Carbenes / Alkylidenes

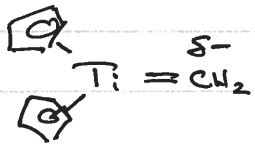
$L_n M = CR_2$ - metal C formal double bond.

- Historically, carbenes were officially considered to fall into one of two types - There are more now

Fischer Type Carbenes

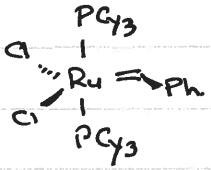
- Mostly Cr Group (Cr, Mo, W) or Fe Group
- Stabilized by attached Heteroatom (O here)
- Reactivity - Electron poor at C
- Analogy to ester carbonyls has been made

Schrock Type Carbenes (Alkylidenes)



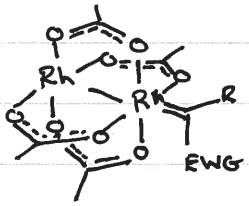
- Early transition metal
- Electron rich at Carbon
- Example - Tebbe Reagent (Wittig Rxn Analogue)

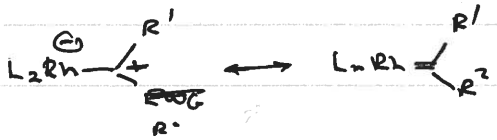
- Newer Metathesis Carbenes
  - Some $Mo^{II(VI)}$, most $Ru^{II(IV)}$ i.e



- Have seen them lumped in with both types above
- No great M-C bond polarity; likes alkenes & cycloaddition processes.

- Diazo-Derived Carbenes - usually Rh^{II} $R{=}N_2{-}R'$ + $Rh_2(OAc)_4$





- Good for cyclopropanations, C-H insertions
- C is electrophilic, due to EWG invariably on carbene carbon.

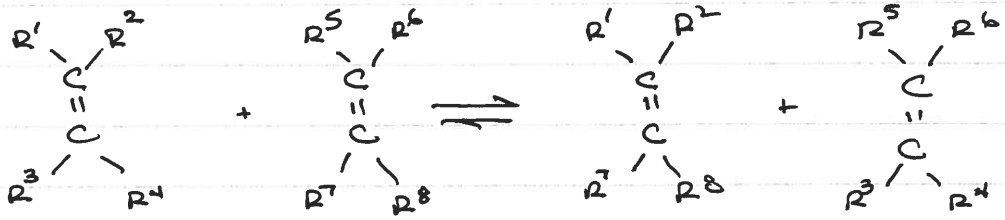
SIMPLEST PICTURE OF BONDING

SINGLET CARBENE

METATHESIS OF ALKENES (+) - BY FAR THE MOST SYNTHETICALLY IMPT.

CHAUVIN & SCHROCK GRUBBS NOBEL 2005

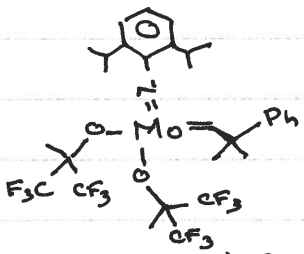
CONVERSION OF



- BY A SERIES OF 2+2 CYCLOADDITIONS AND RETRO- 2+2 CYCLOADDNS.

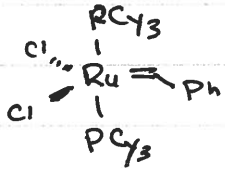
MAY BE CONSIDERED INSERTION RXNS.

- THE MAIN CATALYSTS



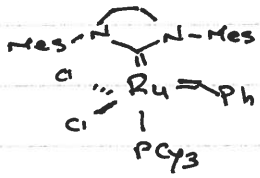
SCHROCK (PRE) CATALYST

- HIGH REACTIVITY
- LESS STABLE, LESS EASILY HANDLED
- NOT V. FUNCTIONAL GROUP TOLERANT



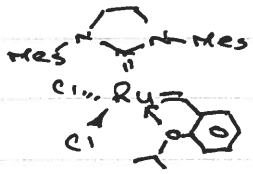
GRUBBS 1ST GENERATION (G1)

