Exploring Green Catalysis

Overview of the Activity:

When designing catalysts, there are many intersecting contributors that must be kept in mind. As we strive for creating more green-focused chemistry and catalysts, it is important to consider factors such as metal choice, ligand selection, reaction conditions, and overall sustainability. Green catalysis aims to reduce environmental impact while maintaining or improving reaction efficiency. This escape room activity is designed to reinforce these principles through a fun, collaborative, and challenge-based experience. Participants will apply their knowledge of catalysis and green chemistry concepts to solve a series of puzzles that highlight key aspects of sustainable catalyst design.

Get together in a team of 2-3 people. Using the provided information within the workbook plus your personal experience, work with your team to get through the three different puzzles within this 'escape room.' Each puzzle will have a code or answer that can be inputted into the corresponding virtual lock (Flippity QR code below), which will allow your group to progress to the next puzzle. Good luck and think green!

Overall Learning Objectives:

- To be able to analyze the interconnected components of catalyst design.
- To recognize the role of catalysis in green chemistry.
- To demonstrate collaborative problem solving in a team context

QR Code for the Virtual Lock

Puzzle 1: Dissociative Mechanisms

Objectives

Ligand dissociation from a metal center is the first step in many reaction mechanisms, creating a vacant site in which an incoming small molecule can bind (Figure 1). Both the donicity and steric bulk of the ligands in the coordination complex influence the rate of ligand dissociation.

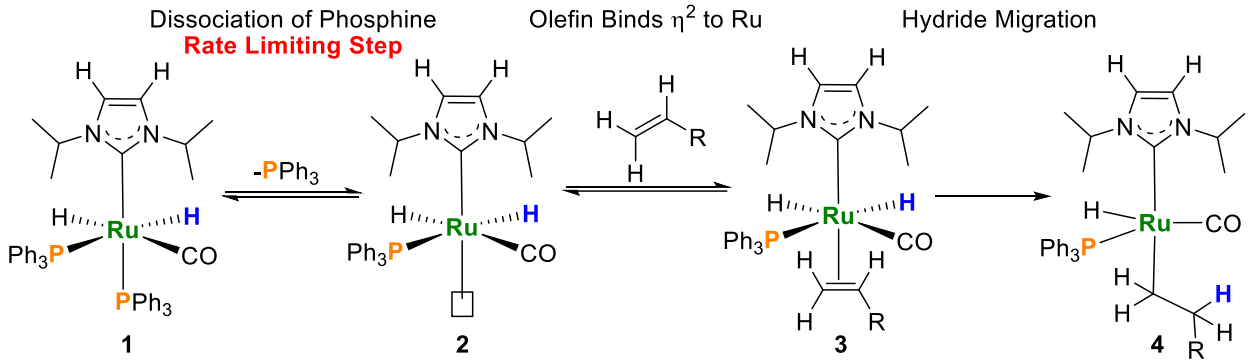
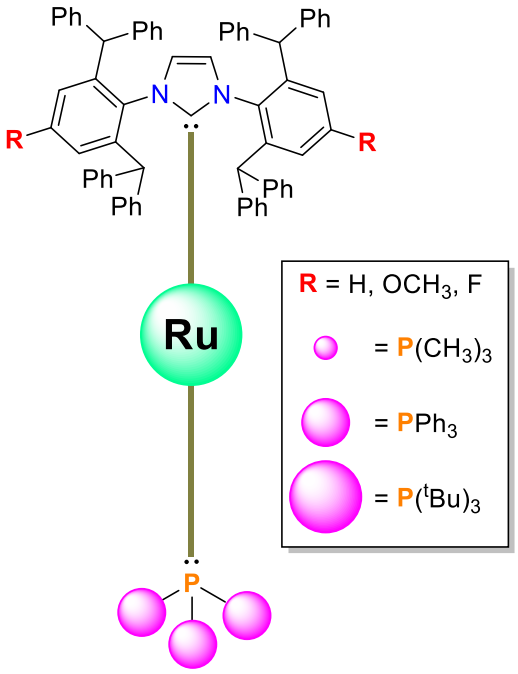


Figure 1. The dissociation of a phosphine ligand from Grubbs catalyst allowing for an incoming olefin to bind to the metal center.

Using the research notes provided, determine which ligand pairings would result in the *fastest* and *slowest* rate in the dissociation of the phosphine from the metal center.

HINT: Flippity (lock #1), *fastest* (PR_3 before NHC), *slowest* (PR_3 before NHC).



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September 3rd, 2025

Synthesis of NHC-Ru-CO derivatives

Observations: Addition of excess carbon monoxide to a solution of $[(NHC)Ru(H)_2(CO)(PPh_3)_2]$ results in loss of both phosphine ligands and formation of the corresponding carbonyl species.

IR Spectroscopy:

NHC Functional Group	Frequency of *trans*-CO stretch (cm^{-1})
H	1975
F	2016
OCH_3	1952

Free CO IR stretching frequency = 2143 cm^{-1}

CO-M sigma bond M to CO pi backbonding

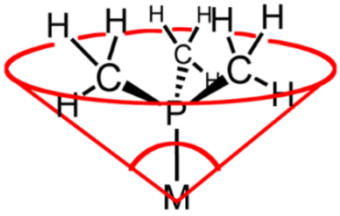
September 7th, 2025

Crystal Structures of NHC Complexes

Observations: Crystals of $[(NHC)Ru(H)_2(CO)(PR_3)_2]$ R = H, PPh_3 and R = OCH_3, $P(^tBu)_3$ were grown via pentane diffusion into a 0.5 mL THF solution of complex at -40°C over 14 days under nitrogen.

IR Spectroscopy:

NHC	Ru-C Bond Length (Å)	PR_3 Cone Angle (°)
R = H, PPh_3	1.687(2)	145
R = OCH_3, $P(^tBu)_3$	1.621(3)	182



From: Project Scientist
To: Co-op Student
Subject: Dissociative Mechanisms – Catalyst Examination.

Date: August 29th, 2025

Dear Jane,

Interesting FT-IR results, do not forget to review the *Trans*-Effect before drawing conclusions. Model the bond lengths for Monday's research update.

Thank you,
Dr. Kamoren Hedilhof

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Senior Scientist, Catalyst Co.

Helpful References:

1. S. Vanicek, M. Podewitz, C. Hassenrück, M. Pittracher, H. Kopacka, K. Wurst, T. Müller, K. R. Liedl, R. F. Winter, B. Bildstein, *Chem. Eur. J.* **2018**, *24*, 3165.

2. Hopkinson, M. N.; Richter, C.; Schedler, M.; Glorius, F. An Overview of N-Heterocyclic Carbenes. *Nature* **2014**, *510* (7506), 485–496. https://doi.org/10.1038/nature13384.

