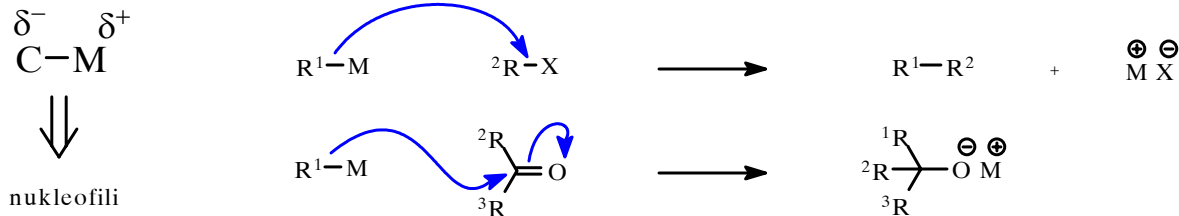


## REAKCIJE ORGANOMETALNIH JEDINJENJA



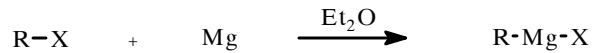
Reaktivnost organometala proporcionalna je elektropozitivnosti M

Najčešće korišćeni: Mg, Li, Cu, Zn, Cd

### Grignard-ov reagens

1900 otkriven

1912 Nobelova nagrada



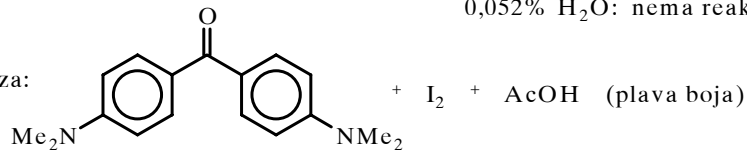
\* Reaktivnost R-X: prim > sec > tert > vinil > aril  
I > Br > Cl

\* Aktiviranje Mg: I<sub>2</sub>, MeI, BrCH<sub>2</sub>CH<sub>2</sub>Br, K/MgCl<sub>2</sub>,...

\* Uticaj H<sub>2</sub>O: BuBr + Mg  $\xrightarrow{Et_2O}$  BuMgBr

suv Et <sub>2</sub> O:	5 min
0,02% H <sub>2</sub> O:	27 min
0,052% H <sub>2</sub> O:	nema reakcije

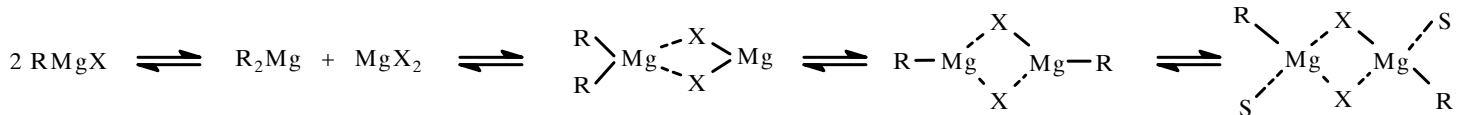
\* Kvalitativna analiza:



\* Kvantitativna analiza: RMgX + H<sub>2</sub>O  $\longrightarrow$  R-H

\* Struktura: RMgX • Et<sub>2</sub>O      RMgX • 2Et<sub>2</sub>O

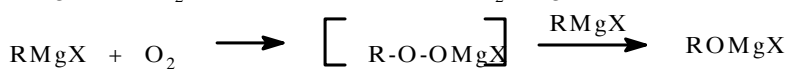
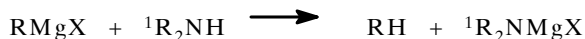
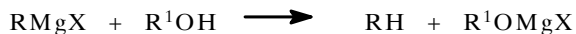
### Schlenk-ova ravnoteža



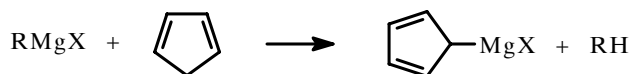
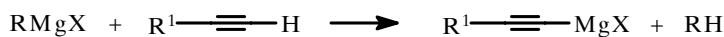
Uticaj koncentracije  
(na ravnotežu dimer  $\rightleftharpoons$  monomer)

S = rastvarač

Reaktivnost: trenutno reaguje sa H<sub>2</sub>O, ROH, ArOH, RCOOH, R<sub>2</sub>NH, O<sub>2</sub>



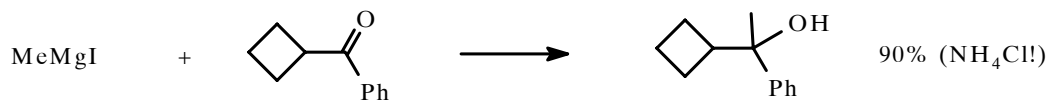
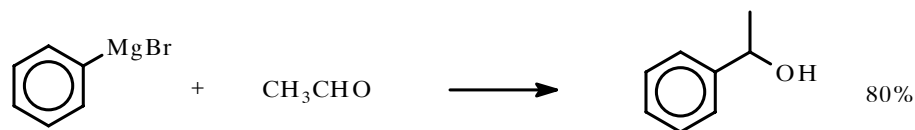
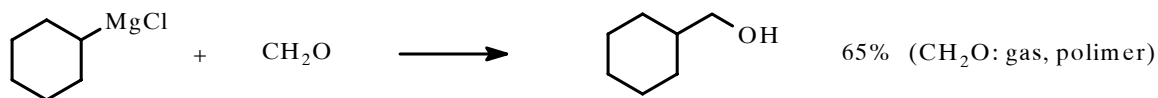
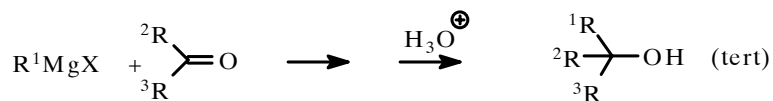
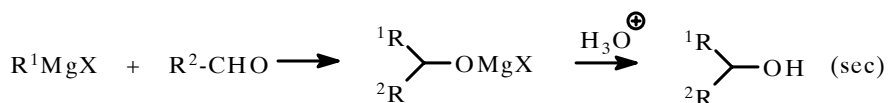
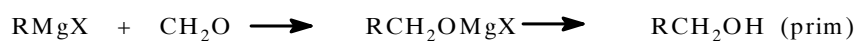
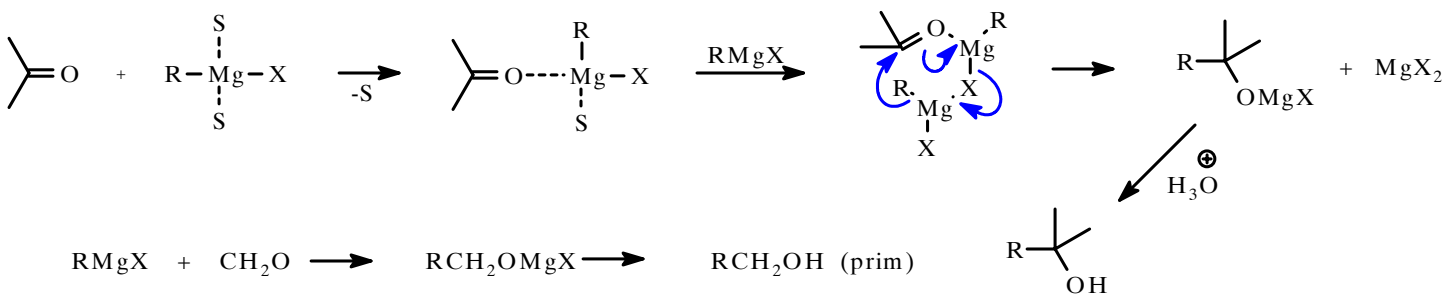
RMgX je jaka baza

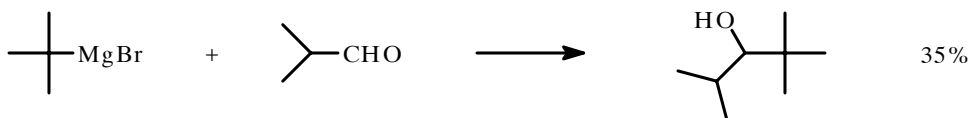
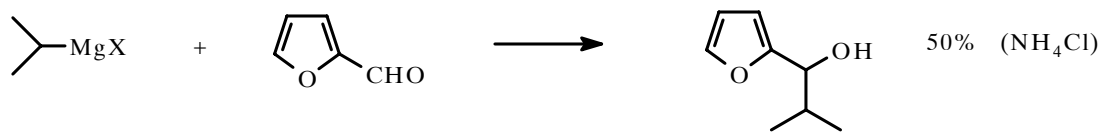
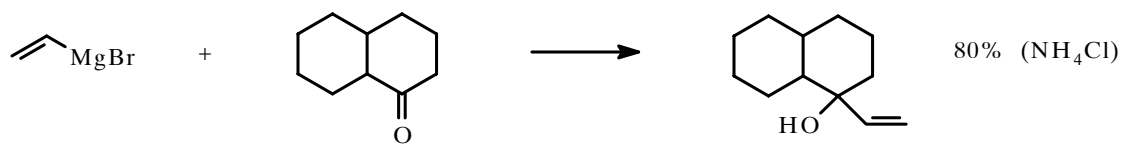


Redosled reaktivnosti funkcionalnih grupa sa Grignard-ovim reagensom:



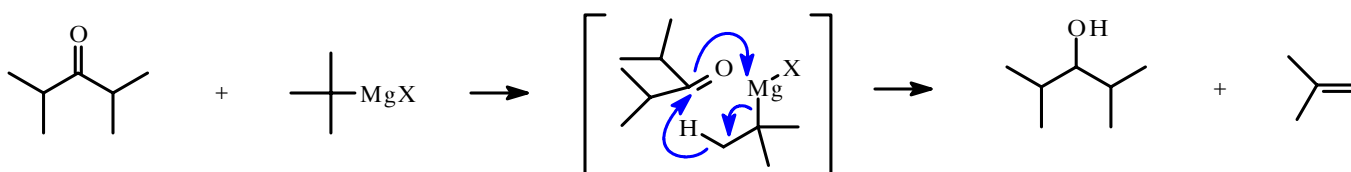
Reakcije sa karbonilnim jedinjenjima



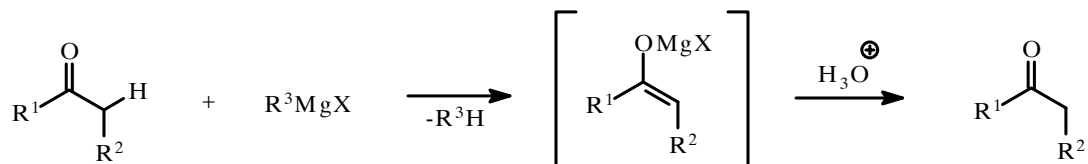


### Sporedne reakcije

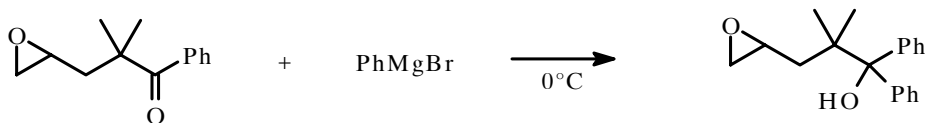
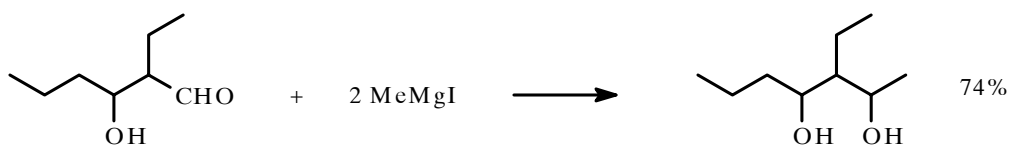
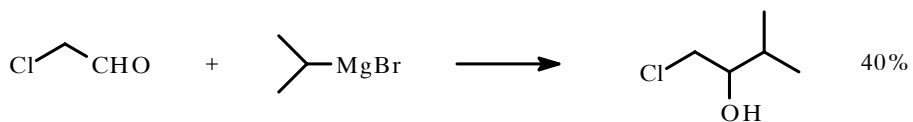
1) Redukcija ( $\beta$ -hidridna migracija) kada postoje sterne smetnje



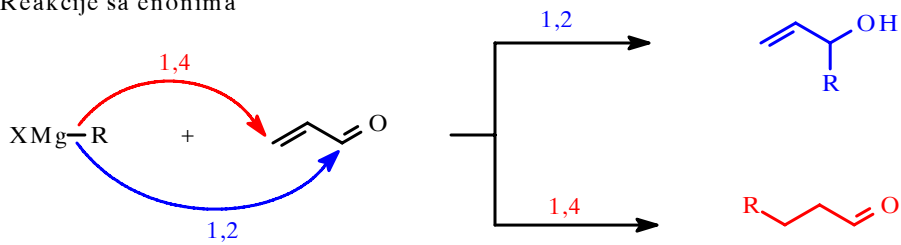
2) Enolizacija



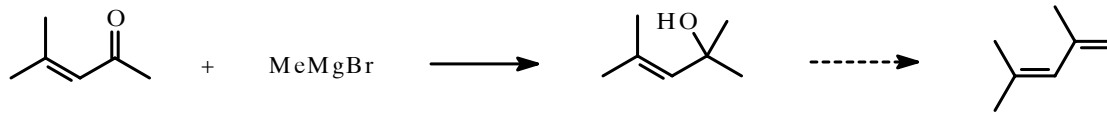
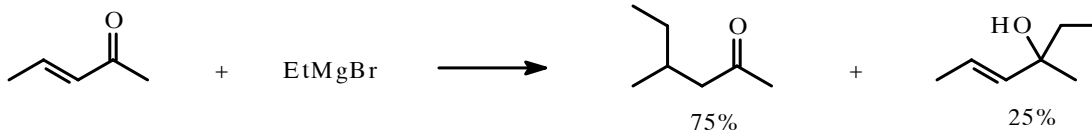
### Reakcije sa polifunkcionalnim jedinjenjima



