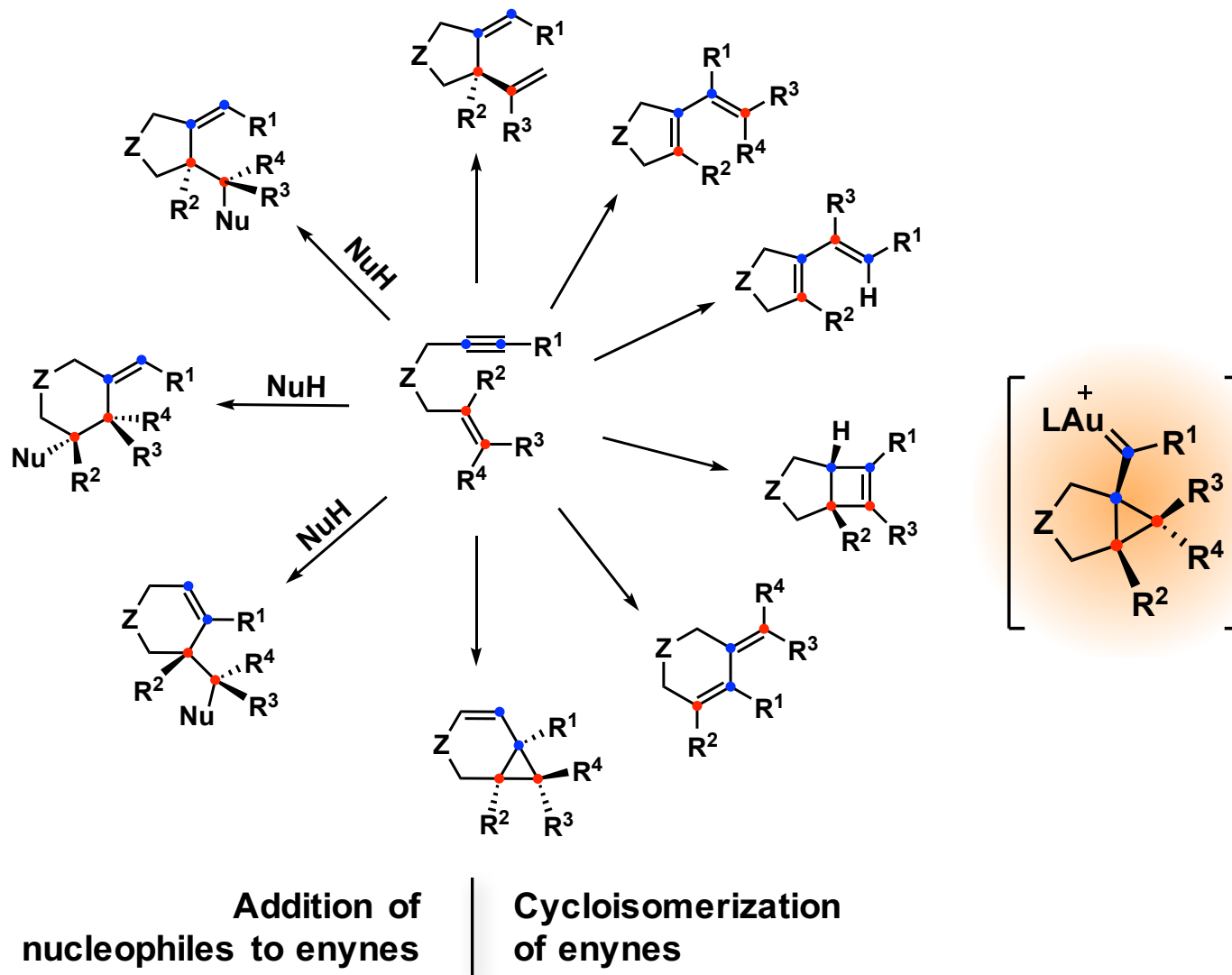


Building Molecular Diversity with Gold(I) Carbenes

Antonio M. Echavarren

Institute of Chemical Research of Catalonia (ICIQ)





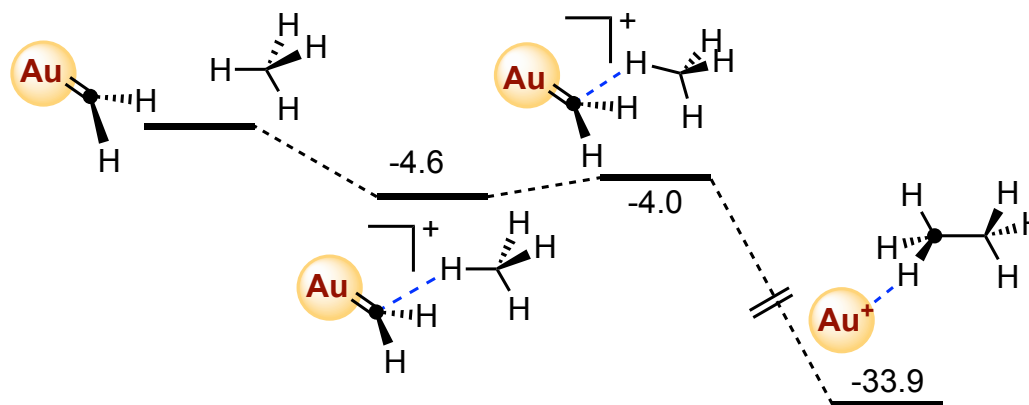
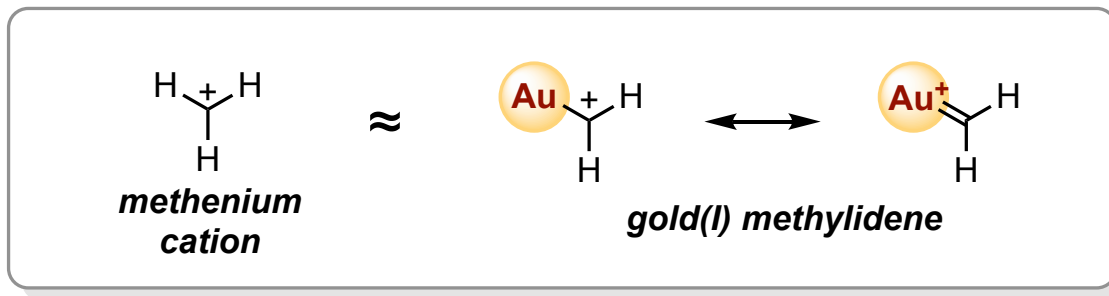
Echavarren, Muratore, López-Carrillo, Escribano-Cuesta, Huguet, Obradors, *Organic Reactions* **2017**, 92, chapter 1.

Pd(II): Trost, Tanoury, *J. Am. Chem. Soc.* **1988**, 110, 1636; Trost, Hashmi, *Angew. Chem. Int. Ed.* **1993**, 32, 1085.

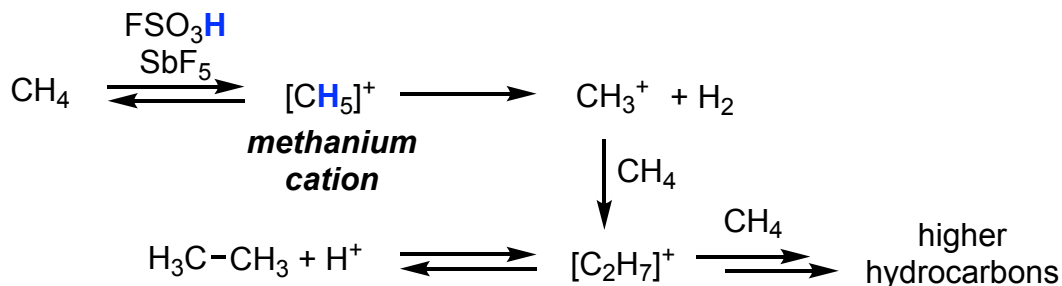
Ru(II): Chatani, Murai, et al. *J. Am. Chem. Soc.* **1998**, 120, 9104.

Pt(II): Fürstner et al. *J. Am. Chem. Soc.* **2000**, 122, 6785; Echavarren et al. *J. Am. Chem. Soc.* **2000**, 122, 11549.

Au(I): ... Toste, Fürstner, Hashmi, Zhang, Fensterbank, Liu, Gagosz, Michelet, Marinetti, Shin, Widenhoefer ...

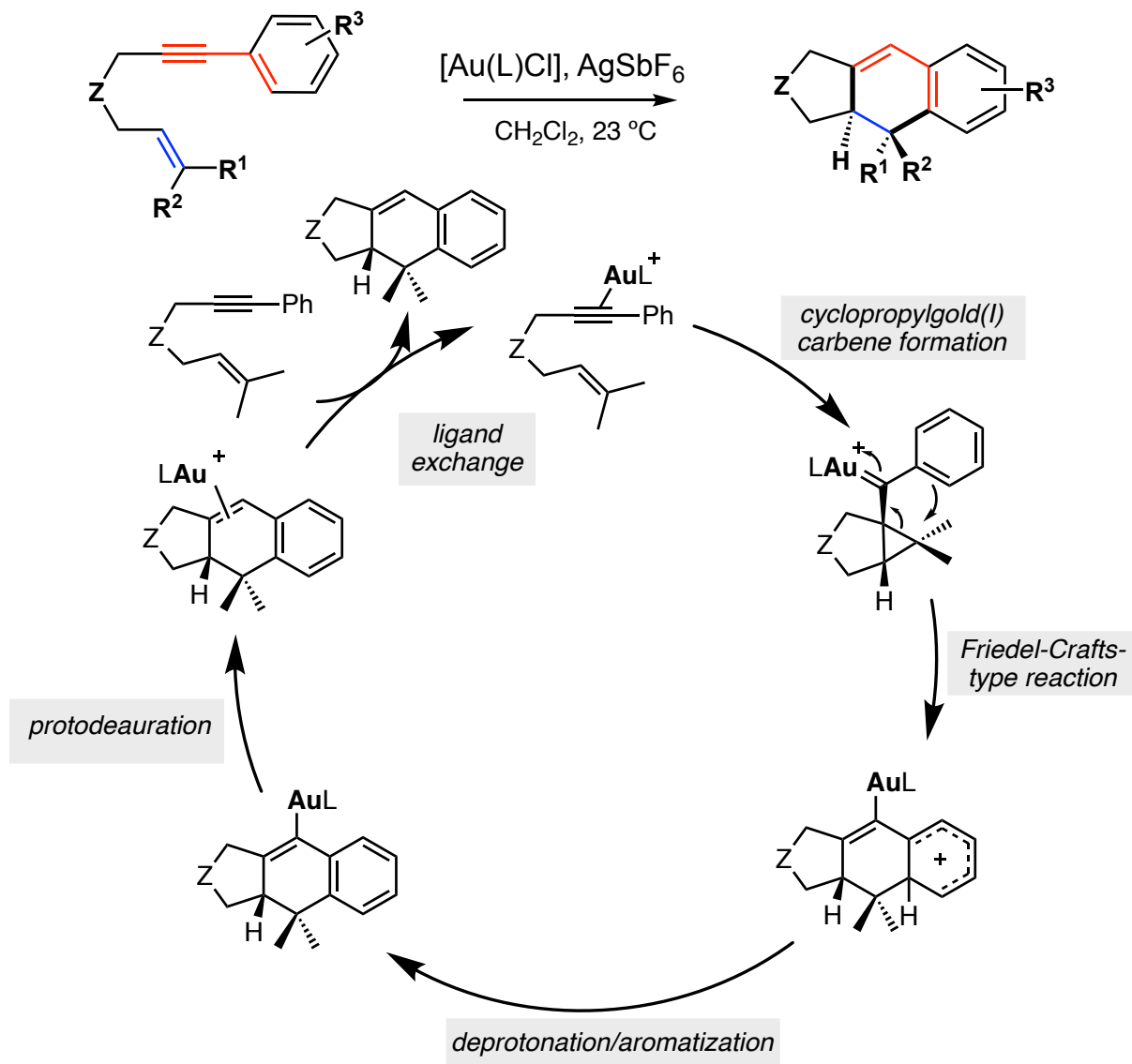


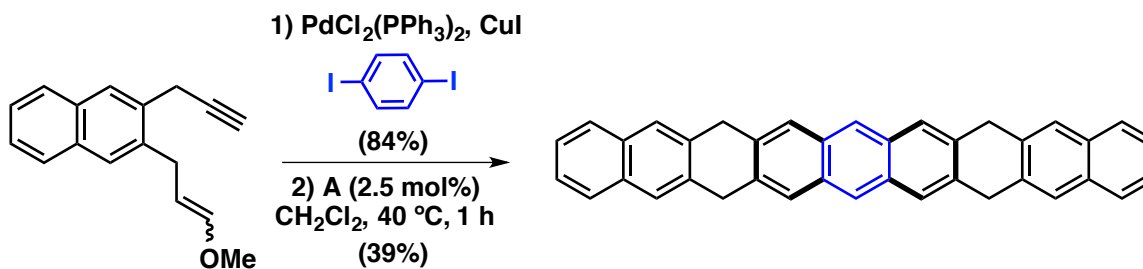
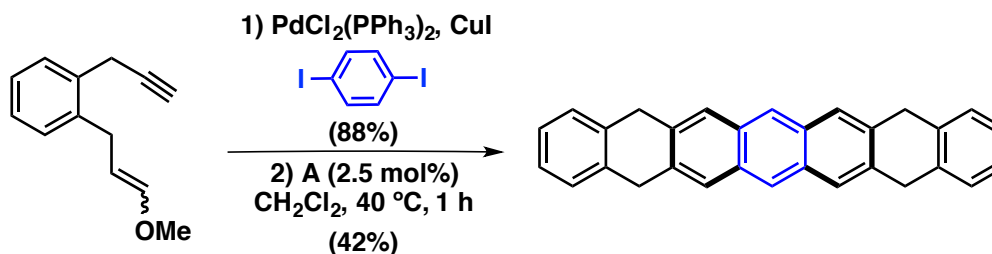
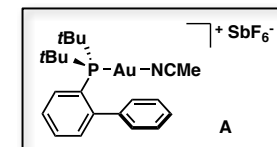
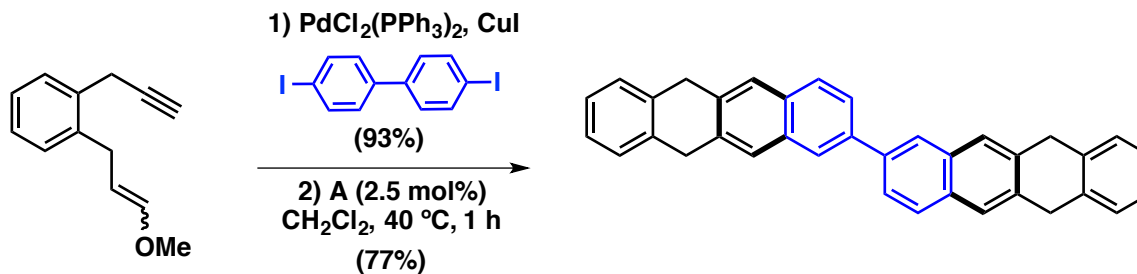
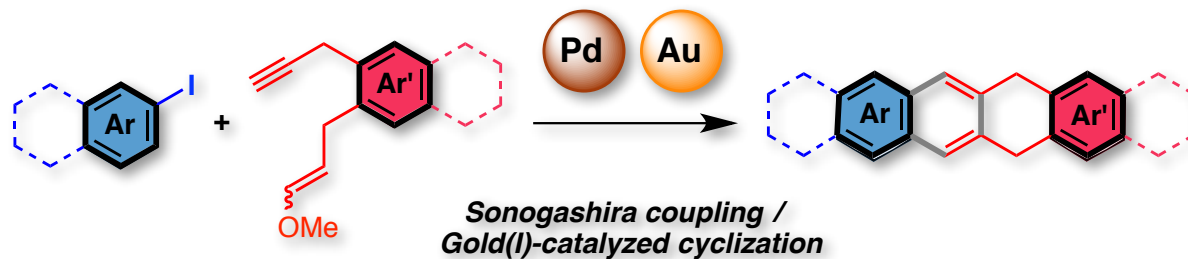
Zhou, Li, Wu, Schlangen, Schwarz, *Angew. Chem. Int. Ed.* **2016**, *55*, 441. Zhou, Li, Schlangen, Schwarz, *Acc. Chem. Res.* **2016**, *49*, 494



Olah, Lukas, *J. Am. Chem. Soc.* **1967**, *89*, 2227. Olah, Schlosberg, *J. Am. Chem. Soc.* **1968**, *90*, 2726. Olah, Klopman, Schlosberg, *J. Am. Chem. Soc.* **1969**, *91*, 3261. Olah, Halpern, Shen, Mo, *J. Am. Chem. Soc.* **1971**, *93*, 1251

