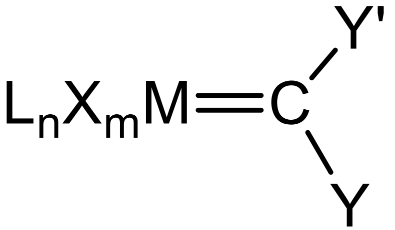
Transition metal carbene complexes



Y= R, H, heteroatom…

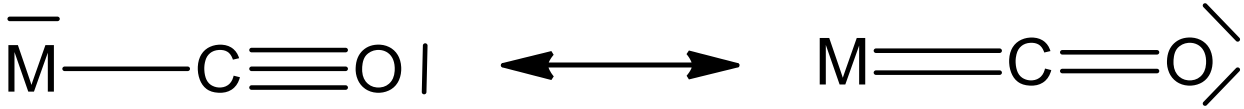
Carbene: organic ligand featuring a divalent carbon donor atom

Broad class of compounds with widely different properties, very intensively studied in the course of the last 50 years (carbene transfer to organic molecules, olefin metathesis, preparation of π-extended organometallic compounds for nonlinear optics, N-heterocyclic carbenes etc.).

Technologically useful compounds characterized by a **very broad reactivity spectrum**, going from reactive, transient complexes, whose existence can only indirectly be determined, to compounds in which the carbene moiety acts as supporting ligand, remaining unaffected even under drastic reaction conditions.

Transition metal carbene vs. CO complexes

In transition metal carbonyl complexes, the donor-acceptor synergism can be represented in terms of an intermediate bonding situation between two limit resonance forms:



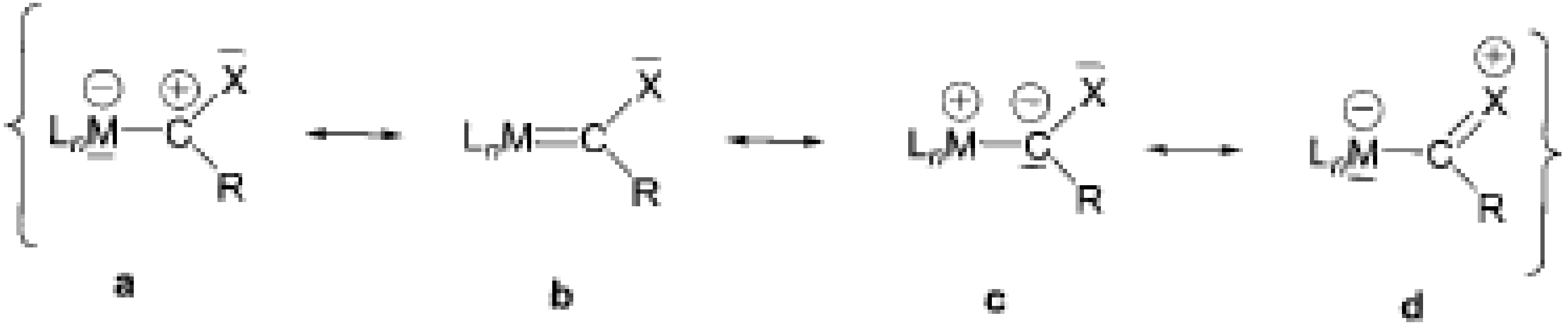
Furthermore, independently of the relative weight of the two resonance forms (i.e. of the extent of backbonding):

1) The metal-CO bond is always represented as a single bond;

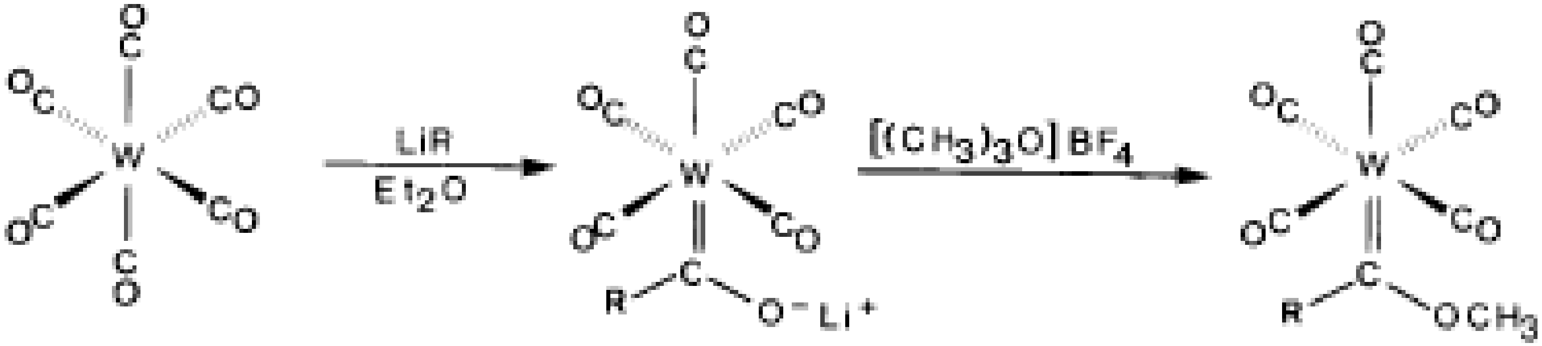
2) Bond formation invariably implies the accumulation of a partial positive charge on the carbonyl carbon.

Transition metal carbene vs. CO complexes

As we will see, in the case of TM-carbene complexes, limit resonance forms of the same kind can be written.
In these resonance forms, though, both positive and negative formal charges on C appear; indeed, **the experimental polarity of the M-C bond is highly variable**.
Furthermore, although traditionally the M-carbene bond has been always represented as a double bond, today in some cases representation as a single bond is commonly accepted.

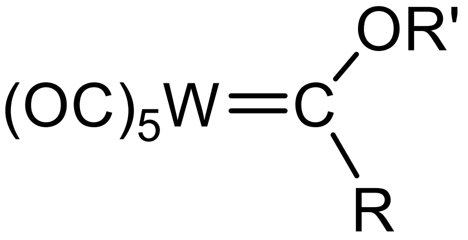


TM carbene complexes – Fischer carbenes



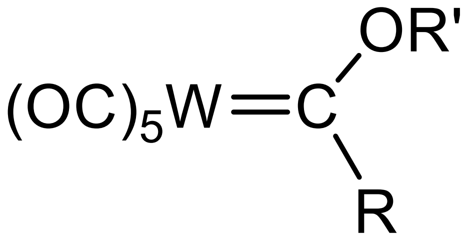
Fischer et al., Angew. Chem. Int. Ed. Engl. 3 (1964) 580

The intermediate acylate complex is stable, isolable and characterizable



$(OC)_5W{=}C(OR')R$

TM carbene complexes – Fischer carbenes



- TM from the right side of the d block;
- TM in low formal oxidaton state;
- Complex typically with 18 electrons;

–π-accepting supporting ligands ;

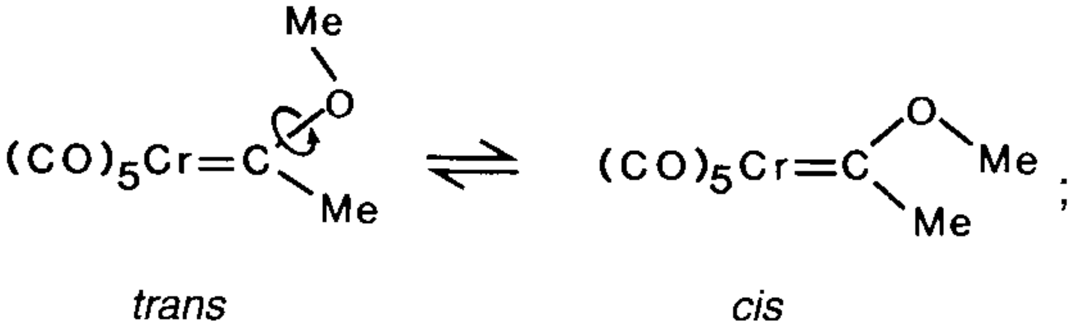
–π-donating substituents on the carbene C;

Reasonably stable complexes (in particular in the case of group 6 metals) which can be treated as organic molecules (purification by chromatography, modification, functionalization etc.); not very air sensitive, moderately light sensitive (see below).

TM carbene complexes – Fischer carbenes

Properties of Fischer carbenes:

- The M-C bond is shorter than a single M-C bond, but generally longer than a M-C(CO) bond;
- carbene C sp^2 hybdridized;
- C-O bond (or, in general, C-X bond) shorter than a single bond; furthermore, restricted rotation around the C-X bond, determined e.g. by variable temperature NMR;

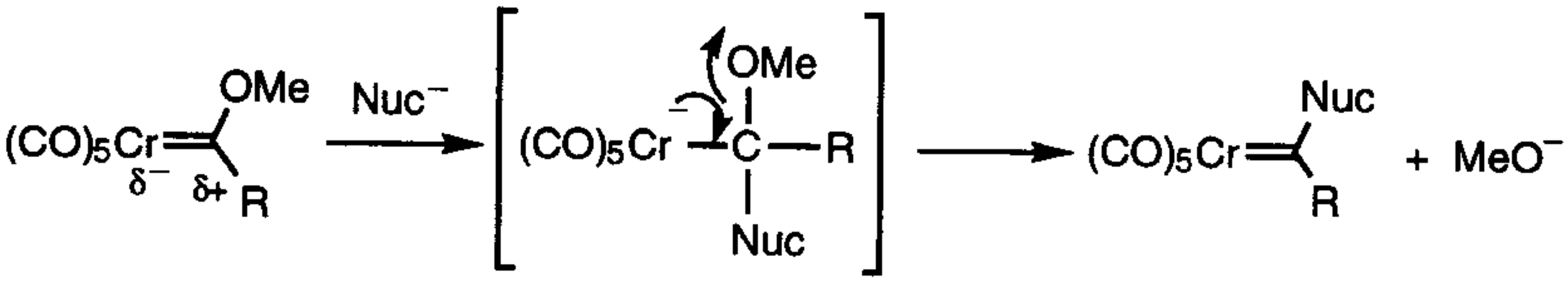


- carbene C electron-poor and consequently electron-withdrawing: if R= H, δ= 12-22 ppm in the ^{1}H-NMR spectrum;

TM carbene complexes – Fischer carbenes

Reactivity of Fischer carbenes:

- carbene C <u>electrophilic</u>; possibility of nucleophilic substitution of OR’ with other π-donating groups, even chiral ones;

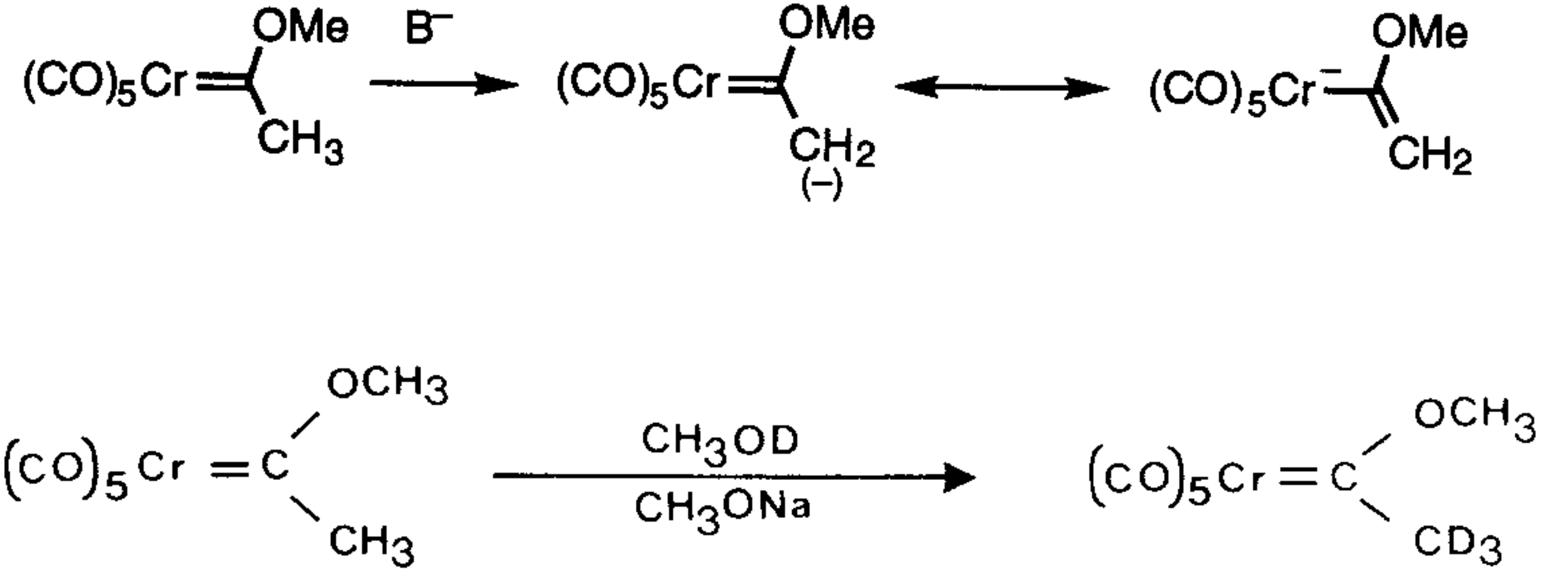


Nuc = $R'O^-$, NH_3, RNH_2[12]

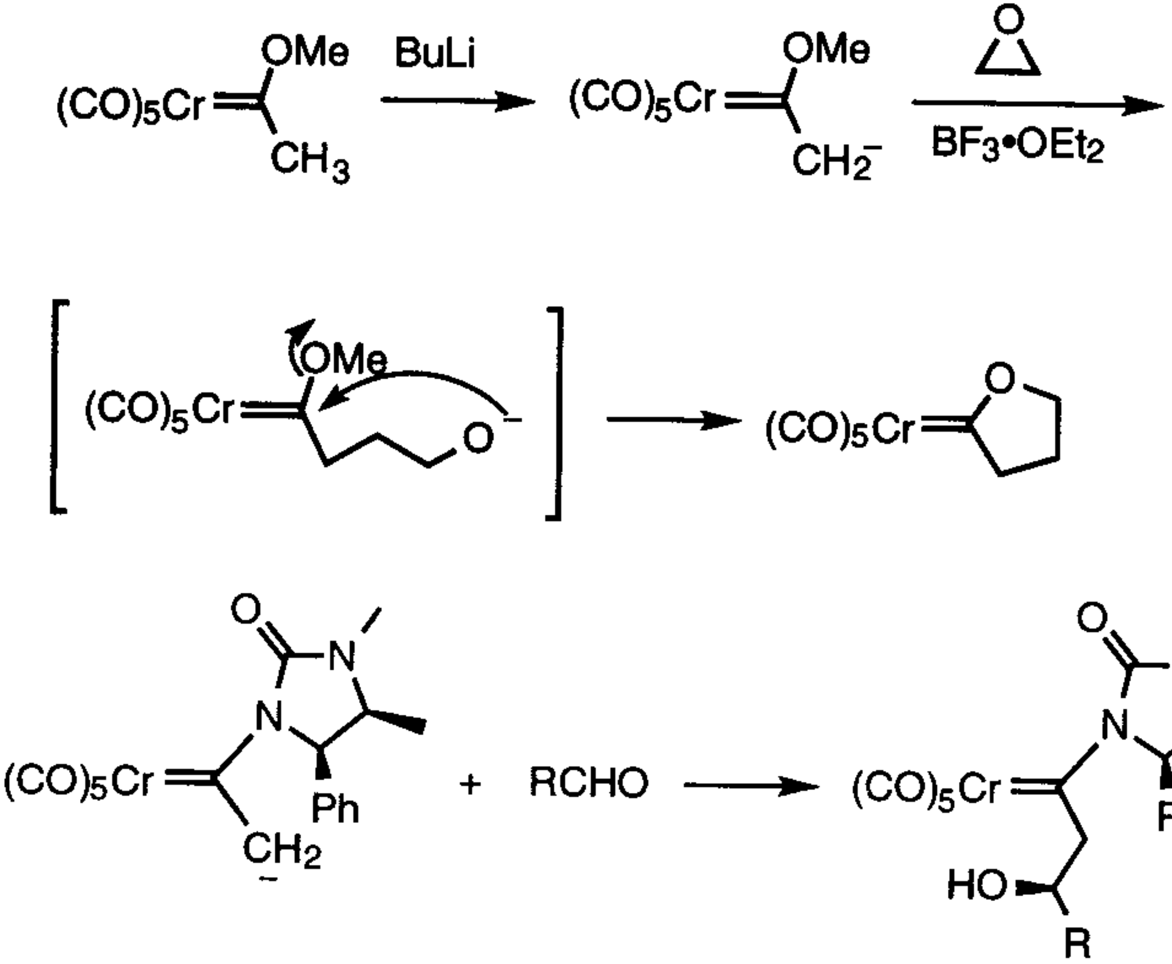
<u>Small</u> R_2NH, RSH

TM carbene complexes – Fischer carbenes

- protons in α to the carbene C are quite acid (pK_a ca.12); possibility of deprotonation (with strong bases which deprotonate irreversibly the carbene!) and use as nucleophiles of the resulting carbanions (however: α-ramification destabilizes the carbene!); possibility of enantioselective reactions;

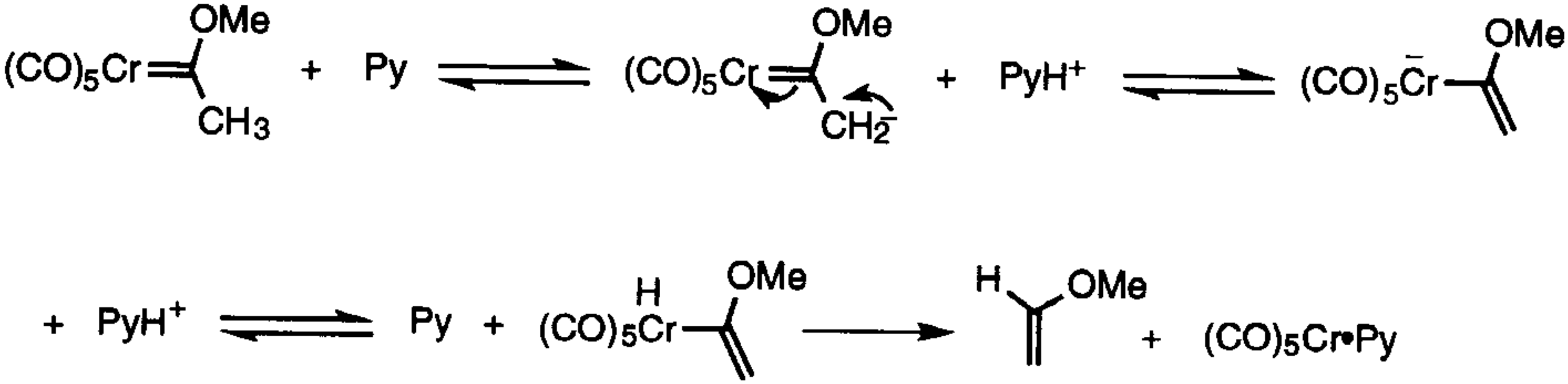


TM carbene complexes – Fischer carbenes



In the last case, elimination of water is possible, with formation of a double bond conjugated to the carbene.

