

CHEMIA ORGANICZNA – MECHANIZMY I REAKCJE

Marcin Budny

marcin@chemicalforum.eu
<http://www.newchemistry.eu>

**Katedra Chemii Organicznej
Wydział Chemii UMK**



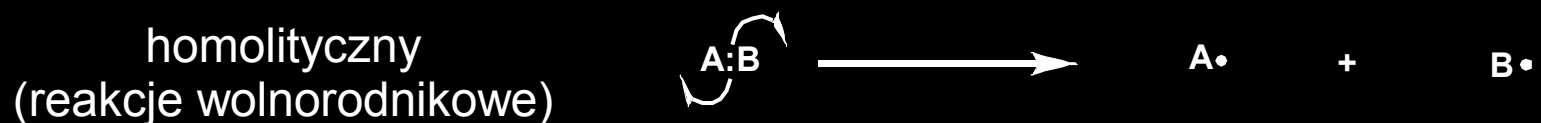
Przeciwności się przyciągają,
Ale miłość to chemia, nie fizyka

www.demotywatory.pl

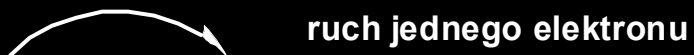
Reakcje w chemii organicznej



Rozpad wiązań



W mechanizmach reakcji pokazujemy ruch elektronów



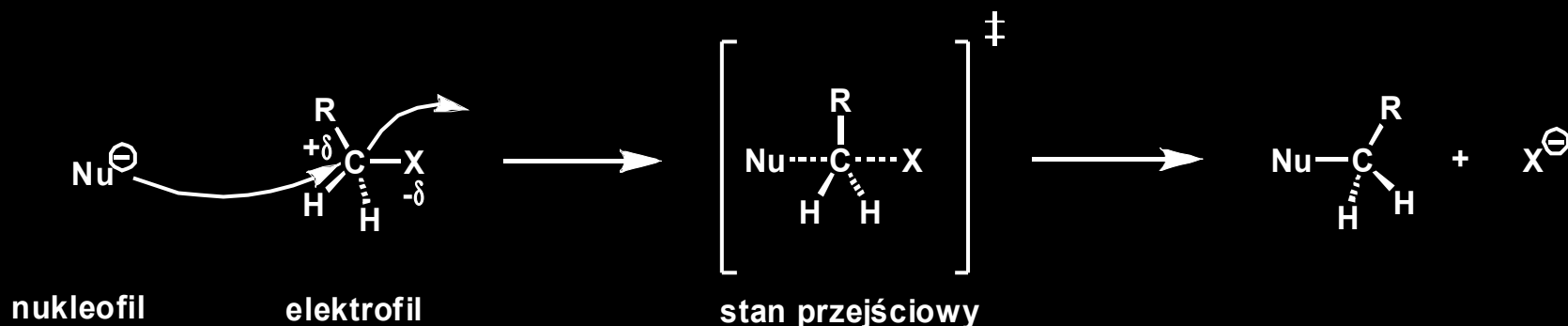


Nukleofil – bogaty w elektrony (anion, wolna para elektronowa, elektrony π)

Elektrofil – ubogi w elektrony (kation, deficyt elektronów, „niezapełnione orbitale”)

Przewidywanie przebiegu reakcji jonowych:
identyfikacja nukleofila, elektrofila i centrów reakcyjnych

Substytucja nukleofilowa dwucząsteczkowa, Sn2



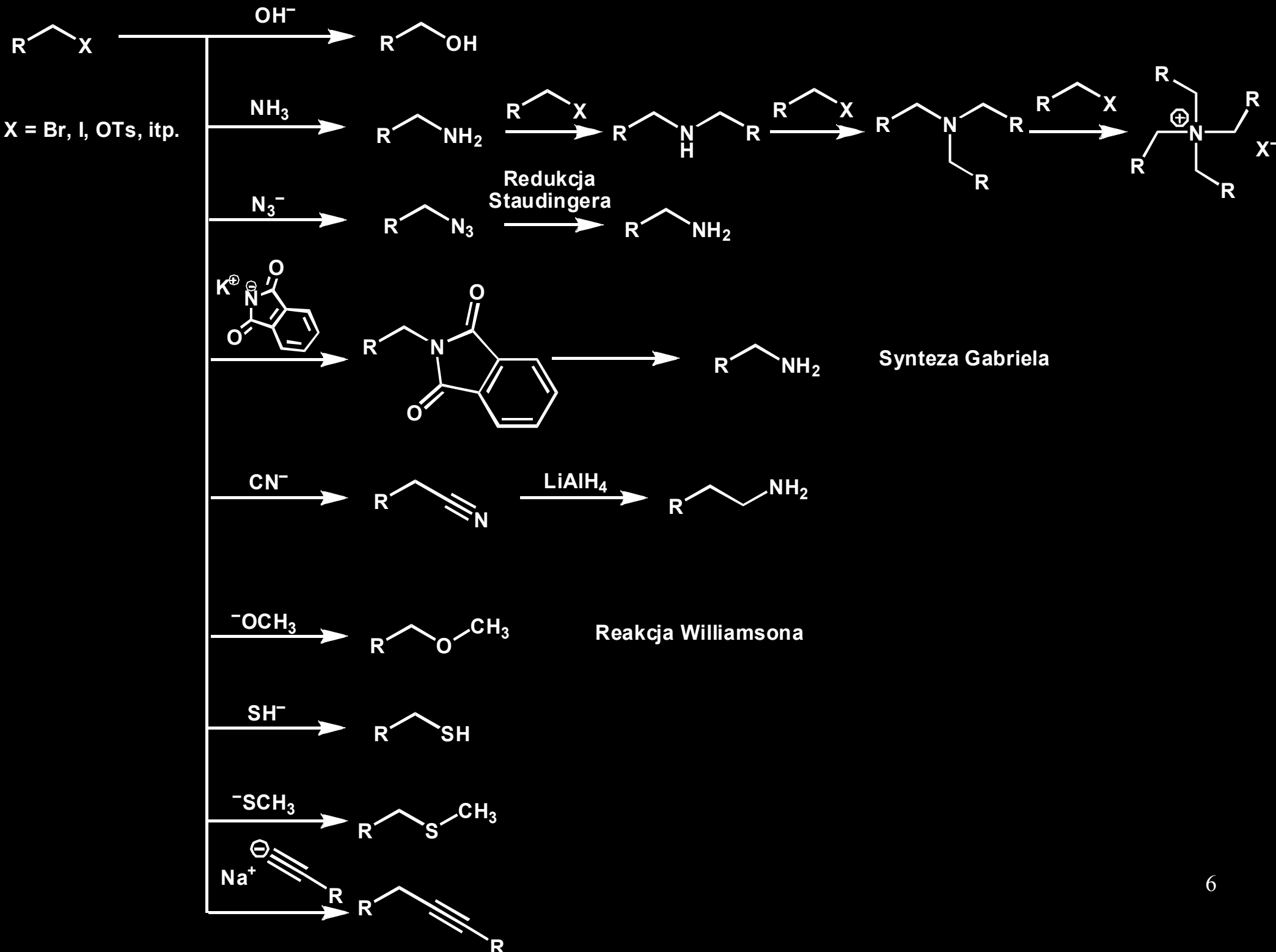
szybkość reakcji zależy od stężeń obu reagentów

elektrofile: 1° i 2° chlorki, bromki, jodki, tosylany

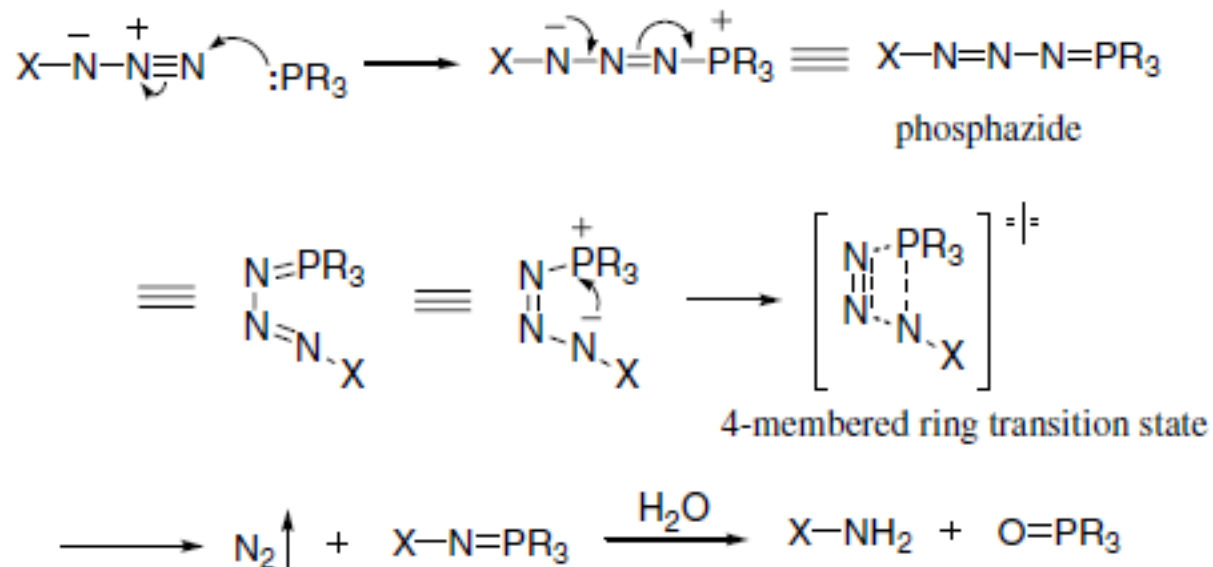
nukleofile: OH^- , I^- , HS^- , CN^- , N_3^- , nukleofile węglowe,

rozpuszczalniki: słabo solwujące aniony, np. dimetyloformamid (DMF)
dimetylosulfotlenek (DMSO), tetrahydrofuran (THF), inne rozpuszczalniki

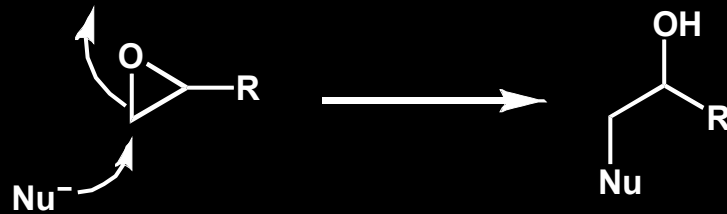
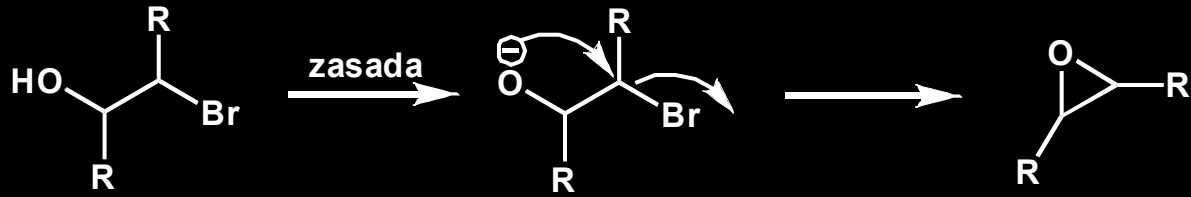
katalizatory: katalizatory przeniesienia fazowego, etery koronowe



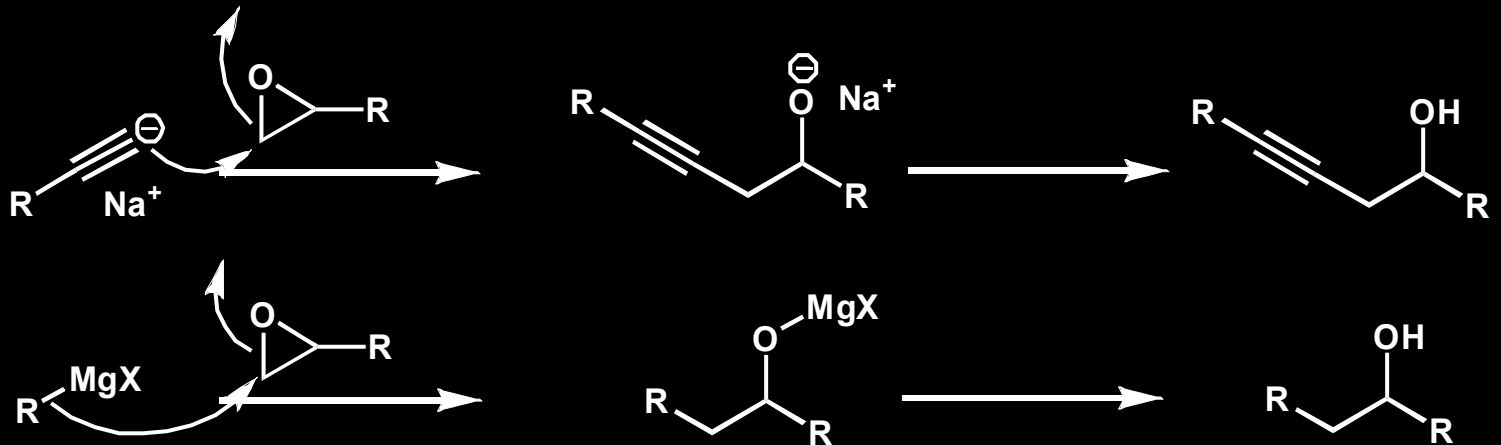
Redukcja Staudingera



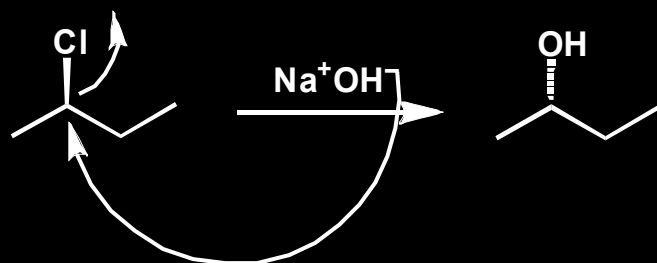
Epoksydy



Nukleofile węglowe są szczególnie użyteczne:



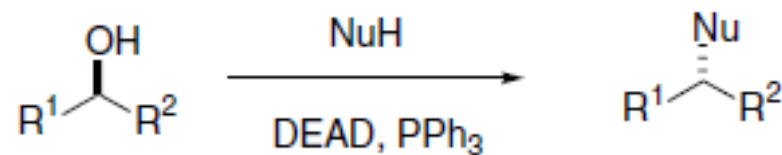
Stereochemia reakcji Sn2

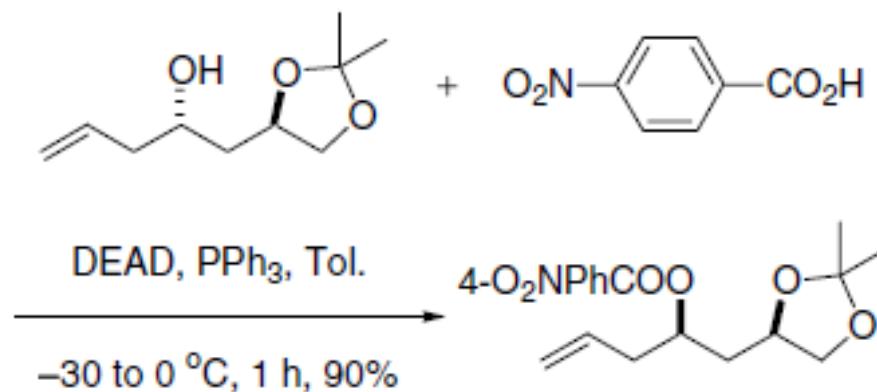
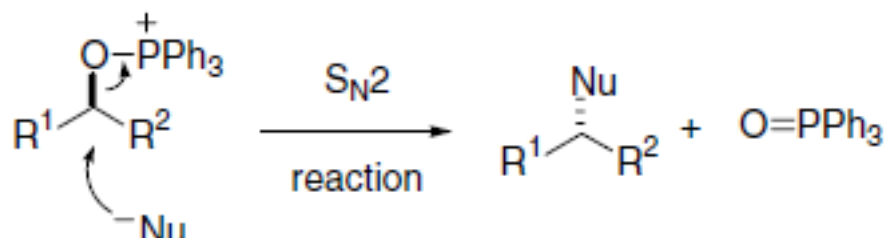
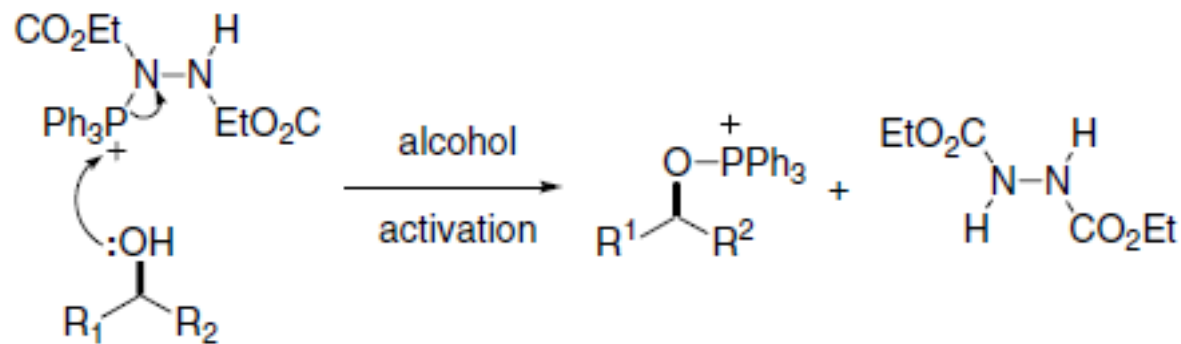
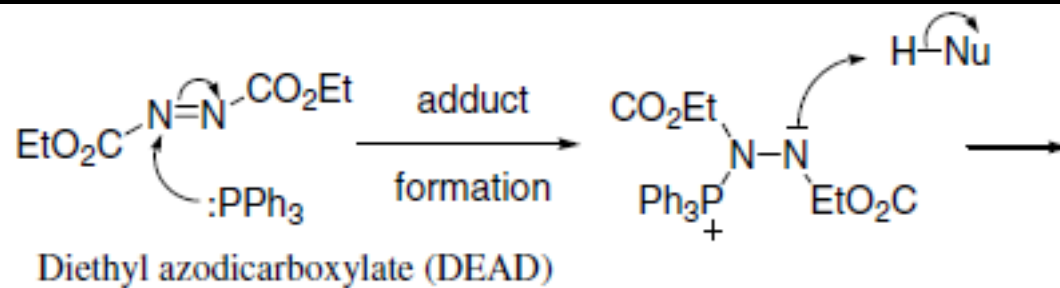


Sn2:
inwersja konfiguracji
na centrum chiralności

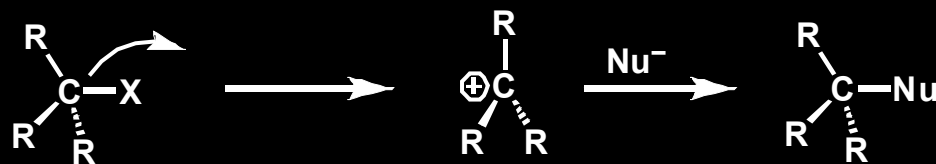
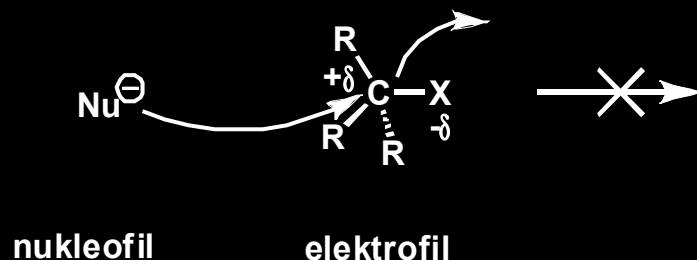
Mitsunobu reaction

S_N2 inversion of an alcohol by a nucleophile using diethyl azodicarboxylate (DEAD) and triphenylphosphine.





Substytucja nukleofilowa jednocząsteczkowa, S_N1

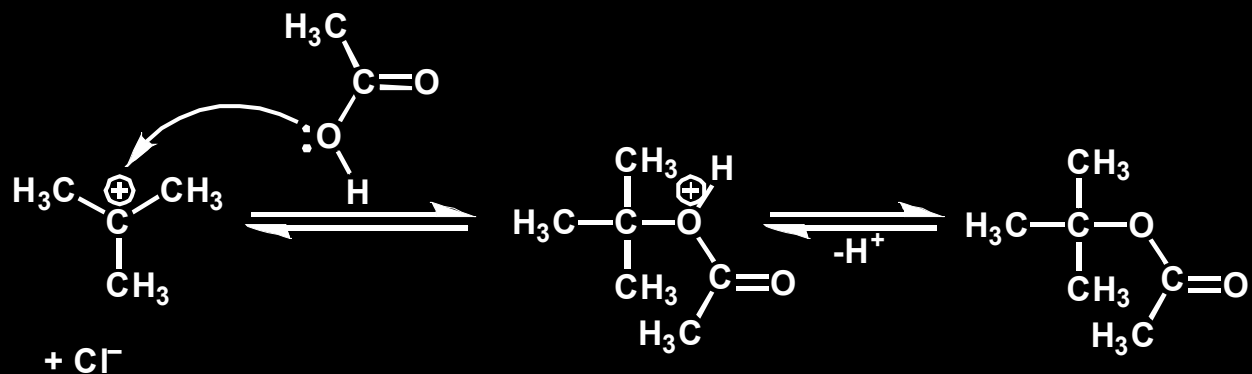
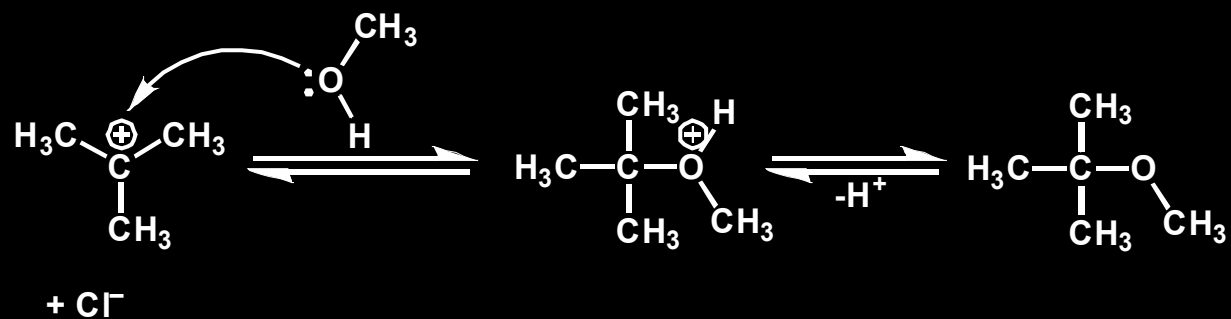
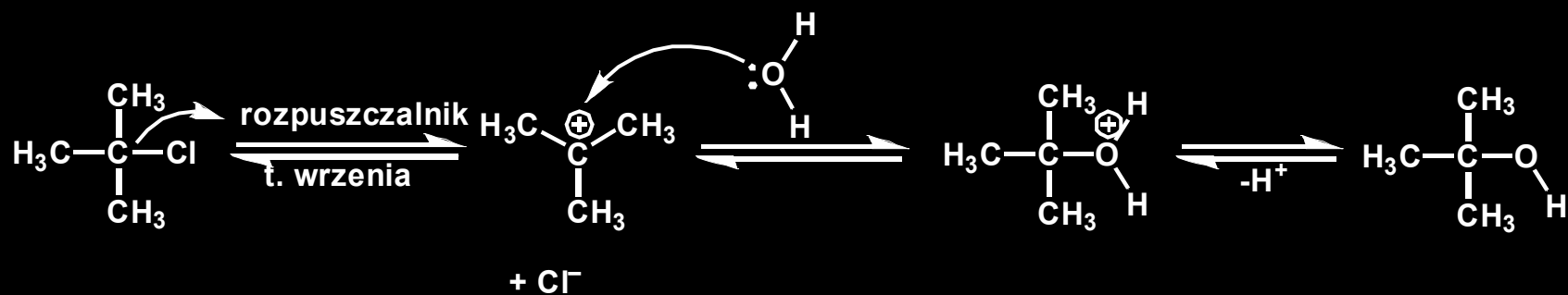


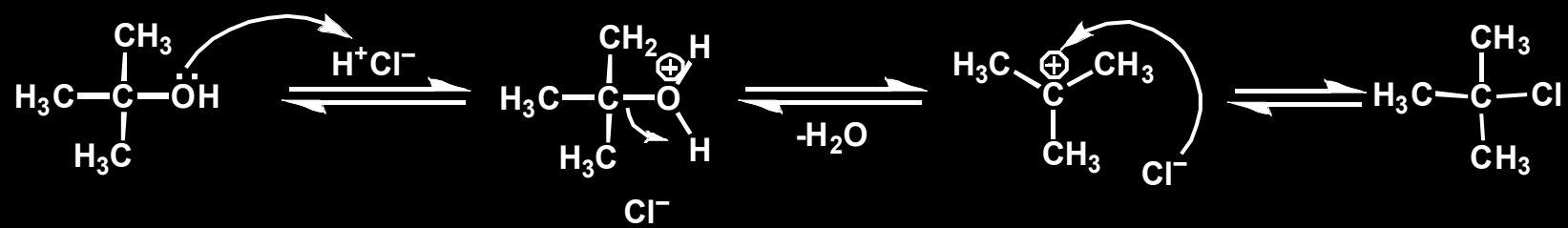
elektrofile: 3° halogenki, tosylany, alkohole itp.

nukleofile: alkohole, woda, mocne zasady dają złe rezultaty

rozpuszczalniki: solwatuujące aniony (alkohole, woda, kwasy karboksylowe)

