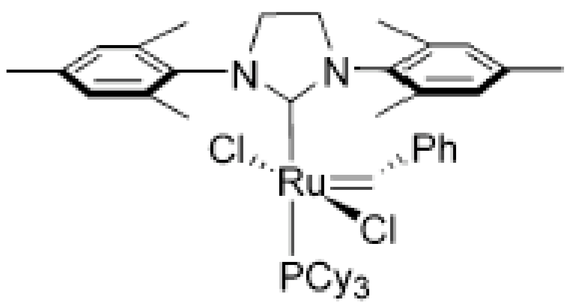
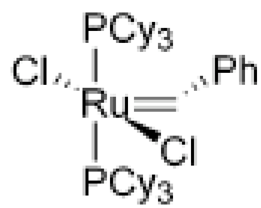
A General Model for Selectivity in Olefin Cross Metathesis

R.H. Grubbs, *JACS* ASAP.

Common Metathesis Catalysts



1



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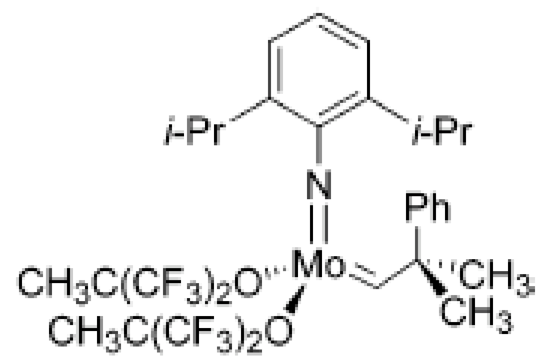
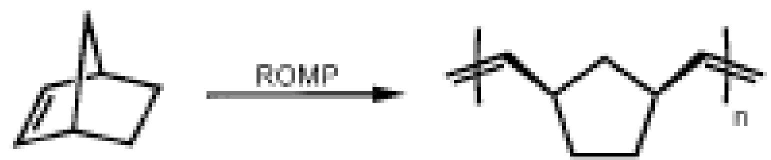