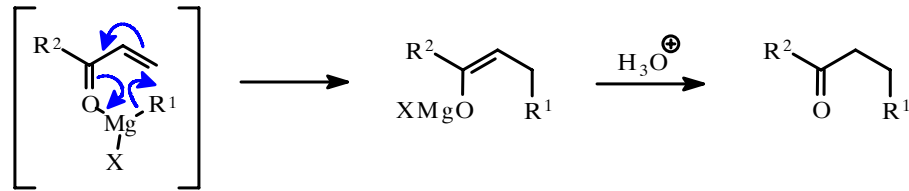
Reakcije sa enonima



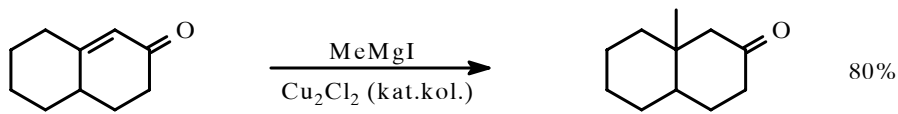
Sterni efekti



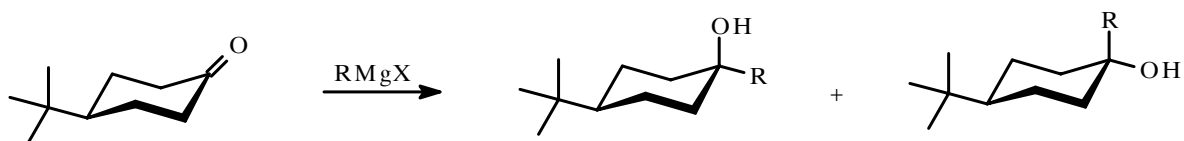
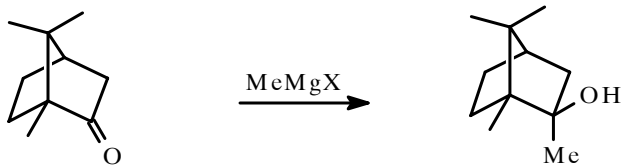
Mehanizam:



1,4-adicija: dodatkom Cu(I) soli



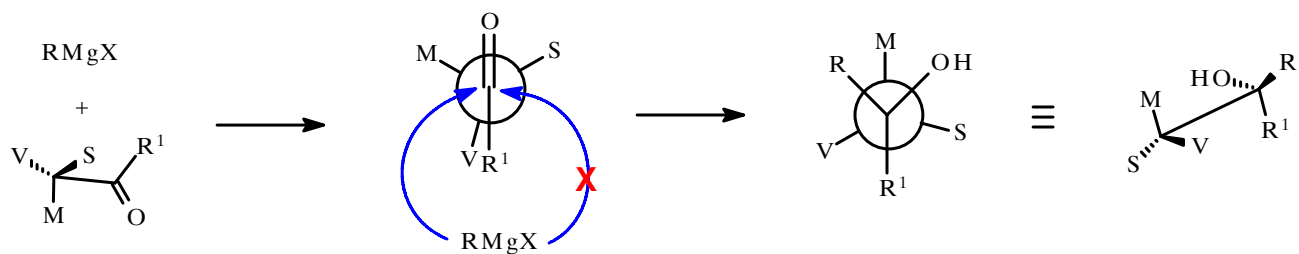
Stereohemija adicije  
(ciklični sistemi)



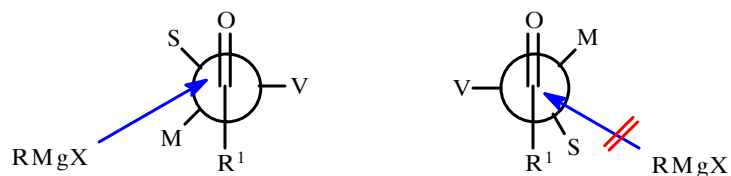
R = Me	53	:	47
R = Et	71	:	29
R = <i>t</i> -Bu	100	:	0

Stereohemija adicije  
(aciklični sistemi)

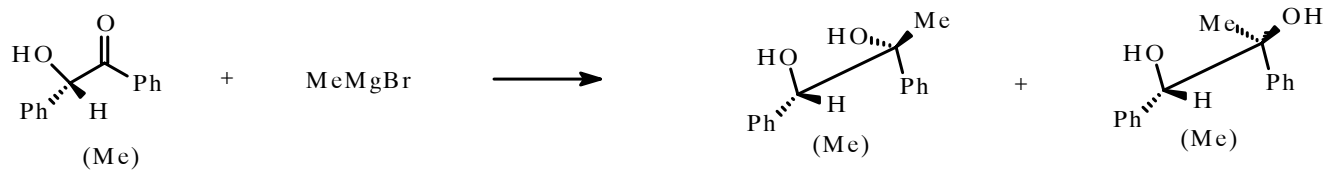
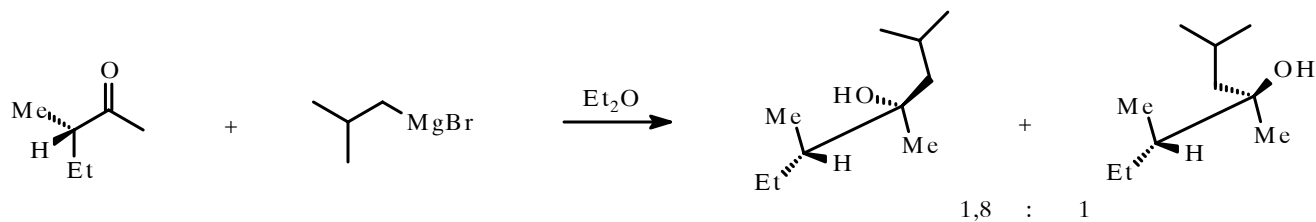
Cram-ovo pravilo



Felkin-Ahn-ovo pravilo

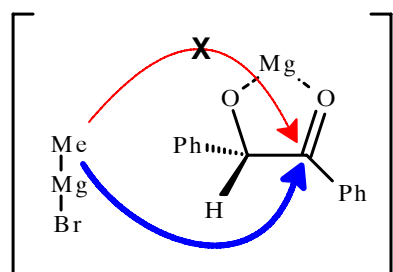


Pravila ne važe  
kada je moguća  
helatacija!

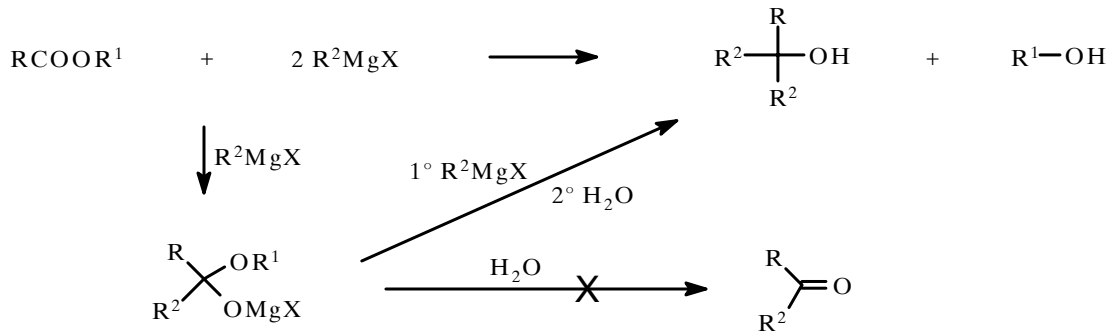


96 : 4

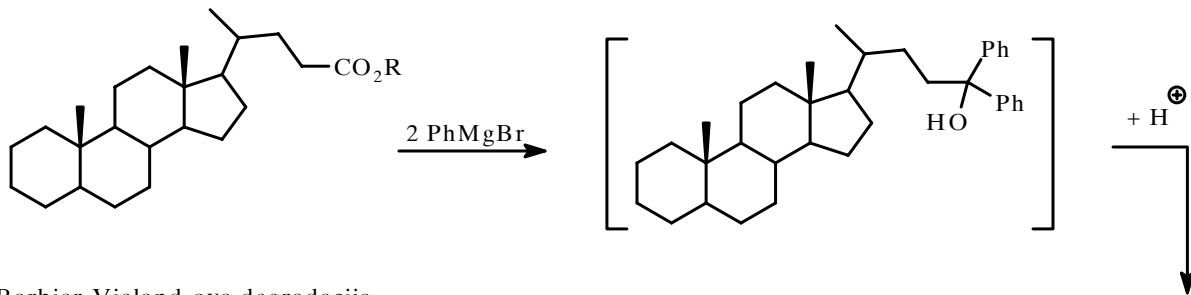
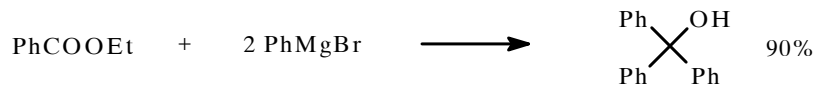
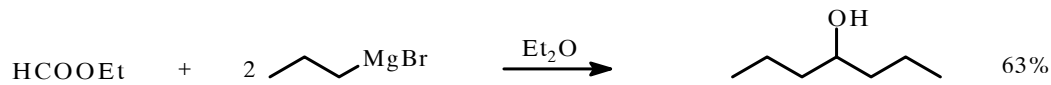
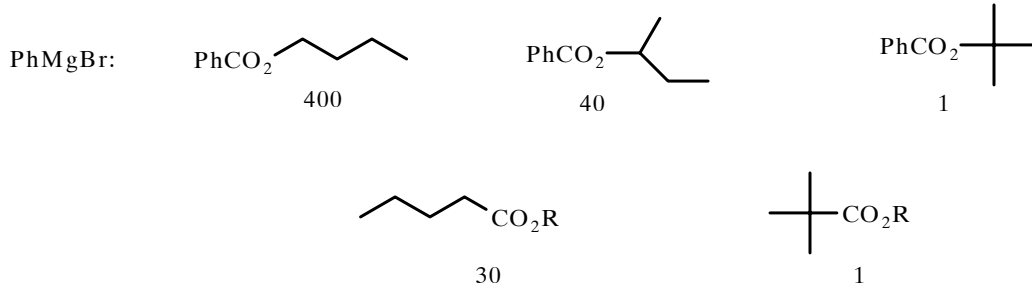
(66 : 34)



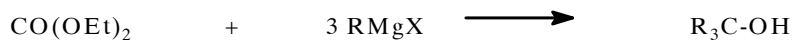
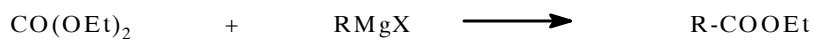
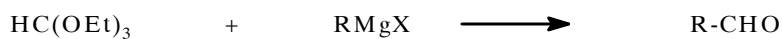
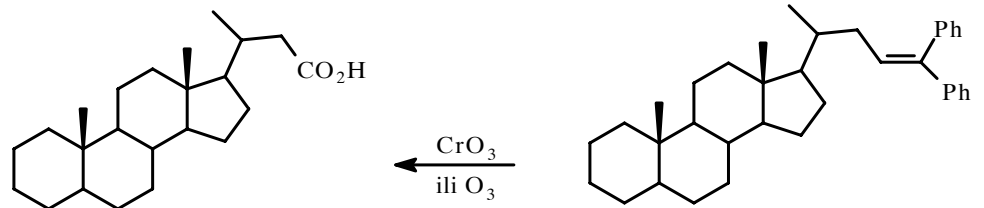
Reakcije sa estrima

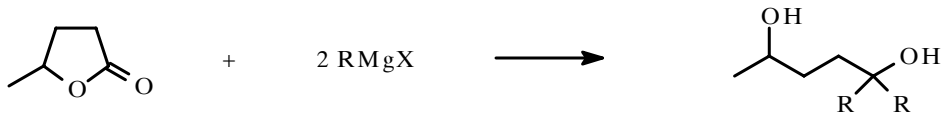
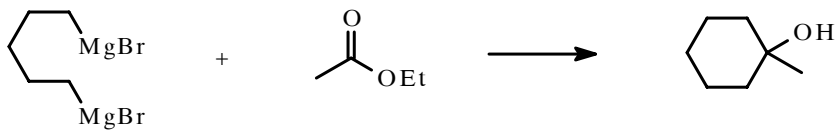


Reaktivnost: prim > sec > tert

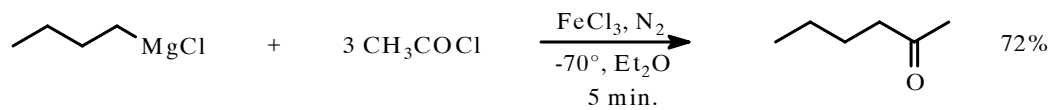
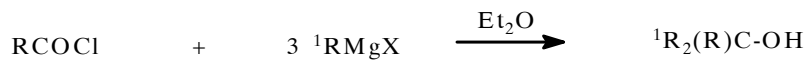
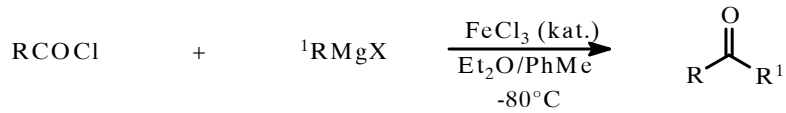


Barbier-Vieland-ova degradacija

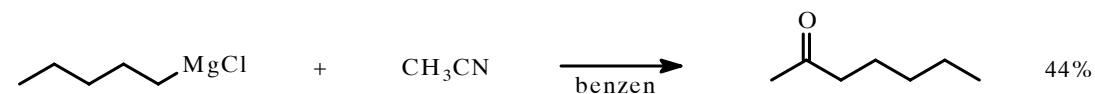
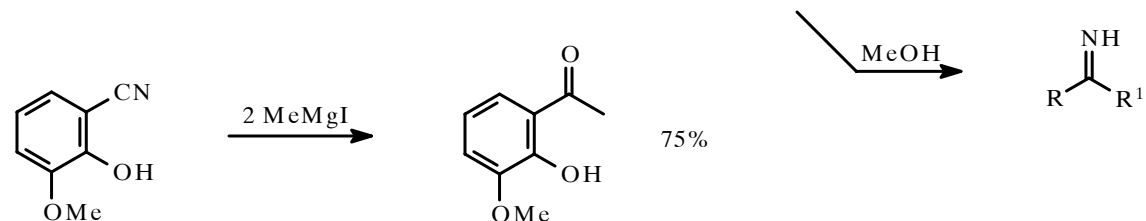
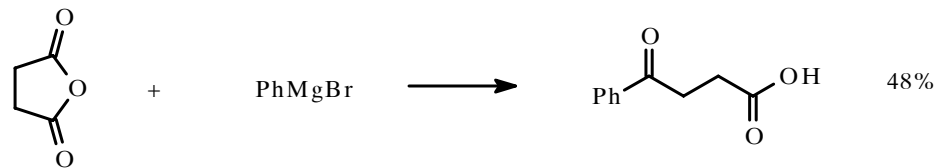
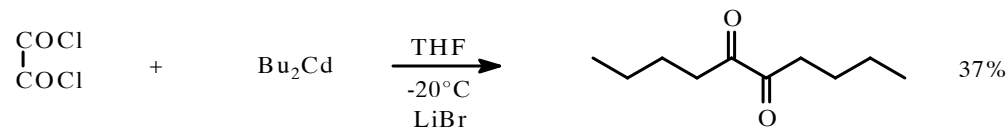
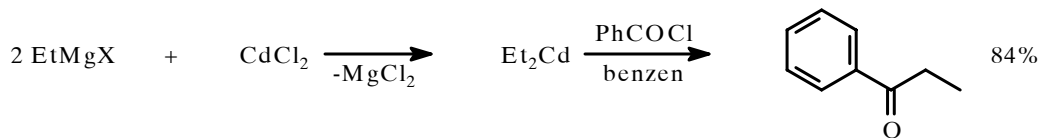
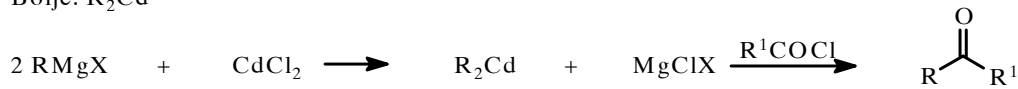