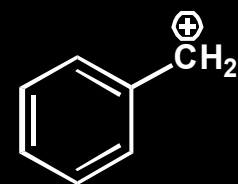
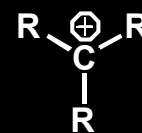
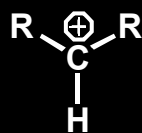
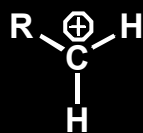
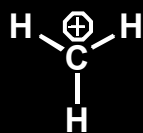
Sn1: reakcje solwolizy



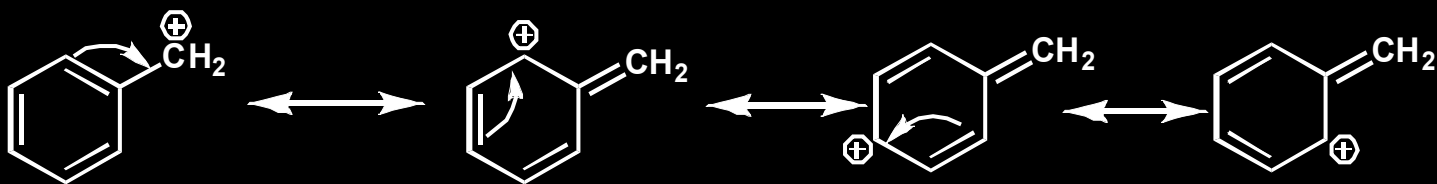


Karbokationy: trwałość

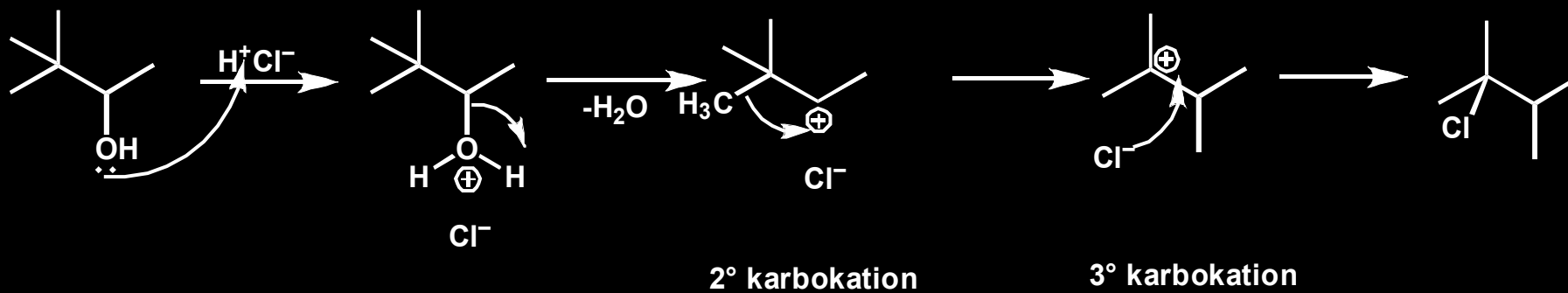
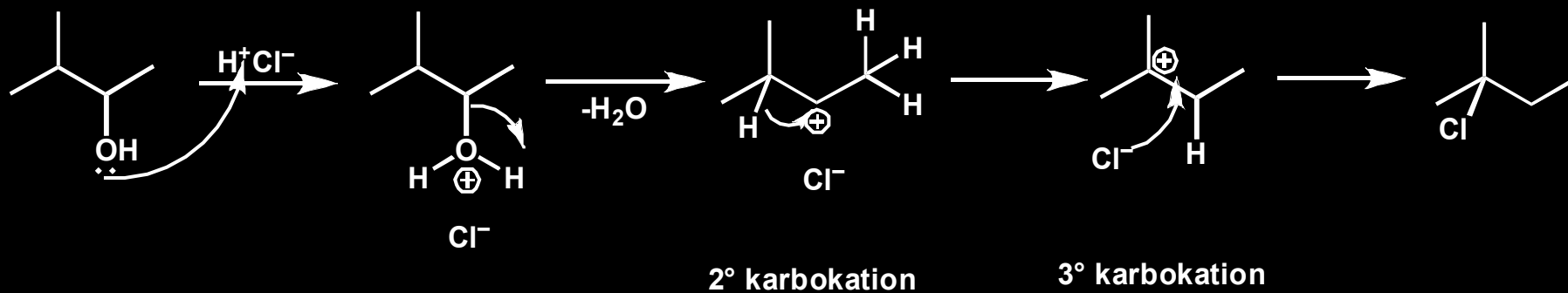
rosnąca trwałość karbokationów



benzylowy



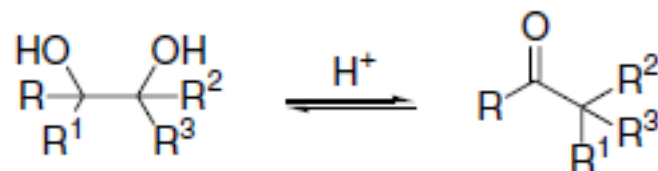
Karbokationy: przegrupowania



Przegrupowanie pinakolowe

Pinacol rearrangement

Acid-catalyzed rearrangement of vicinyl diols (pinacols) to carbonyl compounds.

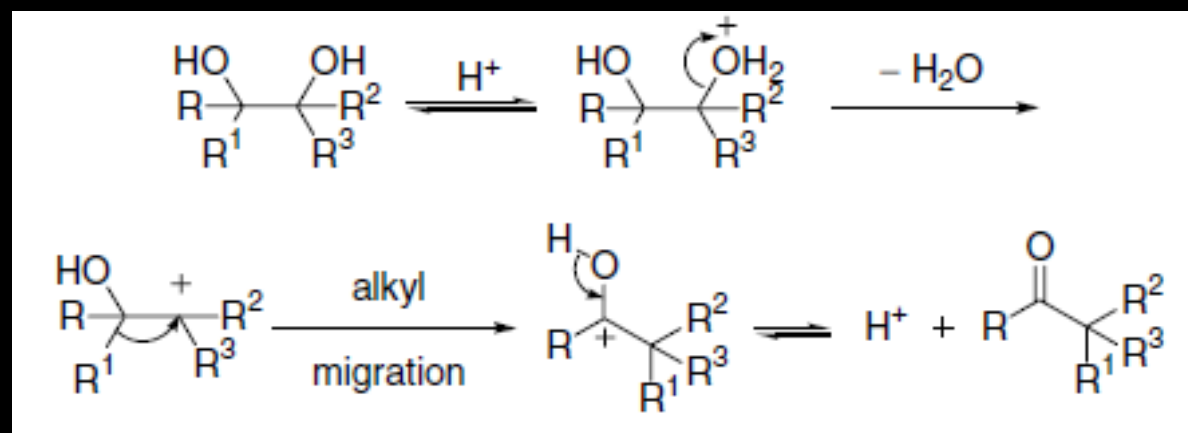


The most electron-rich alkyl group (more substituted carbon) migrates first.
The general migration order:

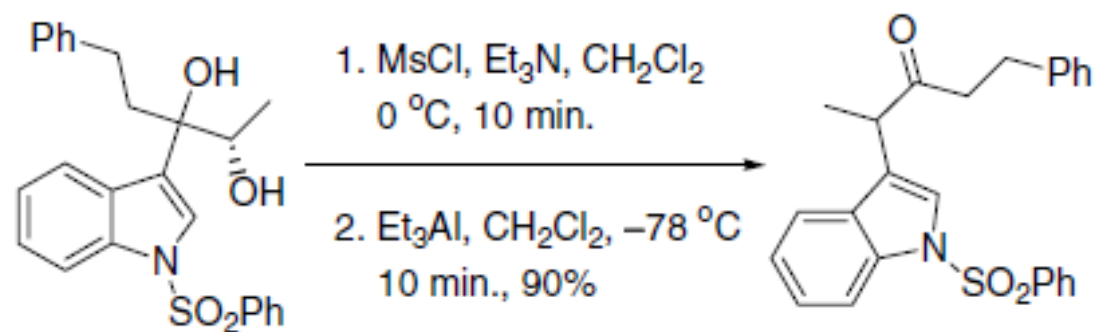
tertiary alkyl > cyclohexyl > secondary alkyl > benzyl > phenyl >
primary alkyl > methyl >> H.

For substituted aryls:

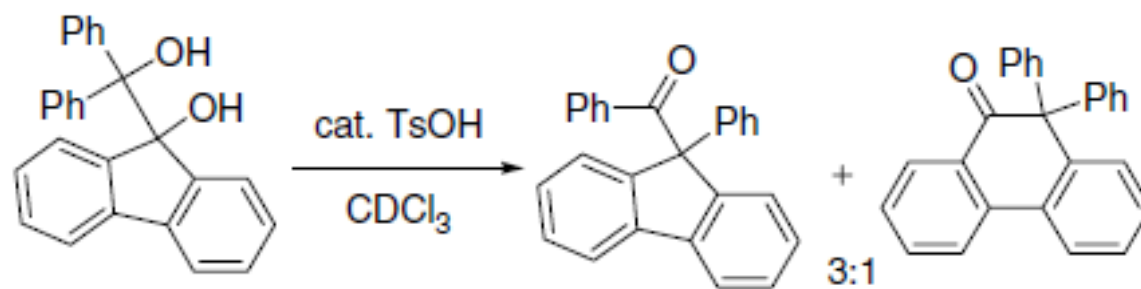
p-MeO-Ar > *p*-Me-Ar > *p*-Cl-Ar > *p*-Br-Ar > *p*-MeOAr > *p*-O₂N-Ar



Example 1¹²

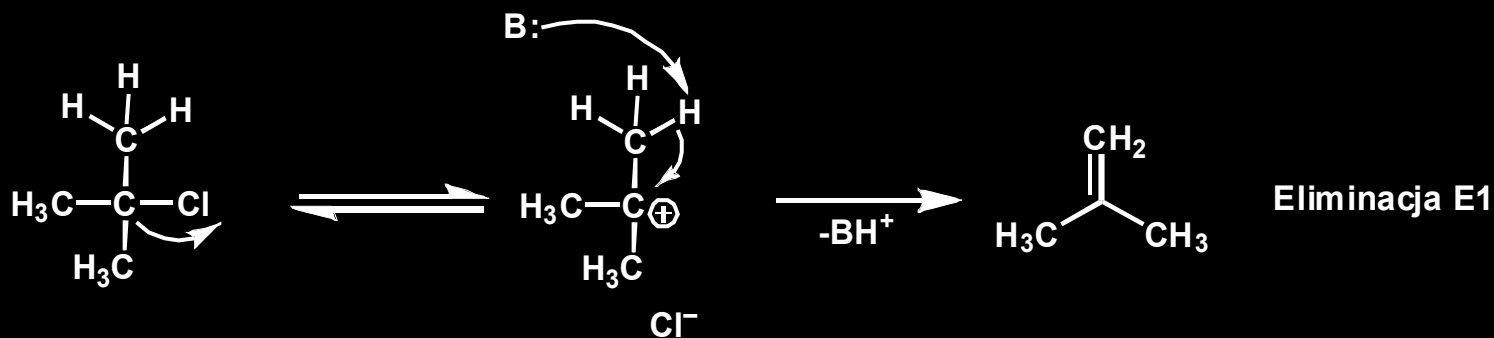
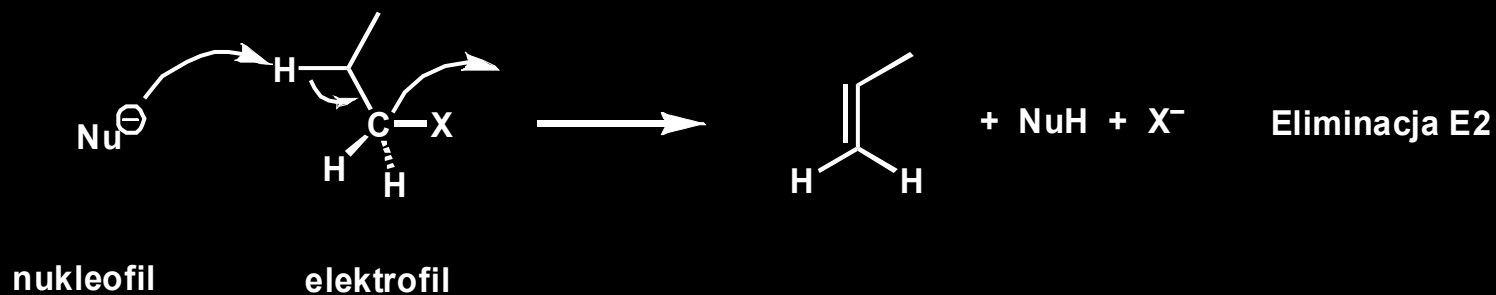
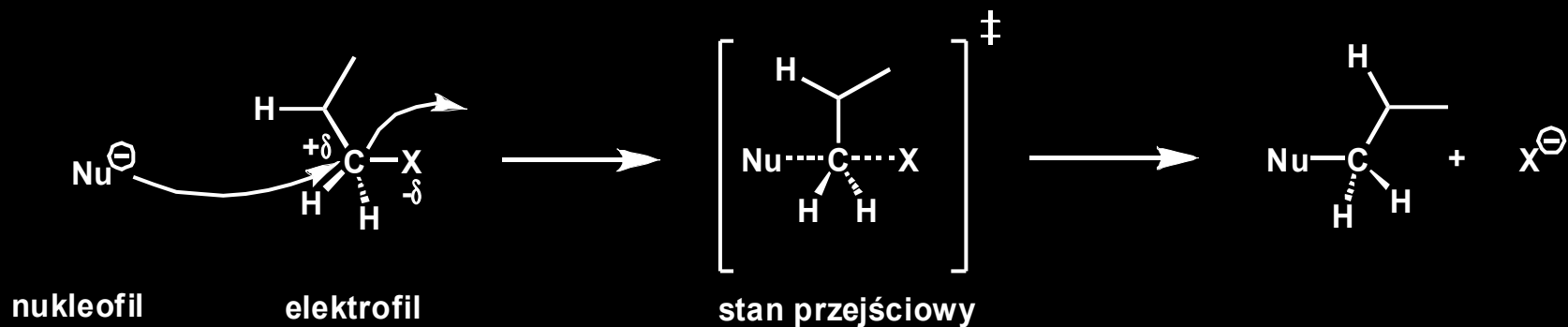


Example 2¹⁴

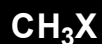


Substytucja vs eliminacja

Reakcje eliminacji często towarzyszą reakcjom substytucji.



