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Wipf Group
Current literature 17 Feb 2018

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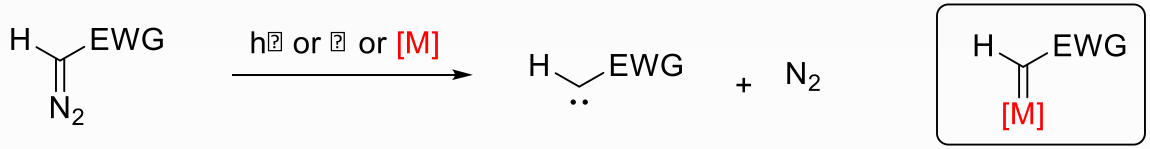
J. Org. Chem., **2018**, *83*, 1026-1032

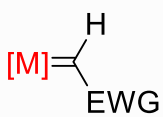
Ru(II)-Catalyzed Cross-Coupling of Cyclopropenes with Diazo Compounds: Formation of Olefins from Two Different Carbene Precursors

Metal Carbenoid

- **Decomposition of diazo compounds** is one of the more common ways to generate carbene due to functional groups versatility

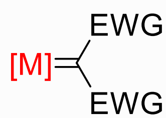


- **Classification of metal carbenoids**



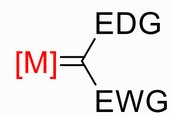
Acceptor

EWG = CO_2R, COR, $CONR_2$, NO_2, SO_2R



Acceptor/Acceptor

EWG = CO_2R, COR, $CONR_2$, NO_2, SO_2R, CN, CF_3

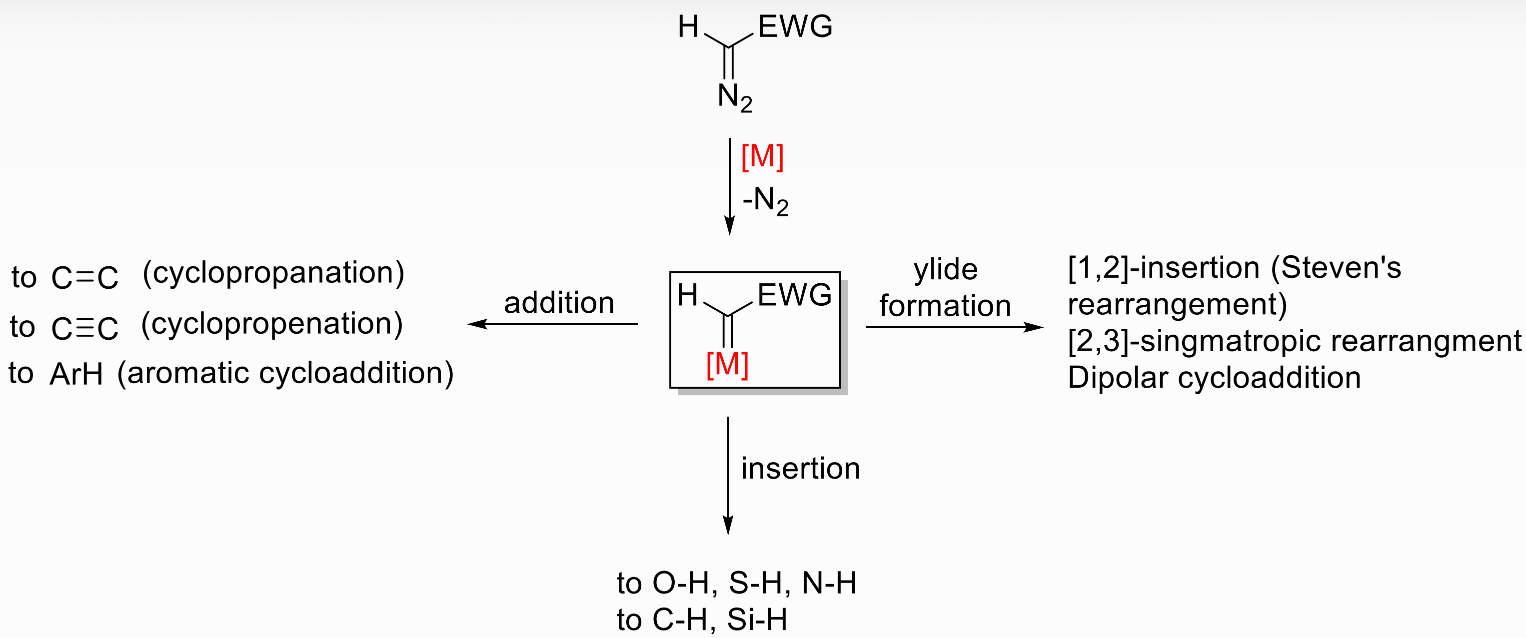


Donor/Acceptor

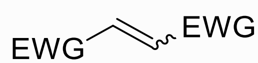
EWG = CO_2R, COR, CN, CF_3
EDG = vinyl, alkynyl, aryl, heteroaryl