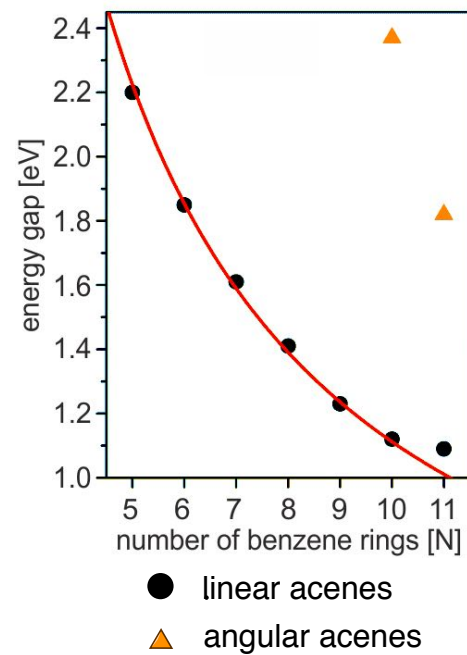
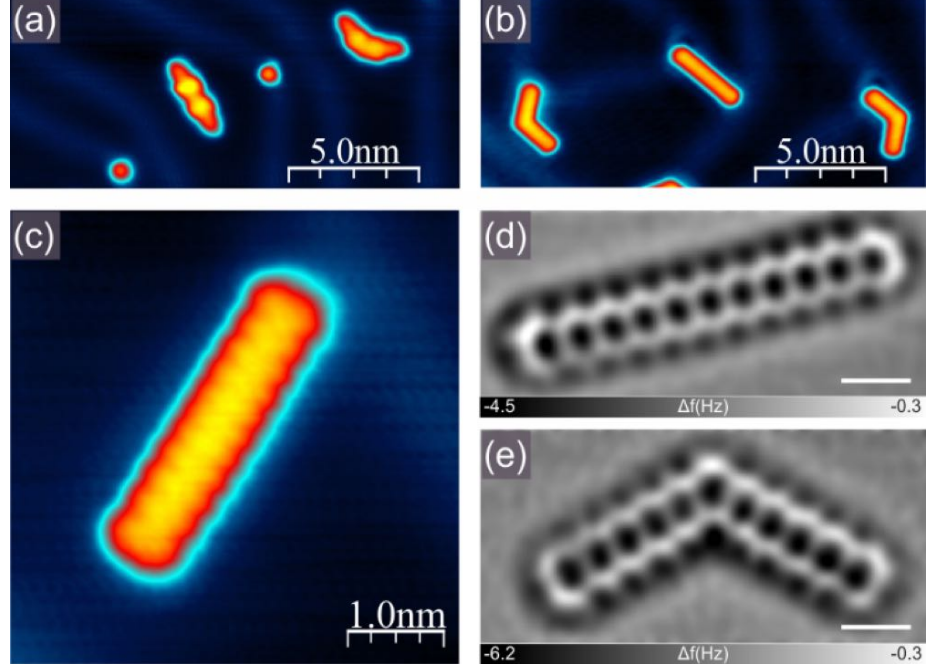
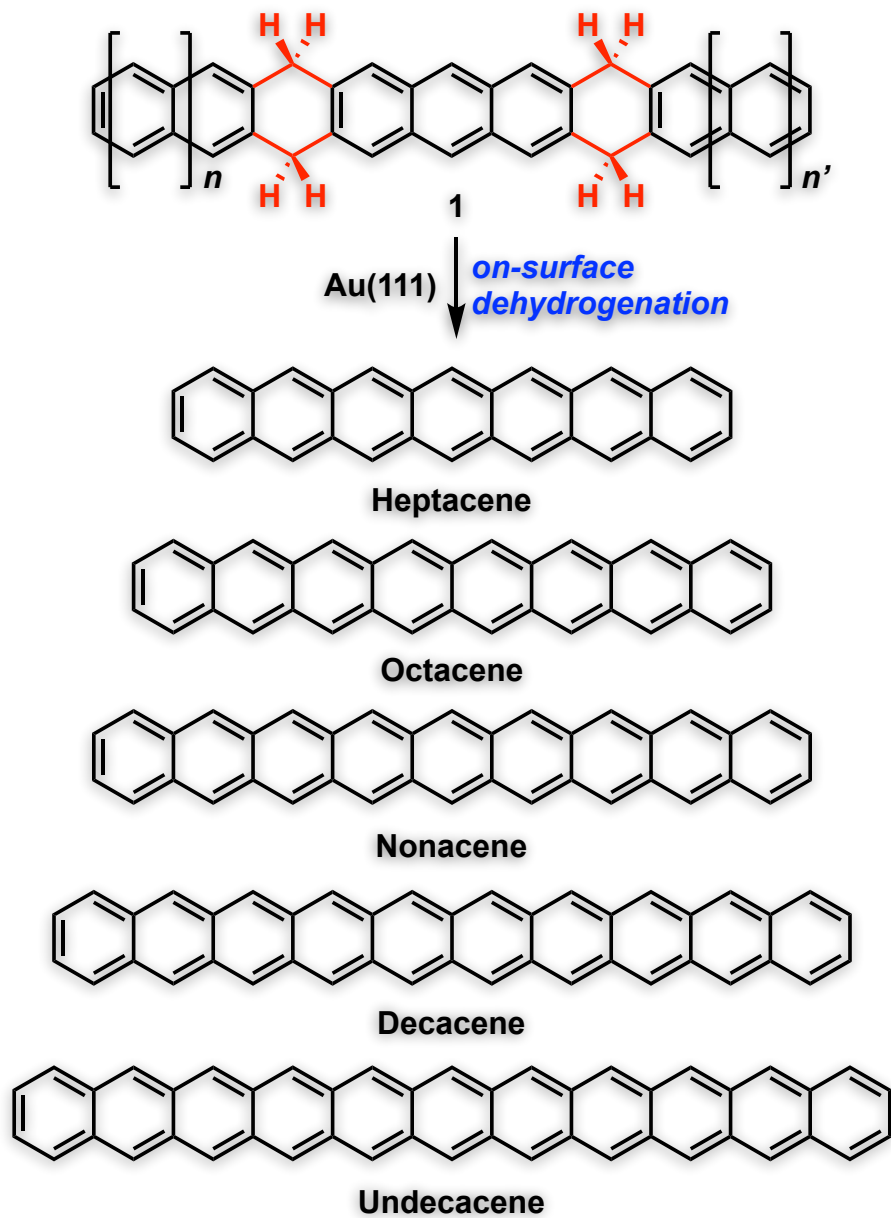
Gold(I)-catalyzed [4+2] cycloaddition of arylalkynes with alkenes





Dorel, McGonigal, Echavarren, *Angew. Chem. Int. Ed.* **2016**, 55, 11120

Zuzak, Dorel, Krawiec, Such, Kolmer, Szymonski, Echavarren, Godlewski, *ACS Nano* **2017**, 11, 9321



The race for the synthesis of higher acenes

ICIQ-Kraków: *Angew. Chem. Int. Ed.* **2016**, 55, 11120
ACS Nano **2017**, 11, 9321; *Angew. Chem. Int. Ed.* **2018**, 57, 10500
StgCompost-Dresden: *Angew. Chem. Int. Ed.* **2017**, 56, 11945;
ACS Nano **2020**, 14, 1011

DECACENE (StgCompost-Dresden)

NONACENE-H4
(ICIQ)

NONACENE
(ICIQ-Kraków)

UNDECACENE
(ICIQ-Kraków)

DODECACENE
(StgCompost-Dresden)

TRIDECACENE
(HIGHER ACENES)

2016

2017

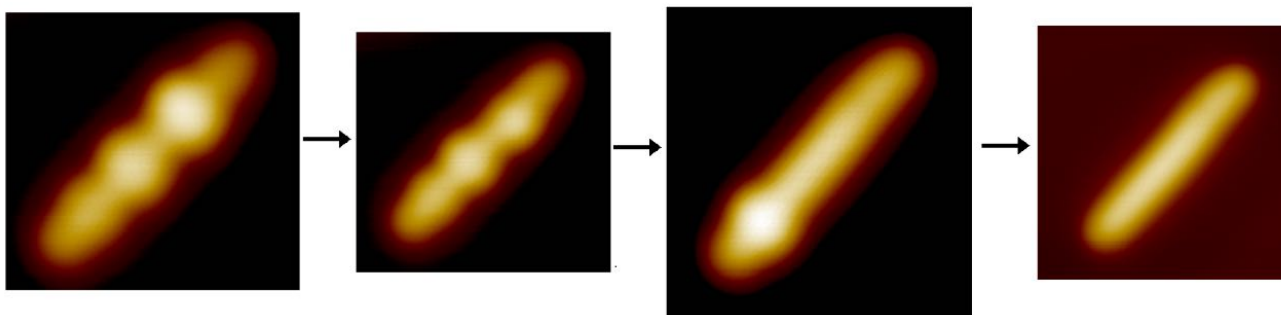
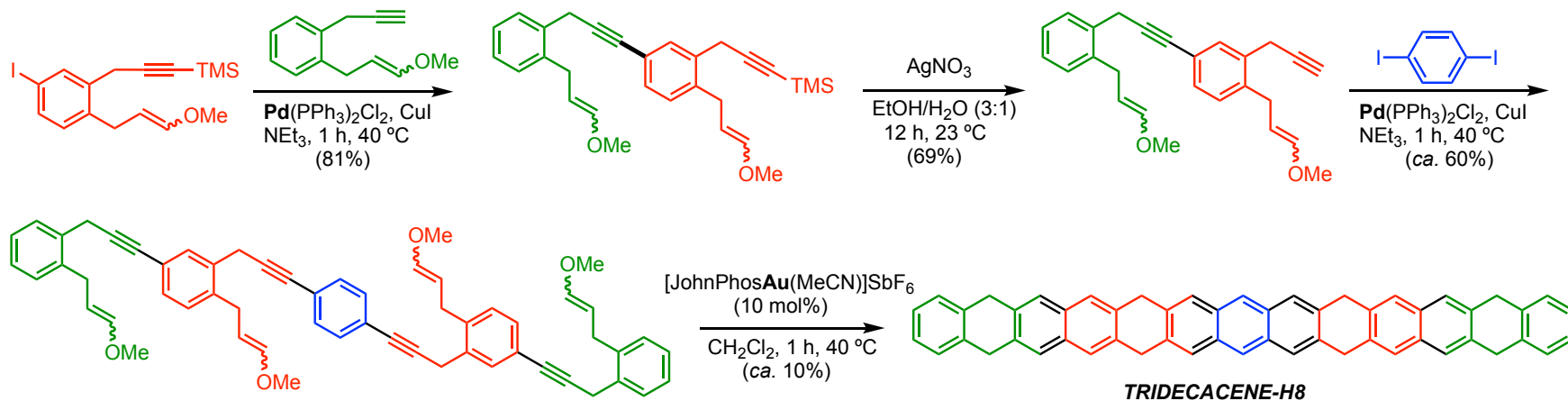
2018

2019

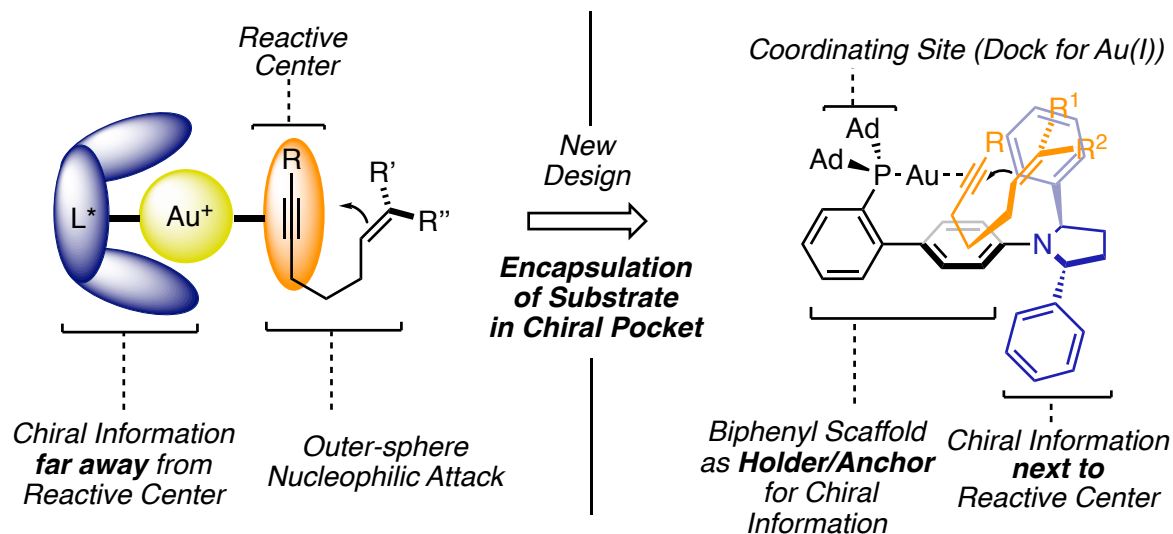
2020

2021

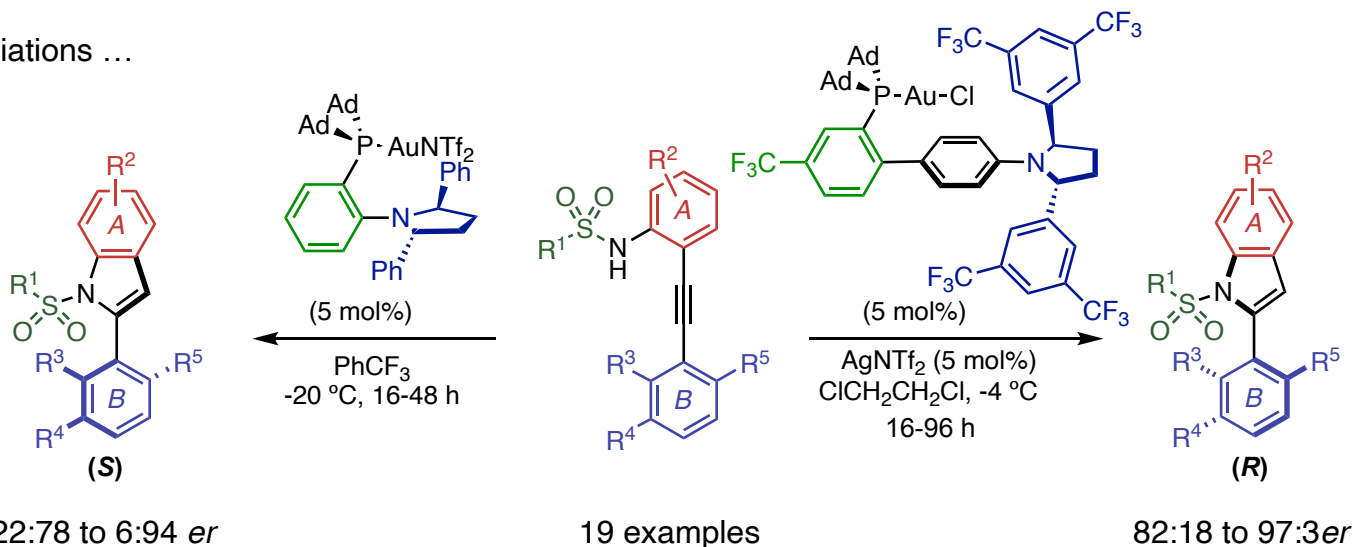
Energy gap
increases to 1.4 eV



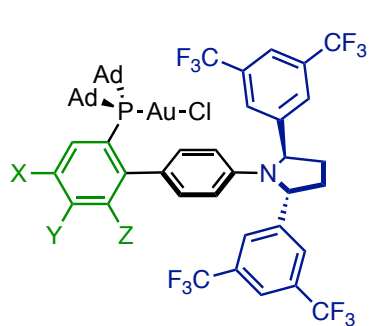
Pyrrolidine BiphenylPhos Ligands



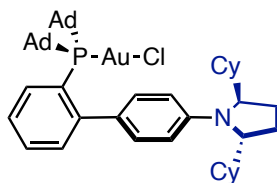
23 variations ...