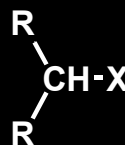
Substytucja vs eliminacja



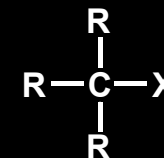
Metylowy



1°



2°



3°

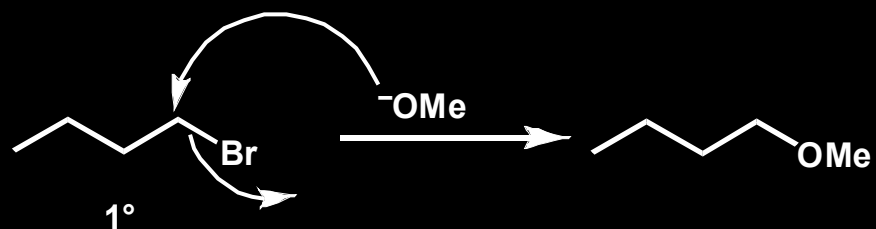
Reakcja Sn2

Głównie reakcja Sn2,
chyba, że stosuje się silne
i stłoczone sterycznie zasady
(tBuOK) - wtedy E2

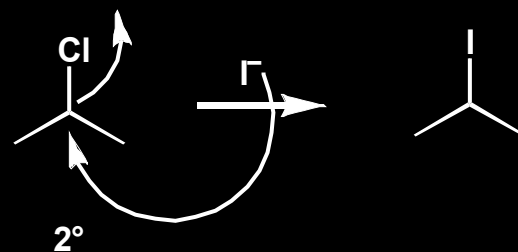
Głównie reakcja Sn2
jeśli stosuje się słabe zasady
(np. I-)
Głównie reakcja E2
jeśli stosuje się mocne zasady
(np. alkoholany)

Reakcja Sn2 wykluczona
Solwoliza - reakcje Sn1/E1
(niskie temperatury - Sn1)
Silne zasady (np. alkoholany) - E2

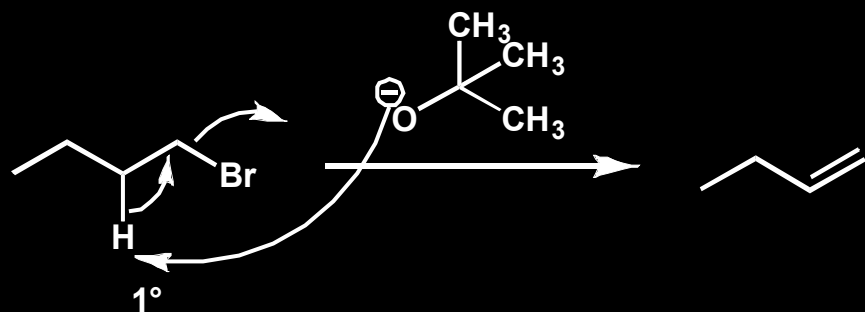
Substytucja vs eliminacja



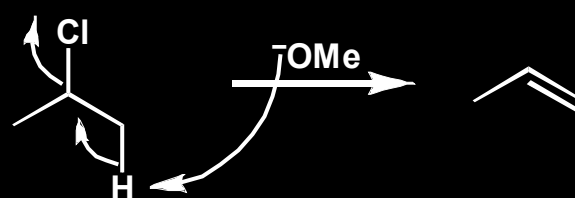
Sn2



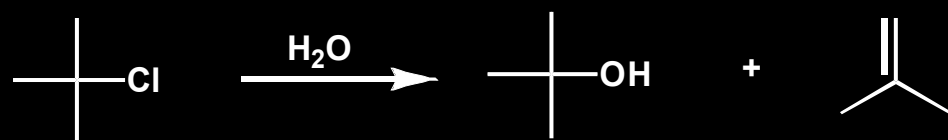
Sn2



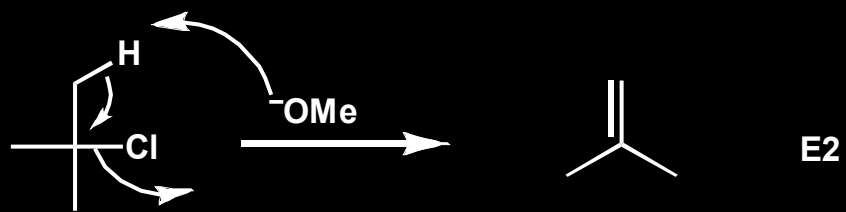
E2



E2

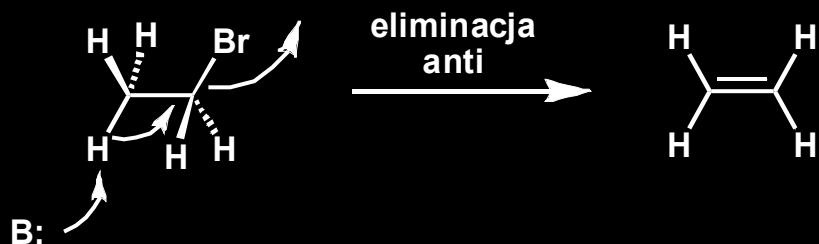


Sn1/E1



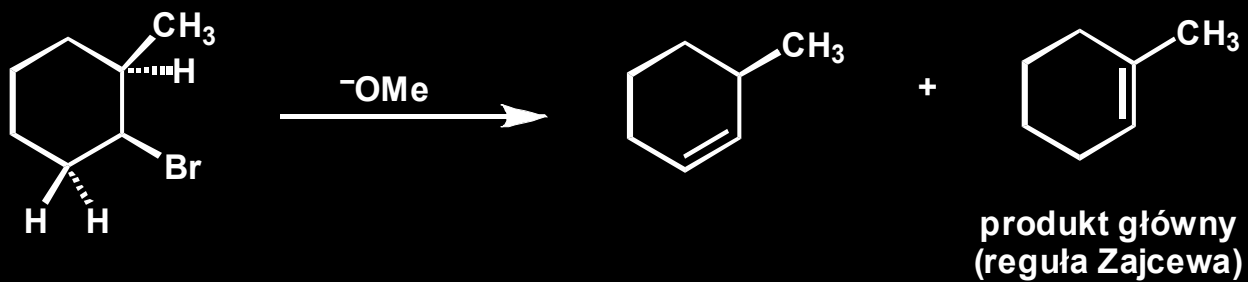
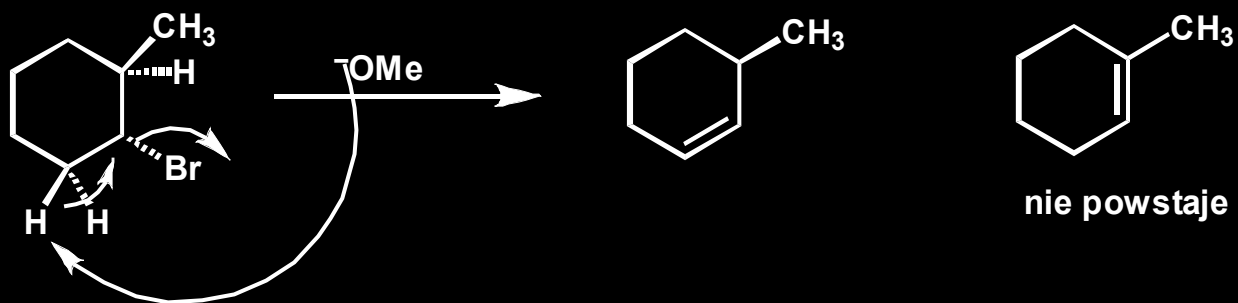
E2

Eliminacja E2 - stereochemia

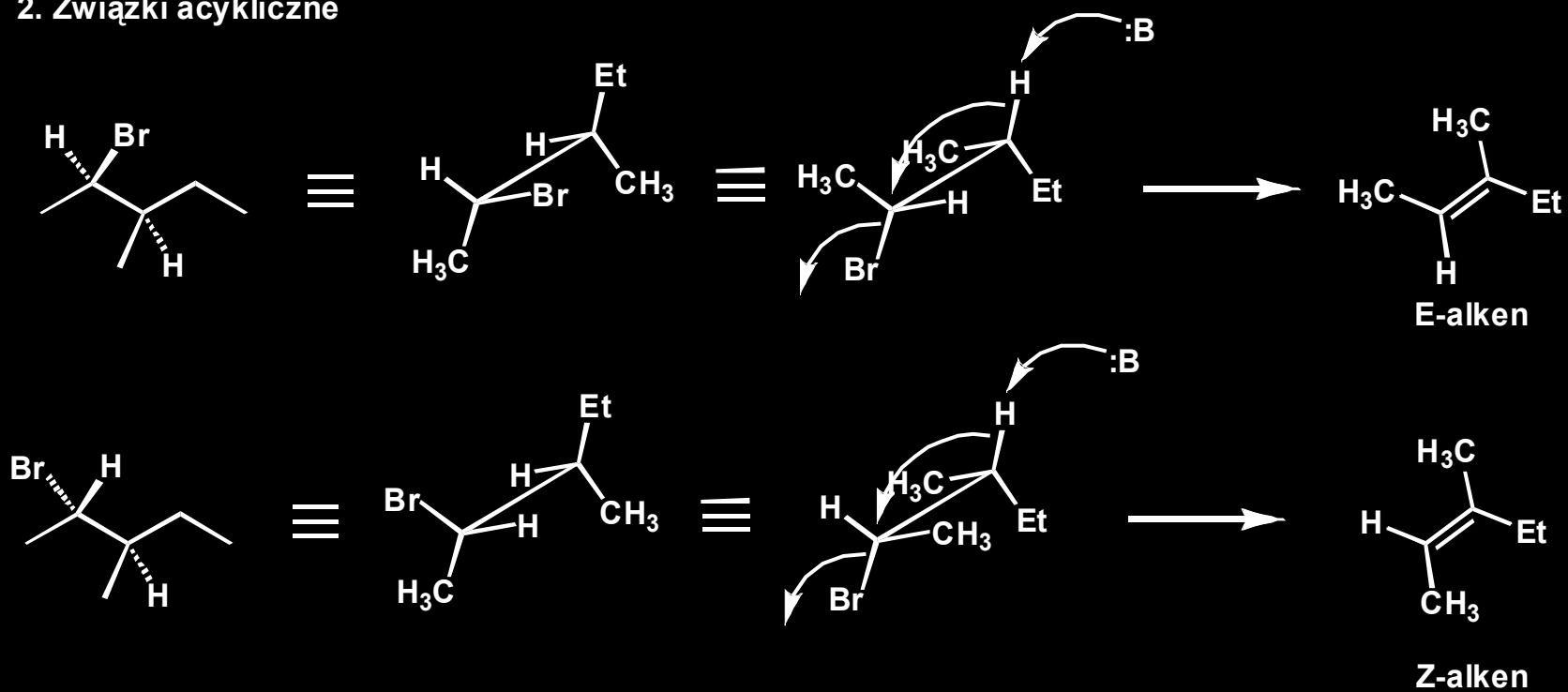


Konsekwencje:

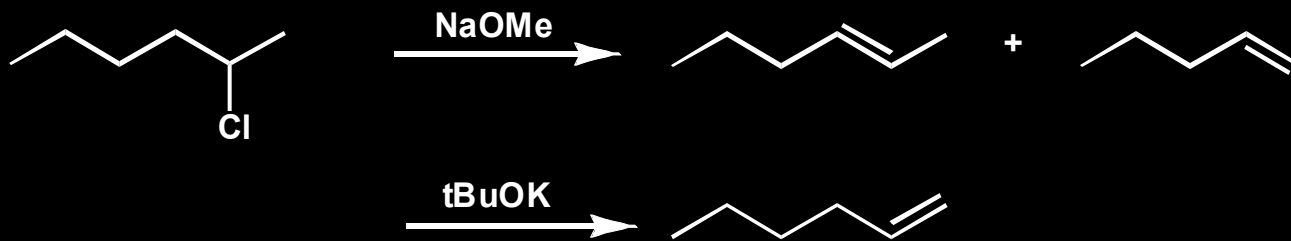
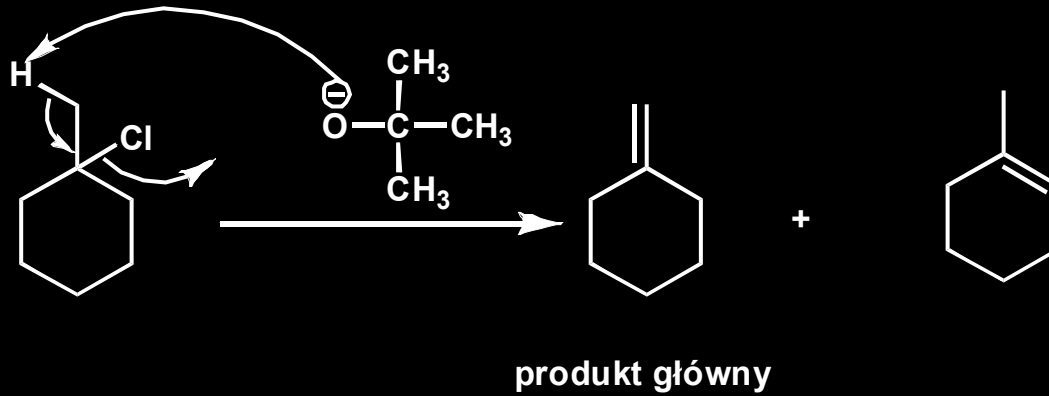
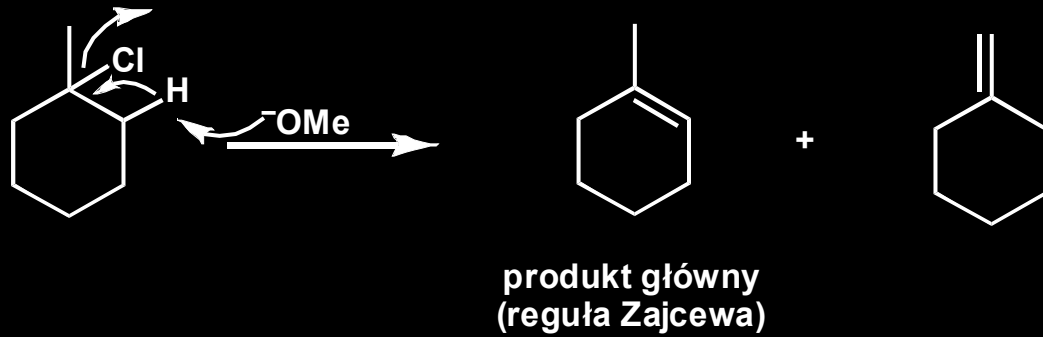
1. Związki cykliczne



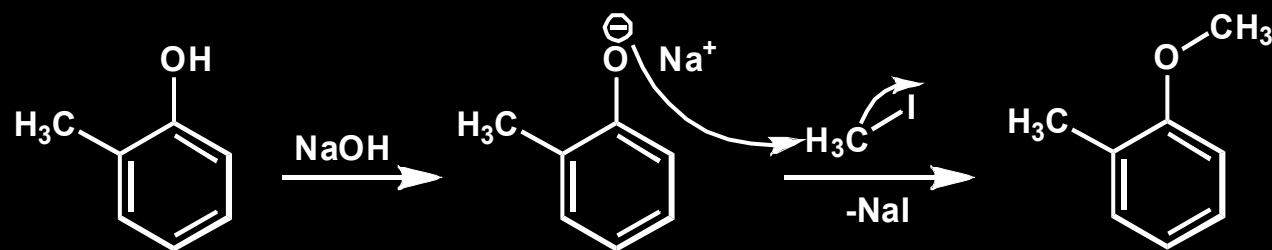
2. Związki acykliczne



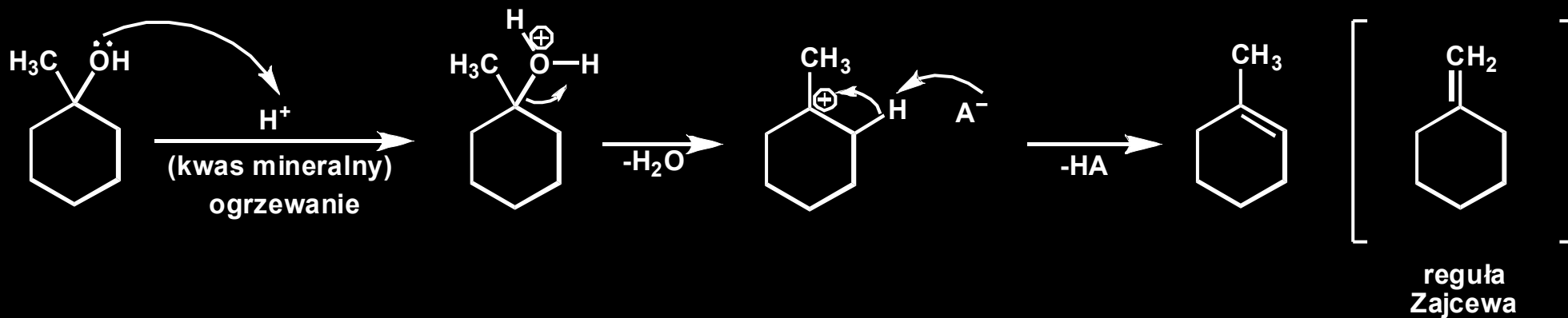
Wpływ zasady



Przykład 1 (Zadanie 5, I etap)

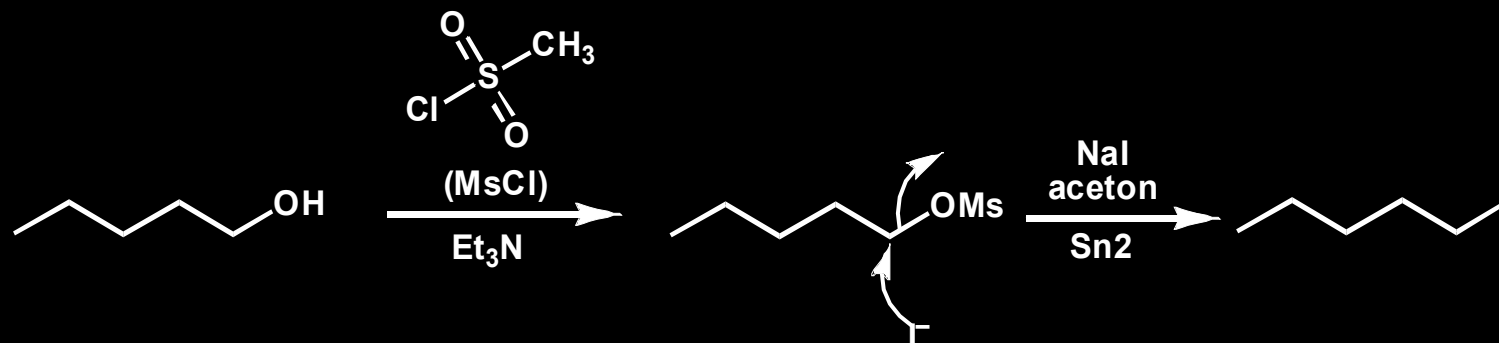
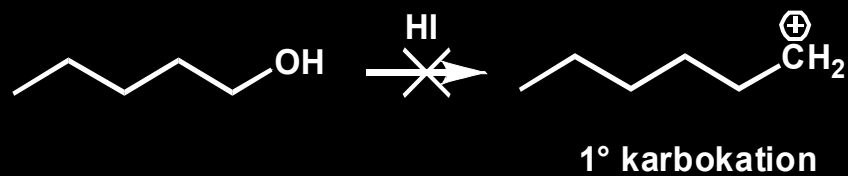


Sn2
Reakcja Williamsona

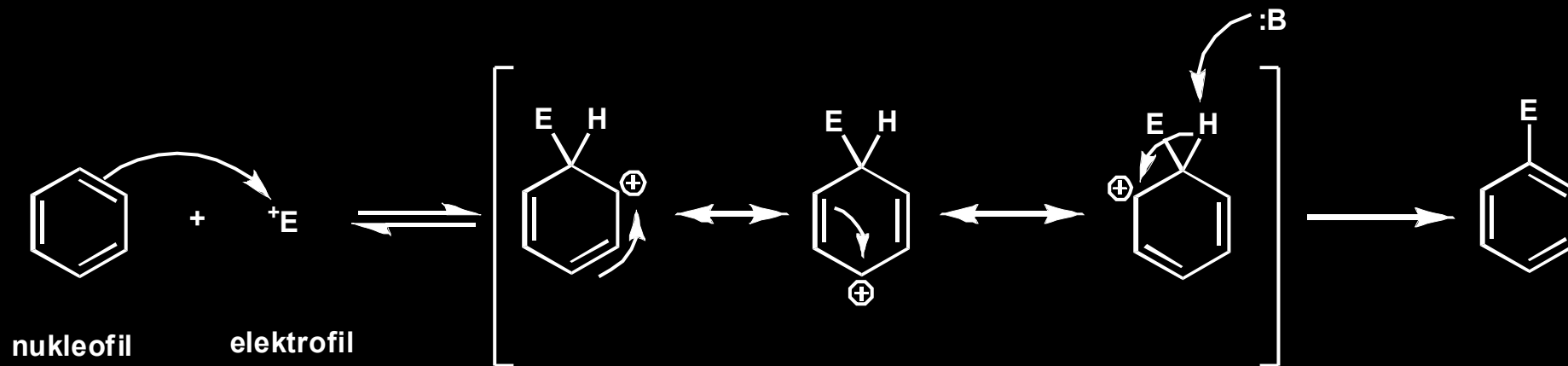


Przykład 2

Jak zrealizować poniższe przejście?



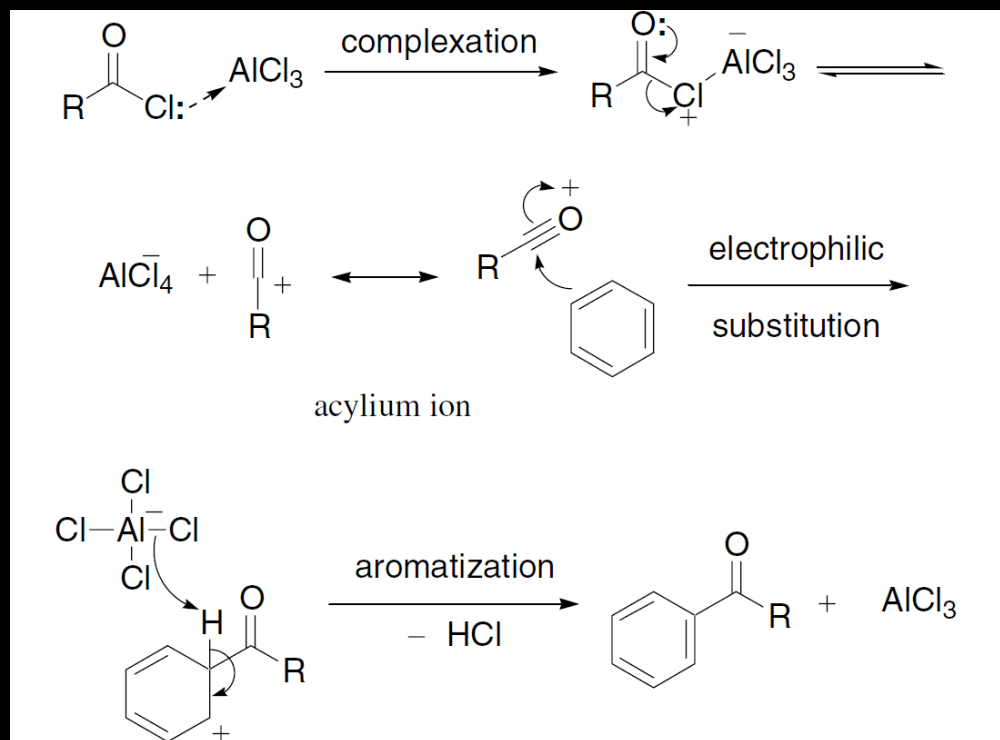
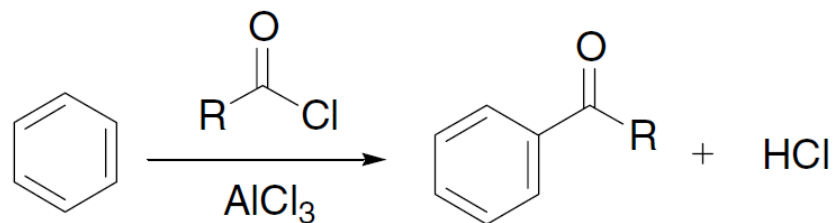
Substytucja elektrofilowa w pierścieniu aromatycznym