- MORE EASILY HANDLED
- V. FUNCTIONAL GRP TOLERANT
- MUCH LESS REACTIVE THAN SCHROCK



GRUBBS 2ND GEN. (G2)

"
"
MORE REACTIVE THAN G1



HOVEYDA-GRUBBS 2 (HG2)

- SOMEWHAT LESS REACTIVE THAN G2
- GOOD FOR e⁻ POOR ALKENES

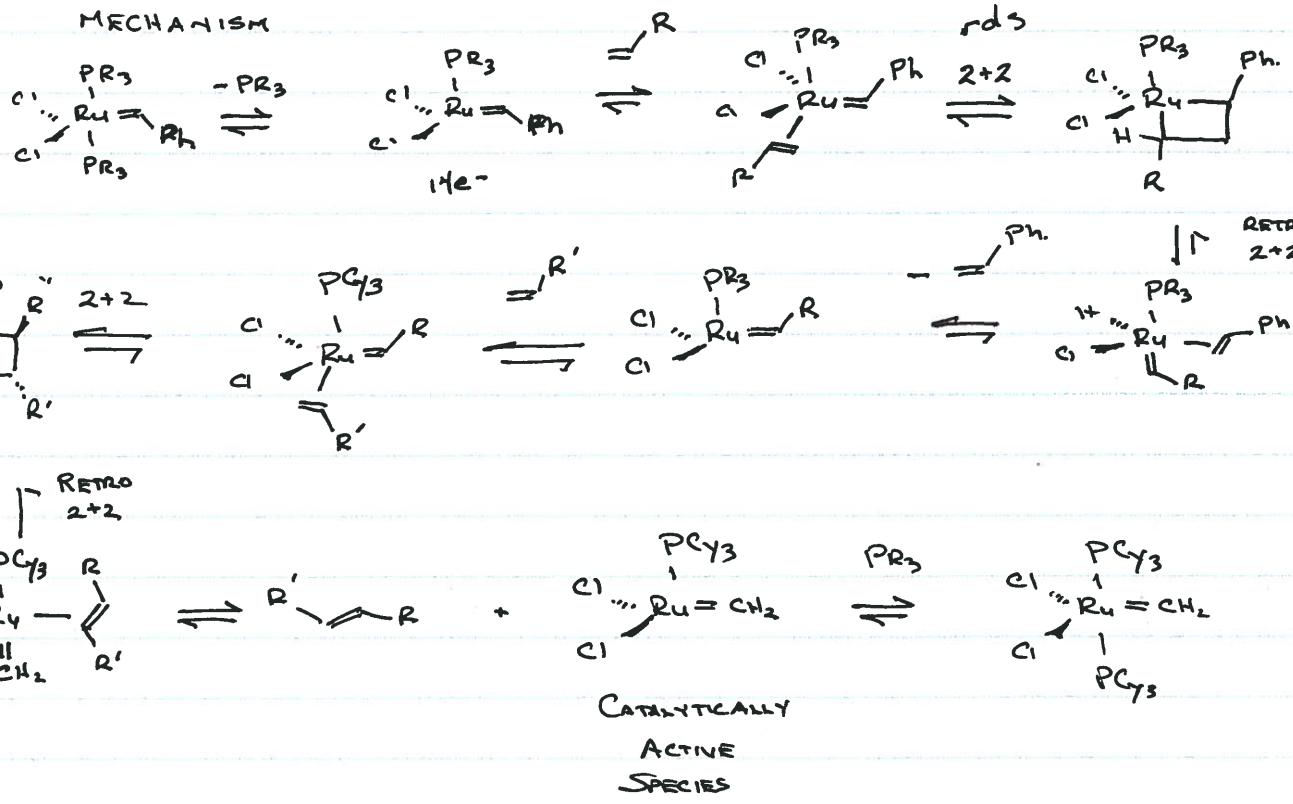
V. ROUGH REACTIVITY (& rel)

