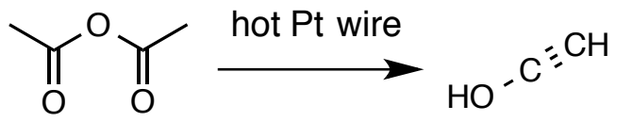
Ketenes

Hai Dao
25/01/2014

Part 1. Introduction

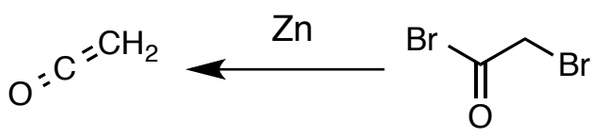
A brief history

1828: Synthesis of urea = the starting point of modern organic chemistry.
1901: Wedekind's proposal for the formation of ketene equivalent (confirmed by Staudinger **1911**)
1902: Wolff rearrangement, Wolff, L. *Liebigs Ann. Chem.* **1902**, *325,* 129.
Wolff adopt a ketene structure in **1912**.
1905: First synthesis and characterization of a ketene: in an efford to synthesize radical **2**, Staudinger has synthesized diphenylketene **3**, Staudinger, H. *et al.*, *Chem. Ber.* **1905**, 1735.
1907-8: synthesis and dicussion about structure of the parent ketene, Wilsmore, *J. Am. Chem. Soc.* **1907**, 1938; Wilsmore and Stewart *Chem. Ber.* **1908**, 1025; Staudinger and Klever *Chem. Ber.* **1908**, 1516.

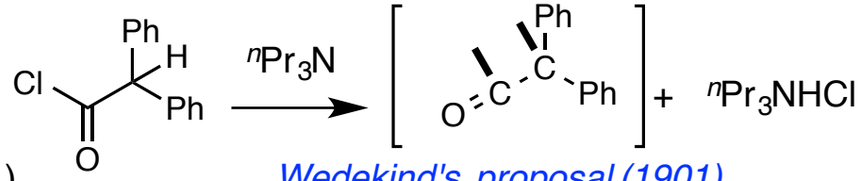


Wilsmore's synthesis and proposal (1907-8)

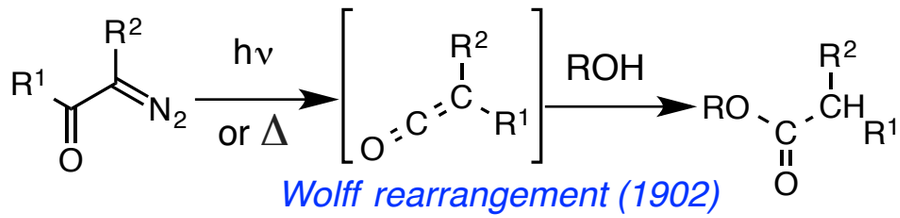
vs.



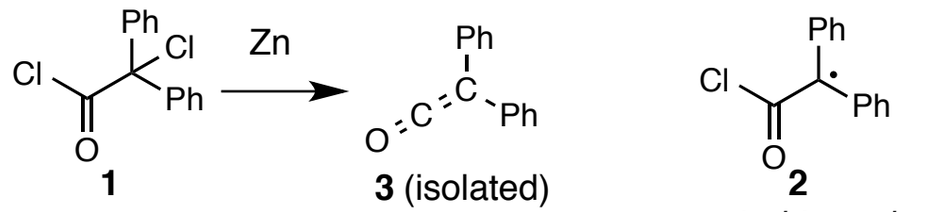
Staudinger's synthesis and proposal (1908)



Wedekind's proposal (1901)



Wolff rearrangement (1902)



1 **3** (isolated) **2**

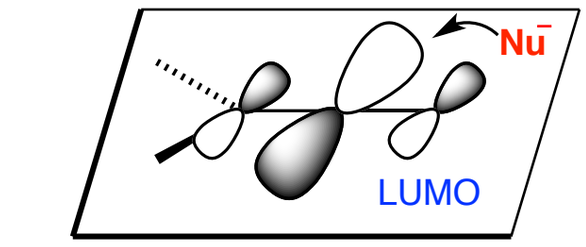
wanted to make

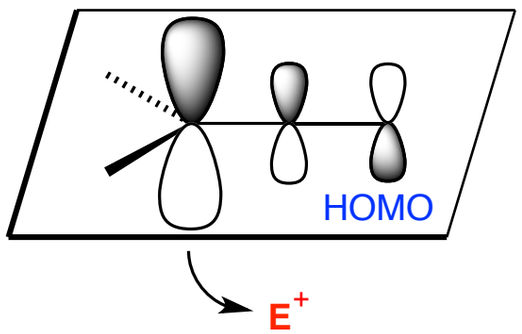
Staudinger's discovery (1905)

Latest books: ketene (Tidwell, **1995**), ketene II (Tidwell, **2006**), Science of Synthesis, *Vol. 23* (**2006**); Latest review: new direactions in ketene chemistry: the land of opportunity (Tidwell *et al.*, *Eur. J. Org. Chem.* **2012**, 1081). Search for ketenes, Google gave 406,000 (*vs.* allenes: 950,000) Jan 23,2014.

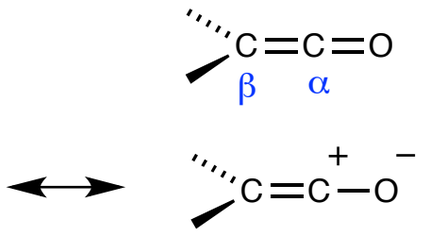
Structure and Physical properties

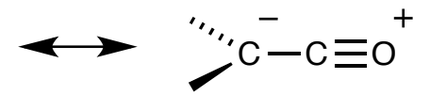
Frontier orbitals



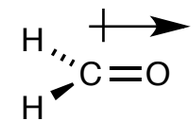


Resonance structure

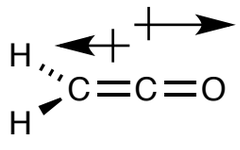




Dipole moment

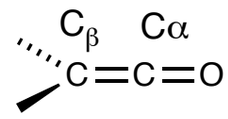


(2.27 D)



(1.45 D)

Spectroscopy data



IR: distinctive absorptions near 2200-2100 cm^{-1} (*vs.* alkene: 1680 cm^{-1}, alkynes: 2200 cm^{-1}; allenes: 1950-1960 cm^{-1}, carbonyl 1760-1665 cm^{-1}).

(IR is frequently used to detect the formation of reactive ketene species)

^{13}C NMR: $\delta_{C\alpha}$ =203-178 ppm; $\delta_{C\beta}$ **= 48-33 ppm**.

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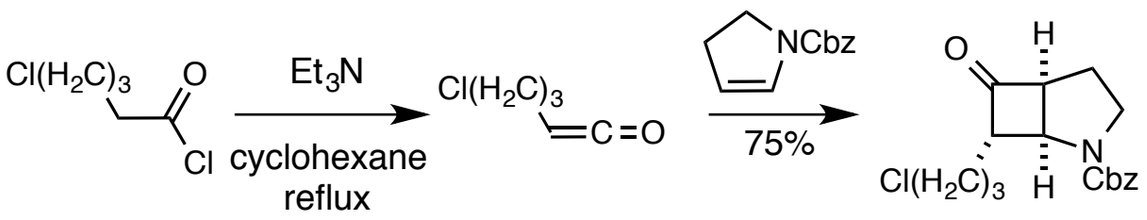
Part 2. Synthesis of Ketenes

Due to its highly reactivity, many ketenes are synthesized *in situ* as intermediates which then react with other reagents to generate products

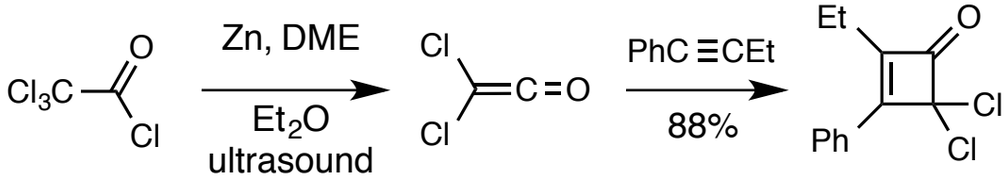
2.1 Ketenes from Carboxylic Acids and Their Derivatives

From Acyl halides and Activated Acids (Wedekind's Method)



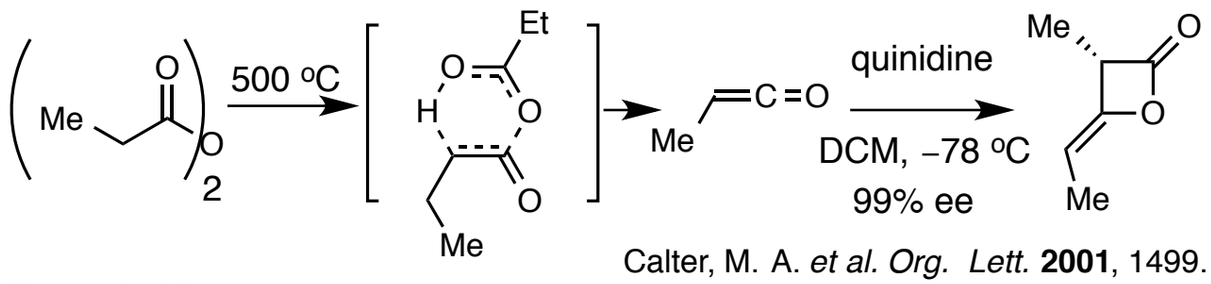
Cevasco, G.; Thea, S. *et al. J. Org. Chem.* **1999**, 5422.

From α-Halo Carboxylic Derivatives (Staudinger's Method)



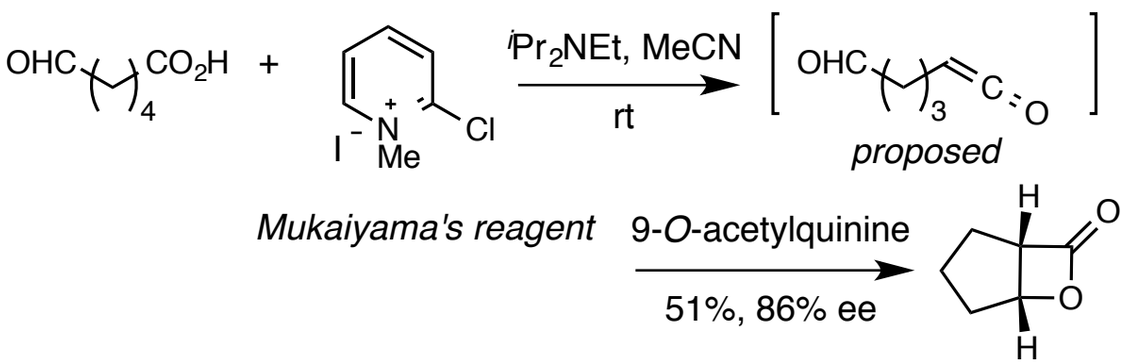
Rizzo, C. J. *et al. Synth. Commun.* **1995**, 2781.

