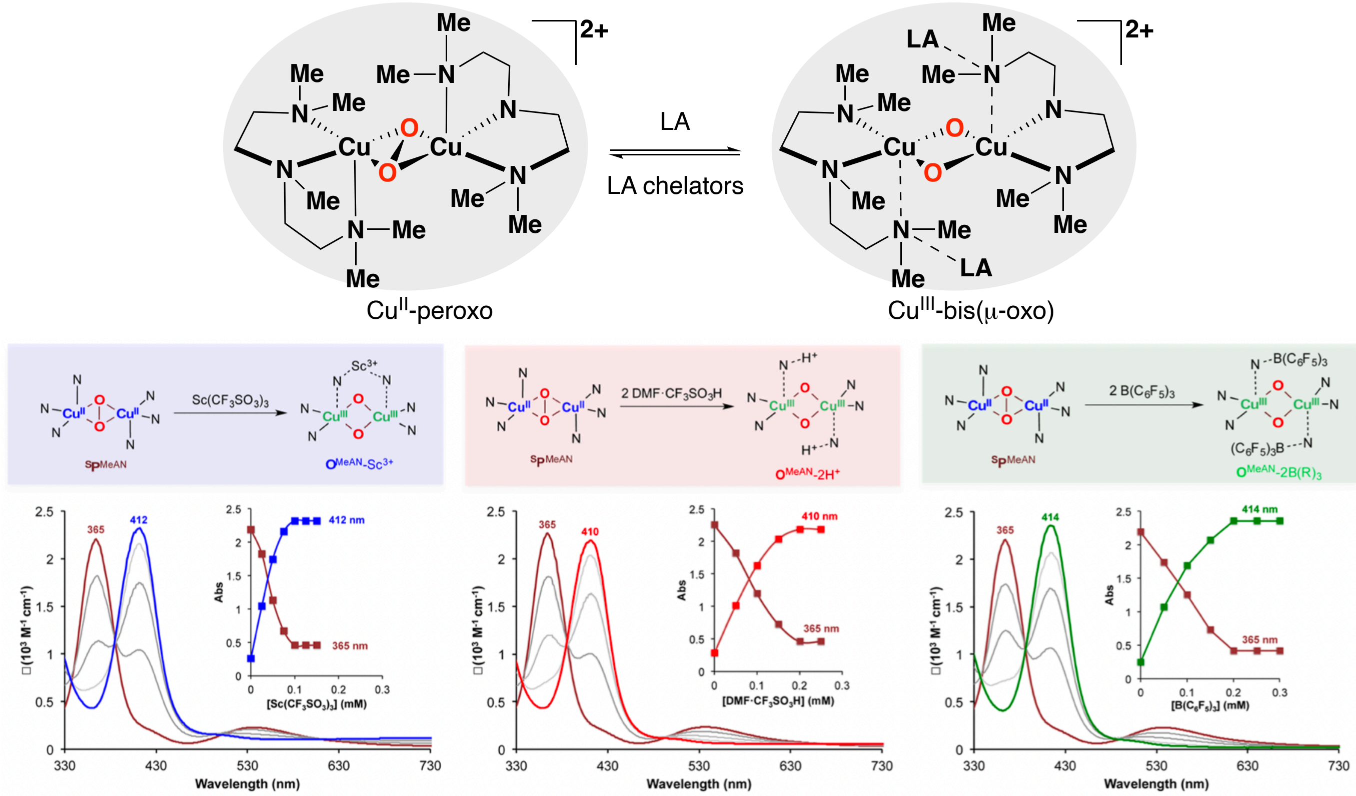




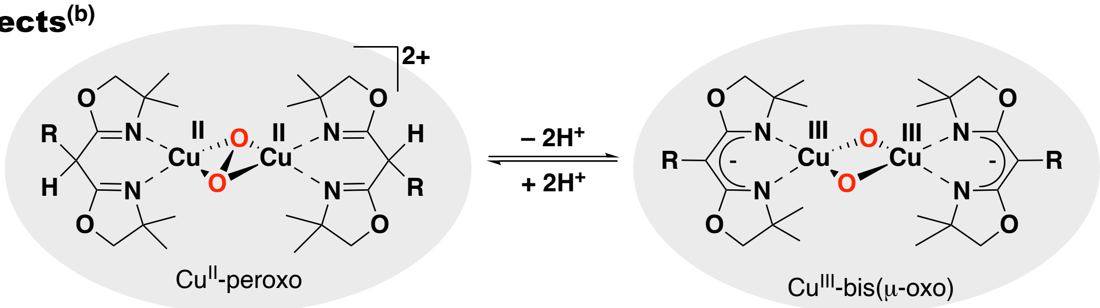
(a) (1) Stack, T. D. *Dalton Trans.* **2003**, *10*, 1881. (2) Tolman, W. B. *Acc. Chem. Res.* **1997**, 30, *6*, 227–237
(b) (1) Stack, T. D. et al. *J. Am. Chem. Soc.* **2006**, *128*, 2654. (2) Stack, T. D. et al. *J. Am. Chem. Soc.* **2006**, *128*, 9268.

1. Introduction

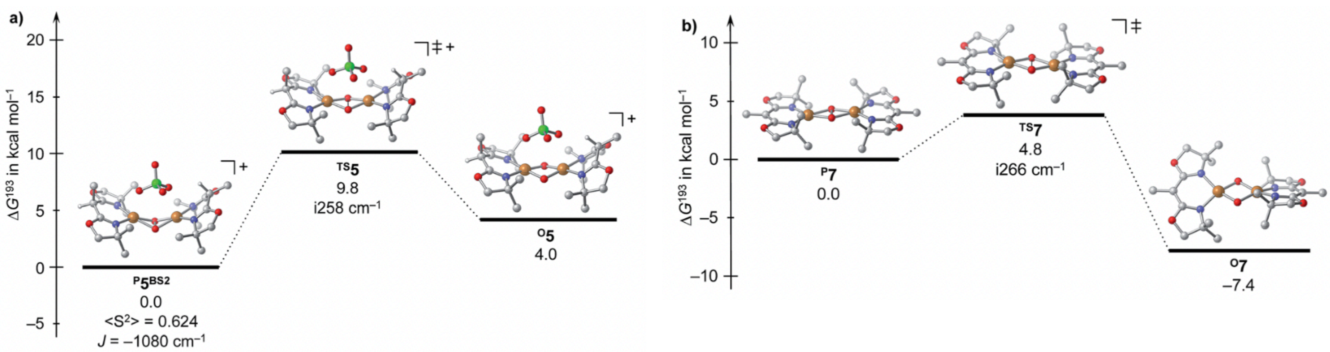
Lewis Acid Additive Effects(a)



pH Effects(b)