Friedel–Crafts reaction

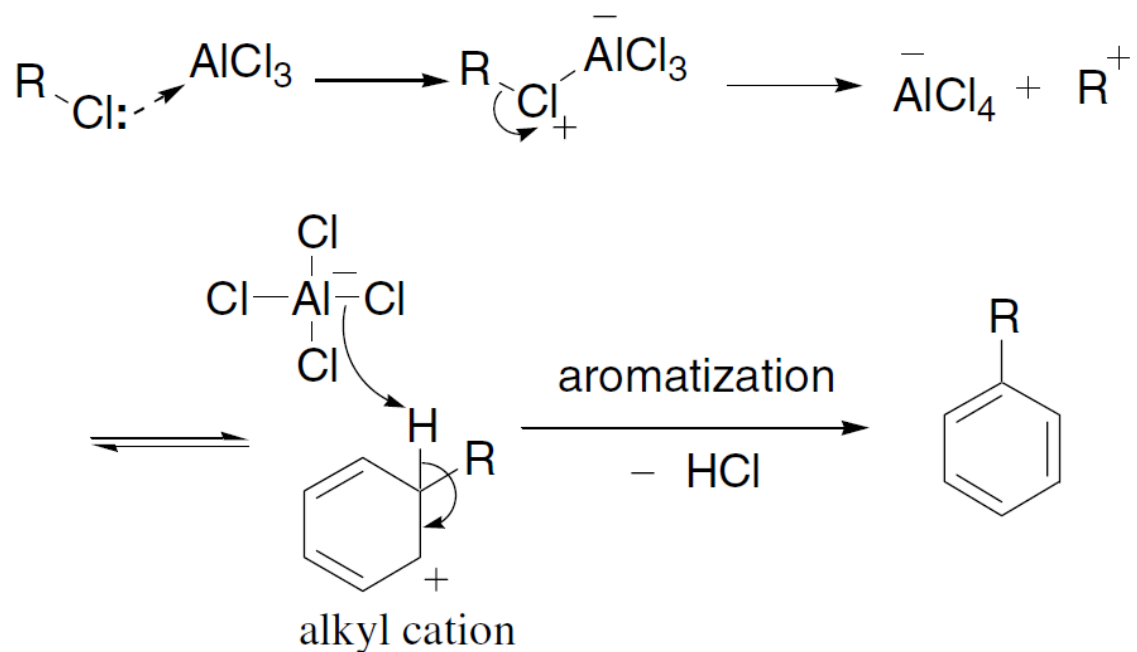
Friedel–Crafts *acylation* reaction:

Introduction of an acyl group onto an aromatic substrate by treating the substrate with an acyl halide or anhydride in the presence of a Lewis acid.



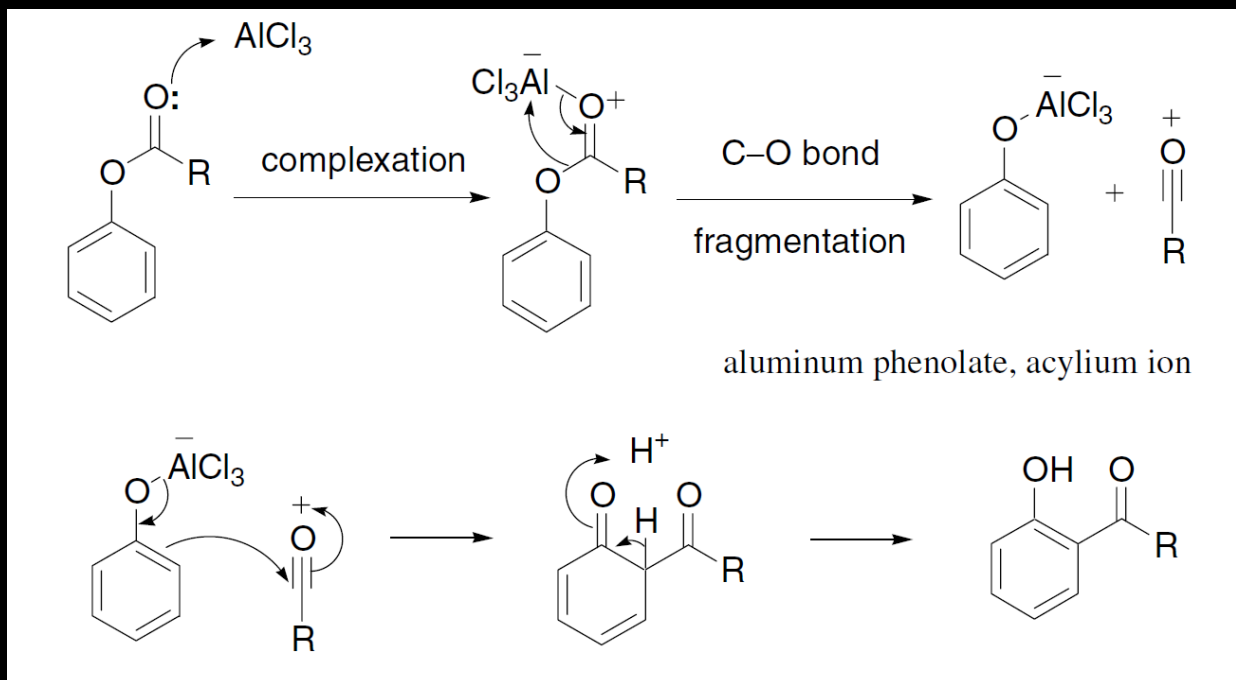
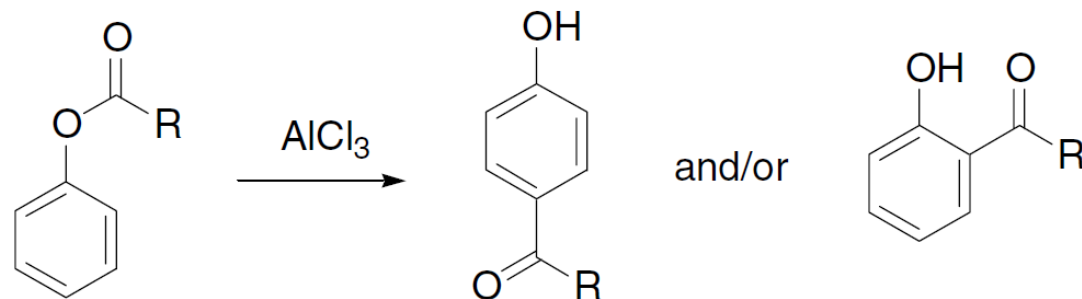
Friedel–Crafts *alkylation* reaction:

Introduction of an alkyl group onto an aromatic substrate by treating the substrate with an alkylating agent such as alkyl halide, alkene, alkyne and alcohol in the presence of a Lewis acid.



Fries rearrangement

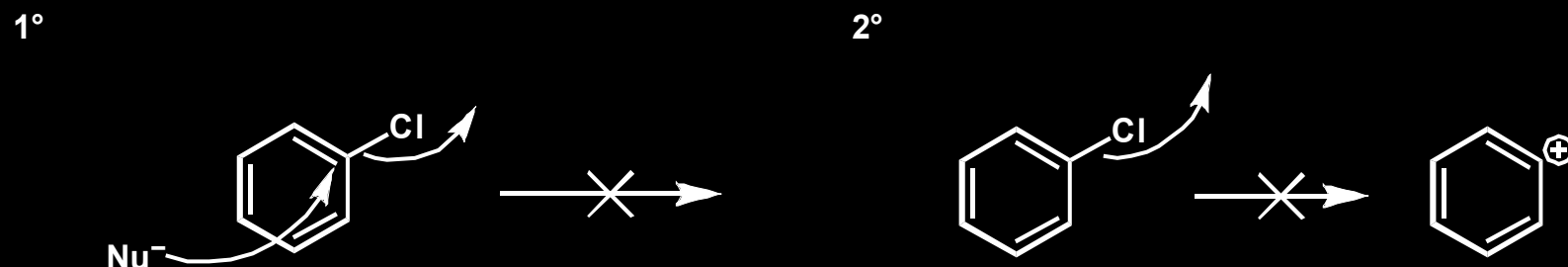
Lewis acid-catalyzed rearrangement of phenol esters and lactams to 2- or 4-ketophenols. Also known as the Fries–Finck rearrangement.



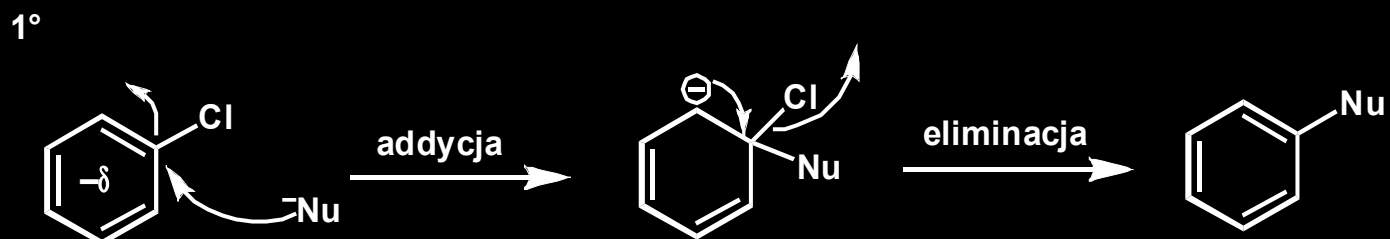
Wysokie temperatury: orto; niskie temperatury, PhNO_2 jako rozpuszczalnik: para.

Substytucja nukleofilowa w pierścieniu aromatycznym

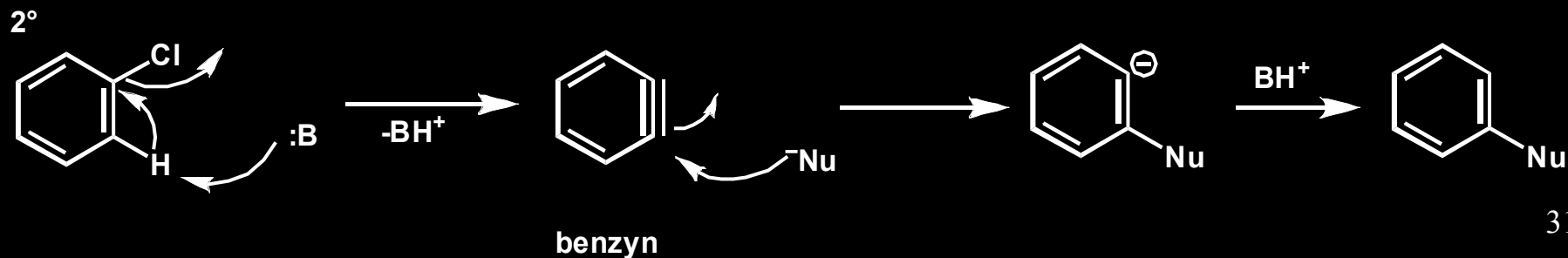
Substytucja nukleofilowa w pierścieniu aromatycznym jest trudna, bo

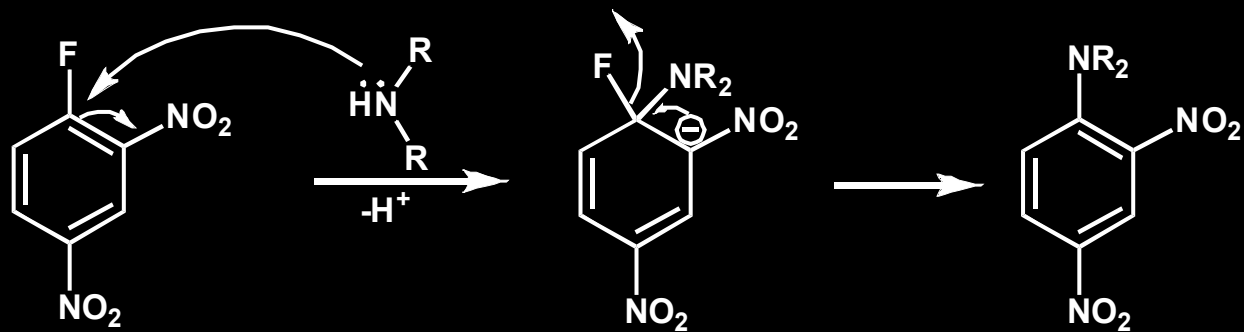


Rozwiązanie:



tylko dla układów ubogich w elektrony (podstawniki elektronoakceptorowe)