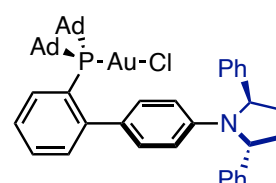
Zuccarello, Mayans Escofet, Scharnagel, Kirillova, Pérez-Jimeno, Calleja, Boothe, Echavarren, *J. Am. Chem. Soc.* **2019**, *141*, 11858. Zuccarello, Nannini, Arroyo-Bondía, Fincias, Arranz, Pérez-Jimeno, Peeters, Martín-Torres, Sadurní, García-Vázquez, Wang, Kirillova, Montesinos-Magraner, Caniparoli, Núñez, Maseras, Besora, Escofet, Echavarren, *JACS Au* **2023**, *3*, 1742



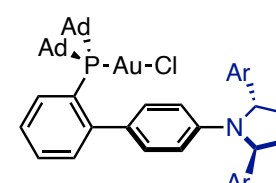
(*R,R*)-**A**: X = Y = Z = H,
 (*R,R*)-**B**: X = CF₃, Y = Z = H
 (*R,R*)-**C**: X = Z = F, Y = H
 (*R,R*)-**D**: X = Z = CF₃, Y = H
 (*R,R*)-**E**: X = Z = H, Y = Me
 (*R,R*)-**F**: X = Z = H, Y = OMe



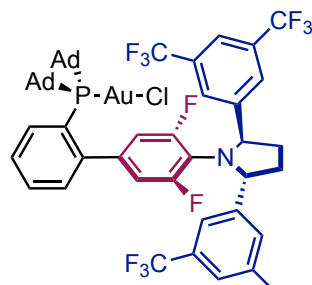
(*R,R*)-**G**, **2a**



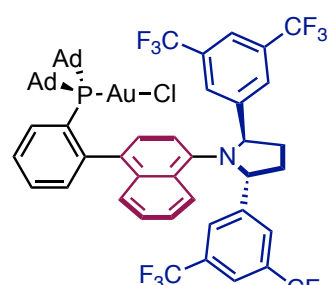
(*R,R*)-**H**, **2a**



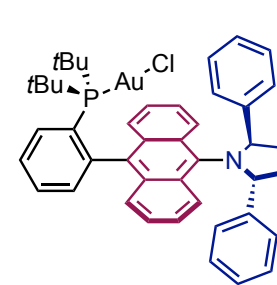
(*S,S*)-**I**: Ar = 1-Naphthyl



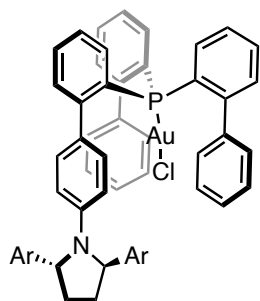
(*R,R*)-**J**



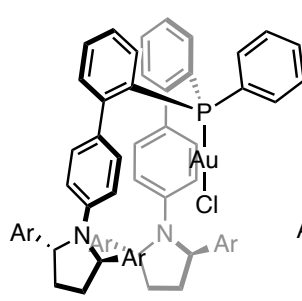
(*R,R*)-**K**, **2a**



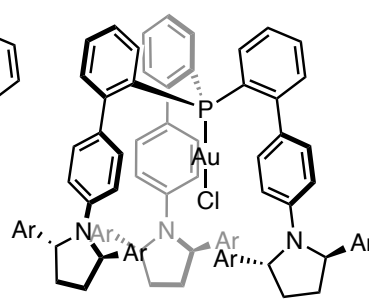
(*R,R*)-**L**, **2a**



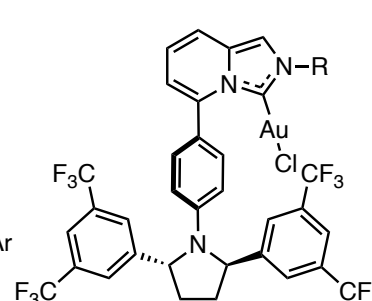
(*R,R*)-**P**



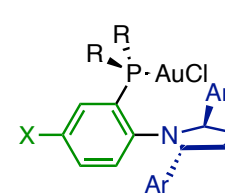
(*R,R*)-**Q**



(*R,R*)-**R**



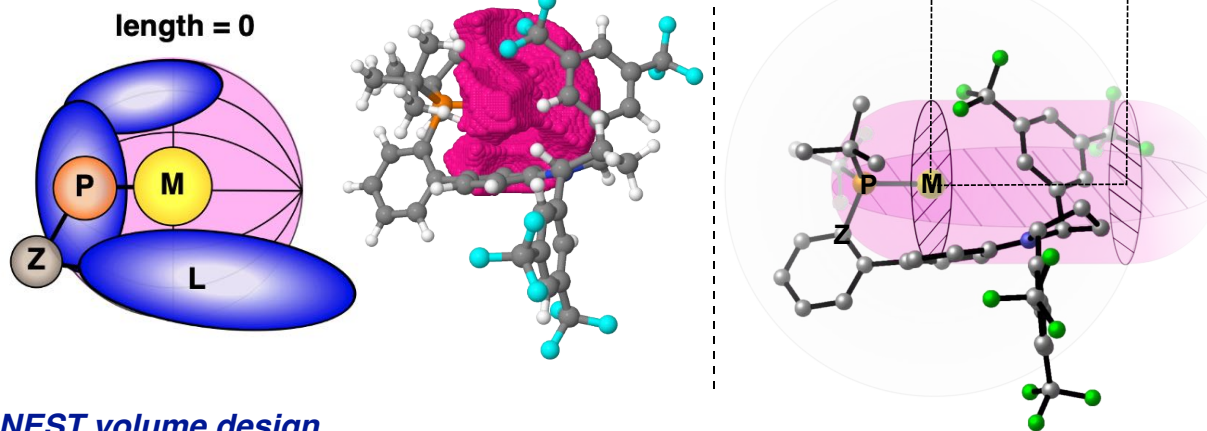
(*R,R*)-**M**: R = 2,4,6-Me₃C₆H₂
 (*R,R*)-**N**: R = 2,6-*i*PrC₆H₃
 (*R,R*)-**O**: R = Ad



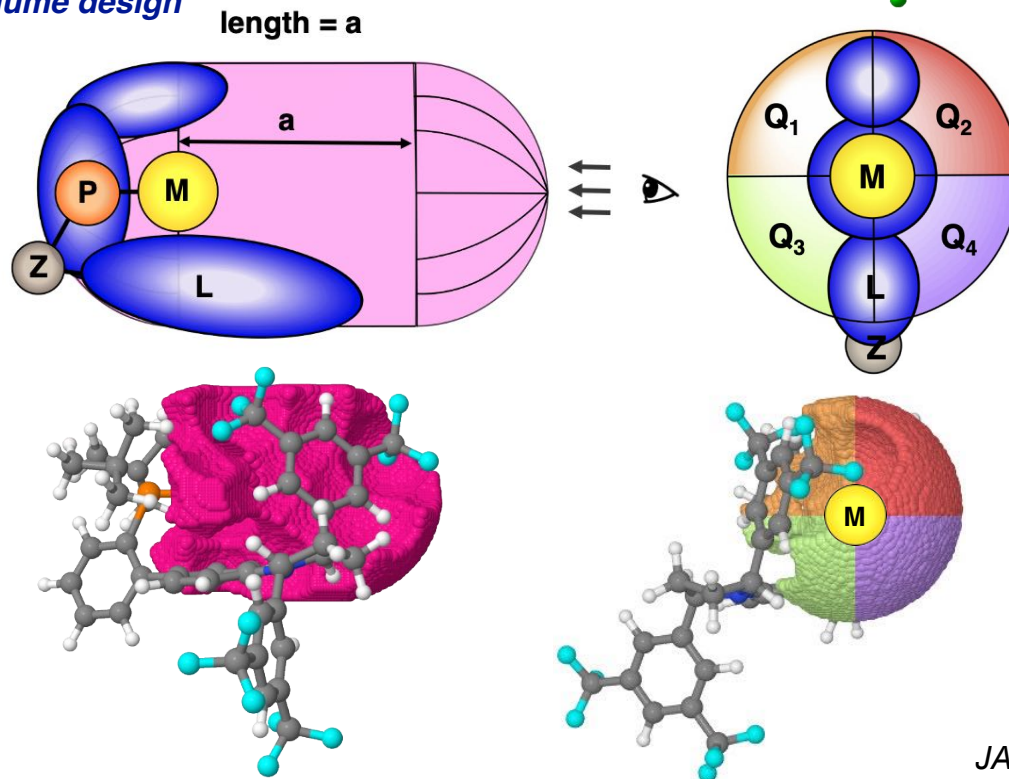
(*R,R*)-**S**: R = Ad, Ar = Ph, X = H
 (*R,R*)-**T**: R = *t*Bu, Ar = Ph, X = H
 (*R,R*)-**U**: R = Ad, Ar = Ph, X = CF₃
 (*R,R*)-**V**: R = *t*Bu, Ar = 3,5-Ph₂C₆H₃, X = H
 (*R,R*)-**W**: R = Ad, Ar = 3,5-Ph₂C₆H₃, X = H

NEST Analysis of the Chiral Binding Pocket

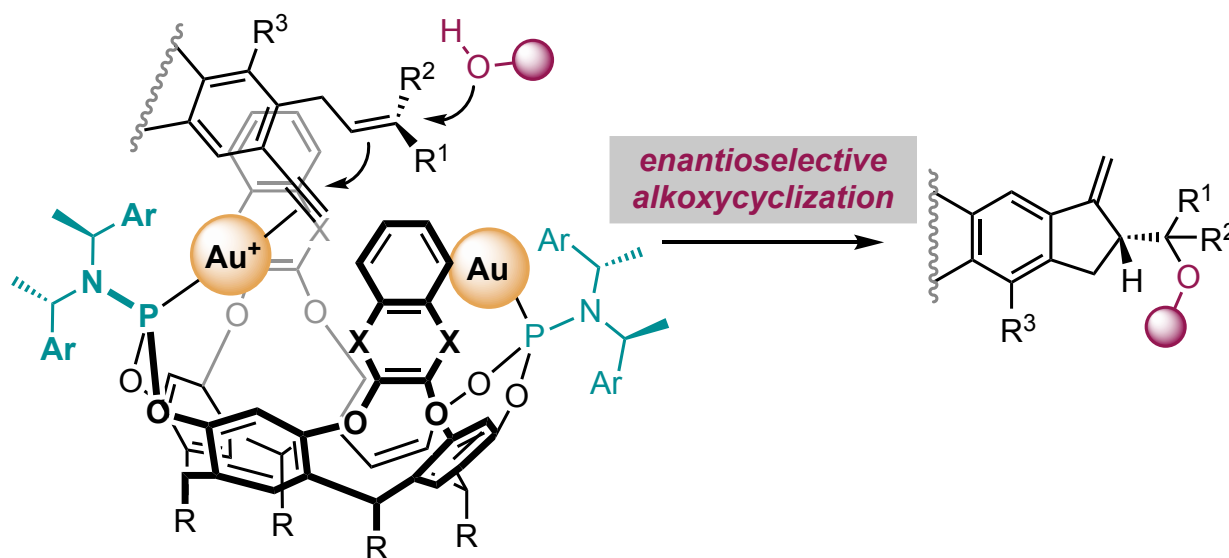
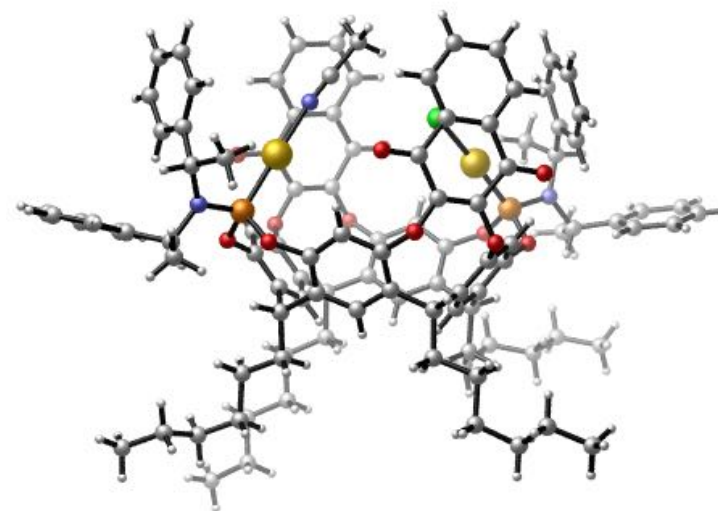
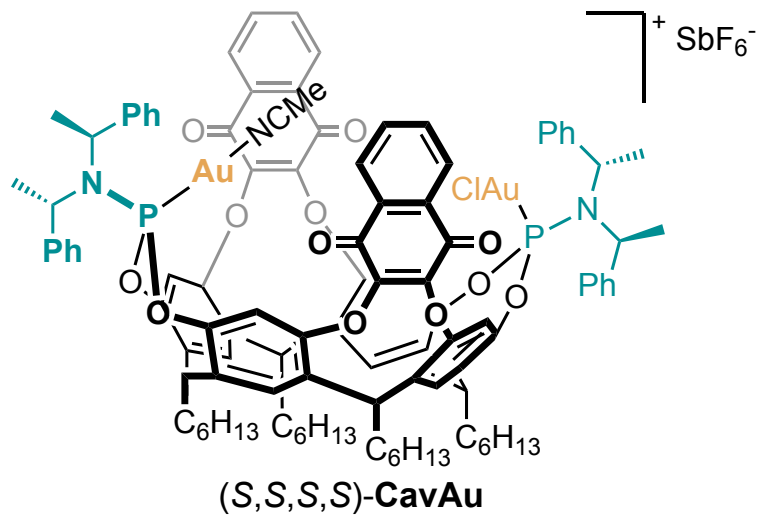
Spherical volume

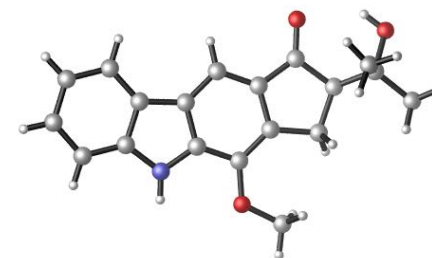
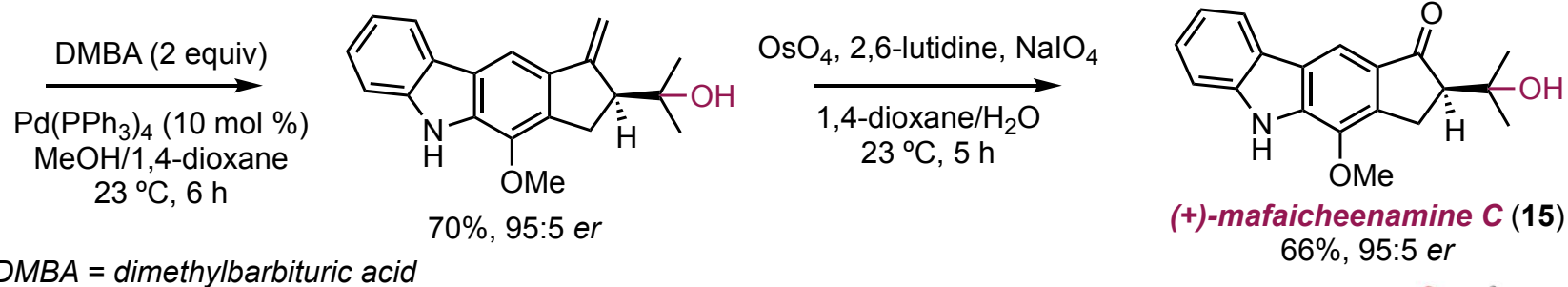
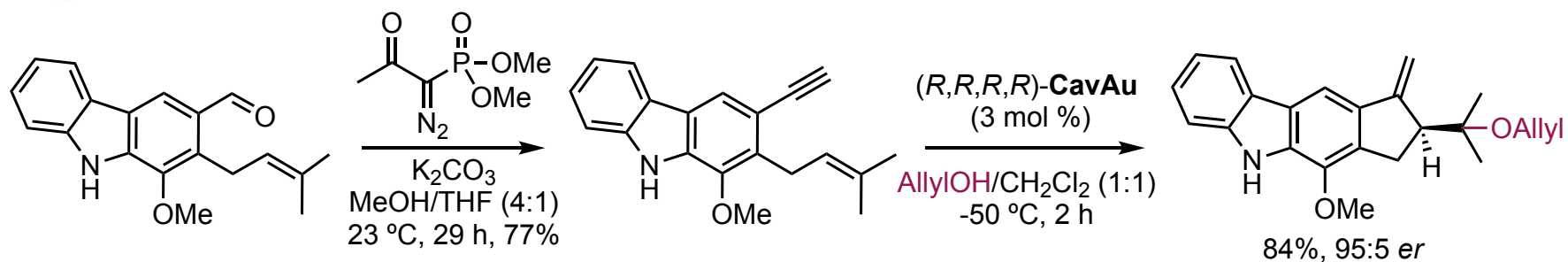
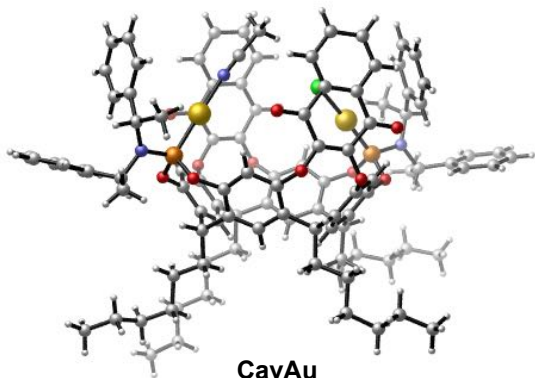