From Acid Anhydrides



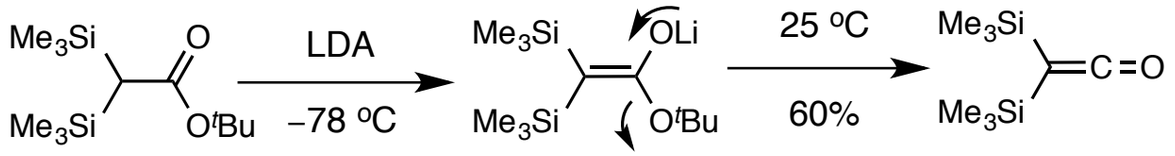
Calter, M. A. *et al. Org. Lett.* **2001**, 1499.

From Acids



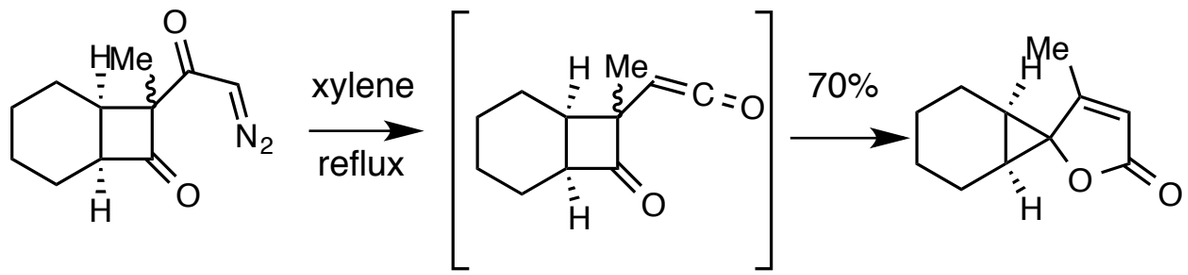
From Esters

E1cB mechanism (crowed esters...) or similar pathway

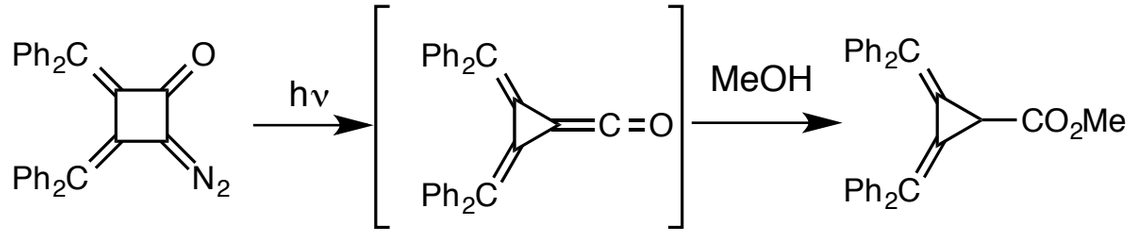


Rethke, M. W. *et al. J. Org. Chem.* **1977**, 2038.

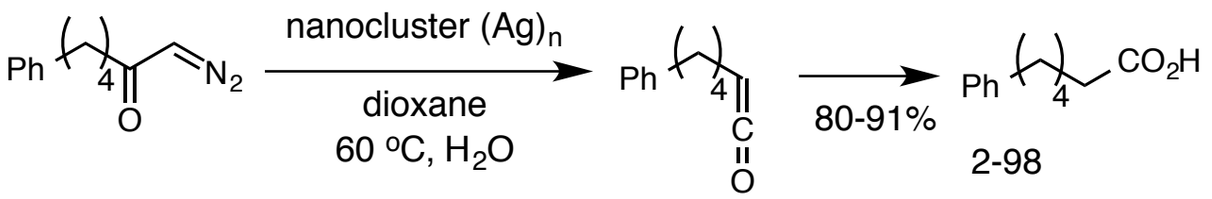
2.2 Ketenes from Diazo Ketones (Wolff's Rearrangement)



Miller, R.D., *et al. J. Org. Chem.* **1991**, 1453



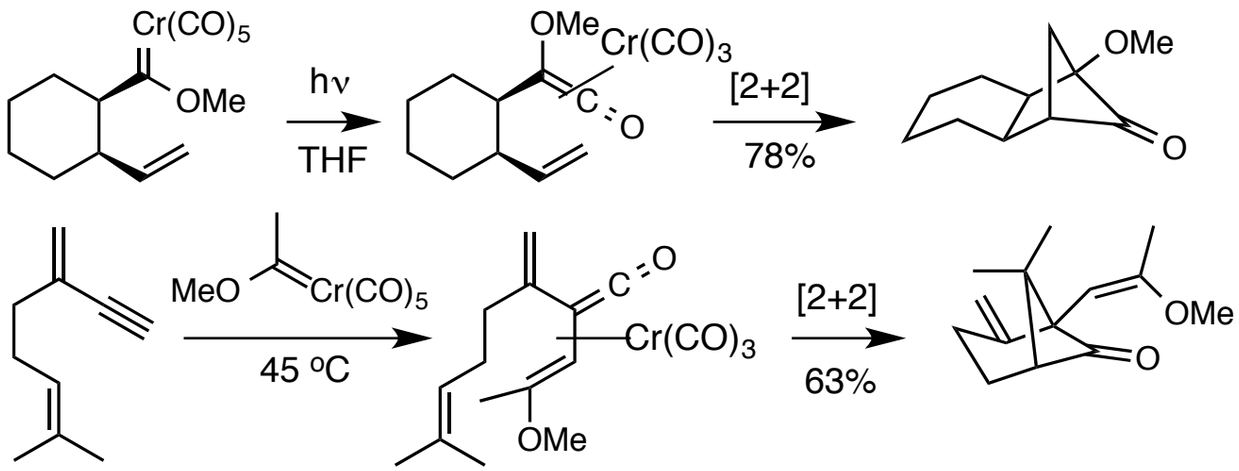
Ueda, K.; Toda, F. *et al. Chem. Lett.* **1975**, 1421.



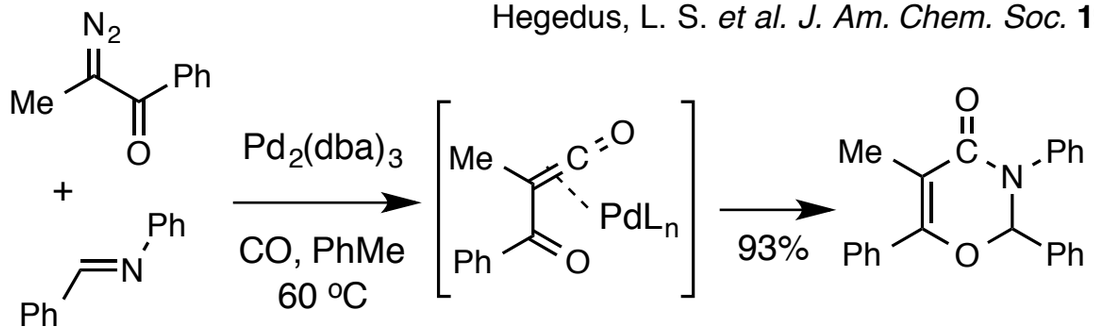
Sudrik, S. G. *et al. Org. Lett.* **2003**, 2355.

other metal catalysts: Ag, Cu, Rh

2.3 Ketenes from Metal Carbene Complexes



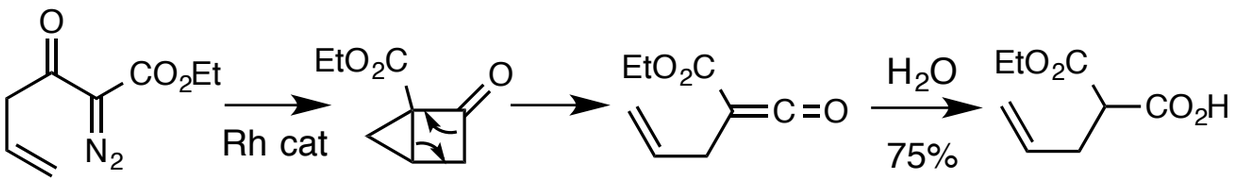
Hegedus, L. S. *et al. J. Am. Chem. Soc.* **1996**, 7873.



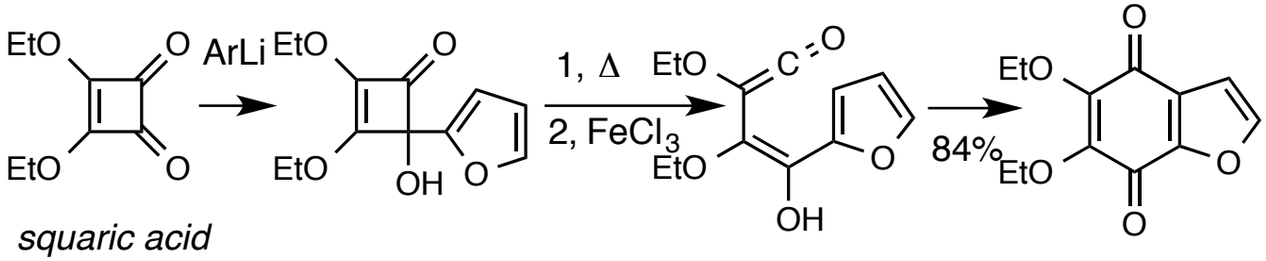
Wang, J. *et al. J. Am. Chem. Soc.* **2011**, 4330.

2.4 Other Methods

From Cyclobutanones and Cyclobutenones



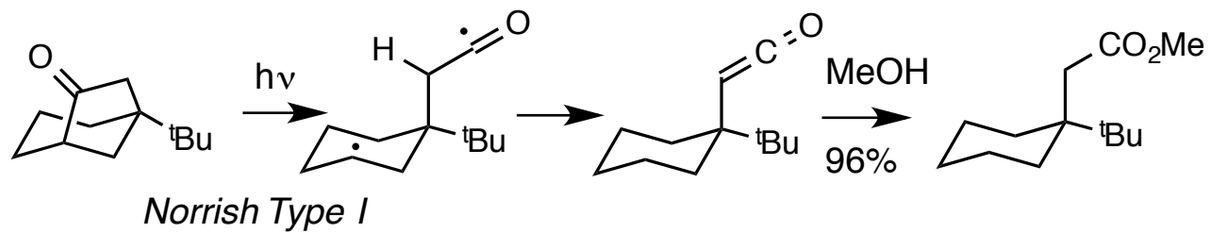
Cai, W. -L. *et al. J. Chem. Soc. Perkin 1* **1996**, 2337.



squaric acid derivative

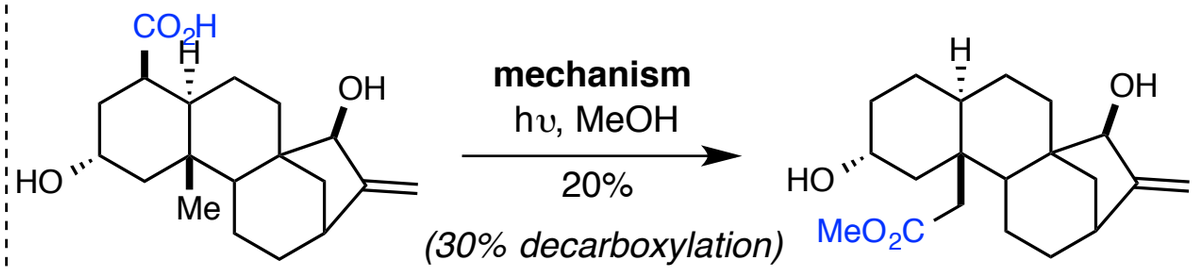
Moore, H. W. *et al. Org. Synth* **1990**, 220.