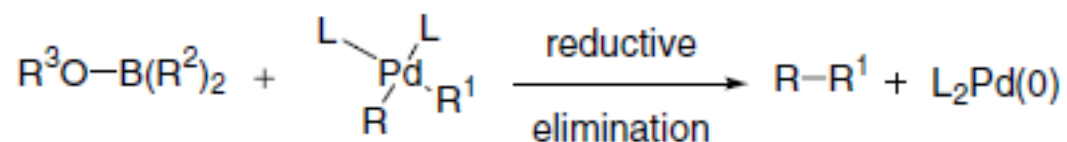
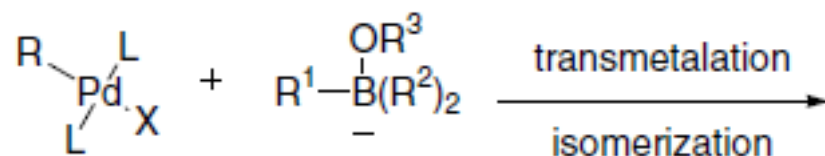
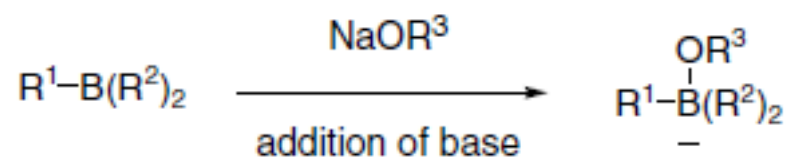
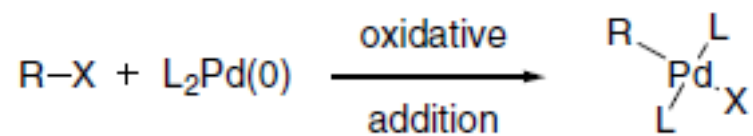
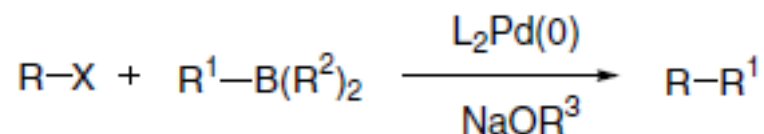


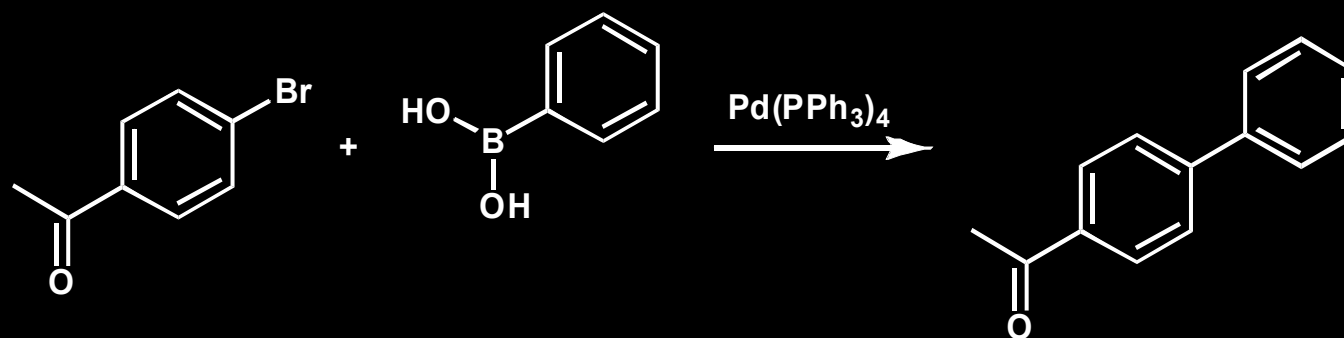
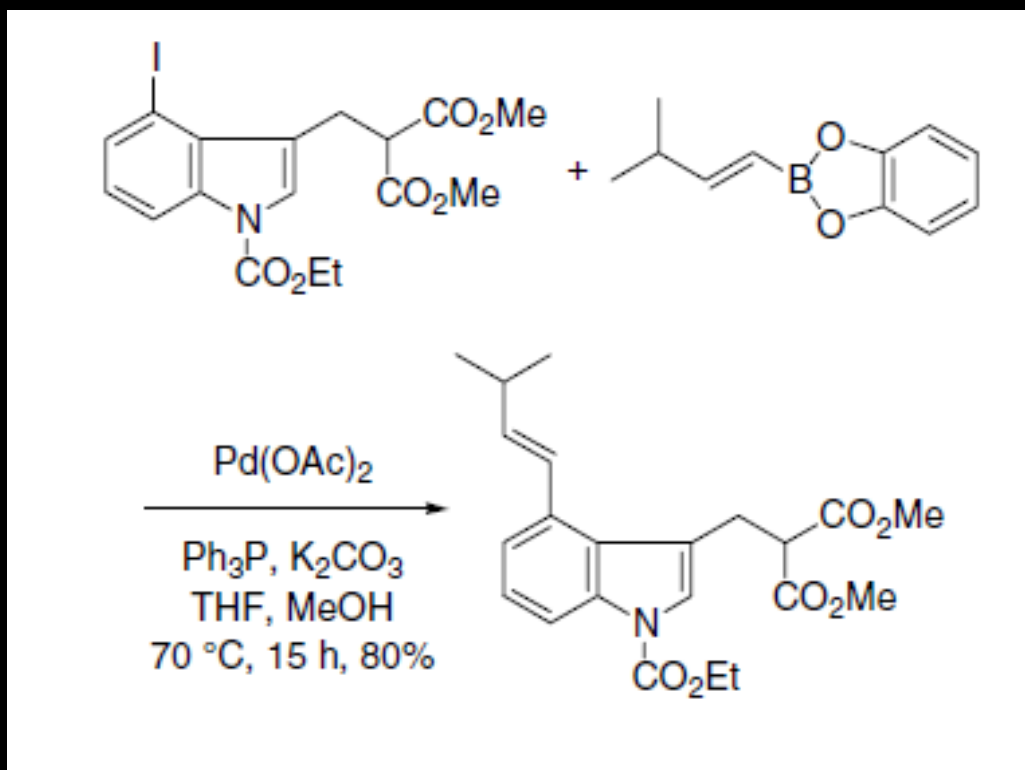
Sekwencjonowanie peptydów metodą Sangera

Sprzężenia

Suzuki coupling

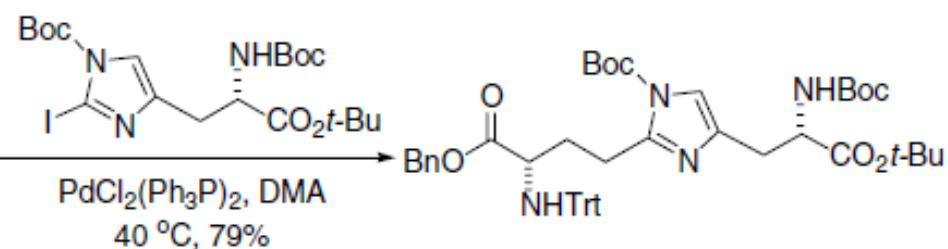
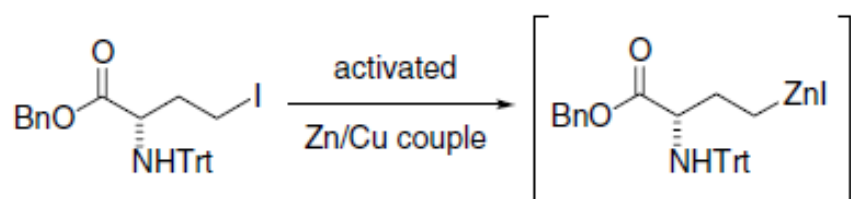
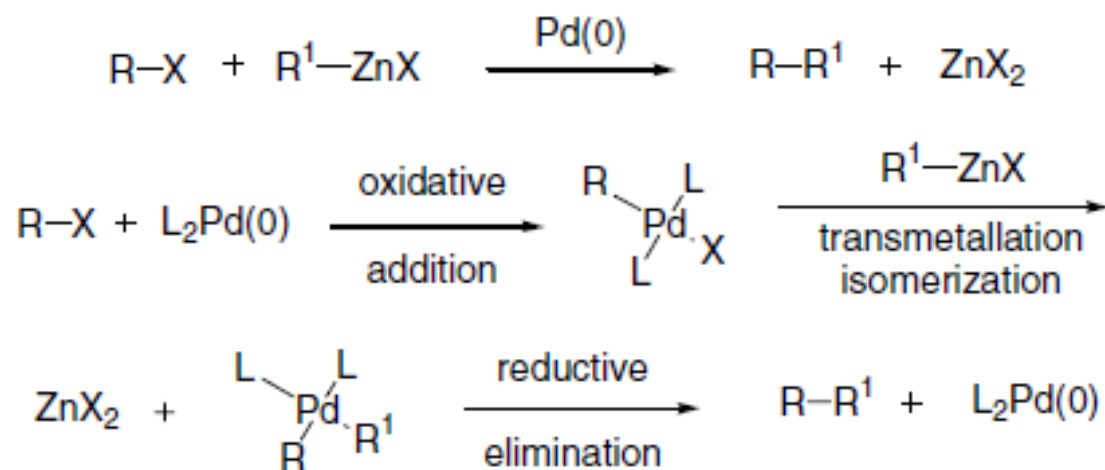
Palladium-catalyzed cross-coupling reaction of organoboranes with organic halides, triflates, *etc.* in the presence of a base (transmetalation is reluctant to occur without the activating effect of a base). For the catalytic cycle, see Kumada coupling on page 345.





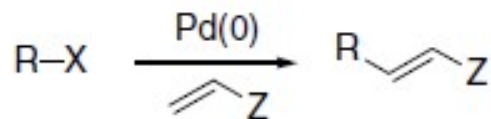
Negishi cross-coupling reaction

Palladium-catalyzed cross-coupling reaction of organozinc reagents with organic halides, triflates, *etc.* It is compatible with many functional groups including ketones, esters, amines, and nitriles. For the catalytic cycle, see the Kumada coupling on page 345.



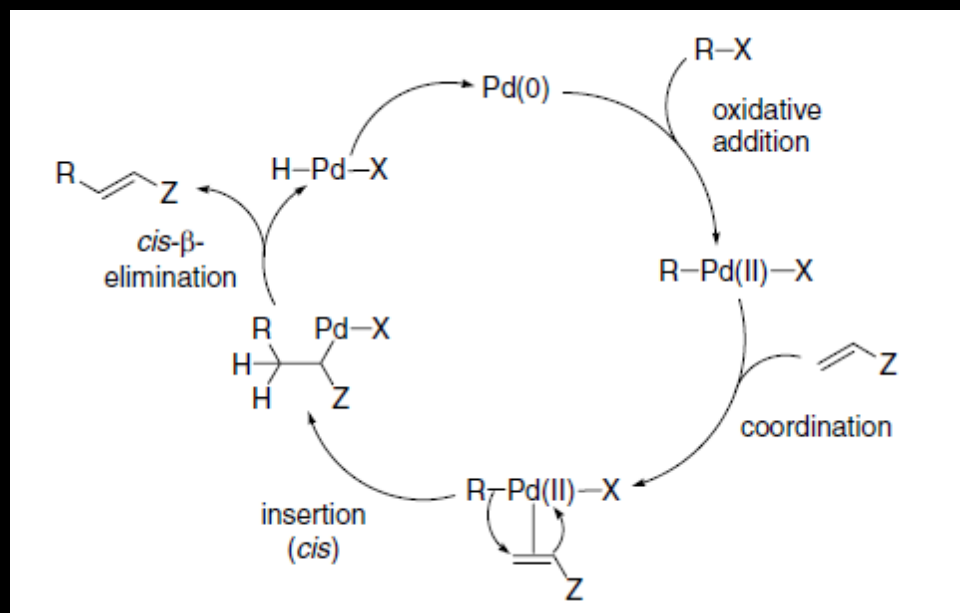
Heck reaction

Palladium-catalyzed coupling between organohalides or triflates with olefins.