NEST volume design

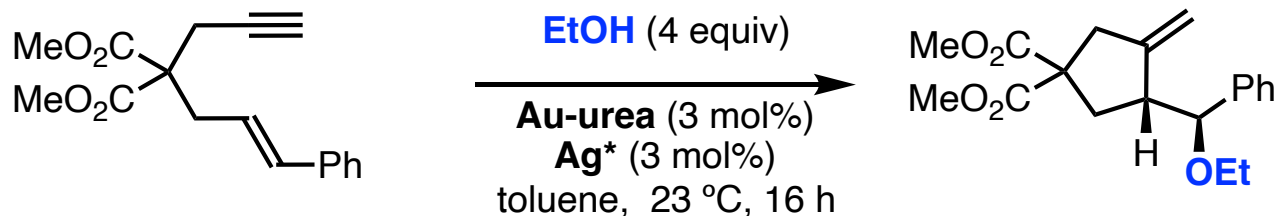


Chiral Gold(I)-Cavitands

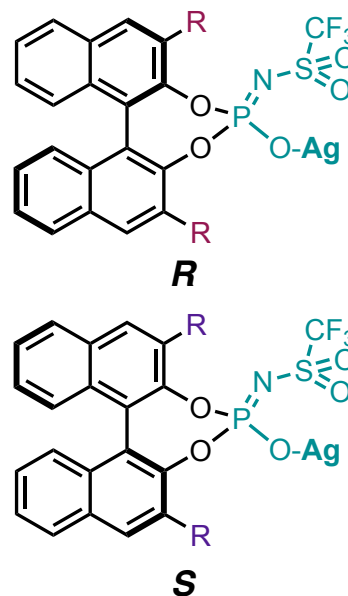
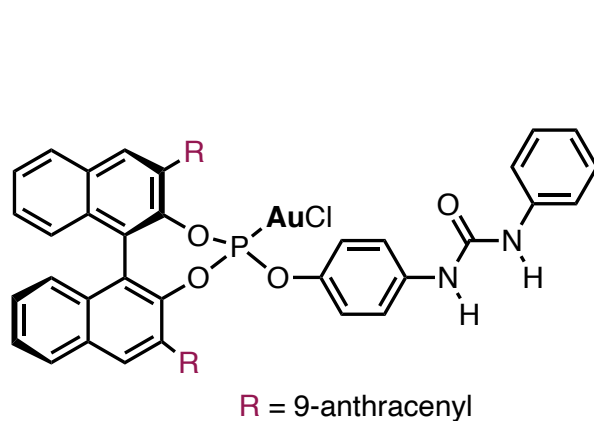




H-bonded Matched Ion Pair Au(I) Catalysis



> 30 examples



87%, 98:2 *er*
matched

85%, 43:57 *er*
mismatched

Martí, Ogalla, Echavarren, *ACS Catal.* **2023**, 13, 10217

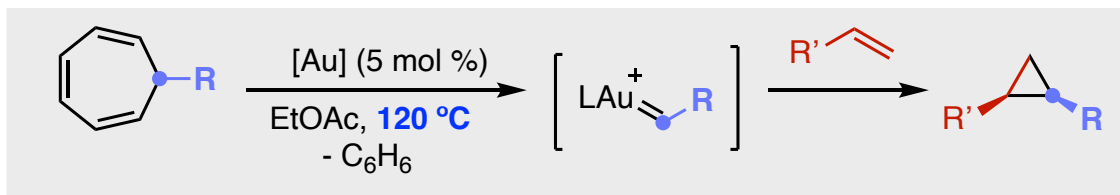
H-bonded Counterion-Directed Enantioselective Au(I) Catalysis:

Franchino, Martí, Echavarren, *J. Am. Chem. Soc.* **2022**, 144, 3497

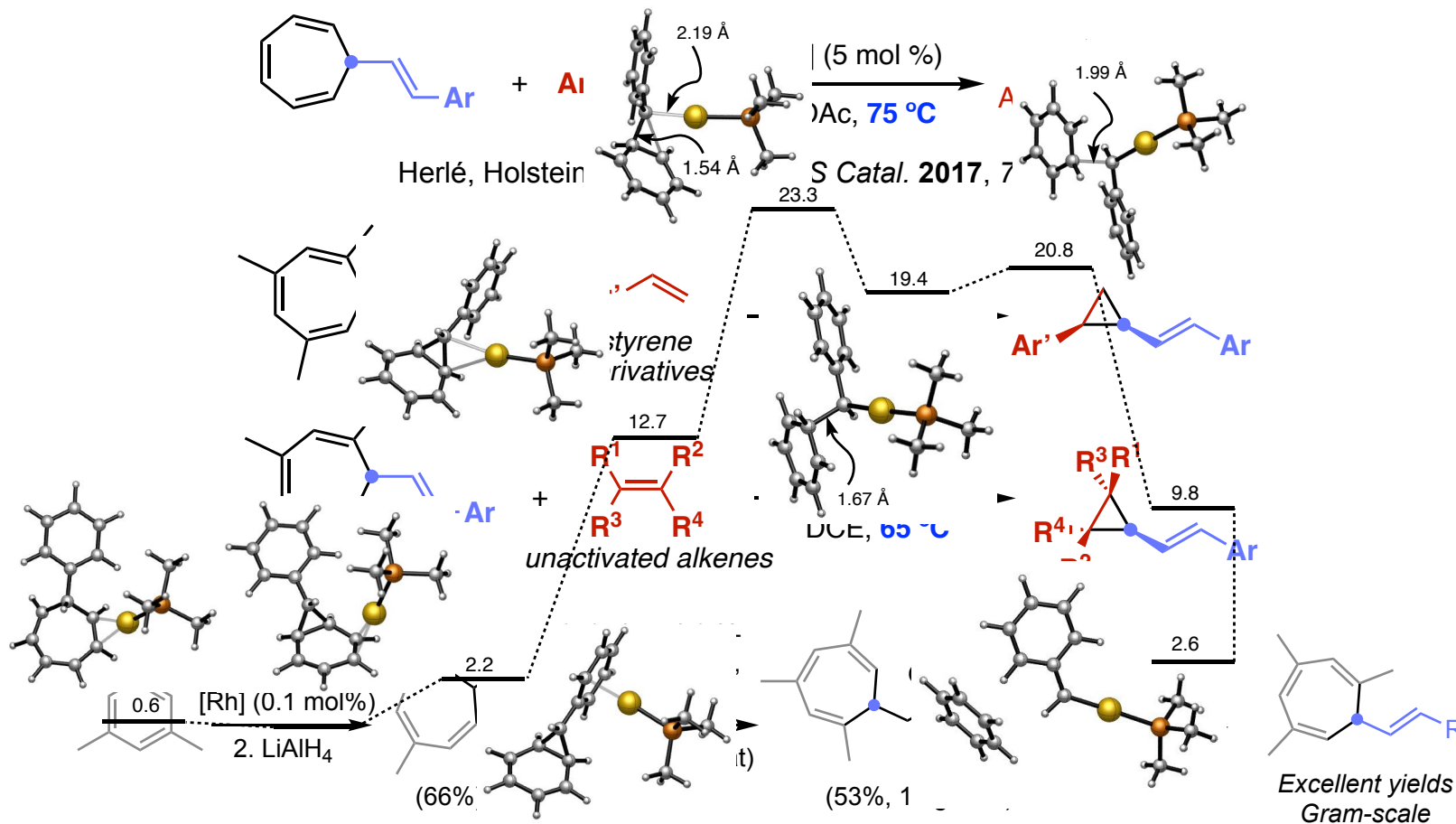
Modular Chiral Gold(I) Phosphite Complexes:

Delpont, Escofet, Pérez-Galán, Spiegl, Raducan, Bour, Sinisi, Echavarren, *Cat. Sci. Technol.* **2013**, 3, 3007

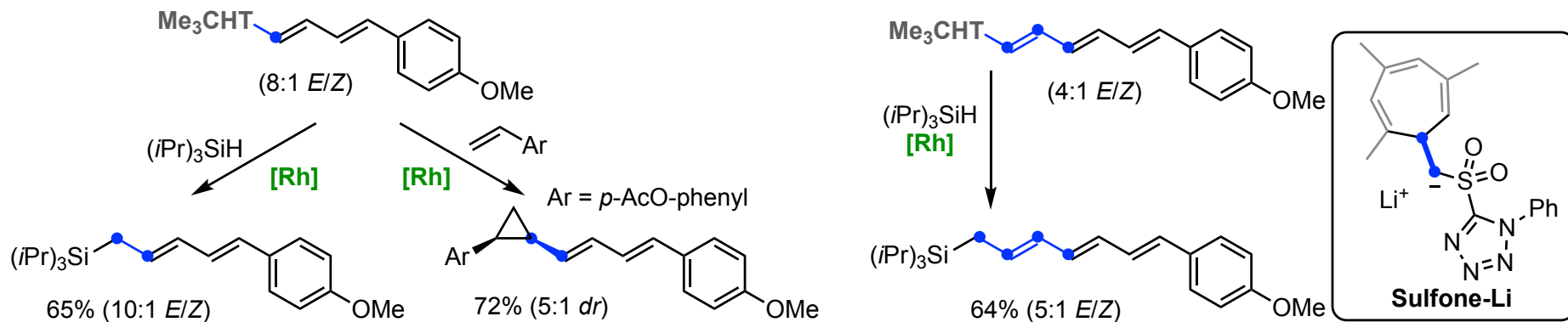
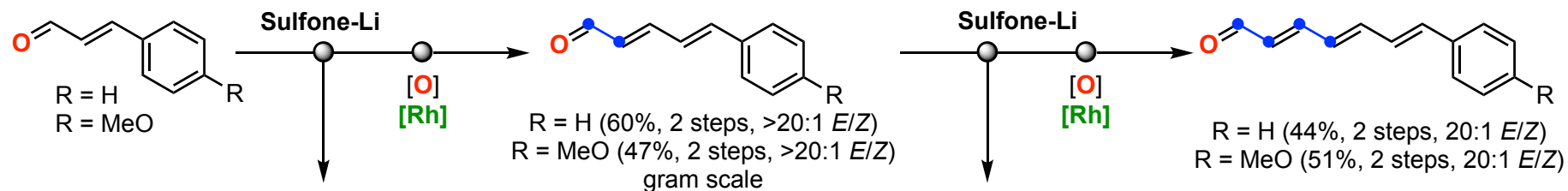
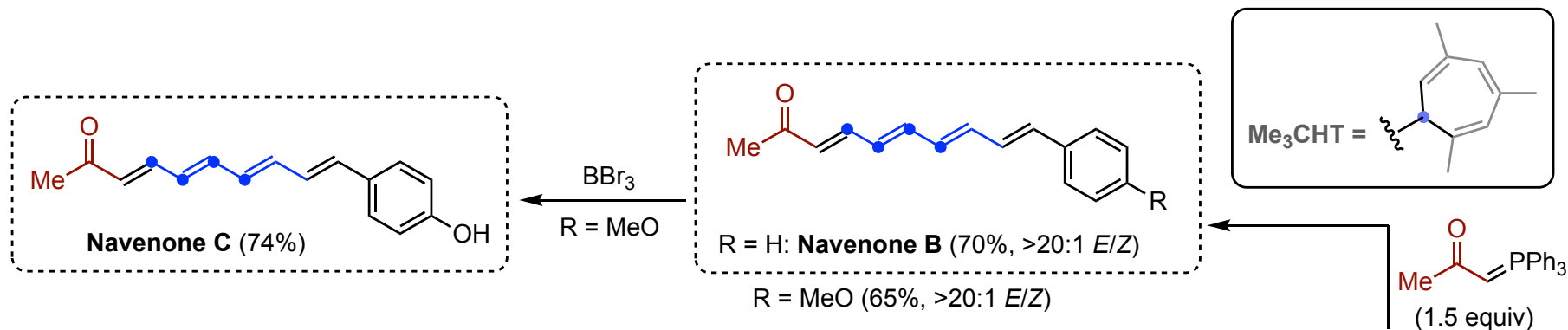
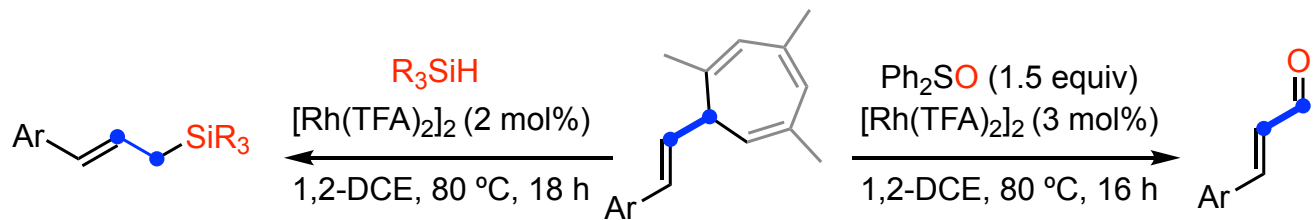
Gold(I) Carbenes by Decarbenation (retro-Buchner reaction)

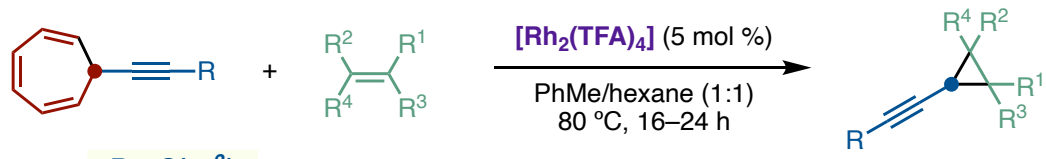


Solorio-Alvarado, Wang, Echavarren, *J. Am. Chem. Soc.* **2011**, 133, 11952. Wang, McGonigal, Herlé, Besora, Echavarren, *J. Am. Chem. Soc.* **2014**, 136, 801. Wang, Muratore, Rong, Echavarren, *Angew. Chem. Int. Ed.* **2014**, 53, 14022. Yin, Mato, Echavarren, *Angew. Chem. Int. Ed.* **2017**, 56, 14591



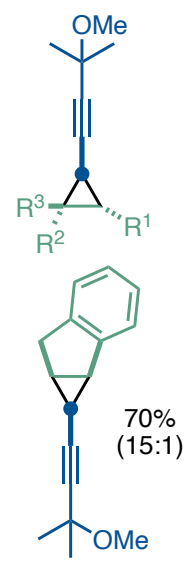
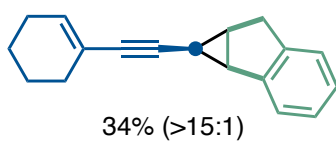
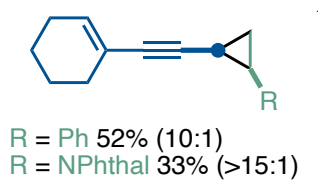
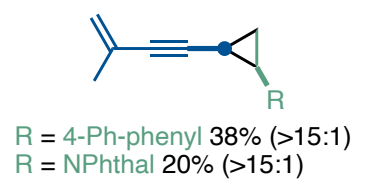
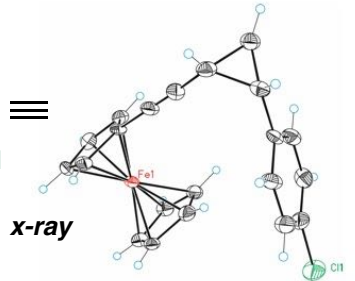
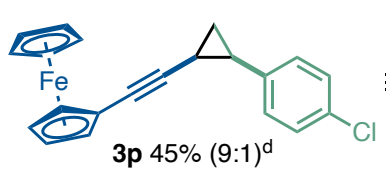
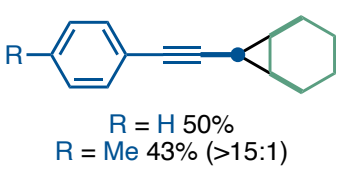
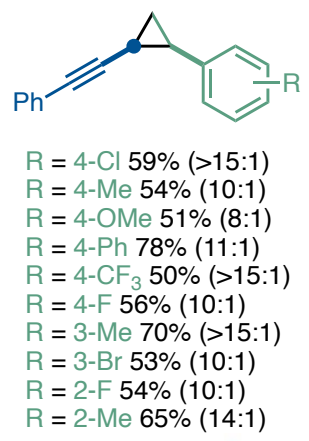
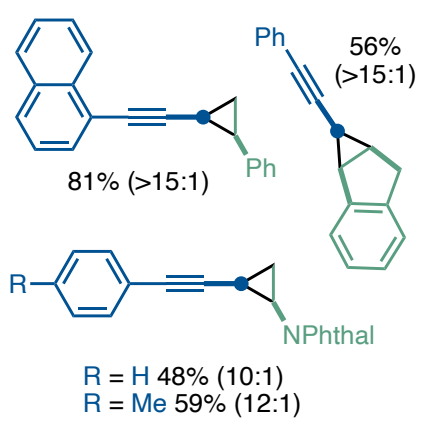
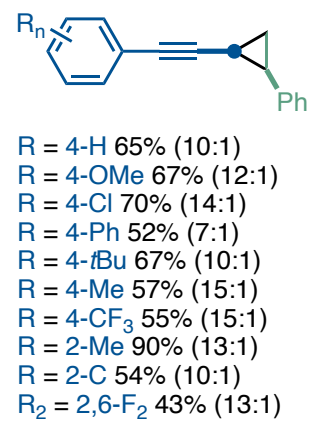
Mato, Herlé, Echavarren, *Org. Lett.* **2018**, 20, 4341