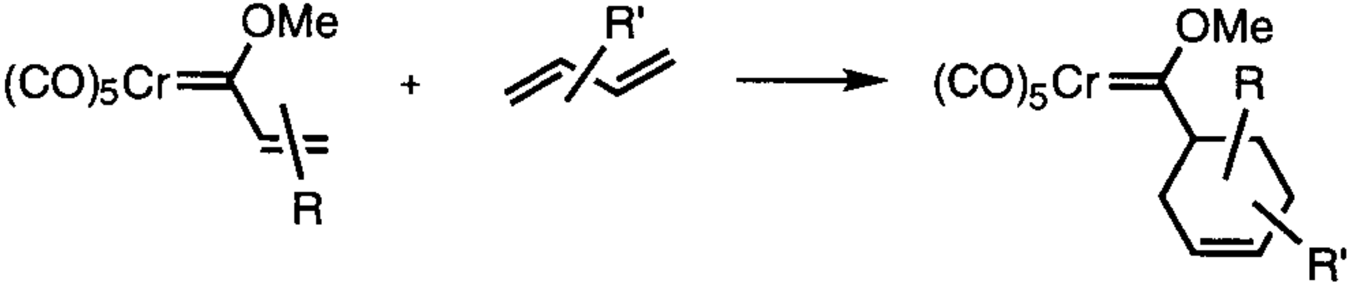
TM carbene complexes – Fischer carbenes



Reversible deprotonation of the carbene can result in its tautomerization to enolether (amide) promoted by the base!

TM carbene complexes – Fischer carbenes

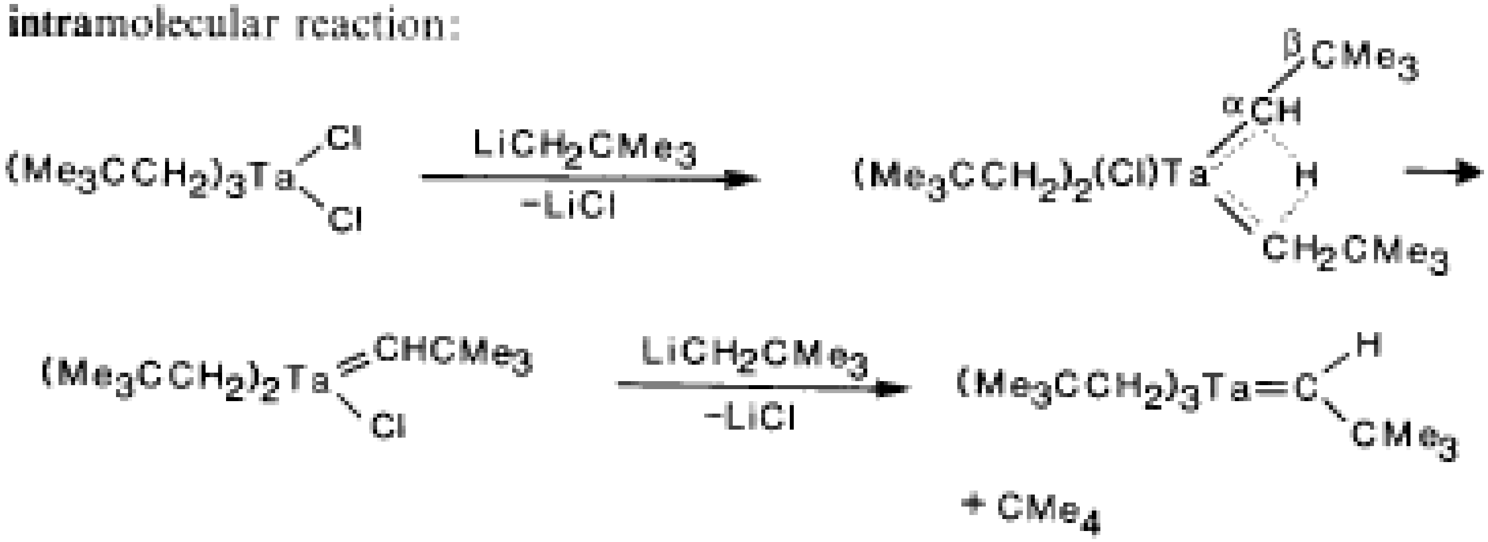
- Double bonds conjugated to the carbene (generated by aldol condensation or starting from reagents such as Li-vinyl) are electron poor and very reactive in Micheal-type additions, 1,3-dipolar cycloadditions or Diels-Alder reactions (reactions 10^4 times faster compared to esters);



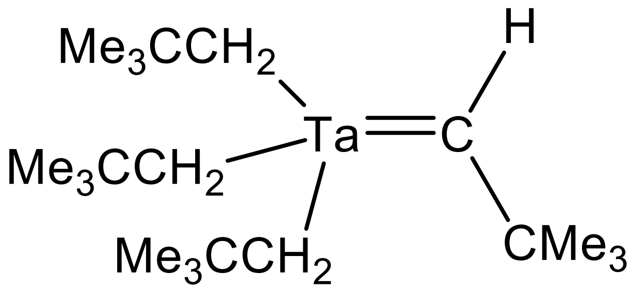
- The carbene is detached from the metal centre upon reaction with ylides (e.g. phosphorus ylides, $R_2P=CR'R''$) forming olefins;

Evident analogy of the Fischer carbene with a carbonyl group!

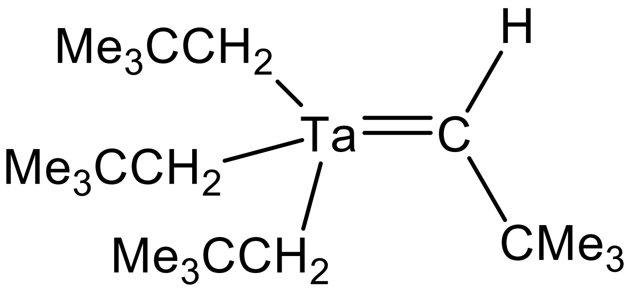
TM carbene complexes – Schrock carbenes



Schrock, J. Am. Chem. Soc. 96 (1974) 6769



TM carbene complexes – Schrock carbenes



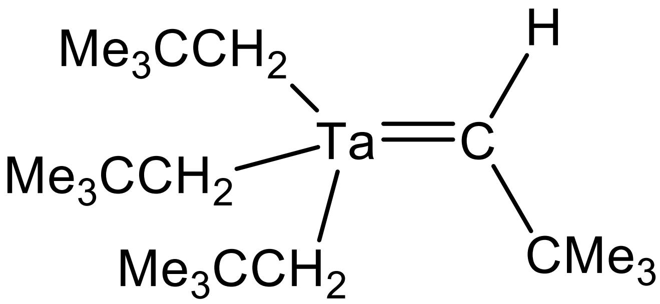
- TM from the <u>left side</u> of the d block;
- metal in <u>high</u> formal oxidation state;
- complexes with typically <u>less than 18 electrons</u>;

–<u>σ-donating</u> supporting ligands;

-<u>H o R as substituents</u> on the carbene C;

<u>Very reactive compounds</u>, which can be manipulated only under an inert atmosphere and anhydrous conditions, but which are also very useful as as reagents/catalysts.

TM carbene complexes – Schrock carbenes



Properties of Schrock carbenes:

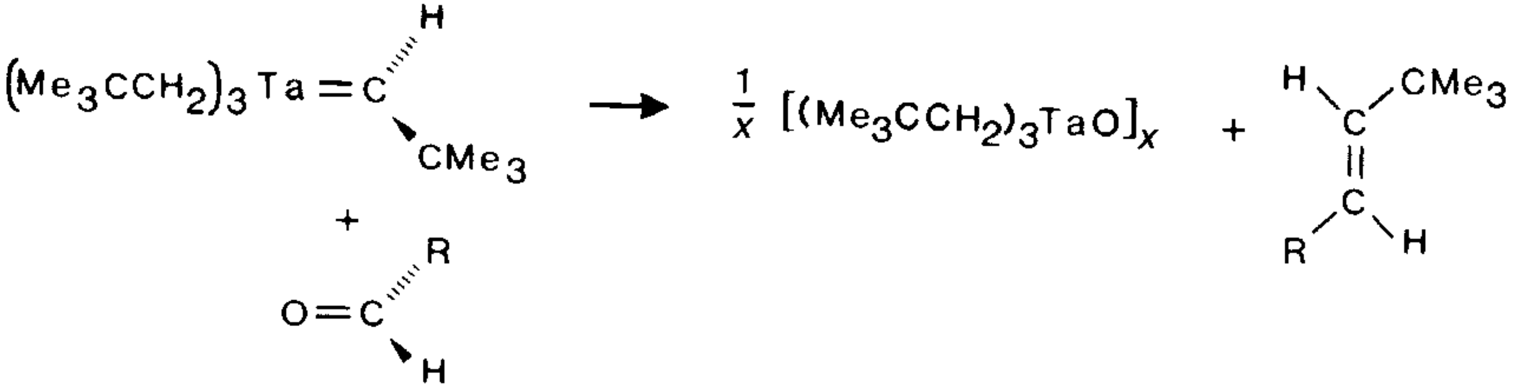
- shorter M-C(carbene) bond with respect to Fischer carbenes;
- geometry of the carbene C often strongly distorted, depending on agostic interactions with the metal centre (e.g. small M=C-H angle, sometimes even lower than 90°);
- C electron rich and consequently electron-donating: H is found at negative δ (e.g. ca. –2) in the ^{1}H-NMR spectrum.

TM carbene complexes – Schrock carbenes

Reactivity of Schrock carbenes:

- carbene C nucleophilic: behaves as ligand (Lewis base) towards strong Lewis acids (e.g. AlR_3);

- The carbene attacks carbonyl compounds (aldehydes, ketones, amides, esters) substituting the oxygen in a Wittig-type reaction;



Evident analogy of the Schrock carbene with an organic ylide!

Fischer carbenes or Schrock carbenes?

Fischer and Schrock carbenes are opposite extremes of TM carbene complexes, at least for what it concerns the polarity of the M-C bond (carbene C electrophilic/nucleophilic).

Such a difference in polarity is not easily detectable without investigating the reactivity of the compound (e.g. the carbene C in the ^{13}C-NMR spectrum falls within a very large interval, typically 150-400 ppm, which is similar for the two kinds of carbene)

It is somewhat difficult to rationalize this difference; it looks even counterintuitive, if one considers e.g. the formal oxidation state of the metal centre (high for Schrock carbenes, low for Fischer carbenes)…

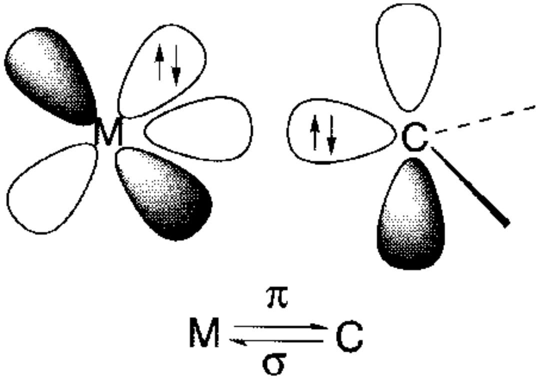
Fischer carbenes or Schrock carbenes?

Today, a generally accepted rationalization considers **different electronic structures of the interacting partners** (carbene + metal centre) for Fischer and Schrock carbenes:

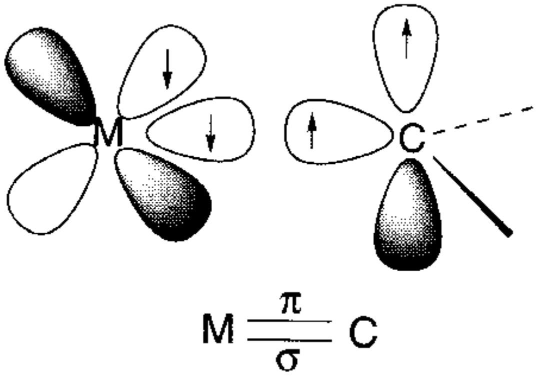
Fischer: low spin metal + singlet carbene → bond interpretation in terms of donation-back donation of electron doublets (analogy with M-CO, carbene as neutral ligand L)

Schrock: high spin metal + triplet carbene → bond interpretation in terms of sum of covalent bonds (σ and π: “classic” double bond, carbene as dianionic ligand X_2)

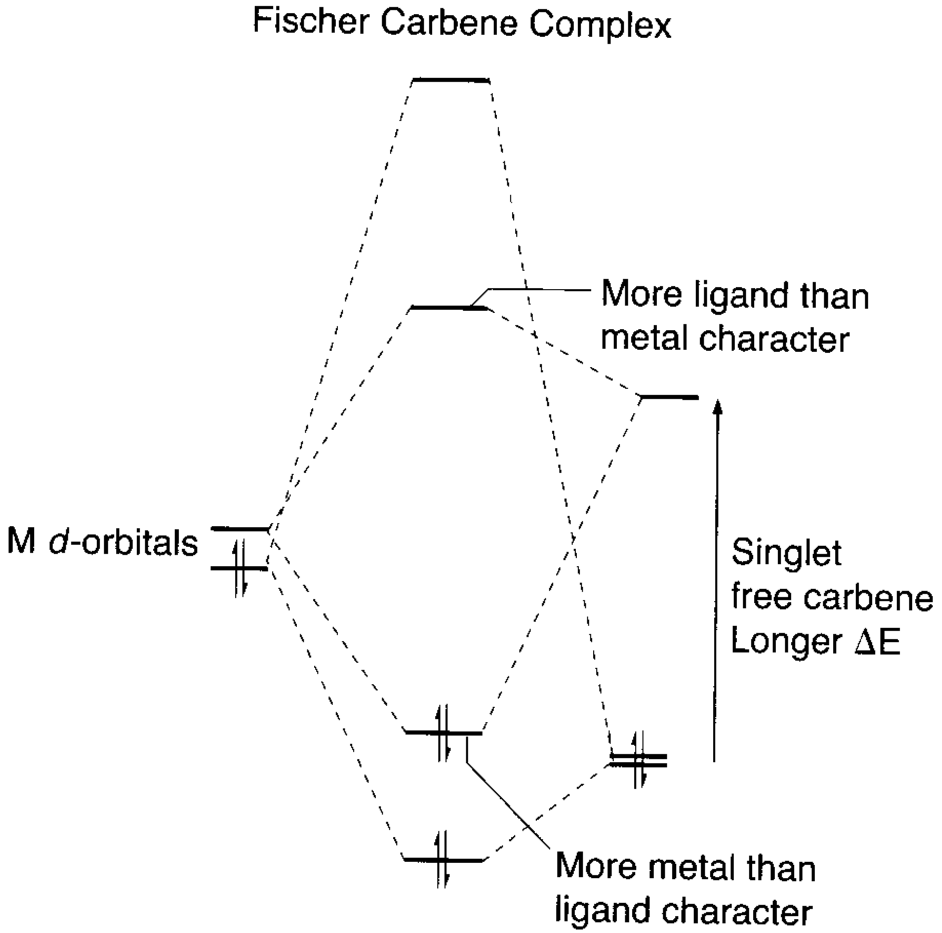
Fischer type

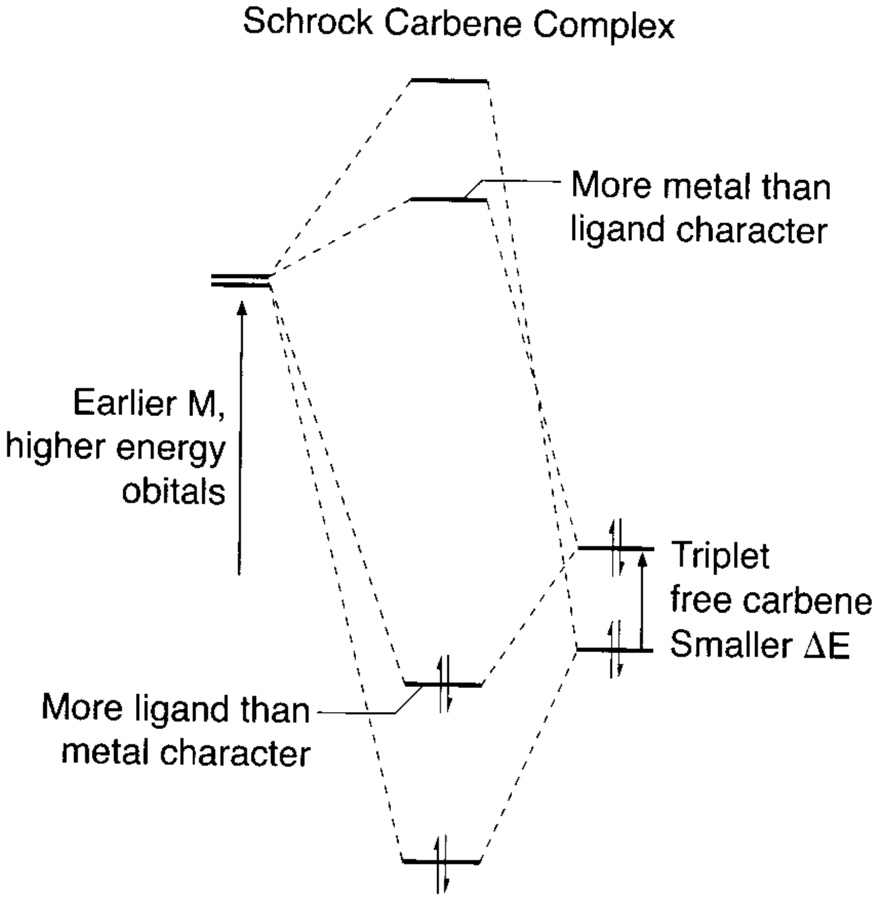


Schrock type



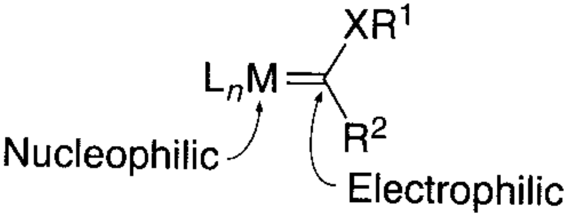
Fischer carbenes or Schrock carbenes?