WILL RIP THE DIENE RIGHT OUT OF YOUR HAND

SOMEWHAT LESS THAN G2

NUMBERS ARE VARIABLE

MECHANISM



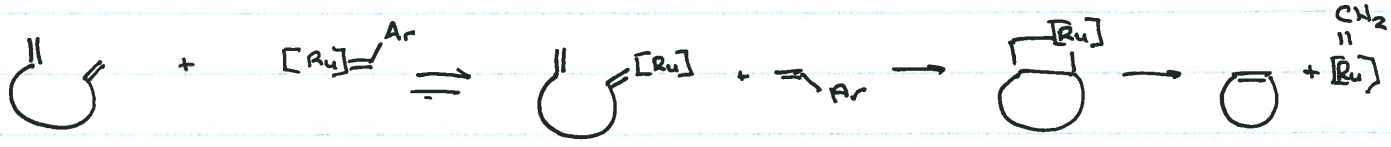
- RXN OFTEN DRIVEN BY LOSS AT END OF VOLATILE ALKENE I.E. $H_2C{=}CH_2$

MAJOR TYPES OF ALKENE METATHESIS:

RCM - RING CLOSING METATHESIS
CM - CROSS METATHESIS
} WILL INCLUDE BRIEFLY ENYNE METATHESIS

ROMP - RING OPENING METATHESIS POLYMERIZATION
ADMET - ACYCLIC DIENE METATHESIS
} WILL NOT DISCUSS Z. WANG?

RCM - MOST IMPORTANT OF THEM ALL

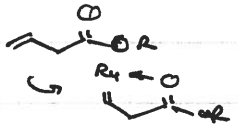


Ru CATALYSTS NORMALLY TOLERATE

ALCOHOLS*, ETHERS*, KETONES, ACIDS, ESTERS*, AMIDES, ARENES

* - ALCOHOLS - ALLYLIC ALCOHOLS CAN BE PROBLEMS IN SLOWER CASES → ETHER, ESTER, ACETALS OR

* - VINYL/ENOL ETHERS - OFTEN TOO UNREACTIVE WITH Ru CATALYSTS

* - ESTERS - OCCASIONAL ISSUES WITH INTERNAL CHELATE  BEING TOO STABLE

- 3° AMINES → USUALLY MAKE AMIDE OR PG'D AMINE

THIOETHERS → Mo OR

PHOSPHINES → Mo OR

PROBLEMATIC

FOR NORMAL (5,6) SIZED RINGS. 

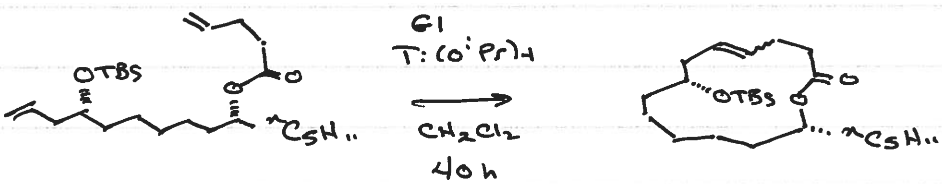
CATALYST	G1	G2	SCHROCK	
DISUB (R=H)	OK	OK	OK	GRUBBS ORG LETT 1999 1, 953
TRISUB (1 R = CH_3)	USUALLY	OK	OK	
TETRASUB. (2 R'S = CH_3	USUALLY NOT	USUALLY	USUALLY.	J. ORG. CHEM 1997, 62, 7310.

SIZE OF RING.

- 3 & 4 - NO, BECAUSE THERMODYNAMIC FORCE IS TO RING OPEN
  - HAS BEEN USED IN ROMP.
- 5, 6 - - USUALLY SEAMLESS
- 7 - FAIR
- 8 - 10 - TOUGHEST DUE TO ENTROPY, SEVERAL EXAMPLES, BUT TEND TO USE EVERY TRICK (LOW CONC.; GEM DIMETHYL/THORPE INGOLD EFFECT)
- >10 - NOT TOO BAD - RXNS TYPICALLY AT LOW CONC. (10^{-3} M) AND WAIT FOR TRANSIENT OLIGOMERS TO UNRAVEL.

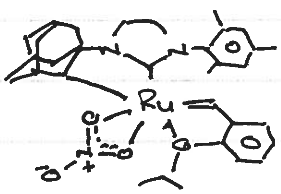
- NOTE: IN RING SIZES ≥ 10 Z - STEREOCHEMISTRY IS NO LONGER MANDATORY, AND Z/E STEREOCHEMICAL CONTROL IS POOR.

i.e.