3. Ligand Substitution Reactions. *Springer eBooks* **2007**, 121–134. https://doi.org/10.1007/978-3-540-46129-6_7.

4. Housecroft, C. E.; Sharpe, A. G. *Inorganic Chemistry*, 5th ed.; New York [Etc.]: Pearson, 2018.

5. Jover, J.; Cirera, J. Computational Assessment on the Tolman Cone Angles for P-Ligands. *Dalton Trans.* **2019**, *48* (40), 15036–15048. https://doi.org/10.1039/c9dt02876e.
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Puzzle 2: Cross Coupling Catalyst Design of Experiment (DOE)

Objectives

The Suzuki-Miyaura cross coupling reaction is heavily used in the synthesis of pharmaceuticals, agrochemicals, and other chemical building blocks. Here, a metal with a vacant site is able to undergo oxidative addition with an aryl halide (Figure 2). Boronic acids are the typical cross coupling partner, although the strength of the transmetalating agent is related to the reactivity of the metal center, with some metals requiring stronger reagents such as Grignard reagents (ex. BrMgR). In the last step of the mechanism, the two aryl groups are reductively eliminated from the metal yielding a new carbon-carbon bond. Because of its prevalence in industry, there is a push to develop greener catalytic processes by utilizing alternative metals to palladium, utilizing simple ligands, performing the reaction under aqueous conditions, etc.

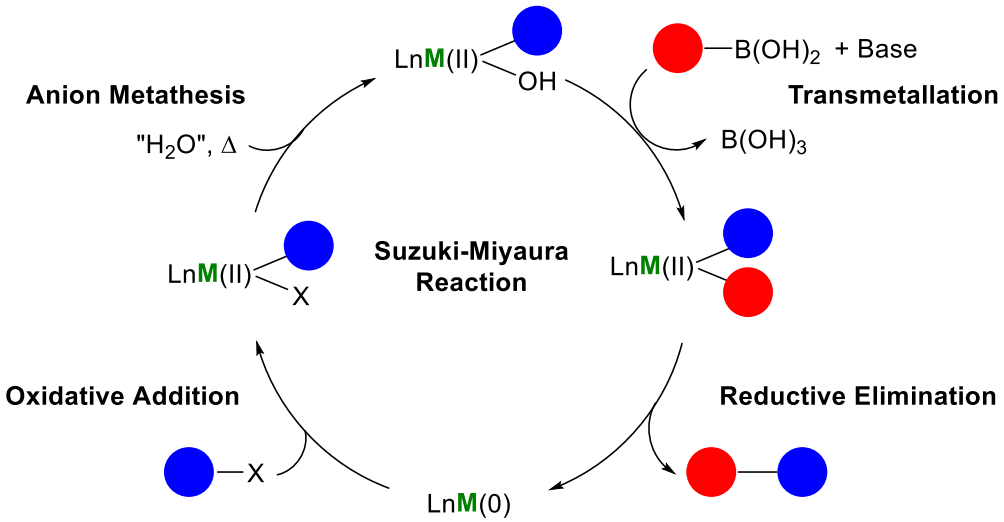


Figure 2. Representative Suzuki-Miyaura cross coupling reaction mechanism.

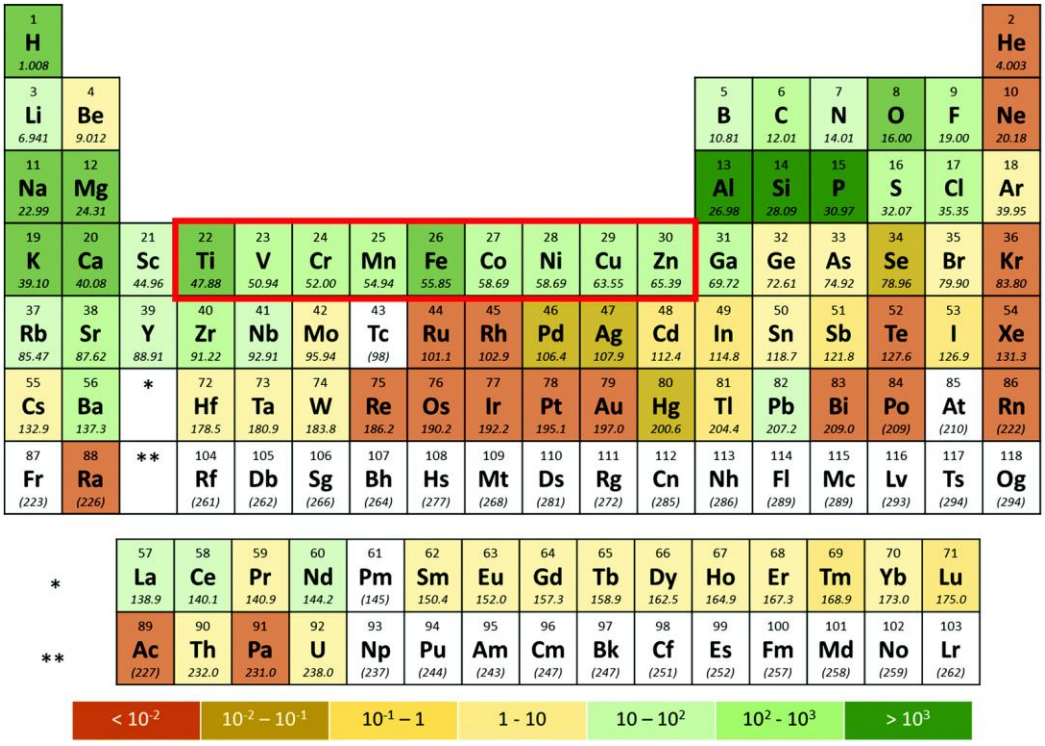
Using the research notes provided, determine the greenest cross coupling process (indicated by the number of green leaves). Recall, each metal may require a unique ligand, and not all complexes are stable in water. A reference guide is provided for the design of experiment (DOE) providing information on which ligands, metals, reagents, and processes are compatible.

HINT: Flippity (lock #2), *metal choice* and *number of leaves*).

From: Project Scientist
To: Co-op Student
Subject: DOE – Note on compatible reagents.
Date: August 21st, 2025

Dear Mohammed,
Internal identification of compatible systems is complete (Chart 1). The systems have been colour coded to indicate compatibility. Reaction conditions must be connected by a common colour indicator (e.g. if you pick one reagent tile with orange, **purple**, and red, and the second tile with blue and **purple**, your common colour is **purple** and every subsequent tile must contain this colour). Note, you will be able to choose your metal only after you've decided on a reaction pathway (reveal Chart 2).

Dr. Kamoren Hedilhof



Elemental abundance (in mg per kg of Earth's crust).

Gourdon, L.; Cariou, K.; Gasser, G. *Chem. Soc. Rev.* **2022**, *51*, 1167-1195.