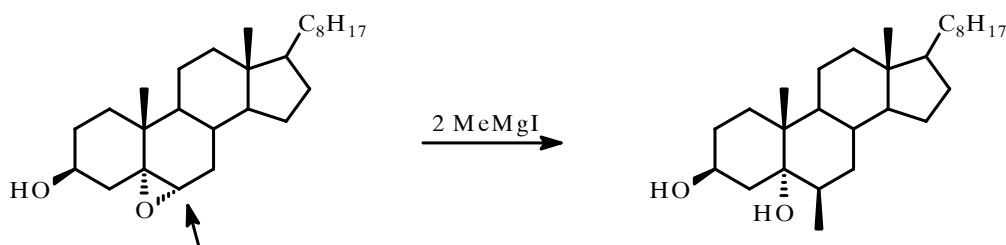
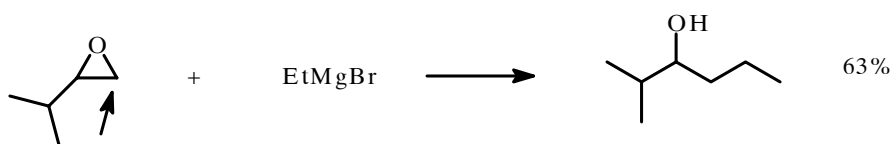
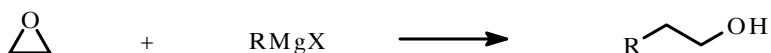
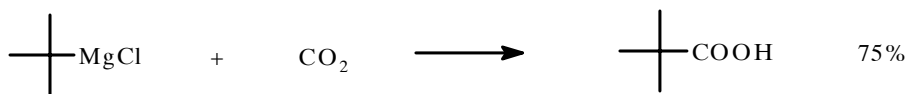
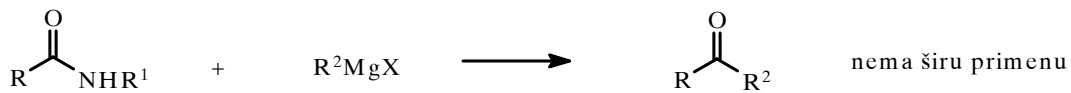


Reakcije sa acil-halogenidima, anhidridima karboksilnih kiselina, nitrilima, amidima i CO<sub>2</sub>

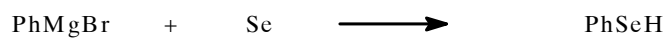
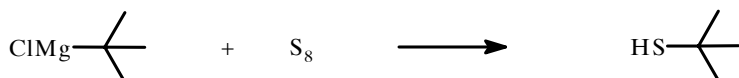
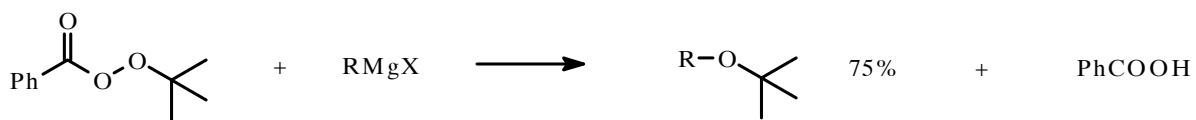
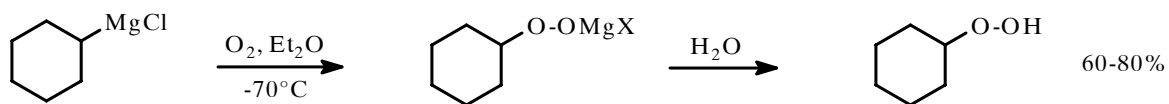


Bolje: R<sub>2</sub>Cd

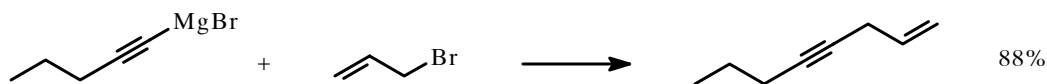
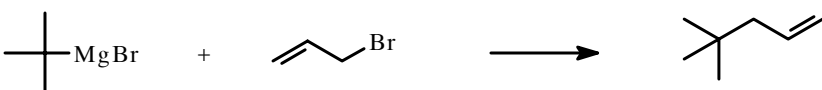
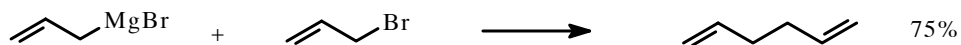
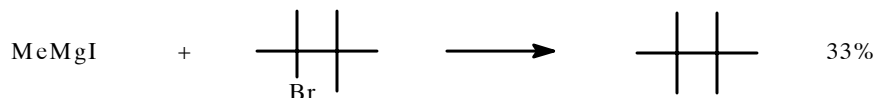
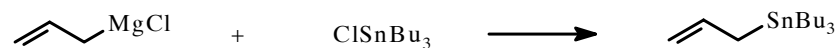
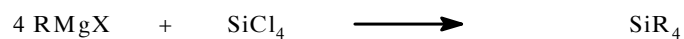
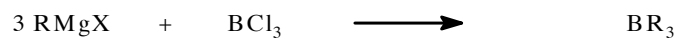
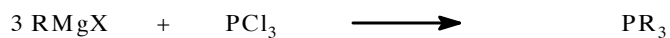




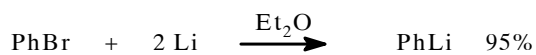
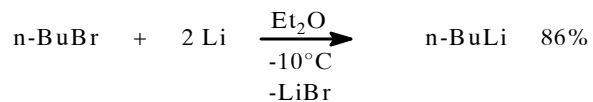
Reakcije sa  $O_2$ ,  $RCO_3R_1$ ,  $S_8$ , Se,  $PCl_3$ ,  $BCl_3$ ,  $SiCl_4$ ,  $CH_2=CH-Br$



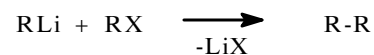




### ORGANOLITIJUMOVA JEDINJENJA



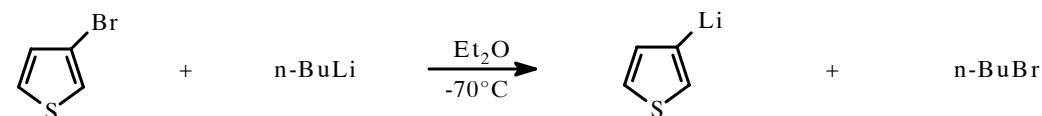
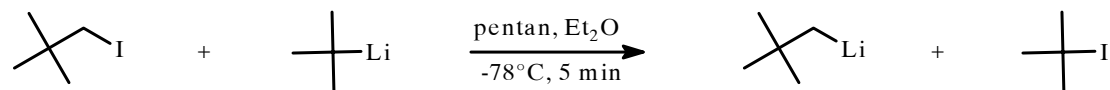
Niska temperatura!  
Sporedna reakcija: Wurtz-ovo kuplovanje



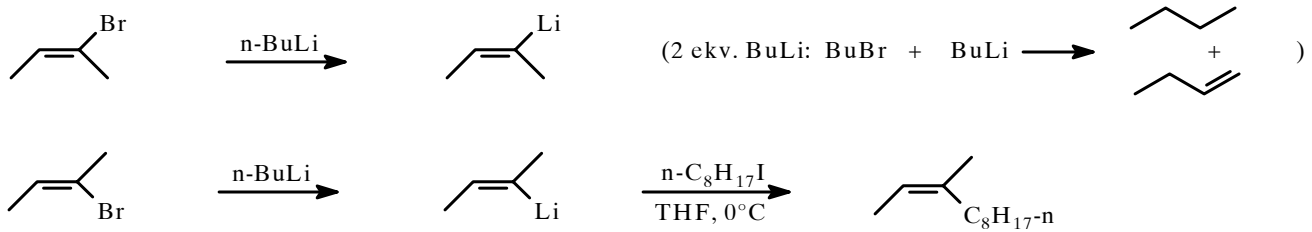
### 2) Li/halogen izmena



ako je  $pK(\text{R-H}) \ll pK(\text{R}^1\text{-H}) \Rightarrow$  Ravnoteža je pomerenka ka  $\text{RLi}$  (  $\rightleftharpoons$  )



Vinil-anjoni su konfiguraciono stabilni:



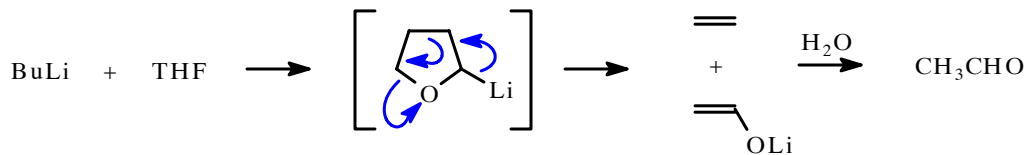
Uticaj rastvarača:

\* RLi mogu biti dimeri, tetrameri, heksameri...

\* dodatak DME ili TMEDA favorizuje reaktivnije, monomernne RLi vrste

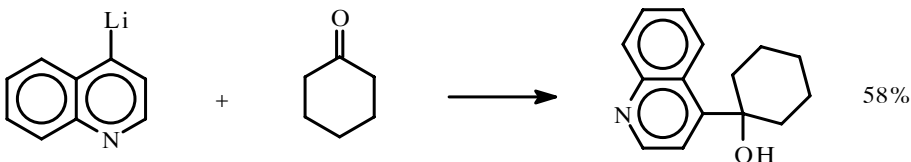
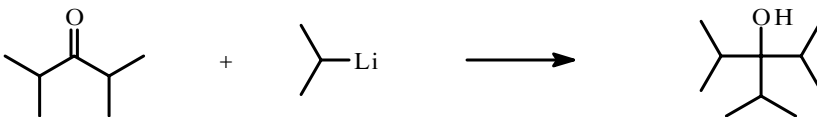
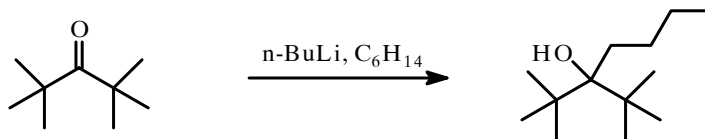


Jake baze  $\Rightarrow$  reaguju sa etarskim rastvaračima na višoj T:

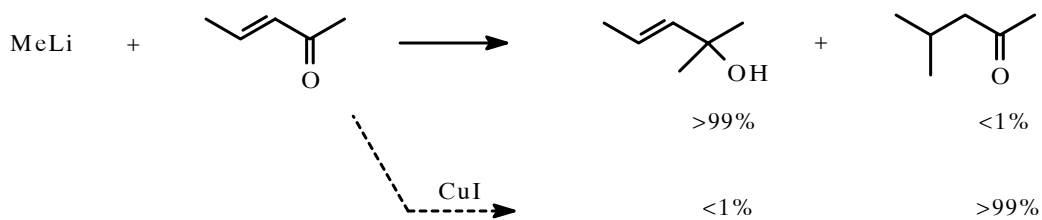


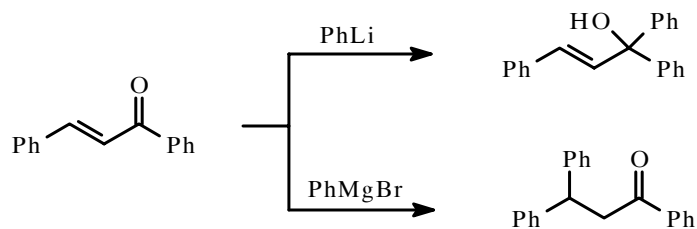
Razlike u odnosu na RMgX:

1) Adicija na C=O grupu - manje osetljivi na sterne smetnje

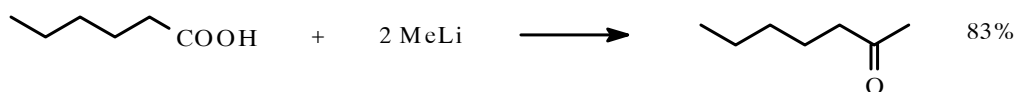
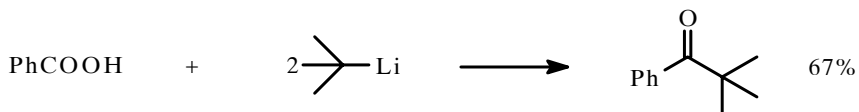


2) Sa enonima: isključivo 1,2-adicija

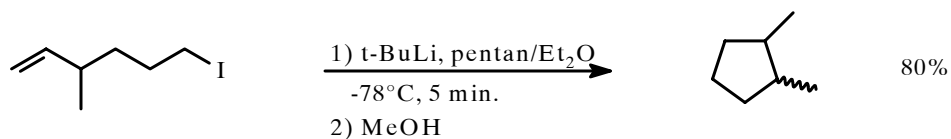
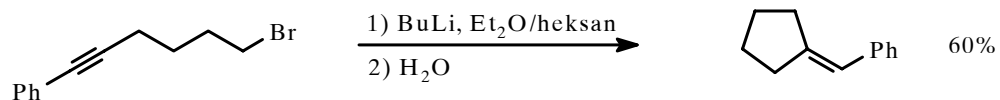