From Cycloalkanones and Enones through Photolysis



Norrish Type I

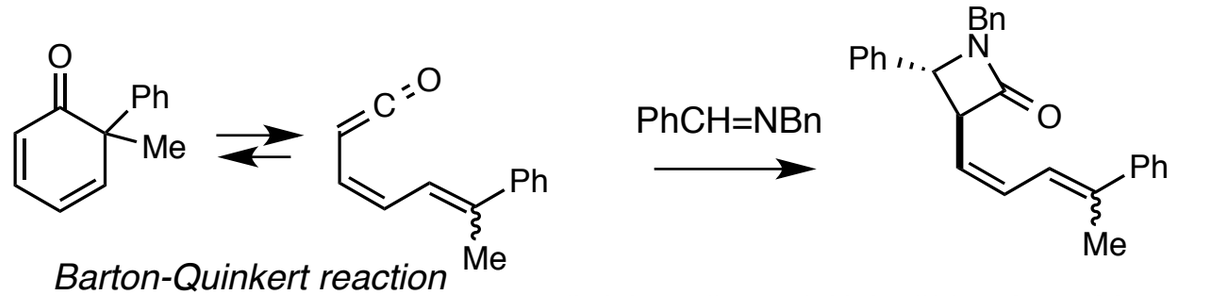
Agosta, W. C.; Wolff, S. *et al. J. Am. Chem. Soc.* **1976**, 4182.



(30% decarboxylation)

Buscemi, S. *et al. Photochem. Photobiol.*, A, **2003**, 145.

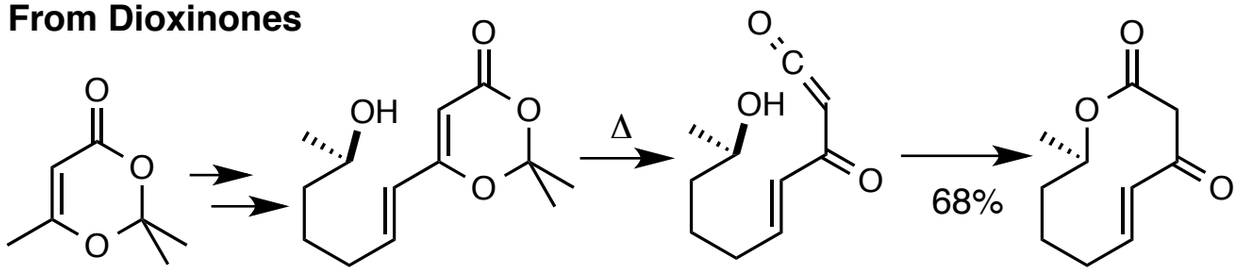
From Cyclohexadienones and Other Cycloalkenones



Barton-Quinkert reaction

Quinkert, G. *et al. Helv. Chim. Acta* **1997**, 1683.

From Dioxinones



comercial available

Boeckmann, R. K. *et al. J. Am. Chem. Soc.* **1989**, 8286.

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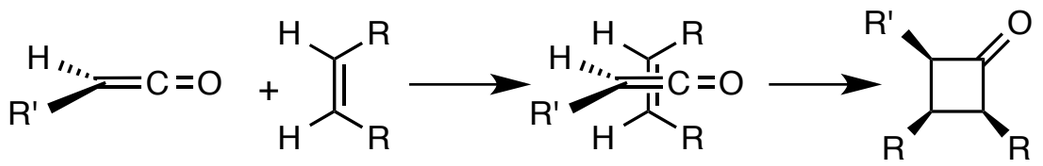
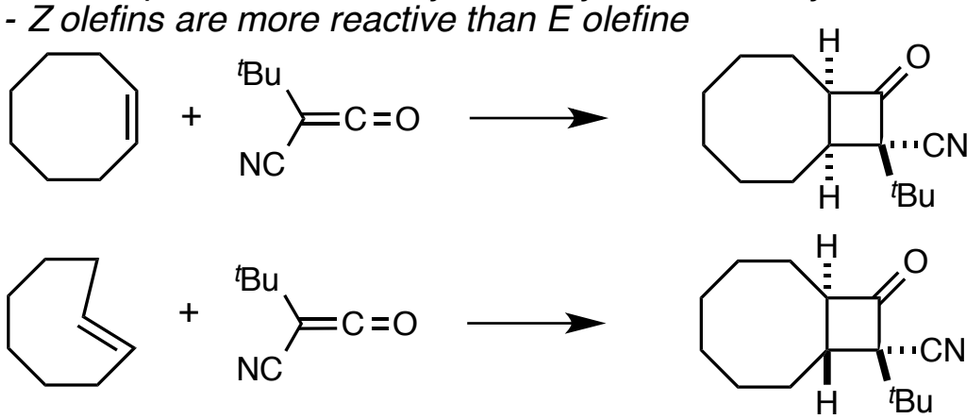
3.1 [2+2] Cycloaddition

Part 3. Reaction of Ketenes

Reaction Mechanism: Concerted [$_\pi 2_s + _\pi 2_a$] vs. Two-step Reaction Involving a Dipolar Intermediate



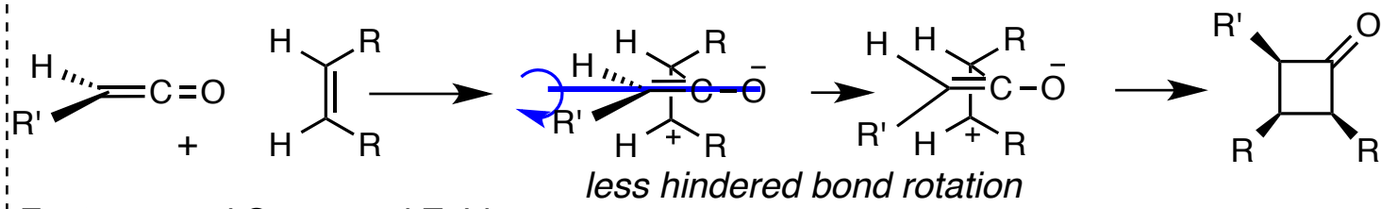
Features and Supported Evidences
- *stereospecific to thermodynamically less stable cyclobutanones*
- *Z olefins are more reactive than E olefine*



Montaigne, R. *et al. Angew. Chem., Int. Ed.* **1968**, 221.

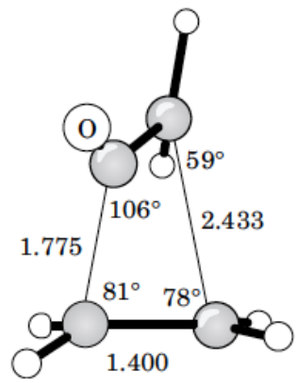
relative reactivity:

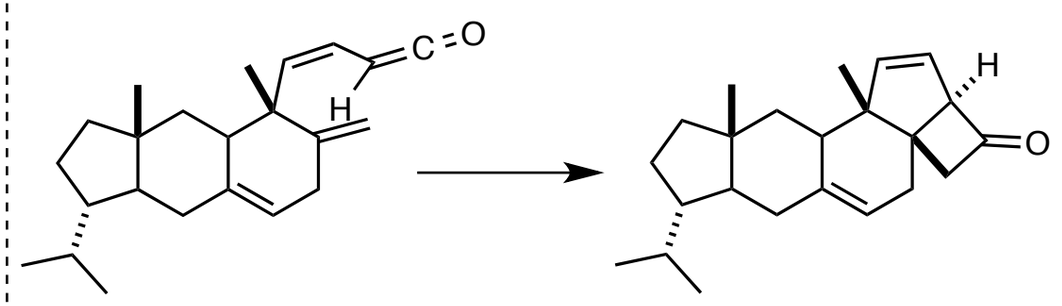
$Cl_2C{=}C{=}O$ > $Ph_2C{=}C{=}O$ > $Me_2C{=}C{=}O$ > $H_2C{=}C{=}O$



less hindered bond rotation

Features and Supported Evidences
- *initial orthogonal approach of the ketene to alkene from the least hindereddirection following by rotation at C2 lead to the same stereochemisty outcome as in concerted mechanism*
- *high level calculation by Houk showed that the forming bond length of the carbonyl carbone is 1.78 Å; the other is 2.43 Å*
- *solvent effects observed (it could be a ground state effect only)*
- *evidence from studies of intramolecular [2+2]*

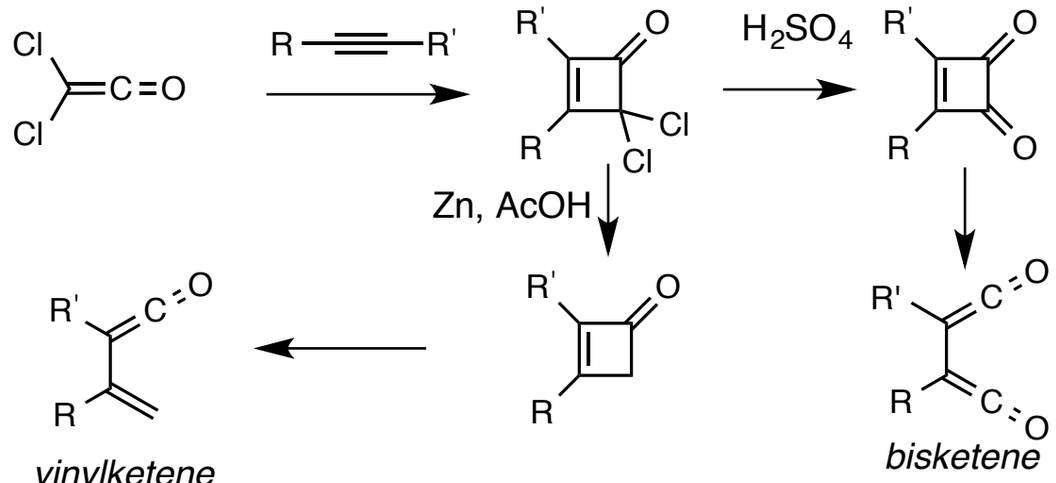




stereochemisty = a net [$_\pi 2_s + _\pi 2_s$]

Retigeranic acid synthesis: Corey, E. J. *et al. J. Am. Chem. Soc.* **1985**, 4339.