Fischer Carbene Complex

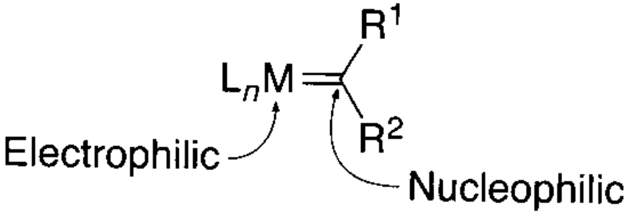

Schrock Carbene Complex

There are not only Fischer/Schrock carbenes…

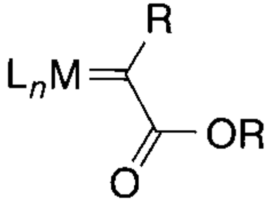
Apart from carbene complexes that are clearly identifiable as Fischer or Schrock carbenes, numerous other complexes exist with intermediate or even alternative reactivity…



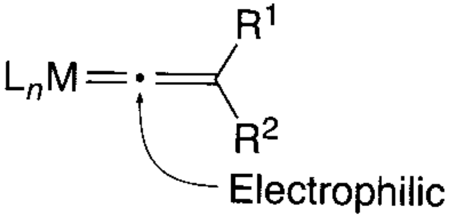
Fischer carbene complexes:
X = O, NR, S
M = low-valent, middle or late transitional metals



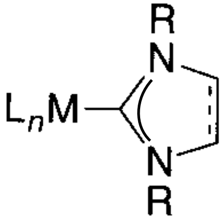
Schrock carbene or Alkylidene complexes:
R^1, R^2 = alkyl or H
M = high-valent carbyl or middle transition metals



Carbenoid complexes:
L_nM = $Rh_2(O_2CR)_4$, N_4Ru, $(N_2O_2)Ru$, or (N, N)Cu



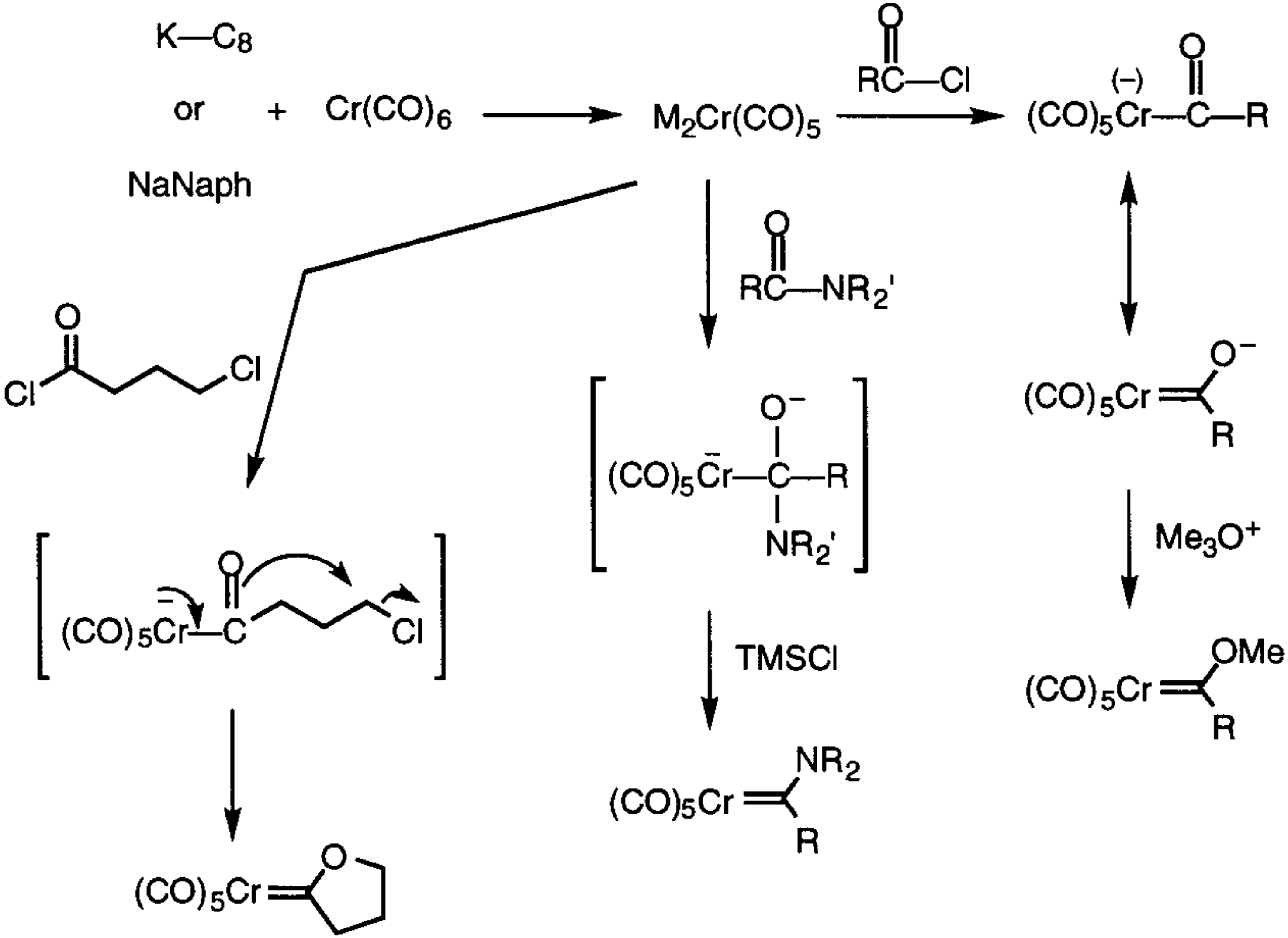
Vinylidene complexes:
R^1, R^2 = H, alkyl or aryl



N-Heterocyclic carbene complexes:
R = aryl or alkyl

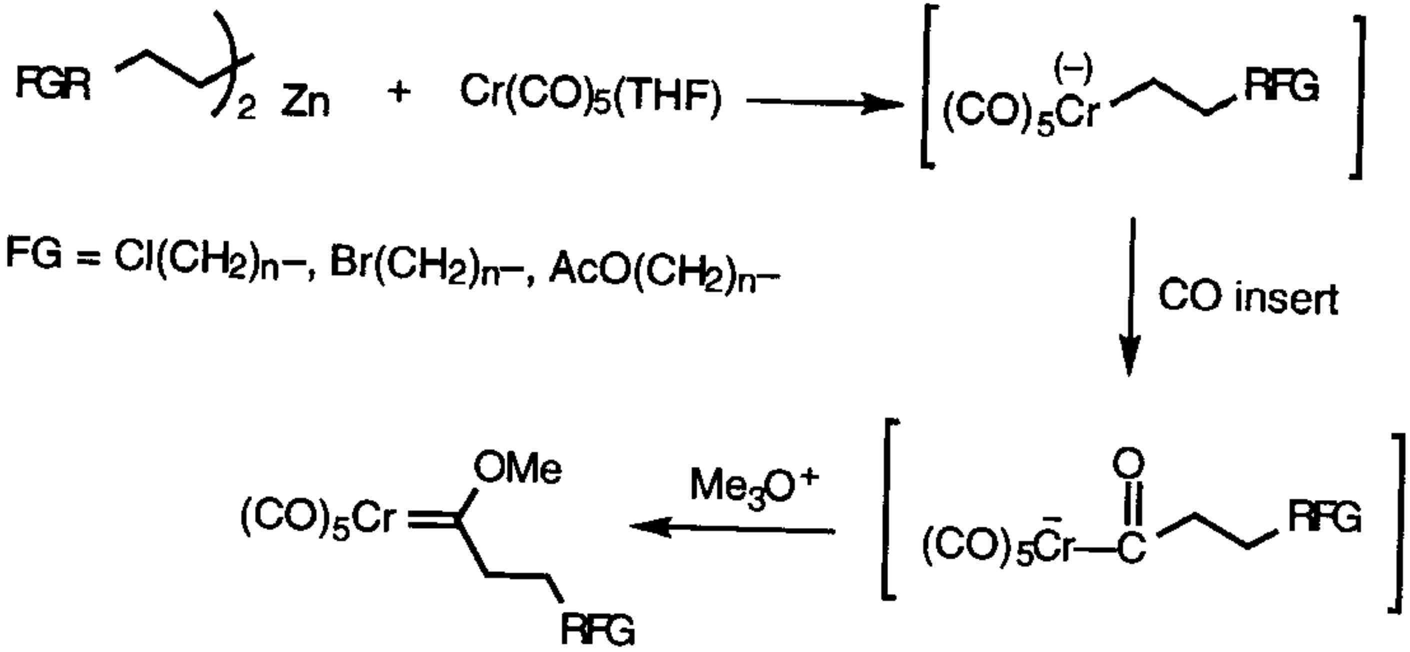
Synthetic methods – Fischer carbenes

All methods for the synthesis of anionic acyl complexes (acylates) can be also employed for the preparation of Fischer carbenes.

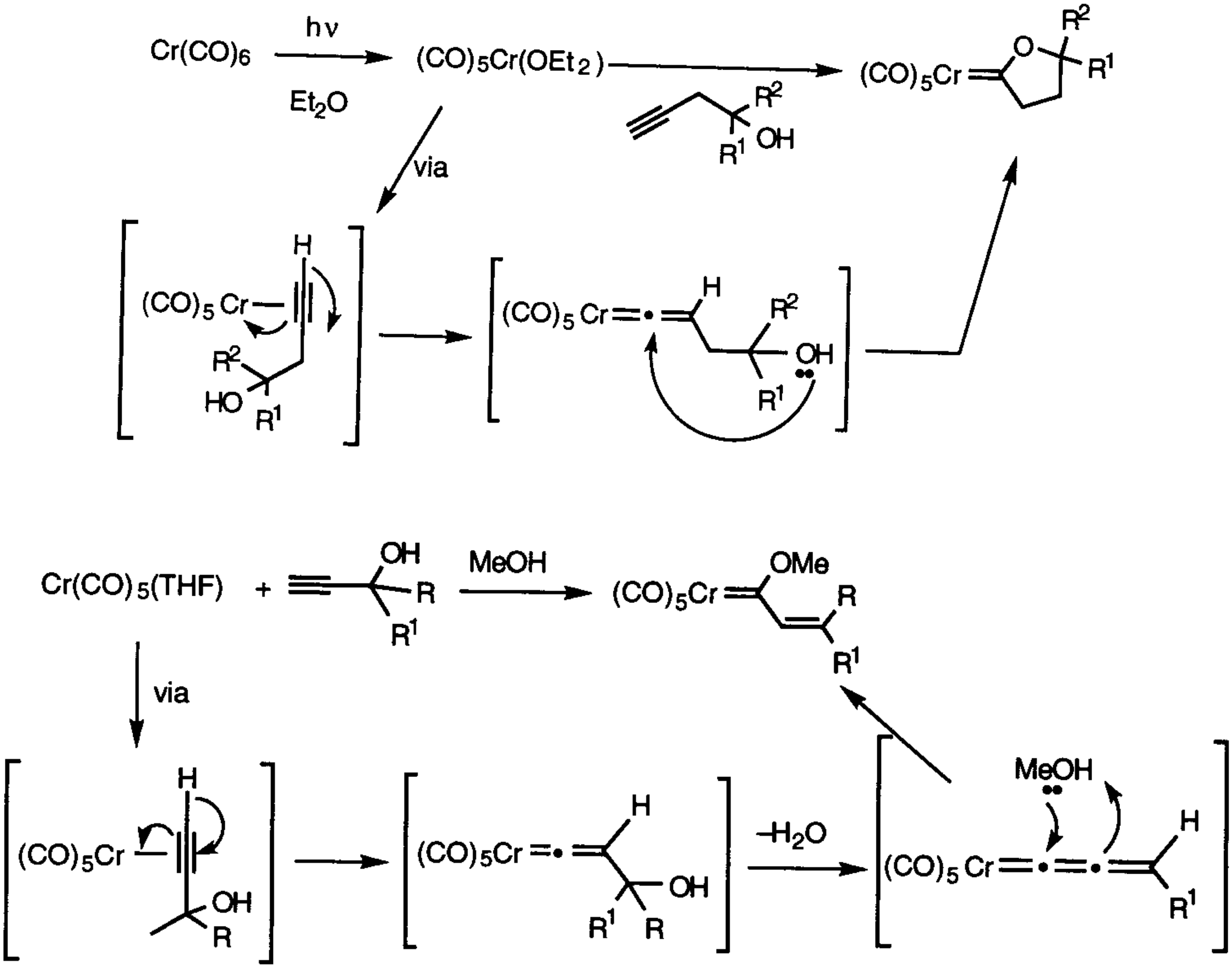


Synthetic methods – Fischer carbenes

All methods for the synthesis of anionic acyl complexes (acylates) can be also employed for the preparation of Fischer carbenes.

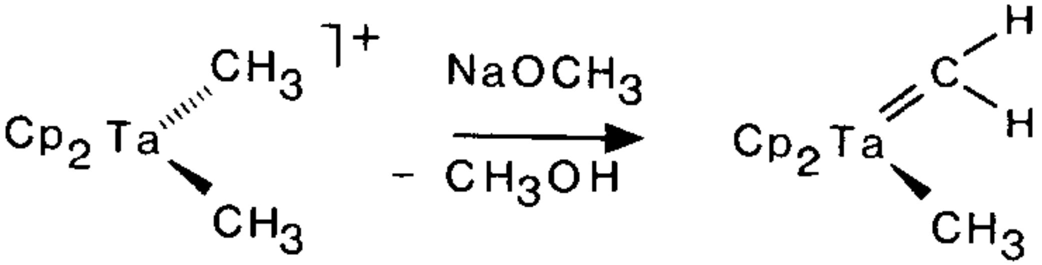


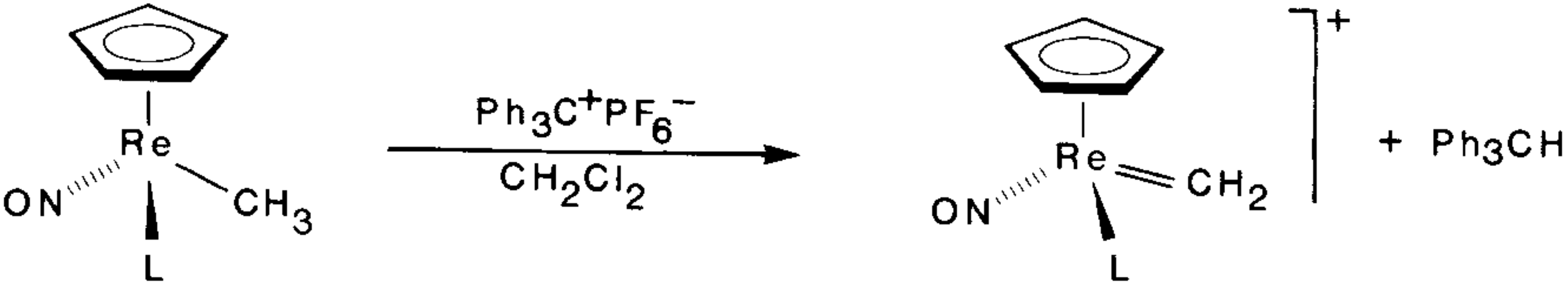
Fischer carbenes from alkynes via vinylidenes



Synthetic methods – Schrock carbenes

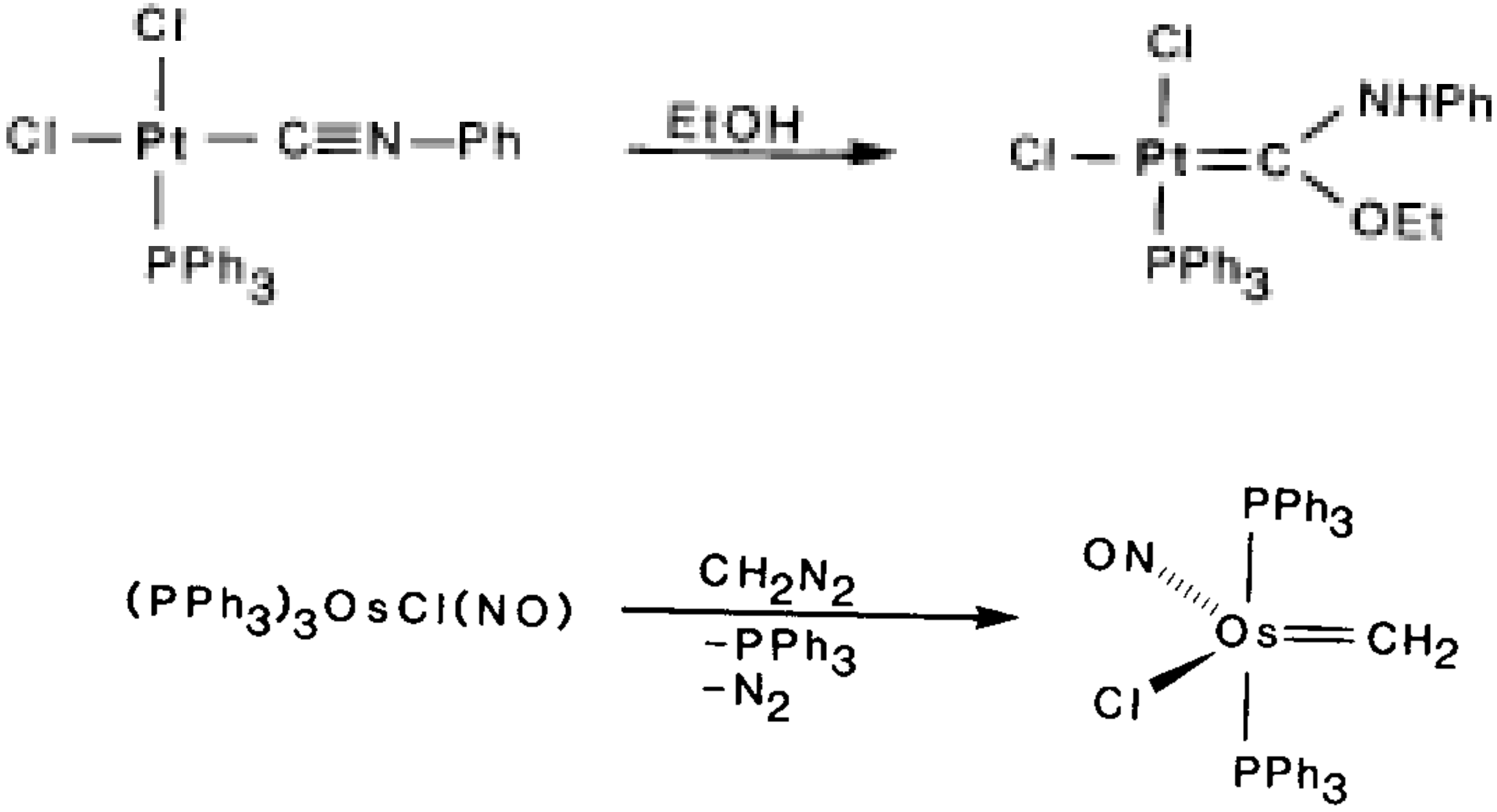
Apart from α-elimination reactions, Schrock carbenes (at least from the point of view of carbene substitution) can be prepared via α-deprotonation or by hydride abstraction from the α carbon of an alkyl ligand.





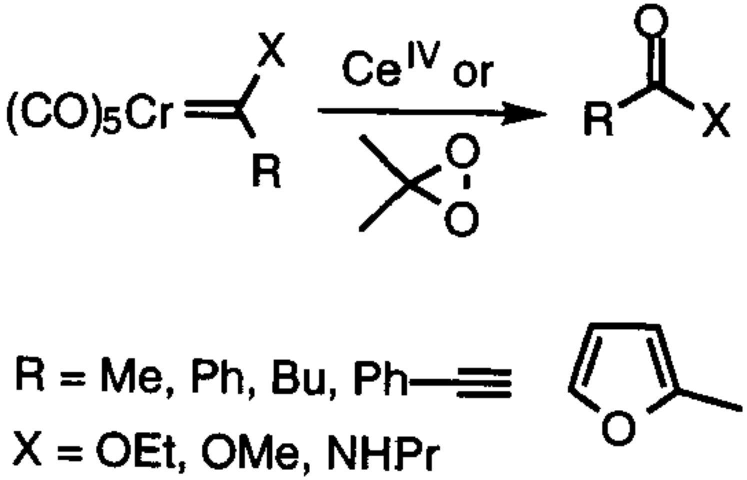
Other methods for the synthesis of TM carbenes

Additional synthetic methodologies for carbene complexes move from other kinds of carbene precursors, such as isonitriles (Fischer) or diazocompounds (Schrock).



