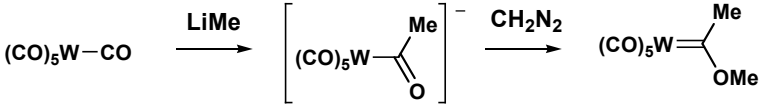
Fischer Carbene Complexes in Organic Synthesis

Ke Chen

Ernst Otto Fischer (1918 -)

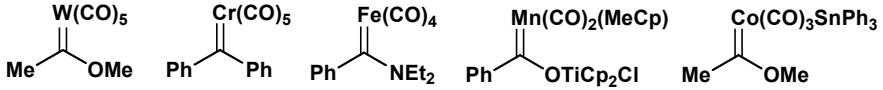
German inorganic chemist. Born in Munich on November 10, 1918. Studied at Munich Technical University and spent his career there. Became director of the inorganic chemistry institute in 1964. In the 1960s, discovered a metal alkylidene and alkylidyne complexes, referred to as Fischer carbenes and Fischer carbynes. Shared the Nobel Prize in Chemistry with Geoffery Wilkinson in 1973, for the pioneering work on the chemistry of organometallic compounds.

Isolation of first transition-metal carbene complex:



E. O. Fischer, A. Maasbol, *Angew. Chem. Int. Ed.,* **1964,** *3*, 580.

Representative Fischer Carbenes:



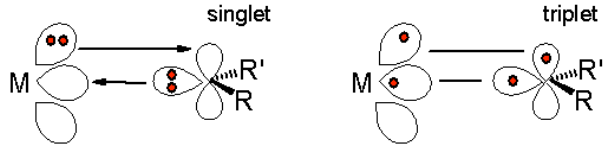
Fischer carbenes are found with :

low oxidation state metals;
middle and late transition metals Fe(0), Mo(0), Cr(0), W(0);
pi-electron acceptor metal ligands;
pi-donor substituents on methylene group such as alkoxy and amino groups.

Other Types of Stabilized Carbenes:

Schrock carbene, named after Richard R. Schrock, is nucleophilic at the carbene carbon atom in an unpaired triplet state.

Comparision of Fisher Carbene and Schrock carbene:



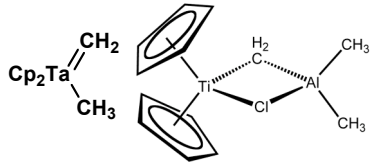
Fischer Schrock

Schrock carbenes are found with:

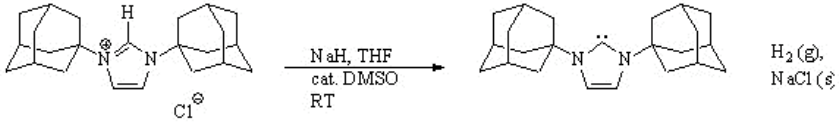
high oxidation states
early transition metals Ti(IV), Ta(V)
non pi-acceptor ligands
non pi-donor substituents

A.B. Charette *J. Am. Chem. Soc.* **2001**, *123*, 11829.

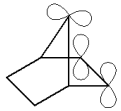
Representatives:



Persistent carbenes, isolated as a crystalline solid by Anthony J. Arduengo in 1991, can exist in the singlet state or the triplet state.



Foiled carbenes were defined as "systems where stabilization is obtained by the inception of the facile reaction which is foiled by the impossibility of attaining the final product geometry". They only exist in the singlet state.



Rolf Gleiter, Ronald Hoffman *J. Am. Chem. Soc.* **1968**, *90,* 5457 - 5460.
Jean-Luc Mieusset and Udo H. Brinker *J. Am. Chem. Soc.* **2006**, *128,* 15843 - 15850.

Fischer Carbene Complexes in Organic Synthesis

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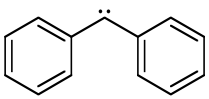
Advantages over regular carbenes
- From fleeting intermediates to powerful reagents

1. Improved stability

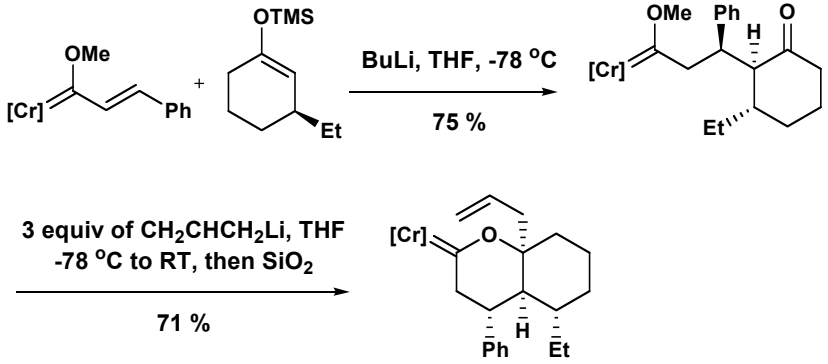
Typical carbenes such as diphenyl carbene have lifetimes in the nanosecond regime.