(a) acidic condition **(b) neutrality condition**



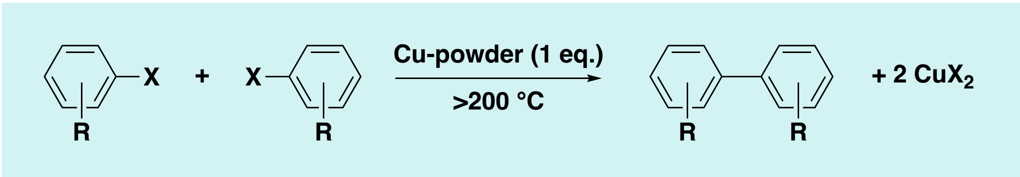
(a) Karlin, K. D. et al. *J. Am. Chem. Soc.* **2017**, *139*, 3186.
(b) Meyer, F. et al. *Chem. Sci.* **2017**, *8*, 3031.

2. Copper

2-1) Cu Catalyzed Reaction –Mechanism

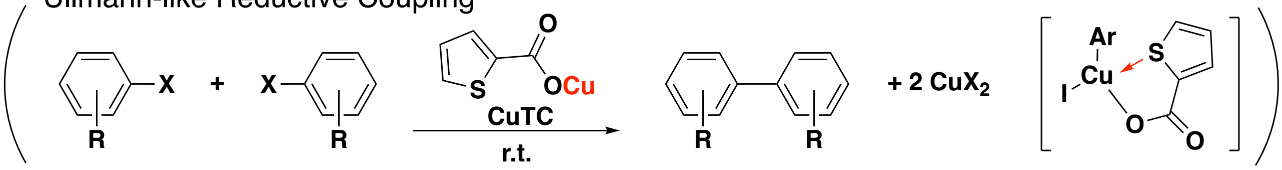
(a) Cu^{I} / Cu^{III} Catalytic Cycle
(b) Cu^{I} / Cu^{II} / Cu^{III} Catalytic Cycle
(c) Single Electron Transfer (Cu^{II} / Cu^{I})