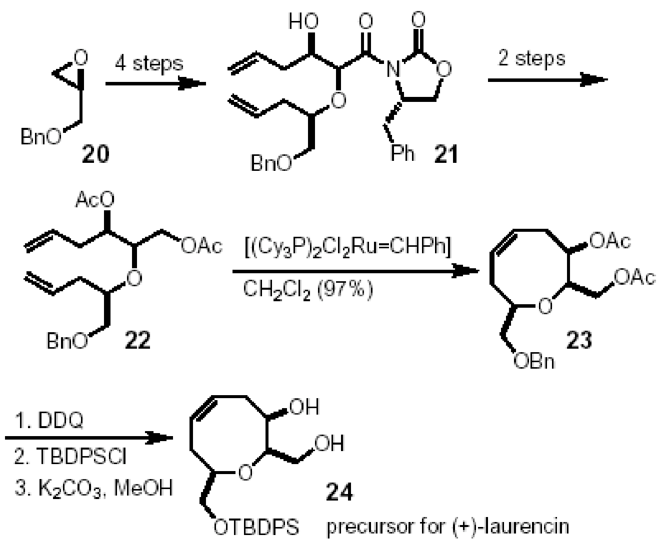
3

Examples of Metathesis

- Ring Opening Metathesis Polymerization



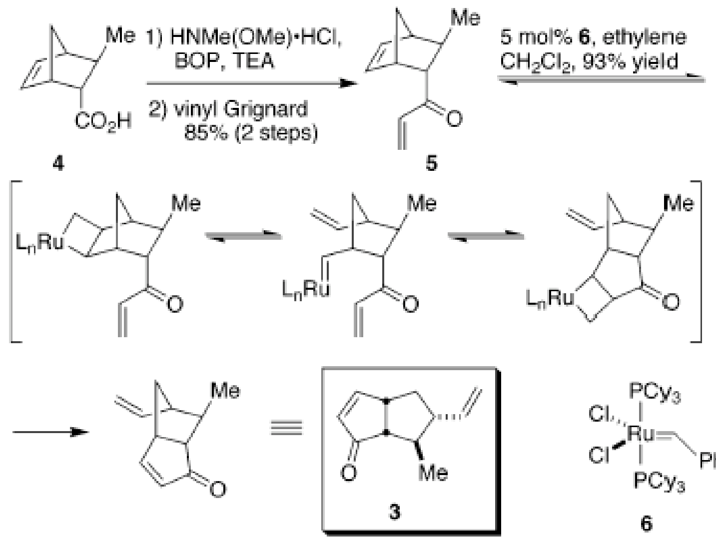
- Ring Closing Metathesis



Angew. Chem. Int.Ed. **2003**, 42, 1900

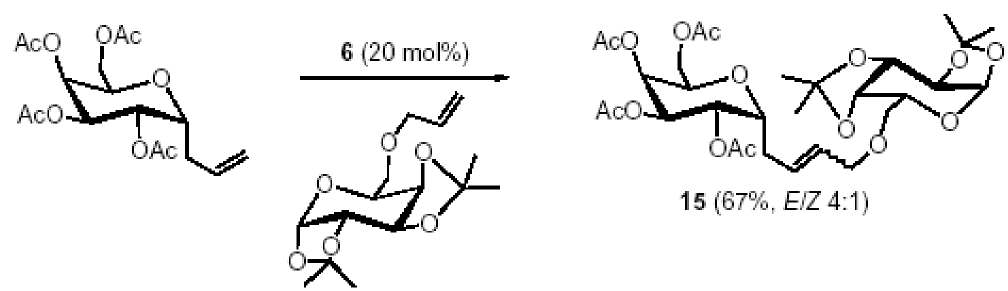
Examples of Metathesis Cont.

- Ring Opening/Ring Closing Metathesis



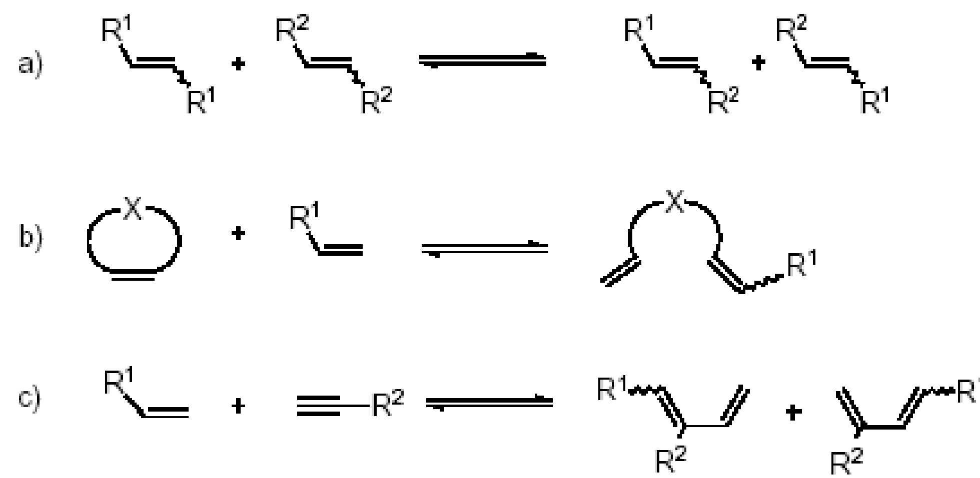
J. AM. CHEM. SOC. 2002, *124*, 9974–9975