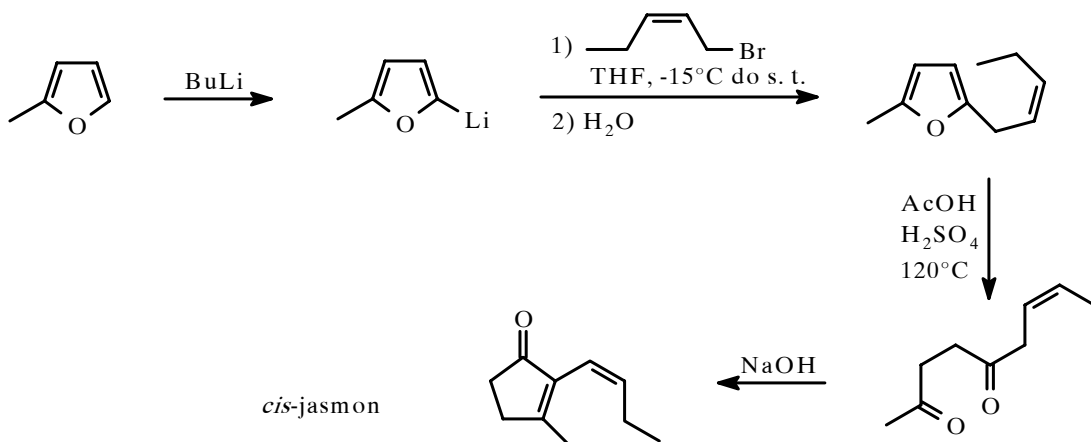
3) Reakcija sa karbonskim kiselinama (solima): dobra metoda za dobijanje ketona

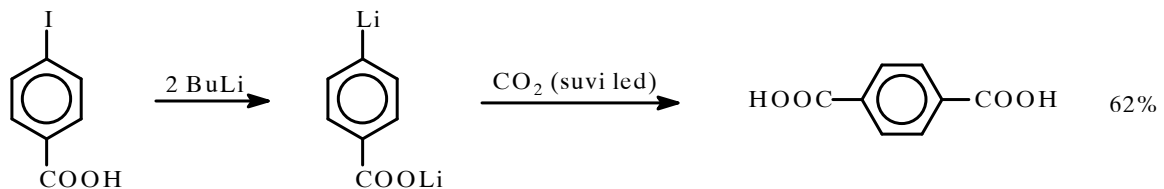
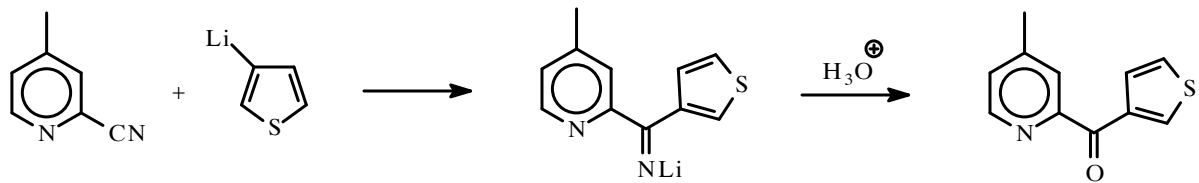
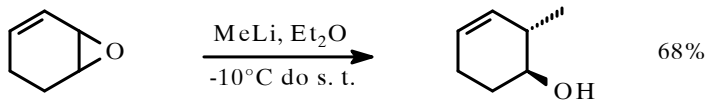


4) Adicija (intramolekulska) na C=C i C≡C veze (neaktivirane)



5) Ostale reakcije: slično RMgX, ali efikasnije

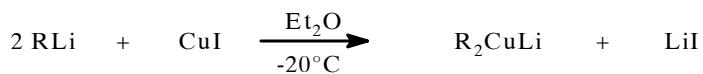




### ORGANOBAKARNI REAGENSI (ORGANOKUPRATI)

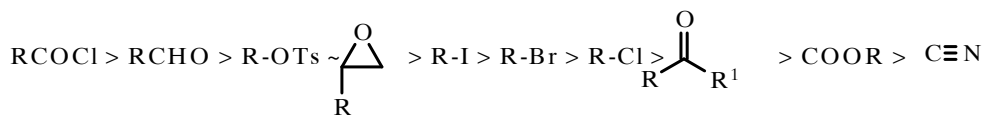
Dobijanje: 1) "Katalitički" reagensi:  $\text{RMgX}$  ( $\text{RLi}$ ) +  $\text{CuBr}$  (katalitička količina; takođe:  $\text{CuCl}$ ,  $\text{CuI}$ ,  $\text{CuBr} \cdot \text{Me}_2\text{S}$  i dr.)

2) Stehiometrijski kupratni reagensi - Gilman-ov reagens

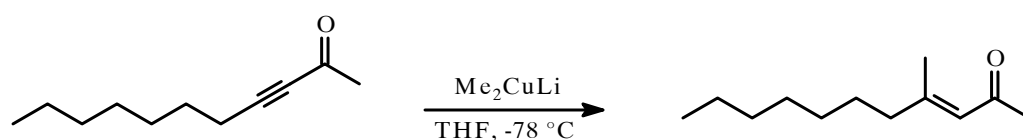
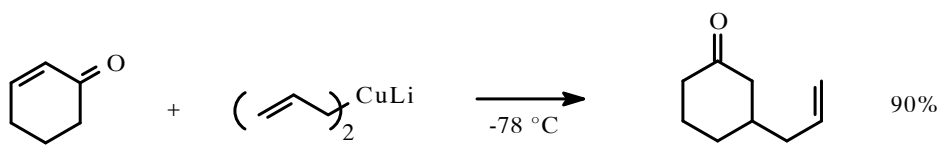
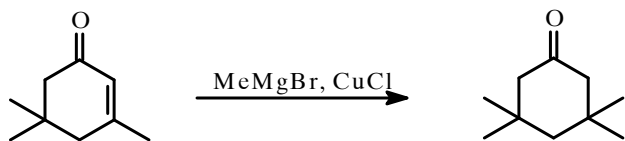
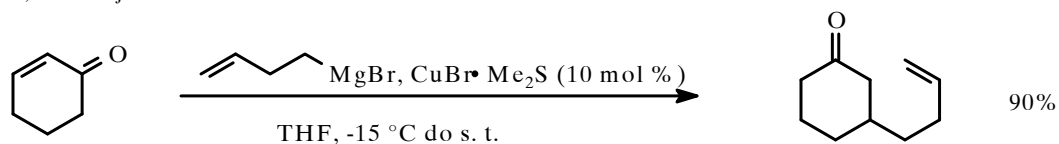


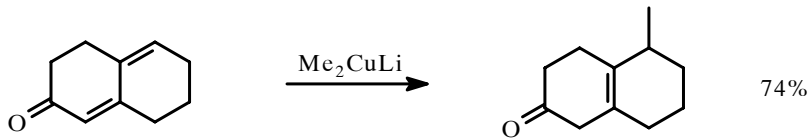
R = prim, sec, tert  
 moguće prisustvo funkcionalnih grupa

Reaktivnost:



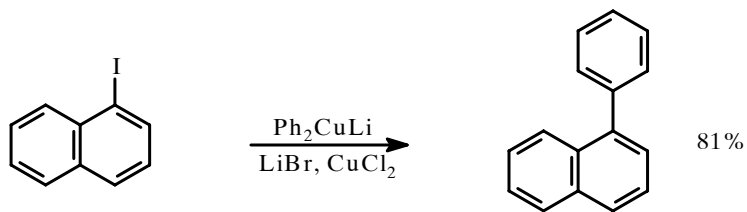
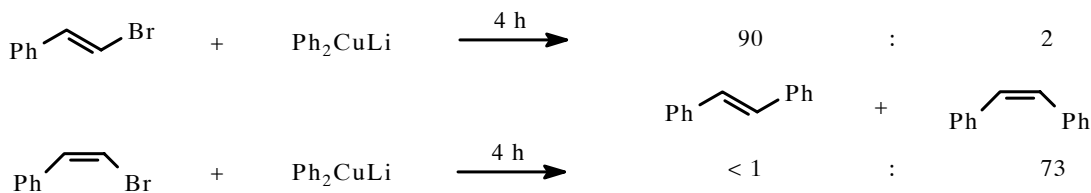
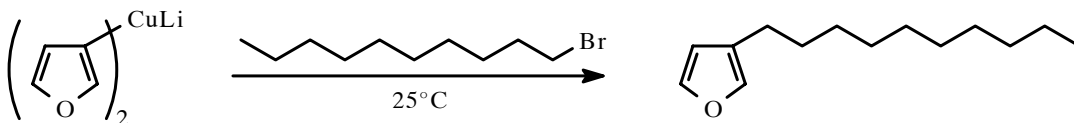
1,4-Adicije:





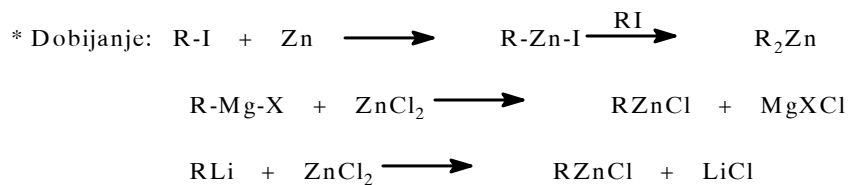
Kuplovanje:  ${}^1R_2CuLi + {}^2R-X \longrightarrow {}^1R-R^2$

${}^2R-X$ : prim THF > Et<sub>2</sub>O X = OTs, I, Br, Cl, OMs  ${}^1R$ : sp<sup>3</sup>, sp<sup>2</sup>

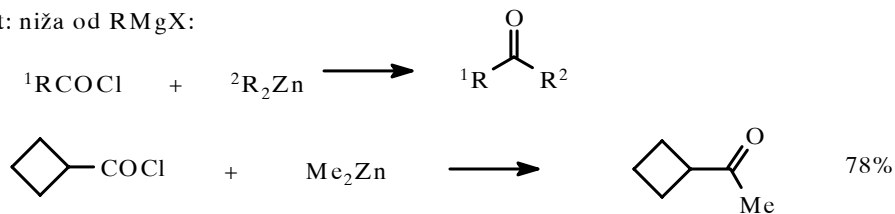


Reakcije sa  $\triangle$ , RCOCl,  ${}^1RCOR^2$  - slično reakcijama Grignard-ovog reagensa

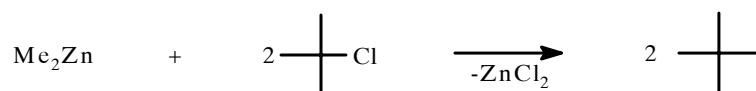
### ORGANOCINKOVA JEDINJENJA



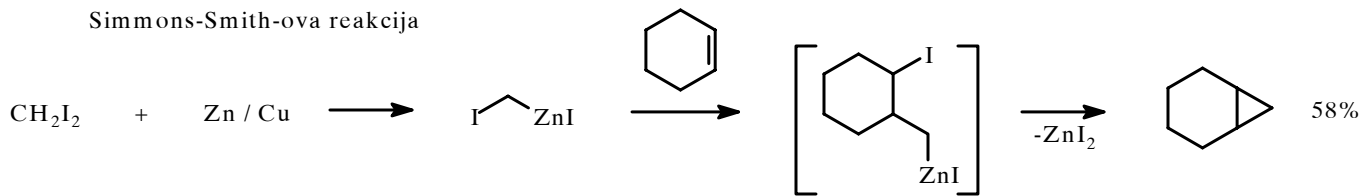
\* Reaktivnost: niža od RMgX:



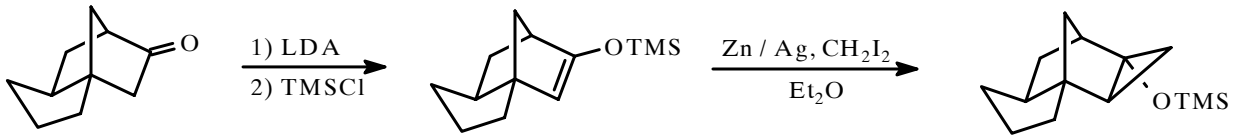
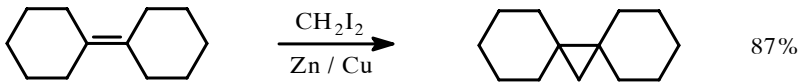
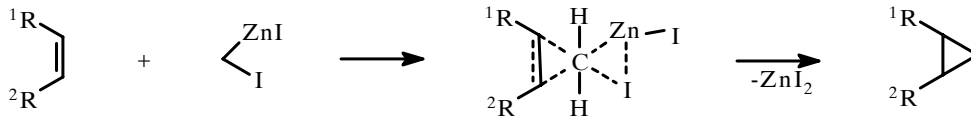
\* Kuplovanje sa tercijskim alkil-halogenidima:



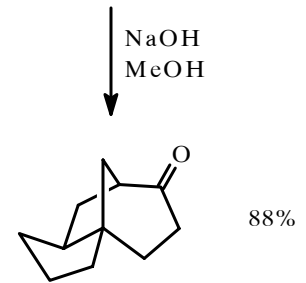
Simmons-Smith-ova reakcija



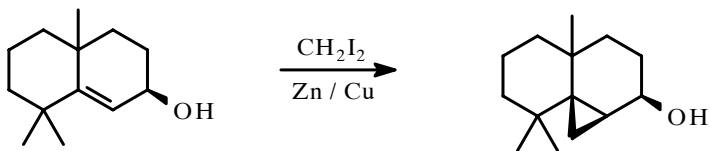
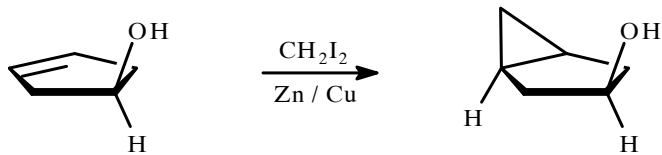
Mehanizam:



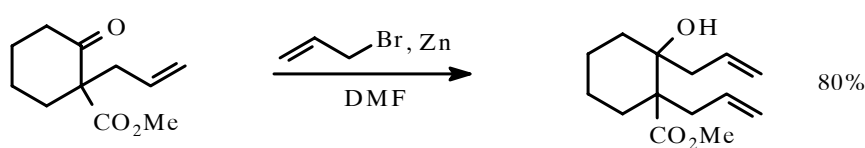
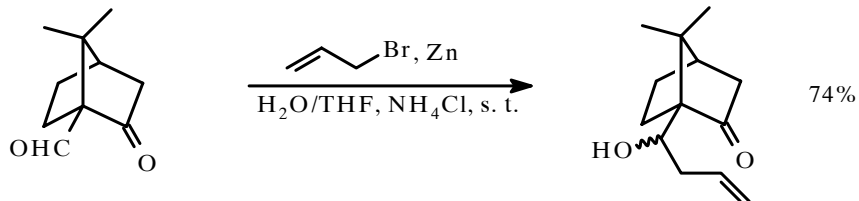
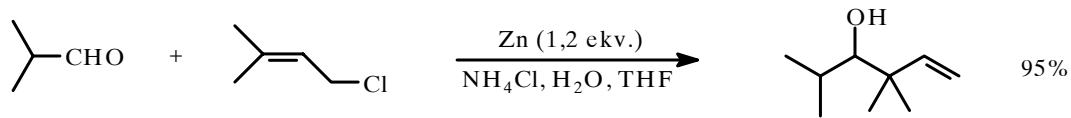
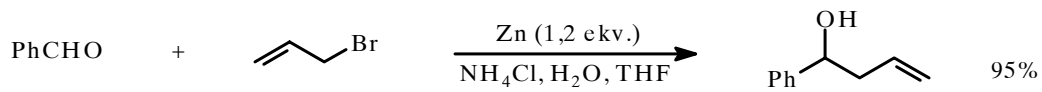
IZnCH<sub>2</sub>I ne reaguje sa: OH, R-C(=O)-R, COOR



