北京大学
PEKING UNIVERSITY
School of Chemical Biology&Biotechnology
化学生物学与生物技术学院

Palladium-Catalyzed Oxidative Carbocyclizations

Superior: Prof. Yong Huang

Reporter: Yan Fang

Oct. 15th 2012

Contents

Contents

Background:

➢ Carbocyclizations

Annulation process
involving carbon-carbon bond formation via carbometalation.

Usually **promoted by transition metals** or their complexes, not by typical elements.

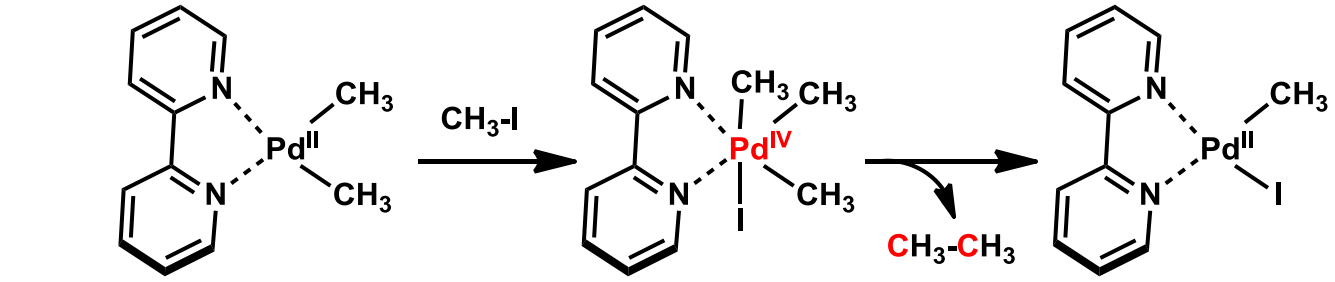
Cobalt, Iro [illegible] conium

Pd^0,Pd^{II}, and Pd^{IV}

Ojima, M. Tzamarioudaki, Z. Li, R. J. Donovan, *Chem. Rev.***1996**, *96*, 635.
D. C. Powers, T. Ritter, *Acc. Chem. Res.***2012**, *45*, 840.

Background:

➢ Pd^{II}/Pd^{IV} Catalytic Cycle



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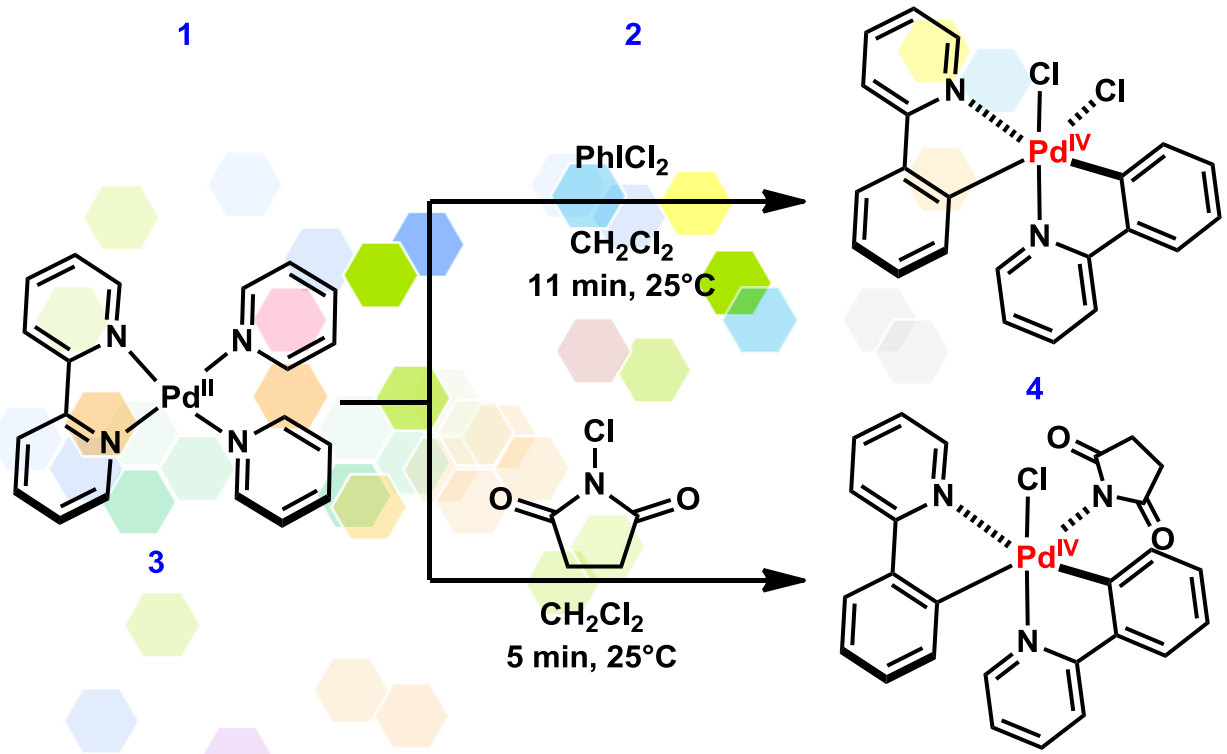
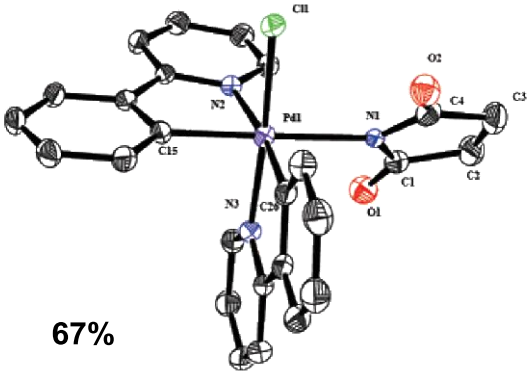


3 4 5

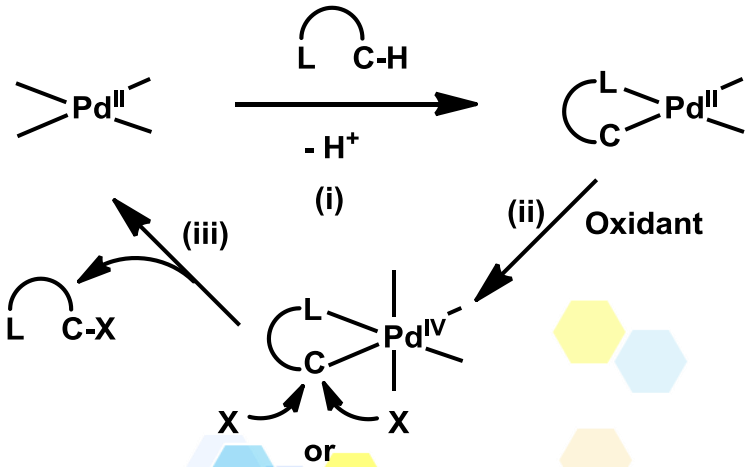


5

K. MuÇiz, *Angew. Chem. Int. Ed.* **2009**, *48*, 9412.
Salena R. Whitfield and Melanie S. Sanford, *J. Am. Chem. Soc.* **2007**, *129*, 15142.

Background:

➢ Pd^{II}/Pd^{IV}Catalytic Cycle



Allison R. Dick, Kami L. Hull, Melanie S. Sanford, *J. Am. Chem. Soc.* **2004**, *126*, 2300.

➢Oxidants for a Pd^{II}/Pd^{0} Catalytic Cycle

Ag^{I}, Cu^{II}, TBHP, BQ, O_2

➢Oxidantsfor a Pd^{II}/Pd^{IV} Catalytic Cycle

$PhI(OAc)_2$, $PhI(O_2CCF_3)_2$, $PhI(O_2CtBu)_2$, H_2O_2

Youqian Deng, Andreas K. A. Persson, Jan-E. Backvall, *Chem. Eur. J.* **2012**, *18*, 11498.

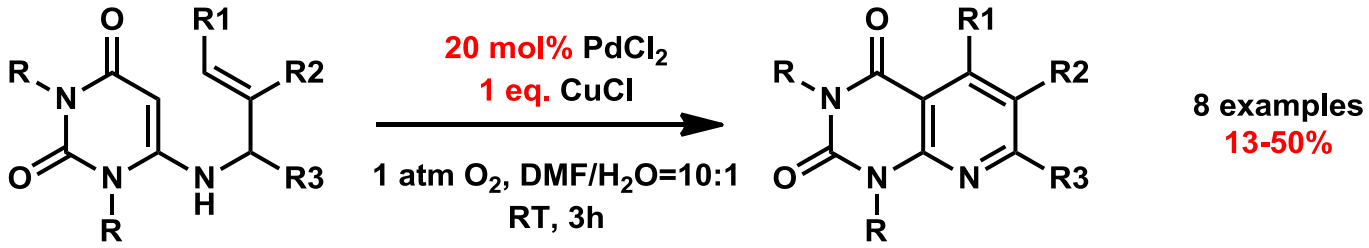
Contents

Contents

- Carbocyclization via a Pd^{II}/Pd^{0} Catalytic Cycle
  - alkenes involving β-H elimination
  - arene–alkenes
  - allenynes
  - enynes
  - others

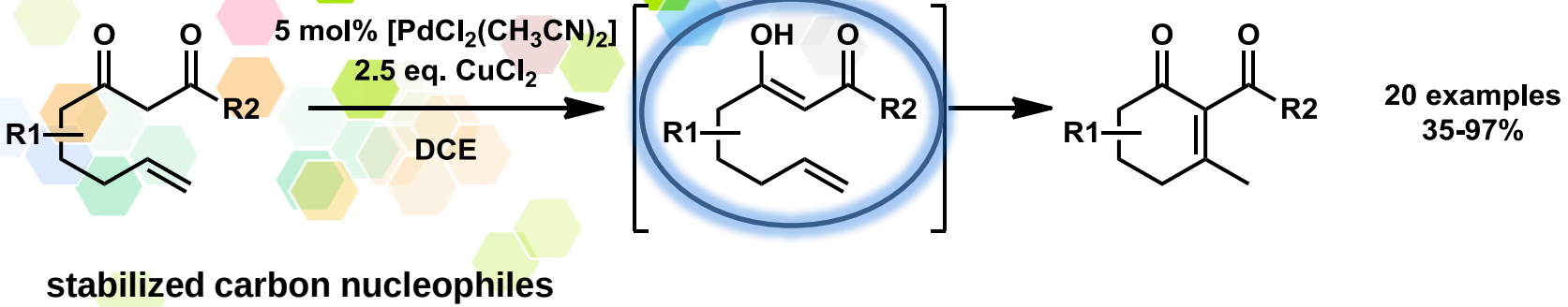
Carbocyclization via a Pd ^{II}/Pd ^{0} Catalytic Cycle（1）

➢diones



T. Itoh, T. Imini, H. Ogura, N. Kawahara, T. Nakajima, K. A. Watanabe, *Chem. Pharm. Bull.* **1985**, *33*, 1375.

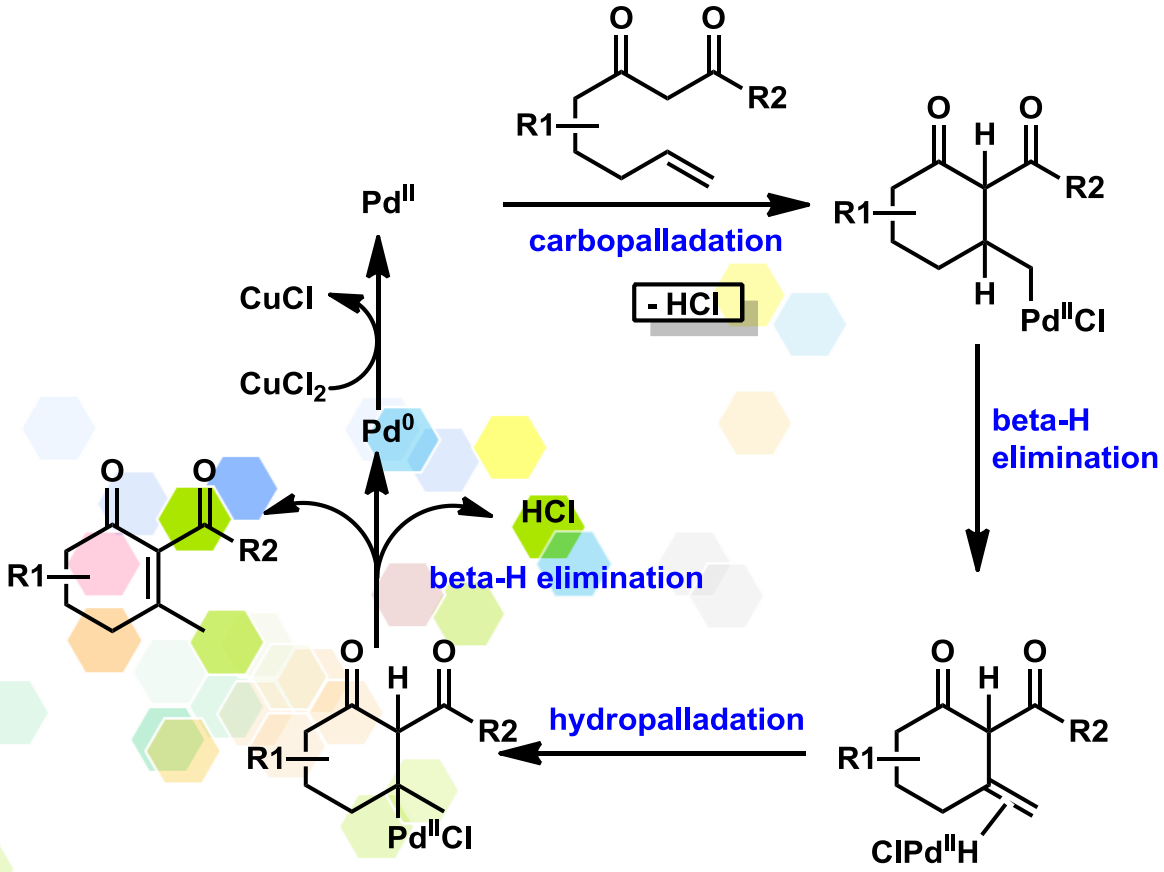
➢unactivated olefins



T. Pei, X. Wang, R. A. Widenhoefer, *J. Am. Chem. Soc.* **2003**, *125*, 648.
C. Liu, X. Wang, T. Pei, R. A. Widenhoefer, *Chem. Eur. J.* **2004**, *10*, 6343.

Carbocyclization via a Pd ^{II}/Pd ^{0} Catalytic Cycle（1）

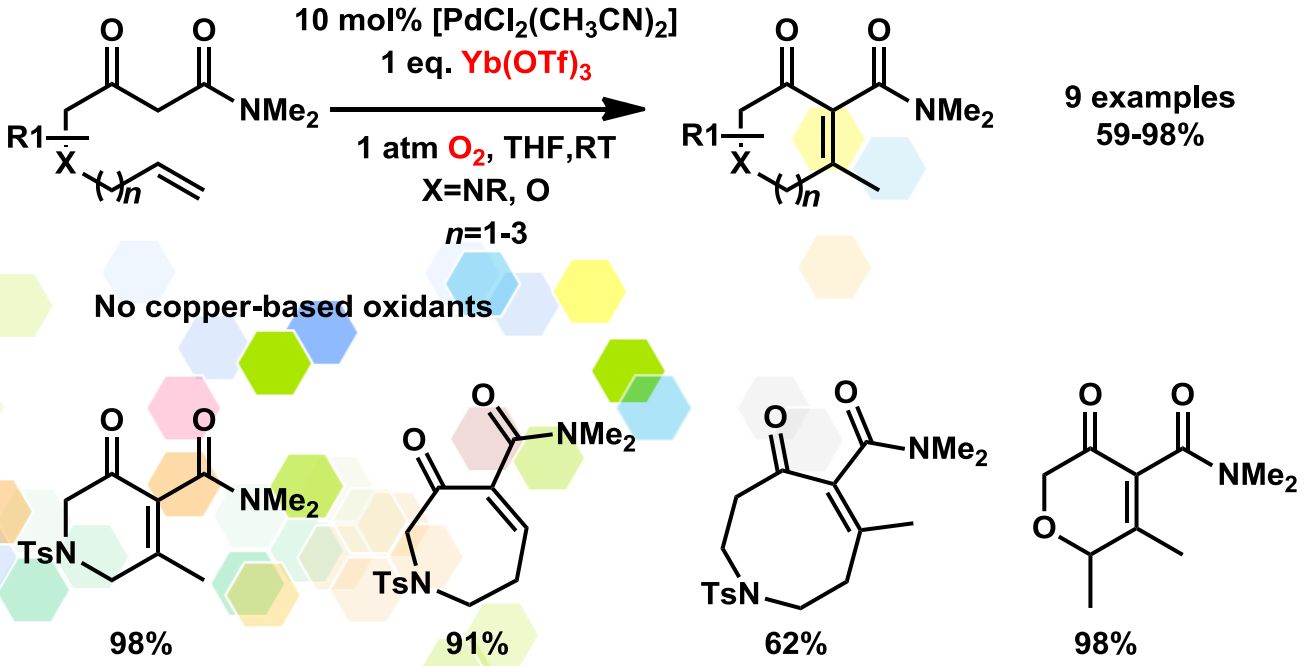
➢**unactivated olefins**



T. Pei, X. Wang, R. A. Widenhoefer, *J. Am. Chem. Soc.* **2003**, *125*, 648.
C. Liu, X. Wang, T. Pei, R. A. Widenhoefer, *Chem. Eur. J.* **2004**, *10*, 6343.