Chem. Rev., **2003**, *103*, 2861−2903

Metal Carbenoid Reactions



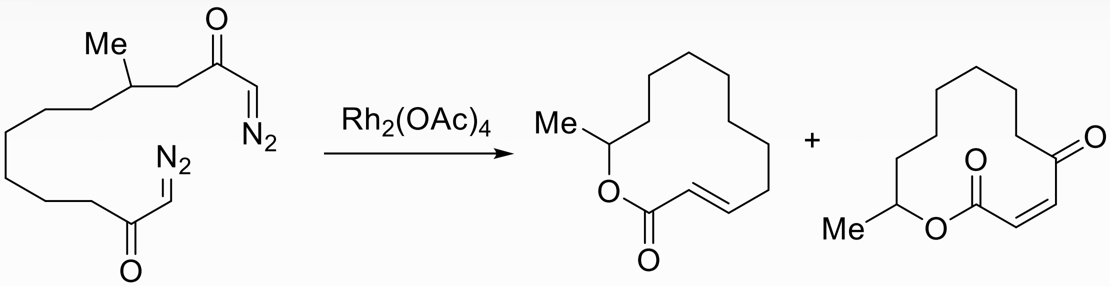
Competing side reaction: carbene dimerization!



Chem. Rev. **1998**, *98*, 911−935

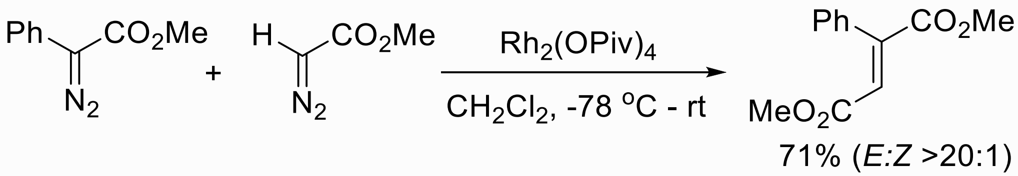
Useful Synthetic Tool: Chemoselective Carbene Dimerization

- ***Intramolecular***



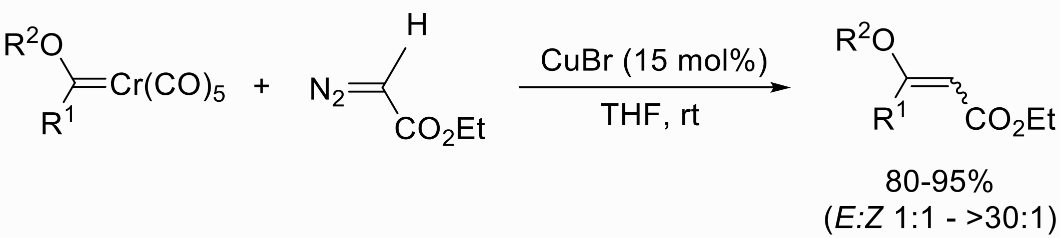
Doyle, *Org. Lett.*, **2000**, *2*, 1777-1779
Similar work: Che[1], Ru(II)-porphyrin cat. *Z*-selective

- ***Intermolecular***



Davies, *Angew. Chem. Int. Ed*. **2011**, *50*, 2544 –2548
Similar work: Sun[2,3], Au(I) and Cu(II) cat. *Z*-selective

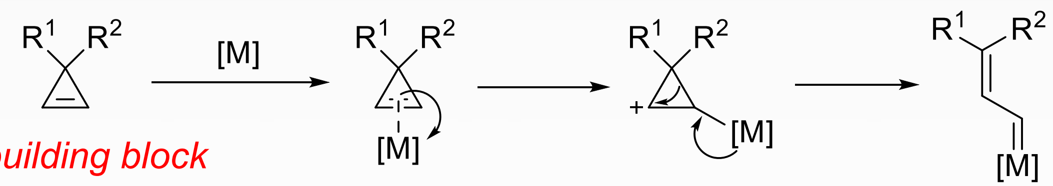
- ***Intermolecular: different carbene precursors***