- Cross Metathesis

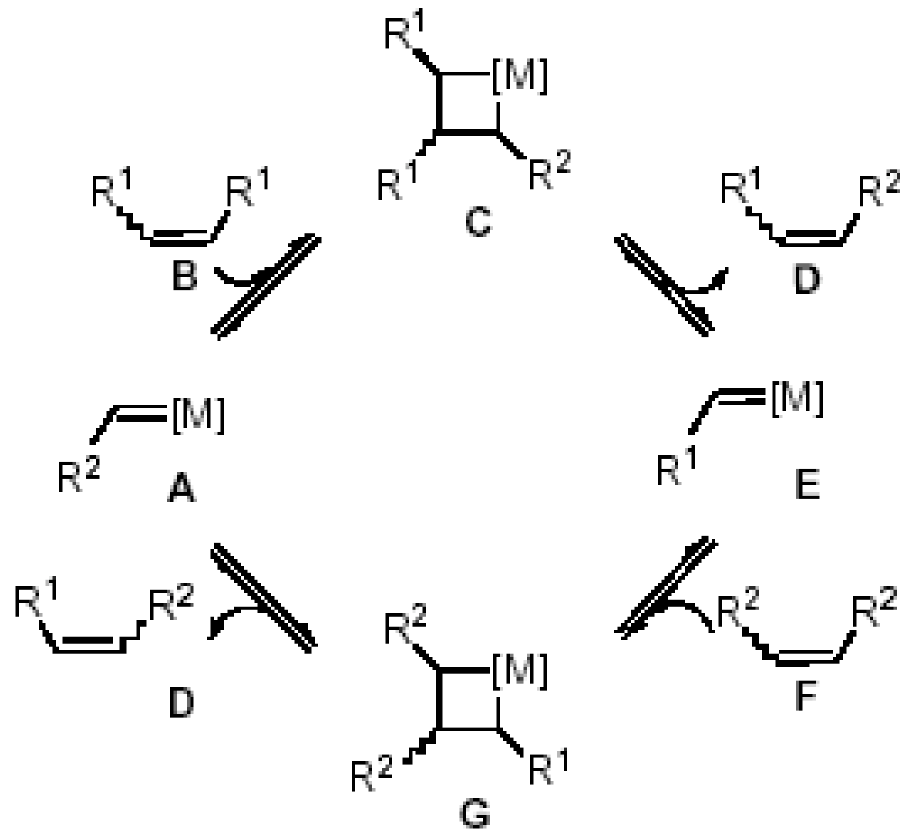


Cross Metathesis(CM)

- The mutual exchange of alkylidene fragments between two olefins promoted by metal-carbene complexes
- There are 3 major variations on this theme: a) CM, b) Ring Opening CM and c) intermolecular enyne metathesis



Metathesis Mechanism



Problems with CM

- Not a large driving force unlike ROMP or RCM
- Low product selectivity, mixtures of homodimers or polymers can be formed
- Poor Stereoselectivity in the produced olefin.
- Lack of a model that predicts selectivity.

Classification of Olefins for CM

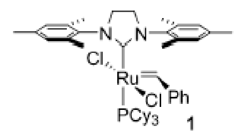
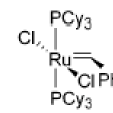
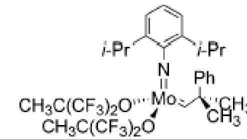
olefin reactivity ↑

- 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)

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

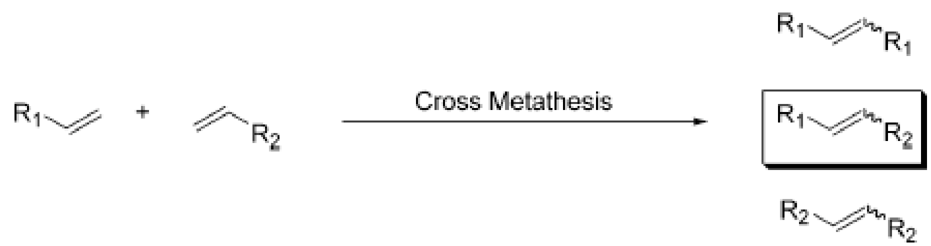
Reaction between two olefins of same type (non-Type I) = *Non-selective*