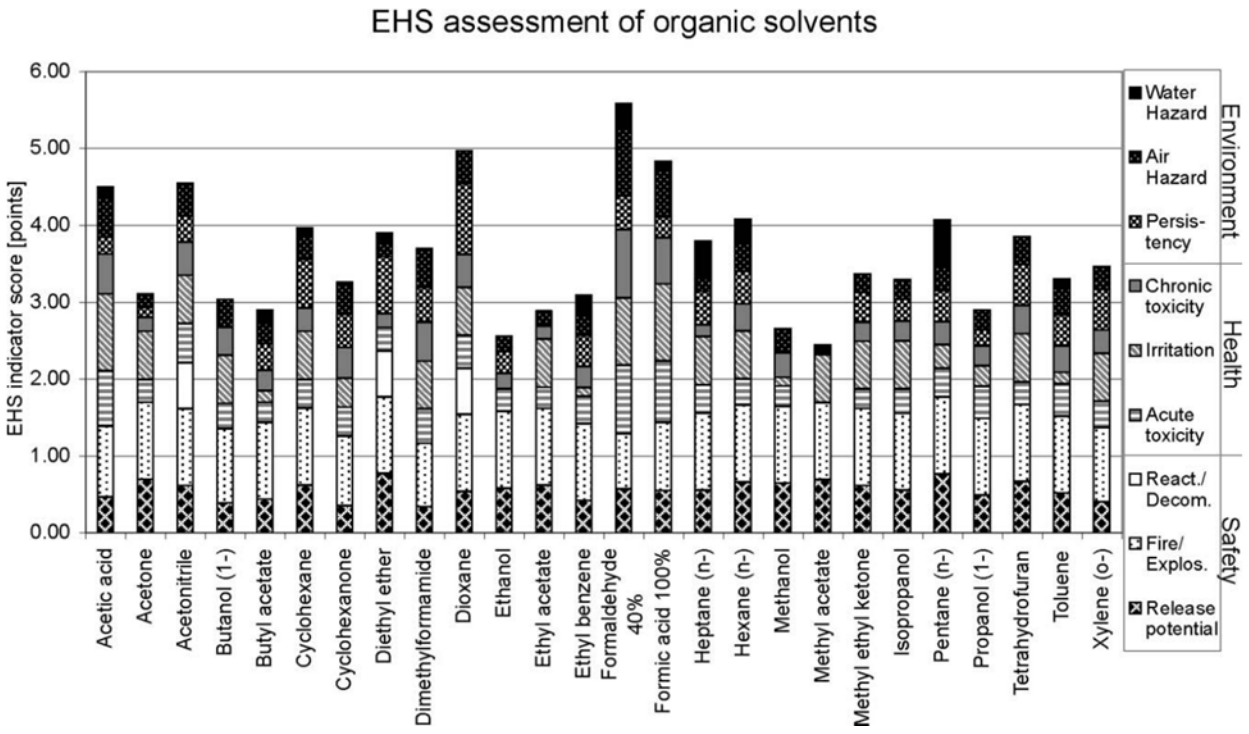
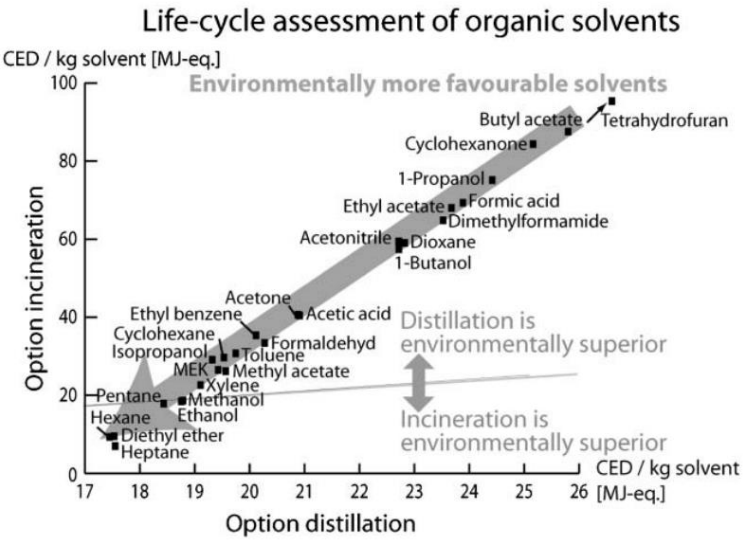


Table 1. Environmental Health and Safety (EHS) assessment of common organic solvents.



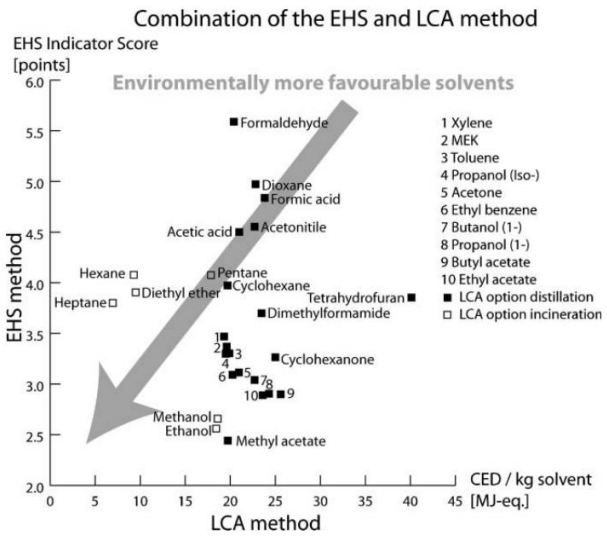
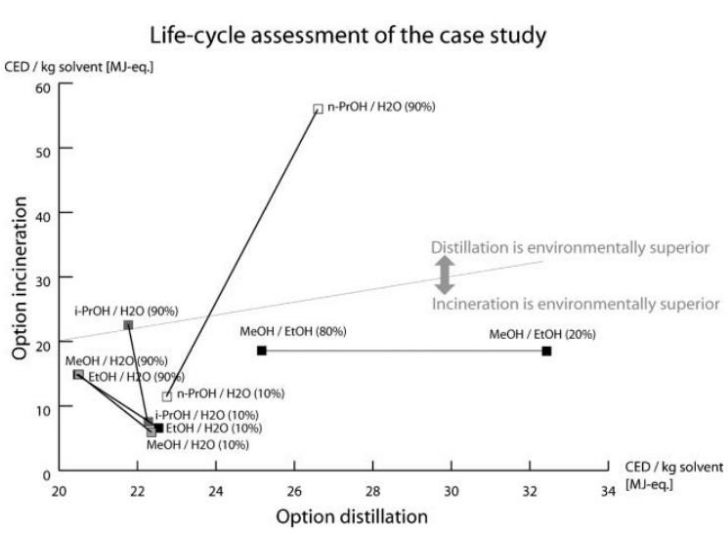


Table 2. (Left) Life cycle assessment (LCA) of common organic solvents highlighting incineration and distillation disposal methods.

Table 3. (Right) Combined EHS and LCA data representing a global environmental indicator for common organic solvents.