Ullmann Coupling[(a)]

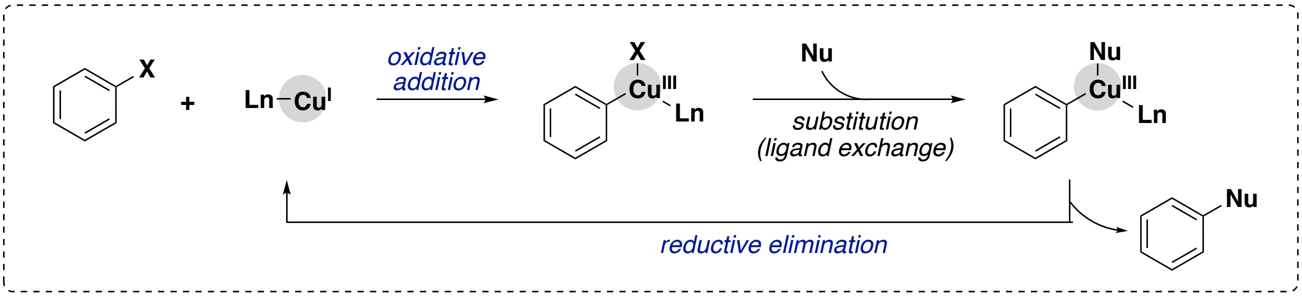


Fritz Ullman (1875-1939)

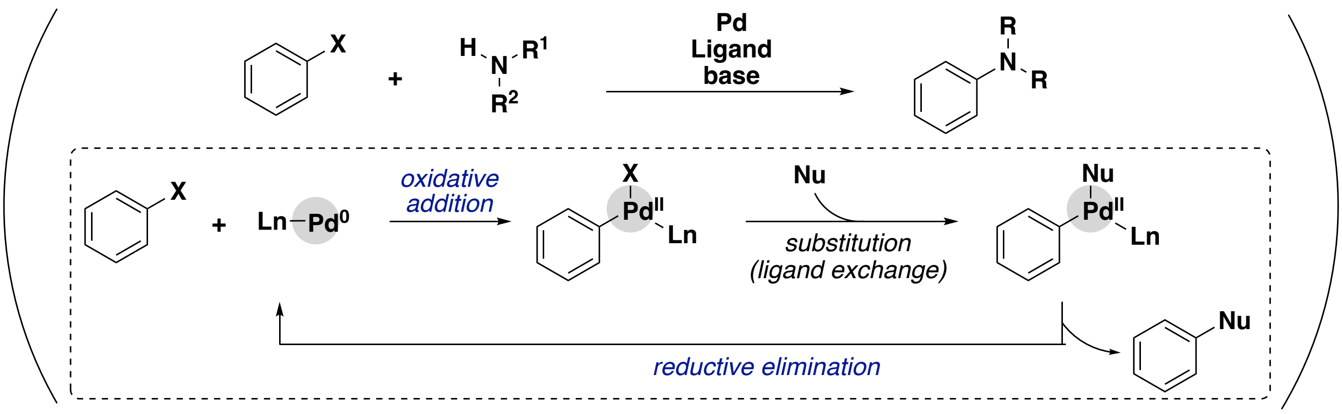
Ullmann-like Reductive Coupling



(a) Cu^{I} / Cu^{III} Catalytic Cycle[(c)]



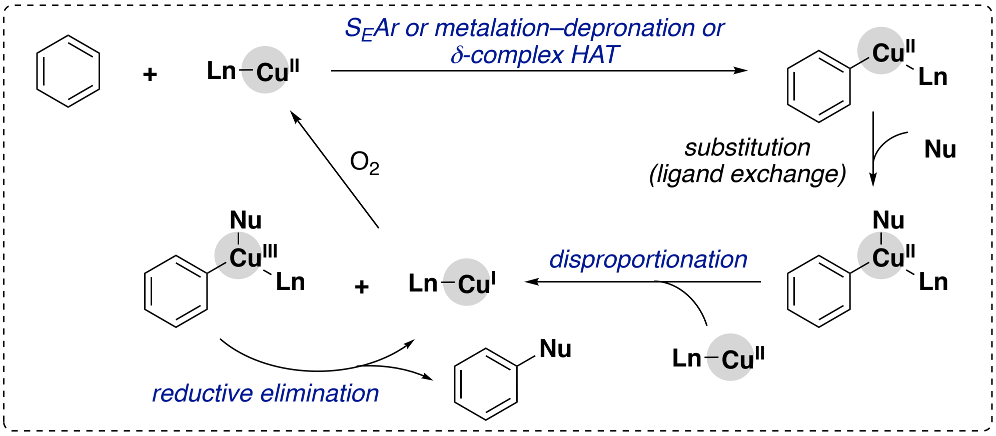
Buchwald–Hartwig reactions mediated by Pd