Carbene detachment (transfer) reactions

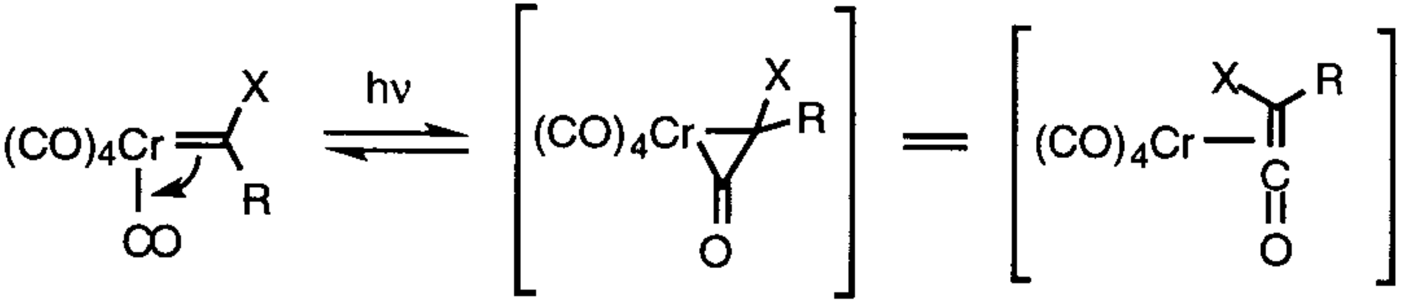
Carbene ligands can be conveniently removed from the metal centre by oxidation, in which case the metal is substituted by an oxygen atom (carbene removal as carbonyl).



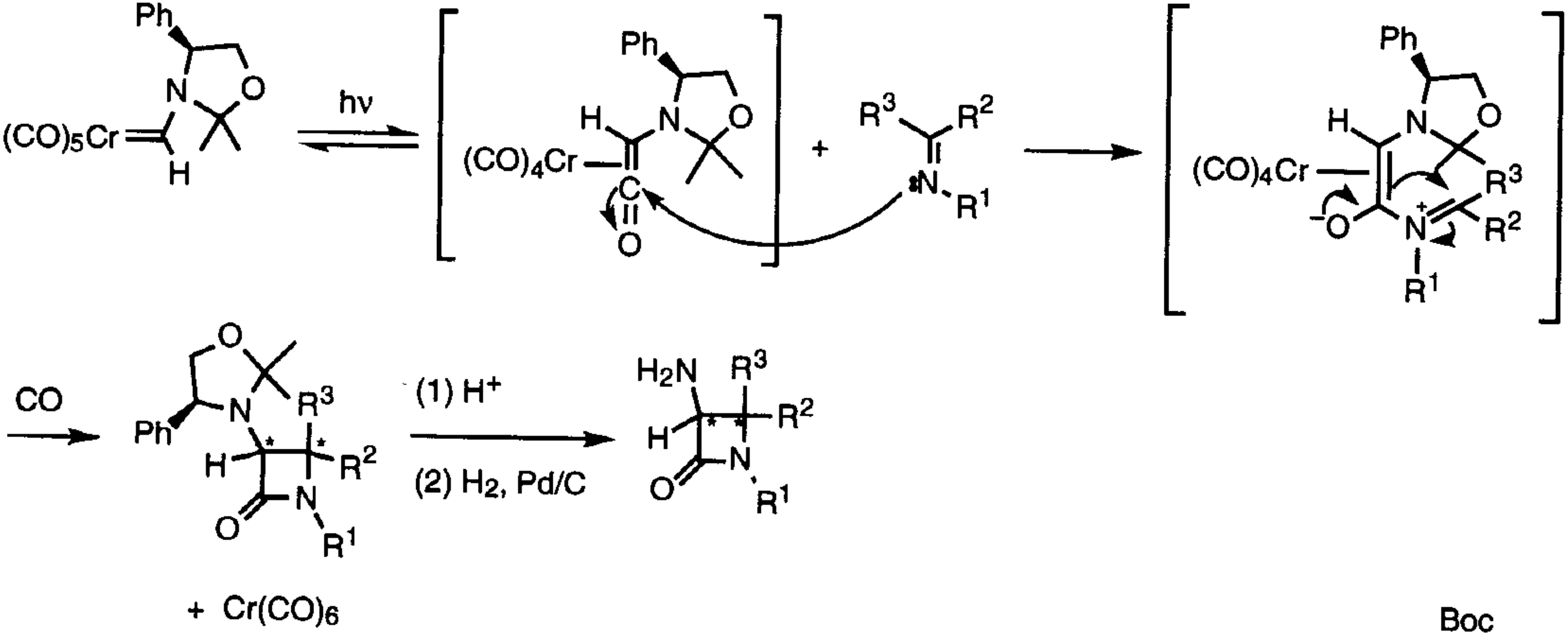
It is possible to employ to this aim also the base-promoted tautomerization to enolethers (see above).

Equilibrium carbene - ketene

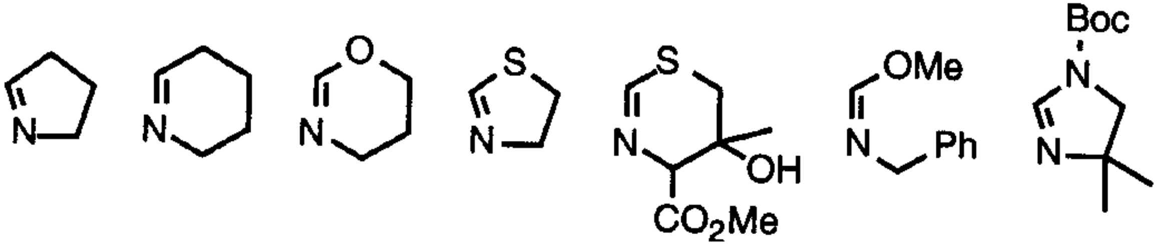
Upon irradiation of Fischer carbenes it is not only possible to remove a carbonyl ligand, but also to promote a carbene-coordinated ketene equilibrium. Such equilibrium is in general perfectly reversible (by switching off the irradiation the Fischer carbene is reformed), but not if the reaction medium contains substances able to react with the ketene…

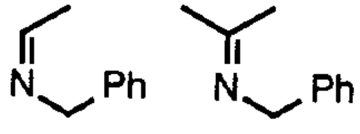


Equilibrium carbene - ketene

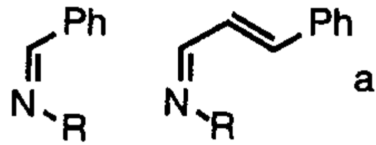


Imine =



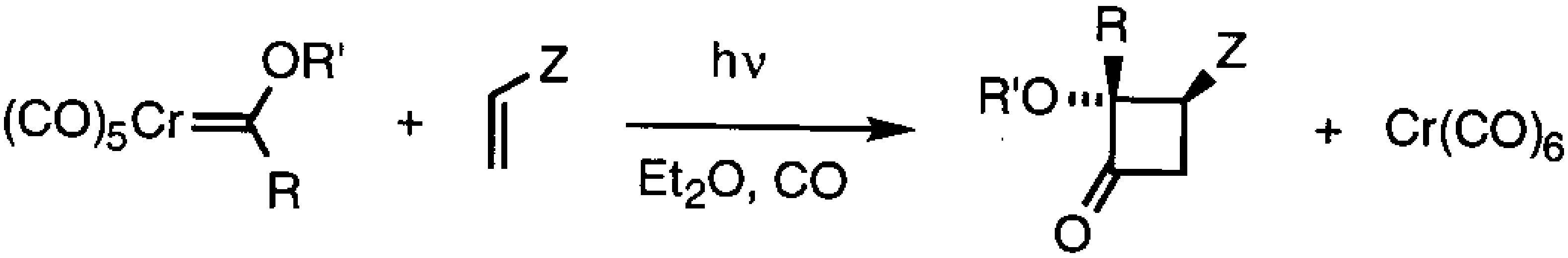


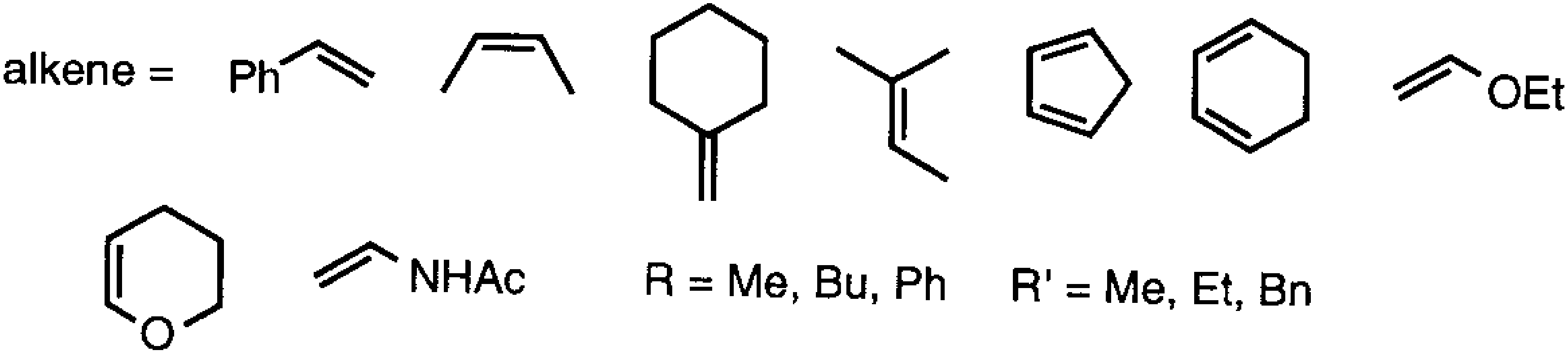
Note !



are *not* diastereoselective

Equilibrium carbene - ketene

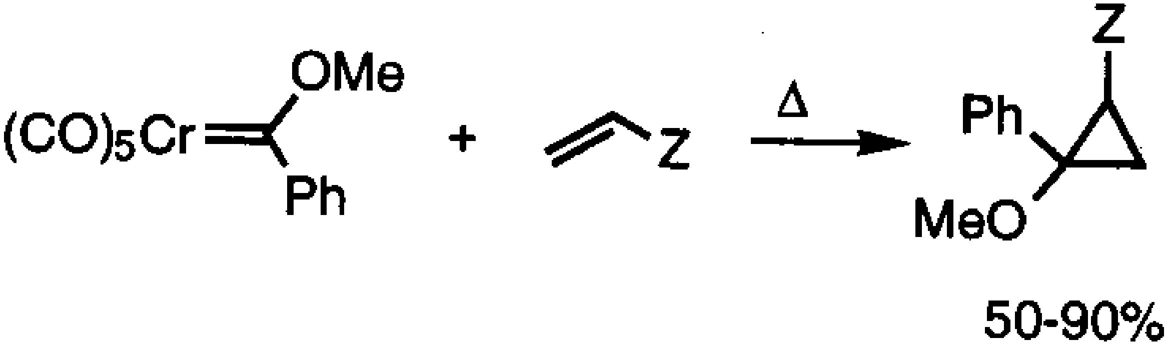




R = Me, Bu, Ph   R' = Me, Et, Bn

Carbene detachment (transfer) reactions

TM carbene complexes, like carbenoid compounds of the main group elements, can transfer the carbene ligand to typical carbene acceptors, such as olefins (cyclopropanation reactions).

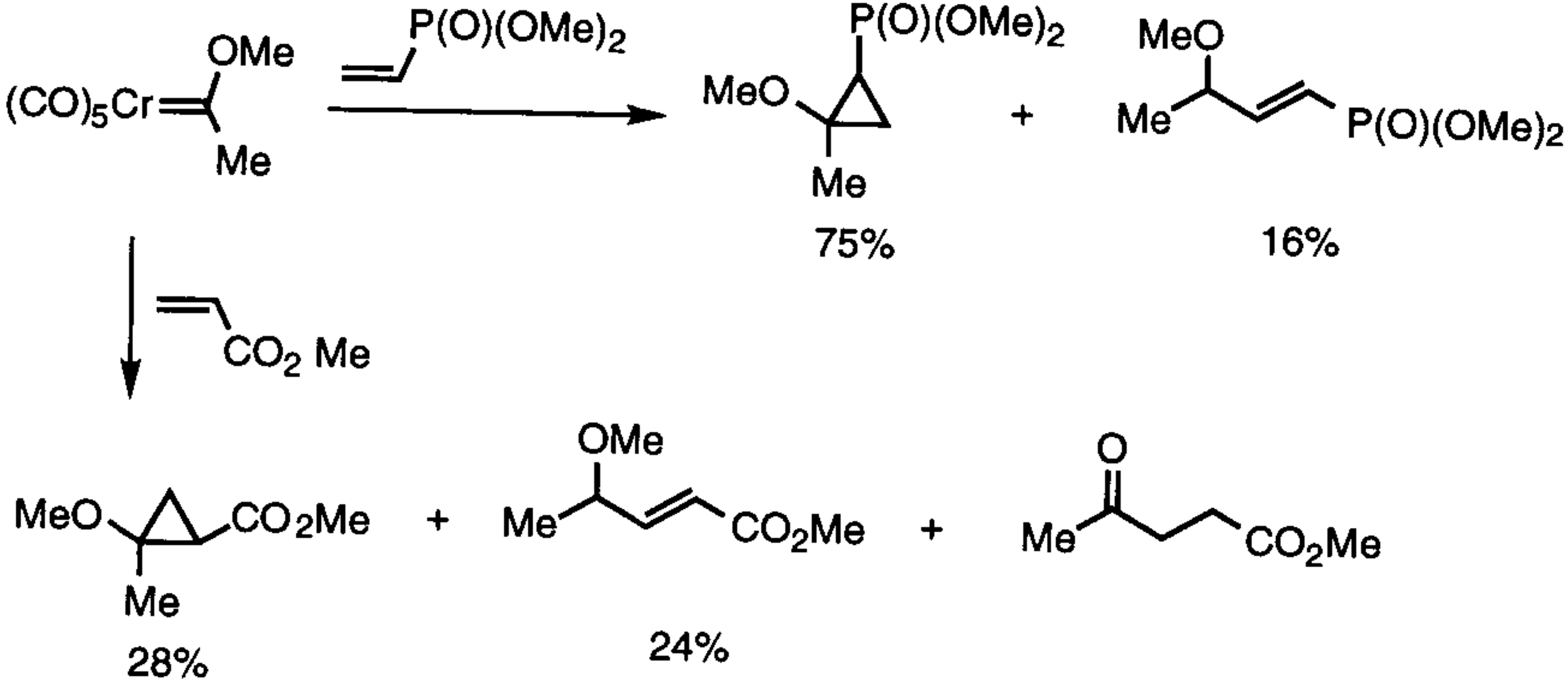


Z = CO_2Me, $CONMe_2$, CN, $P(O)(OMe)_2$, SO_2Ph

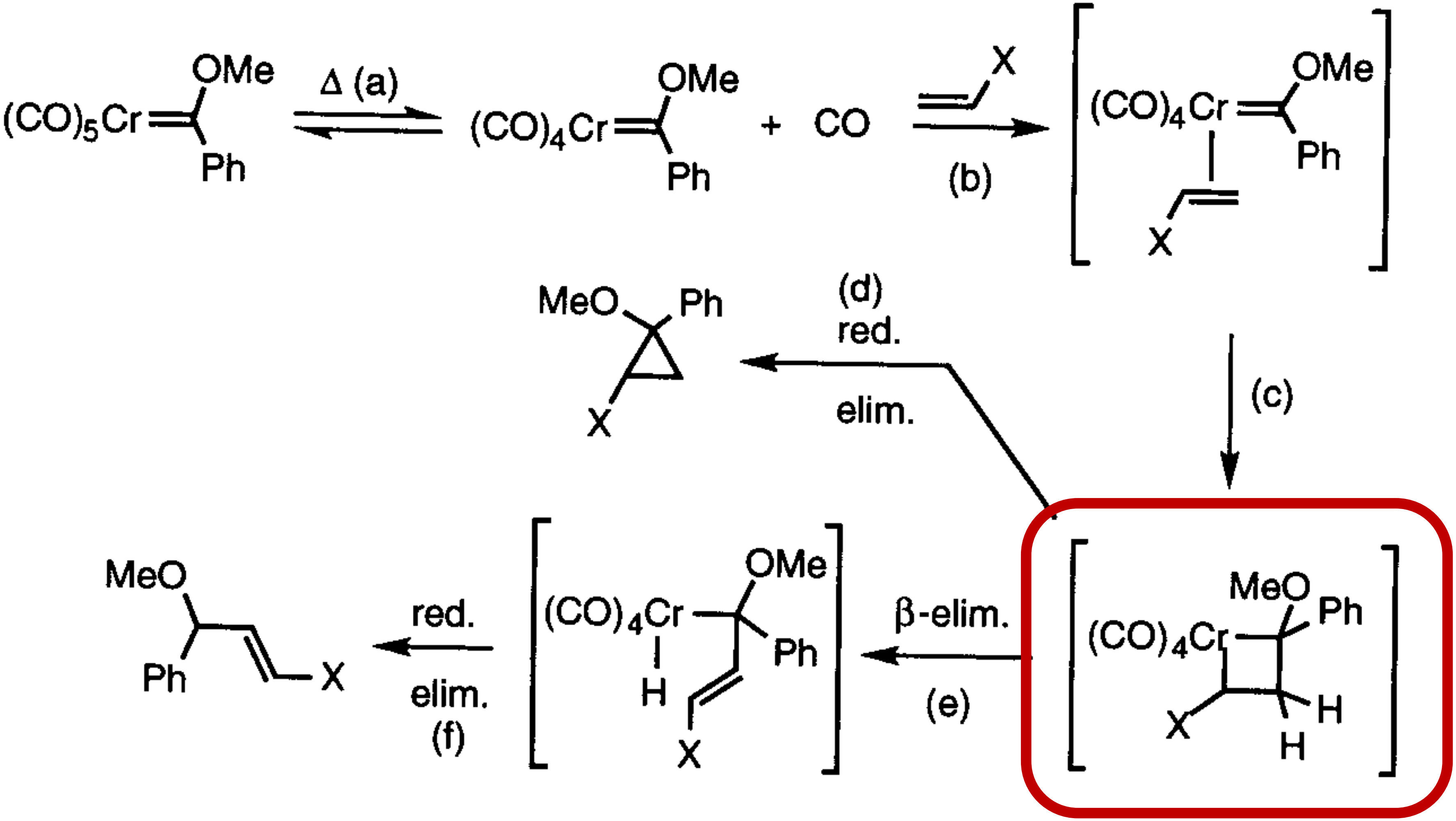
Starting from Fischer carbenes as reagents, this reaction is however possible only with electron-poor olefins (substituted with electron-withdrawing groups).

Carbene detachment (transfer) reactions

Starting from Fischer carbenes as reagents, these reactions proceed <u>without</u> the intermediation of free carbenes; furthermore, the presence of coproducts of formal insertion of the carbene in an olefin C-H bond requires a suitable mechanistic hypothesis.