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

Olefin type	 1	 2	 3
Type I **(fast homodimerization)**	terminal olefins,[6] 1° allylic alcohols, esters,[6h,20] allyl boronate esters,[6f] allyl halides,[6f,6i] styrenes (no large ortho substit.),[6c,d,f,i] allyl phosphonates,[6d] allyl silanes,[25] allyl phosphine oxides,[6h] allyl sulfides,[6h] protected allyl amines[6h]	terminal olefins,[8] allyl silanes,[14,18,19] 1° allylic alcohols, ethers, esters,[8,19,21] allyl boronate esters,[10f] allyl halides[17]	terminal olefins,[11a,b,12,14] allyl silanes[11b]
Type II **(slow homodimerization)**	styrenes (large ortho substit.),[6d,f] acrylates,[6b,i] acrylamides,[6c] acrylic acid,[6c] acrolein,[6b,24] vinyl ketones,[6b] unprotected 3° allylic alcohols,[6f,h] vinyl epoxides,[6b] 2° allylic alcohols, perfluorinated alkane olefins[6b,23]	styrene,[16] 2° allylic alcohols, vinyl dioxolanes,[8] vinyl boronates[8]	styrene,[11a,11b] allyl stannanes[15]
Type III **(no homodimerization)**	1,1-disubstituted olefins,[6a,g] non-bulky trisub. olefins,[6a,g] vinyl phosphonates,[6d] phenyl vinyl sulfone,[22] 4° allylic carbons (all alkyl substituents), 3° allylic alcohols (protected)	vinyl siloxanes[16]	3° allyl amines,[14] acrylonitrile[12]
Type IV **(spectators to CM)**	vinyl nitro olefins, trisubstituted allyl alcohols (protected)	1,1-disubstituted olefins,[8] disub. α,β-unsaturated carbonyls, 4° allylic carbon-containing olefins,[8] perfluorinated alkane olefins,[8] 3° allyl amines (protected)[14]	1,1-disubstituted olefins[11a]

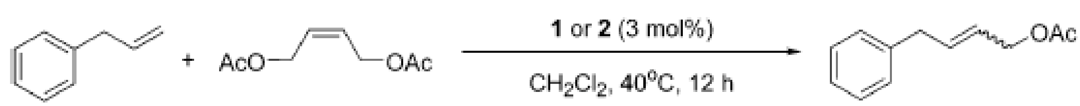
CM with Two Type 1 Olefins

Scheme 3. Statistical Distribution of CM Products



$R_1 : R_2$	CM product selectivity
1:1	50%
2:1	66%
4:1	80%
10:1	91%
20:1	95%

Scheme 4. Nonselective Olefin Cross Metathesis



1 equiv.

2 equiv.

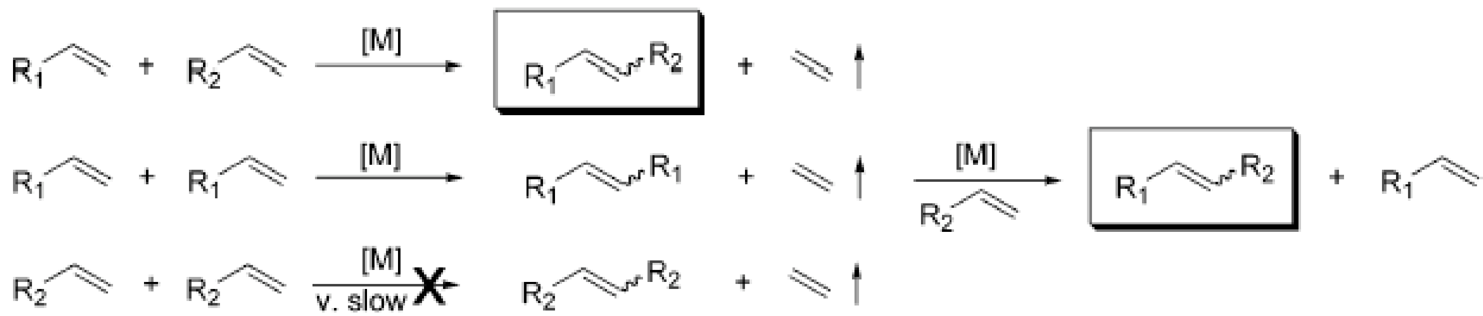
4

80% isolated yield

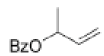
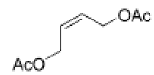
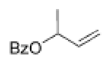
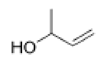
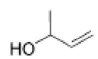
	E/Z ratio
catalyst **1**	7:1
catalyst **2**	3.2:1