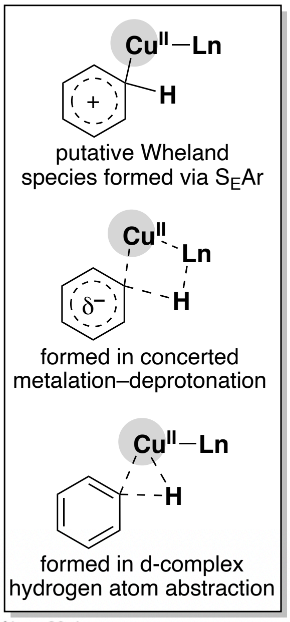


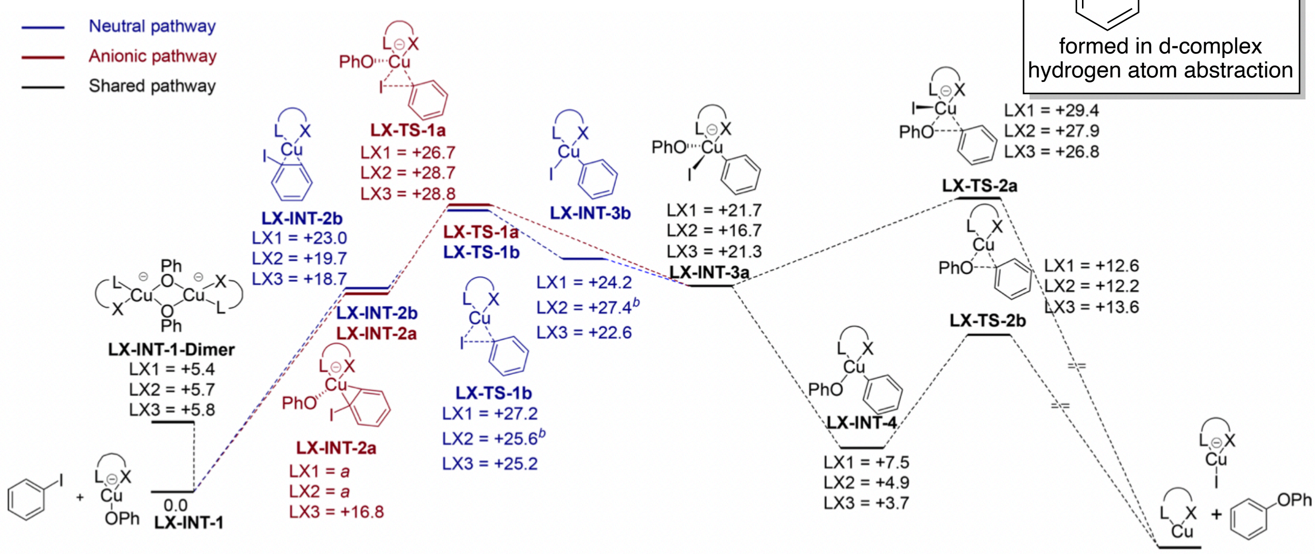
(a) Ullmann, F.; Bielecki, J. *Chem. Ber.* **1901**, *34*, 2174.
(b) Zheng, S.; Zhang, D.; Liebeskind, L. S. *J. Org. Chem.* **1997**, *62*, 2312.
(c) (1)Paul, F.; Patt, J.; Hartwig, J. F. *J. Am. Chem. Soc.* **1994**. *116*, 5969. (2)Guram, A. S.; Buchwald, S. L. *J. Am. Chem. Soc.* **1994**. *116*, 7901.