Carbocyclization via a Pd ^{II}/Pd ^{0} Catalytic Cycle（1）

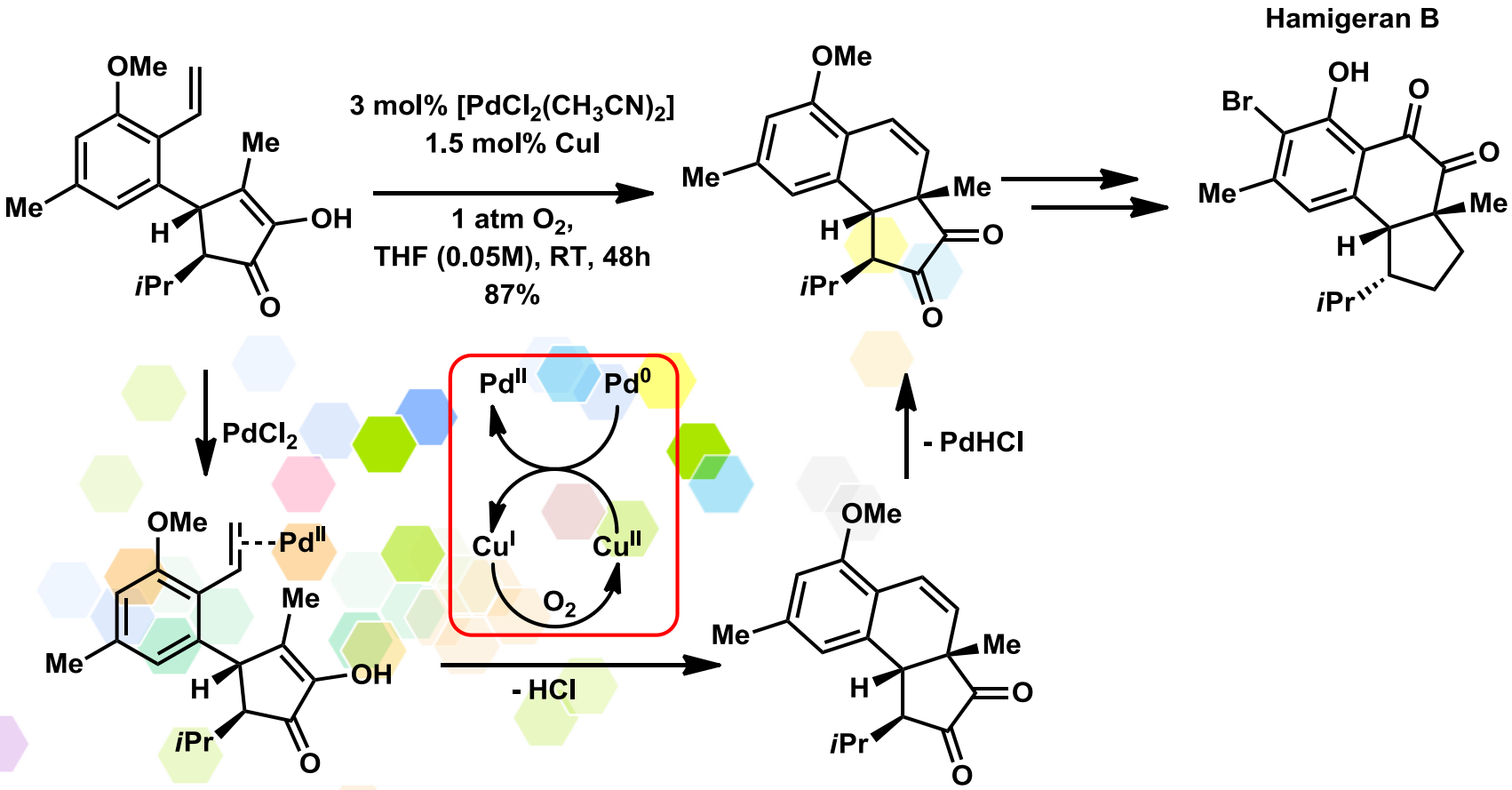
➢γ-heteroalkenyl β-ketoamides



K.-T. Yip, J.-H. Li, O.-Y. Lee, D. Yang, *Org. Lett.* **2005**, *7* , 5717.

Carbocyclization via a Pd ^{II}/Pd ^{0} Catalytic Cycle（1）

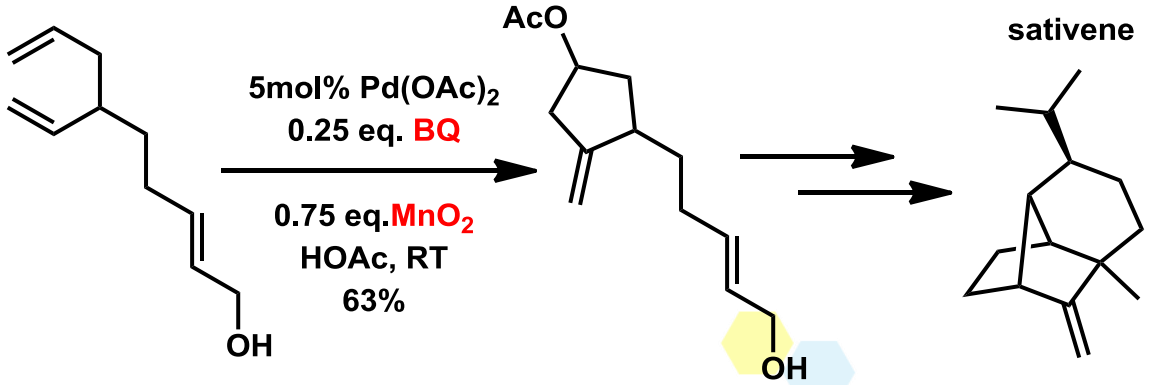
➢α-hydroxyenone



Z. Cai, M. Harmata, *Org. Lett.* **2010**, *12*, 5668.

Carbocyclization via a Pd ^{II}/Pd ^{0} Catalytic Cycle（1）

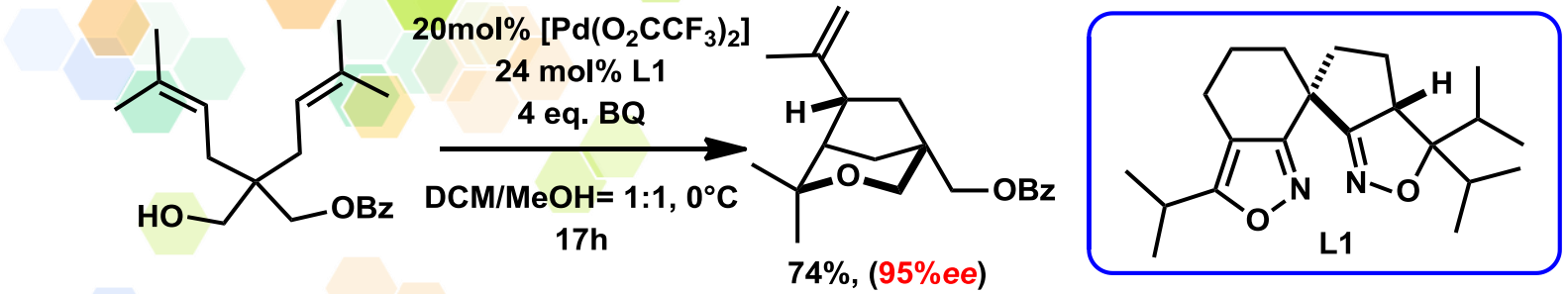
➢dienes



an oxypalladation–insertion sequence

T. Antonsson, C. Moberg, L. Tottie, *J. Org. Chem.* **1989**, *54*, 4914.
T. Antonsson, C. Malmberg, C. Moberg, *Tetrahedron Lett.* **1988**, *29*, 5973.
C. Moberg, K. Nordst ɑrm, P. Helquist, *Synthesis* **1992,** 685.

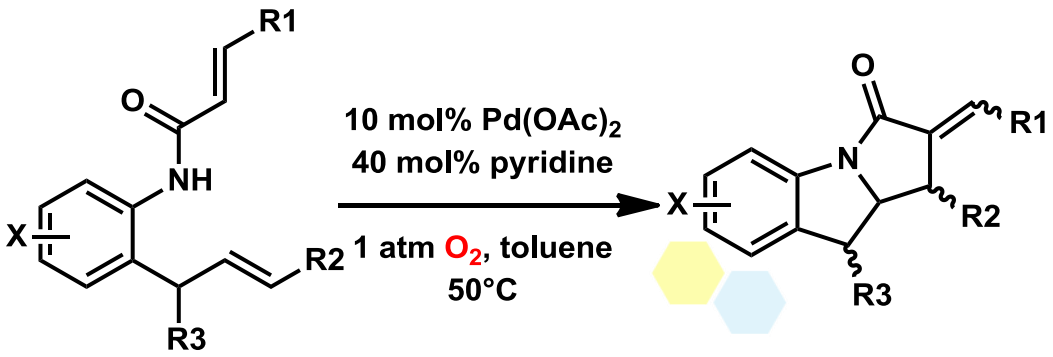
➢dienes in an enantioselective manner



M. A. Arai, M. Kuraishi, T. Arai, H. Sasai, *J. Am. Chem. Soc.* **2001**, *123* , 2907.
P. S. Koranne, T. Tsujihara, M. A. Arai, G. B. Baj-racharya, T. Suzuki, K. Onitsuka, H. Sasai, *Tetrahedron : Asymmetry* **2007**, *18*, 919.

Carbocyclization via a Pd ^{II}/Pd ^{0} Catalytic Cycle（1）

➢**olefin-substituted anilides**



initiated through amidopalladation

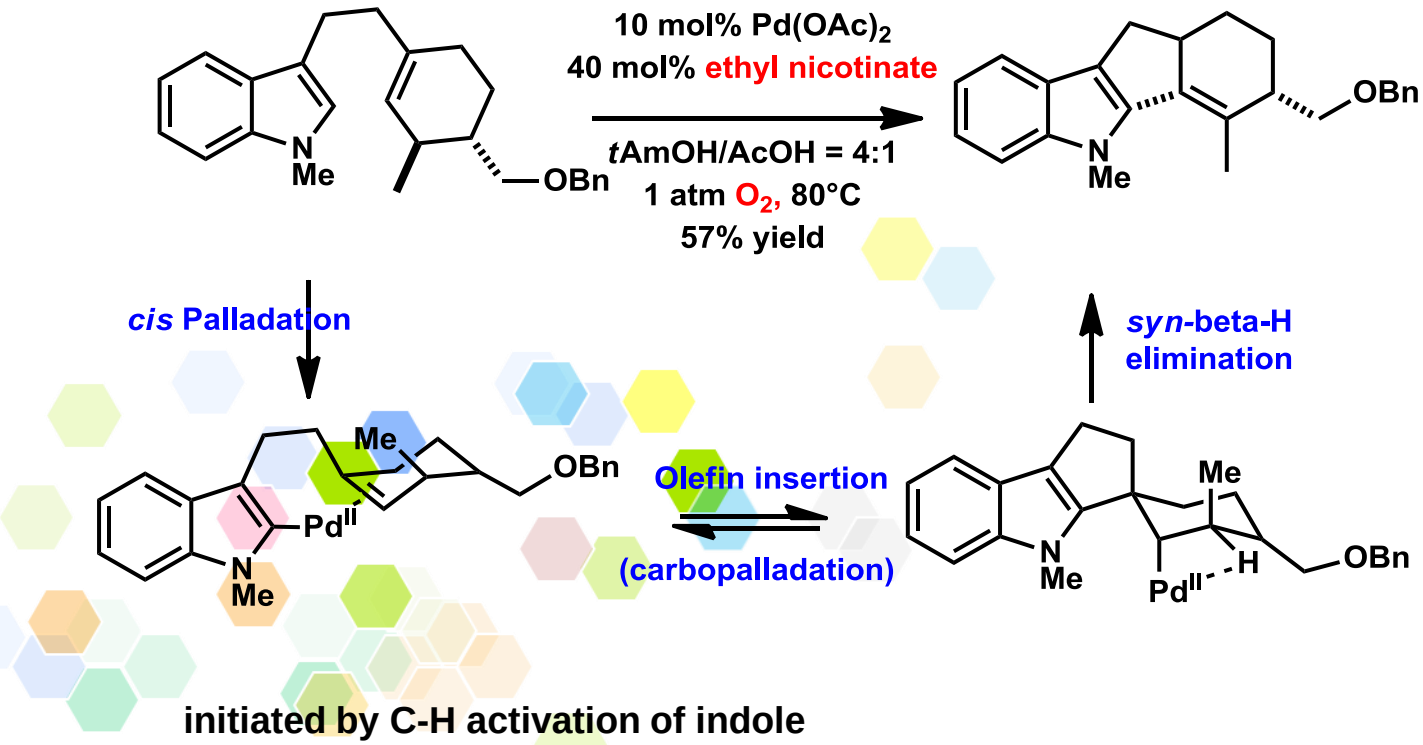
an enantioselective version with a chiral counterpart

an environmentally benign terminal oxidant

K.-T. Yip, M. Yang, K.-L. Law, N.-Y. Zhu, D. Yang, *J. Am. Chem. Soc*. **2006**, *128* , 3130.
K.-T. Yip, N.-Y. Zhu, D. Yang, *Org. Lett*. **2009**, *11*, 1911.
W. He, K.-T. Yip, N.-Y. Zhu, D. Yang, *Org. Lett*. **2009**, *11*, 5626.

Carbocyclization via a Pd ^{II}/Pd ^{0} Catalytic Cycle（2）

➢Carbocyclization of arene–alkenes

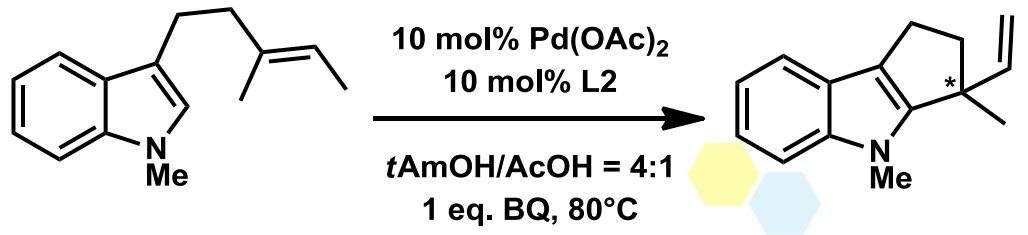


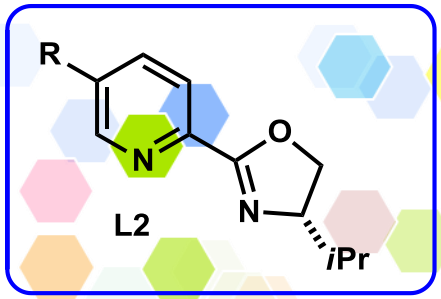
initiated by C-H activation of indole

E. M. Ferreira, B. M. Stoltz, J. *Am. Chem. Soc.* **2003**, *125* , 9578.
E. M. Ferreira, H. Zhang, B. M. Stoltz, *Tetrahedron* **2008**, *64*, 5987.
P. A. Donets, E. V. Van der Eycken, *Synthesis* **2011**, 2147.