Barluenga, *Angew. Chem. Int. Ed*. **2001**, *40*, 3392 –3394
Similar work: Wang[4], difluorocarbene with diazo compound

1. *Org. Lett.*, **2004**, *6*, 1621-1623
2. *Angew. Chem. Int. Ed*. **2014**, *53*, 11070-11074
3. *Org. Lett.*, **2015**, *17*, 4244-4247
4. *Angew. Chem. Int. Ed*. **2016**, *55*, 273-277

Cyclopropene: Vinyl Metal Carbene Precursor

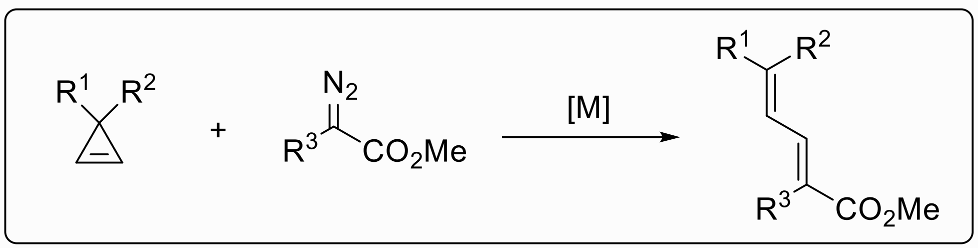


Excellent 3-carbon building block

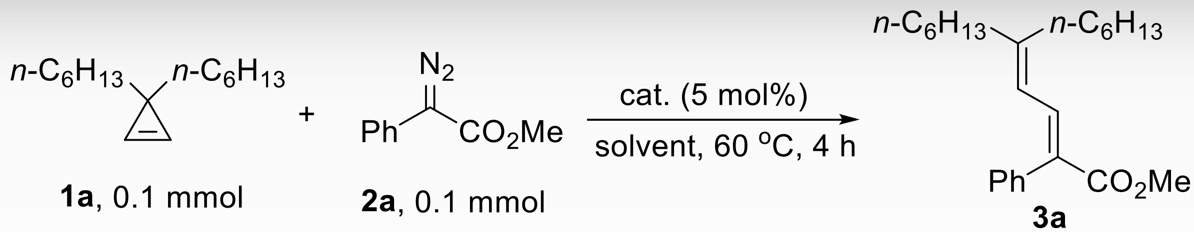
can underdo typical carbene transformations

Angew. Chem. Int. Ed. **2016**, *55*, 9134 –9166

This work:



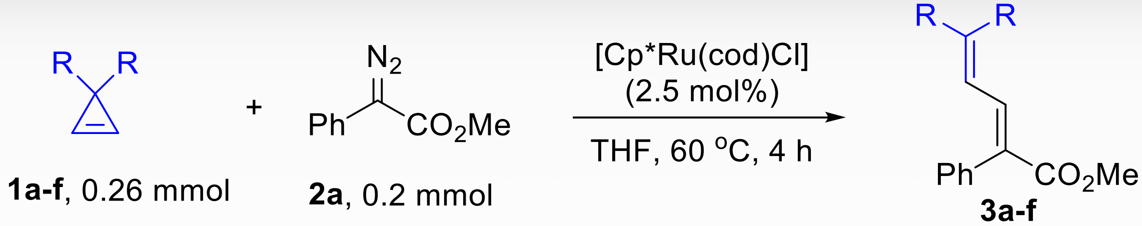
Optimization of Reaction Conditions

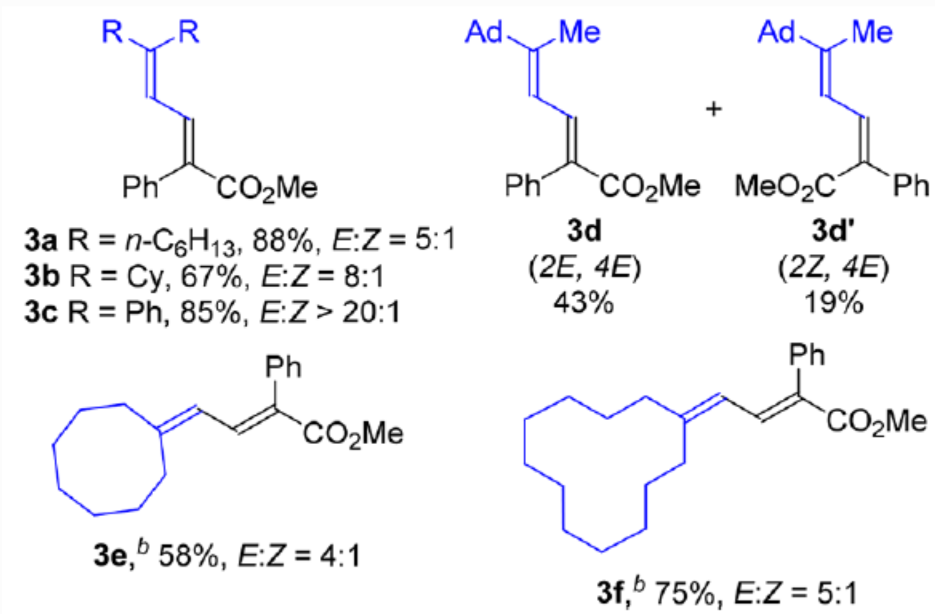


entry	solvent	1a/2a	cat.	yield[a] (%)	E/Z[b]
1	MeCN	1:1	CuI	10	nd[c]
2	MeCN	1:1	AuCl	19	nd
3[d]	MeCN	1:1	$AuPPh_3Cl$	21	nd
4	PhMe	1:1	$[Rh(cod)Cl]_2$	12	nd
5	PhMe	1:1	$[RuCl_2(p\text{-cymene})]_2$	43	3:1
6	PhMe	1:1	$Ru(PPh_3)_3Cl_2$	19	4:1
7	PhMe	1:1	$CpRu(PPh_3)_2Cl$	21	10:1
8	PhMe	1:1	$[RuCl_2(benzene)]_2$	37	2.5:1
9	PhMe	1:1	[Cp*Ru(cod)Cl]	72	3:1
10[e]	THF	1.3:1	[Cp*Ru(cod)Cl]	98 (88[f])	5:1
11[g]	THF	1.3:1	none	0	

[a]NMR yield. [b]Determined by ^{1}H NMR (400 MHz). [c]nd: not determined. [d]5 mol % of AgOTf was used. [e]2.5 mol % of catalyst was used. [f]Isolated yield. [g]The substrates remained unchanged.