[2+2] Cycloaddition with Alkynes

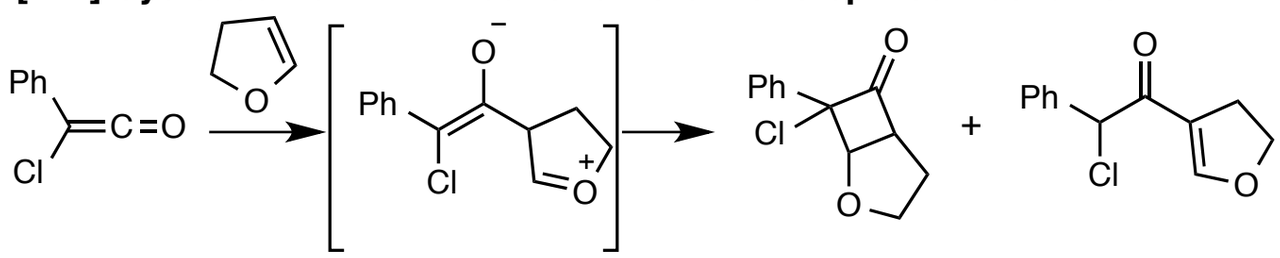


vinylketene

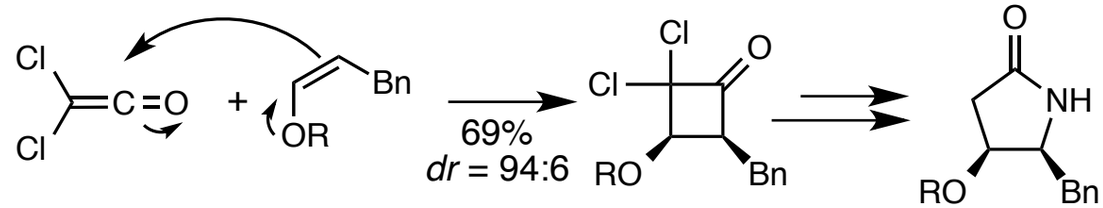
bisketene

Danheiser, R. L. *et al. Tetraherdon Lett.* **1987**, 3299;
Ammann, A. A. *et al. Helv. Chim. Acta* **1987**, 321.

[2+2] Cycloaddition with Electrorich Olefins: Stepwise Mechanism



Reynolds, P. W. *et al. J. Am. Chem. Soc.* **1984**, 4566.



Kanazawa, A. *t al. J. Org. Chem.* **1998**, 4660.

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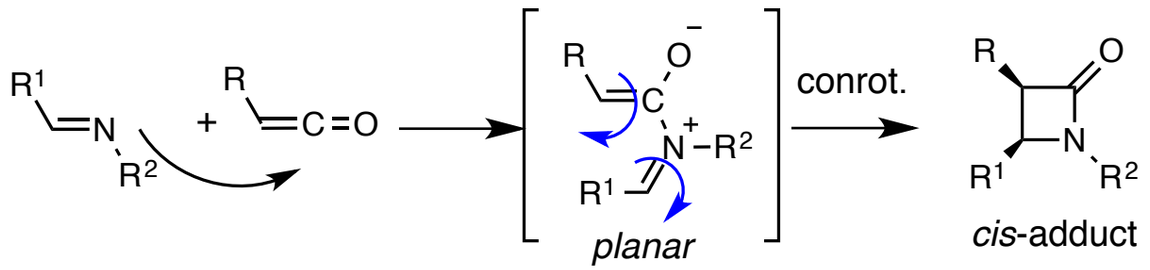
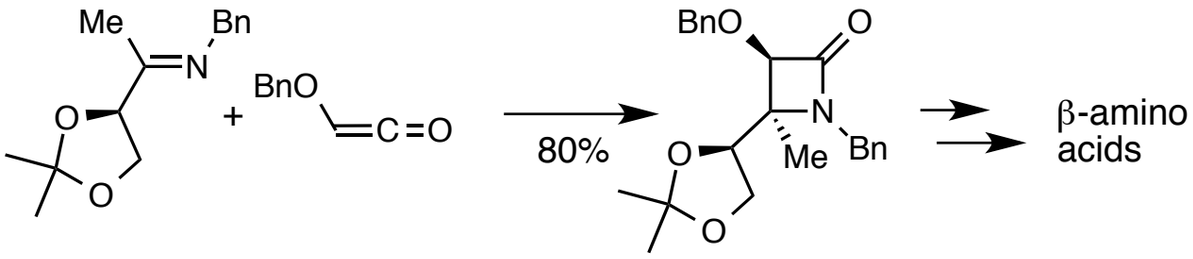
[2+2] Cycloaddition with Imines: Staudinger Ketene-Imine Cycloaddition

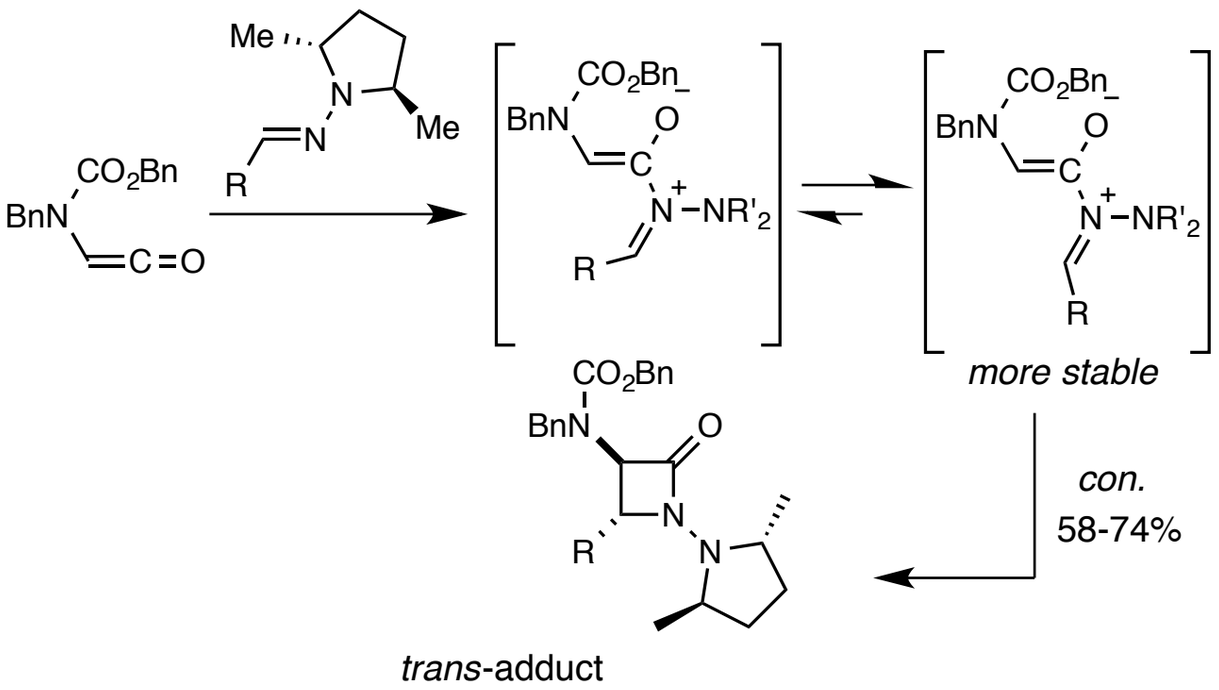
uncatalyzed mechanism: stepwise formation of zwitterion followed by contotatory ring closure to give cis-product



Arrieta, A. *et al. J. Org. Chem.* **1998**, 5869.

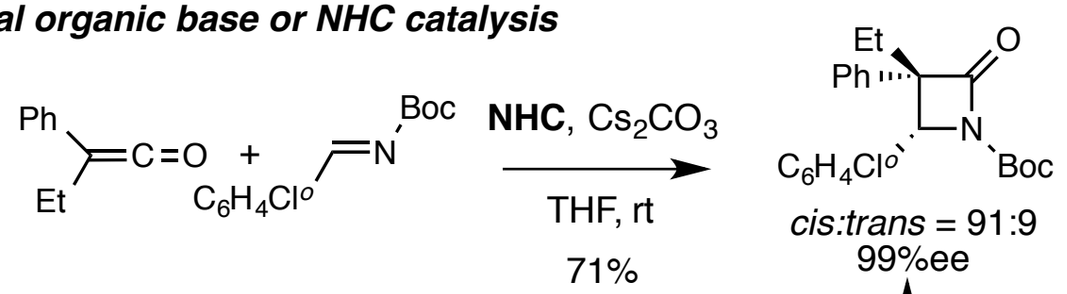


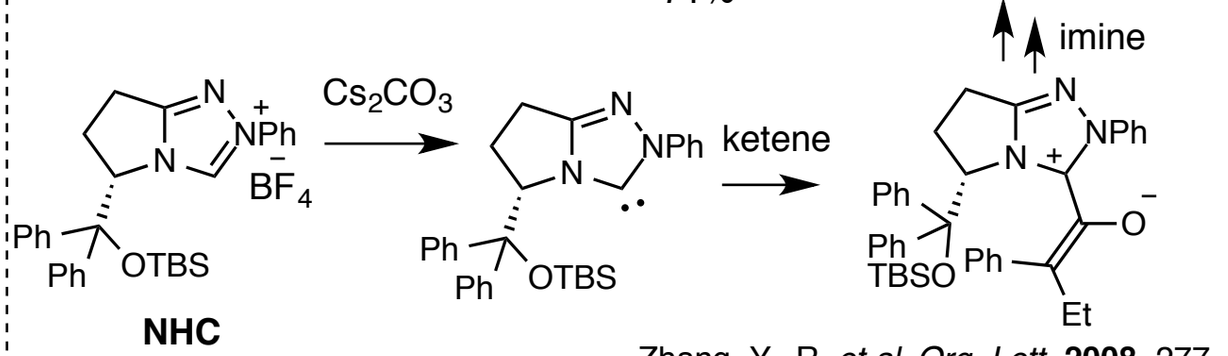
Palomo, C. *et al. Chem. Commun.* **1996**, 1269.