Carbocyclization via a Pd ^{II}/Pd ^{0} Catalytic Cycle（2）

➢**an enantioselective oxidative carbocyclization of indoles**



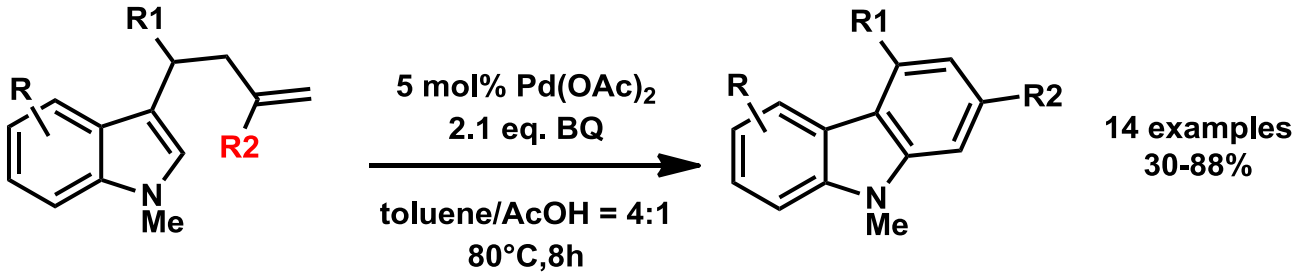


R	Yield(%)	ee(%)
H	39	43
CO_2Et	59	32

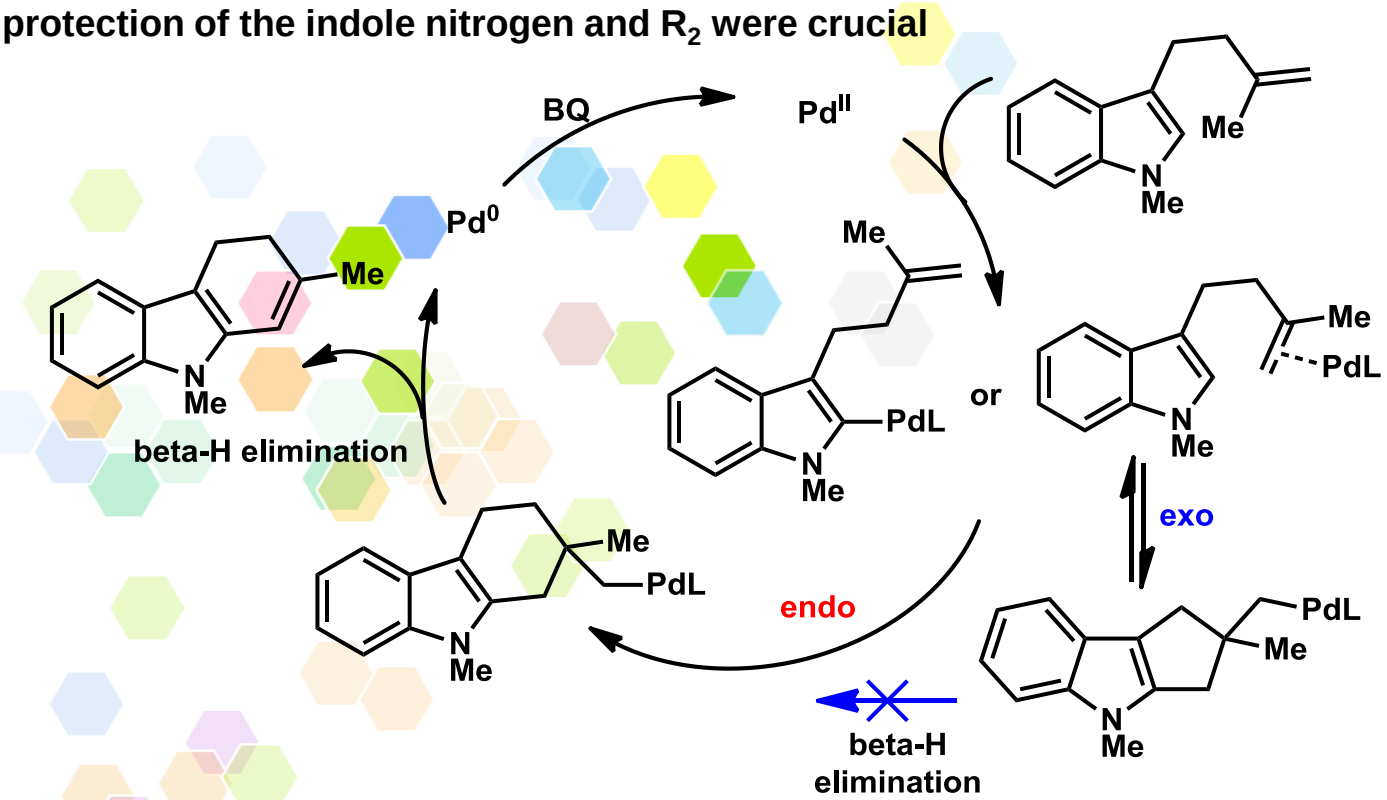
J. A. Schiffner, A. B. Machotta, M. Oestreich, *Synlett* **2008**, 2271.
J. A. Schiffner, T. H. W çste, M. Oestreich, *Eur. J. Org. Chem.* **2010,** *75*, 174.

Carbocyclization via a Pd ^{II}/Pd ^{0} Catalytic Cycle（2）

➢**indoles**



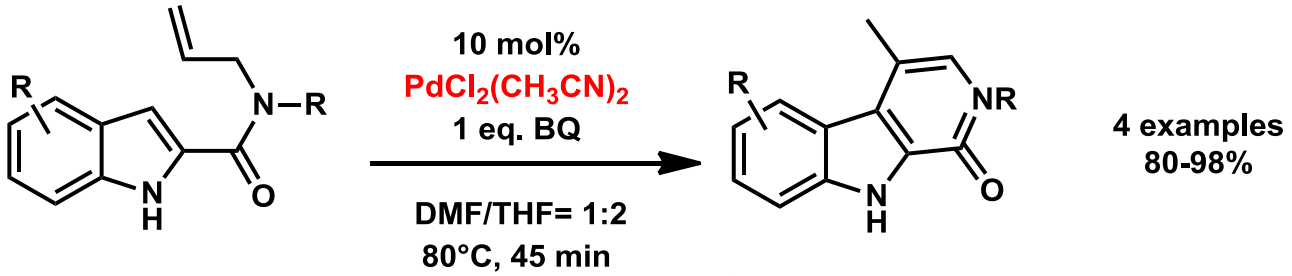
protection of the indole nitrogen and R_2 were crucial



A. Kong, X. Han, X. Lu, *Org. Lett.* **2006**, *8*, 1339.

Carbocyclization via a Pd ^{II}/Pd ^{0} Catalytic Cycle（2）

➢indolecarboxamide

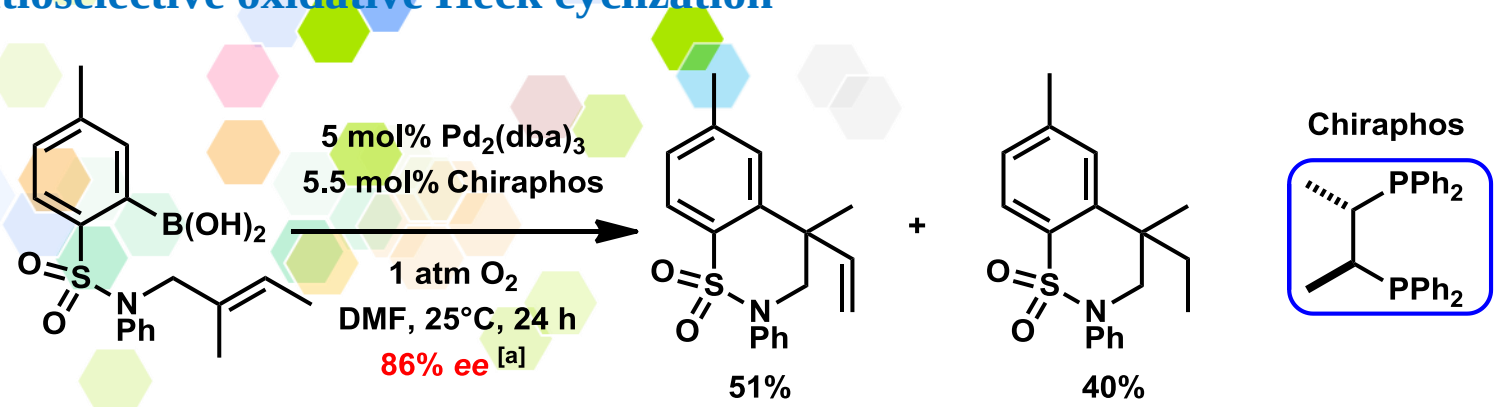


4 examples
80-98%

No need to protect of the indole nitrogen

G. Abbiati, E. M. Beccalli, G. Broggini, C. Zoni, *J. Org. Chem.* **2003**, *68*, 7625.

➢enantioselective oxidative Heck cyclization



[a] The ee value was determined after Pd/C hydrogenation of the two products.

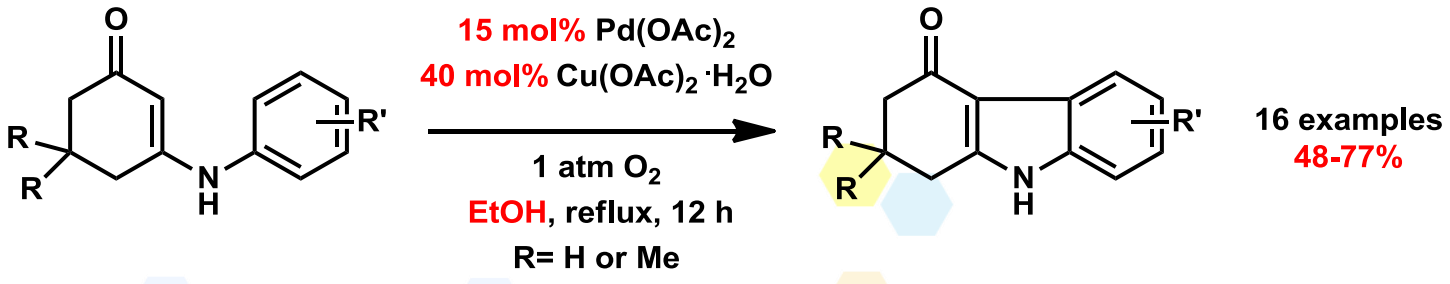
Poor selectivity and limited substrate scope

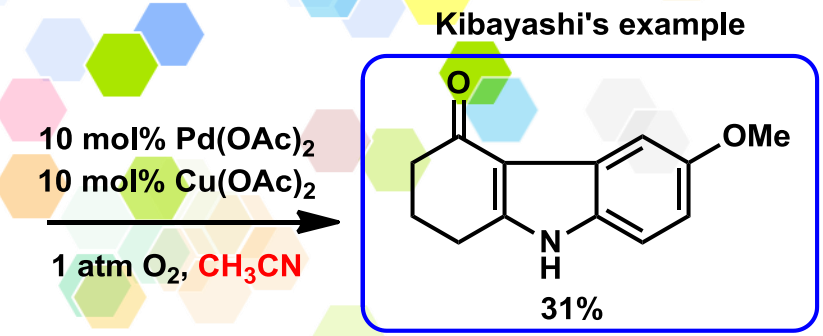
K. Akiyama, K. Mikami, *Heterocycles* **2007**, *74*, 827.

Carbocyclization via a Pd ^{II}/Pd ^{0} Catalytic Cycle（2）

➢anilines

the first catalytic example for the synthesis of carbazoles

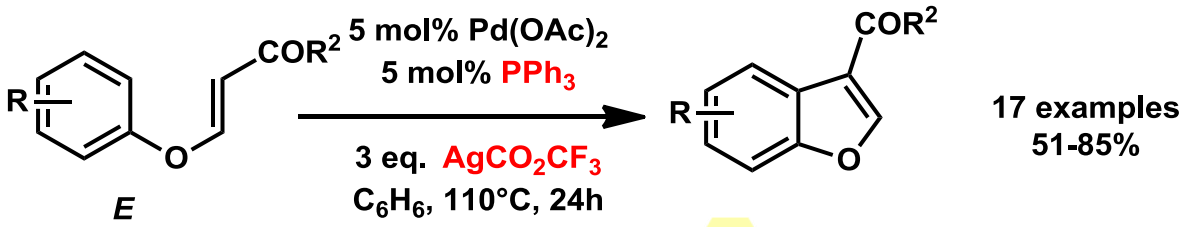




H. Iida, Y. Yuasa, C. Kibayashi, *J. Org. Chem.* **1980**, *45*, 2938.
B. Weng, R. Liu, J.-H. Li, *Synthesis* **2010**, 2926.

Carbocyclization via a Pd ^{II}/Pd ^{0} Catalytic Cycle（2）

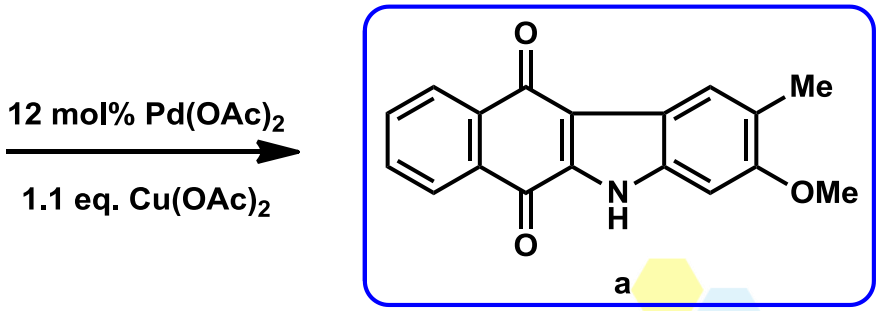
➢**aryl vinyl ethers**



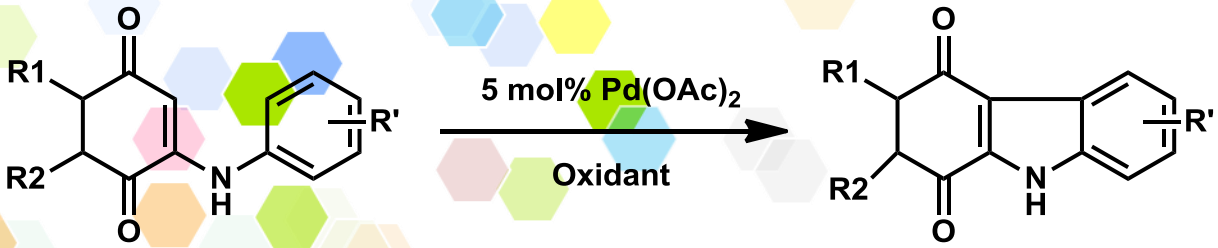
C. Li, Y. Zhang, P. Li, L. Wang, *J. Org. Chem.***2011**, *76*, 4692.