E/Z = 2.7 : 1

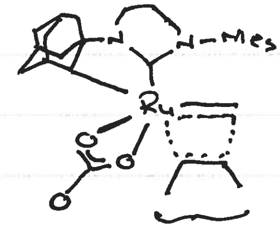
- THERE HAS BEEN WORK DONE ON CONTROLLING ALKENE STEREOCHEMISTRY, AND IF YOU HAVE $$,



0.5g $341
G1 5g $584 (A/L/D) $130 us
G2 2g $774 ; 5g ≈ $300 us
HG2 0.5g $326 ; 1g ≈ $142 us

Z- SELECTIVE GRUBBS CATALYST

VIA



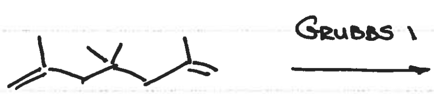
BOTH DOWN

- NOTE - ALKENE ∧ SITE ISOMERIZATION CAN OCCASIONALLY INTERVENE - BENZOQUINONE ADDED AS A SOLUTION *

RELAY RING CLOSING METATHESIS

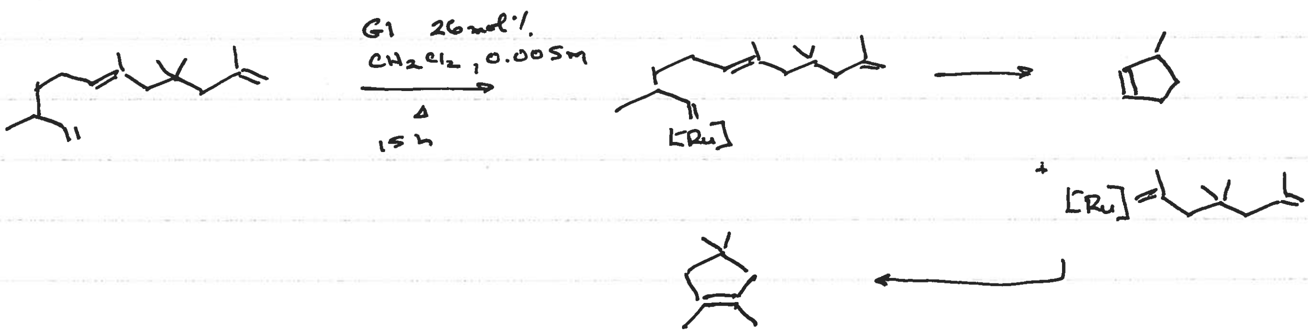
- PROBLEM - IN MANY CASES, THERE CAN BE A DESIRED RCM PRODUCT WHOSE STARTING ALKENES ARE TOO HINDERED TO GO WELL.

i.e.



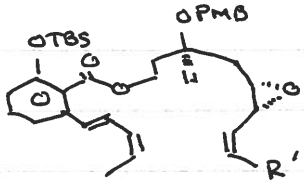
LITTLE PRODUCTIVE RXN

- A SOLUTION TO THIS IS TO CREATE A DIFFERENT STARTING MATERIAL, WITH AN 'ACCESSIBLE' ALKENE, THAT CAN GIVE THE ALKYLIDENE NEEDED FOR RCM INDIRECTLY - CALLED RRCM SOMETIMES

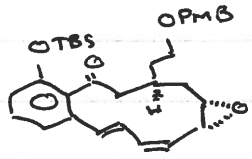


HOYE, T.