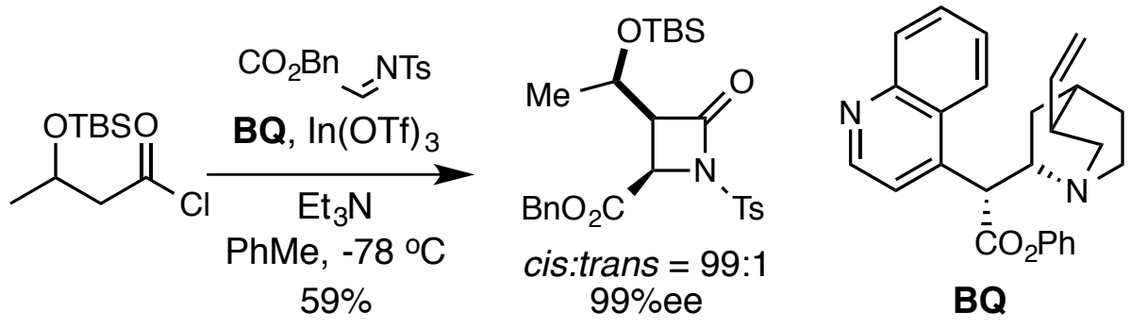
Diez, E. *et al. Org. Lett.* **2004**, 2749.

chiral organic base or NHC catalysis



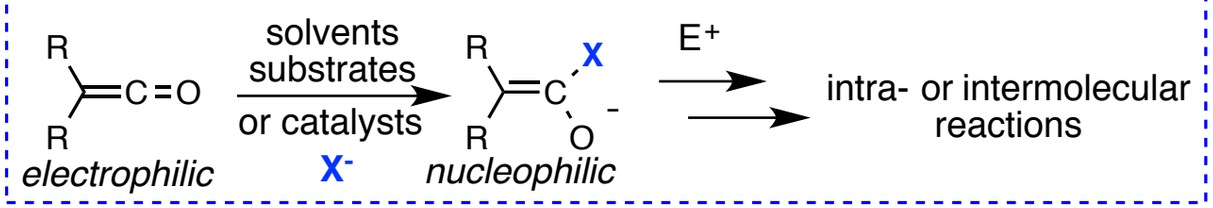


Zhang, Y. -R. *et al. Org. Lett.* **2008**, 277.



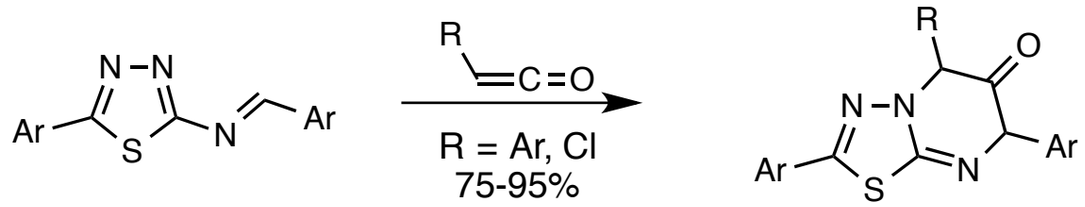
Townsend, C. A. *et al. Org. Lett.* **2009**, 3609.

general reaction mode (apart from concerted [$_{\pi}2_{s}+_{\pi}2_{a}$]):



3.2 Other Cycloadditions

Formal [4+2] Cycloaddition: with electro-deficient dienes



Dutta, B. C. *et al., Chem. Res. (S)* **1999**, 36.

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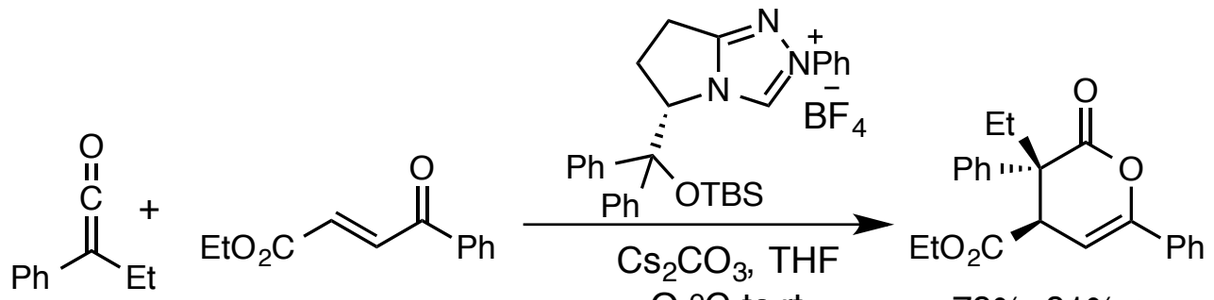
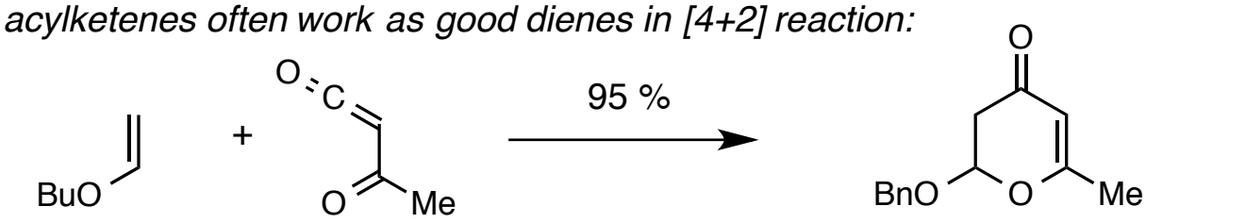


Zhang, Y. -R. *et al. Chem. Eur. J.* **2008**, 8473.

acylketenes often work as good dienes in [4+2] reaction:



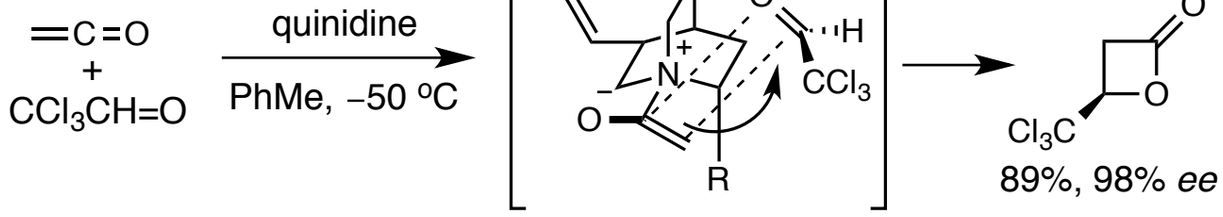
electron rich olefin from dioxinone

Coleman, R. S. *et al. J. Org. Chem.* **1993**, 385.

Cycloaddition with Carbonyl Groups

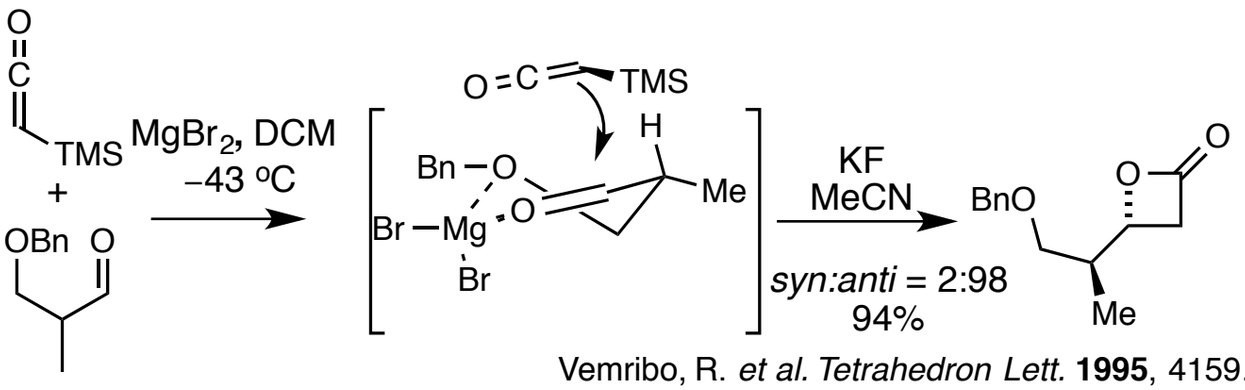
ketenes undergo [2+2] cycloaddition with electrophilic carbonyl group:

Amine base catalyzed reactions



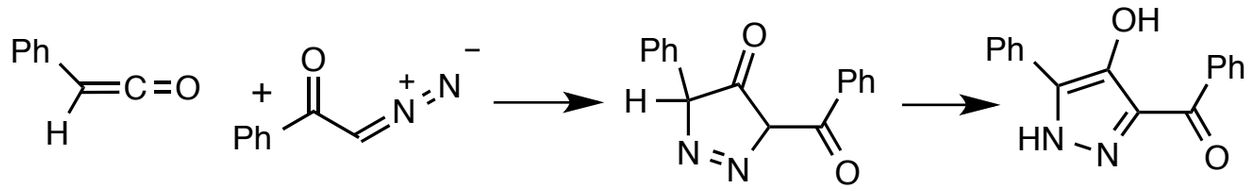
Wynberg, H. *et al. J. Org. Chem.* **1985**, 1977.

Lewis acid catalyzed reactions



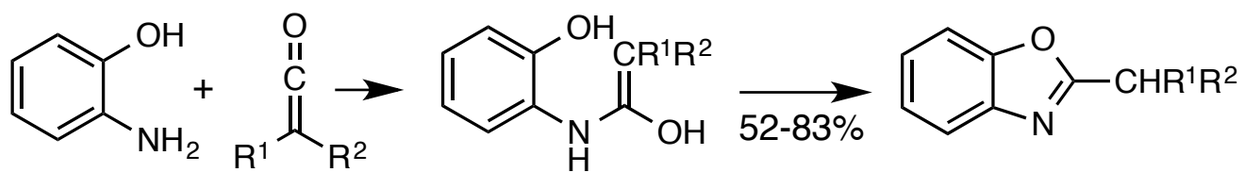
Vemribo, R. *et al. Tetrahedron Lett.* **1995**, 4159.