Carbocyclization via a Pd ^{II}/Pd ^{0} Catalytic Cycle（2）

➢**aminoquinone**



The first example of a palladium-catalyzed synthesis of a carbazoloquinone

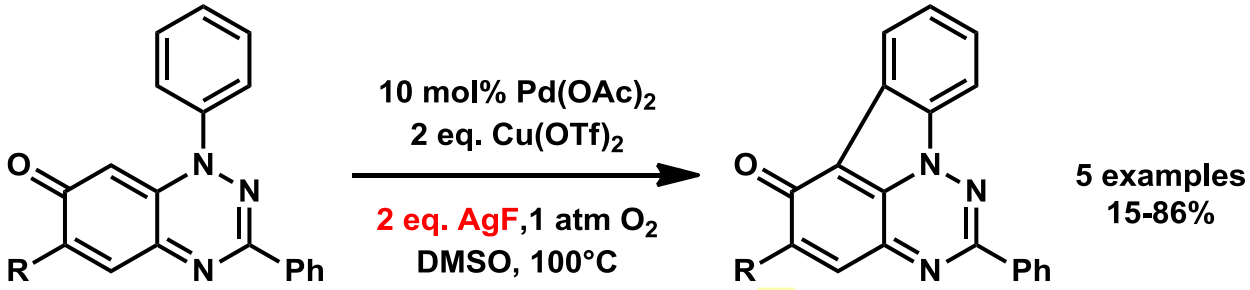


Conditions A:	**5 mol% $Pd(OAc)_2$, 2.5 eq. TBHP, HOAc,90°C**	**6 examples 59-74%**
Conditions B:	**5 mol% $Pd(OAc)_2$, 1 atm O_2, HOAc,95°C**	**3 examples 86-89%**

H.-J. Knolker, N. O'Sullivan, *Tetrahedron* **1994**, *50*, 10893.
H. Hagelin, J. D. Oslob, B. Akermark, *Chem. Eur. J.* **1999**, *5*, 2413.

Carbocyclization via a Pd ^{II}/Pd ^{0} Catalytic Cycle（2）

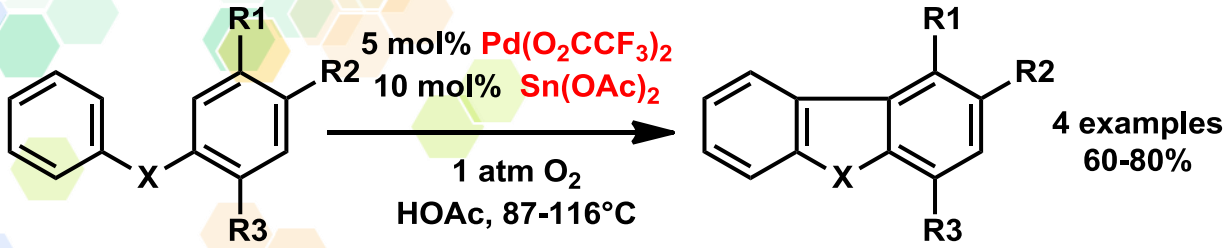
➢benzotriazinones



first example but two equivalents of AgF were necessary

P. A. Koutentis, G. Loizou, D. L. Re, *J. Org. Chem.* **2011**, *76*, 5793.

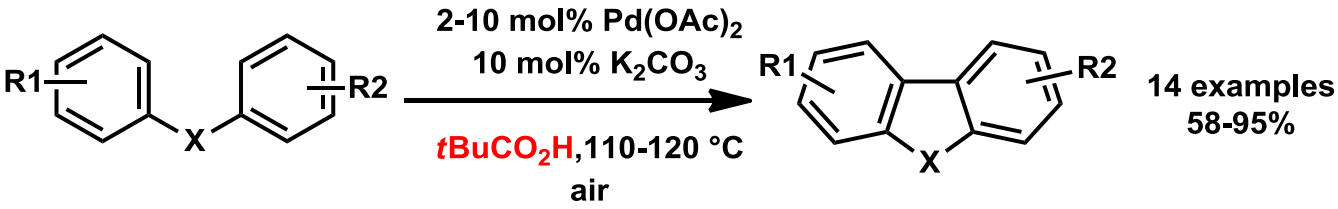
➢Arene–Arene coupling



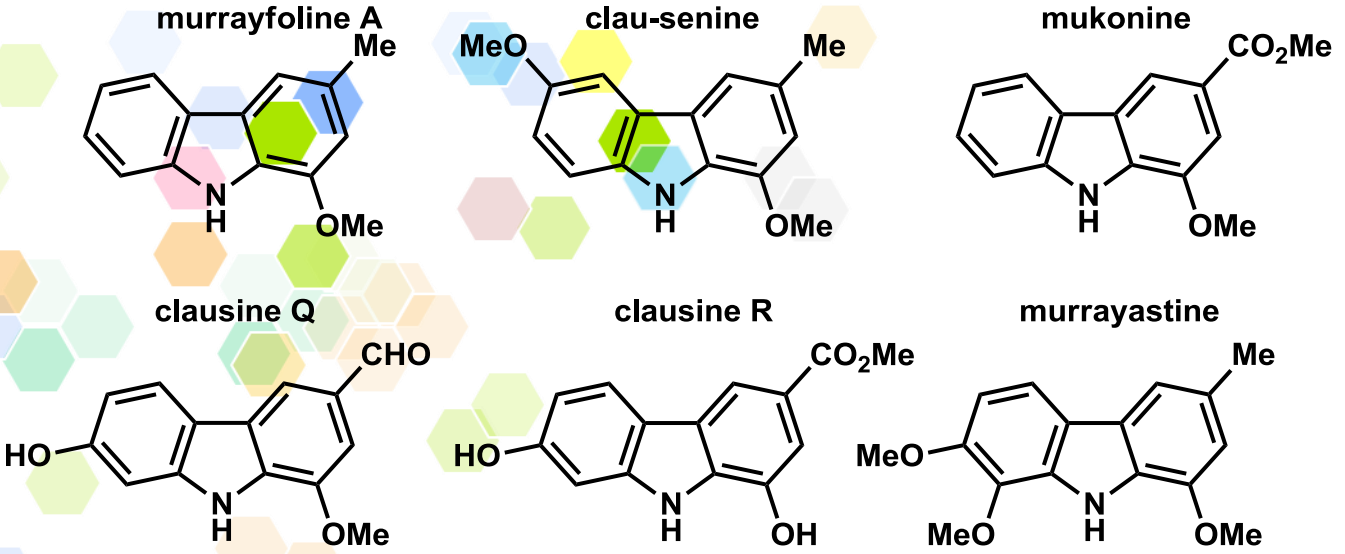
H. Hagelin, J. D. Oslob, B. kermark, *Chem. Eur. J.* **1999**, *5*, 2413.

Carbocyclization via a Pd ^{II}/Pd ^{0} Catalytic Cycle（2）

➢Arene–Arene coupling



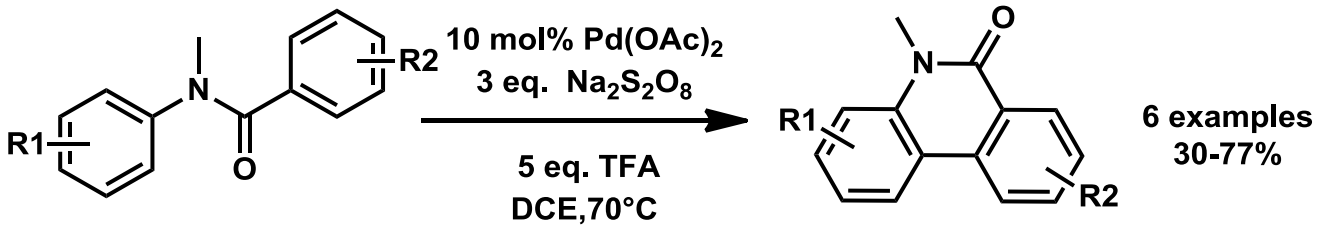
Pivalic acid, not require any additional co-oxidant



B. Ligault, D. Lee, M. P. Huestis, D. R. Stuart, K. Fagnou, *J. Org. Chem*. **2008**, *73*, 5022.
M. Fuchsenberger, R. Forke, H.-J. Knolker, *Synlett* **2011**, 2056.
L. Huet, R. Forke, A. Jger, H.-J. Knolker, *Synlett* **2012**, 1230.

Carbocyclization via a Pd^{II}/Pd^{0} Catalytic Cycle（2）

➢**anilides**

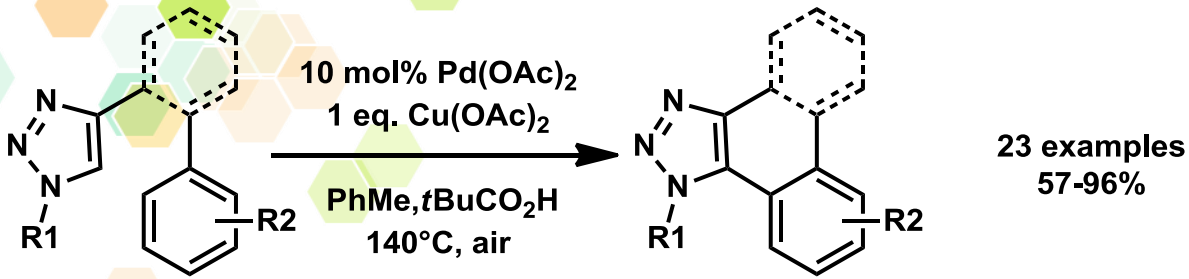


electron-rich substituents are necessary

not limited to anilines, anilides, and indoles

C. S. Yeung, X. Zhao, N. Borduas, V. M. Dong, *Chem. Sci.* **2010**, *1*, 331.

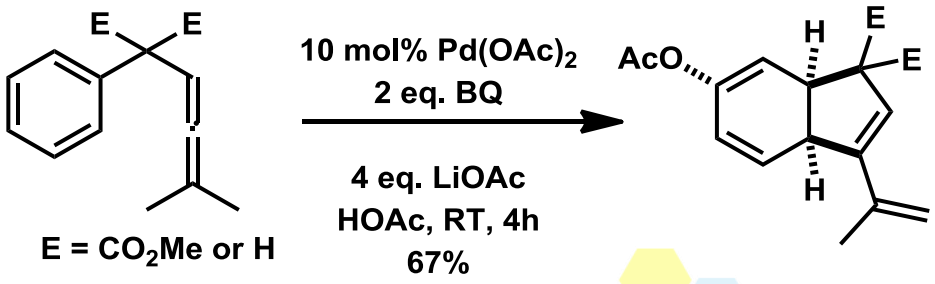
➢**triazole**



L. Ackermann, R. Jeyachandran, H. K. Potukuchi, P. Novak, L. Buttner, *Org. Lett.* **2010**, *12*, 2056.

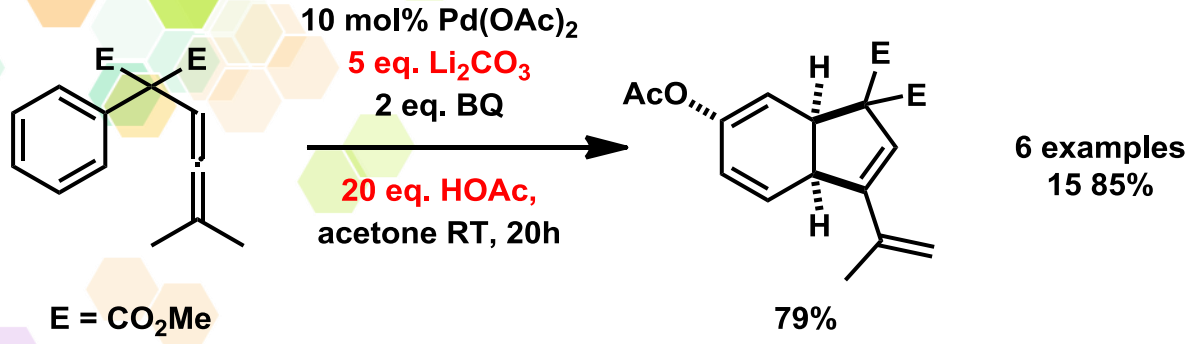
Carbocyclization via a Pd^{II}/Pd^{0} Catalytic Cycle（3）

➢**allenynes**



J. Lofstedt, J. Franzen, J.-E. Backvall, *J. Org. Chem.* **2001**, *66*, 8015.

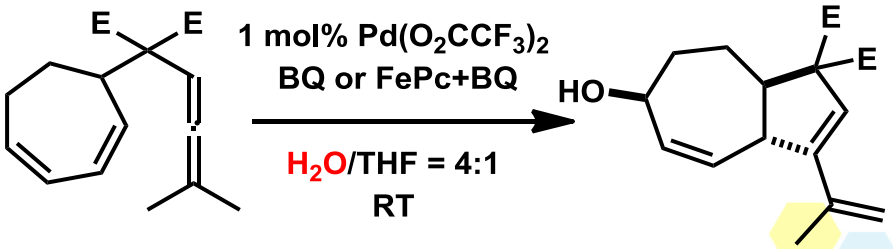
include nucleophiles other than acetate/acetic acid



J. Lofstedt, K. Narhi, I. Dorange, J.-E. Backvall, *J. Org. Chem.* **2003**, *68*, 7243.

Carbocyclization via a Pd ^{II}/Pd ^{0} Catalytic Cycle（3）

➢**dienallenes**

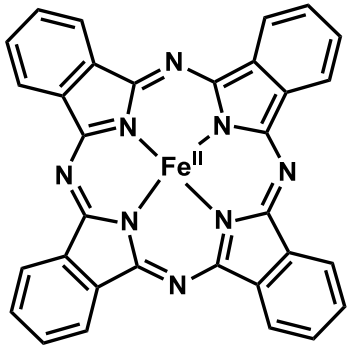


E = CO_2Me

Method A: 2 eq. BQ, 12h 90%

Method B: 1 mol% FePc, 5 mol% BQ 91%

iron(II)-phthalocyanine (FePc)



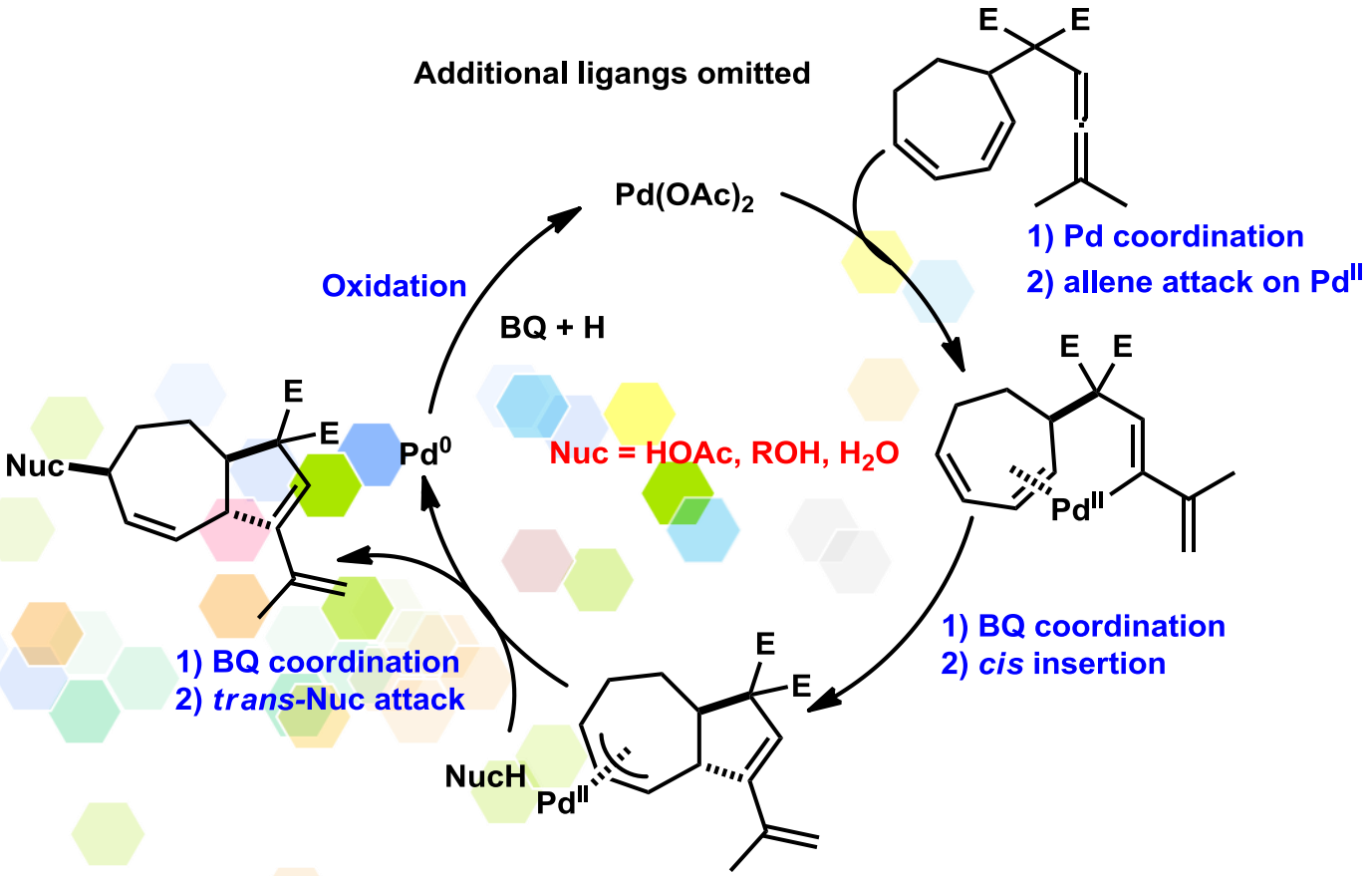
in aqueous media

water as nucleophile

J. Piera, A. Persson, X. Caldentey, J.-E. Backvall, *J. Am. Chem. Soc.* **2007**, *129* , 14120.

Carbocyclization via a Pd^{II}/Pd^{0} Catalytic Cycle（3）

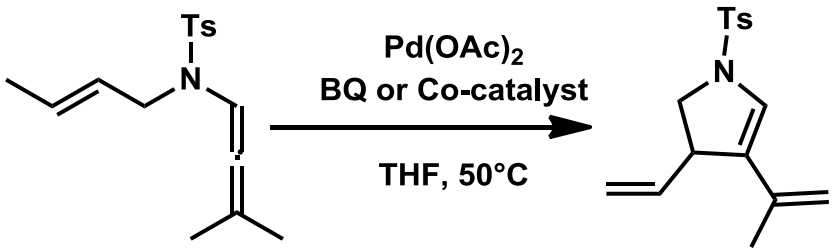
➢**dienallenes**



J. Lofstedt, J. Franzen, J.-E. Backvall, *J. Org. Chem.* **2001**, *66*, 8015.
J. Piera, A. Persson, X. Caldentey, J.-E. Backvall, *J. Am. Chem. Soc.* **2007**, *129* , 14120.