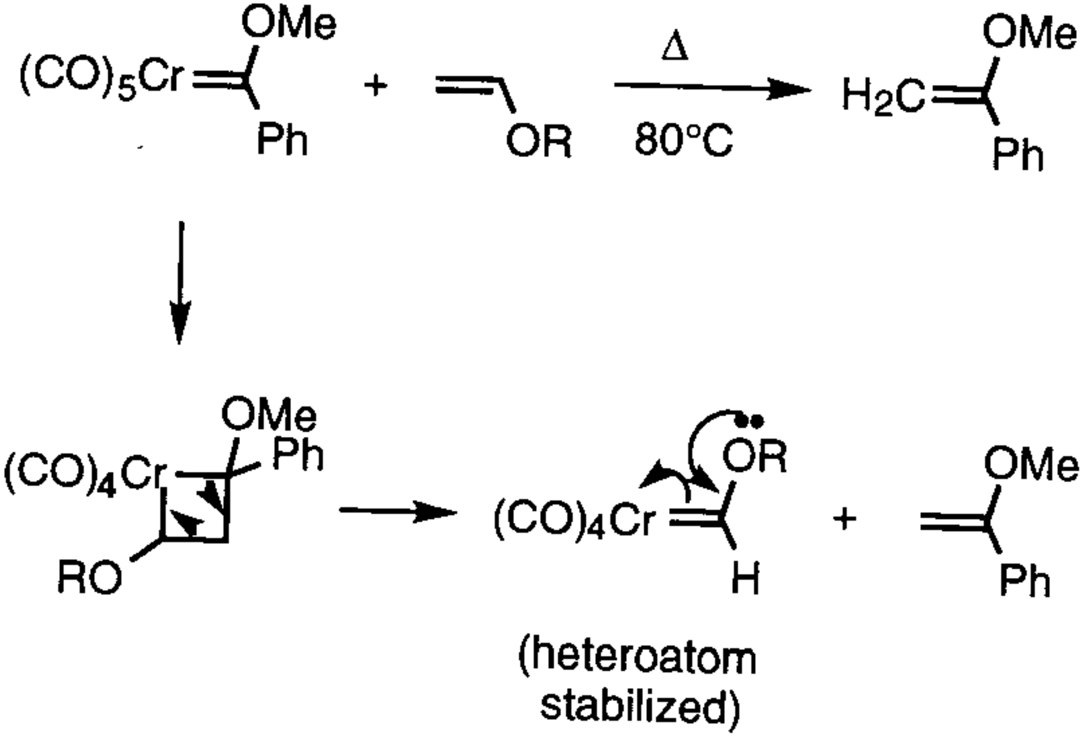
Carbene detachment (transfer) reactions



The metallacyclobutane is the key intermediate of this reaction!

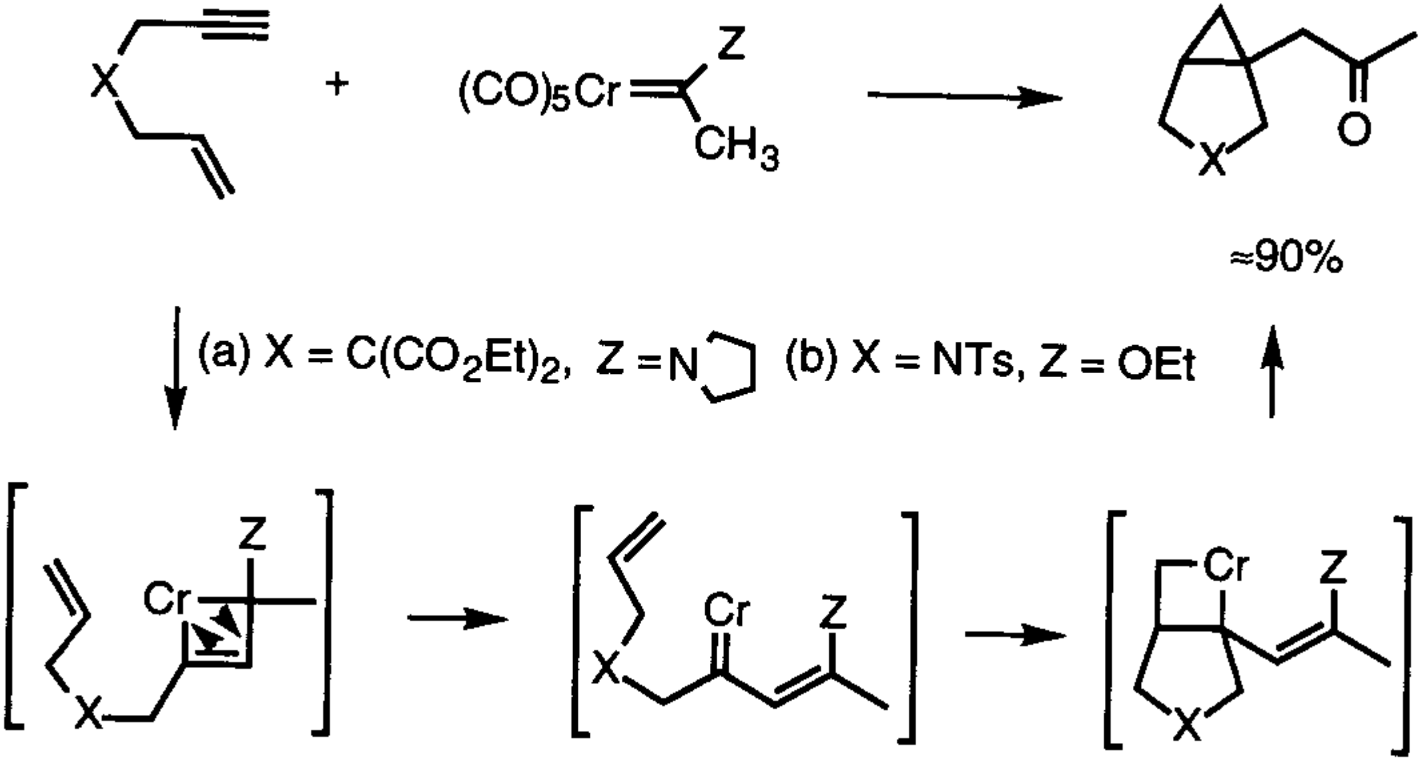
Alkene metathesis

Apart from giving reductive elimination or β-elimination, the metallacyclobutane intermediate can also evolve foming a new carbene ligand and a new olefin (metathesis). However, this happens only if the new carbene complex is stable (the olefin reagent must be electron-rich!).

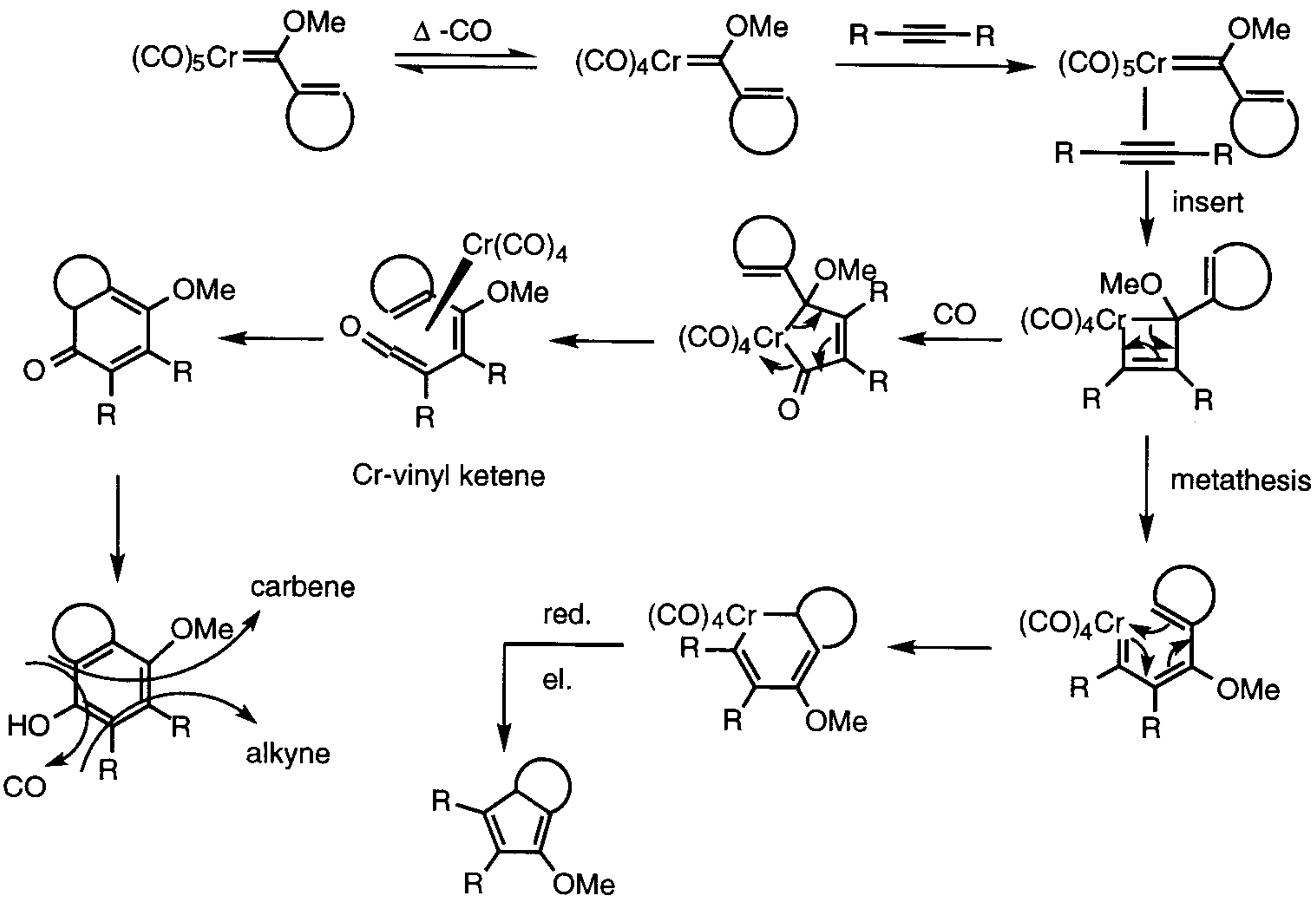


Alkyne metathesis

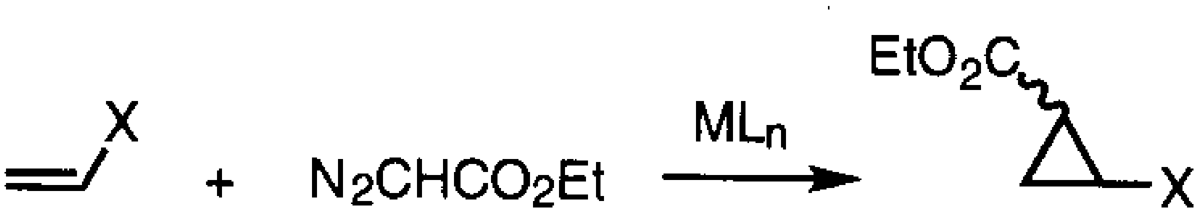
Alkynes can also undergo metathesis with TM carbenes, which upon formation of an intermediate metallacyclobutene produces new metallocarbenes with conjugated double bonds, which can conveniently be made to react further.



The Dötz reaction



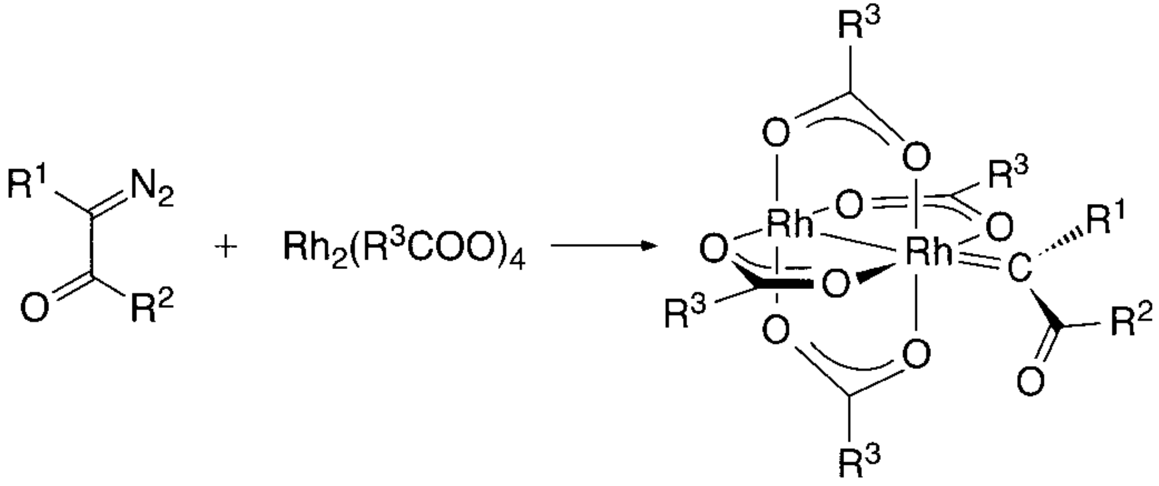
Cyclopropanation with diazocompounds



$ML_n = Rh_2(OAc)_4$, $CuCl{\bullet}P(O\textit{i}\,Pr)_3$, $Rh_6(CO)_{16}$, $PdCl_2{\bullet}2PhCN$

X = $BrCH_2$, $ClCH_2$, PhO, *n* Bu, OAc, OEt, O-*n* Bu, *i* Pr, *t* Bu, $CH_2{=}CPh$

$CH_2{=}CMe$, $CH_2{=}C$-*t* Bu, CH=CHOMe, CH=CHCl, CH=CHPh, CH=CHMe



Cyclopropanation with diazocompounds

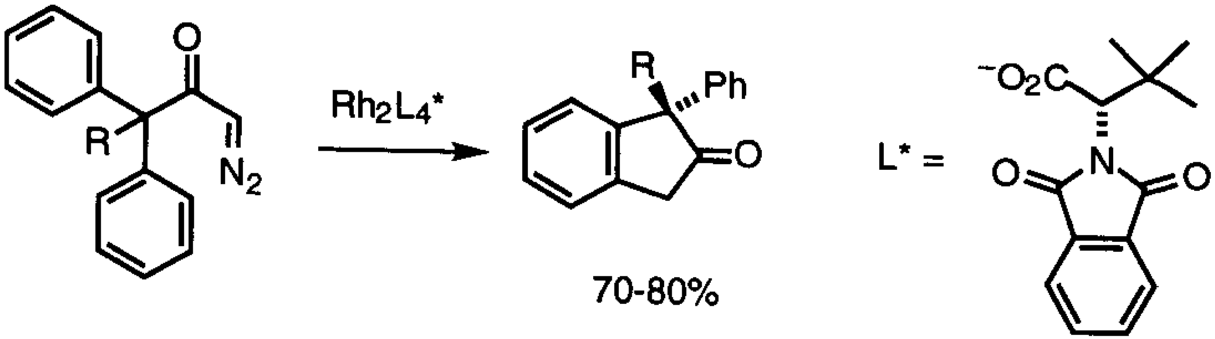
- Fast reaction wich takes place under mild conditions (room T, low catalyst amounts): external attack of the olefin on the coordinated carbene;
- Possibility of highly enantioselective reactions;

Limitations:

- very few diazocompounds are commercially available due to their instability (risk of explosions);
- reaction chemoselectivity (simple carbene dimerization is generally a competitive reaction);
- Diastereoselectivity of the reaction: often *E:Z* isomers are obtained in comparable ratios.

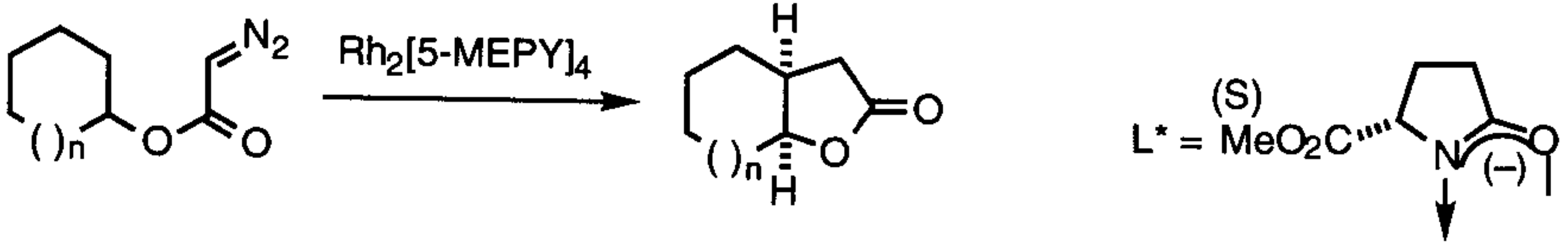
In the absence of C-C double bonds, the reaction can result in the insertion of the carbene in X-H bonds (X= Si, N, O, P, S…) or even in C-H bonds.

C-H insertion of carbenes from diazocompounds



70-80%

88-98% ee

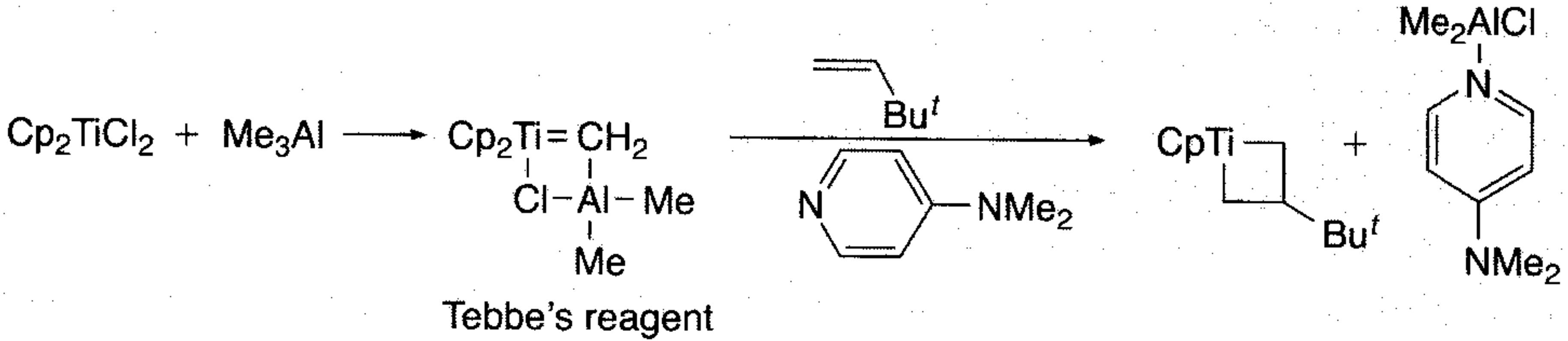


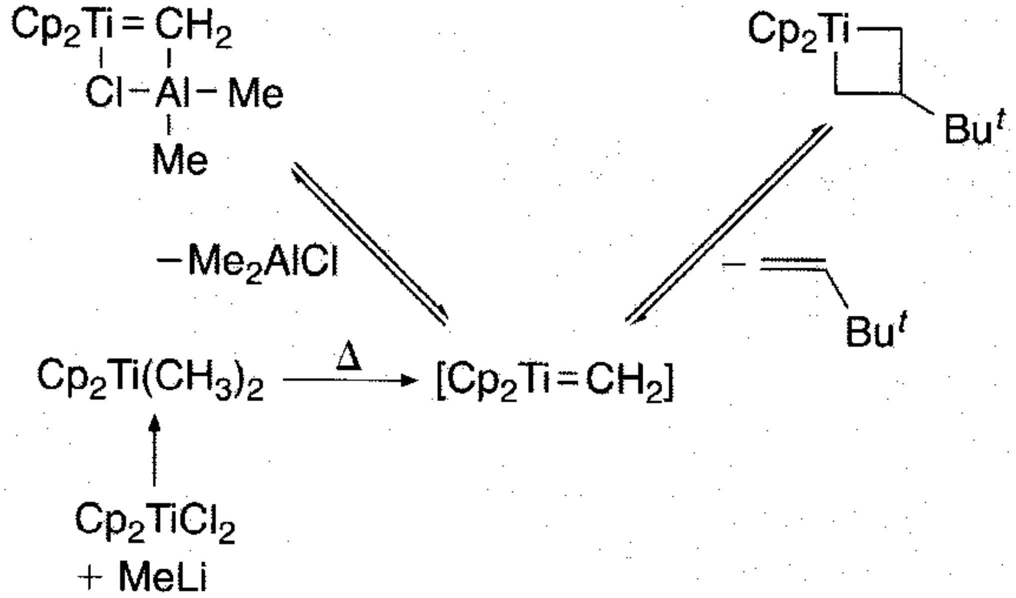
n = 1, 2, 3

97% ee

In the presence of different types of accessible C-H bonds, the chemoselectivity is often imparted by the electronic properties of the ligands at metal.