Most Fischer carbene complexes are stable to air and water and to dilute acids and bases. Despite the high dipole moment of these complexes (~ 4 - 5 Debye), most complexes can be purified by chromatography on silica gel with hexane as eluent and are usually the first compounds to elute. Identification of the fractions from the column containing the carbene complex can simply be done by eye on the basis of their color. The colors of complexes bearing alkoxy groups as the heteroatom-stabilizing group tend to correlate with the hybridzation of the carbon substituent of the carbene carbon. Those with sp_3 carbons usually are yellow, those with sp_2 carbons are normally red and those with sp hybridized carbon substituents are invariably an intense purple/black color.

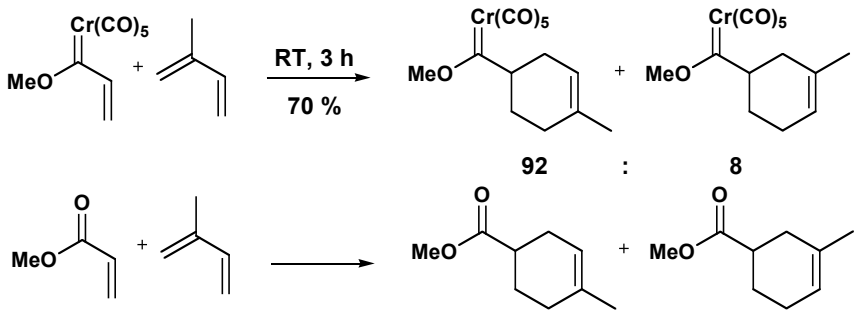
http://www.chemistry.msu.edu/faculty/wulff/myweb$_{26}$/research/carbenes.htm

2. Excellent functional group compatibility - serving as blocking groups in organic synthesis.



J. Barluenga. *J. Am. Chem. Soc.* **2002**, *124*, 9056 -9057.

3. Improved reactivity and selectivity



thermal conditions: RT, 7 months, 54 %	70	:	30
$AlCl_3$, 0.5 h , 50 %	95	:	5

W. Wulff. *J. Am. Chem. Soc.* **1990**, *112*, 3642.

Fischer Carbene Complexes in Organic Synthesis

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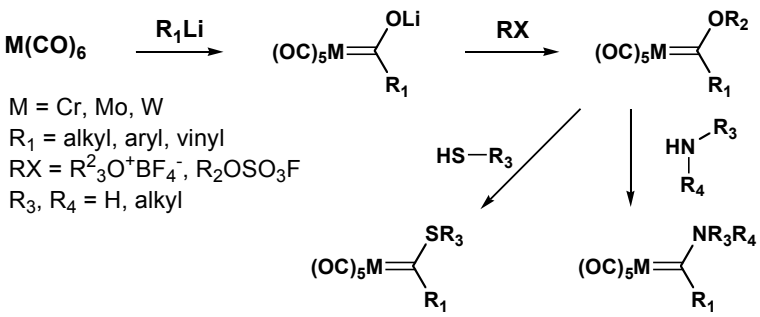
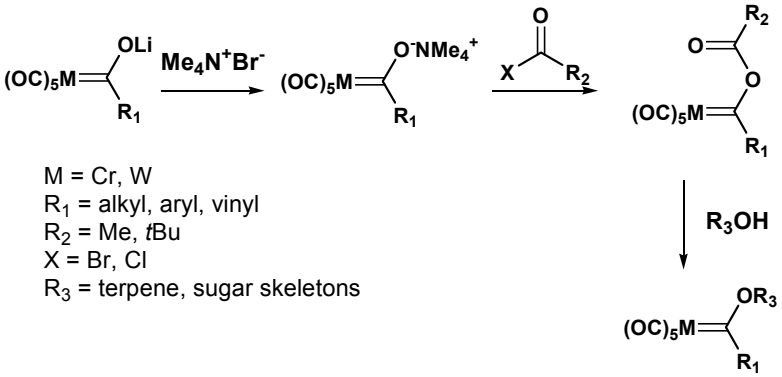
Synthesis of Fischer carbene complexes:

1. Standard Fischer route



M = Cr, Mo, W
R_1 = alkyl, aryl, vinyl
RX = $R^2{}_3O^+BF_4^-$, R_2OSO_3F
R_3, R_4 = H, alkyl

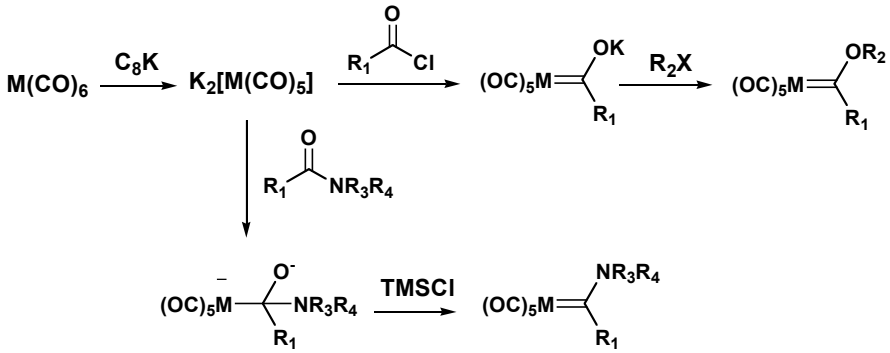
This is the most direct and general approach to Fischer carbene complexes;
Limitations are the availability of organolithium compound and the alkylation reagent.