[3+2] Cycloaddition

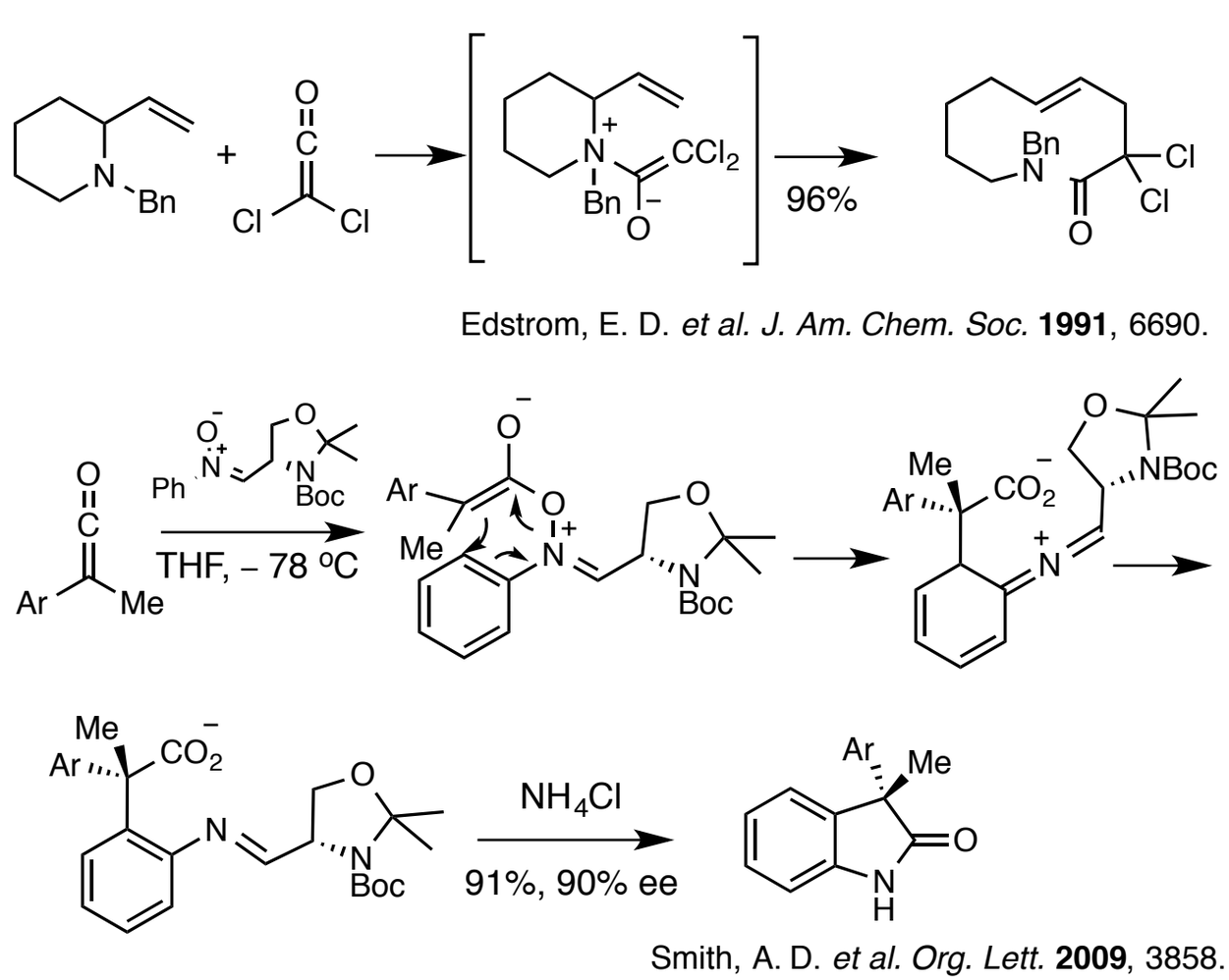


3.3 Other Reactions

Nucleophilic Addition and/or Rearrangement



Olagbemiro, R. O. *et al. Recl. Trav. Chim. Pays-Bas* **1995**, 337.



Edstrom, E. D. *et al. J. Am. Chem. Soc.* **1991**, 6690.

Smith, A. D. *et al. Org. Lett.* **2009**, 3858.

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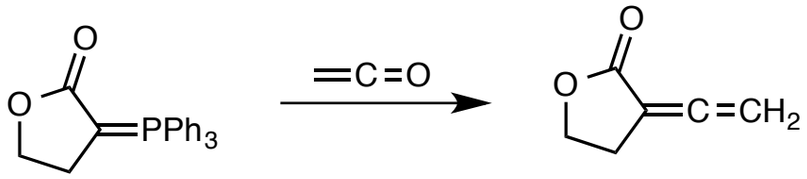
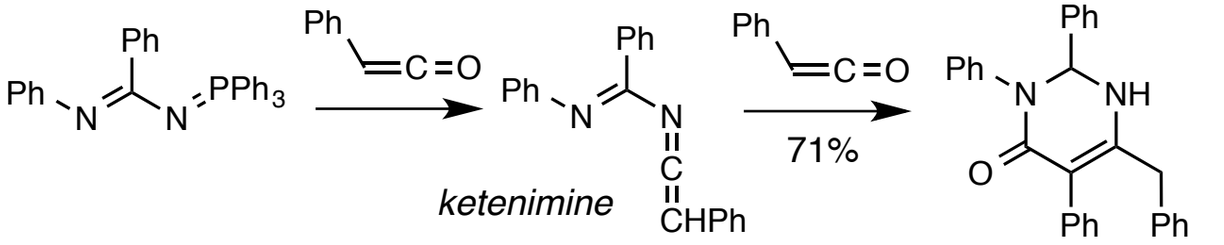
Wittig Reaction

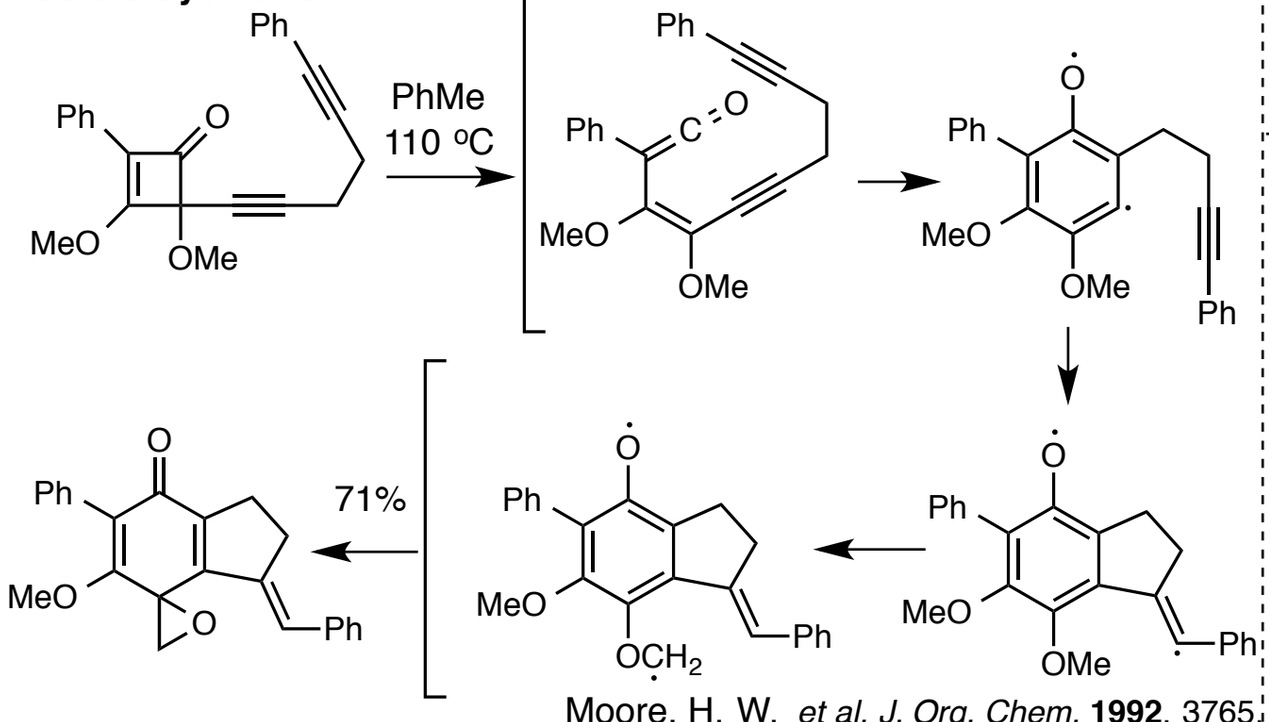


Buono, G. *et al. Tetrahedron Lett.* **1990**, 4859.



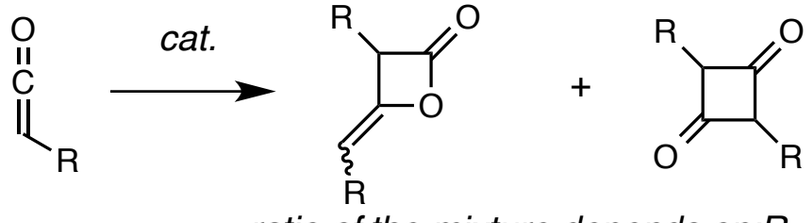
Molina, P. *et al. Tetrahedron Lett.* **1991**, 4041.

Moore's Cyclization



Moore, H. W. *et al. J. Org. Chem.* **1992**, 3765.

dimerization

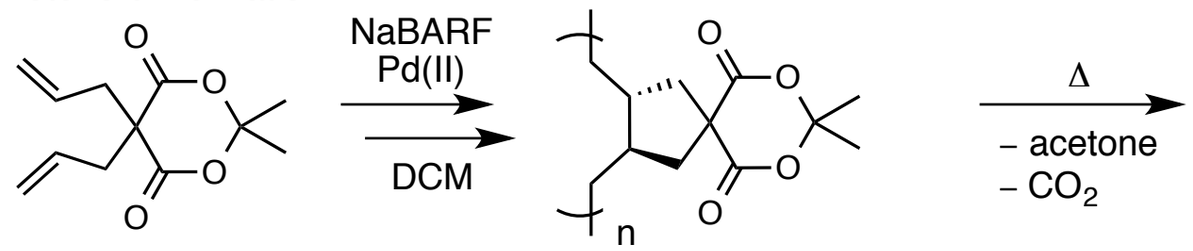


ratio of the mixture depends on:R, cat.

Clemens, R. J. *et al. Chem. Rev.* **1986**, 241.

Ketenes in Polymer Chemistry

New approach for polimer modification: polymer crosslinking through ketene dimerization

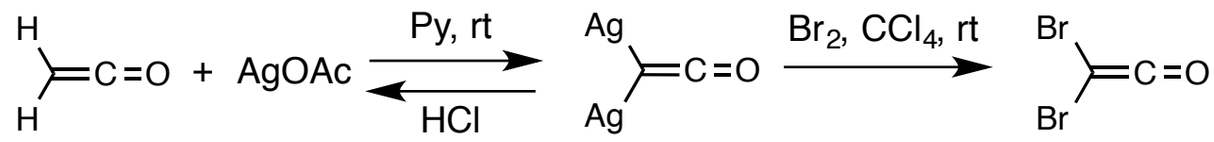


Meldrum's acid derivatives

used for printing submicrometer-scale patterns for microcontact printing

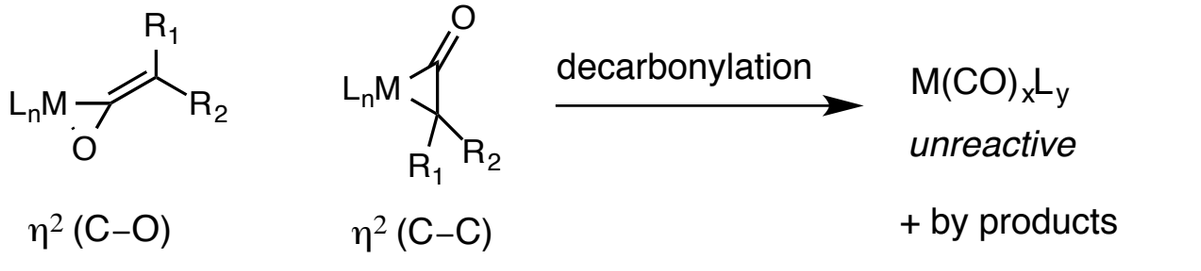
Aida, T. *et al. J. Am. Chem. Soc.* **2011**, 2840.