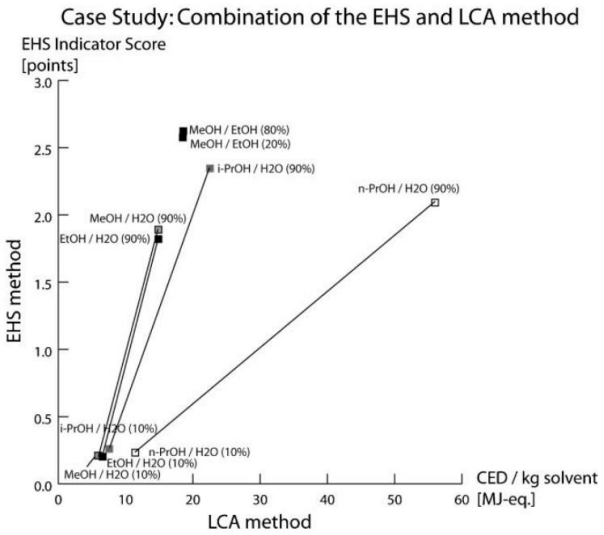
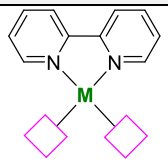
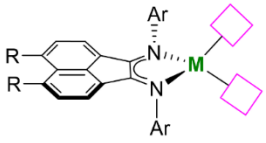
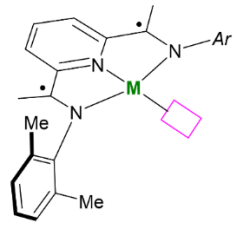
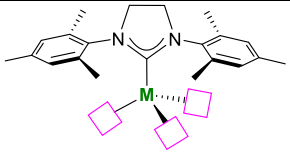
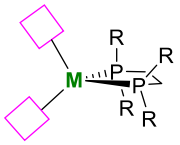


Table 4. (Left) Life cycle assessment (LCA) of common aqueous solvent mixtures highlighting incineration and distillation disposal methods.

Table 5. (Right) Combined EHS and LCA data representing a global environmental indicator for common aqueous solvent mixtures.

Table 6. Available ligands within the company portfolio.

Ligand	Structure	Internal Notes
2,2'-Bipyridine (bipy)		Synthesis: Commercially available Cost: $10.12/1g Hazardous Reagents: volatile organics
Bis(imino)acenaphthenes (BIAN)		Synthesis: In House • 15% molar excess of the aniline with acenaphthenequinone + 3-fold molar excess of $ZnCl_2$ in refluxing acetic acid. **80-95% yield for simple derivatives.** Ref: Cenini et al. *Organometallics* **2002.** Cost: $3.12/1g Hazardous reagents: volatile organics.
Bis(imino)pyridine		Synthesis: In House • Schiff-base condensation of 2 equiv. of the desired aniline with 2,6-diacetylpyridine. **60% yield for simple derivatives.** Ref: Bennett et al. *J. Am. Chem. Soc.* **1998.** Cost: $50.71/1g Hazardous reagents: 97% formic acid, volatile organics.
N-Heterocyclic carbene (NHC)		Synthesis: • Deprotonation of dimesitylimidazolium cation to give "IMes". **89% yield.** Ref: Ison et al. *J. Chem. Educ.* **2012.** Cost: $154.05/1g Hazardous reagents: volatile organics.

Bis(phosphine)		Synthesis: • For symmetric 1,2-*bis*(dichlorophosphino)ethane derivatives, react with appropriate Grignard reagent. **60-70% yield.** Ref: Leight et al. *J. Organomet. Chem.* **1979** Cost: $251.54/1g Hazardous reagents: pyrophorics, volatile organics, phosphines.

From: Projection Manager
To: All Researchers
Subject: Removal of high-risk chemicals from production
Date: August 1st, 2025

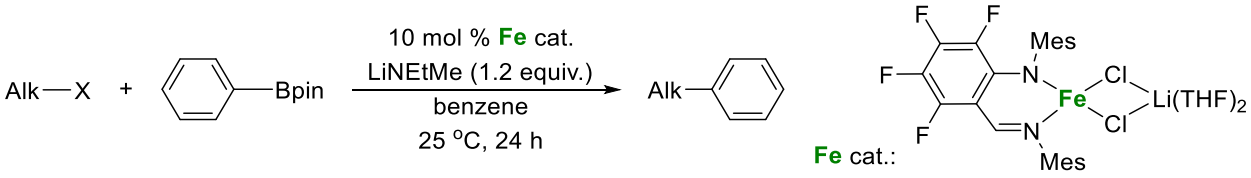
All,
In line with our 2030 sustainable development goals, our health and safety board has concluded that high-risk chemicals (marked with an **!**) cannot be used in new product development. Please avoid their use in synthesis.

Jordyn Eyatoa
Production Manager, Catalyst Co.

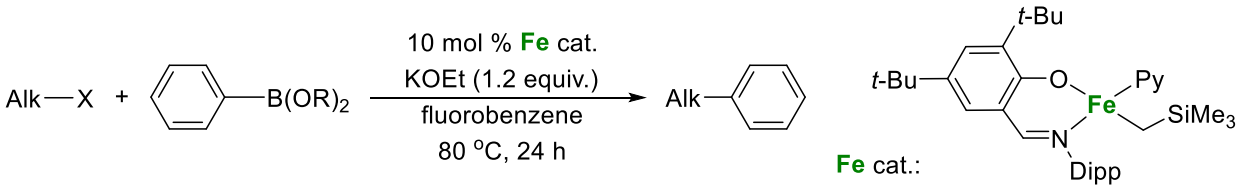
Notes on Suzuki-Miyaura Cross Coupling Reactions

Shown below are select examples of optimized reaction conditions for the Suzuki-Miyaura cross coupling of aryl/alkyl halides and aryl boronic acids/boronates.

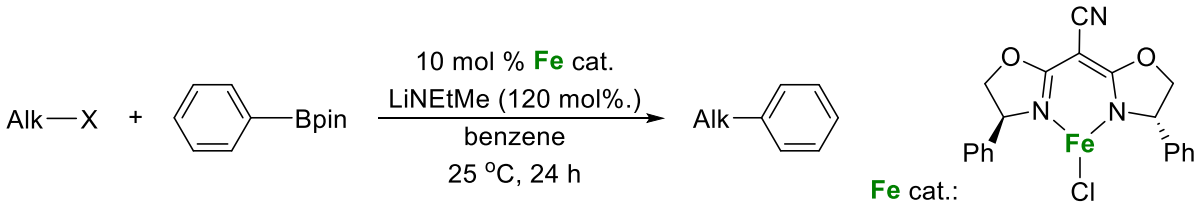
I. Iron Catalyzed Suzuki-Miyaura Cross Coupling:



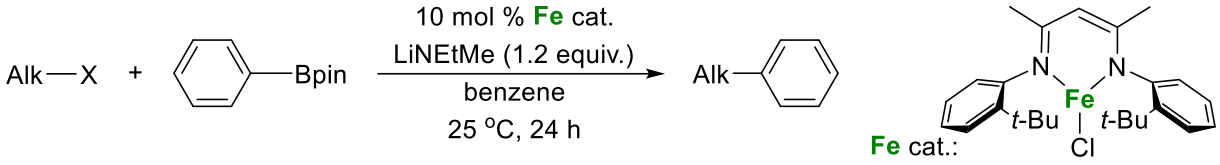
Chen, D.; Lepori, C.; Guillot, R.; Gil, R.; Bezzenine, S.; Hannedouche, J. *Angew. Chem. Int. Ed.* **2024**, *63*, e202408419.



Peterson, P. O.; Joannou, M. V.; Simmons, E. M.; Wisniewski, S. R.; Kim, J.; Chirik, P. J. *ACS Catal.* **2023**, *13*, 2443-2448.