M = Cr, W
R_1 = alkyl, aryl, vinyl
R_2 = Me, *t*Bu
X = Br, Cl
R_3 = terpene, sugar skeletons

This is the standard approach to optically active Fischer carbene complexes bearing alkoxy substituents.

2. Hegedus-Semmelhack approach



M = Cr, W
R_1 = alkyl, aryl, vinyl
R_2X = $R^2{}_3O^+BF_4^-$, R_2OSO_3F
R_3, R_4 = H, alkyl

This strategy combining an organoelectrophile and a metal nucleophile can be extended to the synthesis of aminocarbene complexes.

Recent reviews:

W. D. Wulff, in *Comprehensive Organometallic Chemistry II*, ed. A. W. Abel, F. G. A. Stone and G. Wilkinson, pergamon Press, Oxford, 1995, vol. 12, p. 469
L. S. Hegedus, *ibid.*, vol. 12, p. 549.

Fischer Carbene Complexes in Organic Synthesis

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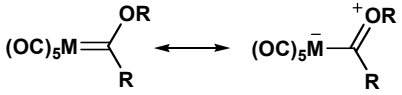
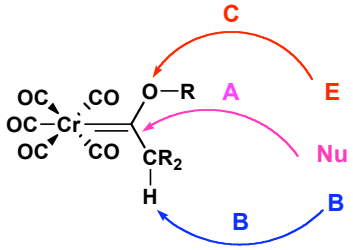
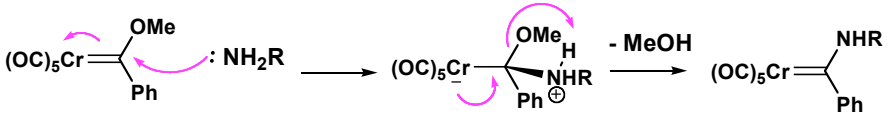
Reaction pattern of carbene complexes:

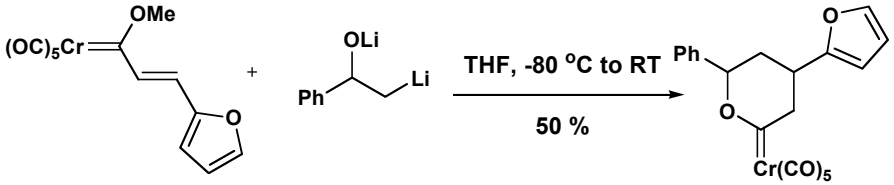
Part I: Ligand-centered



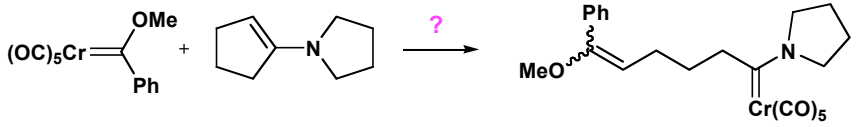


Pattern A: Addition of nucleophiles





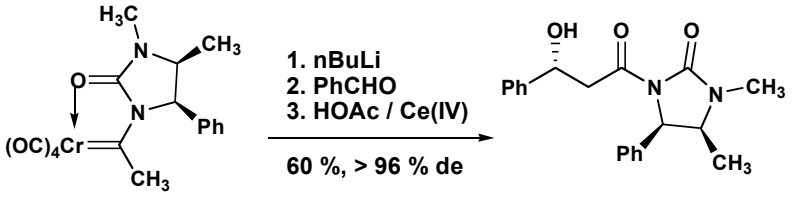
J. Barluengal, *J. Chem. Soc., Chem. Commun.* **1993**, 1068



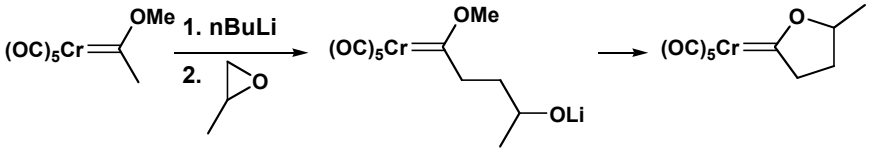
H. Fischer, *Chem. Ber.* **1980**, *113*, 193

Pattern B: Bond formation via metal carbene anions

pKa = 12 **pKa = 25**

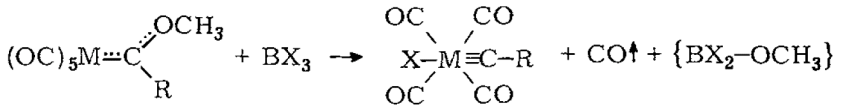


W. Wulff, *J. Org. Chem.*, **1994**, 6882.



B. A. Anderson, *J. Am. Chem. Soc.*, **1993**, *115*, 4602.

Pattern C: Transformation of metal carbenes to metal carbynes



M = Cr, Mo, W; R = CH_3, C_6H_5; X = Cl, Br, I

For reviews on reaction pattern of carbene complexes, see "Carbene Chemistry : From Fleeting Intermediates to Powerful Reagents", chapter 8.