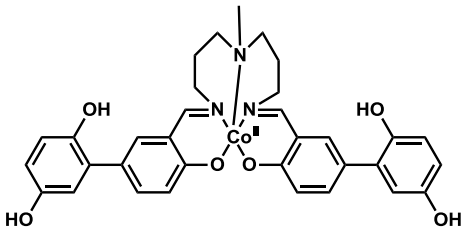
Carbocyclization via a Pd ^{II}/Pd ^{0} Catalytic Cycle（3）

➢**aza-enallenes**



7 examples
64-95%

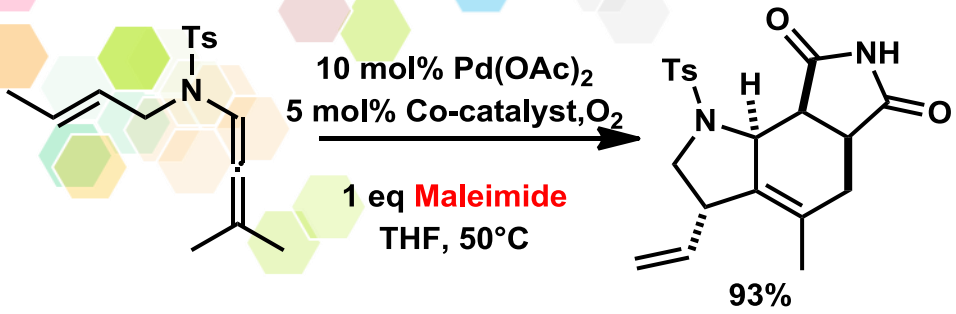
Co-catalyst



Method A: 2 mol% $Pd(OAc)_2$, 1.05 eq. BQ 74%

Method B: 5 mol% $Pd(OAc)_2$, 5 mol% Co-catalyst 94%

in the presence of a dienophile



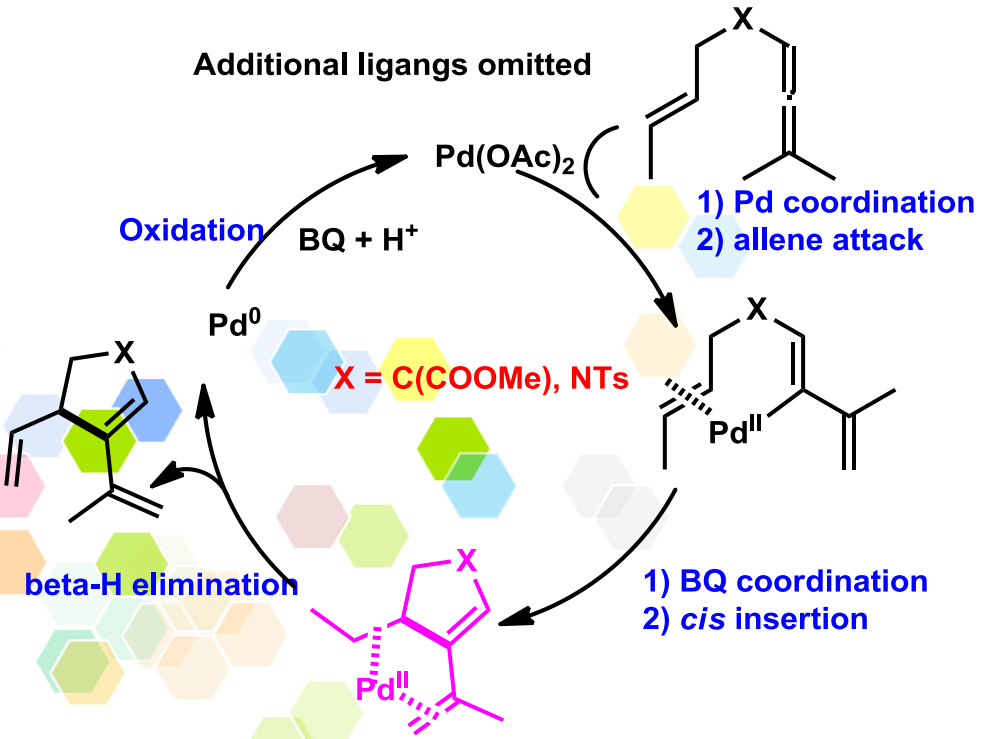
93%

92% *endo, trans/cis* = 85:15

A. K. A. Persson, J.-E. Backvall, *Angew. Chem. Int. Ed.* **2010**, *49*, 4624.

Carbocyclization via a Pd ^{II}/Pd ^{0} Catalytic Cycle（3）

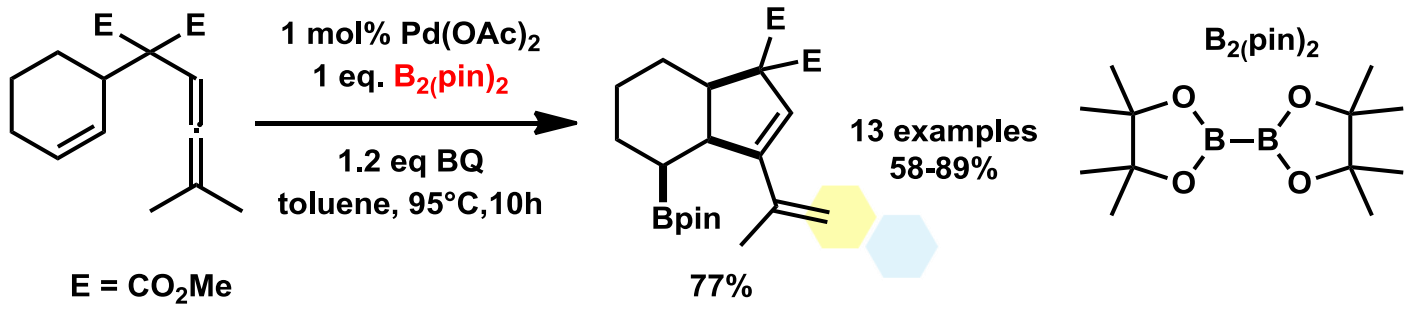
➢**aza-enallenes**



A. K. A. Persson, J.-E. Backvall, *Angew. Chem. Int. Ed.* **2010**, *49*, 4624.

Carbocyclization via a Pd ^{II}/Pd ^{0} Catalytic Cycle（3）

➢**allenynes**

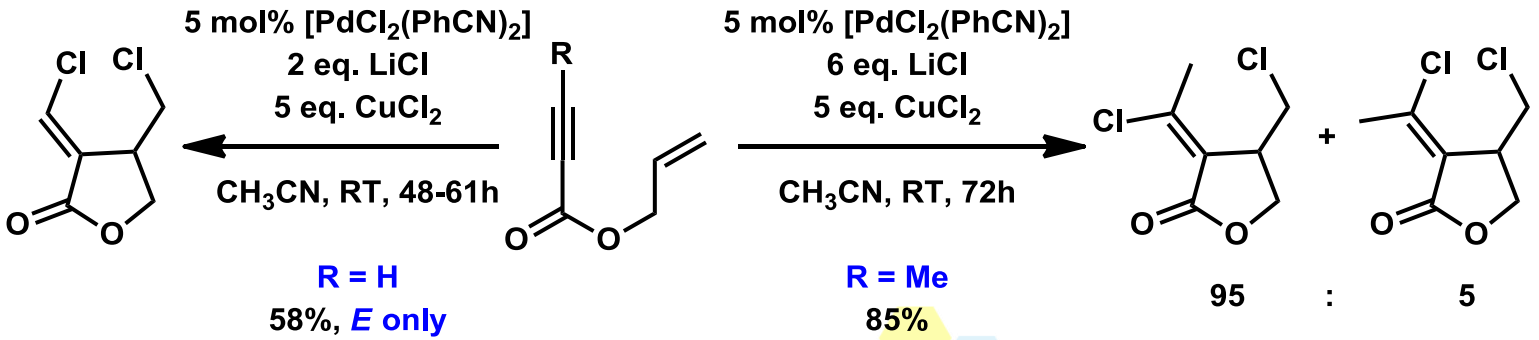


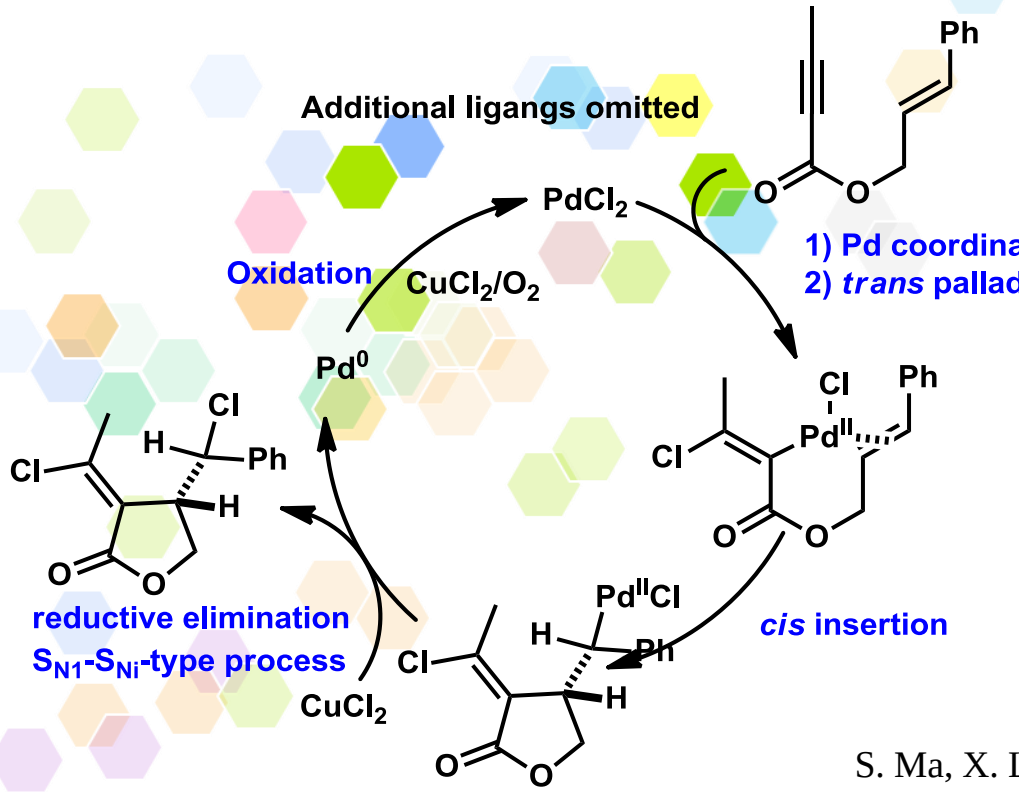
stereoselective cis carboborylation

A. K. A. Persson, T. Jiang, M. T. Johnson, J.-E. Backvall, *Angew. Chem. Int. Ed.* **2011**, *50*, 6155.

Carbocyclization via a Pd^{II}/Pd^{0} Catalytic Cycle（4）

➢**enynes**



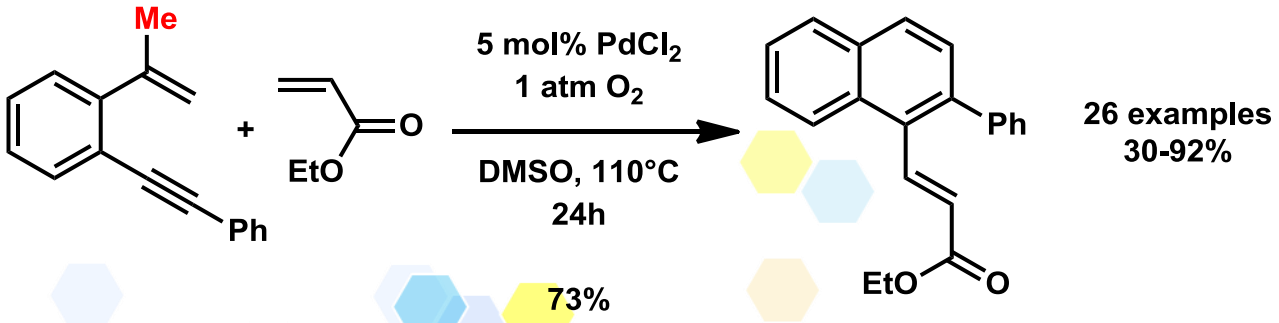


Chloropalladation of the alkyne (cis addition for R = H, trans addition for R = alkyl)