2. Copper

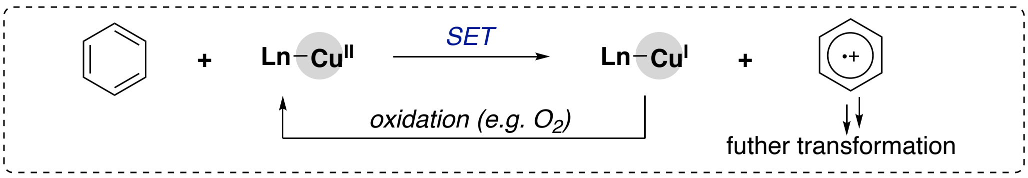
(b) Cu^I / Cu^II / Cu^III Catalytic Cycle[(a)]





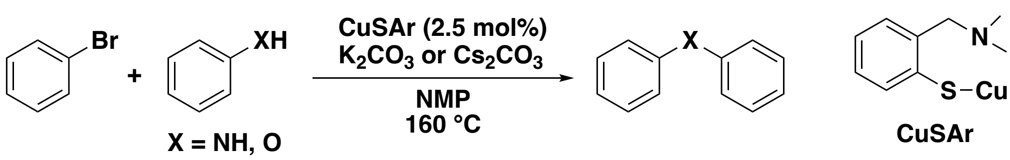


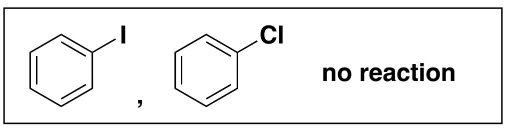
(c) Single Electron Transfer (Cu^II / Cu^I)[(b)]



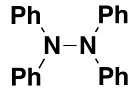
William A. Waters (1869-1948)

Coupling reaction of bromobenzene with nitrogen and oxygen nucleophiles[(c)]





radical scavenger



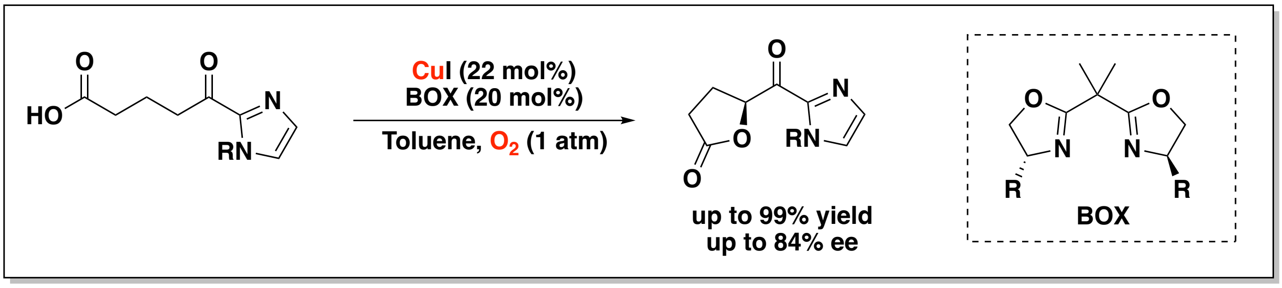
etc.

