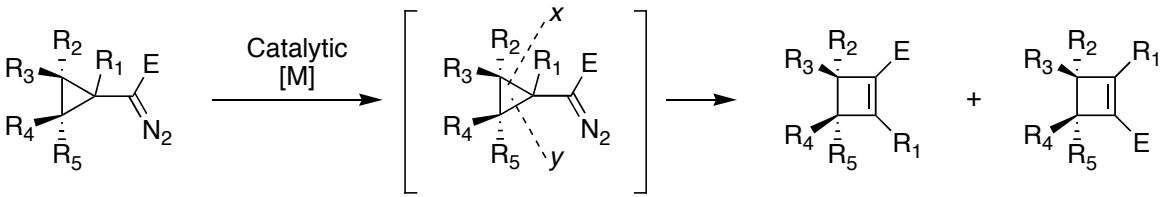
Synthesis of Cyclobutenes by Highly Selective Transition-Metal-Catalyzed Ring Expansion of Cyclopropanes

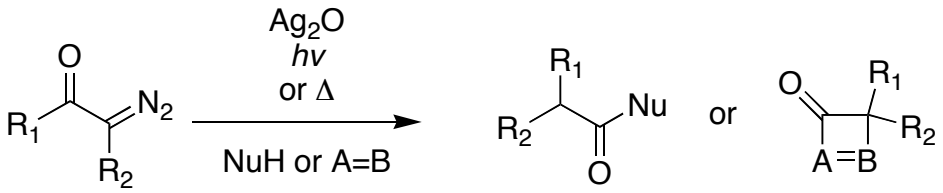


Huadong Xu, Wen Zhang, Dongxu Shu, Jenny B. Werness, and Weiping Tang

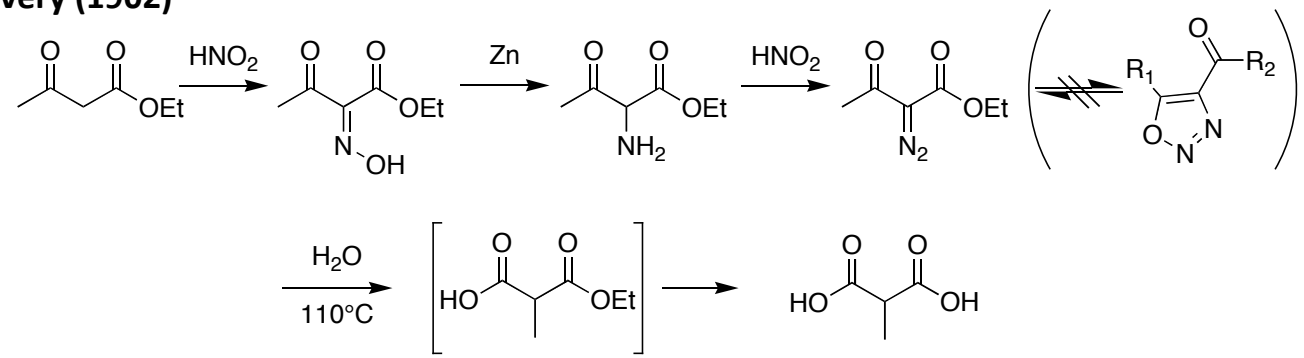
Angew. Chem. Int. Ed. **2008**, *Early View*

Nate Ware, Wipf Group Current Literature 10/18/08

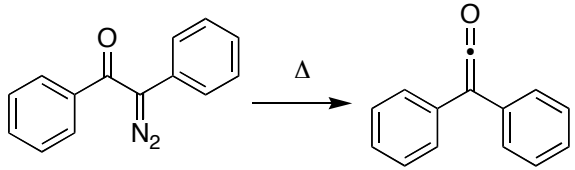
Wolff Rearrangement



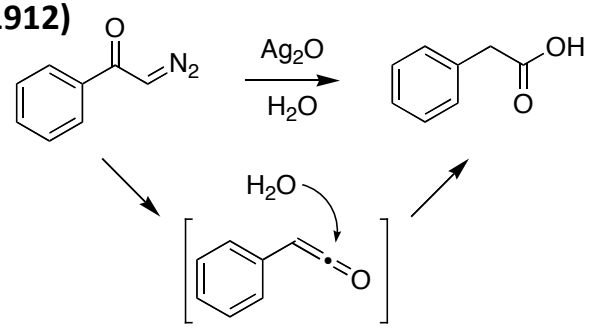
Discovery (1902)