S. Ma, X. Lu, *J. Org. Chem.*.**1993**, *58*, 1245.

Carbocyclization via a Pd ^{II}/Pd ^{0} Catalytic Cycle（4）

➢**aromatic enynes**



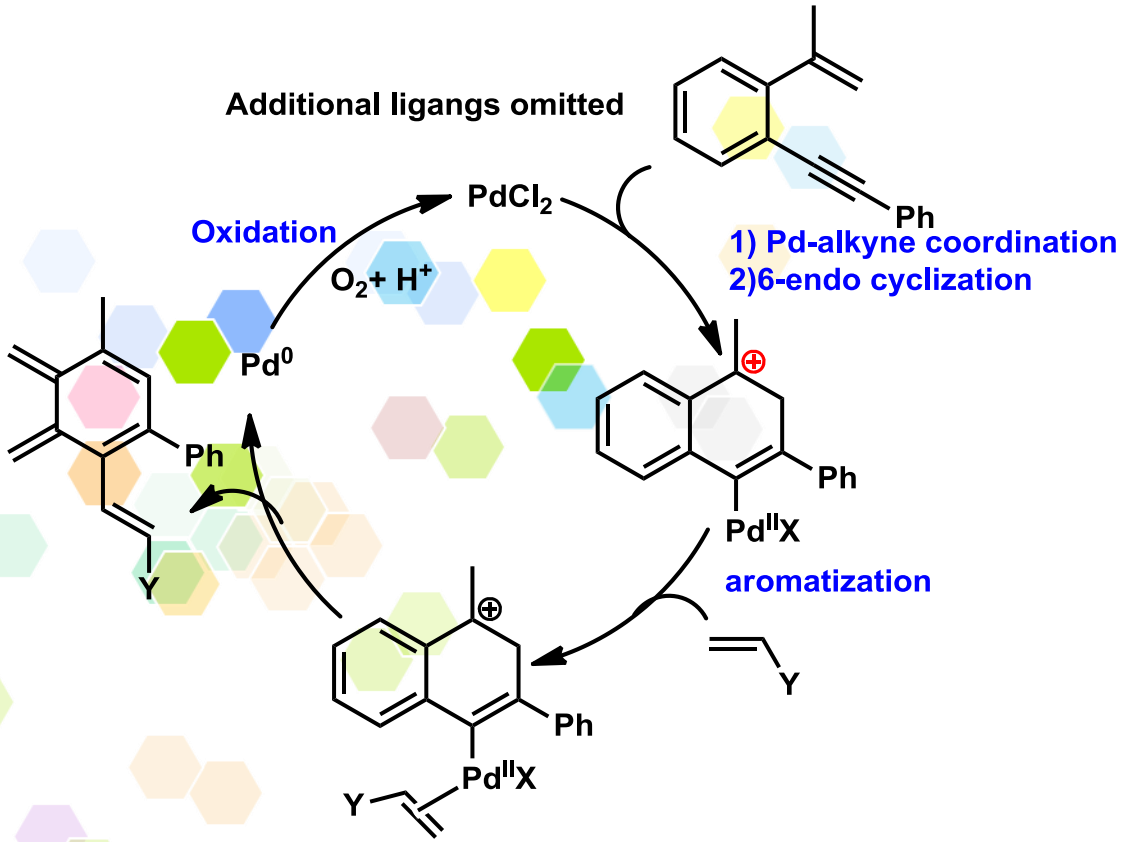
the a-methyl group on the styrene moiety is an absolute necessity

C. Feng, T. P. Loh, *J. Am. Chem. Soc.* **2010**, *132* , 17710.

Carbocyclization via a Pd ^{II}/Pd ^{0} Catalytic Cycle（4）

➢**aromatic enynes**

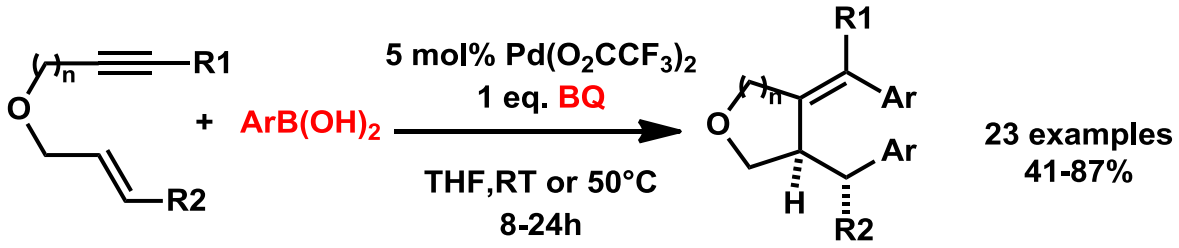
a benzylic cation is stabilized by the methyl group

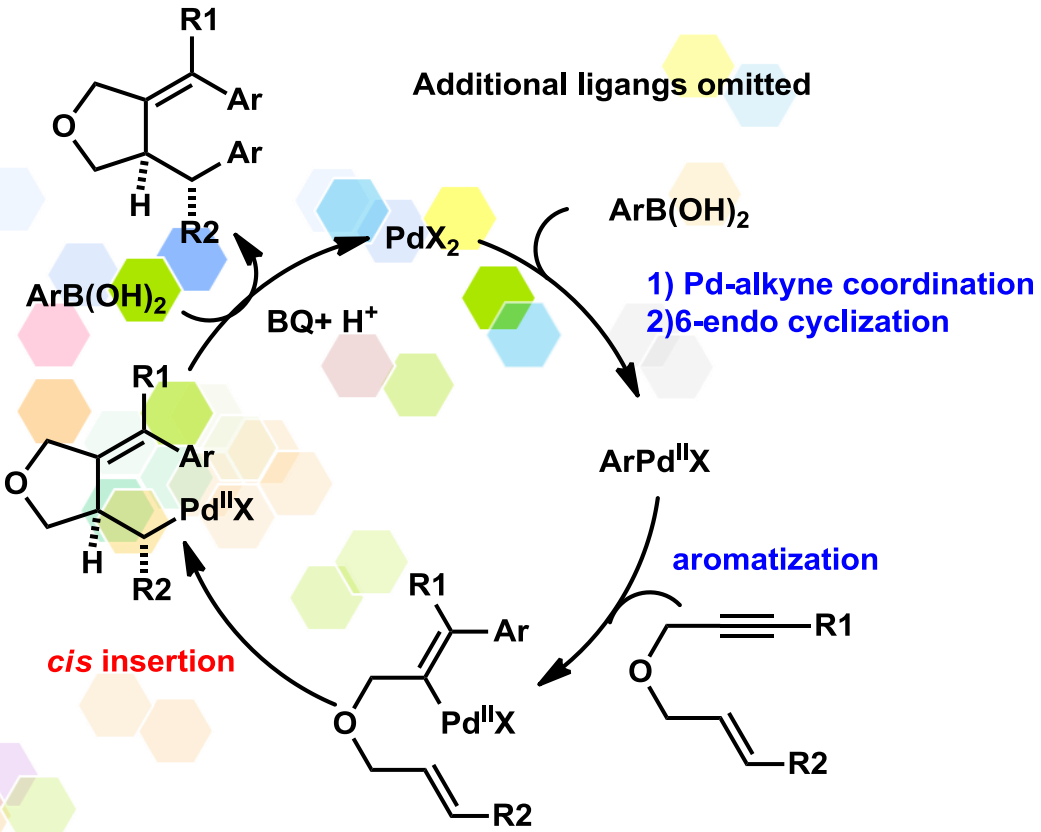


C. Feng, T. P. Loh, *J. Am. Chem. Soc.* **2010**, *132* , 17710.

Carbocyclization via a Pd^{II}/Pd^{0} Catalytic Cycle（4）

➢**oxygen-tethered enynes**

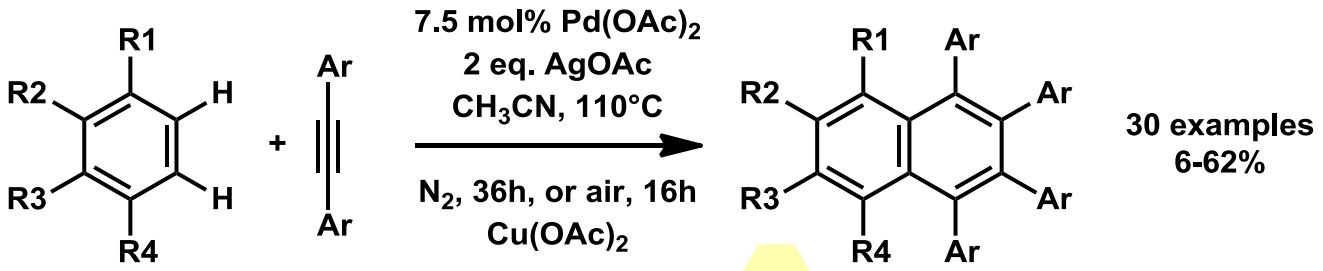




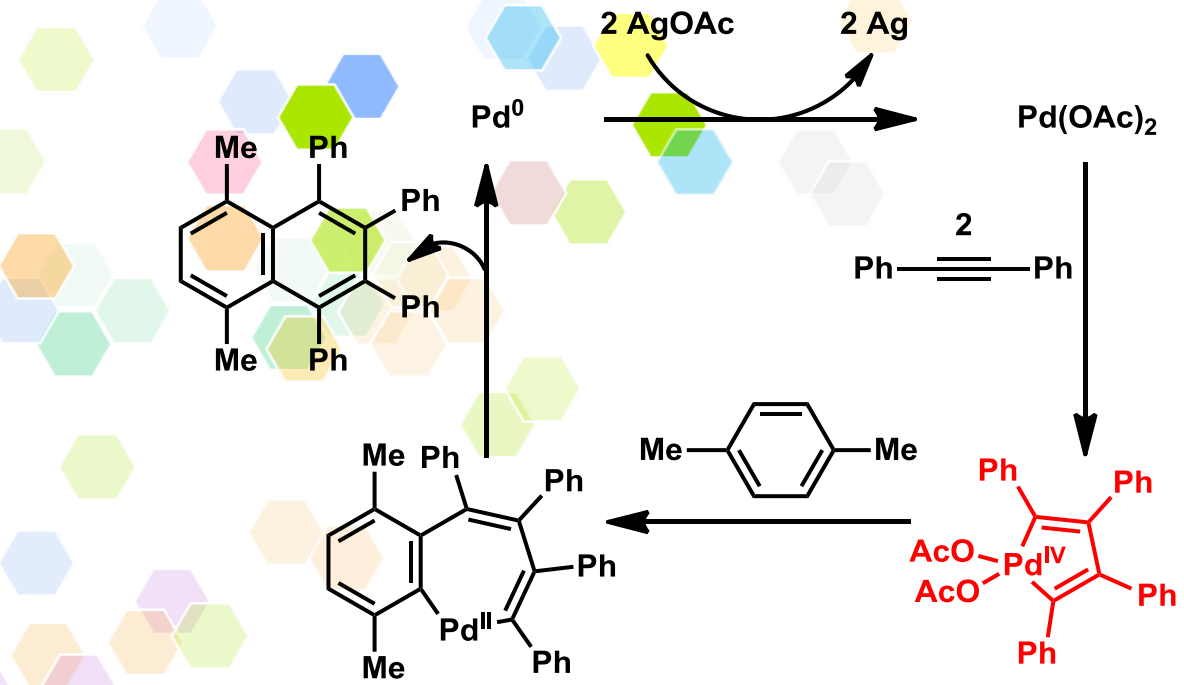
M. Jiang, T. Jiang, J.-E. Backvall, *Org. Lett*. **2012**, *14*, 3538.

Carbocyclization via a Pd ^{II}/Pd ^{0} Catalytic Cycle（2）

➢**naphthalenes**



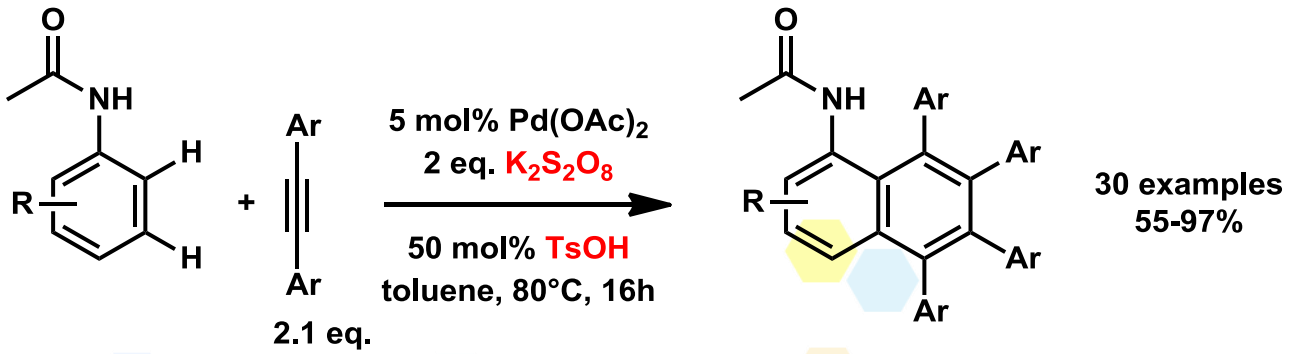
a cyclometallated Pd^{IV} intermediate



Y.-T. Wu, K.-H. Huang, C.-C. Shin, T.-C. Wu, *Chem. Eur. J.* **2008**, *14*, 6697.

Carbocyclization via a Pd ^{II}/Pd ^{0} Catalytic Cycle（2）

➢**amide**

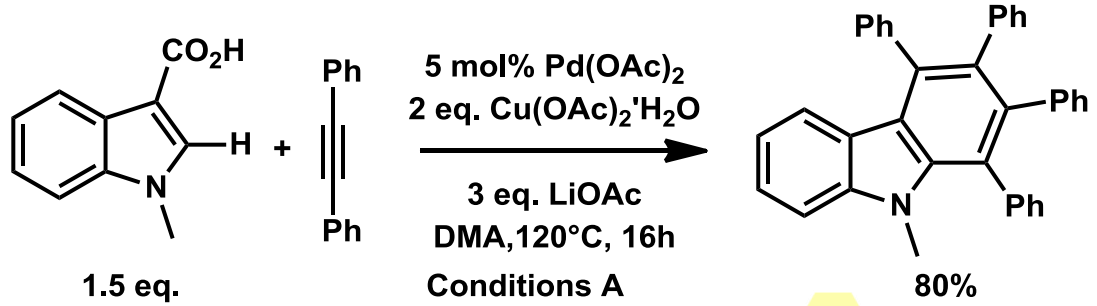


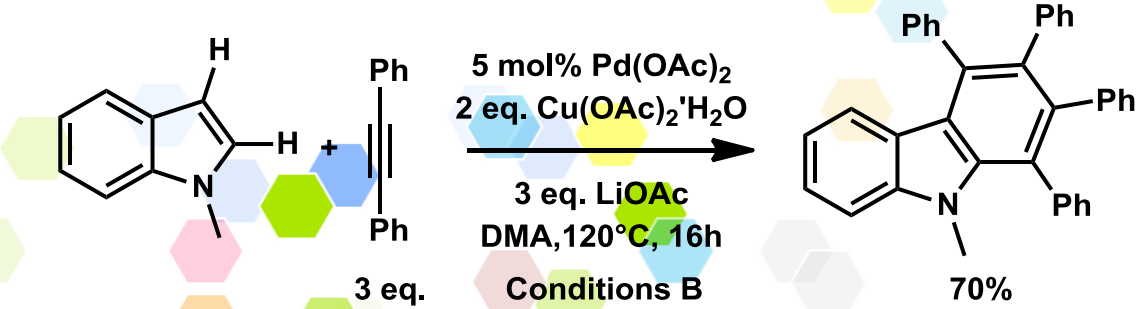
chemo- and regioselective synthesis

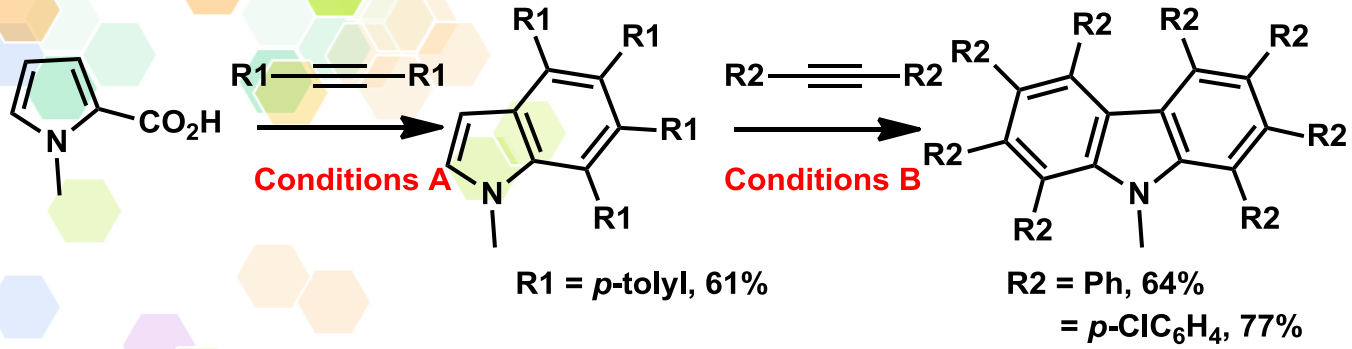
Y.-T. Wu, K.-H. Huang, C.-C. Shin, T.-C. Wu, *Chem. Eur. J.* **2008**, *14*, 6697.