Fischer Carbene Complexes in Organic Synthesis

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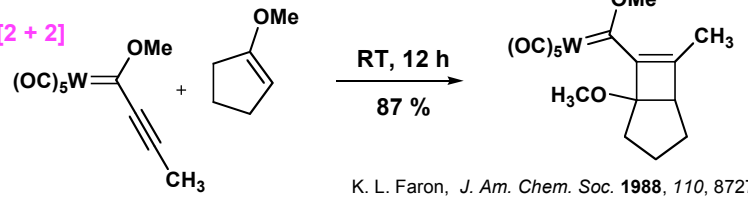
Reaction pattern of carbene complexes:

Part I: Ligand-centered

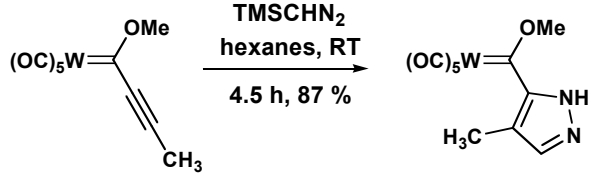
Cycloaddition reactions:

[2 + 2]



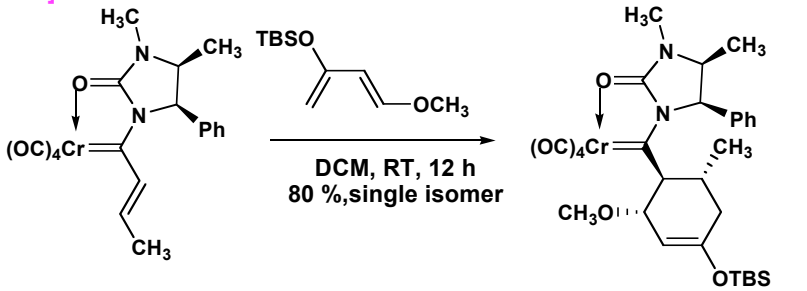
K. L. Faron, *J. Am. Chem. Soc.* **1988**, *110*, 8727 -8729.

[3 + 2]



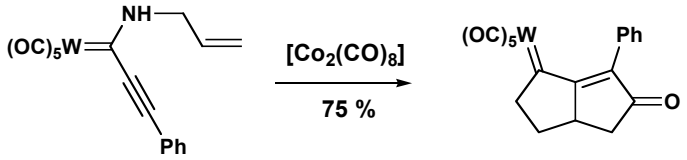
W. D. Wulff, *J. Am. Chem. Soc.* **1986**, *108*, 5229 -5236.

[4 + 2]



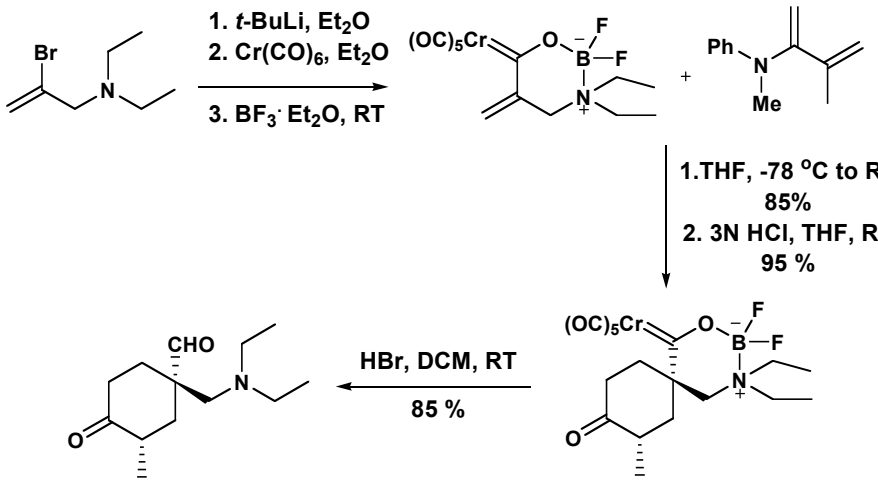
W. D. Wulff, *J. Am. Chem. Soc.* **1997**, *119*, 6438 -6439.