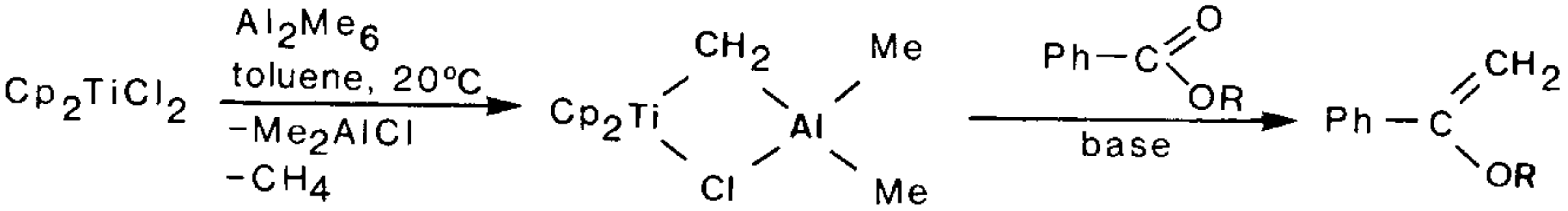
Transfer of Schrock carbenes: the Tebbe reagent



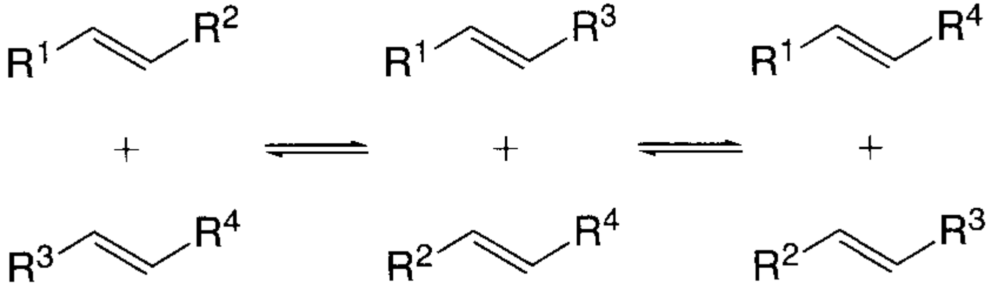


“Grubbs reaction” with the Tebbe reagent

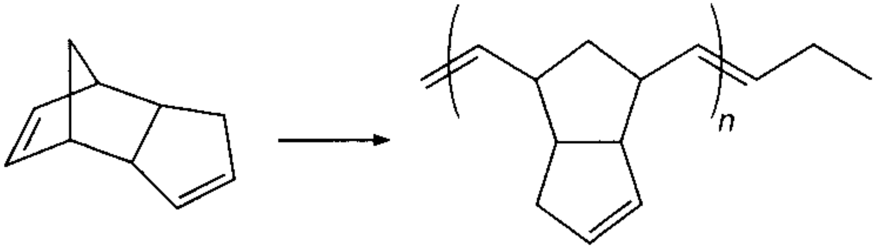
The Tebbe reagent “Cp_2TiCH_2” is analogous to a methylenic ylide, and it consequently transfers the methylene group to substrates containing carbonyl groups, exchanging oxygen with methylene.
Yields are generally higher with respect to classic organic ylides, the tolerance to functional groups is higher and the reaction can be extended from simple carbonyls (aldehydes, ketones) to amides and especially to esters (Grubbs reaction), which usually do not react with organic ylides. Consequently, enamides or enolethers can be produced.



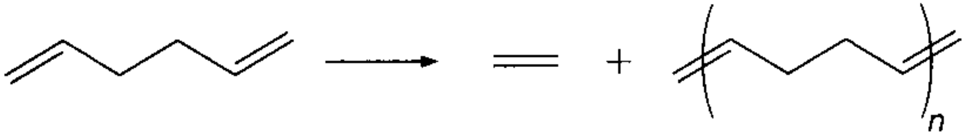
Catalytic olefin metathesis



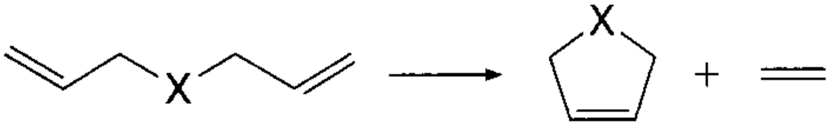
SHOP



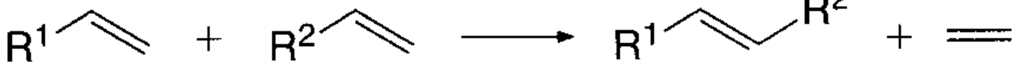
ROMP



ADMET

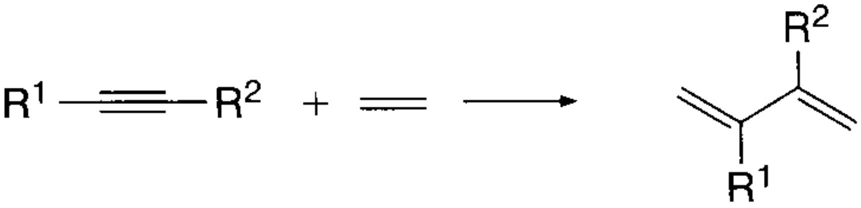


X = O, NTs, $C(CO_2R)_2$ **RCM**

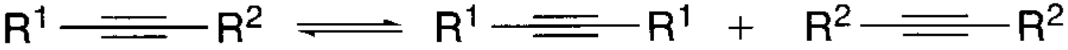


Cross metathesis

Catalytic olefin metathesis

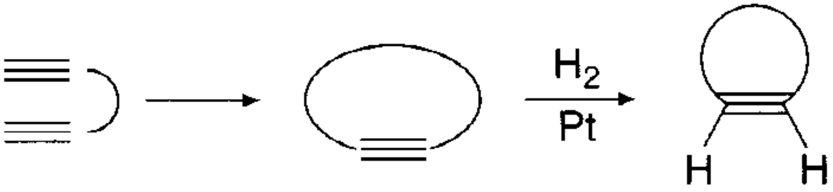


Enyne metathesis



Alkyne metathesis

Alkyne metathesis polymerization



Ring-closing alkyne metathesis

Metathesis – history and catalysts

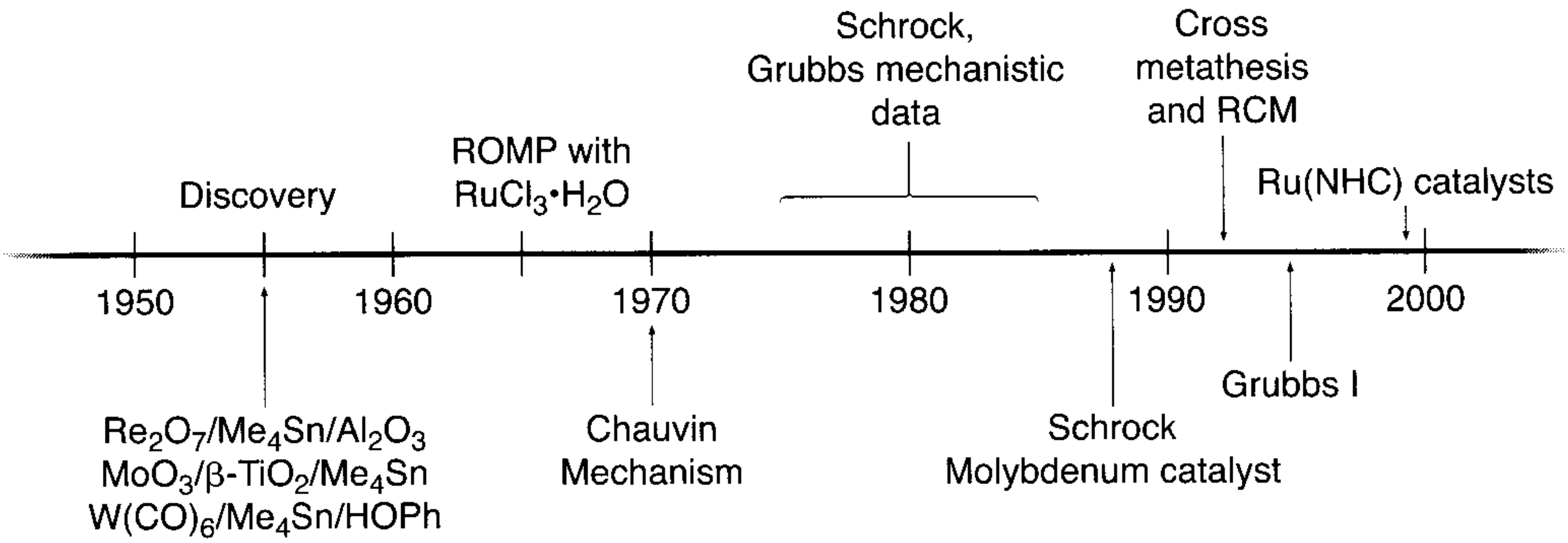
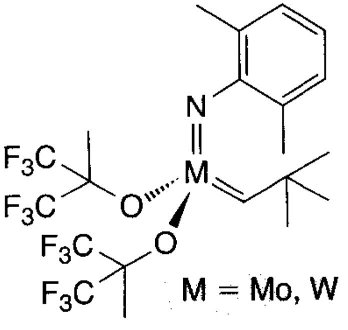
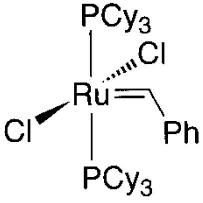


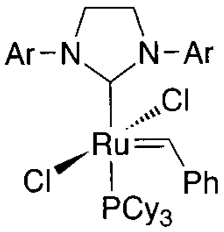
Figure 21.3.
Timeline of olefin metathesis (adapted from Trnka, T. M.; Grubbs, R. H. *Acc. Chem. Res.* **2001**, *34*, 18).



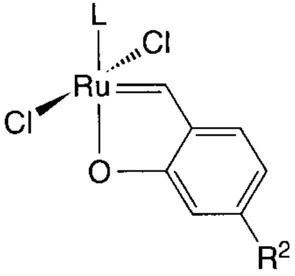
Schrock



Grubbs I



Grubbs II



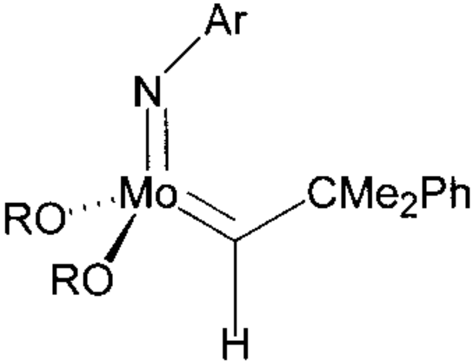
Hoveyda, Blechert, Grela

R = H, L = PCy_3, Hoveyda Gen I
R = H, L = S*i*Mes, Hoveyda Gen II
R = NO_2, L = S*i*Mes, Grela gen II

S*i*Mes =

Ar = 2,6-$Me_2C_6H_3$

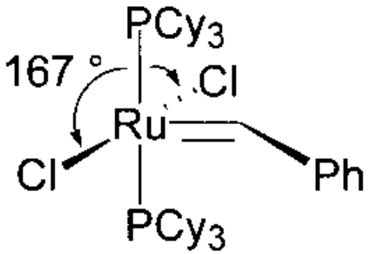
Metathesis – Schrock and Grubbs catalysts



Ar = 2,6-$(i\text{-Pr})_2C_6H_3$
R = $(F_3C)_2(CH_3)C$

Schrock (1990)

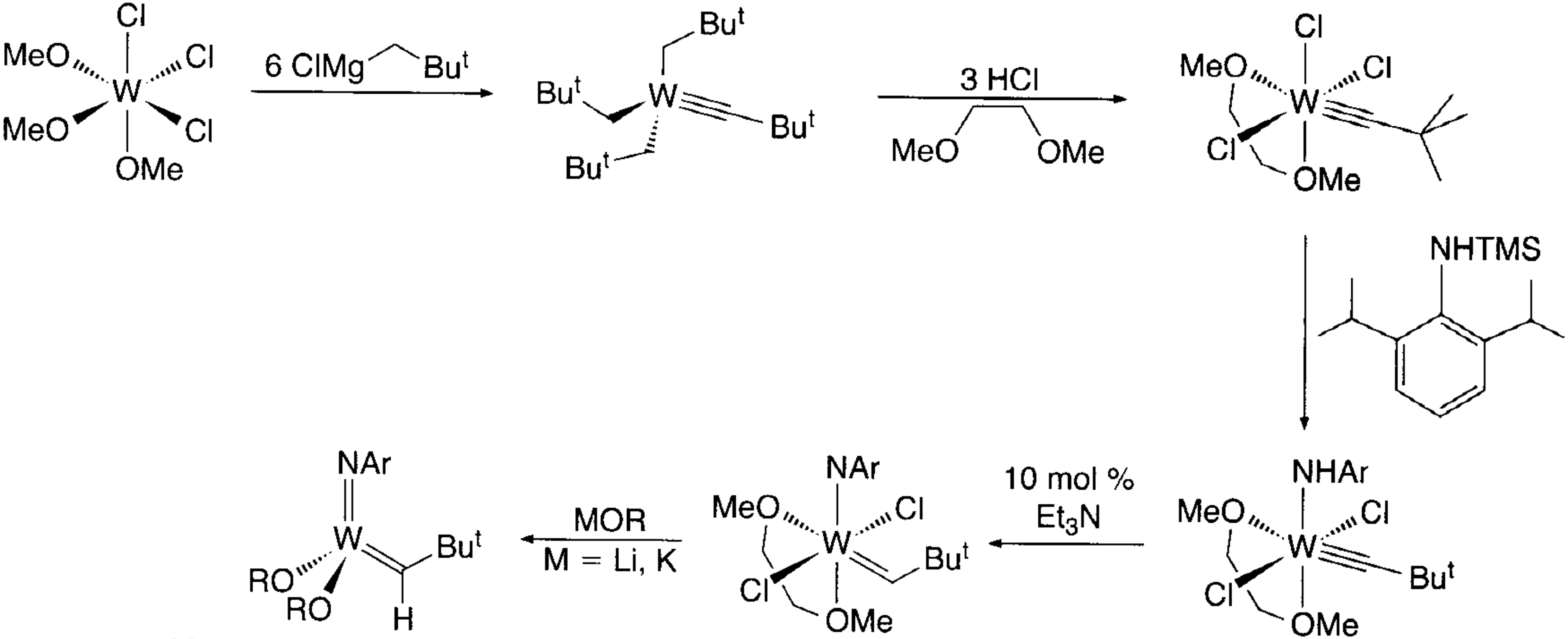
- Highly reactive, hence poor tolerance of functional groups in the substrate.
- The catalytic activity increases with increasing electron-withdrawing nature of R.
- Metathesis of tri- and tetrasubstituted olefins is possible.



Grubbs (1995)

- Tolerance of functional groups (CO, OH, NH_2).
- Selectivity towards sterically unhindered olefins and strained olefins.
- Tri- and tetrasubstituted olefins are not attacked.

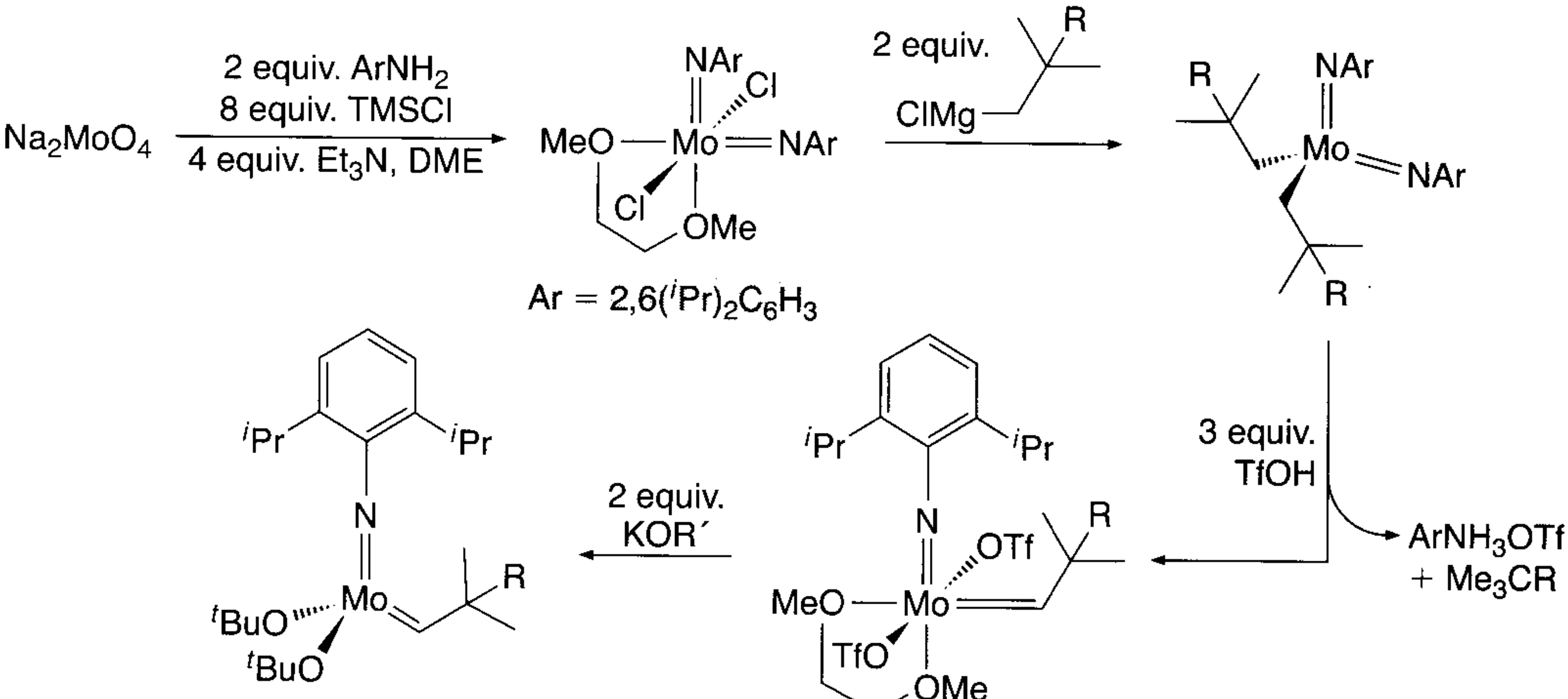
Synthesis of the Schrock catalyst (W)



More stable than anti geometry

R = *t*-Bu, $C(CH_3)(CF_3)_2$

Synthesis of the Schrock catalyst (Mo)