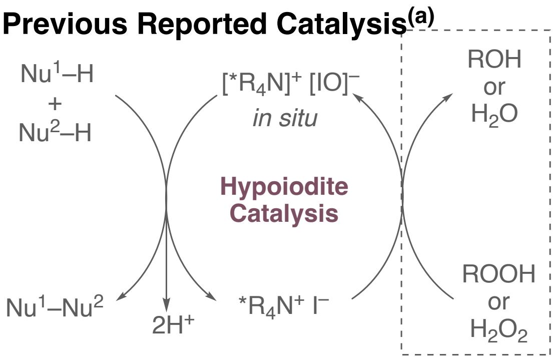
reaction: slowed down / stopped

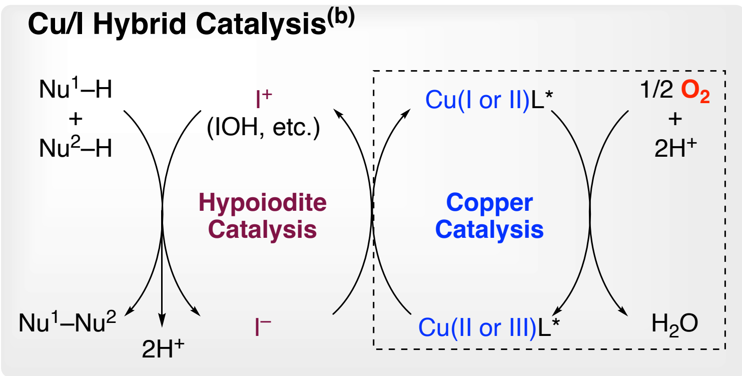
a) (1)Mondal, S.* *ChemTexts* **2016**, *2*, 17. (2)Giri, R.; Brusoe, A.; Troshin, K.; Wang, J. Y.; Font, M.; Hartwig, J. F.* *J. Am. Chem. Soc.* **2018**, *140*, 793-806.
b) Casitas, A.; Ribas, X.* *Chem. Sci.* **2013**, *4*, 2301-2318.
c)Sperotto, E.; Klink, G. P. M.; Koten, G.*, Vries, J. G.* *Dalton Trans.*, **2010**, 39, 10338–10351.

2. Copper

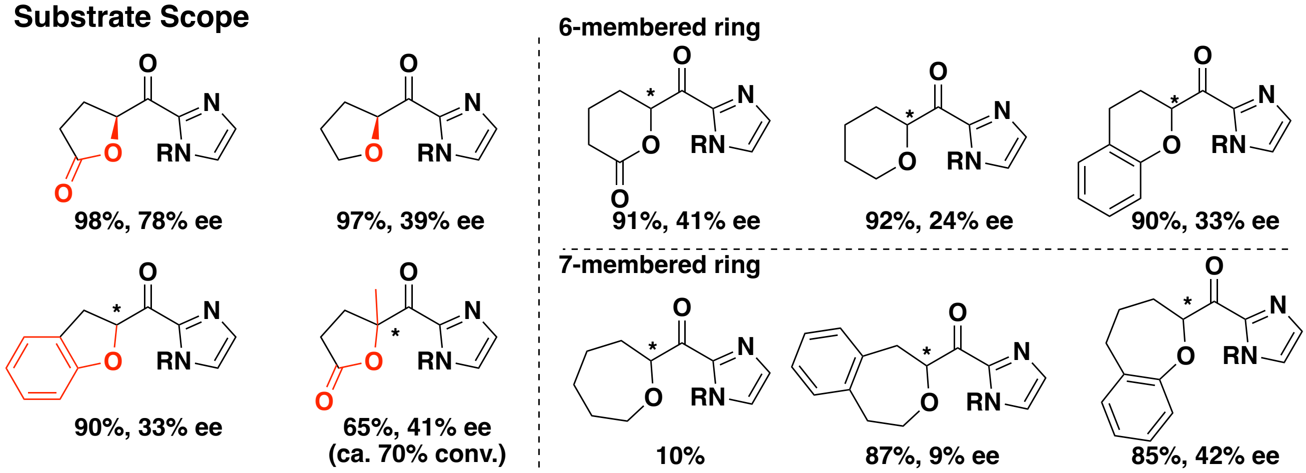
Enantioselective Aerobic Oxidative Coupling with Cu/I Hybrid Catalysis (My Research)