Organometallic Compounds



Silver ketenide
X-ray structure

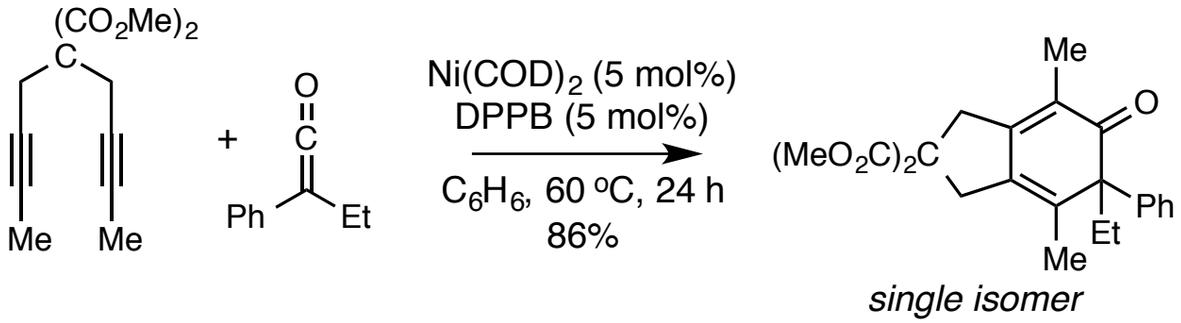
Blues, E. T. *J. Chem. Soc. Perkin Trans. 2*, **1993**, 1631



η^2 (C–O) η^2 (C–C)

modes of ketene coordination with transition metals

To develop the transition metal catalyzed-reaction with ketenes, it is crucial to find the right ligands to stablize the ketene-metal complexes

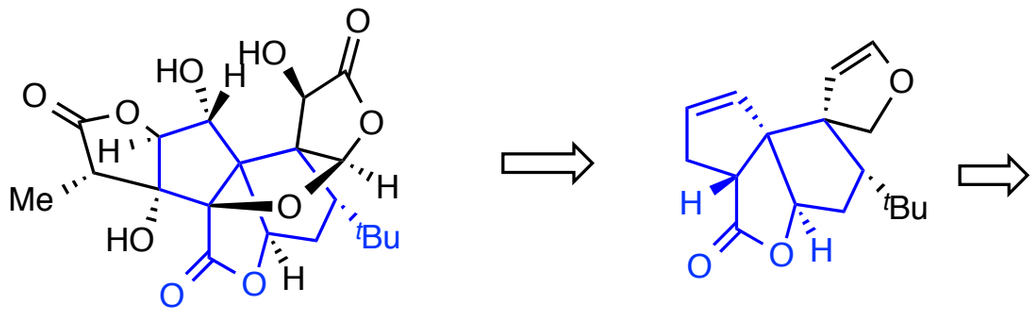


single isomer

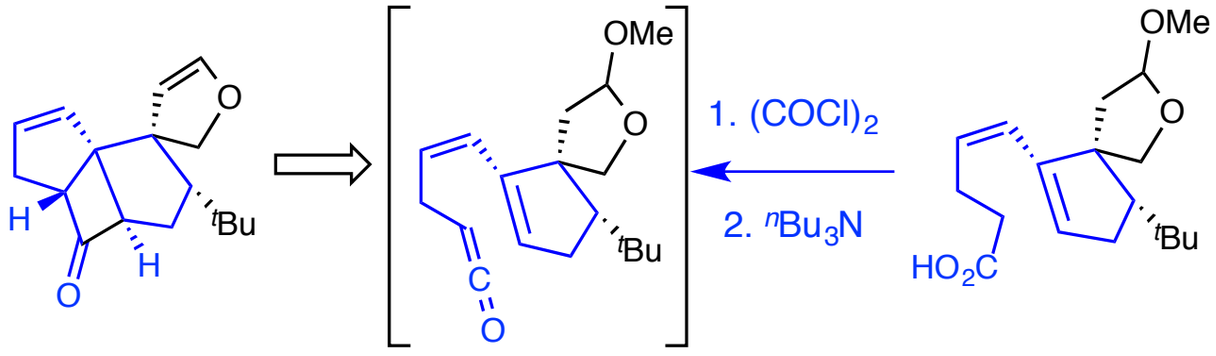
Louie, J. *et al. J. Am. Chem. Soc.* **2011**, 7719.

Part 4. Ketenes in Synthesis

Ginkgolide Synthesis

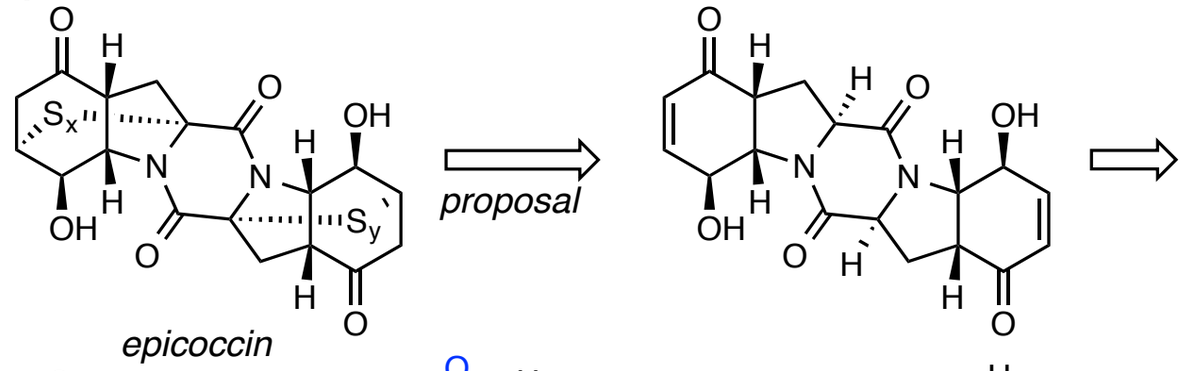


ginkgolide B

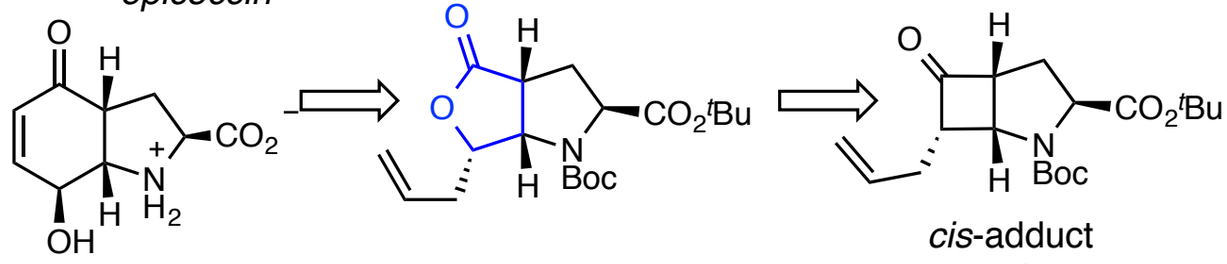


Corey *et al. J. Am. Chem. Soc.* **1998**, 649.

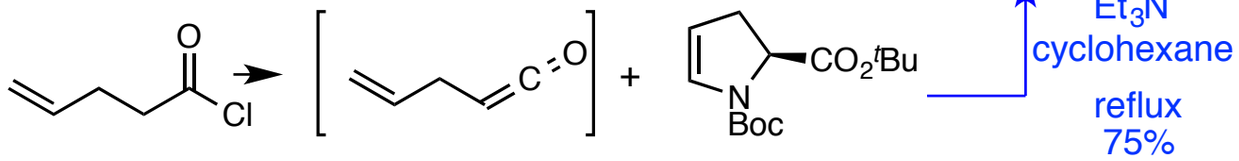
Epicoccins



epicoccin

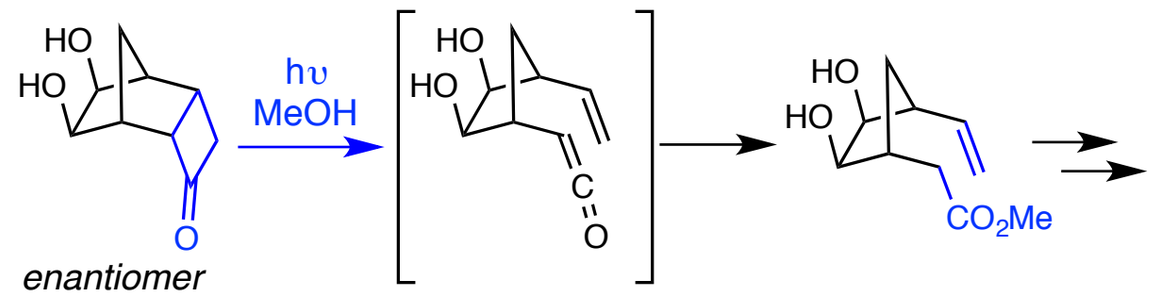


cis-adduct

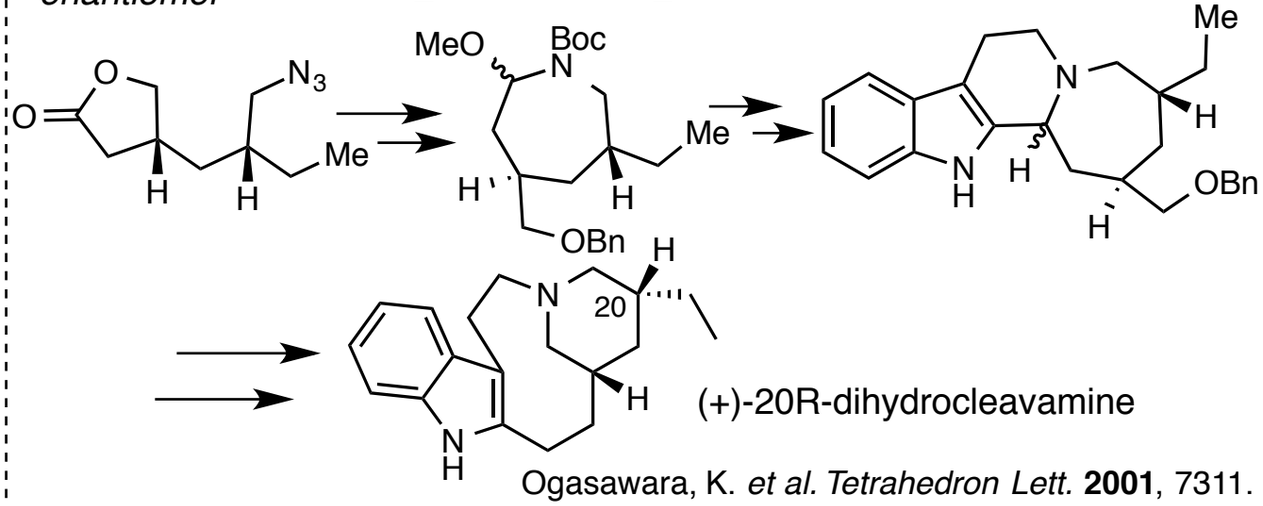


Brase, S *et al. Chem. Eur. J.* **2010**, 11624.