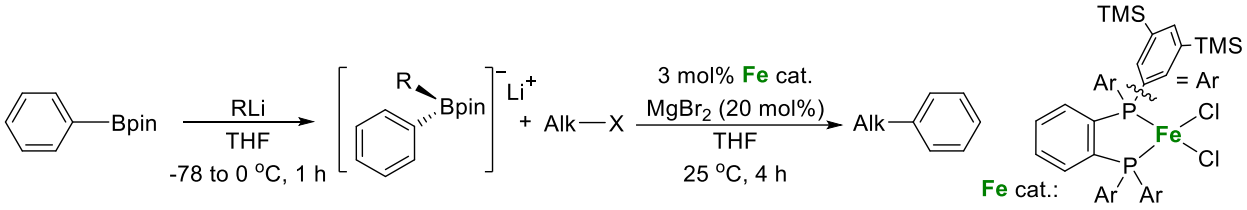


Crockett, M. P.; Tyrol, C. C.; Wong, A. S.; Li, B.; Byers, J. A. *Org. Lett.* **2018**, *20*, 5233-5237.

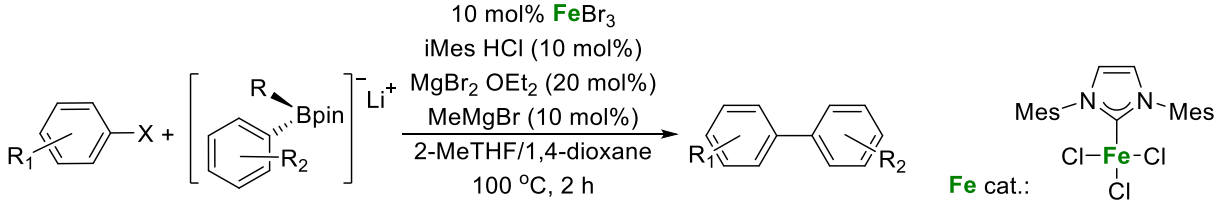


Crockett, M. P.; Wong, A. S.; Li, B.; Byers, J. A. *Angew. Chem. Int. Ed.* **2020**, *59*, 5392-5397.

Alternative strategies for Suzuki-Miyaura Cross Coupling using iron catalysts involve pre-activation of the boronic coupling partner:

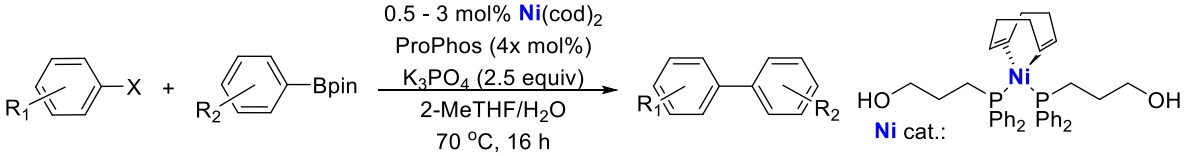


Hatakeyama, T.; Hashimoto, T.; Kondo, Y.; Fujiwara, Y.; Seike, H.; Takaya, H.; Tamada, Y.; Ono, T.; Nakamura, M. *J. Am. Chem. Soc.* **2010**, *132*, 10674-10676.

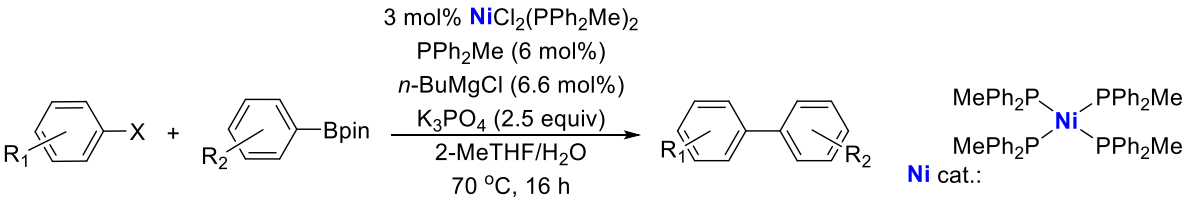


Rowsell, B. J. S.; O'Brien, H. M.; Athavan, G.; Daley-Dee, P. R.; Krieger, J.; Richards, E.; Heaton, K.; Fairlamb, I. J. S.; Bedford, R. B. *Nat. Catal.* **2024**, *7*, 1186-1198.

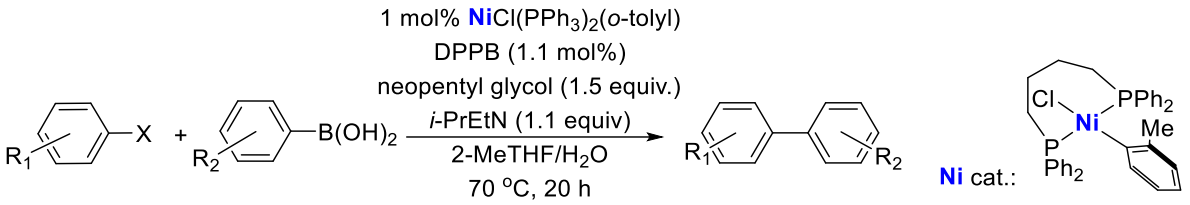
II. Nickel Catalyzed Suzuki-Miyaura Cross Coupling:



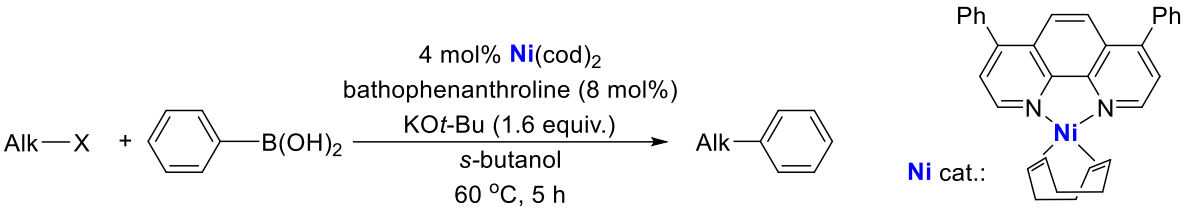
Yang, J.; Neary, M. C.; Diao, T. *J. Am. Chem. Soc.* **2024**, *146*, 6360-6368.



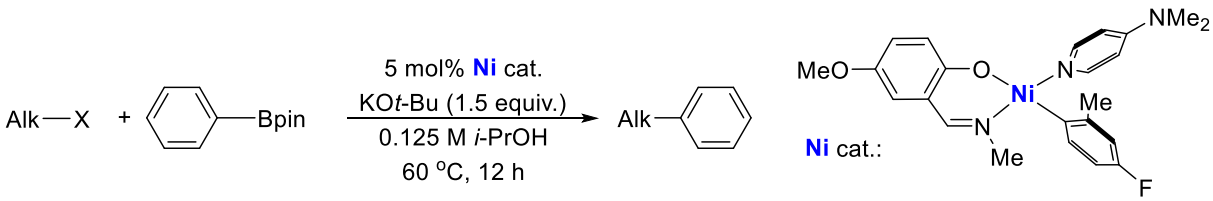
Haibach, M. C.; Ickes, A. R.; Tcyrulnikov, S.; Shekhar, S.; Monfette, S.; Swiatowiec, R.; Kotecki, B. J.; Wang, J.; Wall, A. L.; Henry, R. F.; Hansen, E. C. *Chem. Sci.* **2022**, *13*, 12906-12912



Guo, X.; Dang, H.; Wisniewski, S. R.; Simmons, E. M. *Organometallics*, **2022**, *41*, 1269-1274.