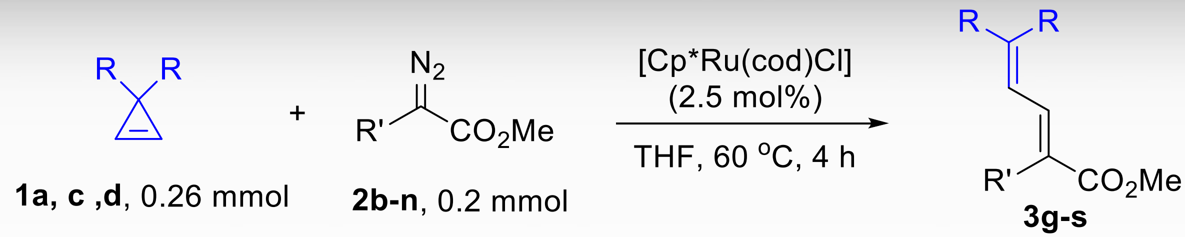
Scope of Cyclopropenes

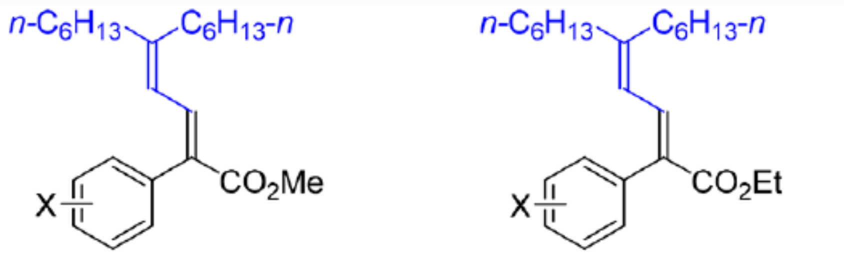




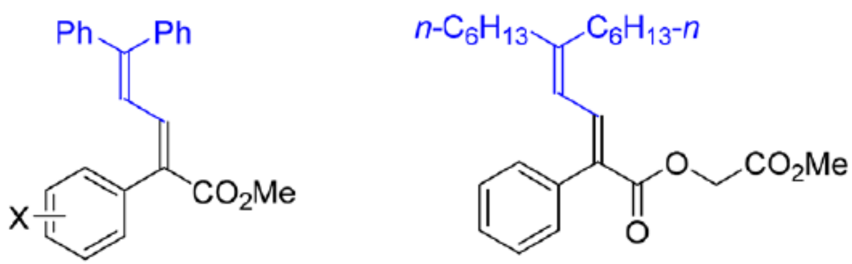
[a]Reaction conditions: **1a–f** (0.26 mmol), **2a** (0.20 mmol), and [Cp*Ru(cod)Cl] (2.5 mol %) in THF (1.0 mL) at 60 °C. All of the yields refer to the isolated products by column chromatography. The ratio of *E*/*Z* was determined by ^{1}H NMR (400 MHz). [b]The reaction time was 12 h, and 1.5 equiv of cyclopropene was used.

Scope of Diazo Precursors

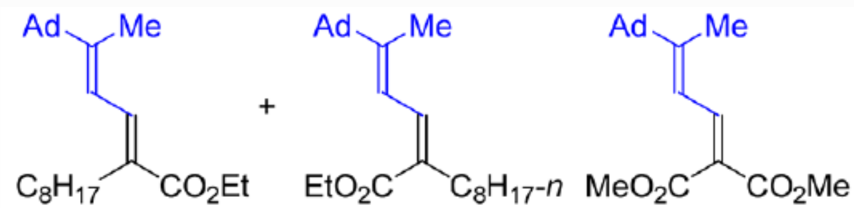




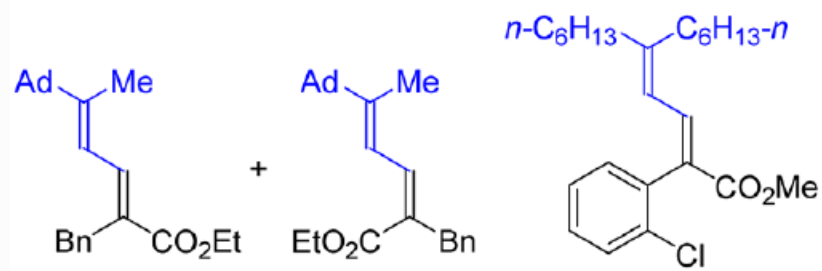
3g, X = 4-OMe, 76%, *E*:*Z* = 3:1
3h, X = 4-Ph, 85%, *E*:*Z* = 4:1
3i, X = 4-Cl, 86%, *E*:*Z* = 5:1[b]
3j, X = 4-Br, 97%, *E*:*Z* = 7:1
3k, X = 2-F, 58%, *E*:*Z* >20:1[b,c]
3l, X = 4-CO_2Me, 67%, *E*:*Z* = 6:1
3m, X = 4-NO_2, 47%, *E*:*Z* = 10:1



3n, X = 4-Me, 87%, *E*:*Z* >20:1
3o, X = 4-CF_3, 71%, *E*:*Z* >20:1
3p, 80%, *E*:*Z* = 3:1

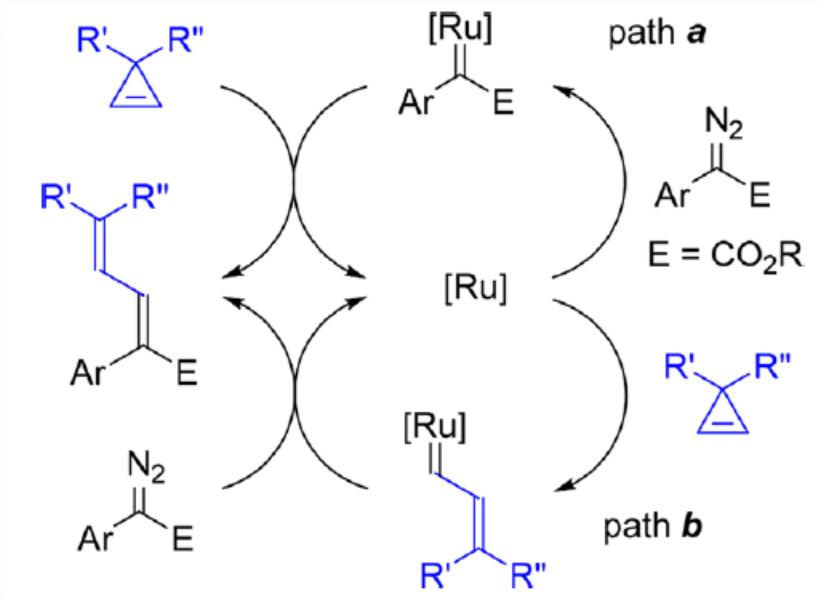


3q, 54%[d]   **3q'**, 27%[d,e]   **3r**, 82%[f]