Schröter (1909)



Wolff (1912)



L. Kurti, B. Czako, *Strategic Application of Named Reactions in Organic Synthesis*, **2005,** Elsevier Inc.

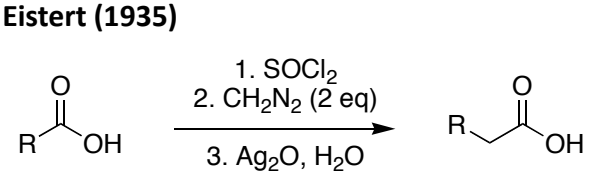
L. Wolff *Justus Liebigs Ann. Chem*. **1902**, 325, 129; **1912**, 394, 23

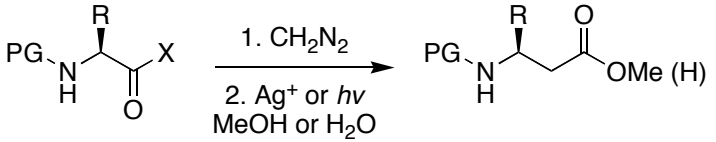
G. Schröter *Ber. Btsch. Chem. Ges*. **1909**, 42, 2336

W. Kirmse E. *J. Org. Chem*. **2002**, 2193

Wolff Rearrangement / Arndt-Eistert Homologation

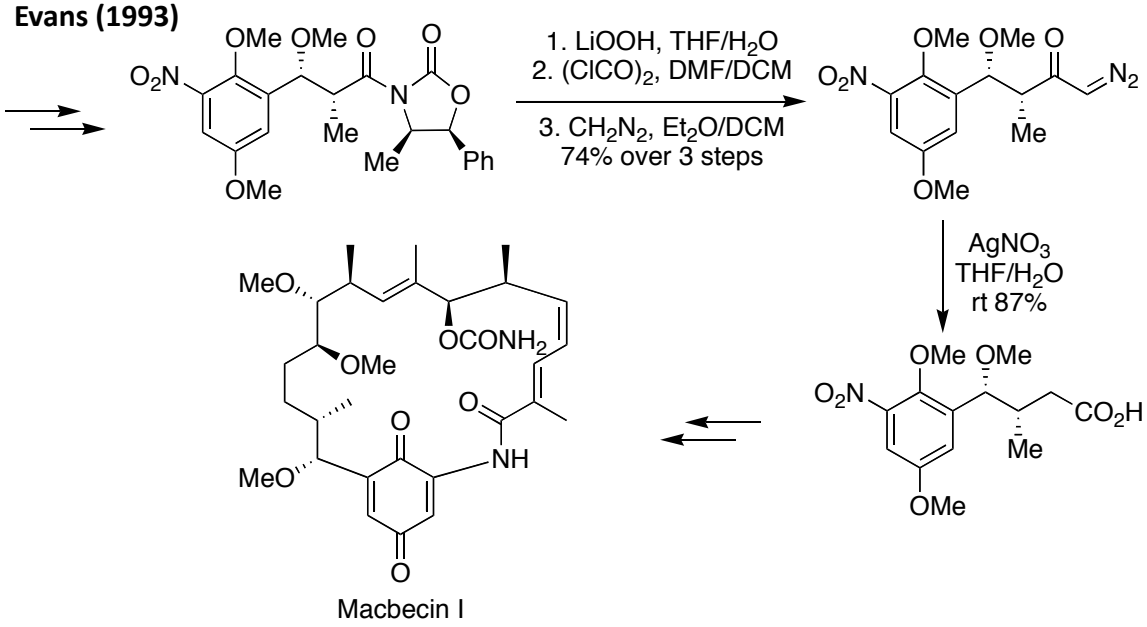
Arndt and Eistert (1935)