Intramolecular Pauson -Khand reaction:



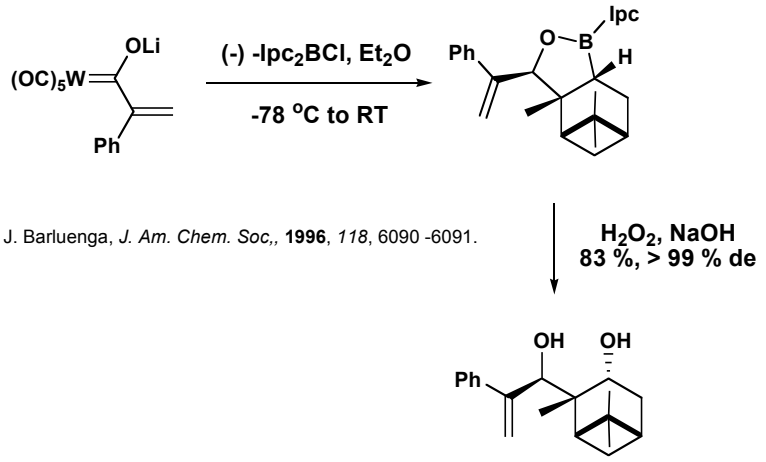
J. M. Moreto. *Angew. Chem. Int. Engl.* **1991**, 11,1470.

Diels-Alder reaction of boroxycarbene complexes:



J. Barluenga. *J. Am. Chem. Soc.* **1998**, *120*, 2514 -2522.

Miscellaneous cases



J. Barluenga, *J. Am. Chem. Soc,,* **1996**, *118*, 6090 -6091.

Fischer Carbene Complexes in Organic Synthesis

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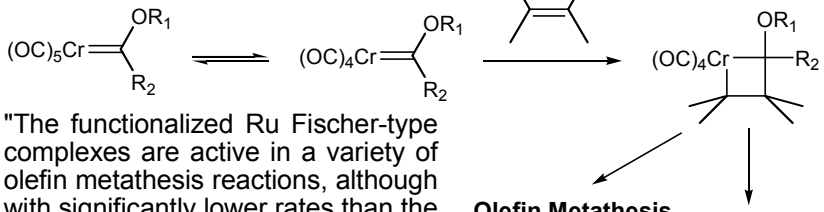
Reaction pattern of carbene complexes:

Part II: Metal-centered

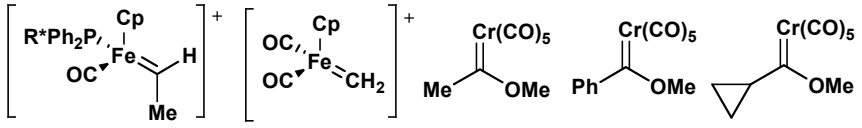
1. Reaction with olefins

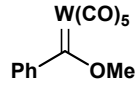


"The functionalized Ru Fischer-type complexes are active in a variety of olefin metathesis reactions, although with significantly lower rates than the corresponding carbon analogues."

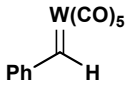
R, H. Grubbs, *Organometallics.* **2002**, *21*, 2153 -2164.

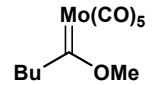
General carbene complexes used in cyclopropanation reactions:





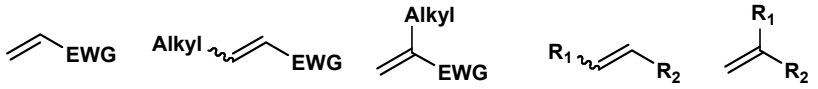
(leads to olefin metathesis product)



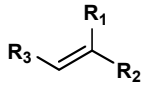


(less stable)

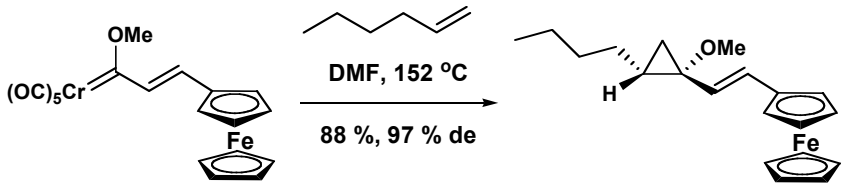
Suitable olefins:

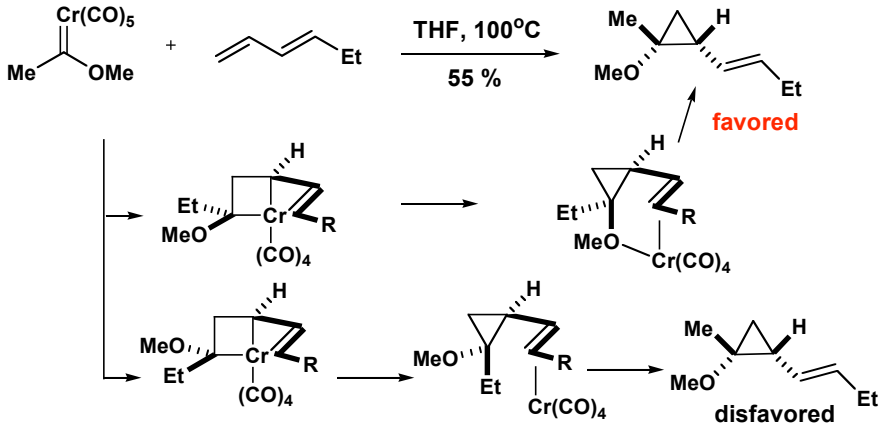


R_1, R_2 = akyl, aryl

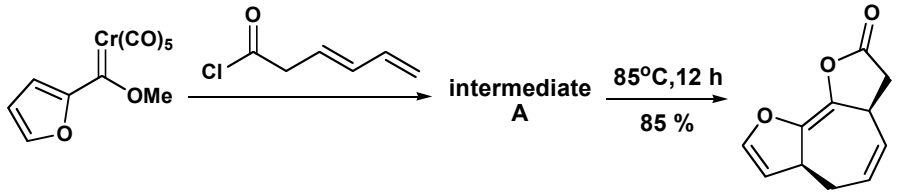


R_1, R_2 and R_3 = alkyl
requires stronger electrophilic metal carbenes





J. Am. Chem. Soc. , 113, 23, **1991,** 8916-8921



Chemtracts - Organic Chemistry. **17**, 67 -71, **2004**

Fischer Carbene Complexes in Organic Synthesis

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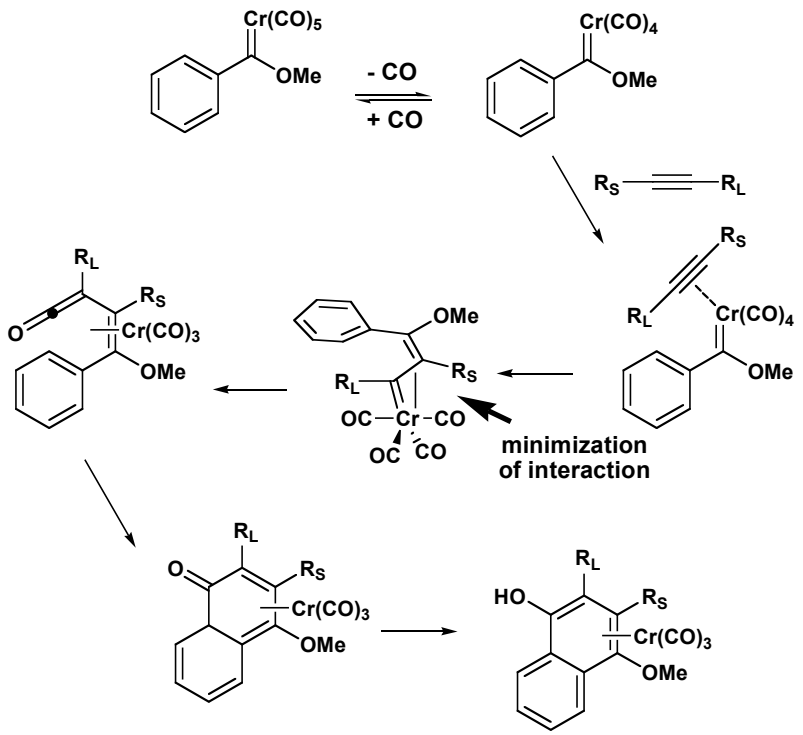
Reaction pattern of carbene complexes:

Part II: Metal-centered

2. Benzannulation (Dotz reaction)



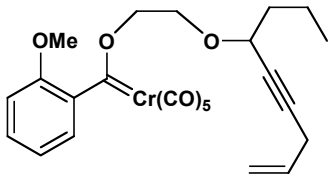
Suitable metal:

Cr (metal of choice)
Mo (furan formation occasionally)
W (favor 3 + 2 cycloaddtion)
Mg (low yields)

Compatible substitution pattern:

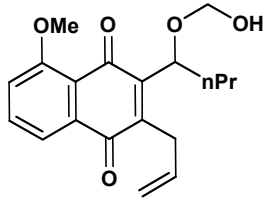
Aryl carbenes with various substituents
Naphthyl and heteroaryl carbenes
Vinyl carbenes bearing alkyl substituents