General CM of Type 1 and Type 2/3 Olefins

Primary Reactions in Cross Metathesis of Type I with Type II/III

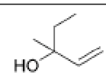
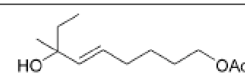
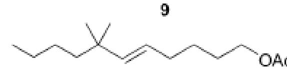
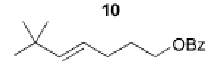
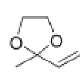
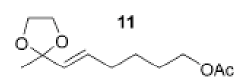
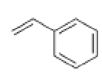
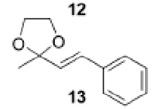


Results of CM of Type 1 and Type 2/3 Olefins

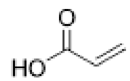
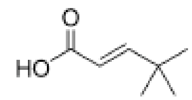
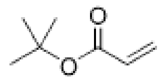
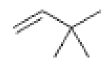
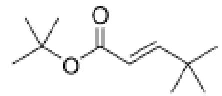
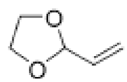
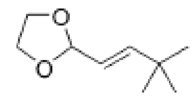
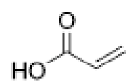
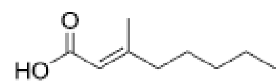
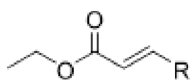
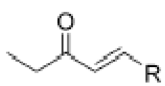
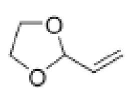
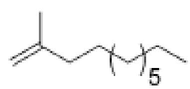
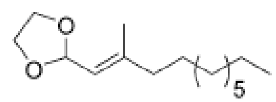
Entry	2° Allylic Alc.	Cross Partner (Equiv)		Product	Iso. Yield (%)	E/Z ratio[a]
1			(1.8)	 5	38	18:1
2			(2.0)	 6	82	10:1
3			(2.0)	 7	92	13:1
4			(1.0)	 7	50 62[b]	14:1 14:1
5			(0.5)	 8	53	6.7:1

NMR. [b] Reaction performed at 23 °C.

Allylic Olefin Cross Metathesis[a]

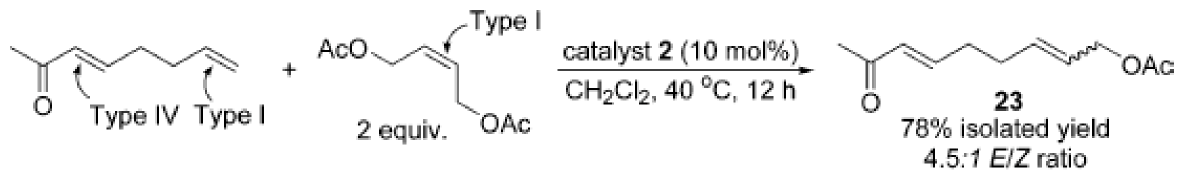
Entry	4° Allylic Olefin	Equiv.	CM Partner	Product	Isolated Yield[b] (%)
1		2.0		 9	93
2		2.0		 10	90
3		excess		 11	99
4		1.0		 12	91
5		2.0		 13	70

Results of CM of Type 2 and Type 3 Olefins

Entry	Type II	Type III (Equiv)		Product	Isolated Yield (%)
1			(neat)		73
2			(neat)		73
3			(neat)		75
4			(4.0)		83[a]
5			(4.0)		55[a] R=H 83[a] R=Me
6			(4.0)		26[a] R=H 68[a] R=Me
7			(1.0)		67[b]