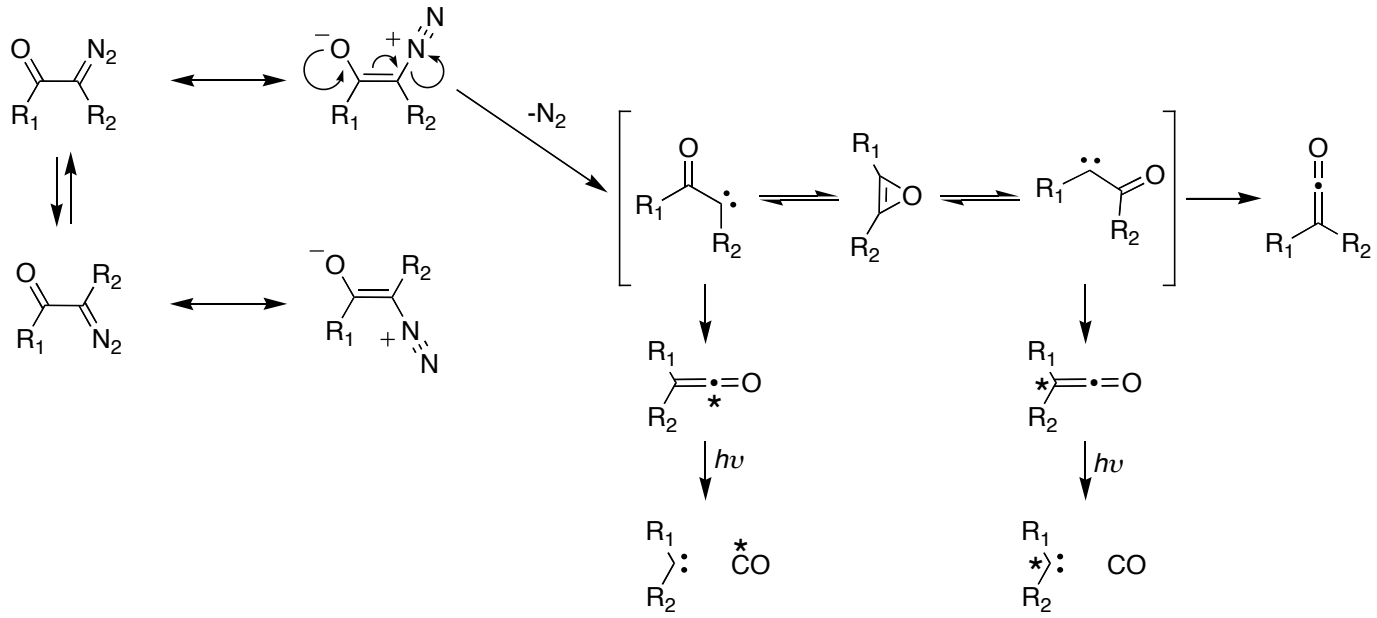
PG = Cbz, Fmoc, Boc
X = -Cl, -F, mixed anhydride, $-OC_6F_5$

Evans (1993)



L. Kurti, B. Czako, *Strategic Application of Named Reactions in Organic Synthesis*, **2005,** Elsevier Inc.
D.A. Evans , et al. *J. Org. Chem*. **1993**, 58, 471
W. Kirmse E. *J. Org. Chem*. **2002**, 2193

Wolff Rearrangement – Mechanism

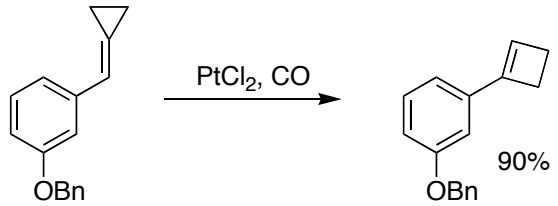


In the gas phase there significant participation by the oxirene.
In solution, oxirene participation is very solvent and temperature dependant.

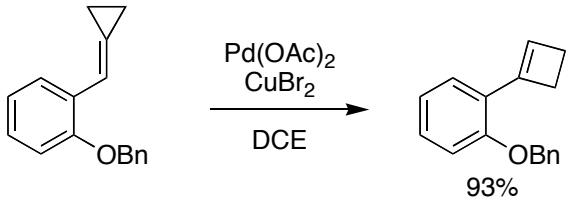
L. Kurti, B. Czako, *Strategic Application of Named Reactions in Organic Synthesis*, **2005,** Elsevier Inc.
M. Torres, E.M. Lown, H.E. Gunning, O.P. Strausz. *Pure App Chem* **1980**, 52, 1623