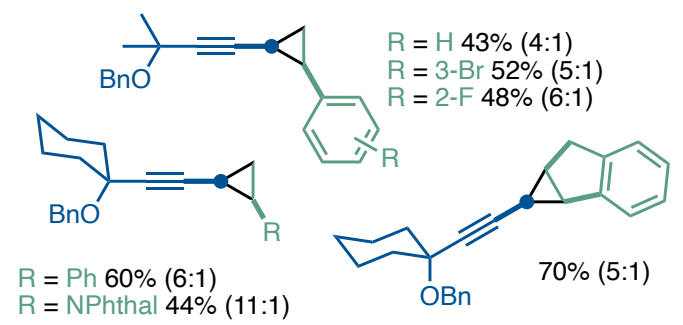
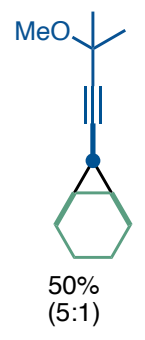
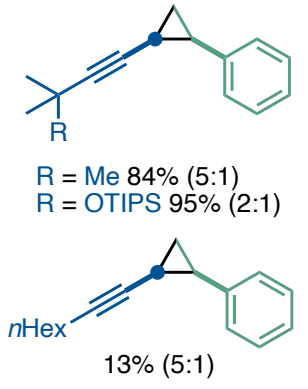


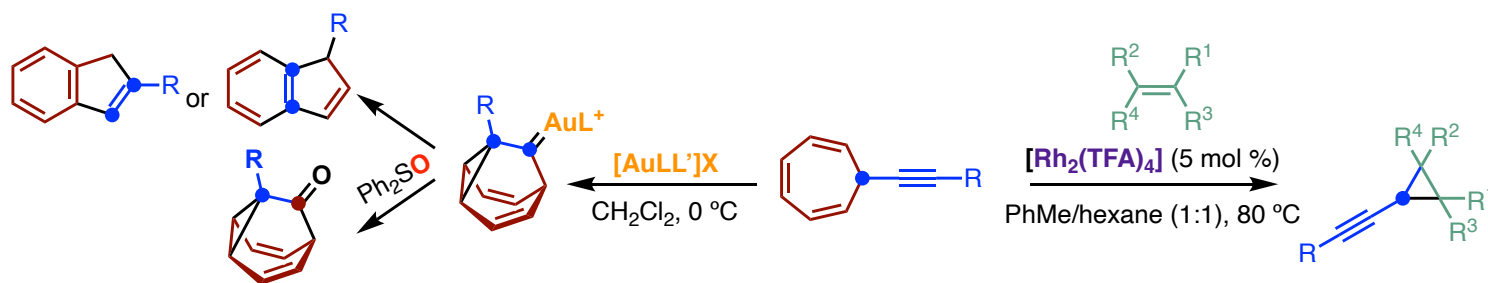
$R = C(sp^2)$

$R = C(sp^3)$



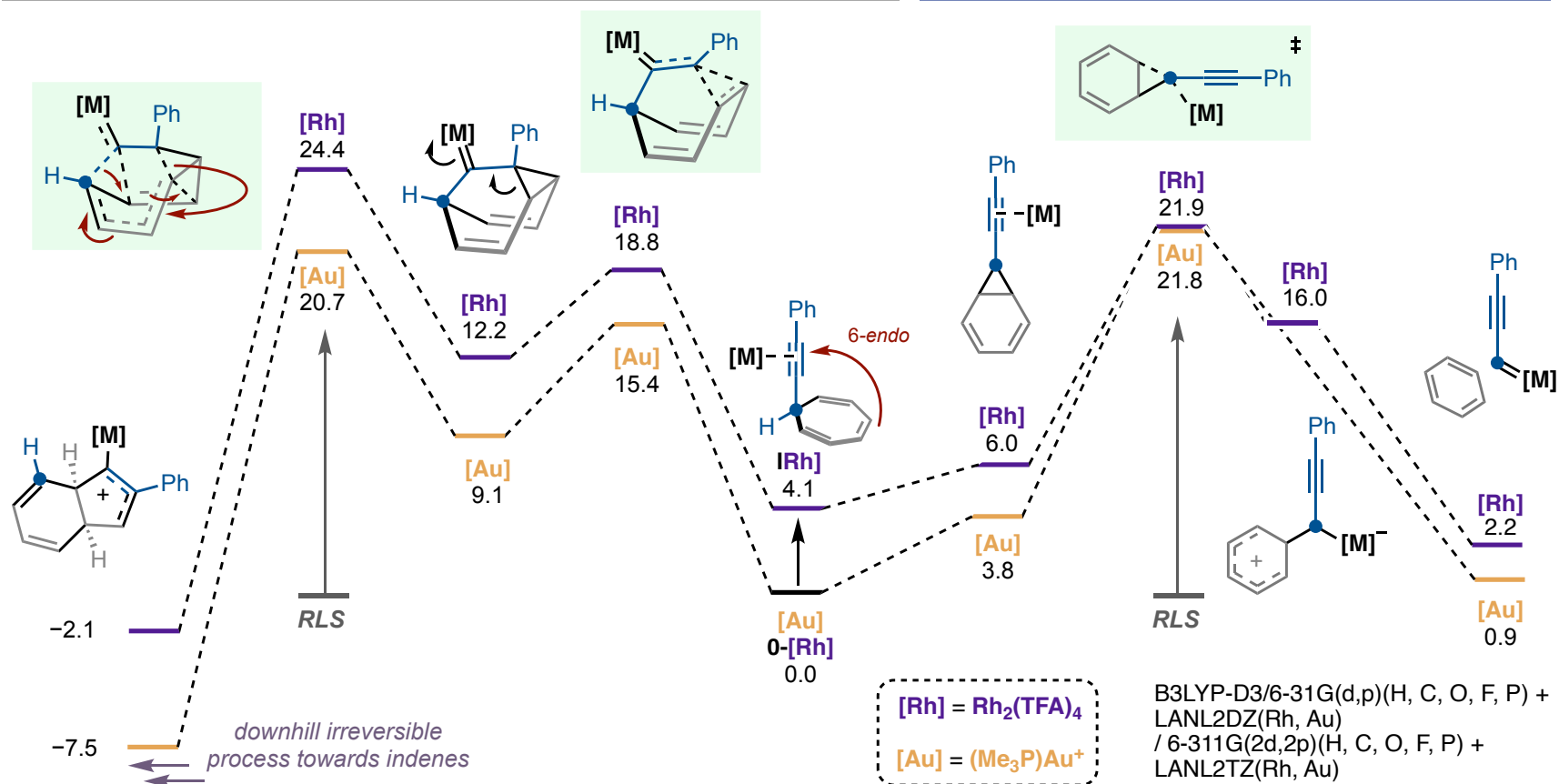
$R^1 = R^2 = \text{H}, R^3 = \text{Ph}$ 78% (5:1)
 $R^1 = R^2 = \text{H}, R^3 = 4\text{-Tol}$ 70% (10:1)
 $R^1 = R^2 = \text{H}, R^3 = \text{NPhthal}$ 70% (5:1)
 $R^1 = \text{Ph}, R^2 = \text{H}, R^3 = \text{Ph}$ 80% (>50:1)
 $R^1 = \text{H}, R^2 = \text{Me}, R^3 = \text{Ph}$ 80% (1.2:1)





6-endo-dig

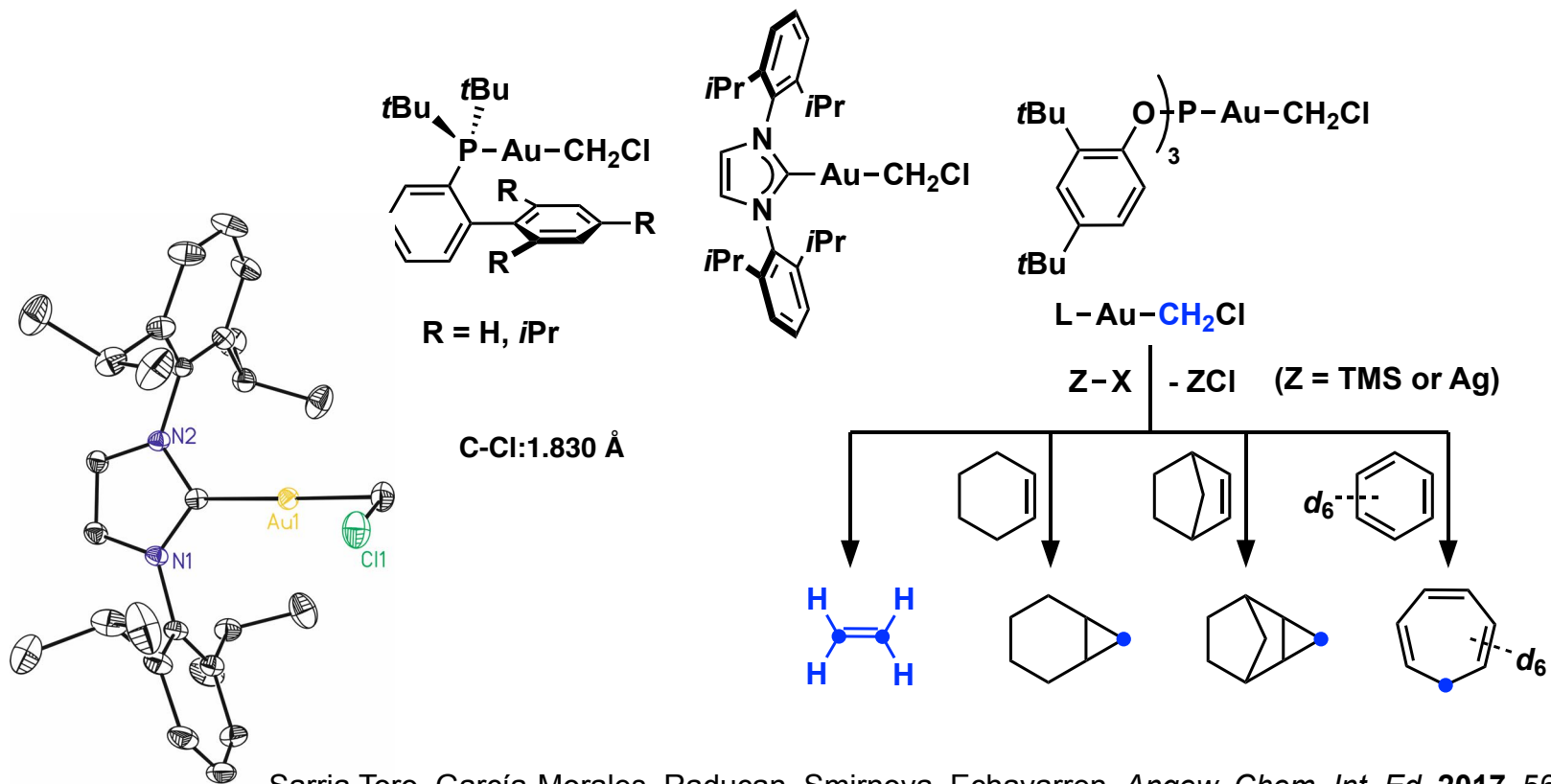
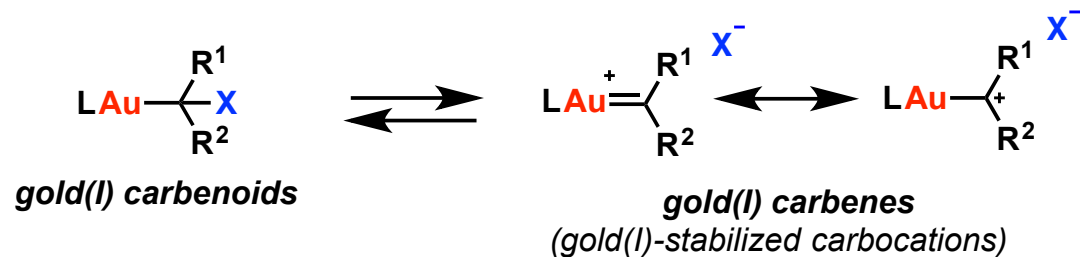
decarbenation

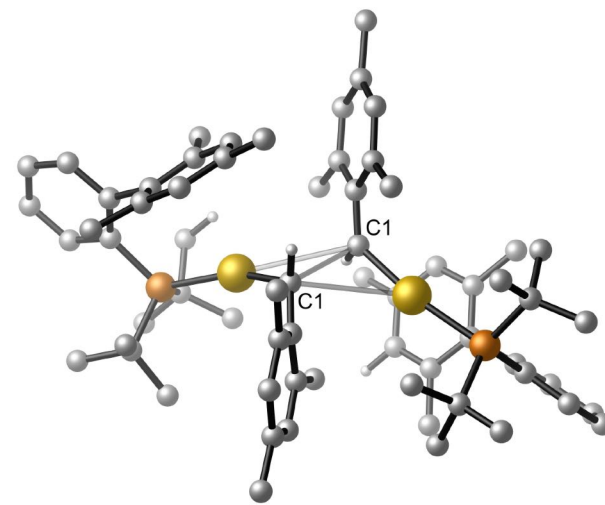
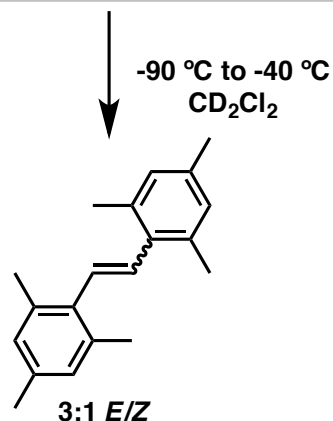
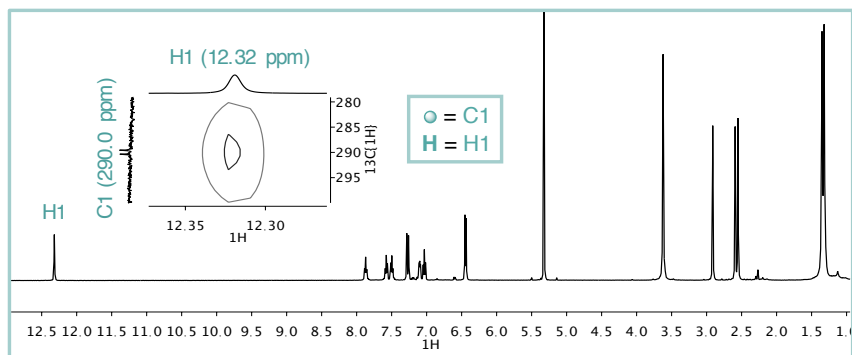
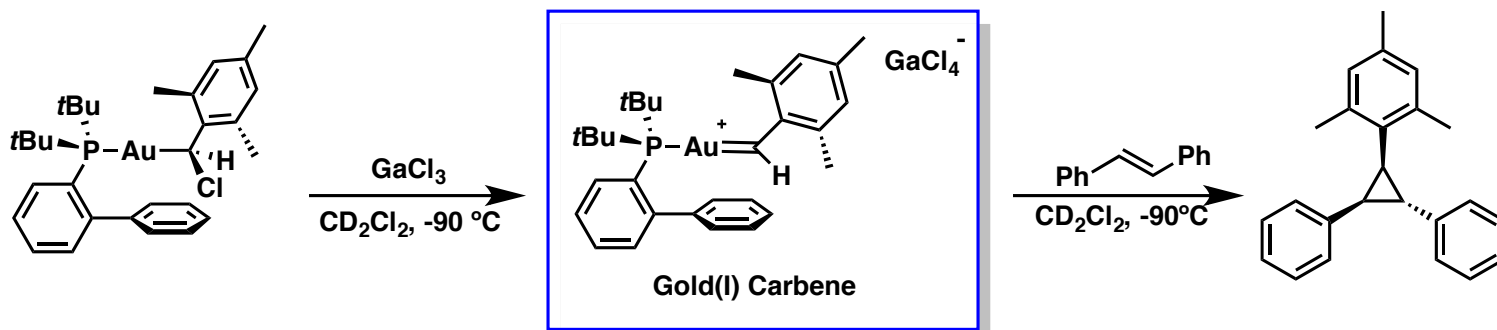
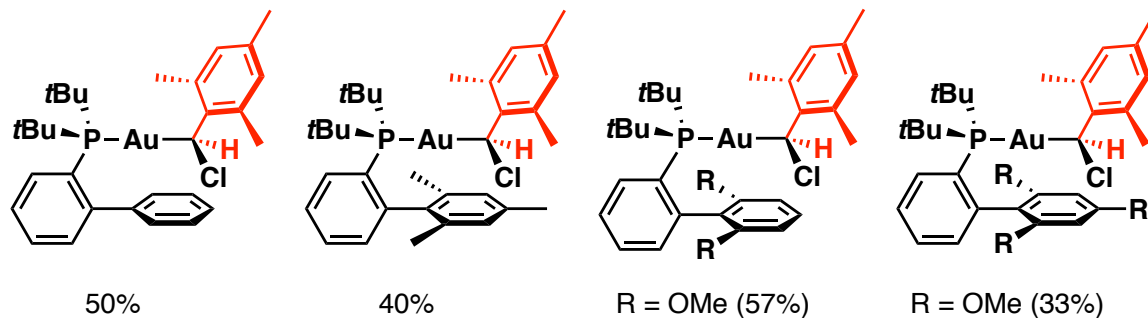