Carbocyclization via a Pd ^{II}/Pd ^{0} Catalytic Cycle（2）

➢**indoles and their carboxylic acid derivatives**



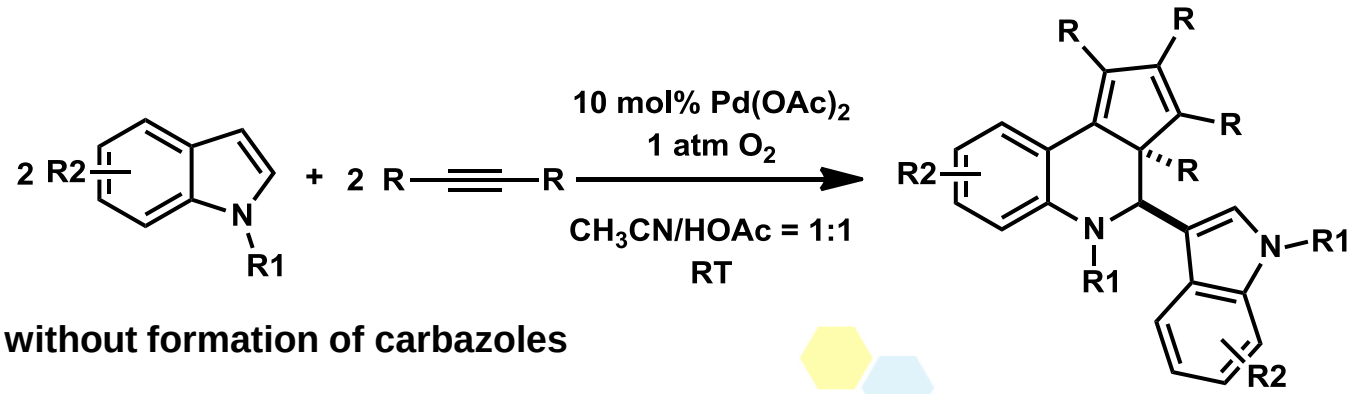




M. Yamashita, H. Horiguchi, K. Hirano, T. Satoh, M. Miura, *J. Org. Chem.* **2009**, *74*, 7481.
M. Yamashita, K. Hirano, T. Satoh, M. Miura, *Org. Lett.* **2009**, *11*, 2337.

Carbocyclization via a Pd ^{II}/Pd ^{0} Catalytic Cycle（2）

➢indoles

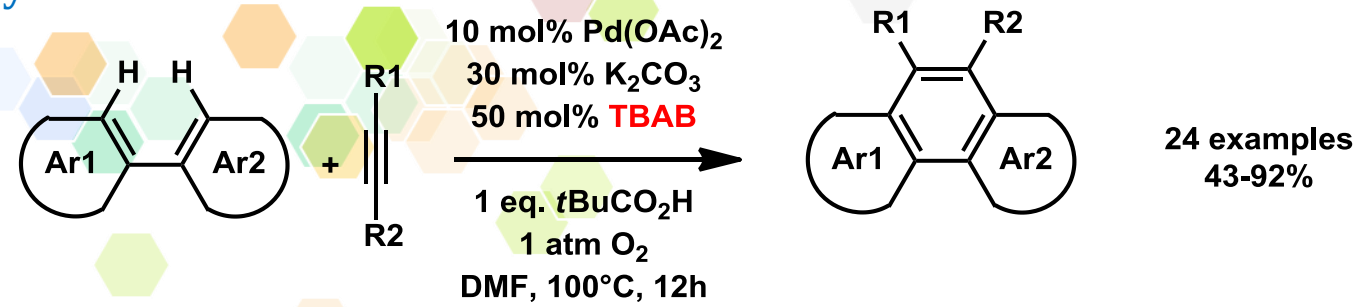


without formation of carbazoles

this ring-expansion reaction involves a dual C-H bond activation, one C-C bond cleavage, and five new C-C bond formations

Z. Shi, B. Zhang, Y. Cui, N. Jiao, *Angew. Chem. Int. Ed.* **2010**, *49*, 4036.

➢biaryls

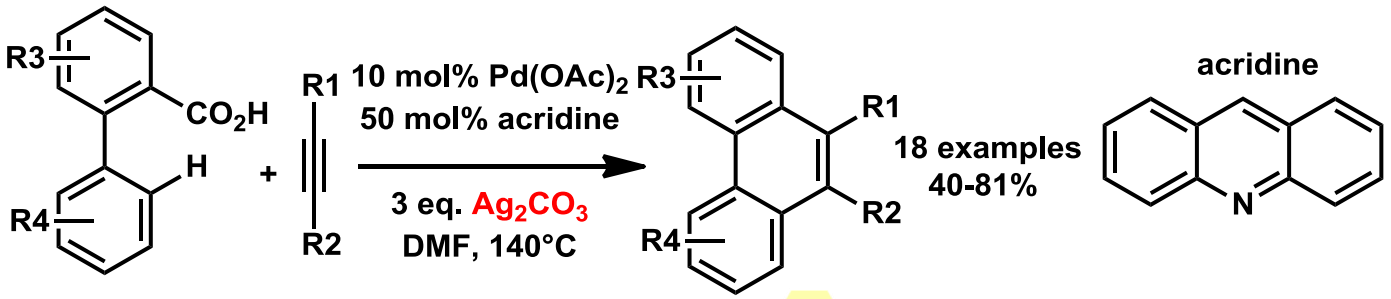


first palladium-cata-lyzed cycloaromatization of biaryls

Z. Shi, S. Ding, Y. Cui, N. Jiao, *Angew. Chem. Int. Ed.* **2009**, *48*, 7895.

Carbocyclization via a Pd ^{II}/Pd ^{0} Catalytic Cycle（2）

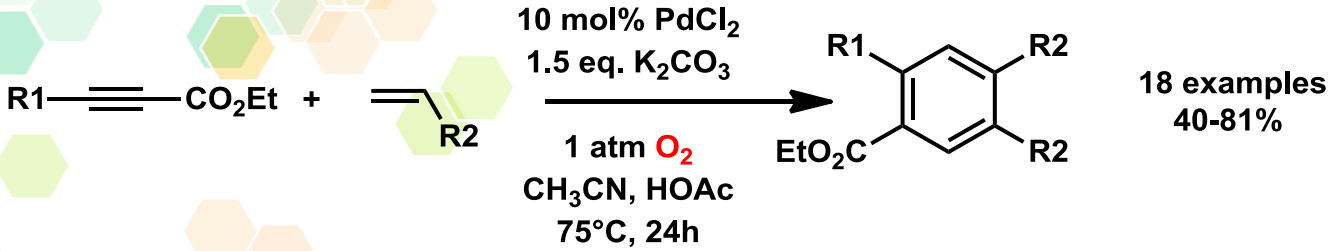
➢phenylbenzoic acids



difficult to determine
whether decarboxylation occurs at an early stage or at the end of the catalytic cycle.

C. Wang, S. Rakshit, F. Glorius, *J. Am. Chem. Soc.* **2010**, *132*, 14006.

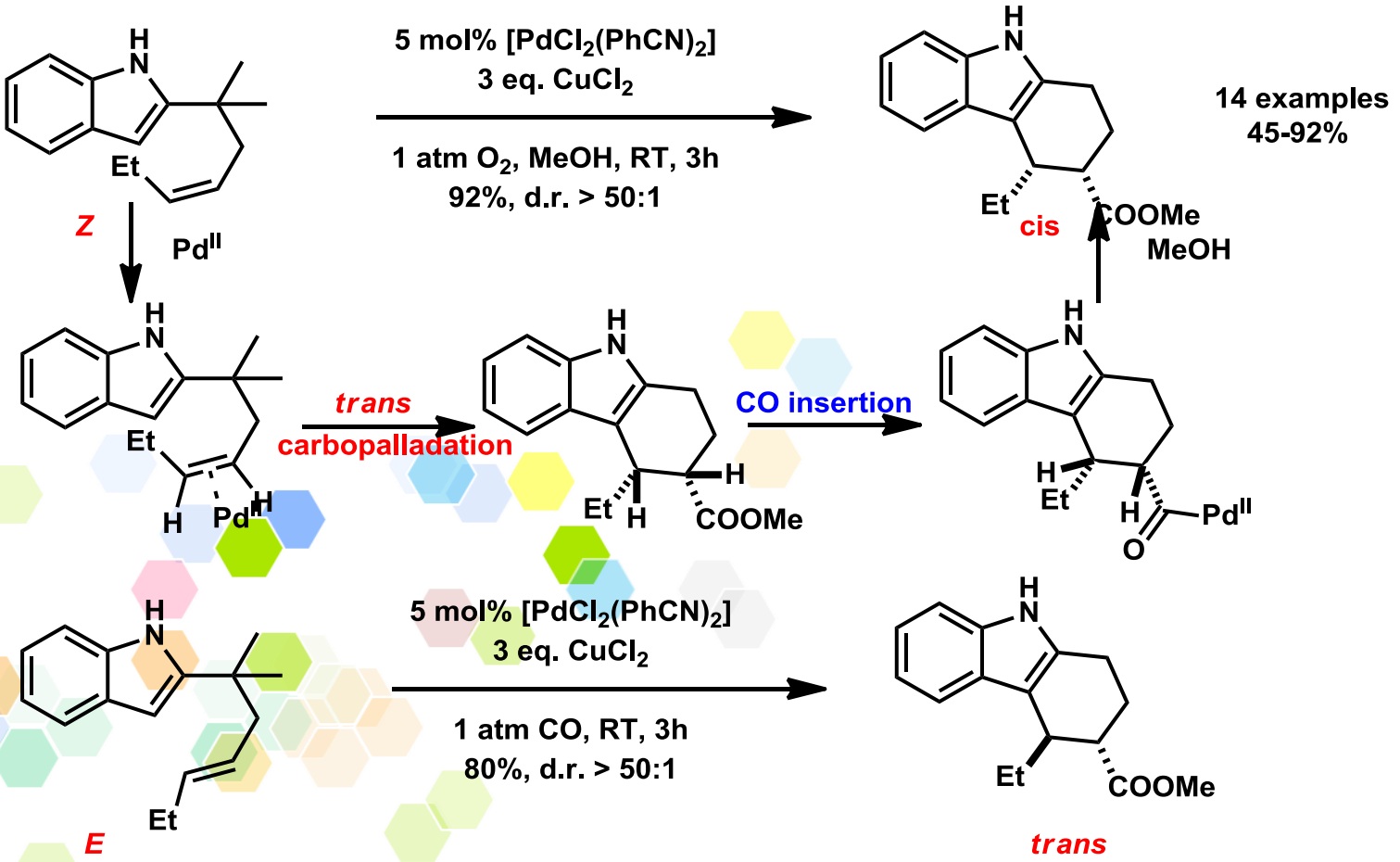
➢alkynes



P. Zhou, L. Huang, H. Jiang, A. Wang, X. Li, *J. Org. Chem.* **2010**, *75*, 8279.

Carbocyclization via a Pd^{II}/Pd^{0} Catalytic Cycle（5）

➢others

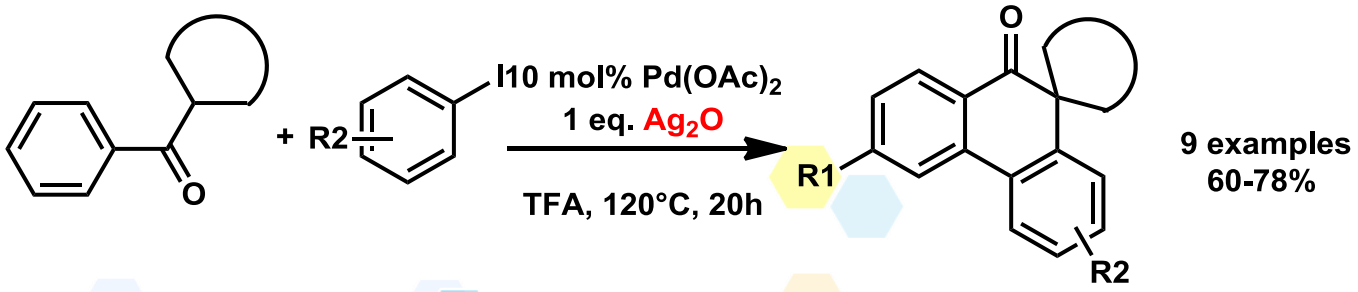


protection of the indole N- H group is not necessary

C. Liu, R. A. Widenhoefer, *Chem. Eur. J.* **2006,** *12*, 2371.

Carbocyclization via a Pd ^{II}/Pd ^{0} Catalytic Cycle（5）

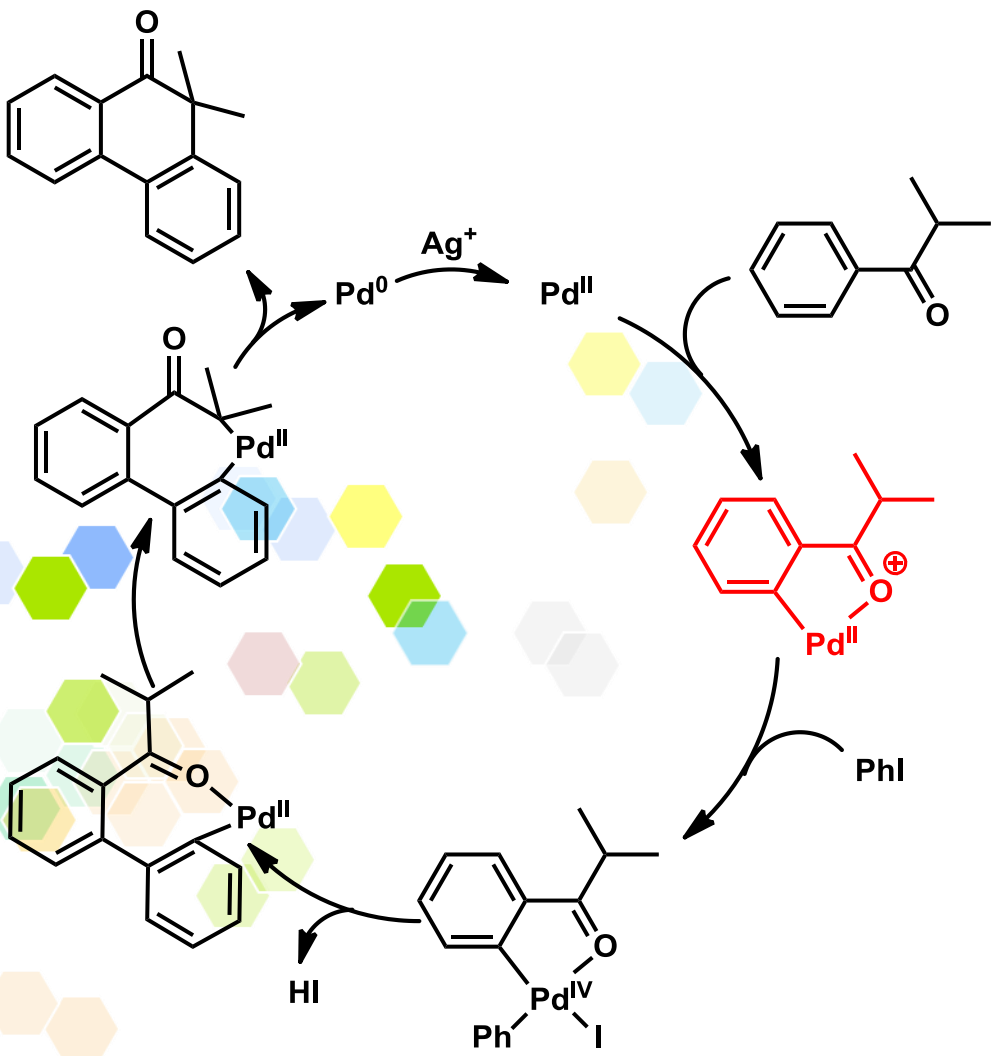
➢**others**



P. Gandeepan, K. Parthasarathy, C.-H. Cheng, *J. Am. Chem. Soc.* **2010**, *132* , 8569.

Carbocyclization via a Pd ^{II}/Pd ^{0} Catalytic Cycle（5）

➢**others**



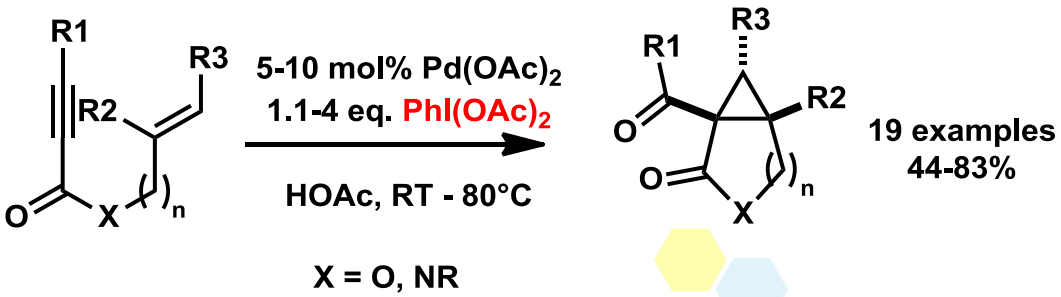
P. Gandeepan, K. Parthasarathy, C.-H. Cheng, *J. Am. Chem. Soc.* **2010**, *132* , 8569.