Ring Expansion Reactions to get Cyclobutenes

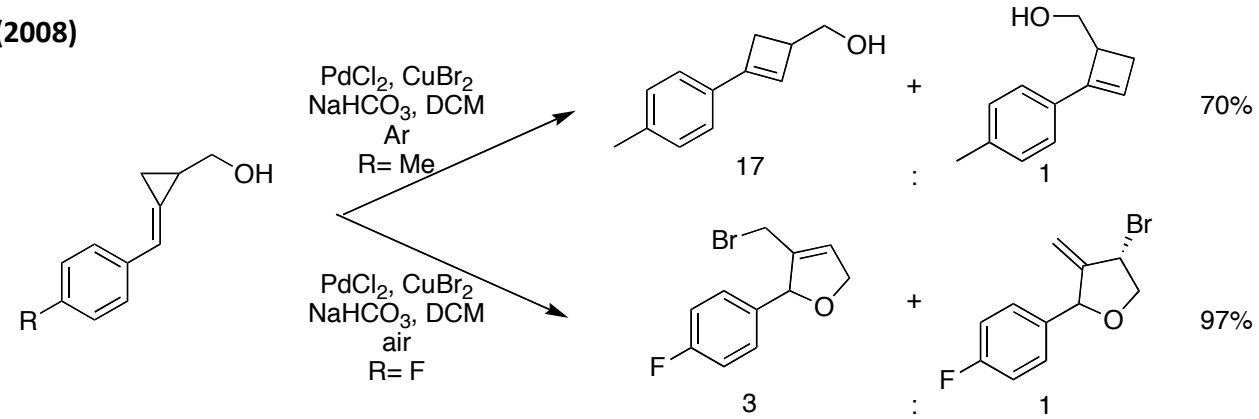
Fürstner (2006)



Shi (2006)



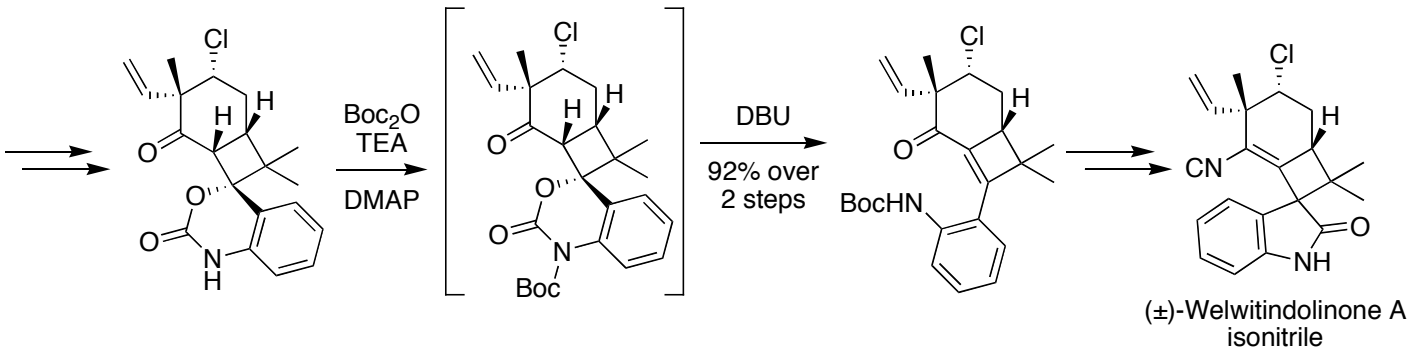
Shi (2008)