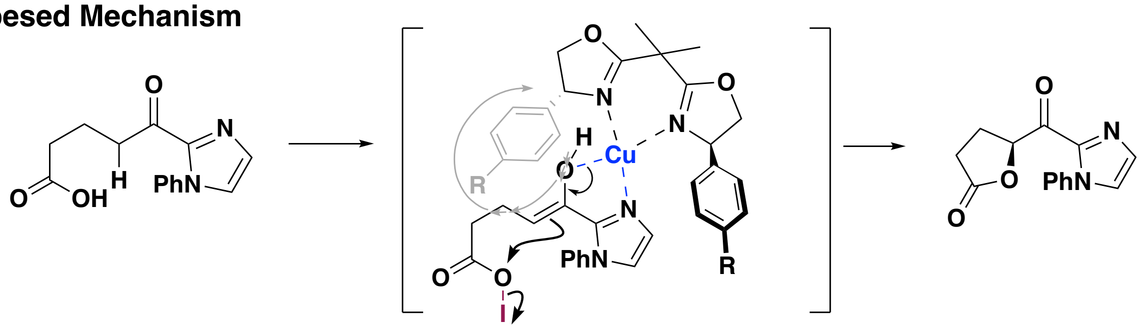




Substrate Scope



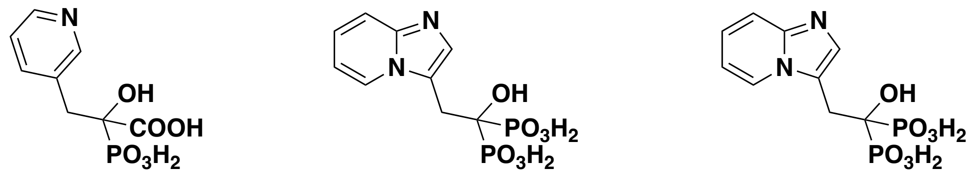
Propesed Mechanism



(a) Selected reviews: M. Uyanik, K. Ishihara, *ChemCatChem* **2012,** *4*, 177. Yusubov, M. S.; Zhdankin, V. V. *Resour. Effic. Technol.* **2015**, *1*, 49.
(b) Selected reviews on Cu aerobic oxidation catalysis:S. E. Allen, R. R. Walvoord, R. Padilla-Salinas, M. C. Kozlowski, *Chem. Rev.* **2013**, *113*, 6234. S. D. McCann, S. S. Stahl, *Acc. Chem. Res.* **2015**, *48*, 1756.

4. Proposal

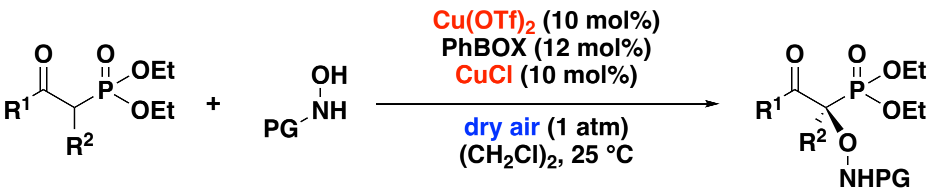
α-Hydroxy Phosphonic Acid Derivatives

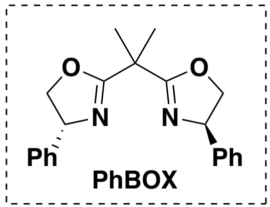


3-PEHPC | Risedronic Acid | Minodronic Acid

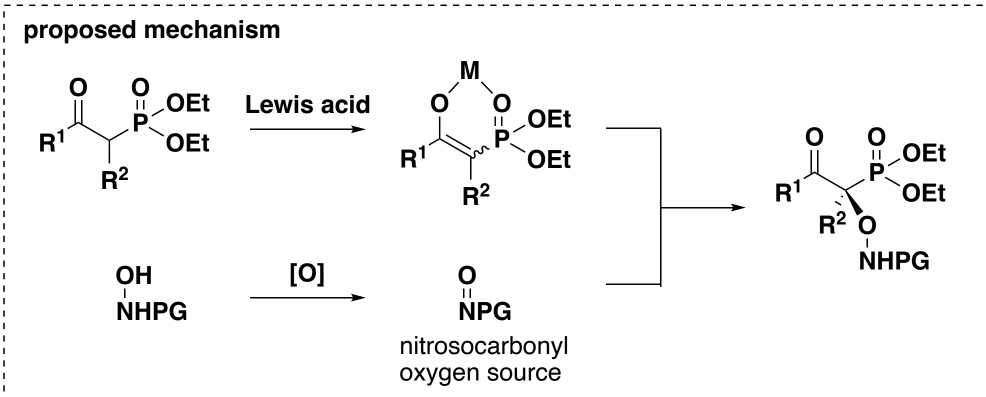
excellent inhibitory bioactivities towards a wide range of enzymes
(renin, HIV protease, and various classes of protein tyrosine kinases etc.)