(+)-20R-dihydrocleavamine



enantiomer



Ogasawara, K. *et al. Tetrahedron Lett.* **2001**, 7311.

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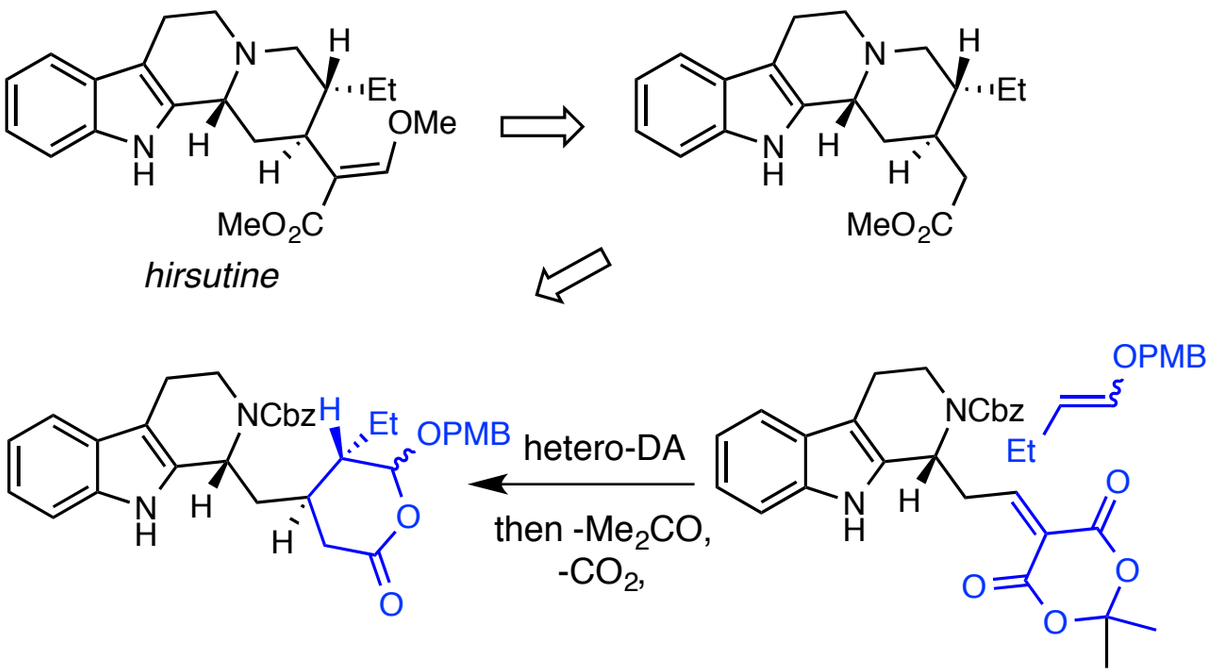
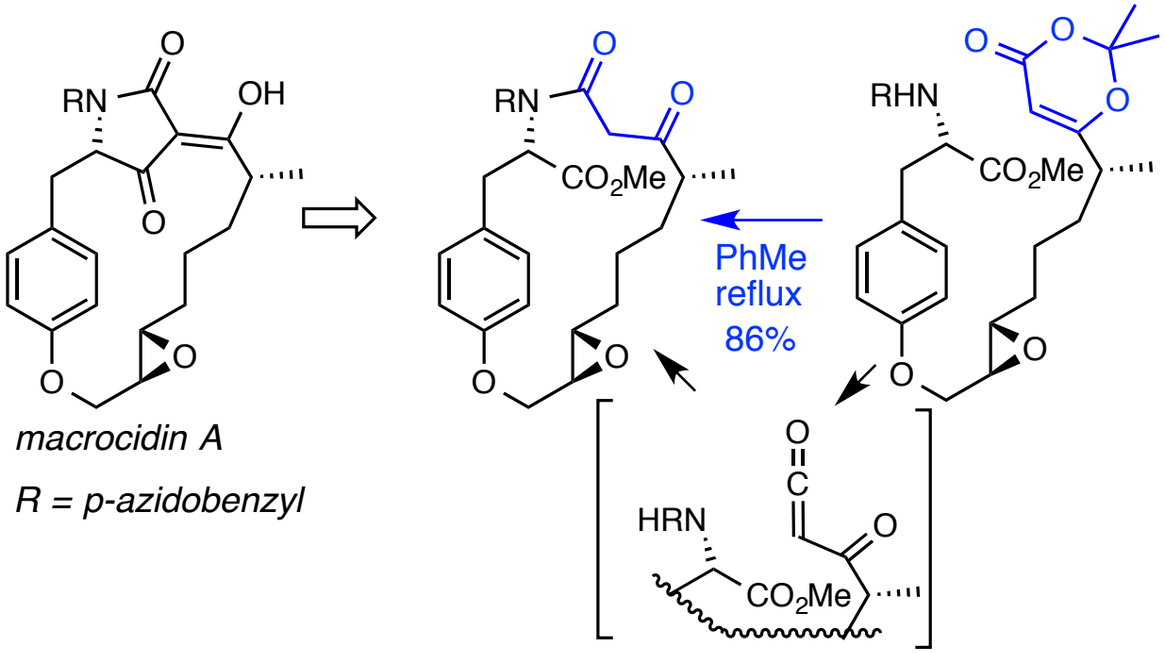
Hirsutine Synthesis



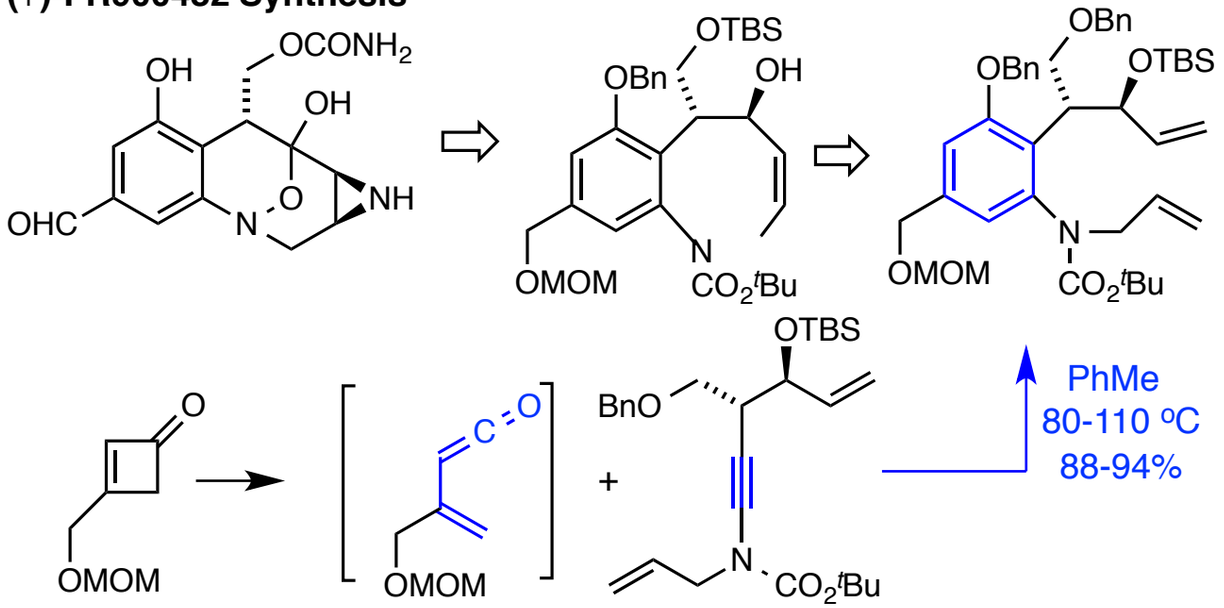
Tietze, L. F. *et al. Angew. Chem. Int. Ed.* **1999**, *38*, 2045.

Macrocidin Synthesis



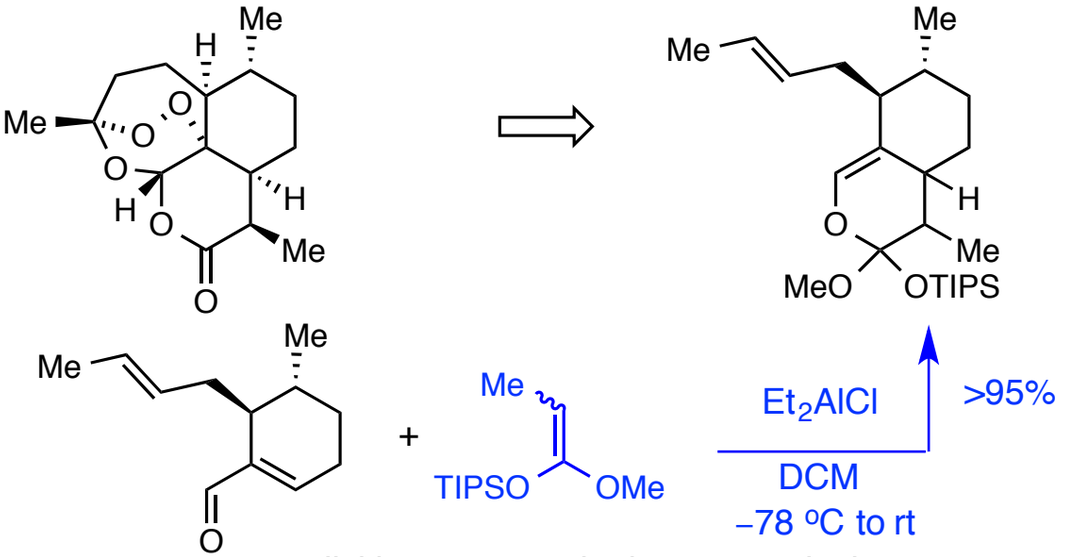
Hoye, T. R. *et al. J. Org. Chem.* **2010**, 7052.

(+)-FR900482 Synthesis



Danheiser, R. L. *et al. J. Org. Chem.* **2011**, 1852.

(+)-Artemisinin Synthesis



silyl ketene acetal = ketene equivalence

Cook. S. P. *et al. J. Am. Chem. Soc.* **2012**, 13577.

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1. Ketenes; Thomas T. Tidwell , John *Wiley and Sons*, **1995**.
2. Ketenes II; Thomas T. Tidwell , John *Wiley and Sons*, **2006**.
3. Science of Synthesis, *Vol. 23* (**2006**)
4. New Directions in Ketene Chemistry: The Land of Opportunity, Tidwell, T. T. *et al. Eur. J. Org. Chem.* **2012**, 1081.