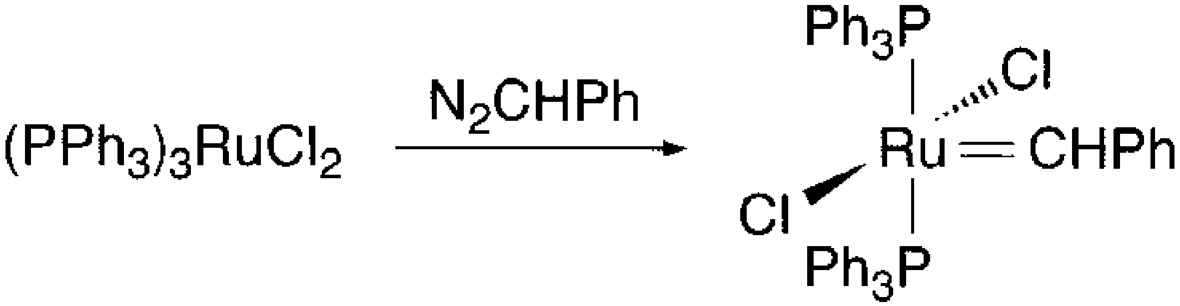
Ar = $2,6(^iPr)_2C_6H_3$

More stable than anti geometry

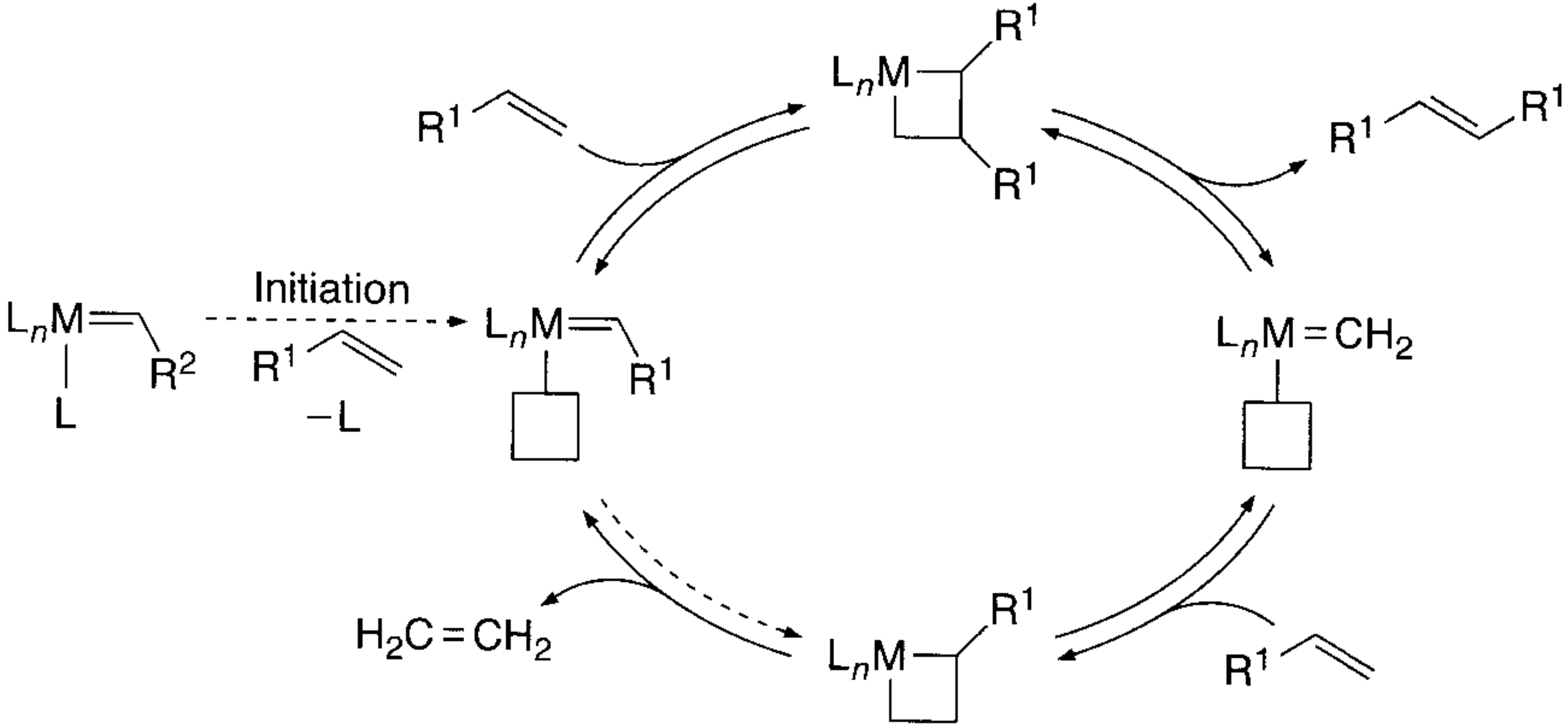
R = Me or Ph
R´ = *t*-Bu, $C(CH_3)(CF_3)_2$

Synthesis of the Grubbs catalyst (1° generation)

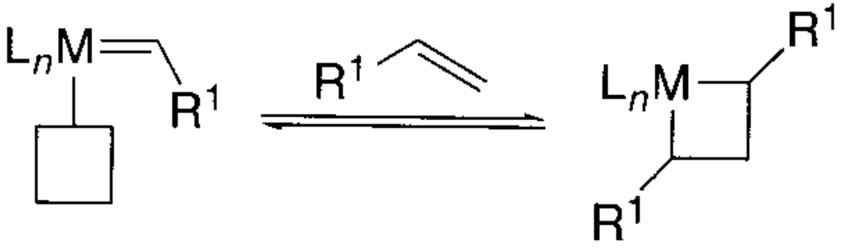
With respect to Schrock catalysts, Grubbs catalysts are less active but more stable, easy to prepare and tolerant towards functional groups and reaction cinditions (the reaction can even be performed in water!). The preference for either typology depends on the particular process to be catalyzed.



Catalytic olefin metathesis - Mechanism



Degenerate [2 + 2] additions (transalkylidenation):



Catalytic olefin metathesis - Mechanism

The catalytic metathesis reaction allows to establish an **equilibrium** between the various olefins that can be synthesized and the starting ones. The reaction can be shifted towards a determined product:

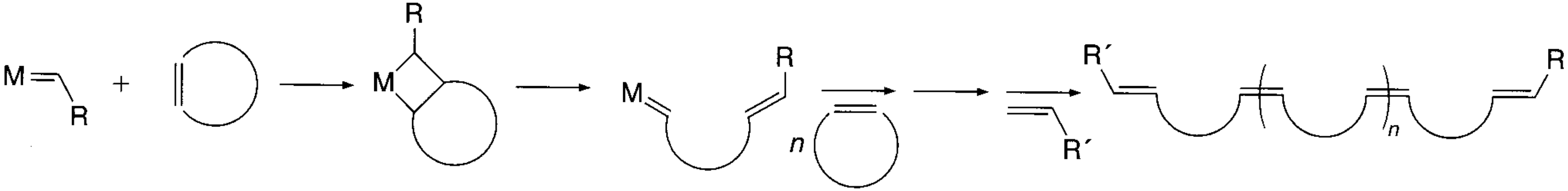
- when the product is thermodynamically favoured by loss of ring strain (ROMP);

- when a volatile olefin coproduct can be removed by evaporation (generally ethylene: ADMET, RCM, CM);

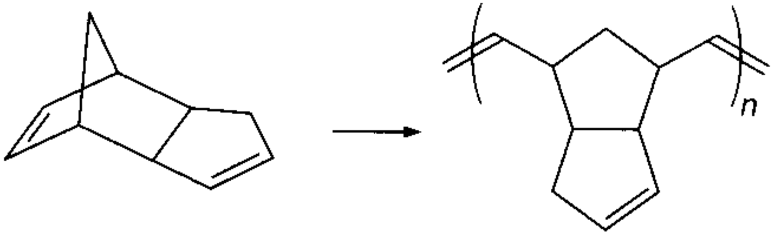
- when dilution or preorientation effects favour cyclic olefins over open chain polyolefins (RCM vs. ADMET);

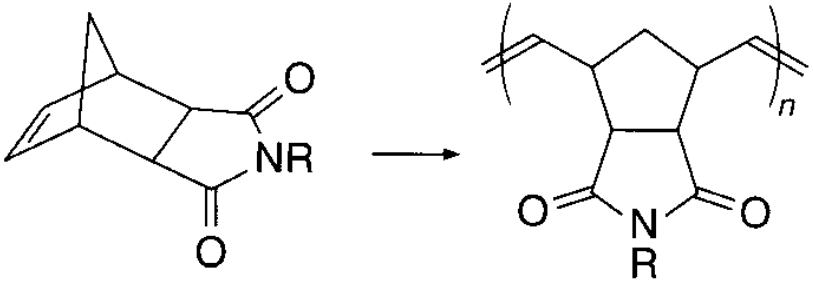
- when a judicious choice of couples of monosubstituted olefin reagents favours the formation of a single product (CM).

ROMP – Synthetic applications

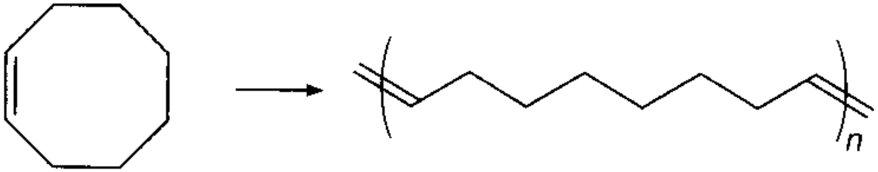


Generally promoted by simple catalytic systems (salts, oxides…); technologically relevant; possibility of living polymerization, hence of production of block copolymers.

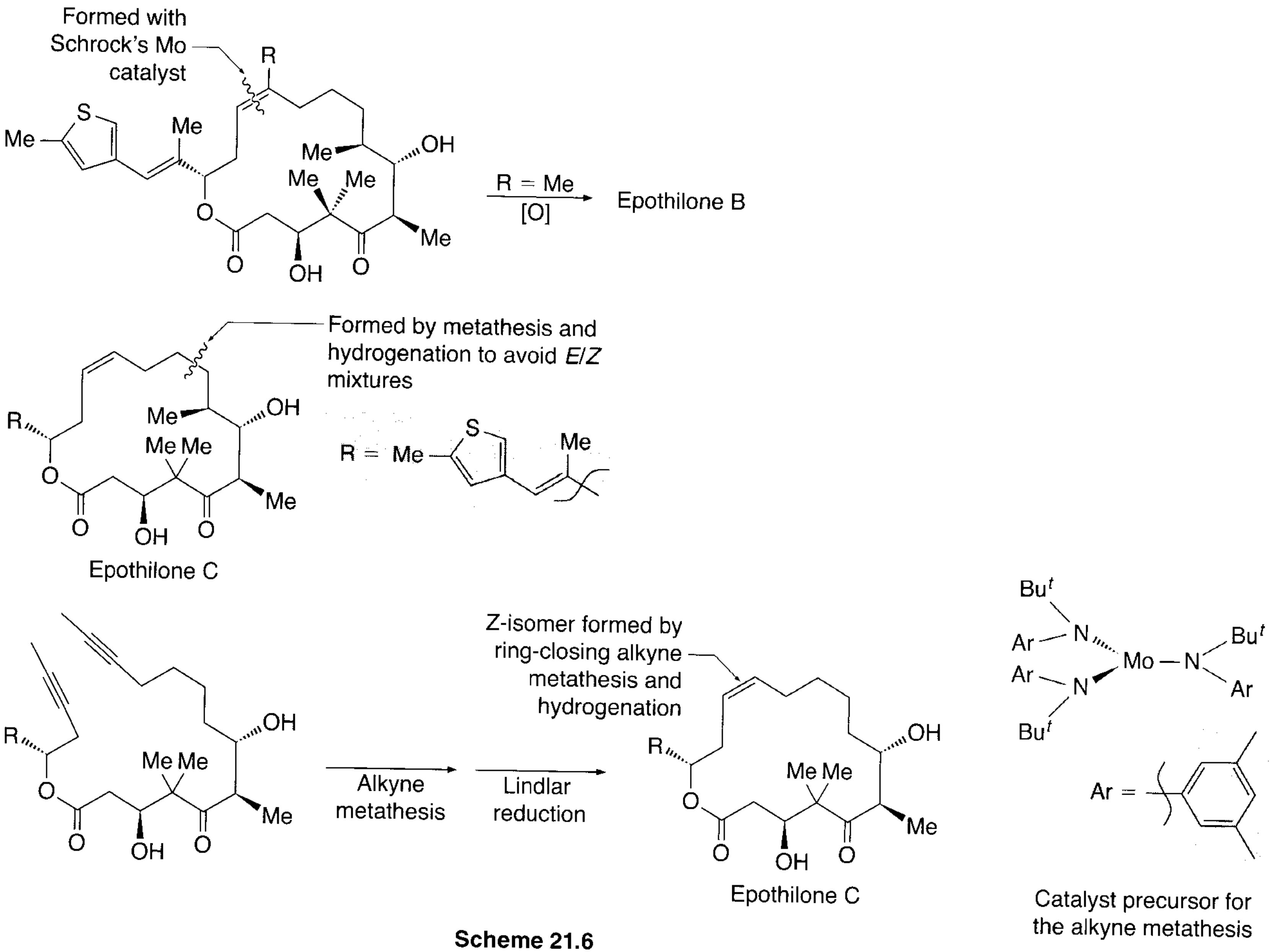




R = Sugar, amino acid, or vancomycin

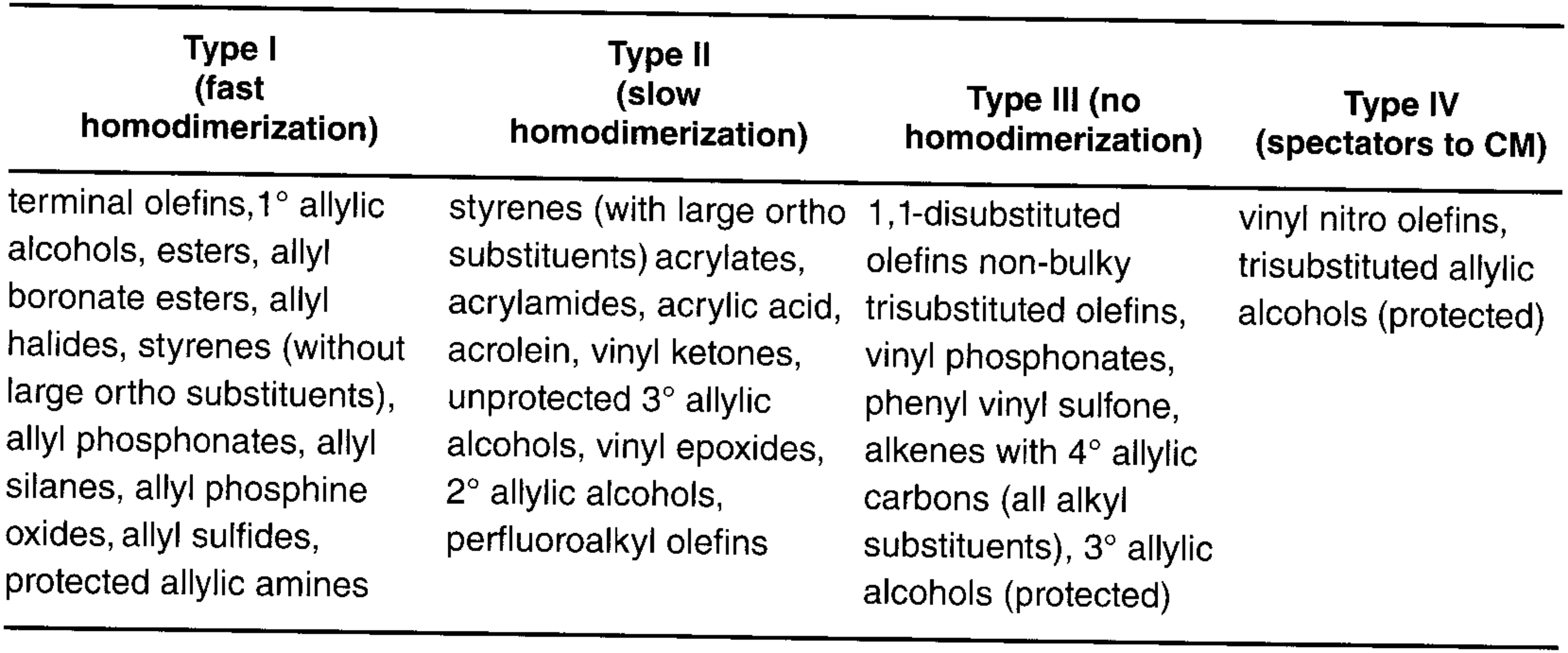


RCM – Synthetic applications

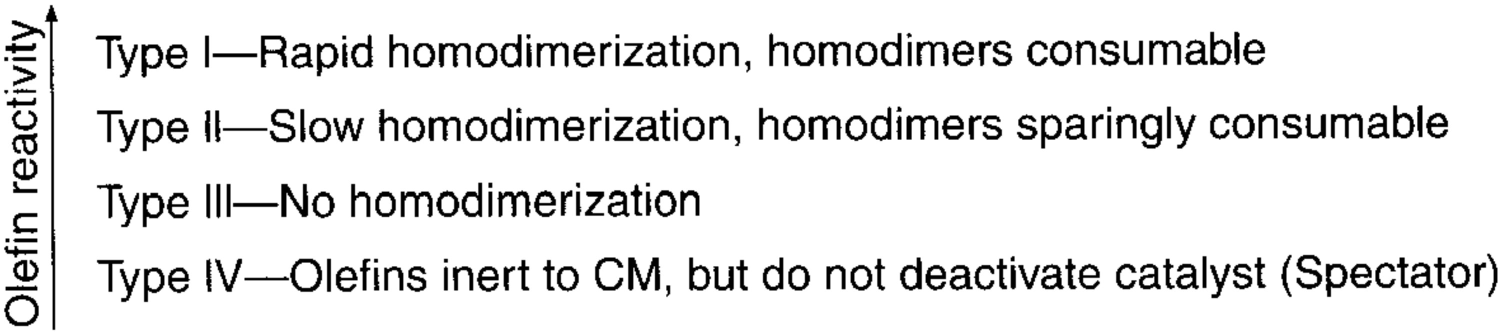


Scheme 21.6

Olefin classification for CM (Grubbs)



Type I (fast homodimerization)	**Type II (slow homodimerization)**	**Type III (no homodimerization)**	**Type IV (spectators to CM)**
terminal olefins, 1° allylic alcohols, esters, allyl boronate esters, allyl halides, styrenes (without large ortho substituents), allyl phosphonates, allyl silanes, allyl phosphine oxides, allyl sulfides, protected allylic amines	styrenes (with large ortho substituents) acrylates, acrylamides, acrylic acid, acrolein, vinyl ketones, unprotected 3° allylic alcohols, vinyl epoxides, 2° allylic alcohols, perfluoroalkyl olefins	1,1-disubstituted olefins non-bulky trisubstituted olefins, vinyl phosphonates, phenyl vinyl sulfone, alkenes with 4° allylic carbons (all alkyl substituents), 3° allylic alcohols (protected)	vinyl nitro olefins, trisubstituted allylic alcohols (protected)



Type I—Rapid homodimerization, homodimers consumable

Type II—Slow homodimerization, homodimers sparingly consumable

Type III—No homodimerization

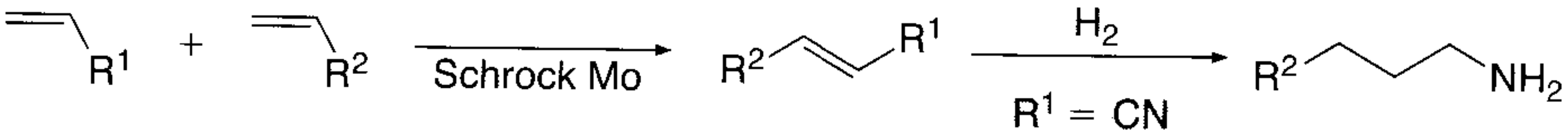
Type IV—Olefins inert to CM, but do not deactivate catalyst (Spectator)