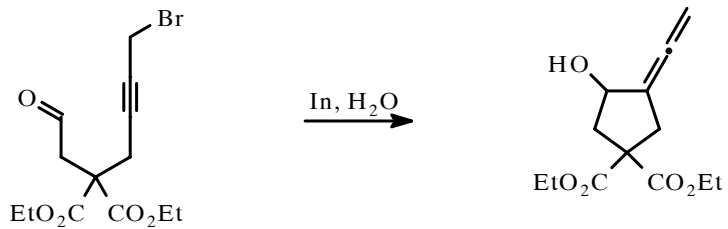
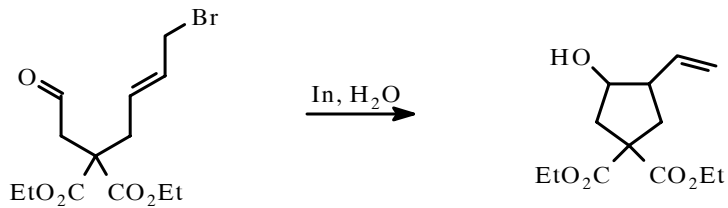
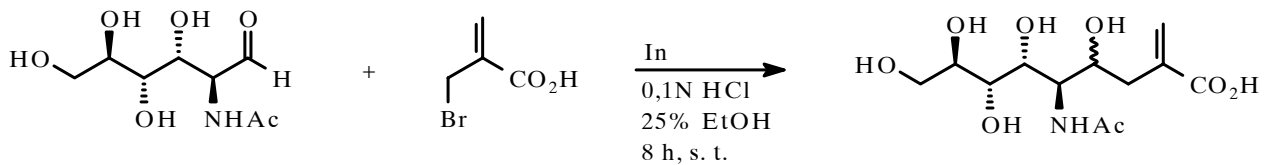
\* Stereoselektivnost



Alilovanje u vodenim uslovima



Bolji: In



## Reakcije organometalnih kompleksa prelaznih metala

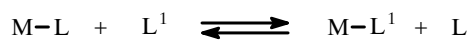
<b>22</b> [Ar] 3d <sup>2</sup> , 4s <sup>2</sup> 4, 3 <b>Ti</b> 47,88 Titan	<b>23</b> [Ar] 3d <sup>3</sup> , 4s <sup>2</sup> 5, 4, 3, 2, 0 <b>V</b> 50,94 Vanadijum	<b>24</b> [Ar] 3d <sup>5</sup> , 4s <sup>1</sup> 6, 3, 2, 0 <b>Cr</b> 51,99 Hrom	<b>25</b> [Ar] 3d <sup>5</sup> , 4s <sup>2</sup> 7, 6, 4, 3, 2, 0, -1 <b>Mn</b> 54,93 Mangan	<b>26</b> [Ar] 3d <sup>6</sup> , 4s <sup>2</sup> 6, 3, 2, 0, -2 <b>Fe</b> 55,84 Gvo`le	<b>27</b> [Ar] 3d <sup>7</sup> , 4s <sup>2</sup> 3, 2, 0, -1 <b>Co</b> 58,93 Kobalt	<b>28</b> [Ar] 3d <sup>8</sup> , 4s <sup>2</sup> 3, 2, 0 <b>Ni</b> 58,69 Nikl
<b>40</b> [Kr] 4d <sup>2</sup> , 5s <sup>2</sup> 4 <b>Zr</b> 91,22 Cirkonijum	<b>41</b> [Kr] 4d <sup>4</sup> , 5s <sup>1</sup> 5, 3 <b>Nb</b> 92,90 Niobijum	<b>42</b> [Kr] 4d <sup>5</sup> , 5s <sup>1</sup> 6, 5, 4, 3, 2, 0 <b>Mo</b> 95,94 Molibden	<b>43</b> [Kr] 4d <sup>6</sup> , 5s <sup>1</sup> 7 <b>Tc</b> 98,90 Tehnecijum	<b>44</b> [Kr] 4d <sup>7</sup> , 5s <sup>1</sup> 8, 6, 4, 3, 2, 0, -2 <b>Ru</b> 101,90 Rutenijum	<b>45</b> [Kr] 4d <sup>8</sup> , 5s <sup>1</sup> 5, 4, 3, 2, 1, 0 <b>Rh</b> 102,90 Rodijum	<b>46</b> [Kr] 4d <sup>10</sup> 4, 2, 0 <b>Pd</b> 106,42 Paladijum
<b>72</b> [Xe] 4f <sup>14</sup> , 5d <sup>2</sup> 6s <sup>2</sup> 4 <b>Hf</b> 178,49 Hafnijum	<b>73</b> [Xe] 4f <sup>14</sup> , 5d <sup>3</sup> 6s <sup>2</sup> 5 <b>Ta</b> 180,94 Tantal	<b>74</b> [Xe] 4f <sup>14</sup> , 5d <sup>4</sup> , 6s <sup>2</sup> 6, 5, 4, 3, 2, 0 <b>W</b> 183,85 Volfram	<b>75</b> [Xe] 4f <sup>14</sup> , 5d <sup>5</sup> , 6s <sup>2</sup> 7, 6, 4, 2, -1 <b>Re</b> 186,20 Renijum	<b>76</b> [Xe] 4f <sup>14</sup> , 5d <sup>6</sup> , 6s <sup>2</sup> 8, 6, 4, 3, 2, 0, -2 <b>Os</b> 190,20 Osmijum	<b>77</b> [Xe] 4f <sup>14</sup> , 5d <sup>7</sup> , 6s <sup>2</sup> 6, 4, 3, 2, 1, 0, -1 <b>Ir</b> 192,22 Iridijum	<b>78</b> [Xe] 4f <sup>14</sup> , 5d <sup>9</sup> 6s <sup>1</sup> 4, 2, 0 <b>Pt</b> 195,08 Platina

Osnovne reakcije organometalnih kompleksa prelaznih metala:

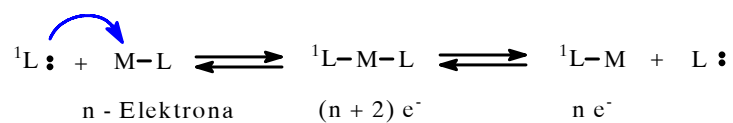
- Izmena liganda;
- Oksidativna adicija/reduktivna eliminacija;
- Migratorna insercija/ $\beta$ -eliminacija;
- Transmetalovanje;
- Nukleofilni napad na koordinirani ligand;
- Elektrofilni napad na koordinirani ligand;
- 2+2 Reakcije



### Izmena liganda



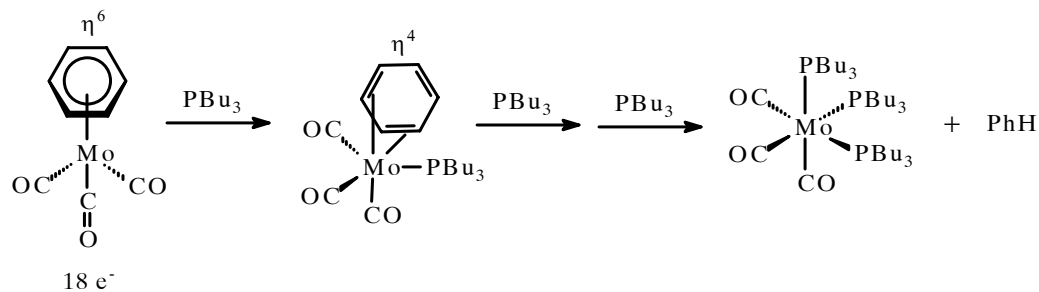
### Asocijativni mehanizam



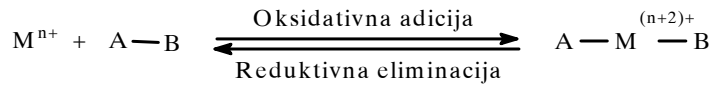
### Disocijativni mehanizam



Primer izmene liganda asocijativnim mehanizmom, uz promenu hapticiteta liganda:



OKSIDATIVNA ADICIJA/REDUKTIVNA ELIMINACIJA

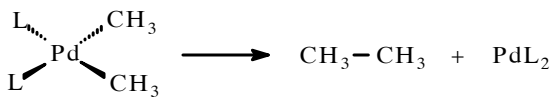
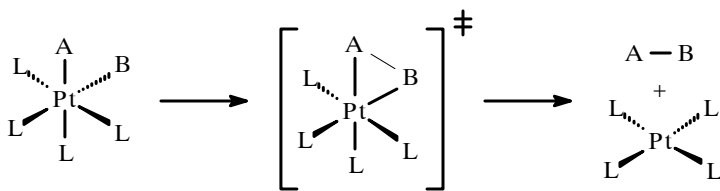
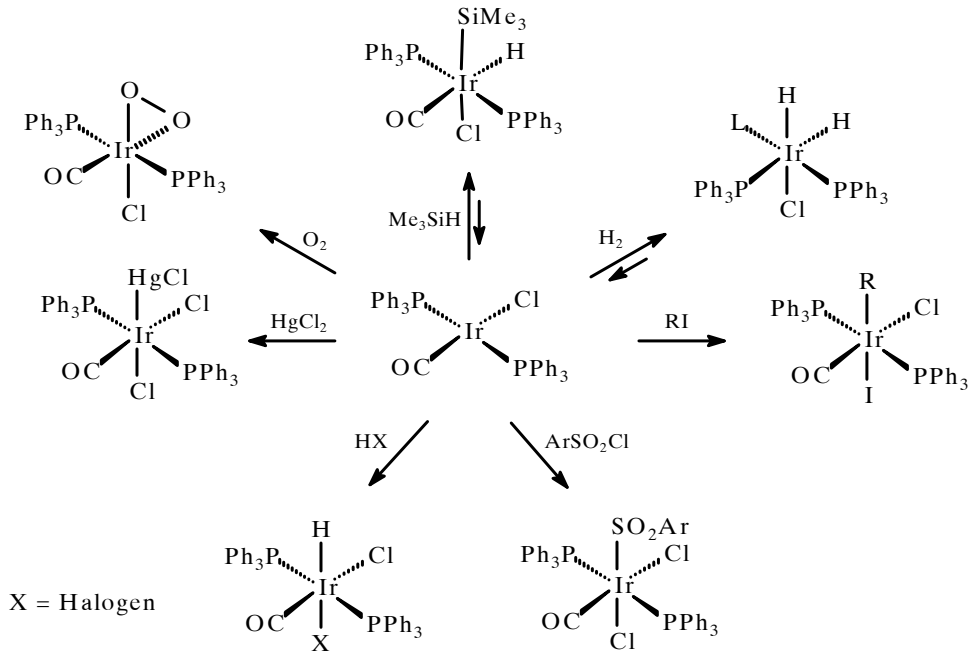


A-B Može biti: a) nepolarno: H<sub>2</sub>, R<sub>3</sub>SiH, R-H

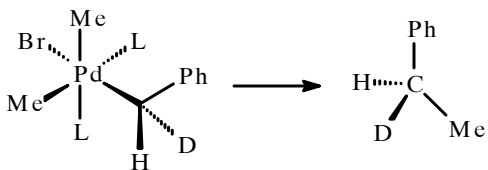
b) polarno: H-X, R-C(=O)-X, X = Br, I

c) nezasićene veze: C=C, O<sub>2</sub>, S<sub>2</sub>, C≡C, [M + || → M< ]

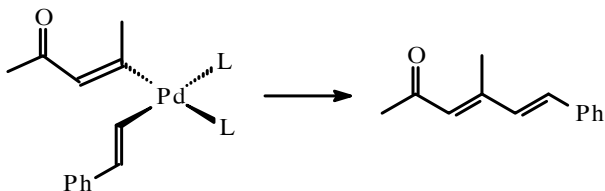
Oksidativne adicije Vaskinog kompleksa



Grupe koje podležu eliminaciji moraju biti u cis-položaju

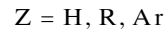
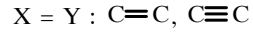
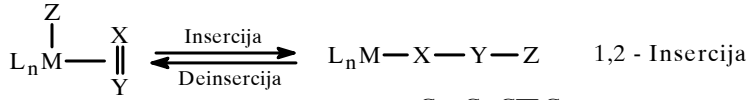
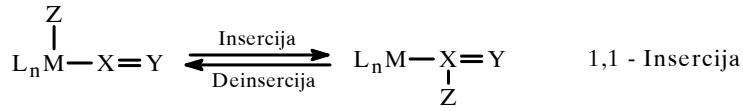


Migracija se vrši sa retencijom konfiguracije na stereocentru

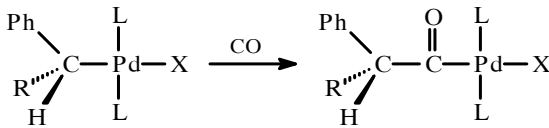
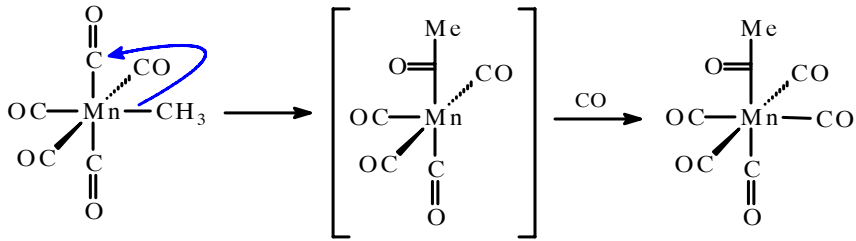


Migracija se vrši sa retencijom geometrijske konfiguracije

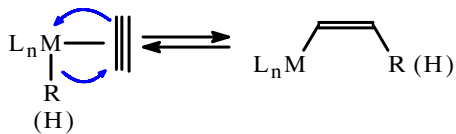
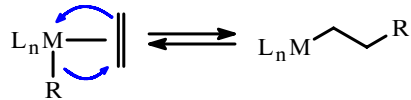
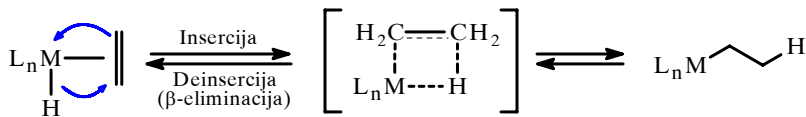
MIGRATORNA INSERCIJA/ $\beta$ -ELIMINACIJA