Electron - neutral alkynes with various substituents

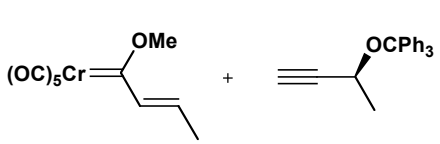


ether, reflux

51 %

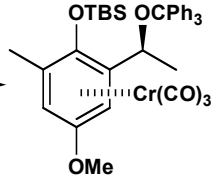


M. F. Semmelhack, *Tetrahedron,* **1985**, 5803.

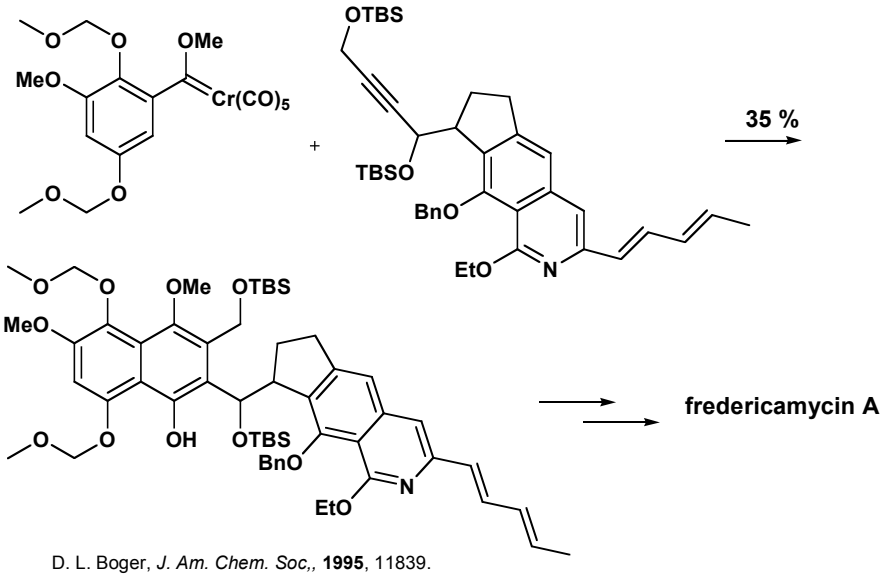


TBSCl, hunig base

> 92 % d. e.



W. D. Wulff, *J. Am. Chem. Soc,,* **1994**, **116**, 6449.

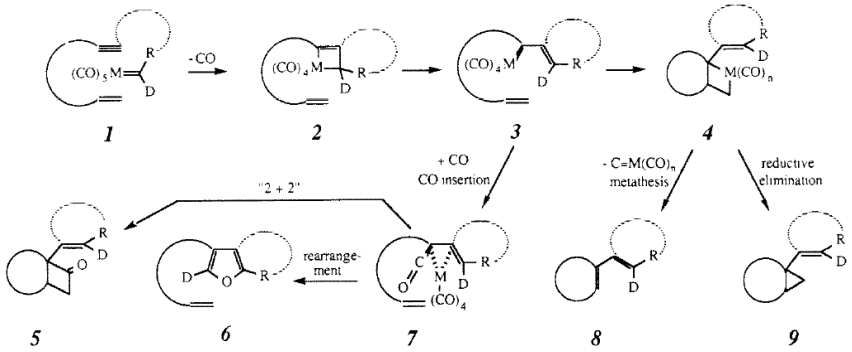


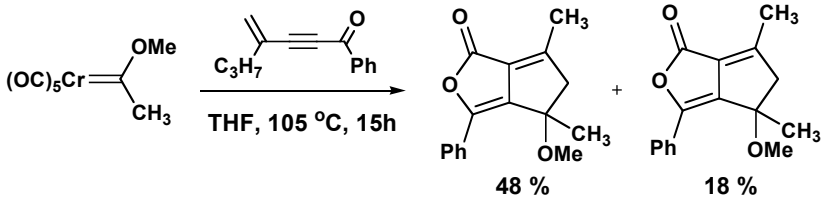
D. L. Boger, *J. Am. Chem. Soc,,* **1995**, 11839.

Reaction pattern of carbene complexes:

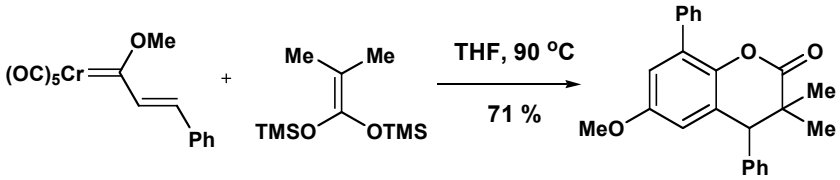
Part II: Metal-centered

3. General Annulation of Fischer carbenes with alkynes and alkenes:

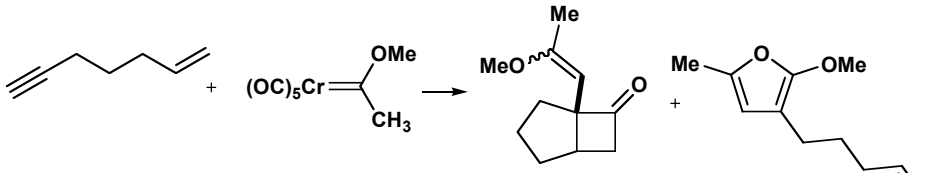




J. Am. Chem. Soc. **1991**, *113*, 5459 - 5461



J. Barluenga, *Org. Lett.*, **2006**, *8*, 2703 -2706.



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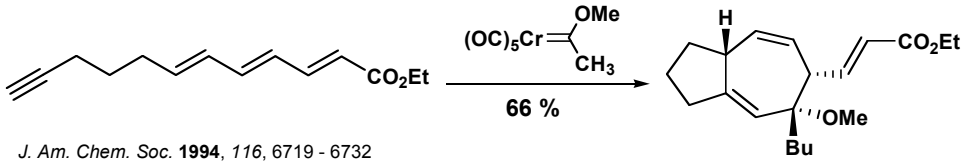