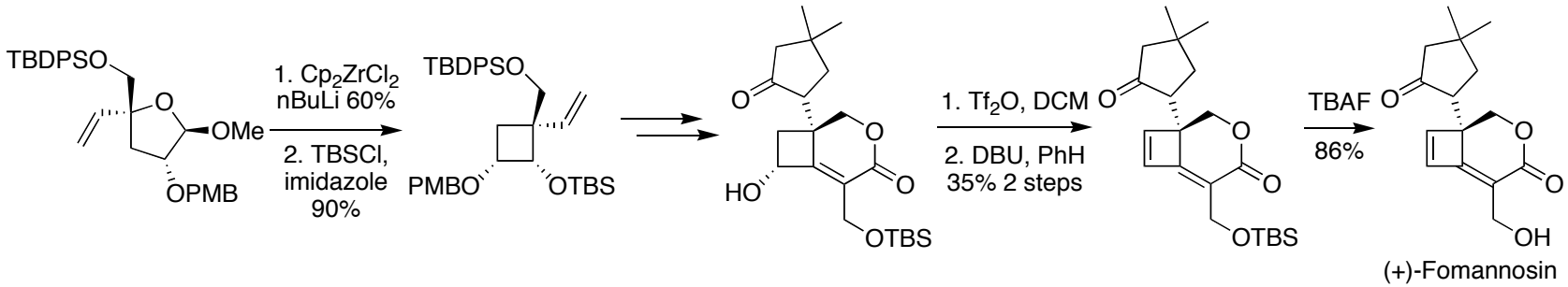
A. Fürstner and C. Aïssa. *J. Am. Chem. Soc.* **2006.** 128, 6306
M. Shi, L.-P. Liu, J. Tang. *J. Am. Chem. Soc.* **2006.** 128, 7430
G.-Q. Tian, Z.-L. Yuan, Z.-B. Zhu, M. Shi. *Chem Commun.* **2008.** 2668

Cyclobutenes in Previous Total Syntheses

Wood (2008)



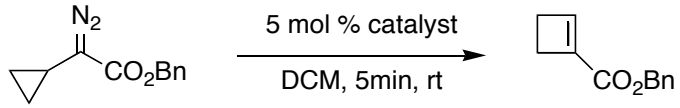
Paquette (2007)



S.E. Reisman, et al *J. Am. Chem. Soc.* **2008.** 130, 2087
L.A. Paquette, X. Peng, J. Yang *Angew. Chem. Int. Ed.* **2007**, 46, 7817

Title Paper - Selection of a Catalyst

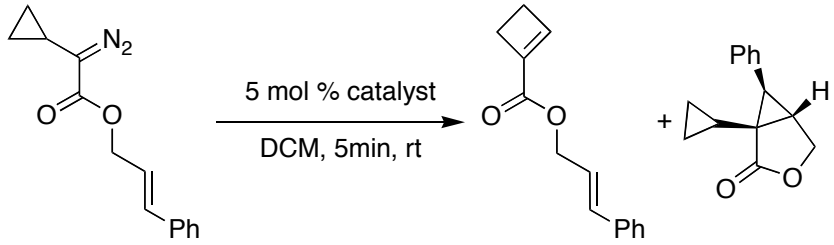
Reactivity:



Entry	Catalyst	Yield[a]
1	$Pd(OAc)_2$	0%[c]
2	$[Ni(cod)_2]$	0%[c]
3	$[AuClPPh_3]$	0%[c]
4	$[RuCl_2(PPh_3)_3]$	0%[c]
5	$[Rh(OAc)_4]$	88%
6	$[Cu(MeCN)_4]PF_6$	80%
7	AgOTf	90% (87% isolated)
8	$[Cu(acac)_2]$[b]	91%

a. Yield by 1H NMR with CH_2Br_2 as internal standard
b. 5 hr reaction time
c. No product by TLC after 5 hrs

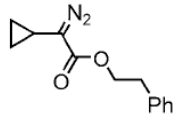
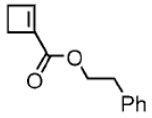
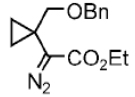
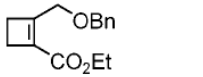
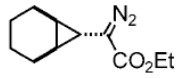
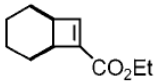
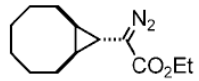
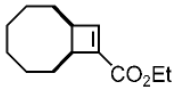
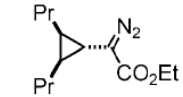
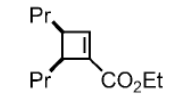
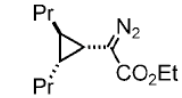
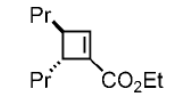
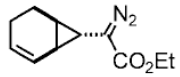
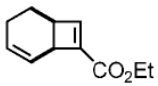
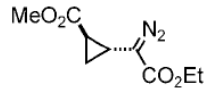
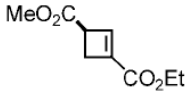
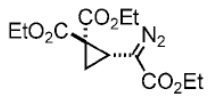
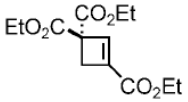
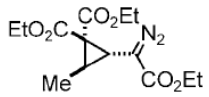
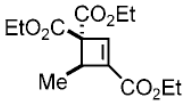
Selectivity:



Entry	Catalyst	Cyclobutene/ Lactone[a]	Yield[b]
1	$[Rh(OAc)_4]$	3:1	91%
2	$[Cu(MeCN)_4]PF_6$	1:0	89%
3	AgOTf	1:0	87%

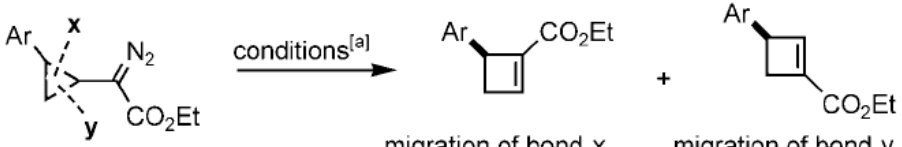
a. Isomeric ratio determined by 1H NMR
b. Isolated yield

Scope of AgOTf Catalyzed Ring Expansion

Cyclopropane		Cyclobutene		Yield	Ratio[b]
3a		**3b**		91%	–
4a		**4b**		77%	–
5a		**5b**		72%	–
6a		**6b**		90%	–
7a		**7b**		71%	single isomer
8a		**8b**		92%	single isomer
9a		**9b**		73%	10:1
10a		**10b**		70%	10:1[c]
11a		**11b**		87%	single isomer
12a		**12b**		77%	single isomer

[a] Conditions: CH_2Cl_2,room temperature, 5 min, 5 mol% AgOTf, unless noted otherwise. Yields given are yields of isolated product. [b] The isomeric ratio was determined by ^1H NMR spectroscopy. [c] −20°C, 30 min.

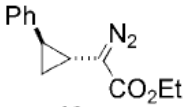
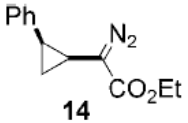
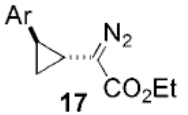
Catalyst Dependant Regioselectivity



13 or **14** (Ar=Ph)
17 (Ar=4-MeOC$_6$H$_4$)

migration of bond x
15
18

migration of bond y
16
19

Cyclopropane	Entry	Catalyst	x/y[b]	Yield
	1	$[Cu(CH_3CN)_4]PF_6$	5:1	–
	2	AgOTf	1:2	–
 **13**	3	$[Rh_2(OAc)_4]$	1:7	–
	4[c,d]	$[Rh_2(octanoate)_4]$	1:9	89%[e]
	5	$[Rh_2(O_2CCPh_3)_4]$	1:4	–
	6	$[Rh_2(O_2CCF_3)_4]$	1:5	–
	7	$[Rh_2(caprolactam)_4]$	1:7	–
	8	heat[f]	2:1	48%[g]
	9[d]	$[Cu(CH_3CN)_4]PF_6$	17:1	93%[e]
 **14**	10	AgOTf	3:1	–
	11	$[Rh_2(OAc)_4]$	1:4	–
	12	heat[f]	1:3	35%[g]
	13	$Ag(O_2CCF_3)$	13:1	–
 **17**	14	$[Cu(CH_3CN)_4]PF_6$	100% **18**	90%[g]
	15	AgOTf	100% **18**	90%[g]
	16	$[Rh_2(OAc)_4]$	1:2	–

[a] CH_2Cl_2, room temperature, 5 min, 10 mol% catalyst, isomeric ratio was determined by ^{1}H NMR spectroscopy, unless noted otherwise. [b] Isomeric ratio of products resulting from the migration of bond x or y. [c] −20°C, 30 min. [d] 5 mol% catalyst. [e] Yield of isolated product. [f] 70°C for 24 h in toluene. [g] Yield determined by ^{1}H NMR spectroscopy in $CDCl_3$, using CH_2Br_2 as the internal standard.

Conclusions

- A transition-metal catalyzed α-cyclopropane ring opening to highly substituted cyclobutenes was developed.
- Chemo- and regioselective conditions were discovered.