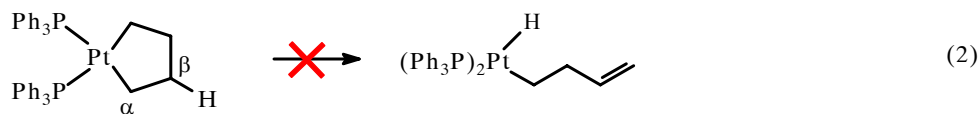
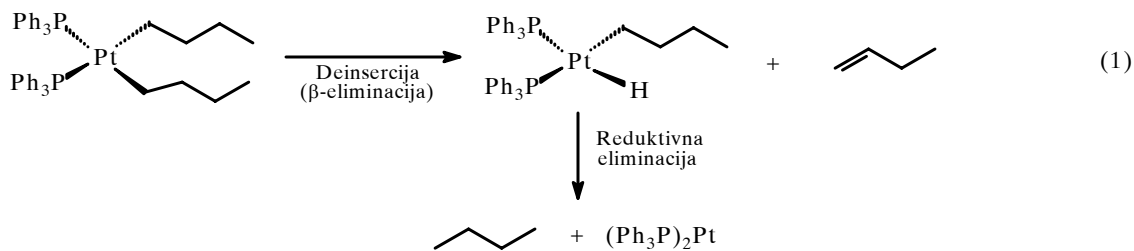
Insercija ugljen-monoksida



Insercija alkena i alkina



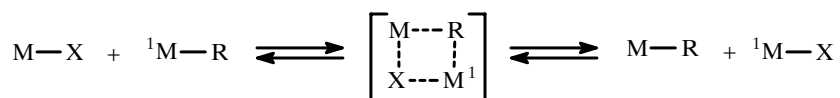
## Deinsercija ( $\beta$ -eliminacija)



Pt,  $\alpha$ -C,  $\beta$ -C i  $\beta$ -H nisu koplanarni

$\Downarrow$   
 Deinsercija je 1000 puta sporija nego kod di-*n*-butil-platinskog kompleksa

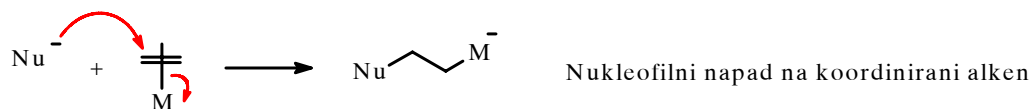
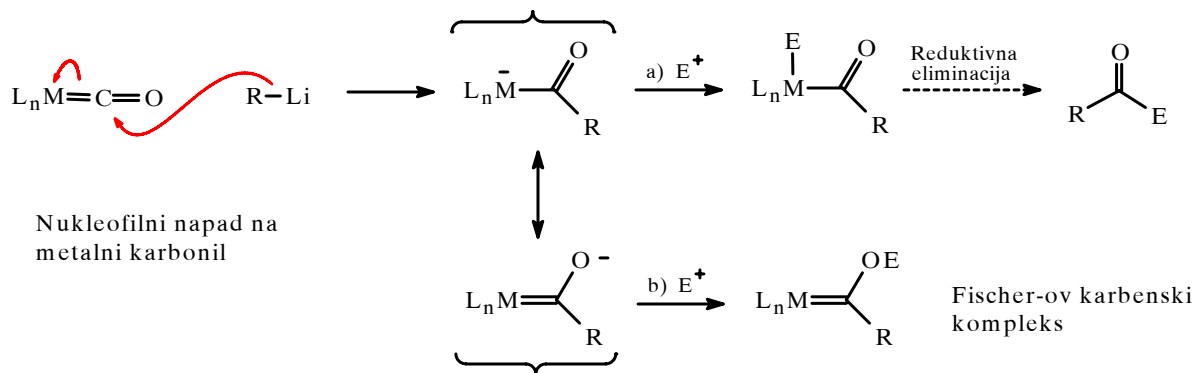
## TRANSMETALOVANJE



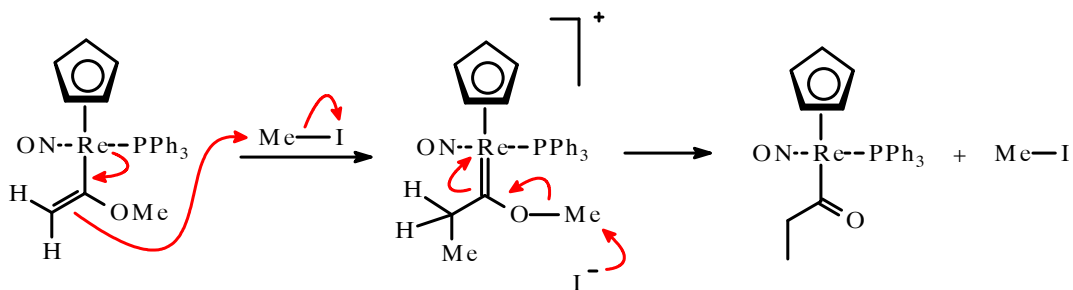
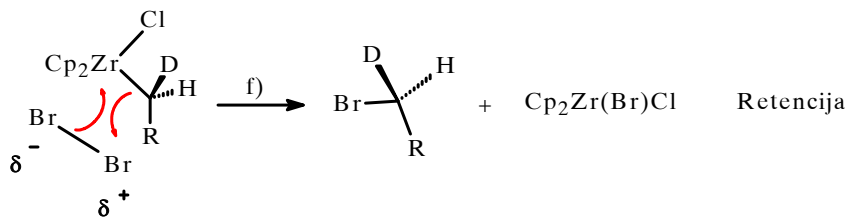
M: Prelazni metal

${}^1\text{M}$ : Metal osnovne grupe: Li, Mg, B, Zn, Si, Sn, Hg, Ge, Zr (takođe prelazni metal)

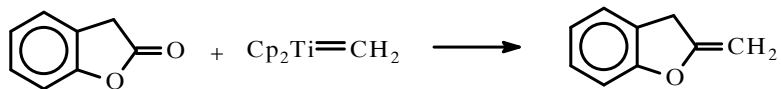
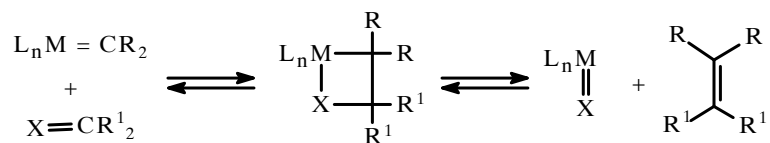
## NUKLEOFILNI NAPAD NA KOORDINIRANI LIGAND



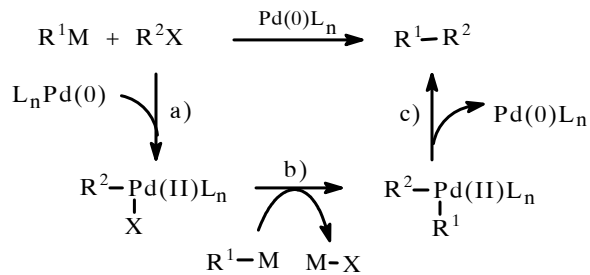
ELEKTROFILNI NAPAD NA KOORDINIRANI LIGAND



2+2 REAKCIJE

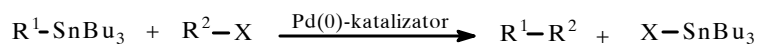


# UKRŠTENA KUPLOVANJA

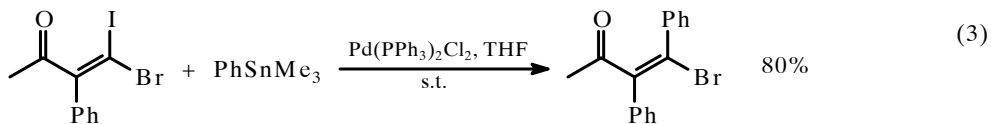
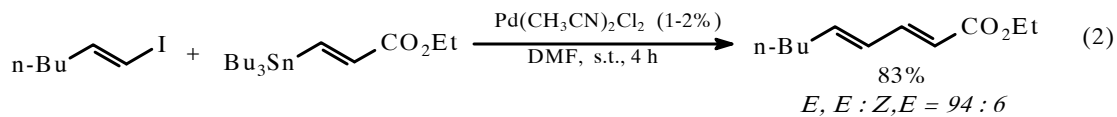
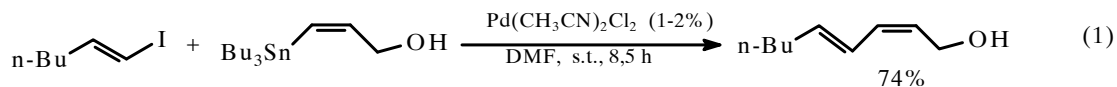


-Stille-ovo kuplovanje (M = Sn)  
 -Suzuki-jevo kuplovanje (M = B)  
 -Negishi (Zn), Hiyama (Si), Kumada (Mg) itd.

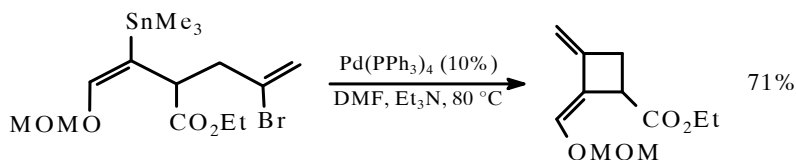
## STILLE-OVO KUPLOVANJE



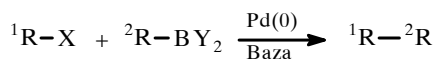
Intermolekulske reakcije: retencija geometrije dvostrukih veza



Intramolekulsko Stille-ovo kuplovanje: pogodno za zatvaranje malih, običnih i velikih prstenova



## SUZUKI-JEVO KUPLOVANJE



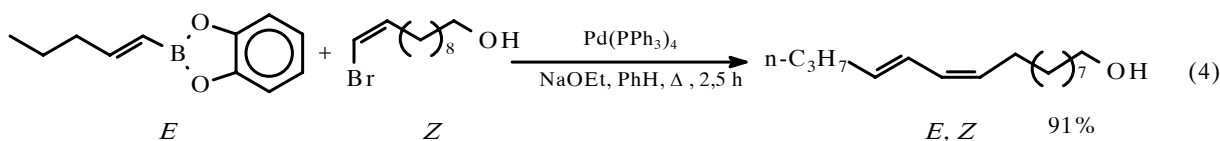
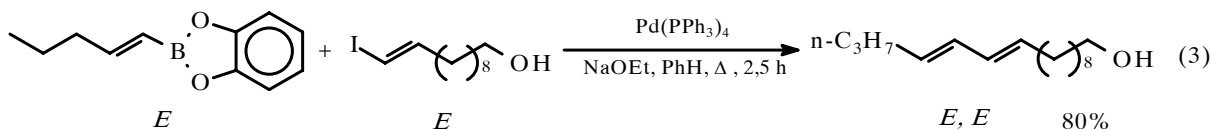
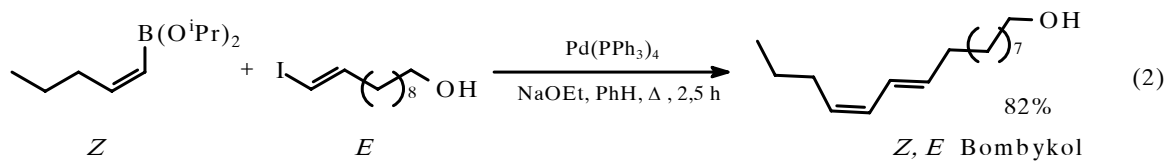
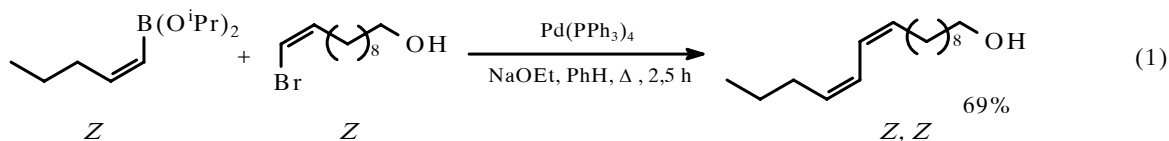
${}^1\text{R}$  = Vinil, aril, alil

${}^2\text{R}$  = Vinil, aril, alil, prim. alkil

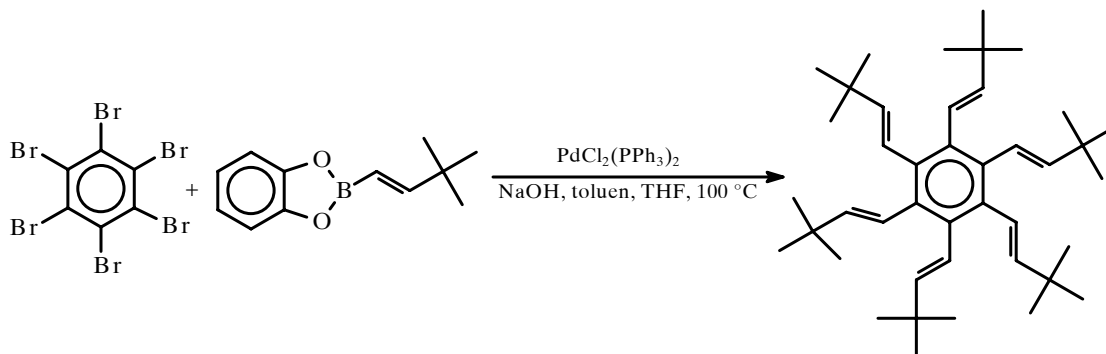
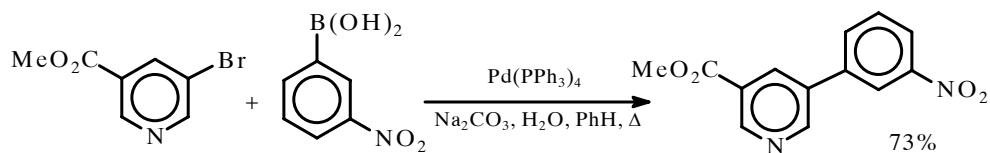
X = I, Br, OTf