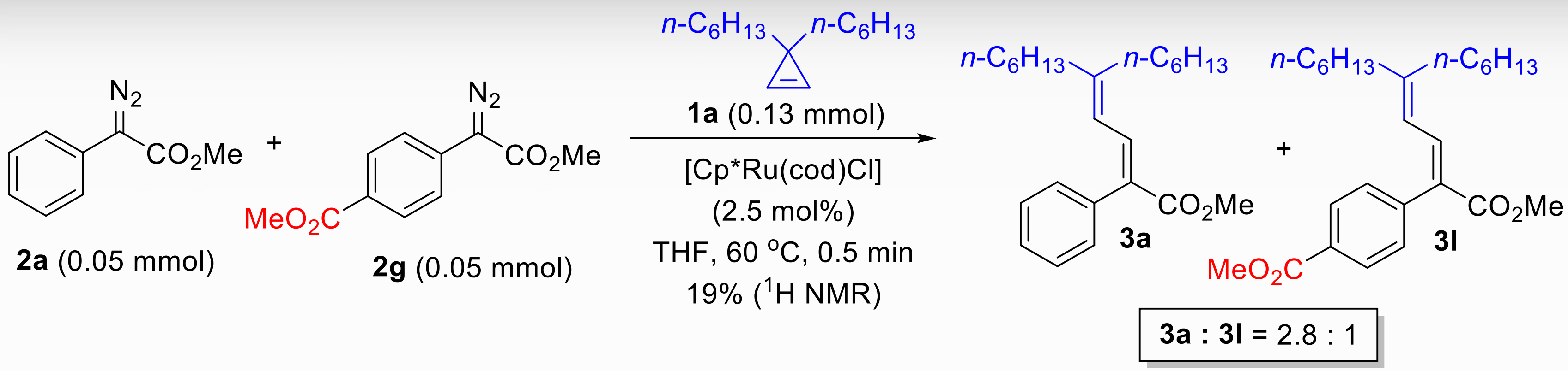
3s, 50%[d]   **3s'**, 25%[d,e]   **3t**, 0%

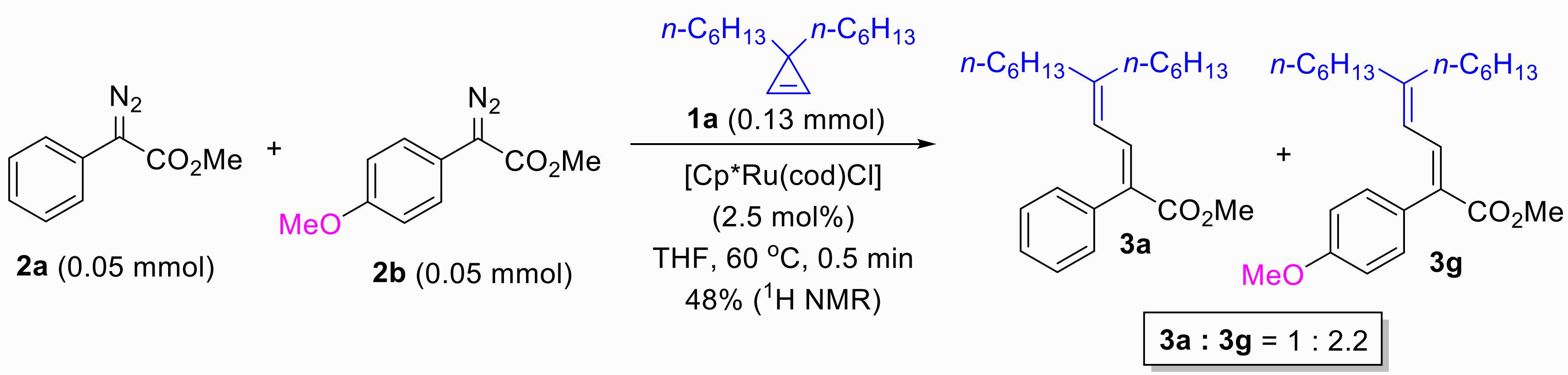
Proposed Reaction Pathways



Which substrate reacts with Ru cat. first?