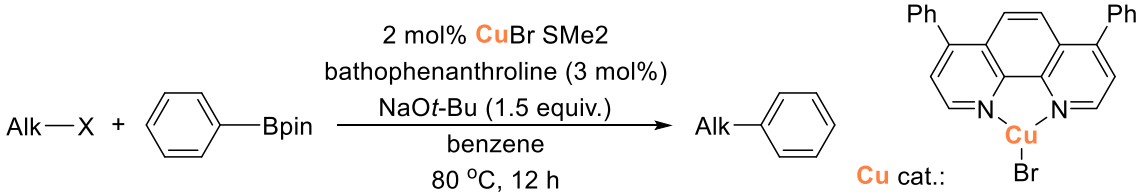


Zhou, J.; Fu, G. C. *J. Am. Chem. Soc.* **2004**, *126*, 1340-1341.

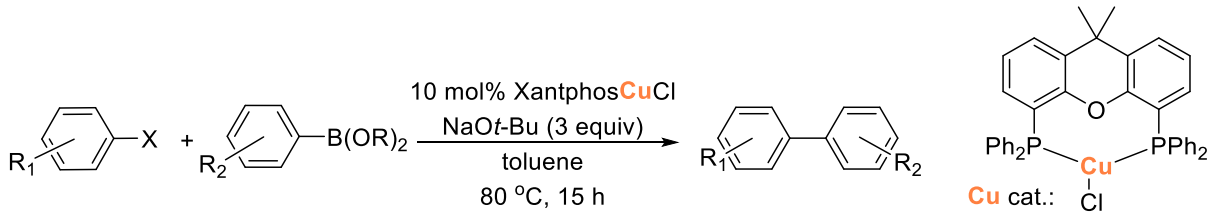


Mills, L. R.; Simmons, E. M.; Lee, H.; Nester, E.; Kim, J.; Wisniewski, S. R.; Pecoraro, M. V.; Chirik, P. J. *J. Am. Chem. Soc.* **2024**, *146*, 10124-10141.

III. Copper Catalyzed Suzuki-Miyaura Cross Coupling:

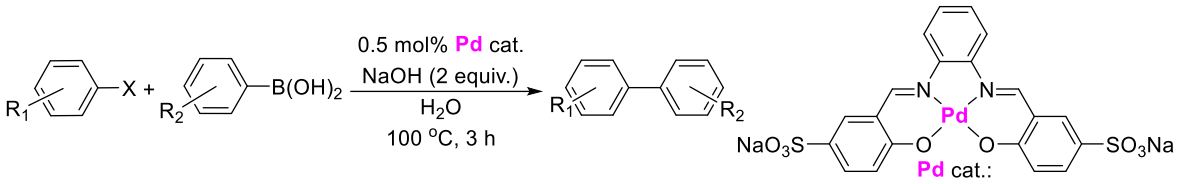


Zhou, Y.; Qiu, L.; Li, J.; Xie, W. *J. Am. Chem. Soc.* **2023**, *145*, 28146-28155.

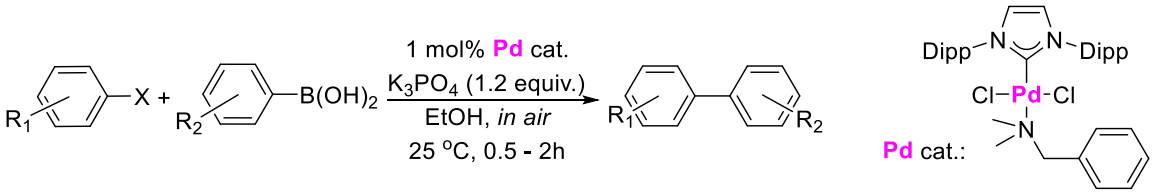


Zhou, Y.; You, W.; Smith, K. B.; Brown, M. K. *Angew. Chem. Int. Ed.* **2014**, *53*, 3475-3479.

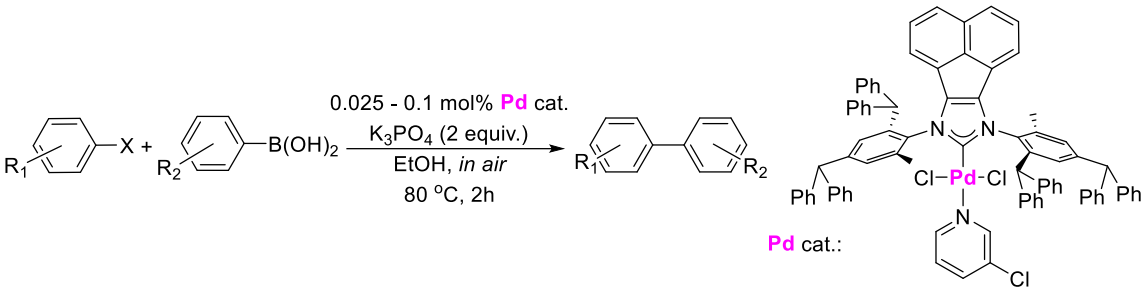
IV. Palladium catalyzed Suzuki-Miyaura Cross Coupling:



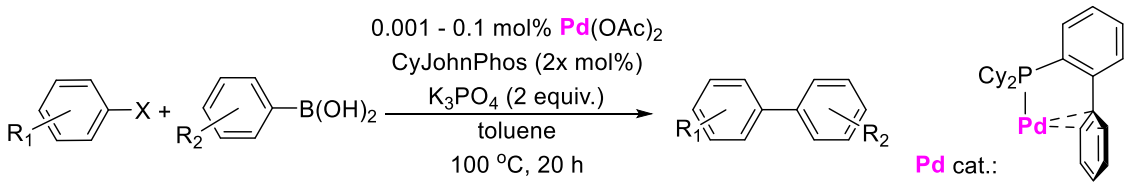
Liu, Y.-S.; Gu, N.-N.; Liu, P.; Ma, X.-W.; Liu, Y.; Xie, J.-W.; Dai, B. *Tetrahedron* **2015**, *71*, 7985-7989.



Chen, M.-T.; Kao, Z.-L. *Dalton Trans.* **2017**, *46*, 16394-16398.



Ouyang, J.-S.; Li, Y.-F.; Huang, F.-D.; Lu, D.-D.; Liu, F.-S. *ChemCatChem*. **2017**, *10*, 371-375.



Wolfe, J. P.; Singer, R. A.; Yang, B. H.; Buchwald, S. L. *J. Am. Chem. Soc.* **1999**, *121*, 9550-9561.