Y = Alkil, OR, OH

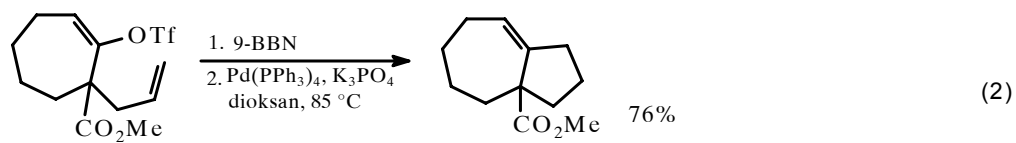
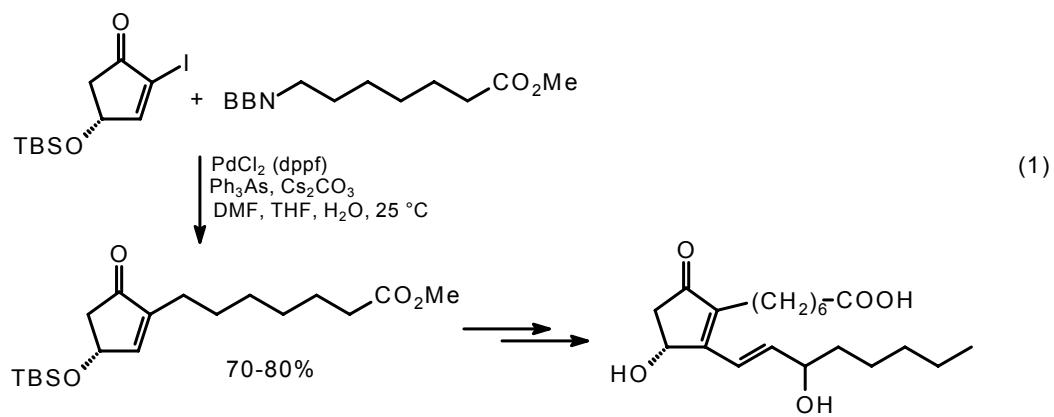
Kuplovanje se vrši sa retencijom geometrijske konfiguracije reakcionih partnera:



Moguća su i kuplovanja dva aromatična jezgra, kao i aromatičnih jezgara sa alkenima:

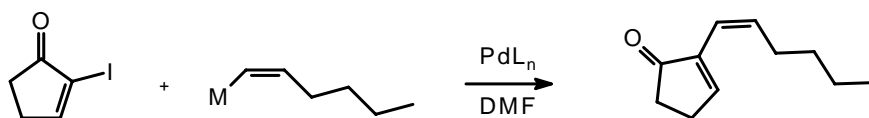
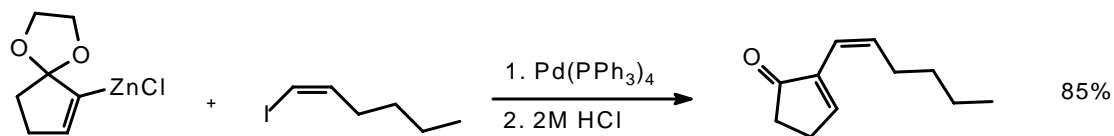
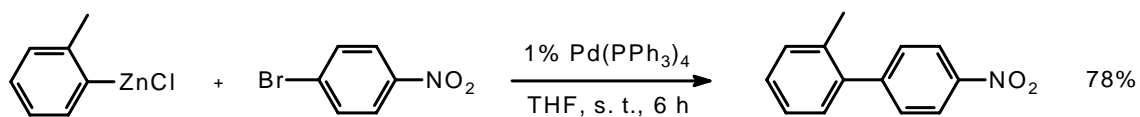
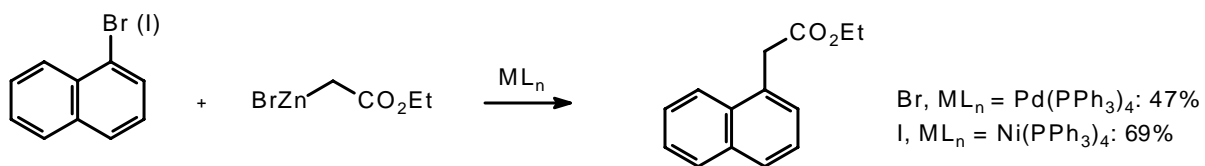
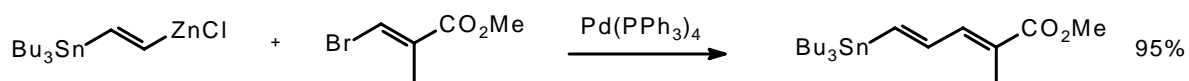


Suzuki-jevo kuplovanje može se primeniti i za stvaranje veze između  $sp^2$  i  $sp^3$  ugljenikovih atoma (reduktivna eliminacija je brža od  $\beta$ -eliminacije):



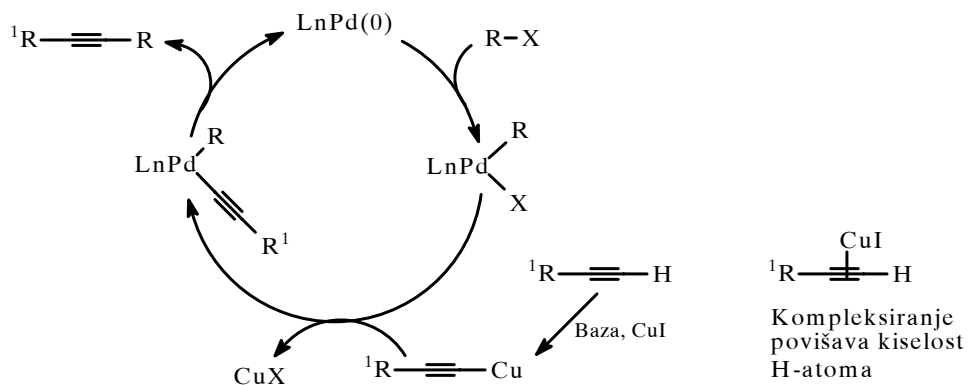
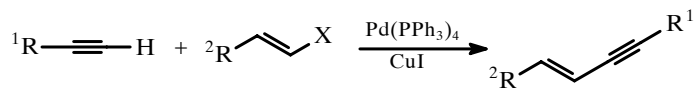


Negishi-jevo kuplovanje (M = Zn, Al, Zr)

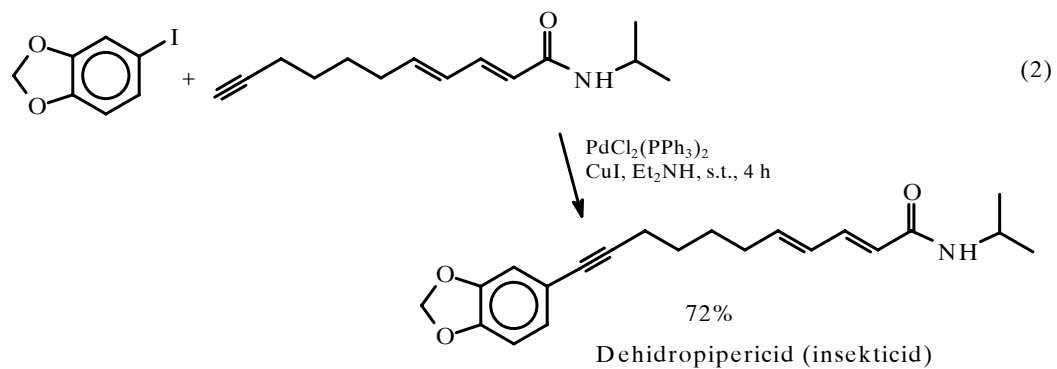
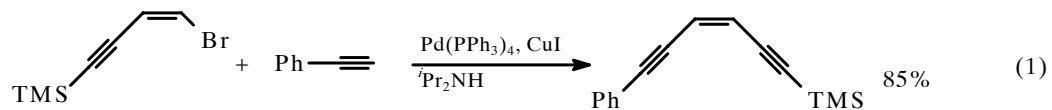


M	Time	Temperature	Yield
Zn <sub>1/2</sub>	1 h	s.t.	100%
Al(Bu-i) <sub>2</sub>	1 h	s.t.	89%
ZrCp <sub>2</sub> Cl	1 h	s.t.	27%
Bu <sub>3</sub> Sn	13 h	65°C	64%

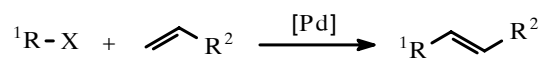
## SONOGASHIRA-INO KUPLOVANJE



Sonogashira-ina reakcija: primena u sintezi:



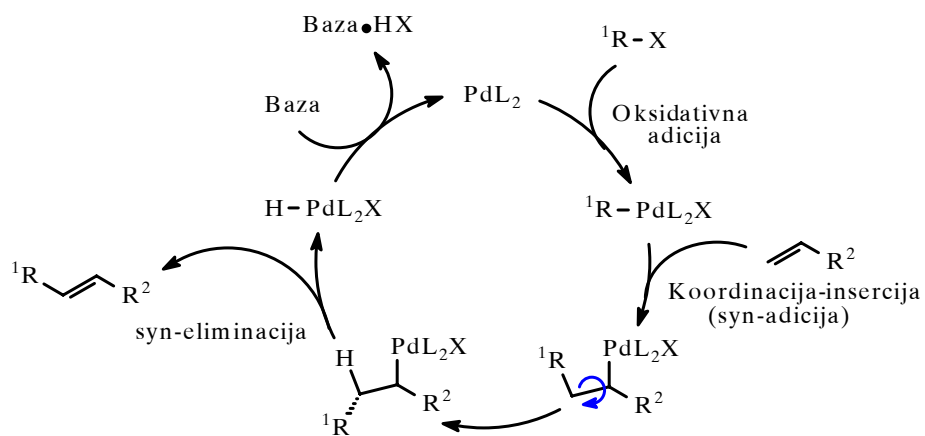
## HECK-OVA REAKCIJA



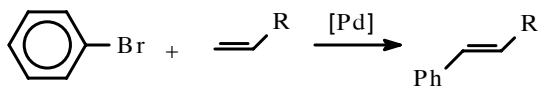
$\text{R}^1$  = Alkenil, aril, alil, alkinil, benzil, alkoksikarbonilmetil

$\text{R}^2$  = Alkil, alkenil, aril,  $\text{CO}_2\text{R}$ , OR,  $\text{SiR}_3$ , itd.

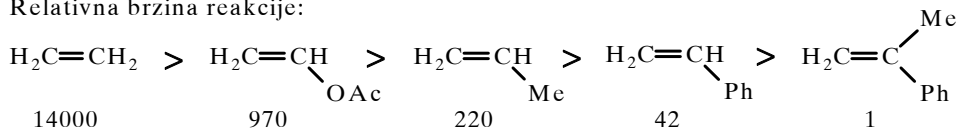
Mehanizam Heck-ove reakcije:



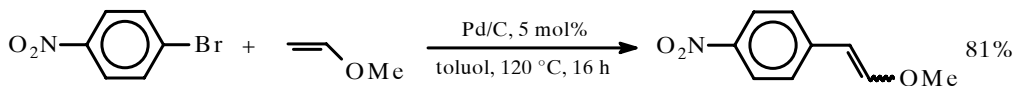
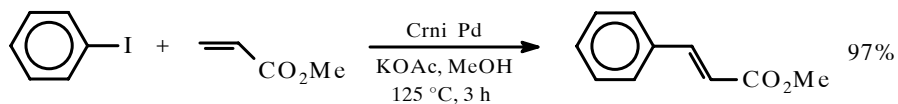
Reakcija je osetljiva na sterne smetnje



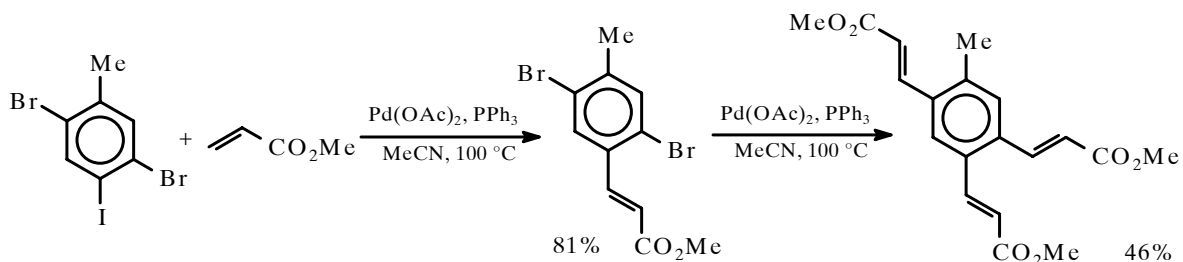
Relativna brzina reakcije:



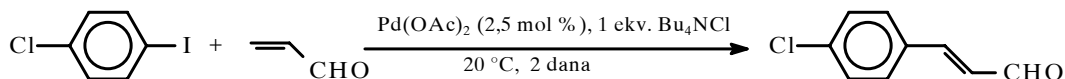
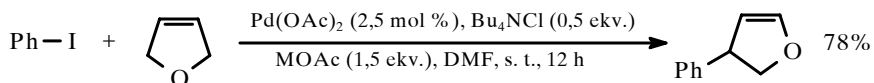
Sa visoko aktivnim elektrofilima nije potreban ligand



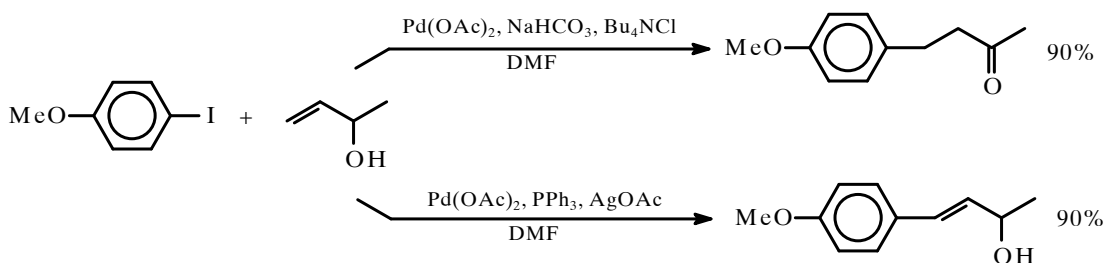
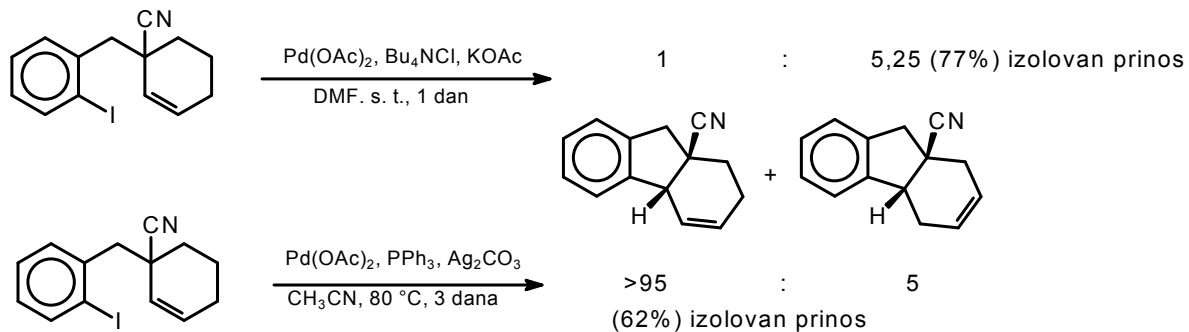
Sa umereno aktivnim elektrofilima koriste se kompleksi Pd(0)