Asymmetric Synthesis of Tertiary α-Hydroxy Phosphonic Acid Derivatives



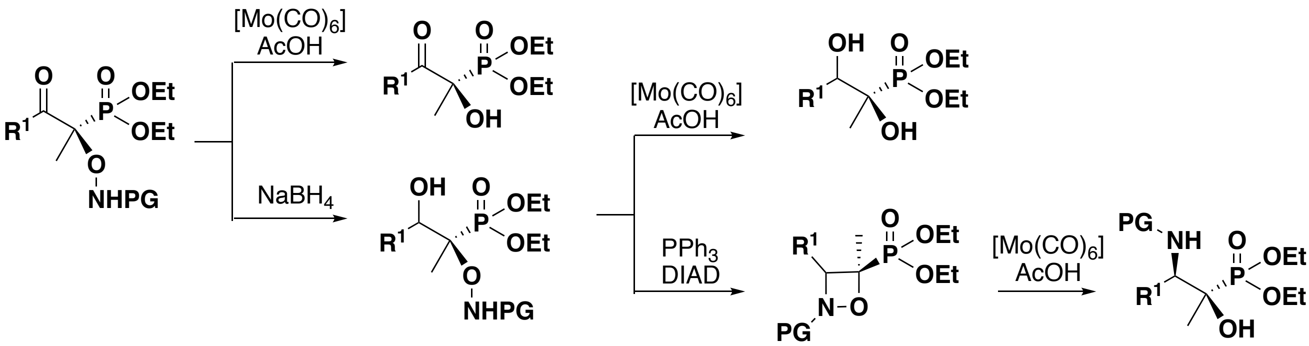


up to 97% yield
up to >99% ee



H. Yamamoto
(1943-)

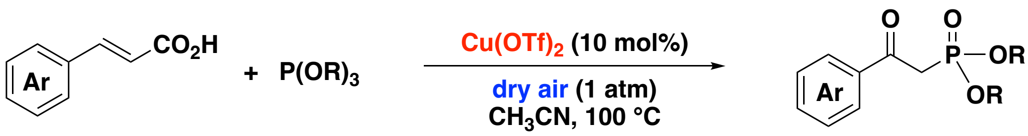
Synthesis of Various Substituted α-Hydroxy Phosphonates

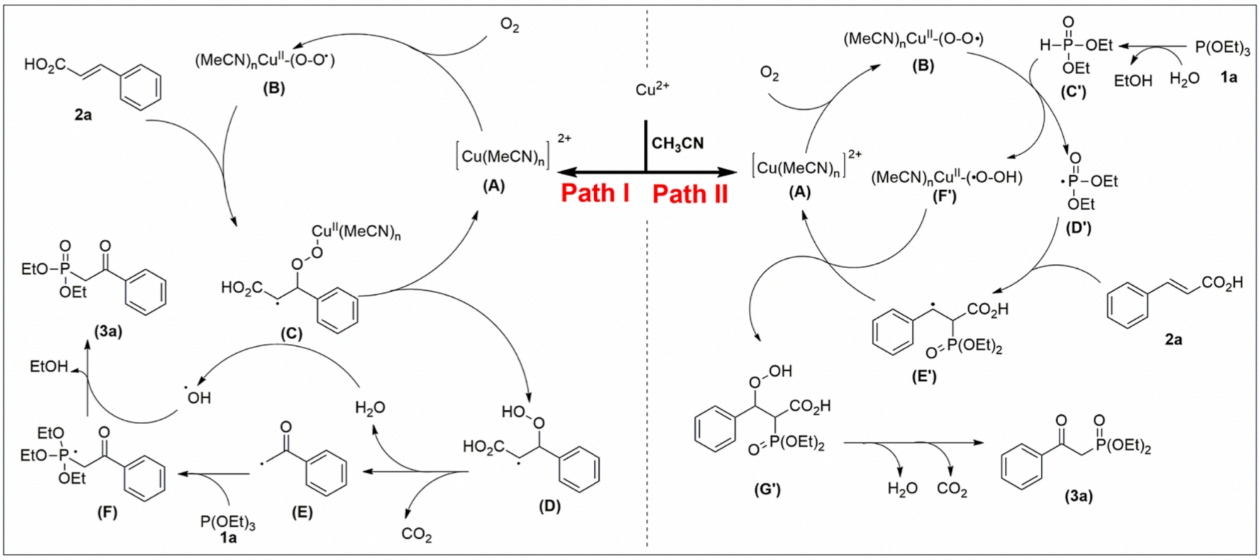


1) Maji, B.* Yamamoto, H.* *Angew. Chem. Int. Ed.* **2014**, *53*, 14472 –14475
Maji, B.* Yamamoto, H.* *Synlett* **2015**, *26*, 1528–1532

4. Proposal

Cu-Catalyzed Aerobic Oxidative/Decarboxylative Phosphorylation[a]





(a) Wong, Y-W. et al. *J. Org. Chem.* **2023**, *88*, 12502–12518