Olefin classification for CM (Grubbs)

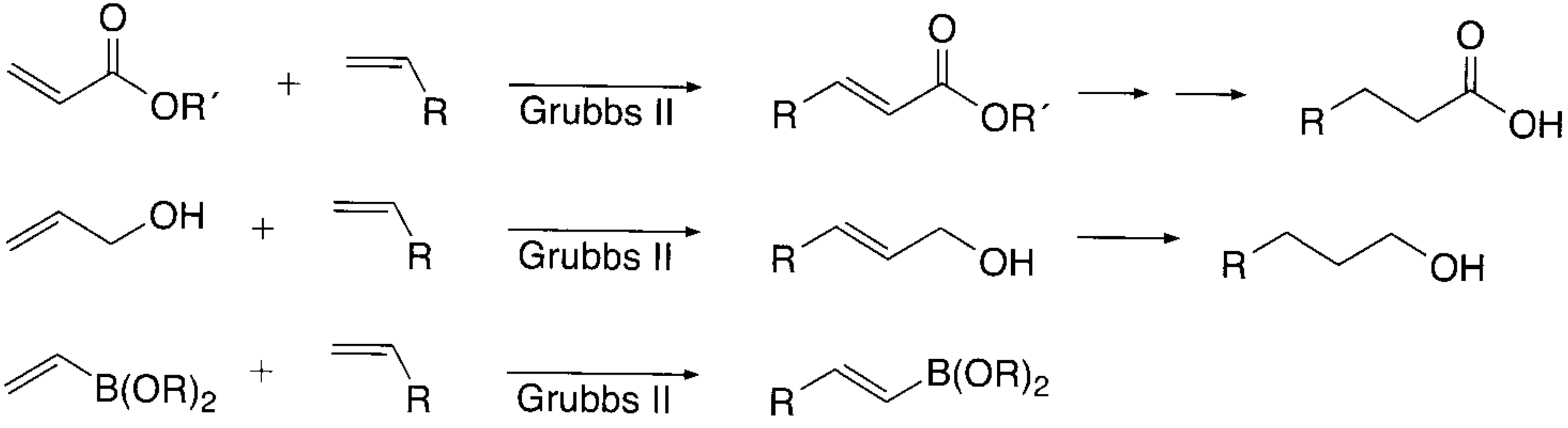
Reaction between two olefins of Type I = *Statistical CM*

Reaction between two olefins of same type (non-Type I) = *Non-selective CM*

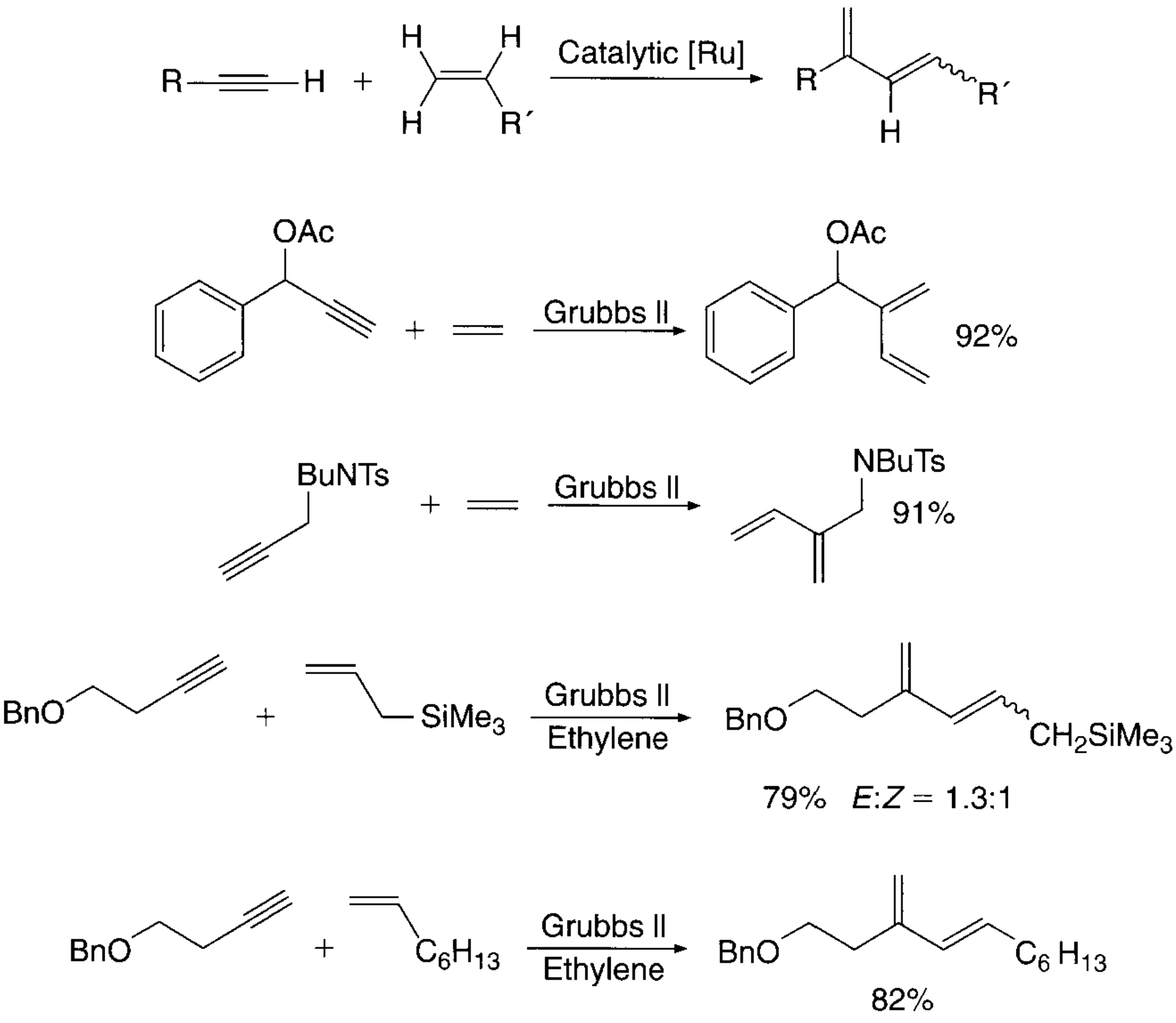
Reaction between olefins of two different types = *Selective CM*



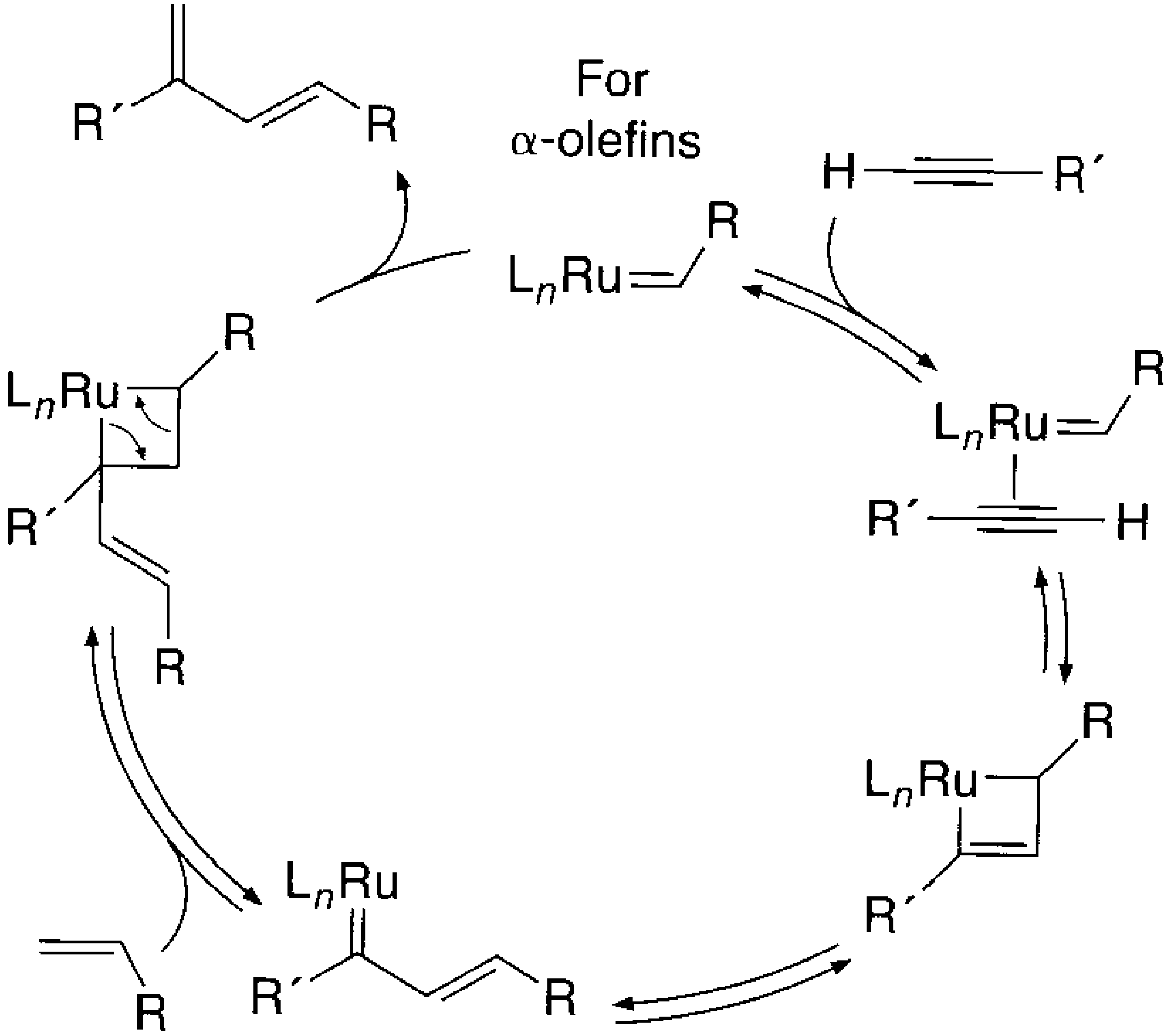
R^1 = CN, Ph or $SiMe_3$
R^2 = alkyl



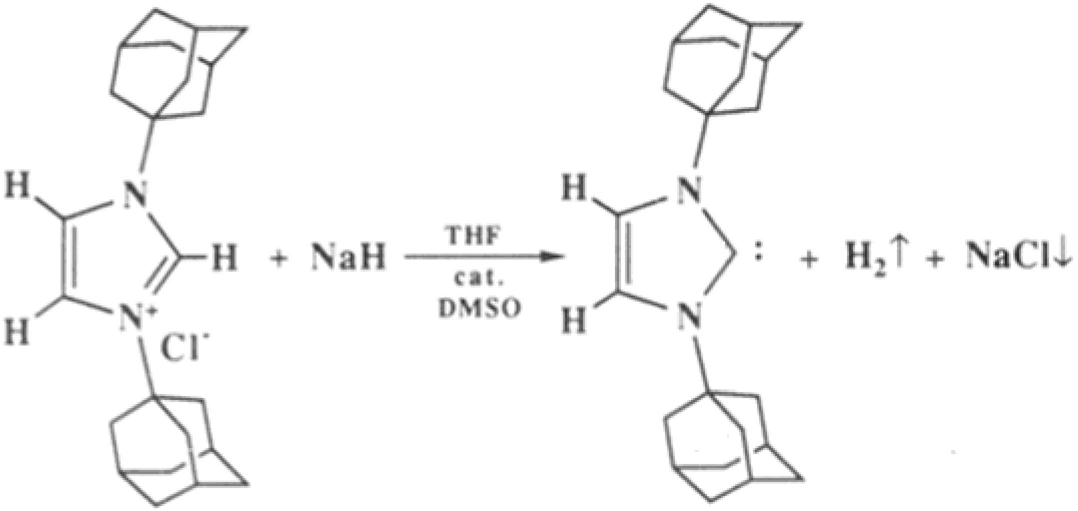
Catalytic ene-yne metathesis



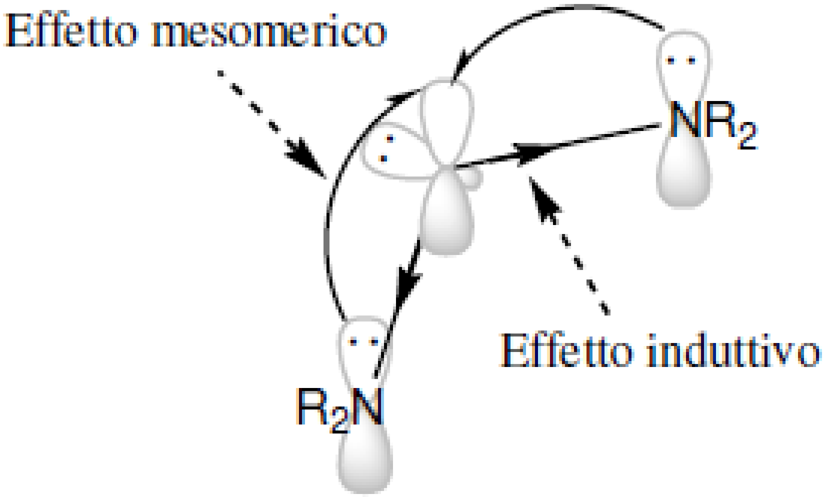
Catalytic ene-yne metathesis - mechanism



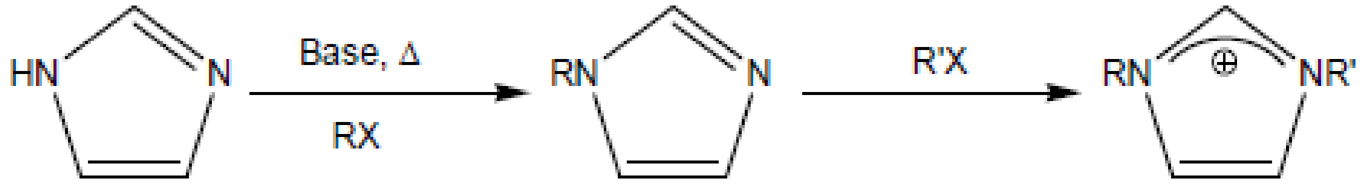
N-heterocyclic carbenes (NHC)

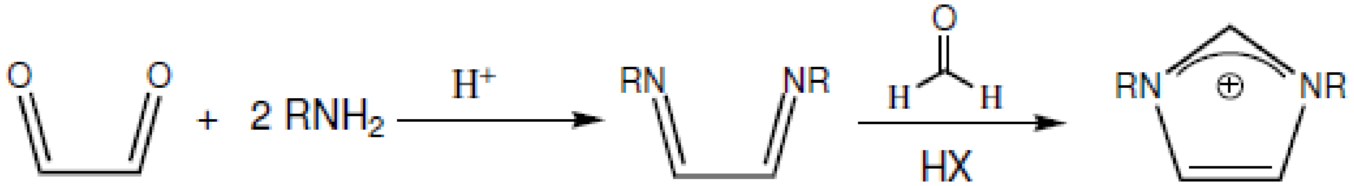


Stable carbenes (isolable, storable, commercially available…) thanks to the electronic effect of the heteroatoms α to C, and to the steric effect of the N-substituents.



N-heterocyclic carbenes (NHC)

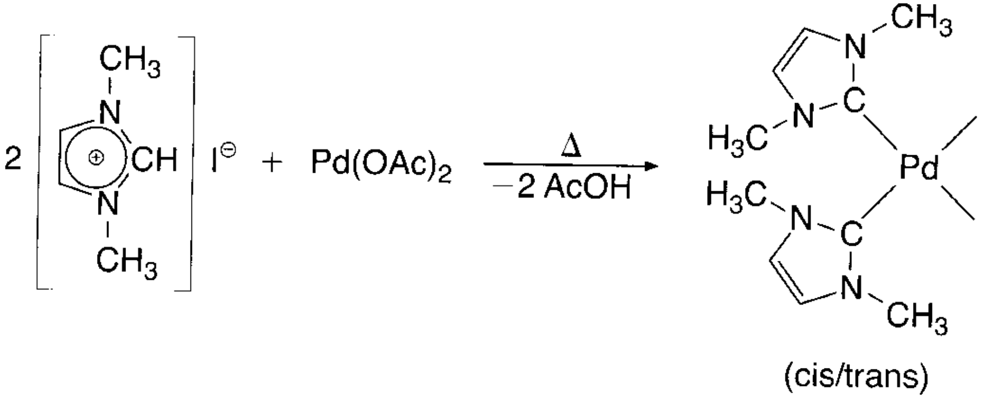




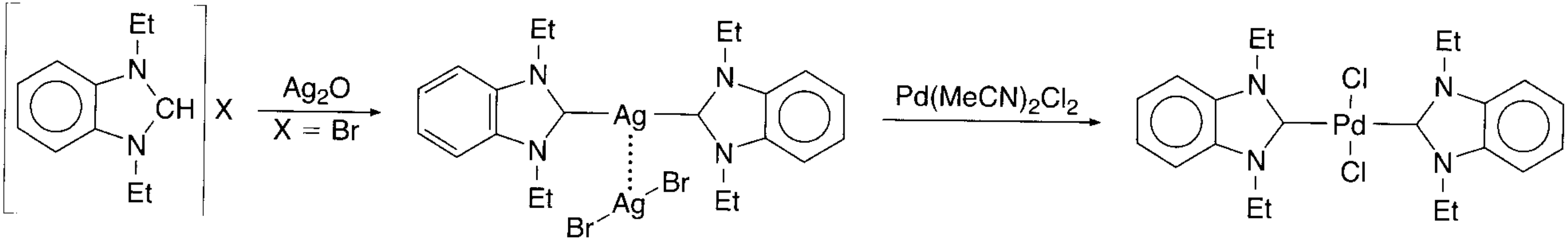
Main synthetic strategies for the preapration of NHC precusors (imidazolium salts and related compounds).

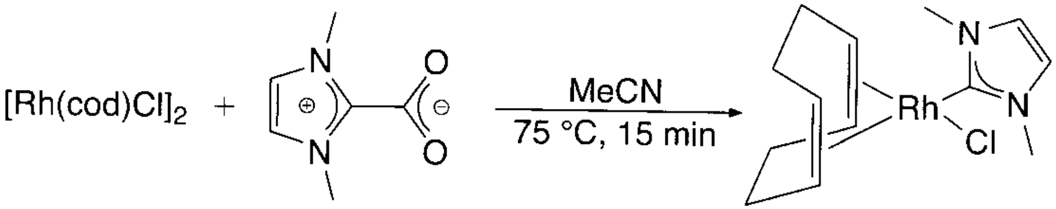
Several other synthetic strategies have been developed for the preparation of other kinds of N-heterocyclic cations.

N-heterocyclic carbenes (NHC)



(13.14)





(13.16)

N-Heterocyclic carbenes(NHC)

NHCs are nowadays extensively studied as supporting ligands towards transition metal centres, since:

- they are strong σ-donors (as trialkylphosphines);

- provide more stable compounds with respect to e.g. phosphines: dissociation equilibria shifted towards the complex, lower risk of decomposition of the complex under drastic reaction conditions;

- Sterically more bulky: possibility to modulate the electronic characteristics independently from steric ones;

- Examples of application: catalytic olefin metathesis (Grubbs II), cross-coupling C-C and C-X, hydrofunctionalizations of C-C multiple bonds…