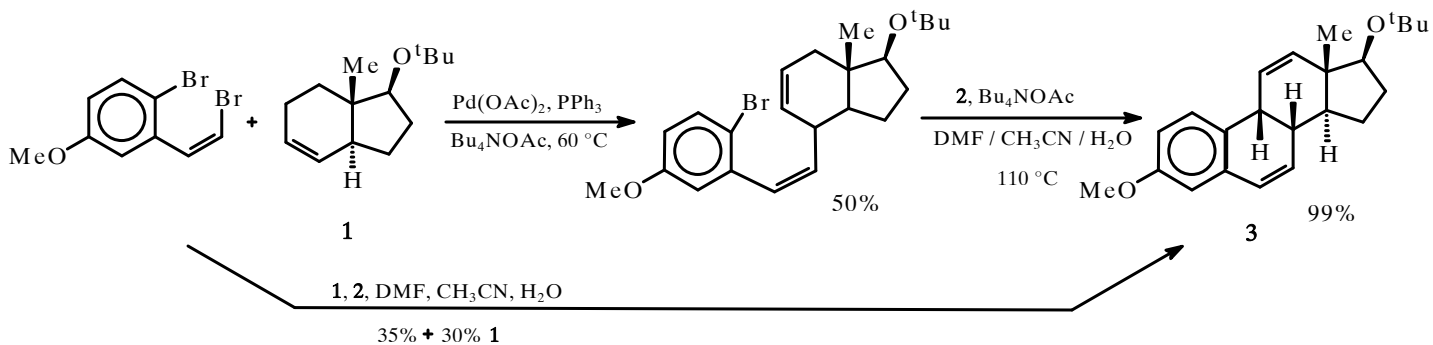
Jeffery-jevi uslovi: dodatak kvaternih amonijum-soli ubrzava reakciju



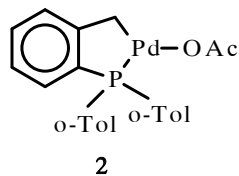
Dodatak srebrnih soli menja mehanizam i selektivnost reakcije



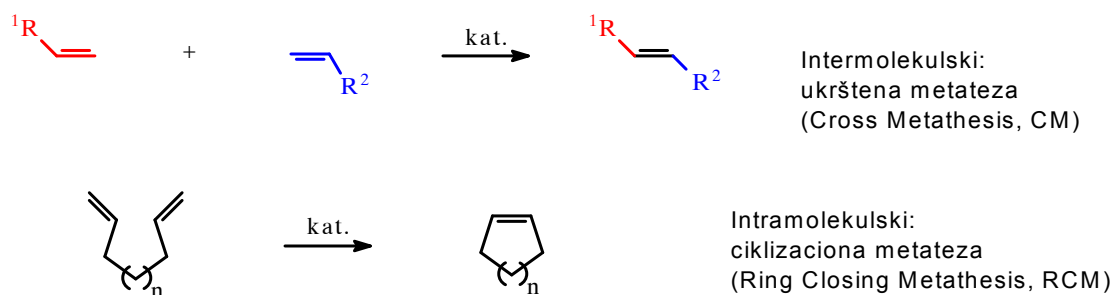
Primena u sintezi



Moguće je izvršiti obe reakcije kao jednu, domino-reakciju, pri čemu nastaje proizvod **3** u prinosu od 35%, uz 30% neizreagovanog supstrata **1**.

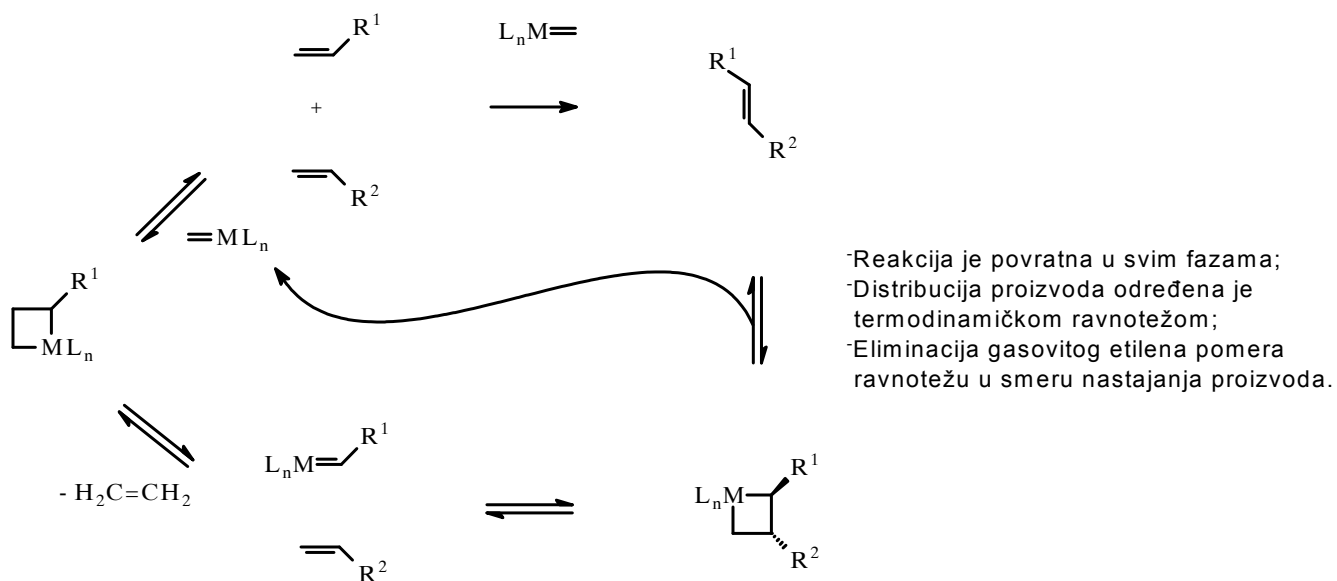


# METATEZA ALKENA (OLEFINSKA IZMENA)

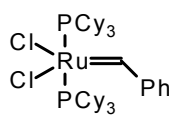


2005: Nobelova nagrada za hemiju: Y. Chauvin, R. Grubbs i R. Schrock

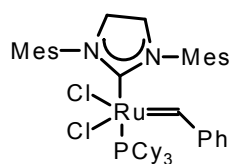
Mehanizam reakcije: Y. Chauvin, 1971.



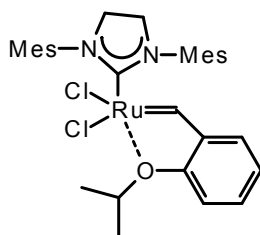
## Katalizatori



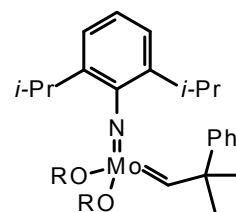
Grubbsov katalizator  
1. generacije



Grubbsov katalizator  
2. generacije

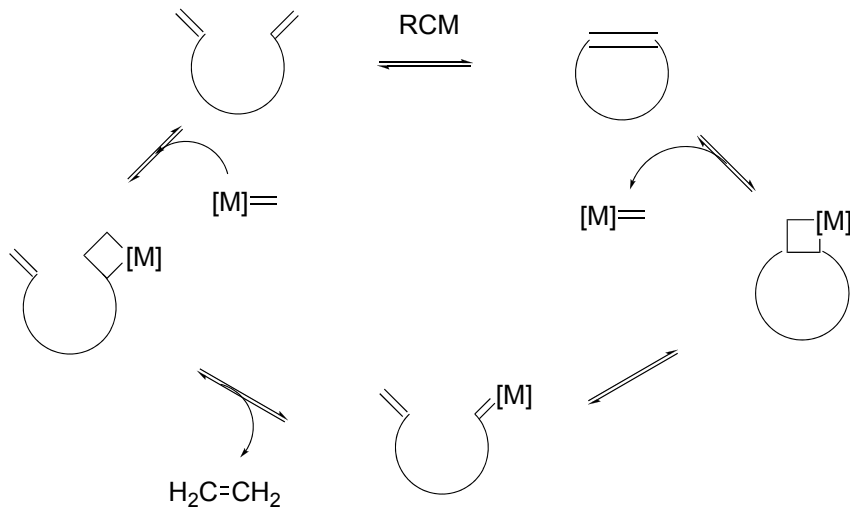


Hoveyda-Grubbs-  
Blechert-ov  
katalizator  
2. generacije

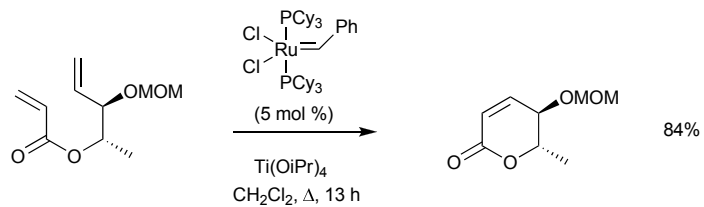
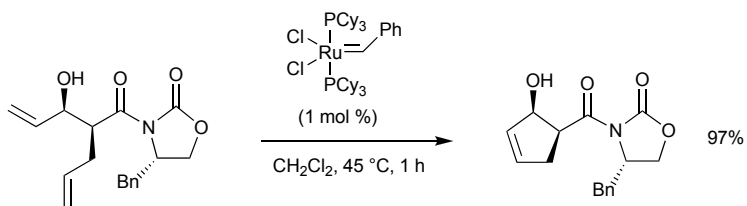


Schrock-ov  
katalizator

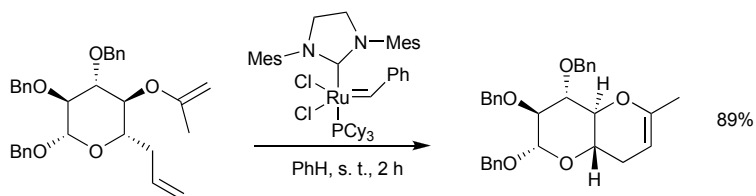
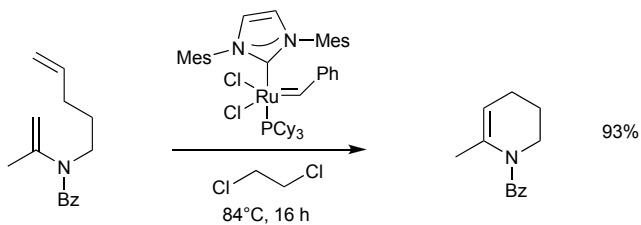
## Mehanizam ciklizacije metateze



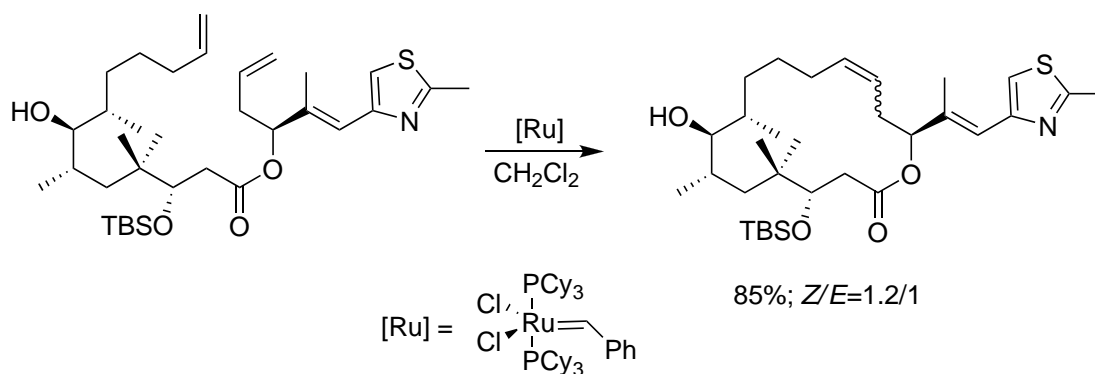
### RCM: Karbociklični prstenovi i laktoni



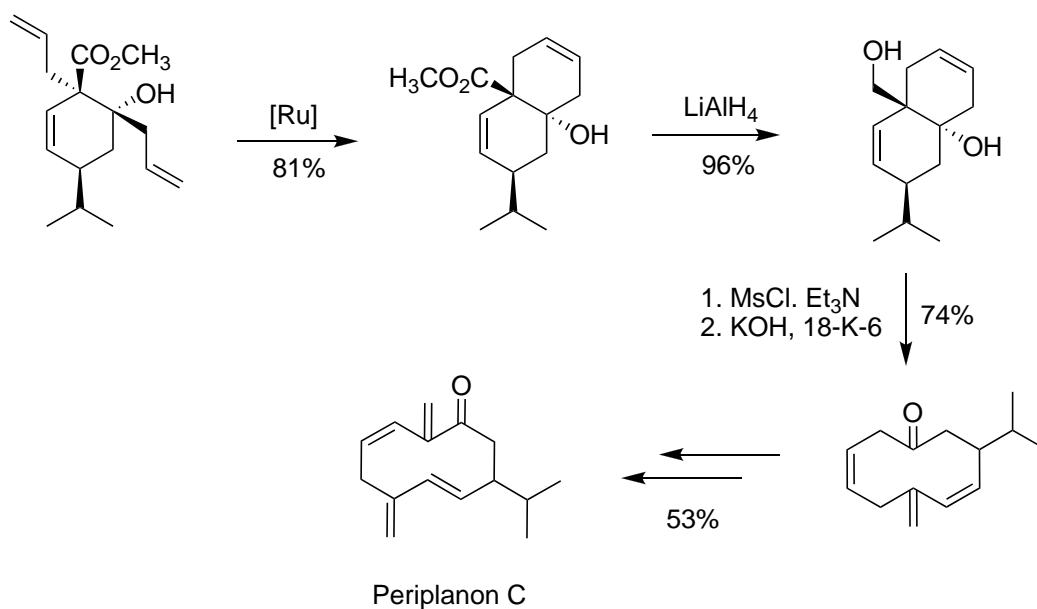
### RCM: Heterociklični prstenovi



RCM: Srednji prstenovi: primer iz sinteze epotilona (antitumorskih agenasa)



Kontrola geometrije alkena: kombinacija: RCM/fragmentacija



Ukrštena metateza