J. AM. CHEM. SOC. 2004, 126, 10210.



HG 2 (10 mol %)
CH_2Cl_2, 0.002 M
Δ



ONLY E,Z -

R' = H

R =

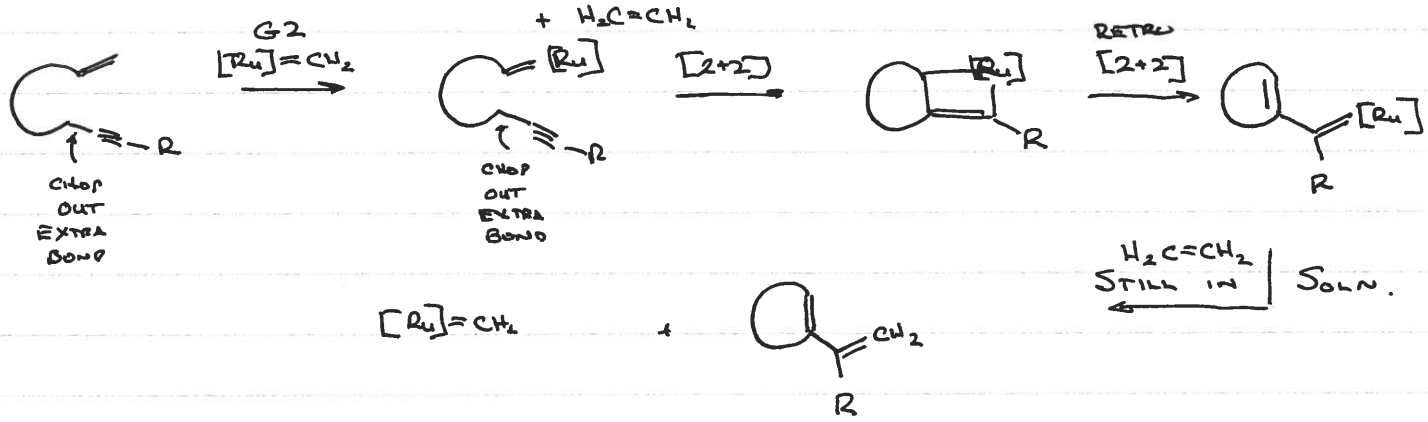
15Z

71 %

PORCO, J.A.
ANGEW. CHEM. INT. ED.
2004, 43, 3601.

ENYNE METATHESIS W/ GI, GII, HG II

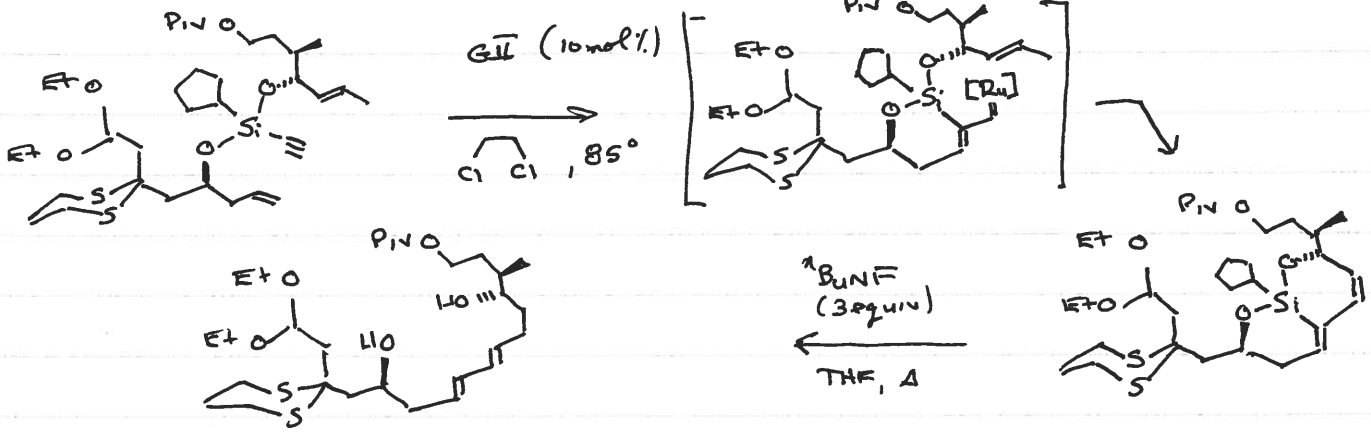
- LOOKS TO ME AS IF ALKYNES ARE SLIGHTLY LESS REACTIVE THAN ALKENES TO THESE CATALYSTS, BUT IT'S CLOSE; SO AN UNPROTECTED ALKYNE WILL PARTICIPATE IN RCM. OUTCOME IS DIFFERENT, BUT OFTEN USEFUL



PRODUCT IS VINYL SUBST. CYCLOALKENE

REVIEW LEE. D. EUR. J. ORG. CHEM. 2011, 4269.
CHEM., EUR. J. 2005, 11, 6118.