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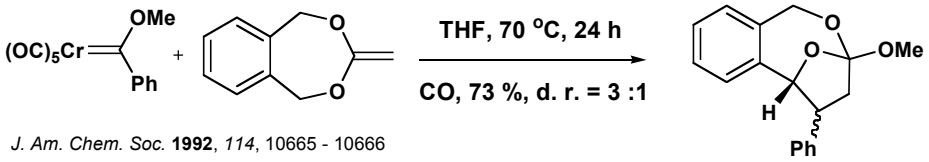

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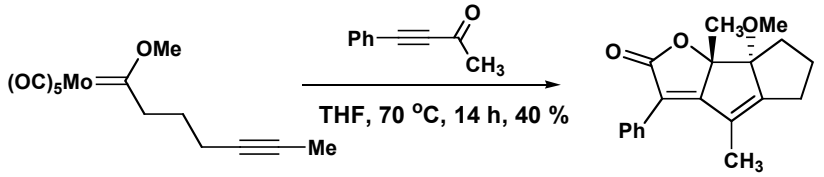

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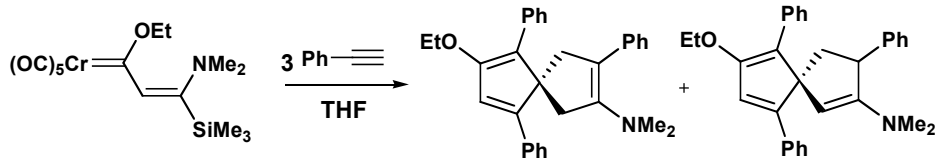

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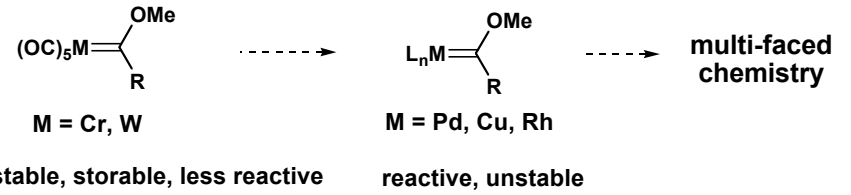
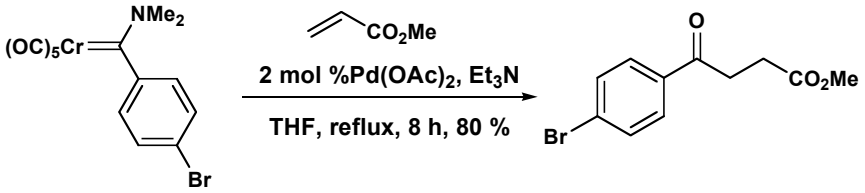
Fischer Carbene Complexes in Organic Synthesis

Ke Chen

State of art:

Group 6 metal carbenes in catalytic carbene transfer reactions





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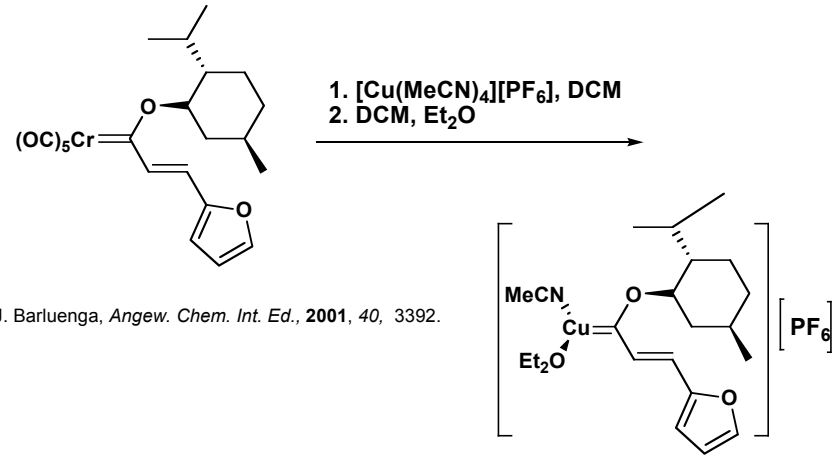

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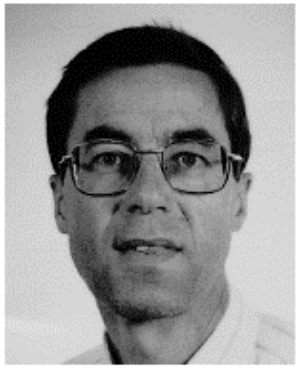

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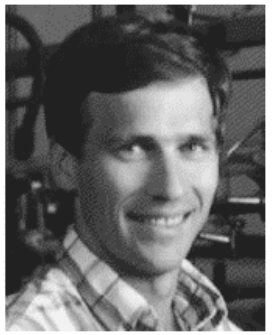

Daniel F. Harvey

Jose Barluenga

Louis S. Hegedus

William D. Wulff