References:

1. Gasperini, M.; Ragaini, F.; Cenini, S. *Organometallics* **2002**, *21*, 2950-2957.
2. Small, B. L.; Brookhart, M.; Bennett, A. M. *J. Am. Chem. Soc.* **1998**, *120*, 4049-4050.
3. Ison, E. A.; Ison, A. *J. Chem. Educ.* **2012**, *89*, 1575-1577.
4. Capello, C.; Fischer, U.; Hungerbuhler, K. What is a green solvent? A comprehensive framework for the environmental assessment of solvents. *Green Chem.* **2007**, *9*, 927-934.

Puzzle 3: Green Catalyst Design for N_2O Reduction.

Objectives

Green catalysis can be considered in three ways:

1. Improving current catalytic processes through design of experiment studies to find greener alternatives.
2. Improving ligand and catalyst design to lower the impact of catalyst synthesis.
3. Targeting the transformation of pollutants to value-added or benign chemicals

Nitrous oxide (N_2O) is a potent greenhouse gas and ozone depletant. It can also be used as a strong oxidant in chemical transformations. With the right catalyst, N_2O can be reduced to nitrogen (N_2) and water (H_2O) in the presence of hydrogen, transforming the pollutant to benign products, safer for the environment. The objective of this puzzle is to select the greenest and most efficient catalyst design for nitrous oxide (N_2O) activation. Using the research notes provided, select the greenest and most efficient catalyst design for nitrous oxide (N_2O) reduction. Rank to donicity of the ligands from most to least, select the ligand with the greenest synthesis, and select a metal to build a catalyst.

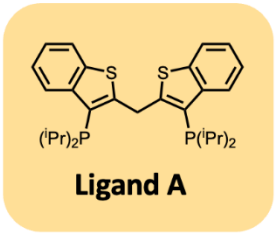
HINT: Flippity (lock #3), *ligand letters, most to least.*
HINT: Flippity (lock #4), *metal name, ligand letter.*

From: Computational Manager
To: Co-op Student
Subject: Density Functional Theory – Reactivity Mapping Issues.
Date: August 21st, 2025

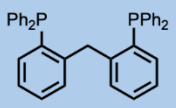
Dear Amanda,

Sorry for the late reply. We have been having issues with our processing computers. All of the computational outcomes are being projected as mazes rather than flow charts! I have run your density functional theory computations alongside the sustainability mapping. Until we fix the problem, all I can provide you with is the maze pieces to select the greenest and most efficient catalyst. You should be able to use your knowledge of the ligand donicity and synthesis to select the right pieces. All you need to do is place the ligands in the correct position on the maze and select the correct metal to get to the desired outcome.
Note, when building your maze ensure the ligand letters are orientated upwards.
****You may only change directions with your metal piece if you hit a wall in the maze****

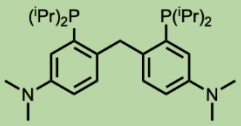
The ligands are colour coded as follows:



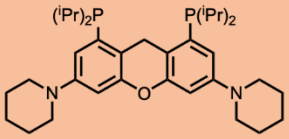
Ligand A



Ligand B

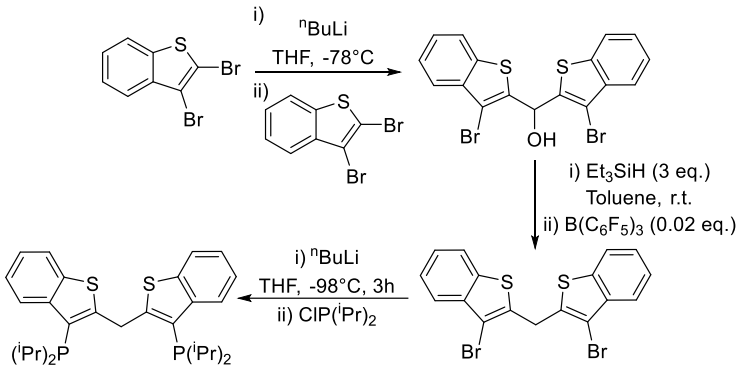
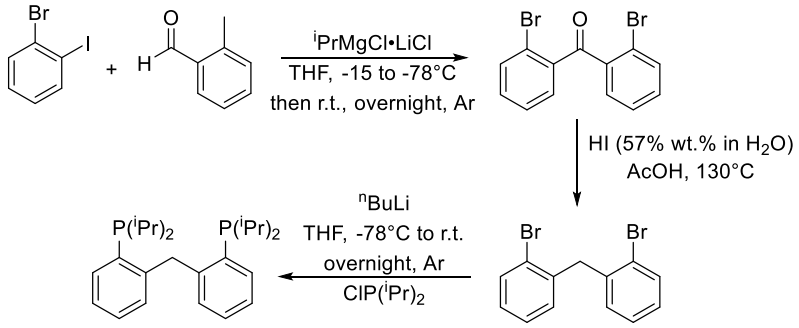
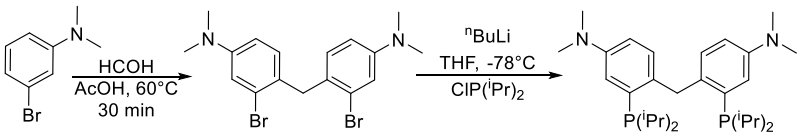


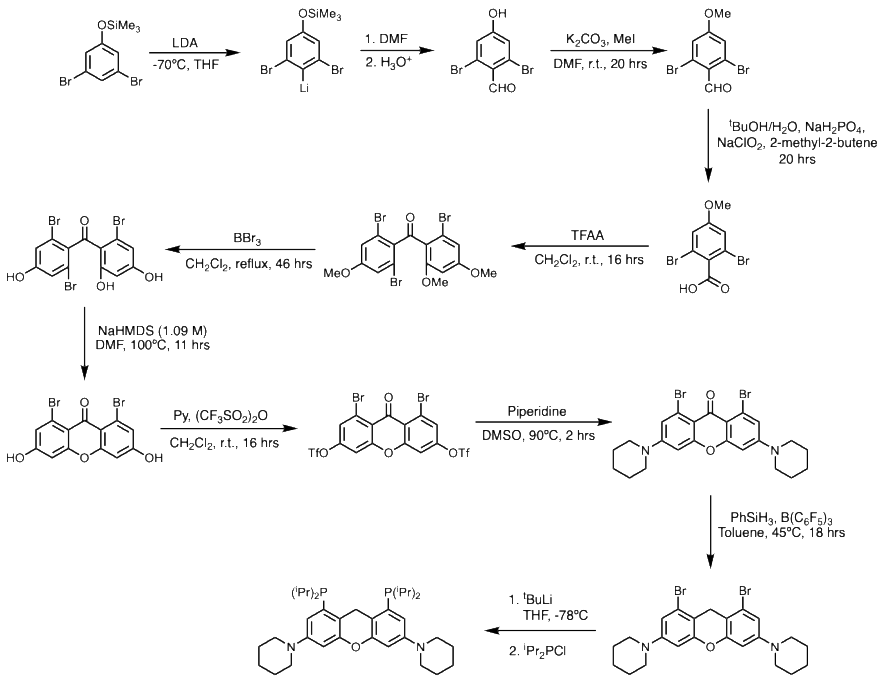
Ligand C



Ligand D

Best of luck!
Dr. Ellen Nickerson
Computational Management, Catalyst Co.