- THIS ALSO GIVES AN OPPORTUNITY (IF THERE'S ANOTHER ALKENE PRESENT) TO DO TANDEM METATHESIS RXNS



61 %

LEE, D.* ORG. LETT. 2009, 11, 2916.

CROSS METATHESIS (CM)

- OTHER MAJOR ORGANIC CHEMISTRY USE OF METATHESIS CHEM.

IDEA 

- THE PROBLEM HERE, IS TO GET SELF / HOMO - METATHESIS

i.e. 

- IT IS POSSIBLE TO SIMPLY JUST ADD AN EXCESS OF ALKENE, AND COUNT ON STATISTICS, AND ASSUMING IT IS CHEAP AND THAT ITS HOMO-DIMER IS READILY REMOVABLE

- MORE COMMONLY DONE SELECTIVELY, SUCH THAT WE HAVE A MORE REACTIVE ALKENE (TO METATHESIS), AND A LESS REACTIVE ONE, AND (MOST OFTEN) TO ADD AN EXCESS AMOUNT OF THE LESS REACTIVE ONE

NOTE: IN THIS CHEMISTRY GRUBBS II IS MUCH MORE COMMONLY USED THAN GRUBBS I - HG II USED SOMETIMES W/ e⁻ POOR ALKENES

- GRUBBS HAS CLASSIFIED ALKENES AS TYPE I THROUGH TYPE IV

TYPE I - ALKENES THAT DO FAST HOMODIMERIZATION; DIMERS WILL RE-ENTER CATALYTIC CYCLE

TYPE II - ALKENES THAT HOMODIMERIZE SLOWLY; DIMERS WILL RE-ENTER CATALYTIC CYCLE ONLY RELUCTANTLY

TYPE III - ALKENES THAT DO NOT HOMODIMERIZE, BUT WILL ENTER METATHESIS W/ MORE REACTIVE ALKENES

TYPE IV - ALKENES COMPLETELY UNREACTIVE TO ANY METATHESIS, BUT CAN WATCH

- CROSS METATHESIS IS USUALLY PERFORMED WITH A TYPE I ALKENE AND AN EXCESS OF A TYPE II OR A TYPE III ALKENE

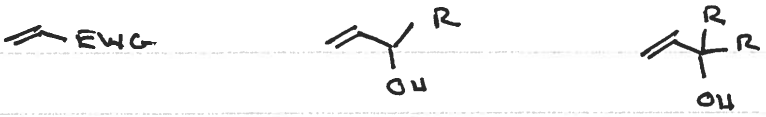
- I WOULD NOT RULE OUT EXAMPLES OF A TYPE II WITH XS TYPE III

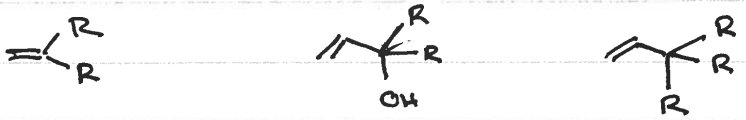
GIVE TABLE FROM: GRUBBS, R.H. J. AM. CHEM. SOC. 2003, 125, 11360.

- A SHORTENED VERSION
- FOR GRUBBS 2

TYPE I 

R = ALKYL, Ac

TYPE II 

TYPE III 

TYPE IV 

- USUALLY GET "MOSTLY" E, BUT E/Z MAY NOT BE GREAT
- OF COURSE, FOR G1 AND HG2 THE TYPE I – TYPE IV LIST WILL BE DIFFERENT

HG2 "ALWAYS" USED WITH CN ACRYLONITRILE, AND GET A SUBSTANTIAL AMOUNT OF Z ISOMER

AMOUNT?	1	:	1	80%	UNUSUALLY GOOD
	1	:	3	"98%"	