Rh(II): Mato, Montesinos-Magraner, R. Sgranyes, Echavarren, *J. Am. Chem. Soc.* **2021**, *143*, 19760

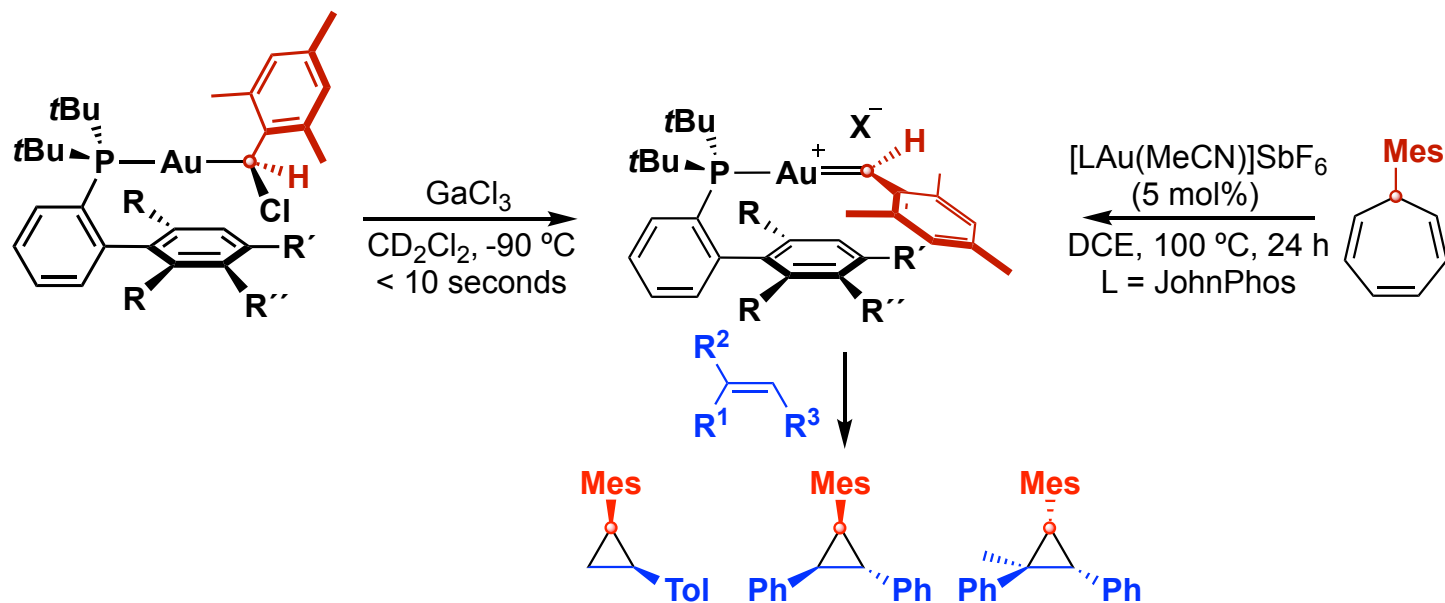
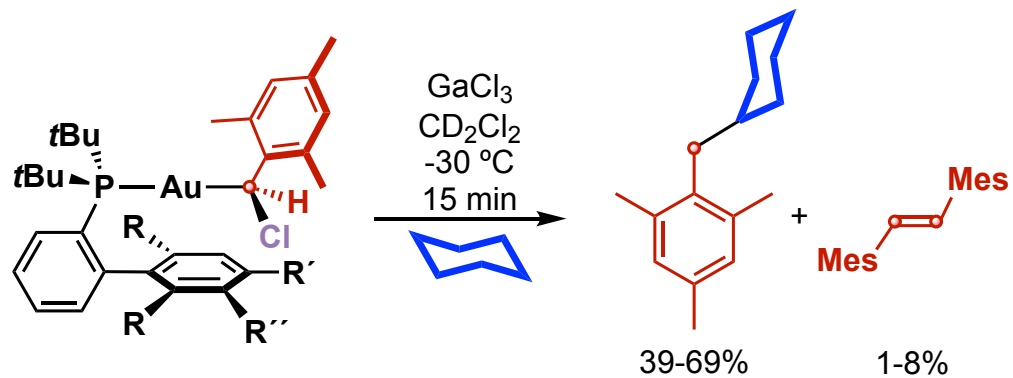
Au(I): McGonigal, de León, Wang, Homs, Solorio-Alvarado, Echavarren, *Angew. Chem. Int. Ed.* **2012**, *51*, 13093.

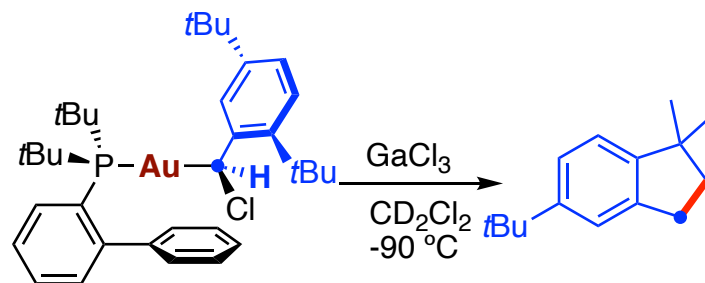
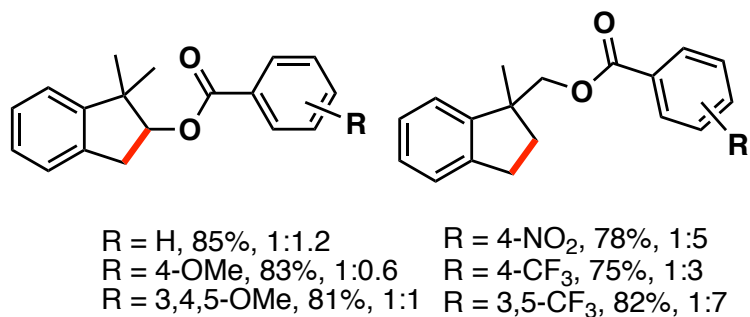
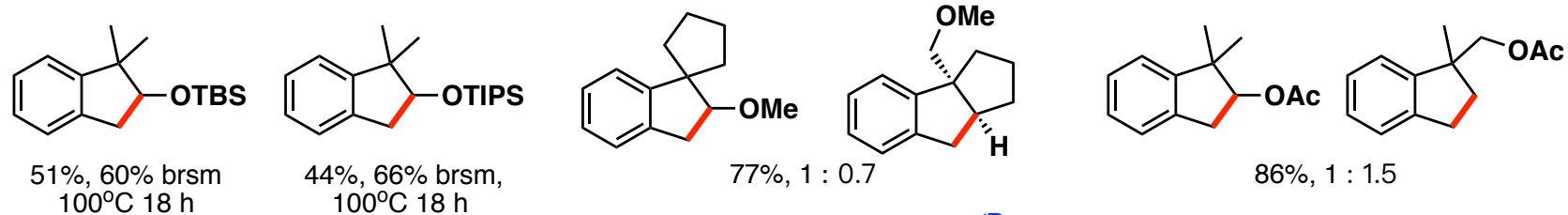
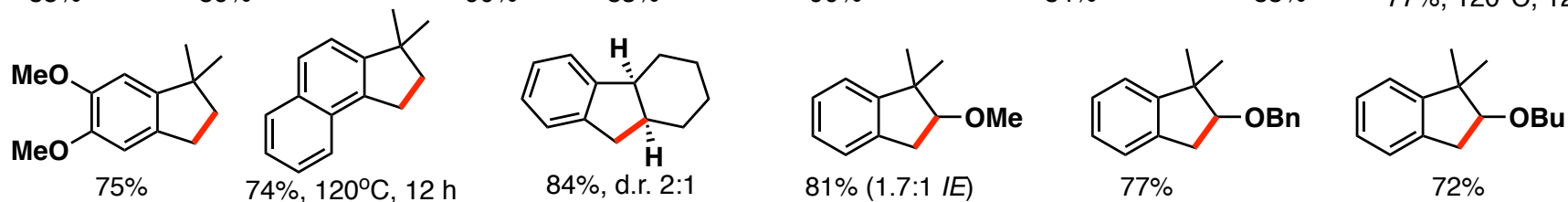
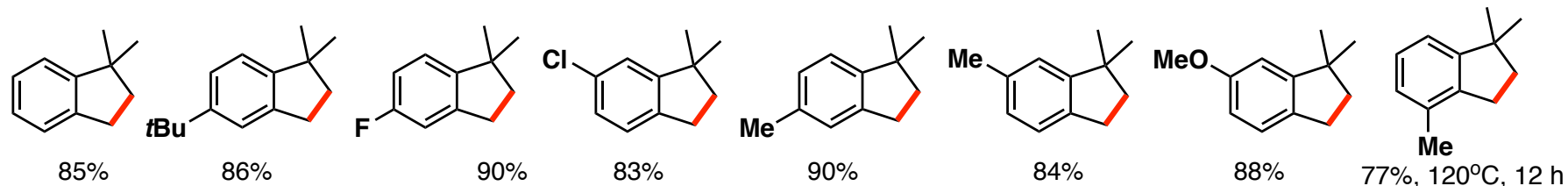
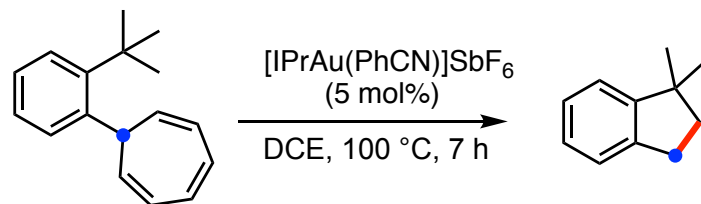
Ferrer, Echavarren, *Angew. Chem. Int. Ed.* **2016**, *55*, 11178



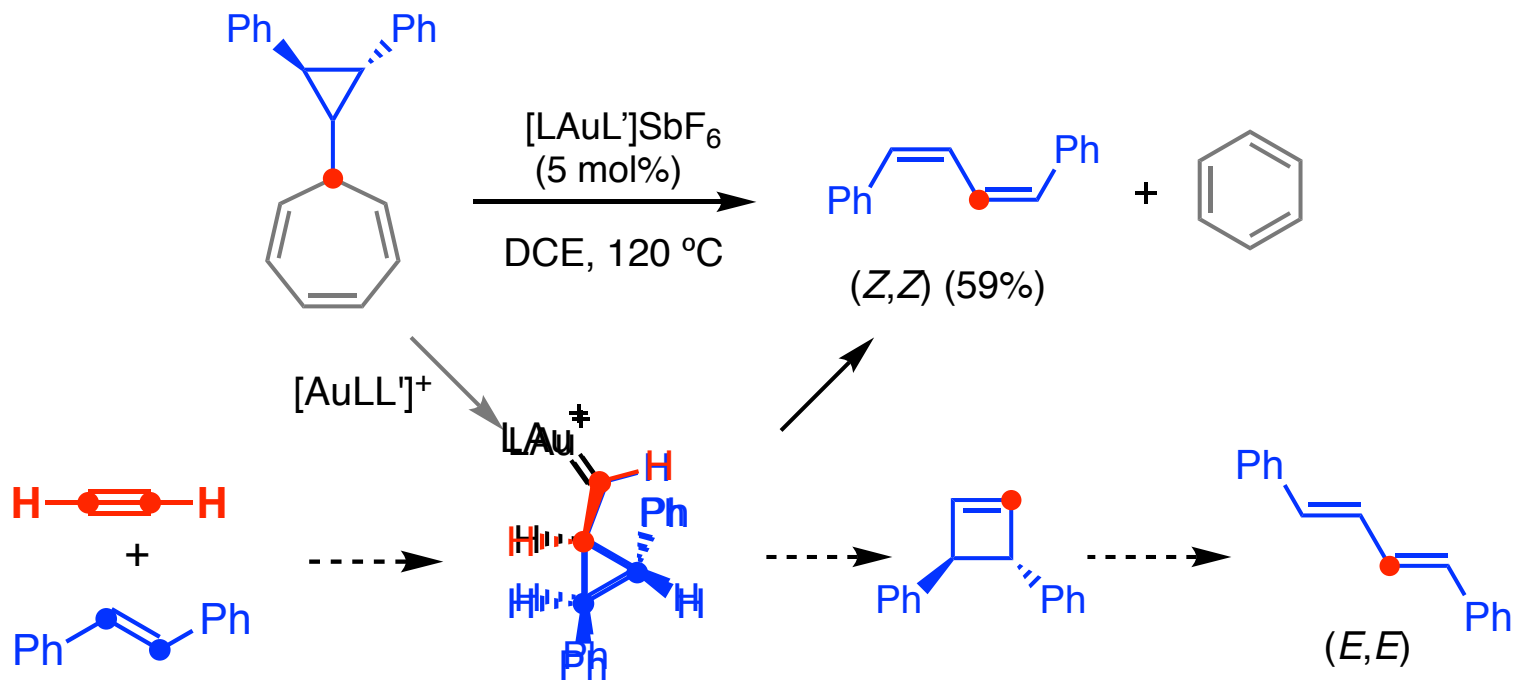


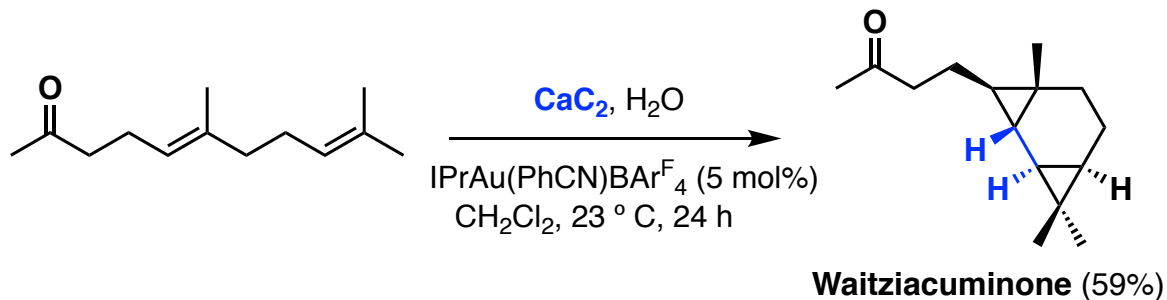
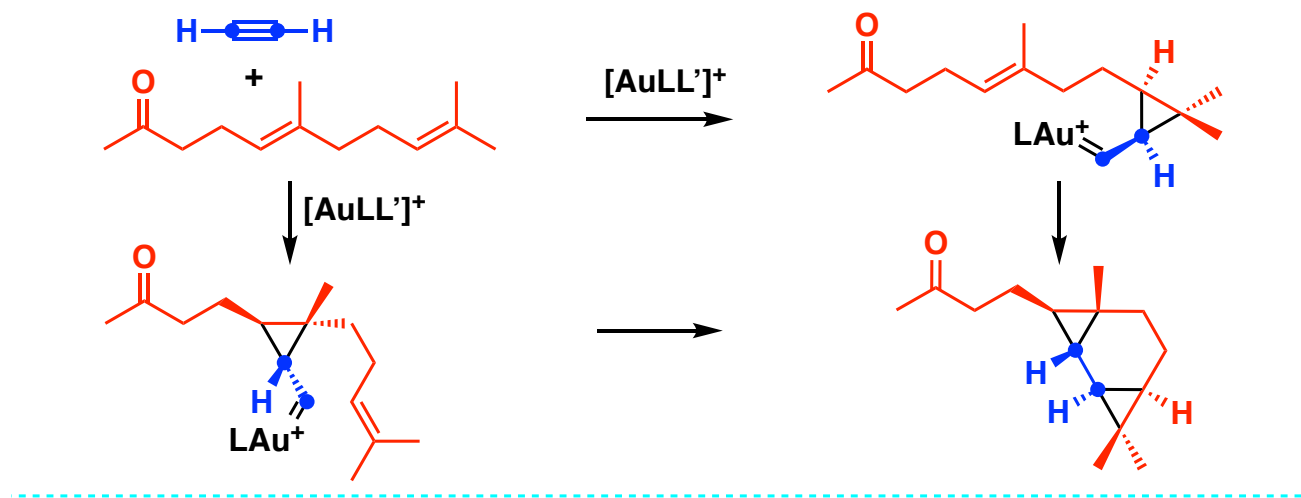
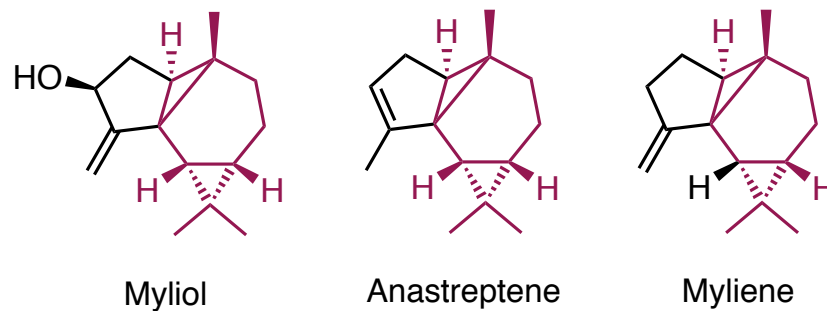
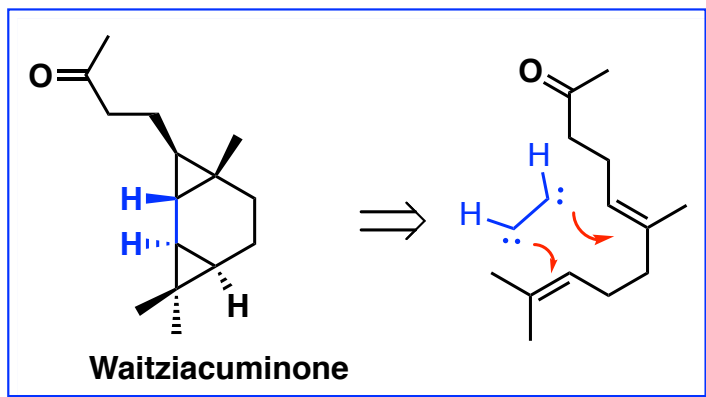
$\Delta G^\ddagger = 6.2 \text{ kcal/mol}$