	Synthesis	Notes
A	 Doyle, L. E.; Piers, W. E.; Borau-Garcia, J. Ligand Cooperation in the Formal Hydrogenation of N_2O Using a $PC_{sp2}P$ Iridium Pincer Complex. *J. Am. Chem. Soc*. **2015**, *137* (6), 2187–2190. https://doi.org/10.1021/ja512602m.	Synthesis must be carried out under a nitrogen atmosphere. Intermediates 1 and 2 are air stable. Step three of the synthesis can only be carried out on a 1-gram scale. Uneven cooling of the reaction vessel causes multiple side products. Hazardous reagents: pyrophorics (step 1 and 3), volatile organics.
B	 Zhao, K.; Wang, H.; Li, T.; Liu, S.; Benassi, E.; Li, X.; Yao, Y.; Wang, X.; Cui, X.; Shi, F. Identification of a Potent Palladium-Aryldiphosphine Catalytic System for High-Performance Carbonylation of Alkenes. *Nat. Commun.* **2024**, *15* (1), 2016. https://doi.org/10.1038/s41467-024-46286-9.	Steps 1 and 3 of the synthesis must be carried out under a nitrogen atmosphere. Intermediates 1 and 2 are air stable. Utilization of Grignard reagent, step 1, is preferable to more reactive lithium reagents. Hazardous reagents: pyrophorics (step 1 and 3), strong acid, volatile organics.
C	 Smith, J. D.; Borau-Garcia, J.; Piers, W. E.; Spasyuk, D. Systematic Dismantling of a Carefully Designed $PC_{carbene}P$ Pincer Ligand via C–C Bond Activations at an Iridium Centre. *Can. J. Chem.* **2016**, *94* (4), 293–296. https://doi.org/10.1139/cjc-2015-0251. Lukinavičius, G.; Umezawa, K.; Olivier, N.; Honigmann, A.; Yang, G.; Plass, T.; Mueller, V.; Reymond, L.; Corrêa Jr, I. R.; Luo, Z.-G.; Schultz, C.; Lemke, E. A.; Heppenstall, P.; Eggeling, C.; Manley, S.; Johnsson, K. A Near-Infrared Fluorophore for Live-Cell Super-Resolution Microscopy of Cellular Proteins. *Nat. Chem.* **2013**, *5* (2), 132–139. https://doi.org/10.1038/nchem.1546.	Step 2 of the synthesis must be carried out under a nitrogen atmosphere. Intermediate 1 is air stable. Hazardous reagents: pyrophorics (step 2), volatile organics.

D	 Da˛ browski, M.; Kubicka, J.; Luliński, S.; Serwatowski, J. A Study on the Metalation of Alkoxydibromobenzenes. *Tetrahedron Lett.* **2005**, *46* (24), 4175–4178. https://doi.org/10.1016/j.tetlet.2005.04.065. Sugawara, S.; Abe, M.; Fujiwara, Y.; Wakioka, M.; Ozawa, F.; Yamamoto, Y. 1,8-Disubstituted Xanthylidene-Based Remote Carbenes: Photolytic Generation and Isolation of Low-Coordinate Palladium(II) Complex. *Eur. J. Inorg. Chem.* **2015**, *2015* (3), 534–541. https://doi.org/10.1002/ejic.201403017. Smith, J. D.; Logan, J. R.; Doyle, L. E.; Burford, R. J.; Sugawara, S.; Ohnita, C.; Yamamoto, Y.; Piers, W. E.; Spasyuk, D. M.; Borau-Garcia, J. Cationic Mono and Dicarbonyl Pincer Complexes of Rhodium and Iridium to Assess the Donor Properties of $PC_{carbene}P$ Ligands. *Dalton Trans.* **2016**, *45* (32), 12669–12679. https://doi.org/10.1039/C6DT02615J.	Total reaction steps: 11 Steps 3, 6, 10, and 11 must be carried out under a nitrogen atmosphere. Several steps require extended periods of heating. Overall reaction mass efficiency is low. Hazardous reagents: pyrophorics, strong bases, reactive boranes, volatile organics.

September 1st, 2025

Synthesis of PCP-Ir-CO derivatives

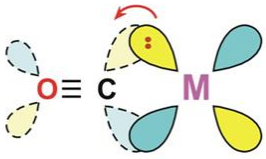
Observations: Addition of $NaB(Ar^F)_4$ to the PCP-Ir-Cl analogues under an atmosphere of CO yielded the dicarbonyl complexes. Placing the dicarbonyl complexes under vacuum resulted in the formation of the desired monocarbonyl.

IR Spectroscopy:

Ligand	Frequency of *trans*-CO stretch (cm^{-1})
A	2048
B	2004
C	1963
D	1974

Free CO IR stretching frequency = 2143 cm^{-1}

CO-M sigma bond



M to CO pi backbonding

From: Project Scientist
To: Co-op Student
Subject: Previous Reactivity Studies
Date: August 27th, 2025

Dear Amanda,

I've done a quick search of the company database. Here is the info that we have on the reactivity of each catalyst.

Complex 1 [Ir+A]: Catalytic hydrogenation of N_2O was difficult due to slow kinetics resulting from formation of two hydride isomers.

Complex 2 [Fe+B]: Previously used as a catalyst for [2+2] cycloadditions.

Complex 3 [Ir+C]: N_2O activation rapid. Catalyst decomposition after 18h.

Thank you,
Dr. Kamoren Hedilhof

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Senior Scientist, Catalyst Co.

References:

1. Doyle, L. E.; Piers, W. E.; Borau-Garcia, J. Ligand Cooperation in the Formal Hydrogenation of N_2O Using a $PC_{sp2}P$ Iridium Pincer Complex. *J Am Chem Soc.* **2015**, *137* (6), 2187–2190. https://doi.org/10.1021/ja512602m.
2. Smith, J. D.; Borau-Garcia, J.; Piers, W. E.; Spasyuk, D. Systematic Dismantling of a Carefully Designed $PC_{carbene}P$ Pincer Ligand via C–C Bond Activations at an Iridium Centre. *Can. J. Chem.* **2016**, *94* (4), 293–296. https://doi.org/10.1139/cjc-2015-0251.
3. Smith, J. D.; Chih, E.; Piers, W. E.; Spasyuk, D. M. Tuning Iridium (I) $PC_{carbene}P$ Frameworks for Facile Cooperative N_2O Reduction. *Polyhedron* **2018**, *155*, 281–290. https://doi.org/10.1016/j.poly.2018.08.054.
4. Hoffbauer, M. R.; Iluc, V. M. [2+2] Cycloadditions with an Iron Carbene: A Critical Step in Enyne Metathesis. *J. Am. Chem. Soc.* **2021**, *143* (15), 5592–5597. https://doi.org/10.1021/jacs.0c12175.
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