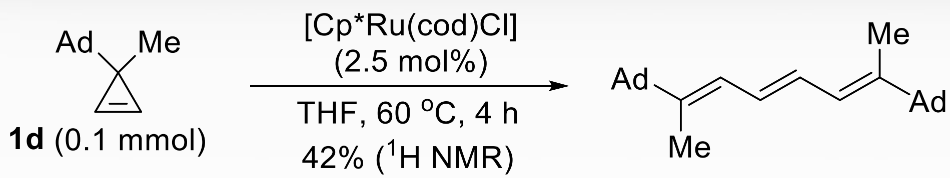
Competition Experiments of the Diazo Compounds

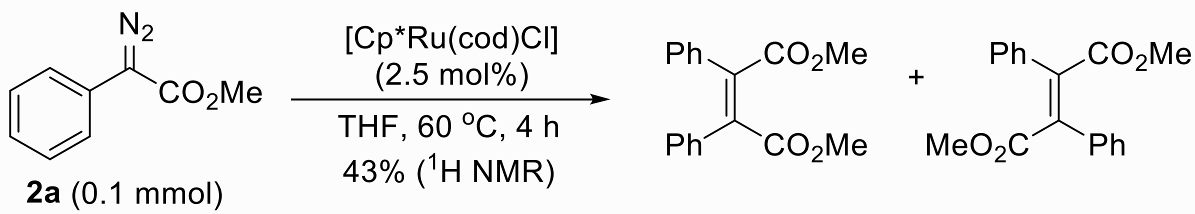




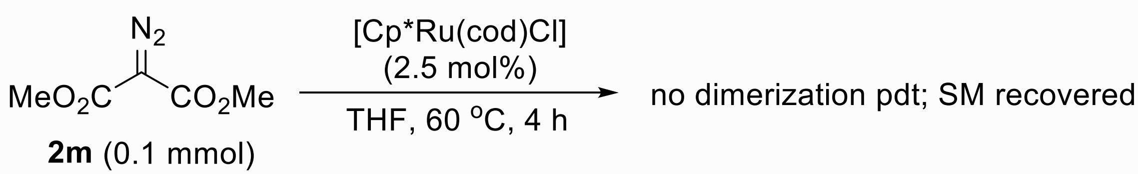
Diazo compound bearing EDG is more reactive
= diazo compound likely functions as ***nucleophile***

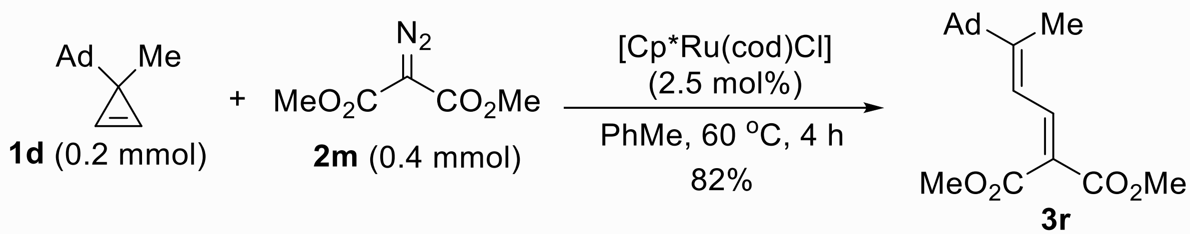
Control Experiments





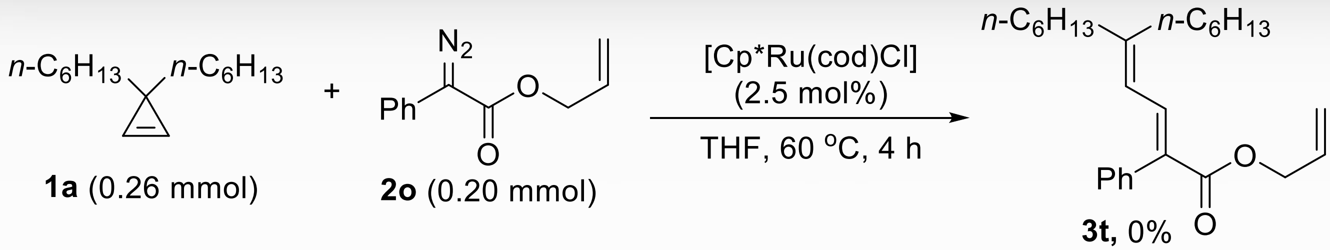
Rate of formation of Ru(II) carbene from cyclopropane or diazo compound is similar