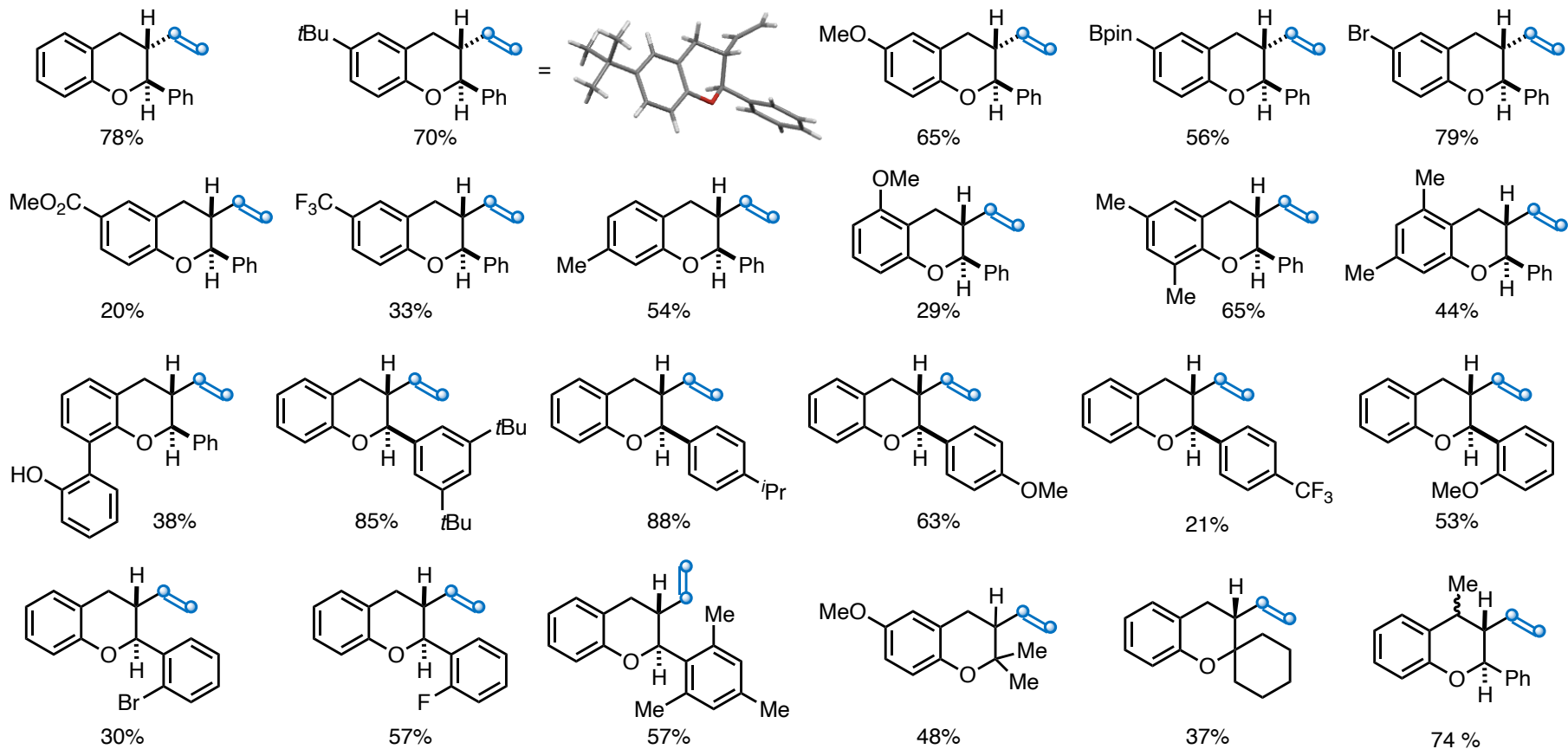
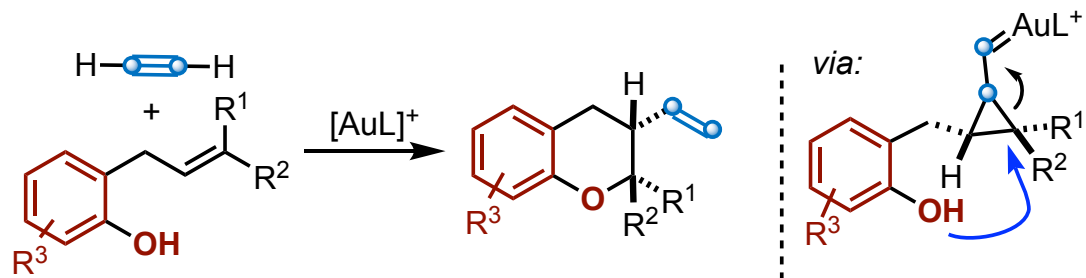


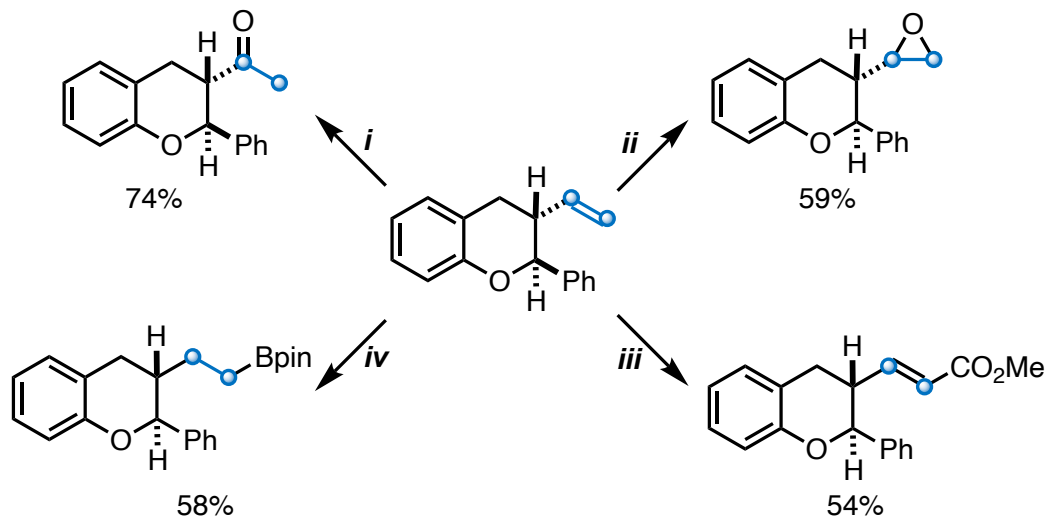
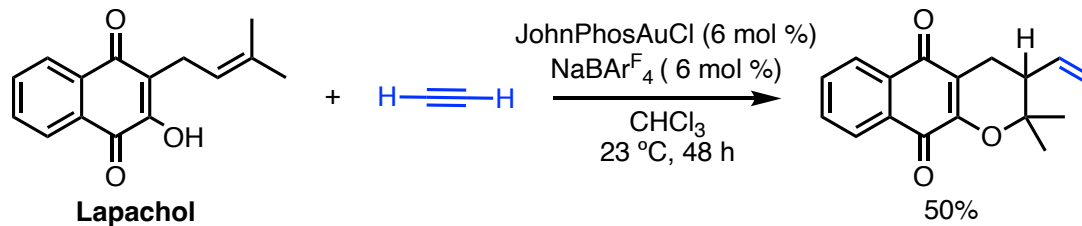
Acetylene as a dicarbene equivalent





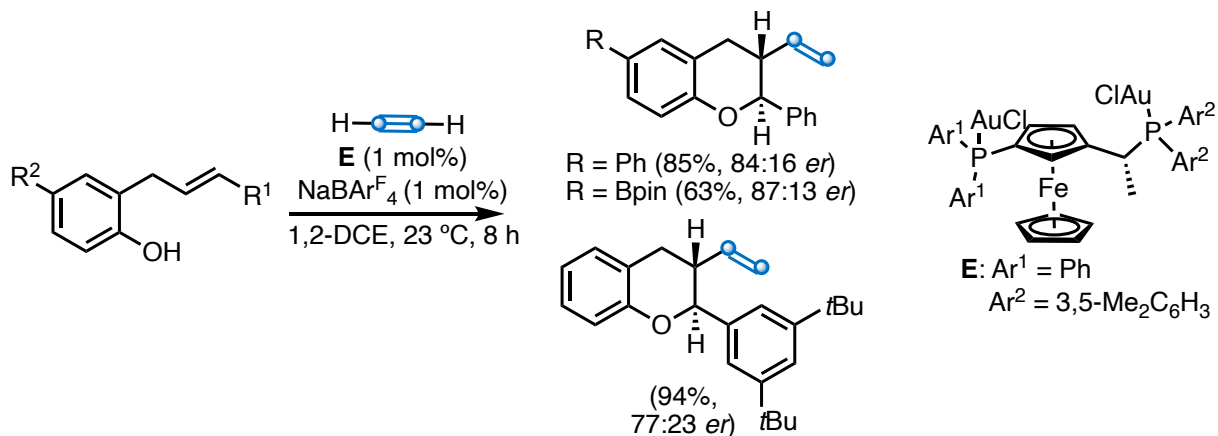
Gold(I)-Catalyzed Intermolecular Aryloxyvinylation



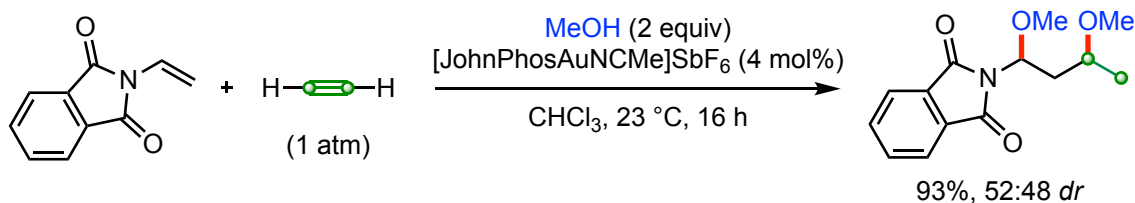
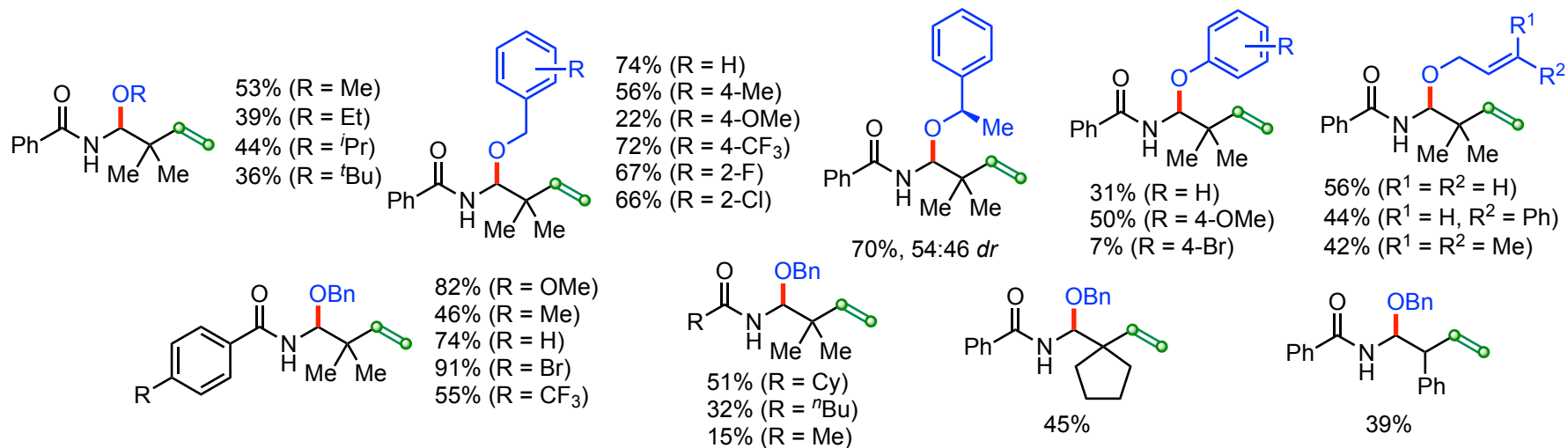
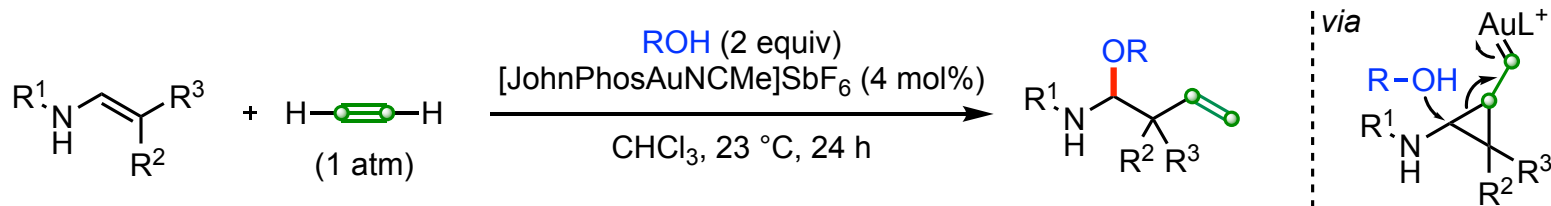


i: O_2 , PdCl_2 , CuCl , aq DMF, 23 °C, 16 h; ii: *m*CPBA, CH_2Cl_2 , 23 °C, 18 h;

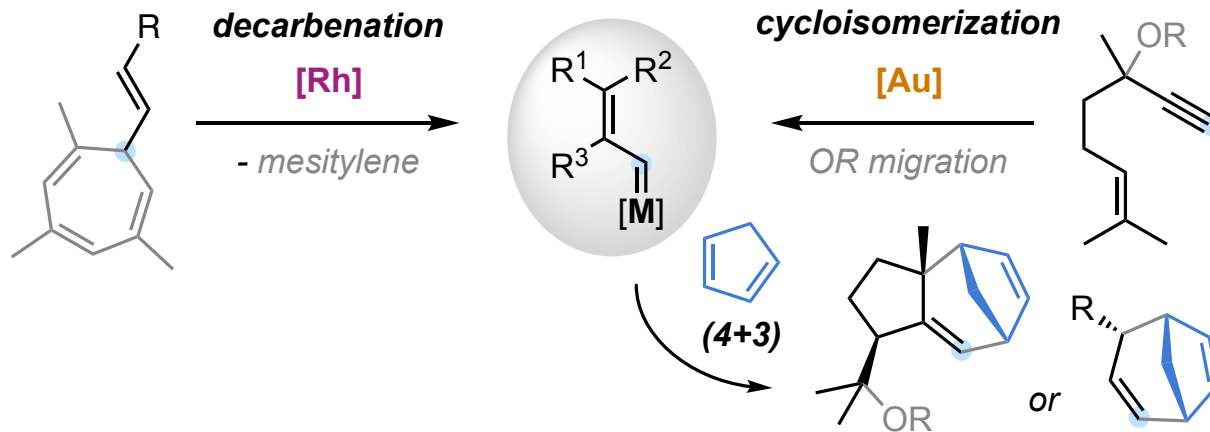
 iii: methyl acrylate, Grubbs 2nd, CuI , Et_2O , 40 °C, 3 h; iv: HBpin, LiHMDS, toluene, 100 °C, 48 h