Contents

- Background
- Carbocyclization via a Pd^{II}/Pd^{0} Catalytic Cycle
- Carbocyclization via a Pd^{II}/Pd^{IV}Catalytic Cycle
- Challenge and Summary
- Acknowledgment

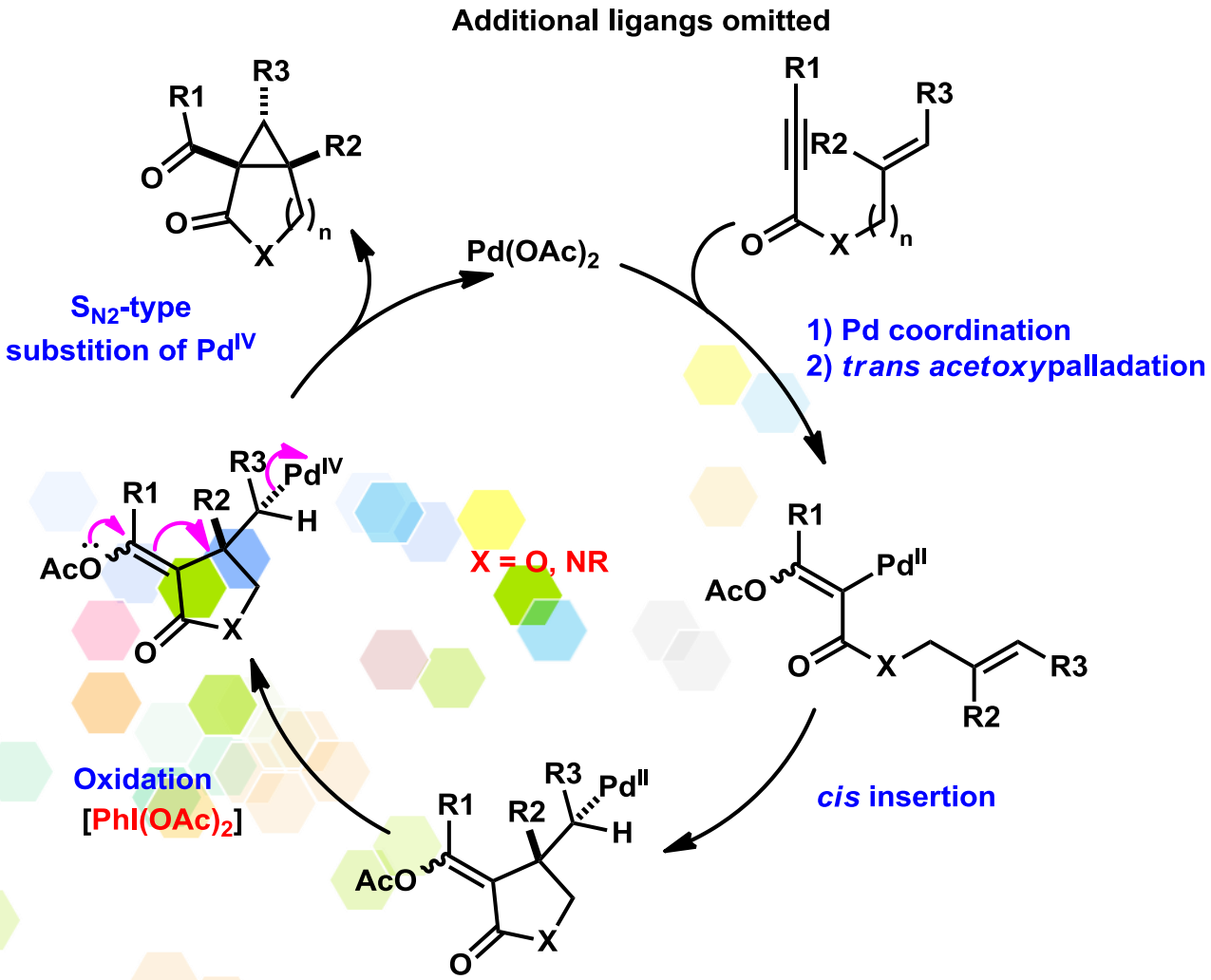
Carbocyclization via a Pd ^{II}/Pd ^{IV} Catalytic Cycle

➢**enynes**



X. Tong, M. Beller, M. K. Tse, J. Am. Chem. Soc. 2007, 129, 4906.
L. L. Welbes, T. W. Lyons, K. A. Cychosz, M. S. Sanford, J. Am. Chem. Soc. 2007, 129, 836.
T. W. Lyons, M. S. Sanford, Tetrahe-dron 2009, 65, 3211.

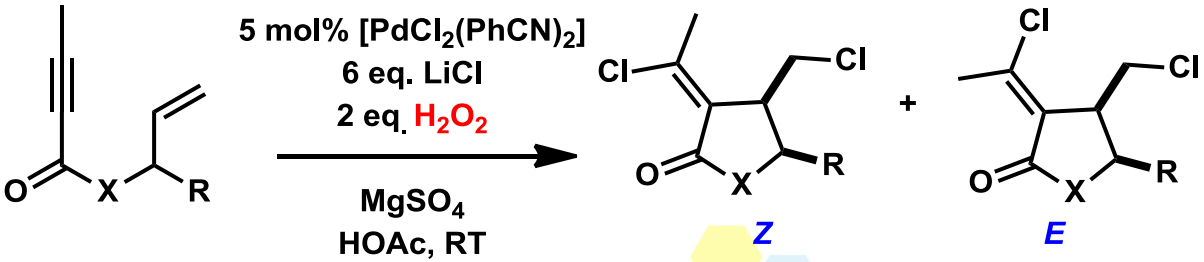
Carbocyclization via a Pd ^{II}/Pd ^{IV} Catalytic Cycle



X. Tong, M. Beller, M. K. Tse, J. Am. Chem. Soc. 2007, 129, 4906.
L. L. Welbes, T. W. Lyons, K. A. Cychosz, M. S. Sanford, J. Am. Chem. Soc. 2007, 129, 836.
T. W. Lyons, M. S. Sanford, Tetrahe-dron 2009, 65, 3211.

Carbocyclization via a Pd ^{II}/Pd ^{IV} Catalytic Cycle

➢**enynes**

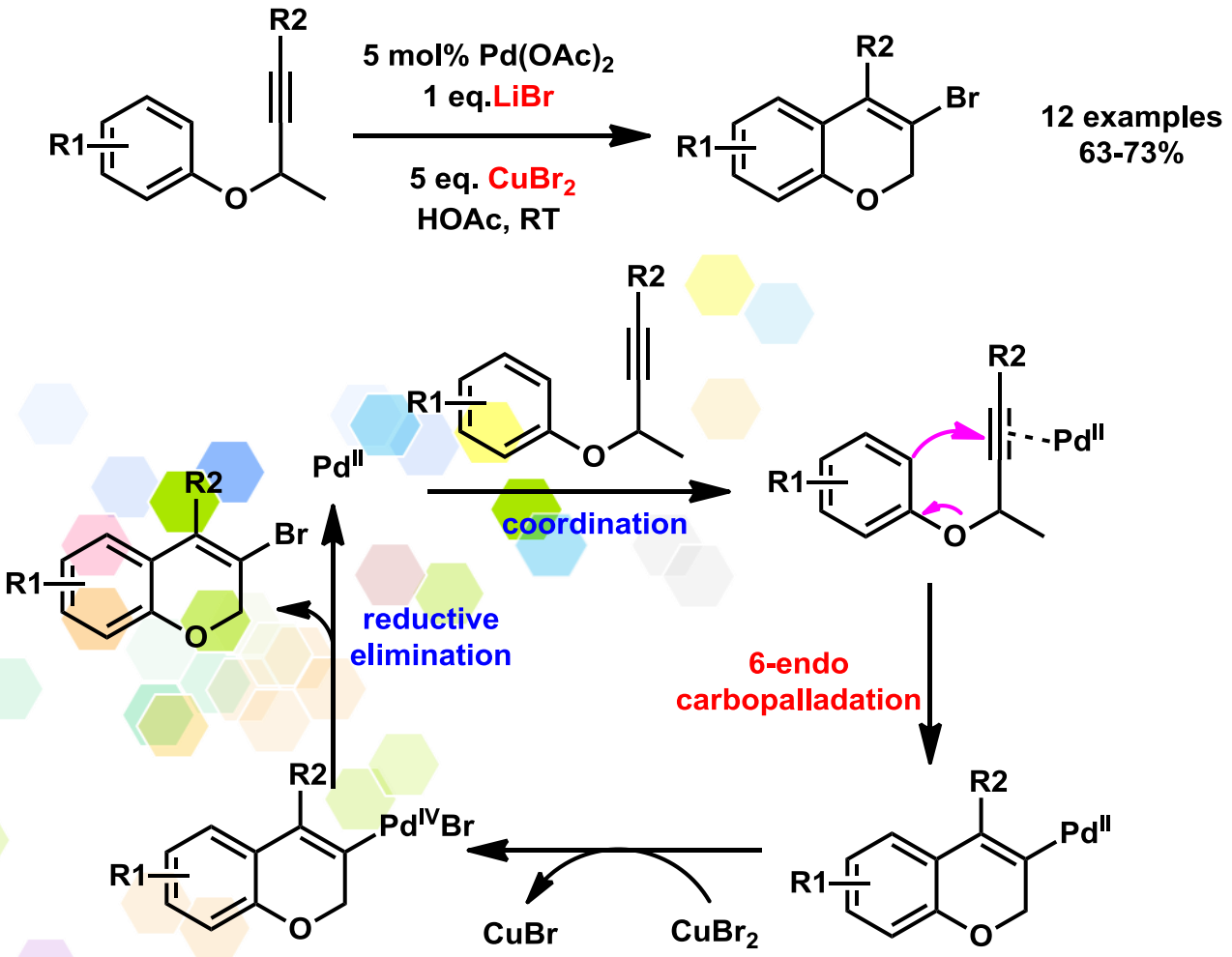


X	R	Yield(%)	*Z*/*E*
O	H	85	90:10
O	Me	60	86:14
O	Ph	58	88:12
NBn	H	67	95:5

G. Yin, G. Liu, *Angew. Chem. Int. Ed.* **2008**, *47*, 5442.

Carbocyclization via a Pd ^{II}/Pd ^{IV} Catalytic Cycle

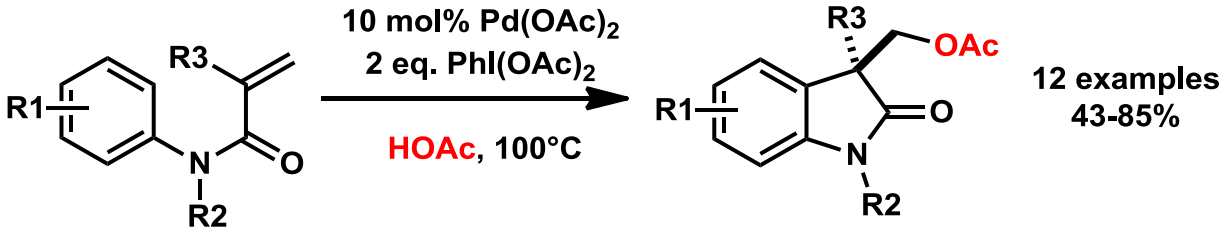
➢**aryl propargyl ethers**

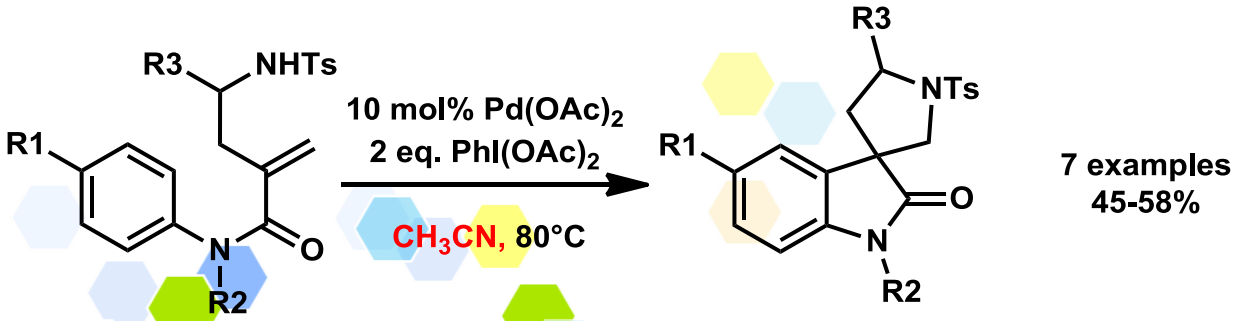


S. Tang, P. Peng, Z.-Q. Wang, B.-X. Tang, C.-L. Deng, J.-H. Li, P. Zhong, N.-X. Wang, *Org. Lett.* **2008,** *10*, 1875.

Carbocyclization via a Pd ^{II}/Pd ^{IV} Catalytic Cycle

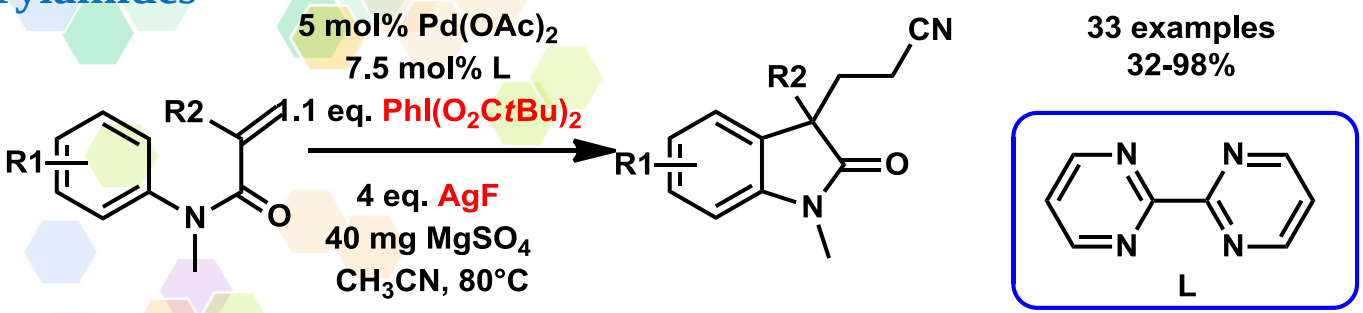
➢A,β-unsaturated alkenes





S. Jaegli, J. Dufour, H. Wei, T. Piou, X. Duan, J.-P. Vors, L. Neuville, J. Zhu, *Org. Lett.* **2010**, *12*, 4498.

➢acrylamides



T. Wu, X. Mu, G. Liu, *Angew. Chem. Int. Ed.* **2011**, *50*, 12578.

Contents

Challenge and Summary :

- **stoichiometric metal salts**
- **Less developmented enantioselective oxidative carbocyclizations**
- **Strong Pd^{II}/Pd^{0} , weak Pd^{II}/Pd^{IV}**
- **Less application in total synthesis**

Efficient Cataytic System

but

More Development Space

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School of Chemical Biology&Biotechnology
化学生物学与生物技术学院

- ***Prof. Yong Huang***
- ***Chengming Wang***
- ***All members here***

Thanks for your attention !