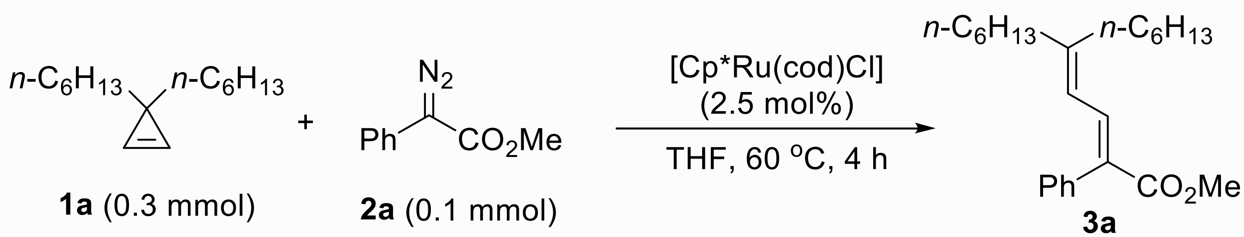


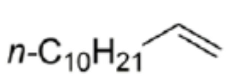


Cyclopropene reacts first with Ru(II) cat.

Effects of Alkenyl Substituents

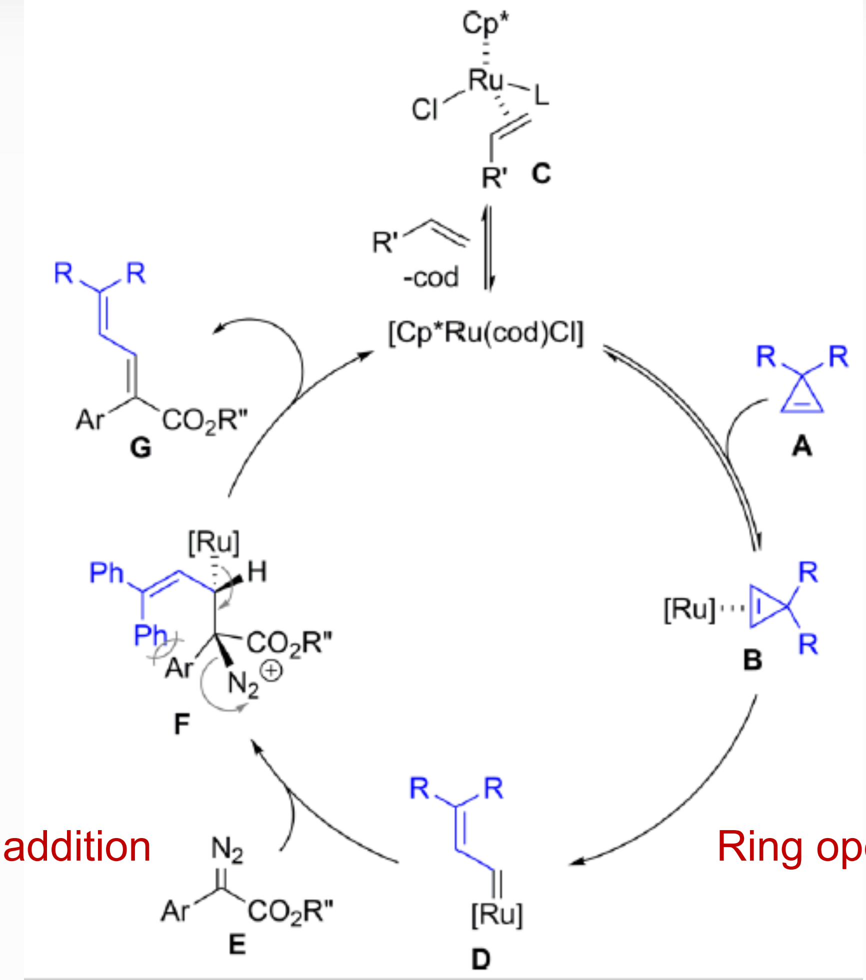




additive (0.13 mmol)	reaction time	yield of **3a**
none	2 min	60%
	4 h	80%
	2 min	37%
	4 h	70%
	2 min	Not determined
	4 h	0%

Alkenyl substituent coordinates with Ru(II) cat., preventing interaction of substrates with the cat.

Proposed Catalytic Cycle



coordination

Ring opening

Nucleophilic addition

Conclusions

- First report of cyclopropene as metal-catalyzed carbene dimerization precursor
- Highly selective substrates – homocoupling not observed
- New addition to the synthetic toolkit to construct C=C bond

Future extensions:

- Improve E/Z selectivity & stereoselectivity
- EWG substituents on cyclopropene
- Narrow substrate scope – limit utility of method