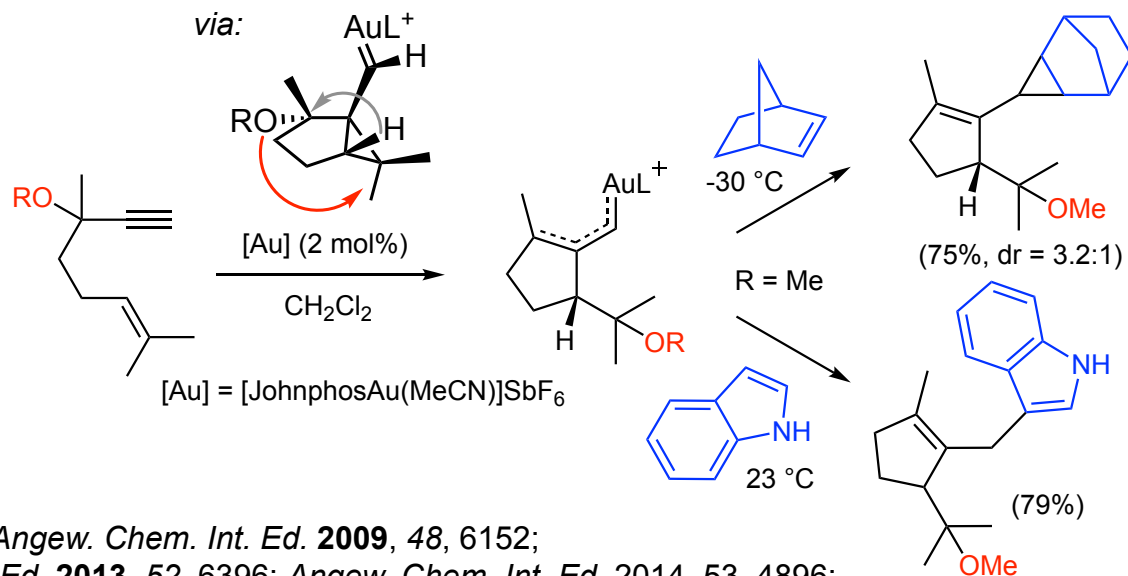
Three-Component Gold(I)-Catalyzed Alkoxyvinylation



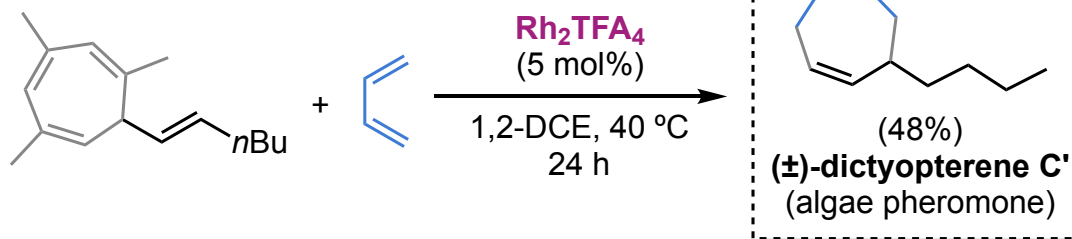
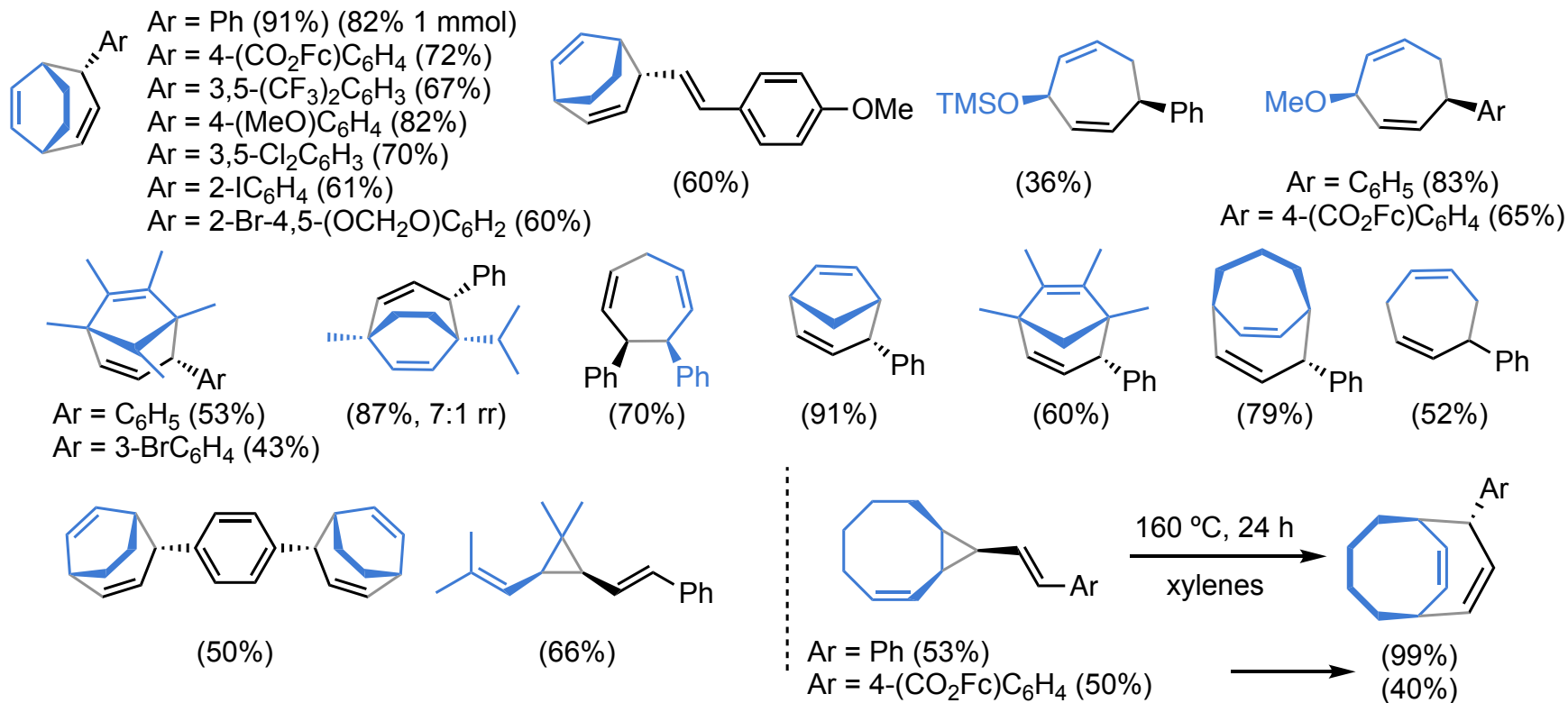
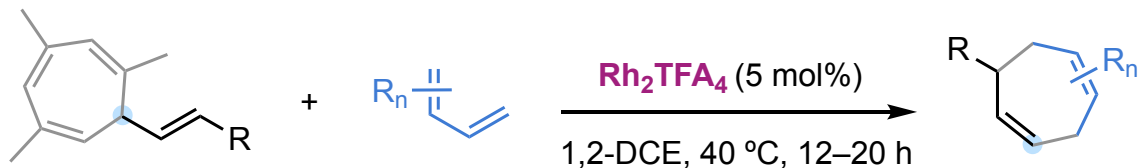
(4+3) Cycloaddition of Metal Carbenes from Cycloheptatrienes or Enynes

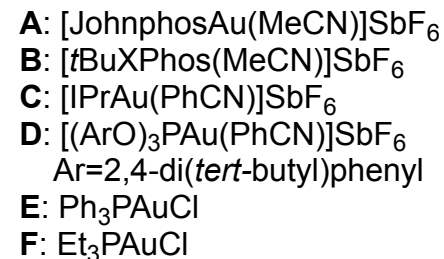
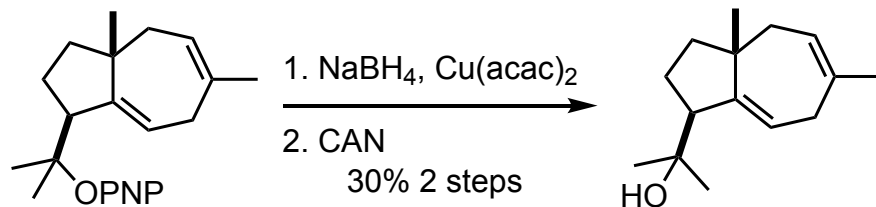
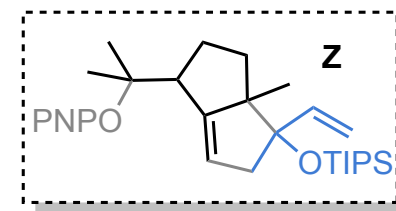
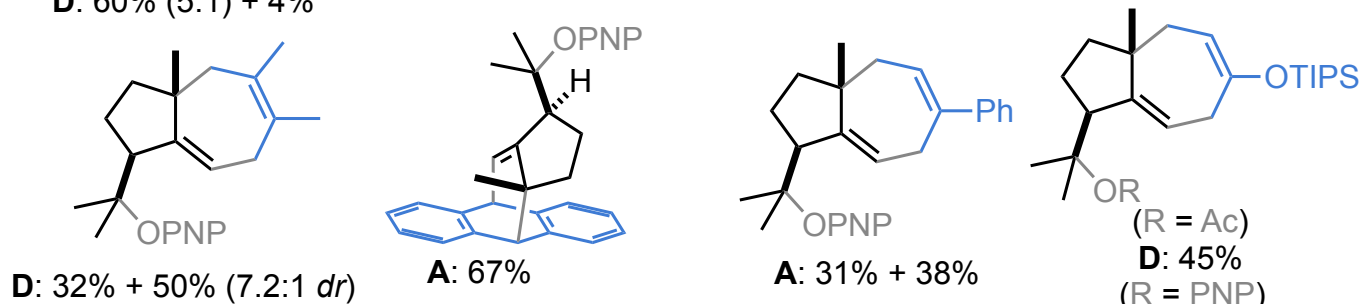
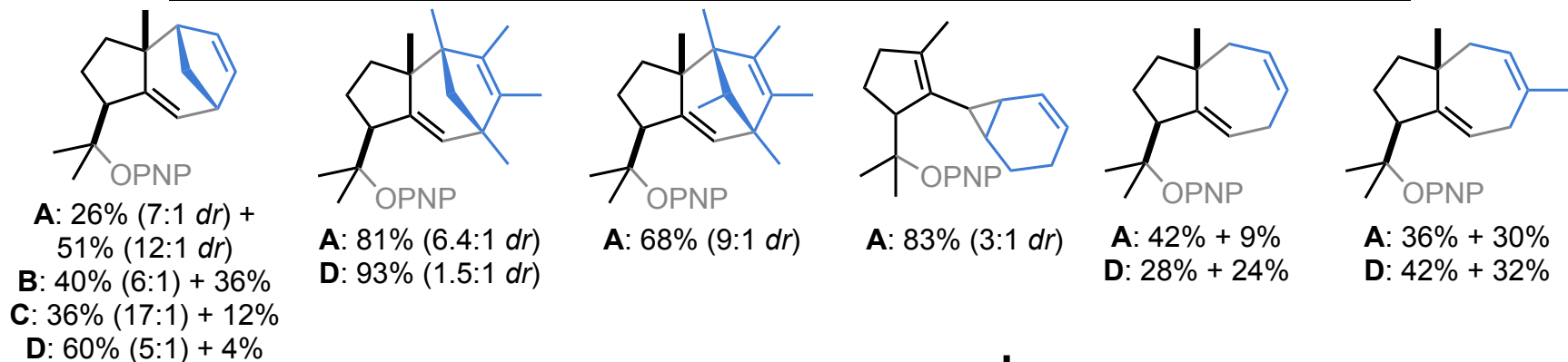
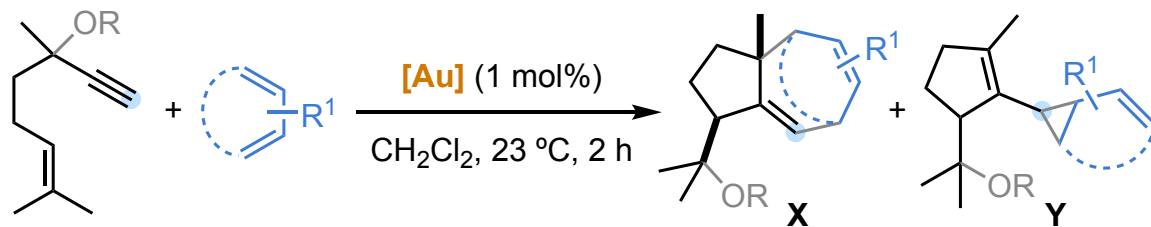


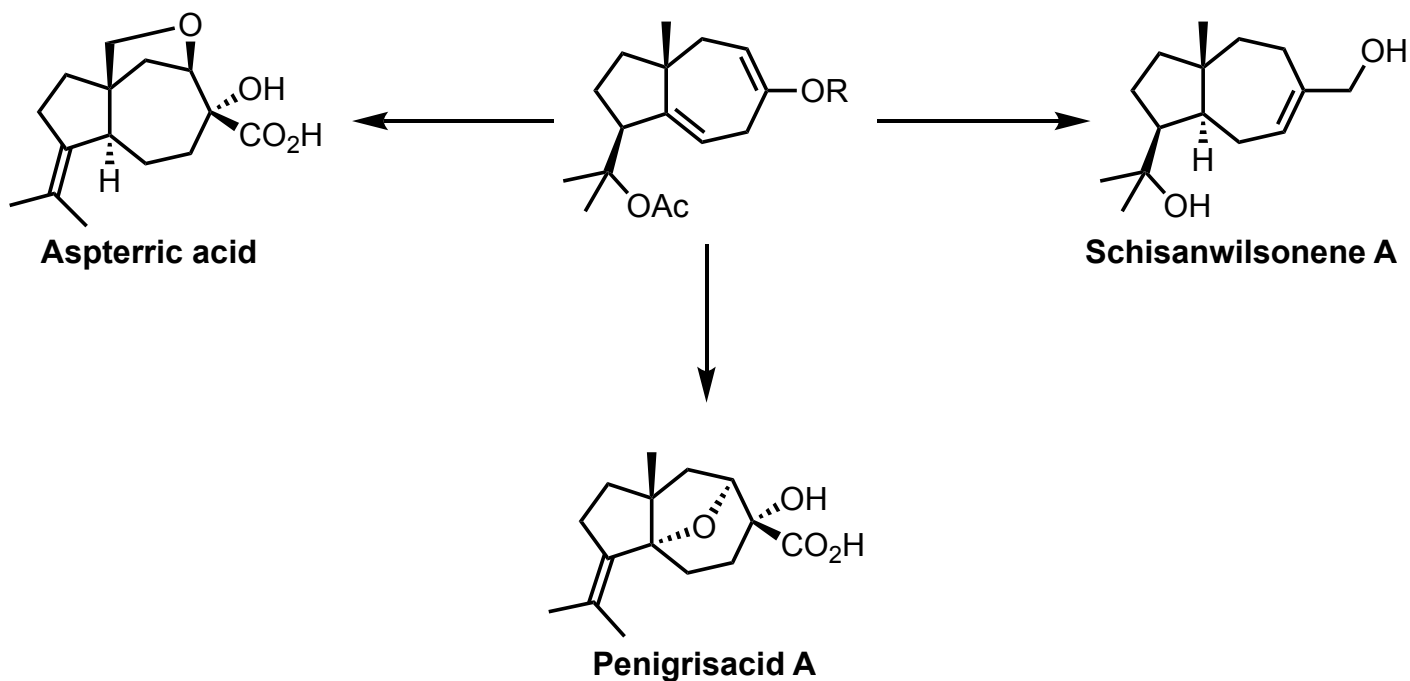
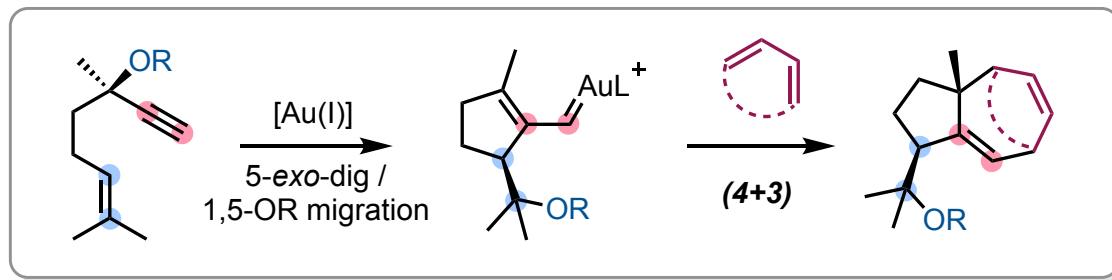
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1,5-OR Migration: *Angew. Chem. Int. Ed.* **2009**, *48*, 6152;
Angew. Chem. Int. Ed. **2013**, *52*, 6396; *Angew. Chem. Int. Ed.* **2014**, *53*, 4896;
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Aspterric acid: Tsuda, Kaneda, Tada, Nitta, Yamamoto, Iitaka, *Chem. Comm.* **1978**, 160

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