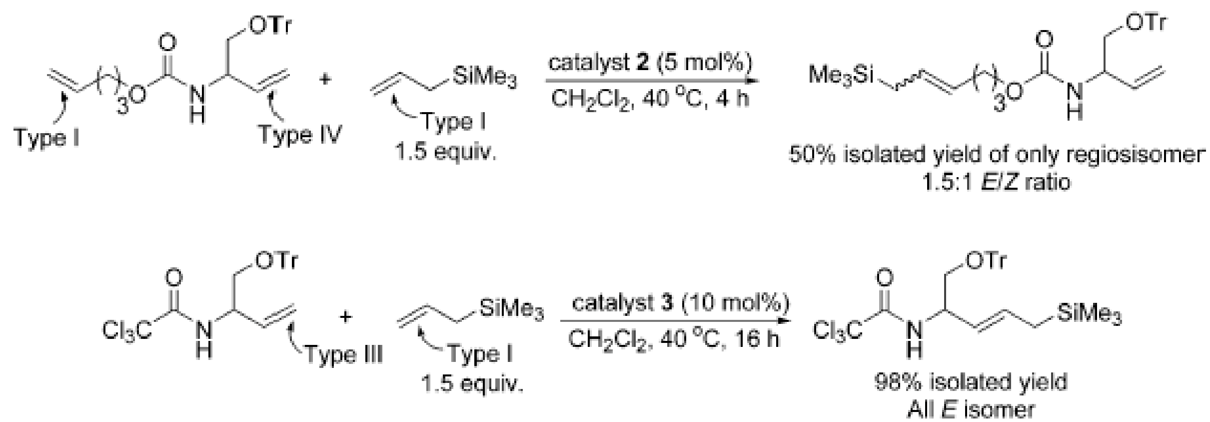
Application of Guidelines

Chemoselective CM Based on Olefin Categorization

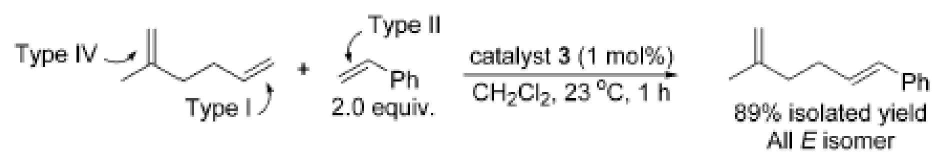


Chemoselective Cross Metathesis Using Catalysts 2 and 3

(A) *Blechert, et al.*



(B) *Crowe and Zhang*



Three Component CM

Scheme 11. Three Component Olefin Cross Metathesis

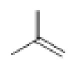
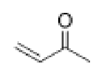
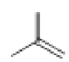
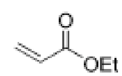
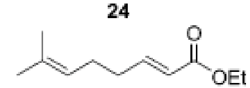
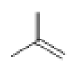
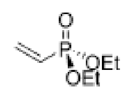
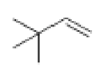
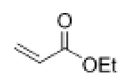
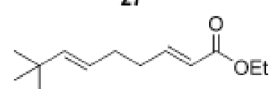
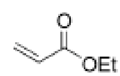
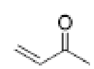
neat *Type III* | 3 eq. *Type I* | 1 eq. *Type II*

24

89% isolated yield

All *E* isomer

Table 8. Three Component Olefin Cross Metathesis[a]

Entry	Method[d]	CM partner Y	CM partner Z	Ratio (Diene:Y:Z)	Product	Isolated Yield (%)
1	A			3:neat:1	 **24**	89
2	A			3:neat:1	 **26**	60
3	A			3:neat:1	 **27**	57[b]
4	A			1:neat:1	 **28**	67[c]
5	B			1:3:1	 **29**	34
6	B			2:3:1	 **25**	47

[a] Using 5−7 mol % of **1** in 0.1−0.2 M refluxing CH_2Cl_2, 12 h. [b] E/Z = 8:1 by ^{1}H NMR. [c] Reaction at 23 °C. [d] Method A = added all components at one time. Method B = added component Z and then added component Y after 4 h.

Conclusions

- There is now a classification of olefins that allows for some predictive abilities in CM.
- These classifications are based on rate of homodimerization and can be influenced by steric and electronic effects as well as protection of alcohols.
- More work needs to be done to develop a model that is more quantitative and less qualitative