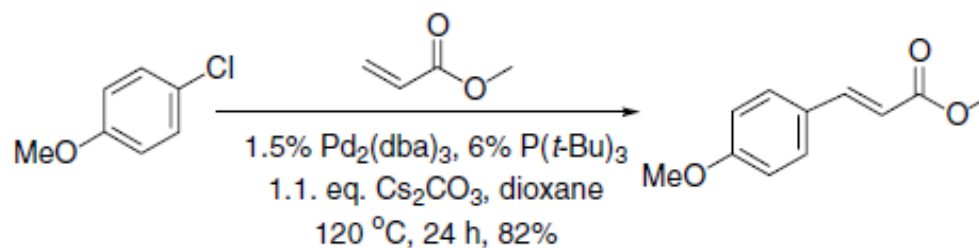


X = I, Br, OTf, Cl, *etc.*

Z = H, R, Ar, CN, CO₂R, OR, OAc, NHAc, *etc.*

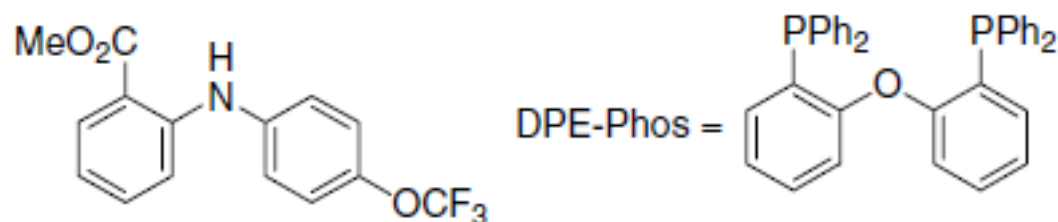
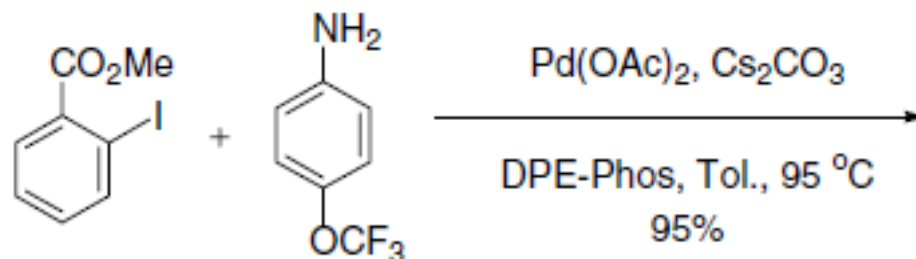
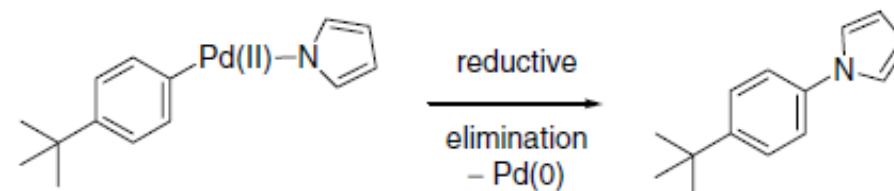
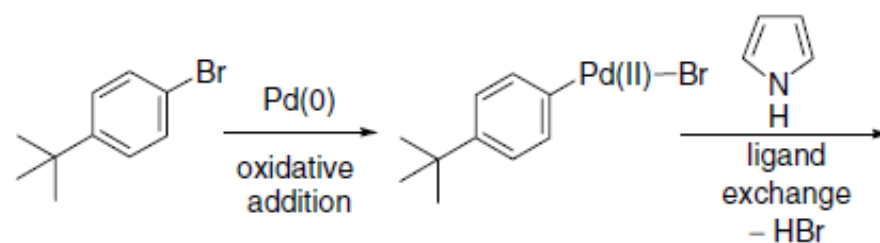
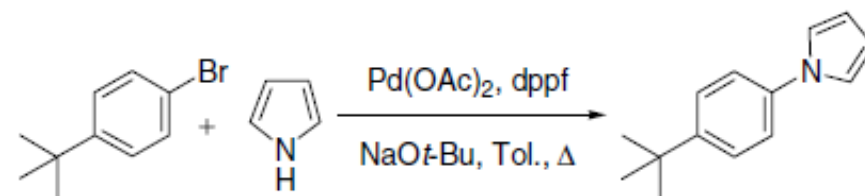


Example 1⁷



Buchwald-Hartwig C-N and C-O bond formation reactions

Direct Pd-catalyzed C-N and C-O bond formation from aryl halides and amines in the presence of stoichiometric amount of base.



Kilka przydatnych reakcji imiennych (name reactions)

<http://www.chemicalforum.eu/index.php?/topic/18111-name-reactions-lista/>
<http://www.organic-chemistry.org/namedreactions/>

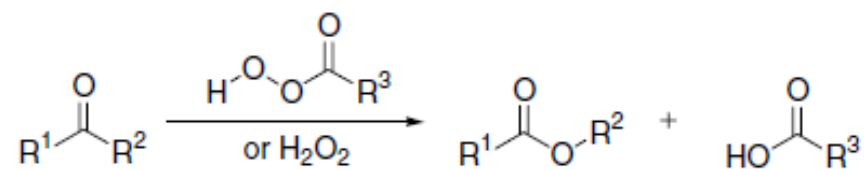
Zadanie B5

Nietypowe syntezy estrów i amidów

Estry i amidy najczęściej otrzymuje się w reakcji zaktywowanego kwasu karboksylowego odpowiednio z alkoholem lub aminą. Niekiedy jednak, związki te można otrzymać w bardziej nietypowy sposób, w wyniku różnego rodzaju przegrupowań. Jedną z takich "niekonwencjonalnych" metod syntezy estrów jest reakcja ketonów z nadkwasami, odkryta przez niemieckich chemików Baeyera i Villigera:

Baeyer-Villiger oxidation

General scheme:



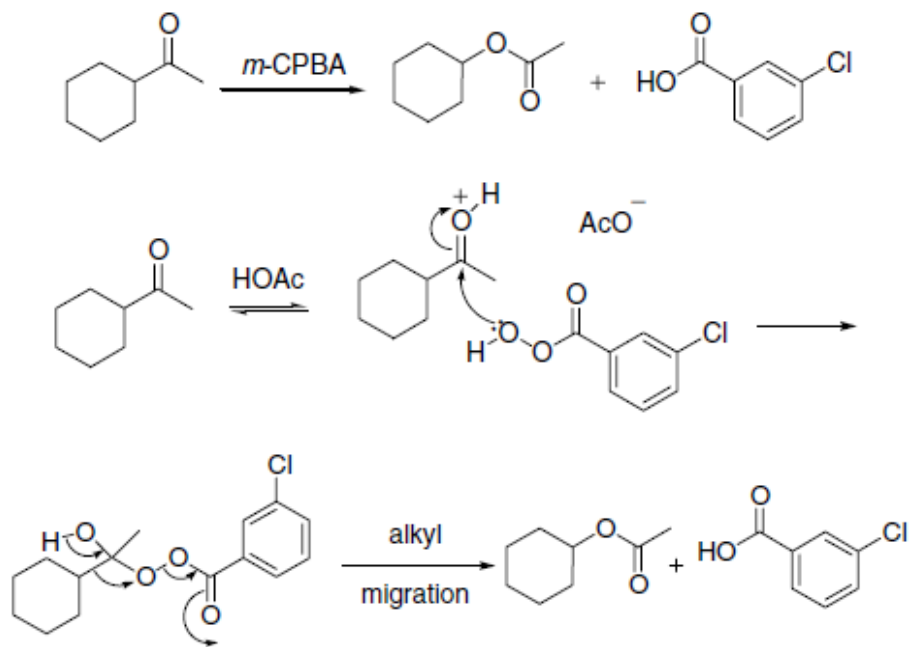
The most electron-rich alkyl group (more substituted carbon) migrates first. The general migration order:

tertiary alkyl > cyclohexyl > secondary alkyl > benzyl > phenyl > primary alkyl > methyl >> H.

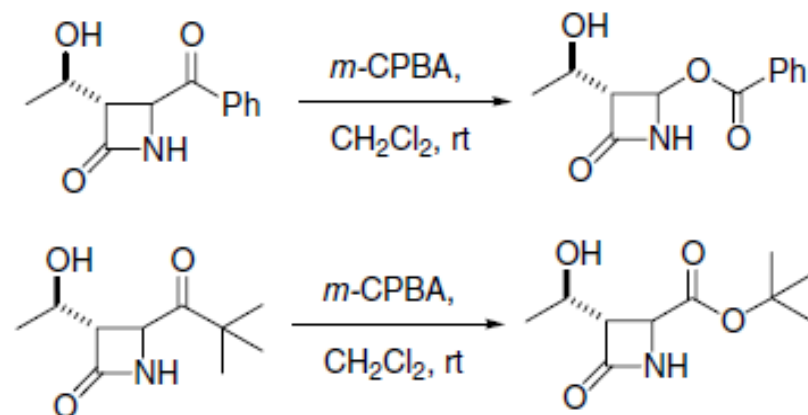
For substituted aryls:

p-MeO-Ar > *p*-Me-Ar > *p*-Cl-Ar > *p*-Br-Ar > *p*-MeOAr > *p*-O₂N-Ar

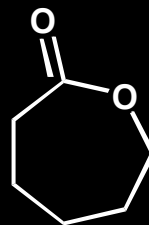
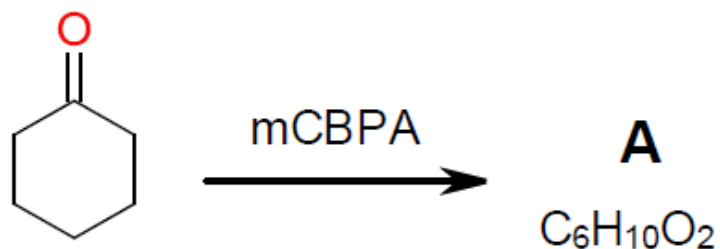
Example 1:



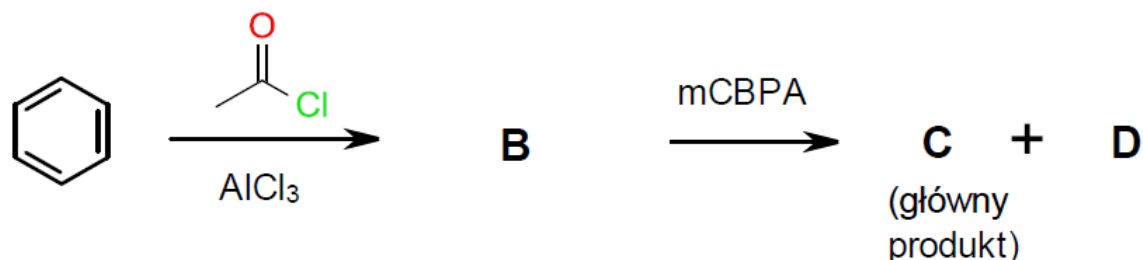
Example 2¹⁰



a. podaj strukturę związku A

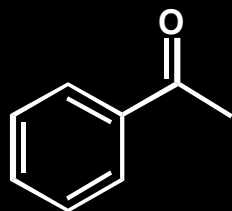


b. podaj struktury związków B, C i D

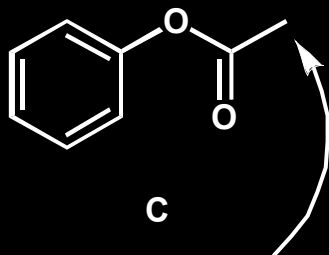


Związek C: ^1H NMR w CDCl_3 , δ ppm: 2,30 (3H, s), 7,05-7,40 (5H, m)

Związek D: ^1H NMR w CDCl_3 , δ ppm: 3,89 (3H, s), 7,35-8,0 (5H, m)

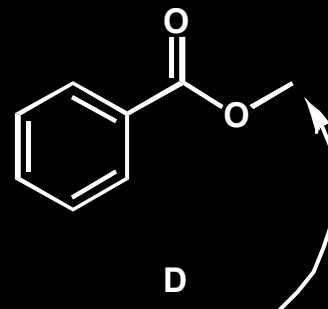


B



C

2.30 ppm

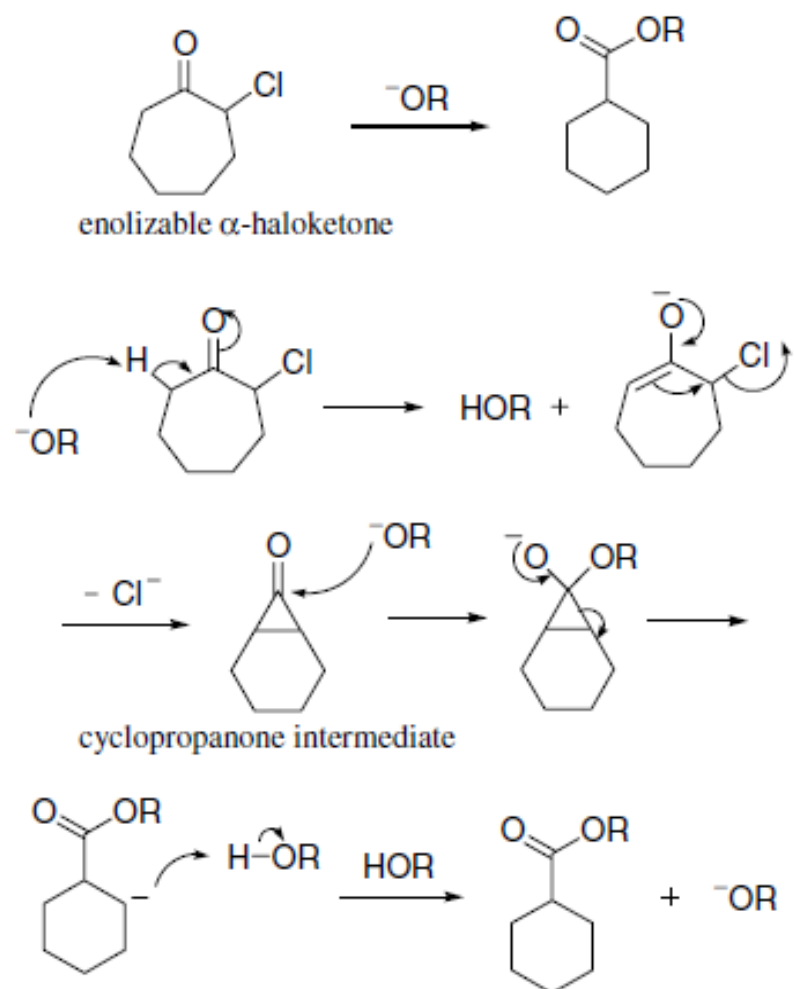


D

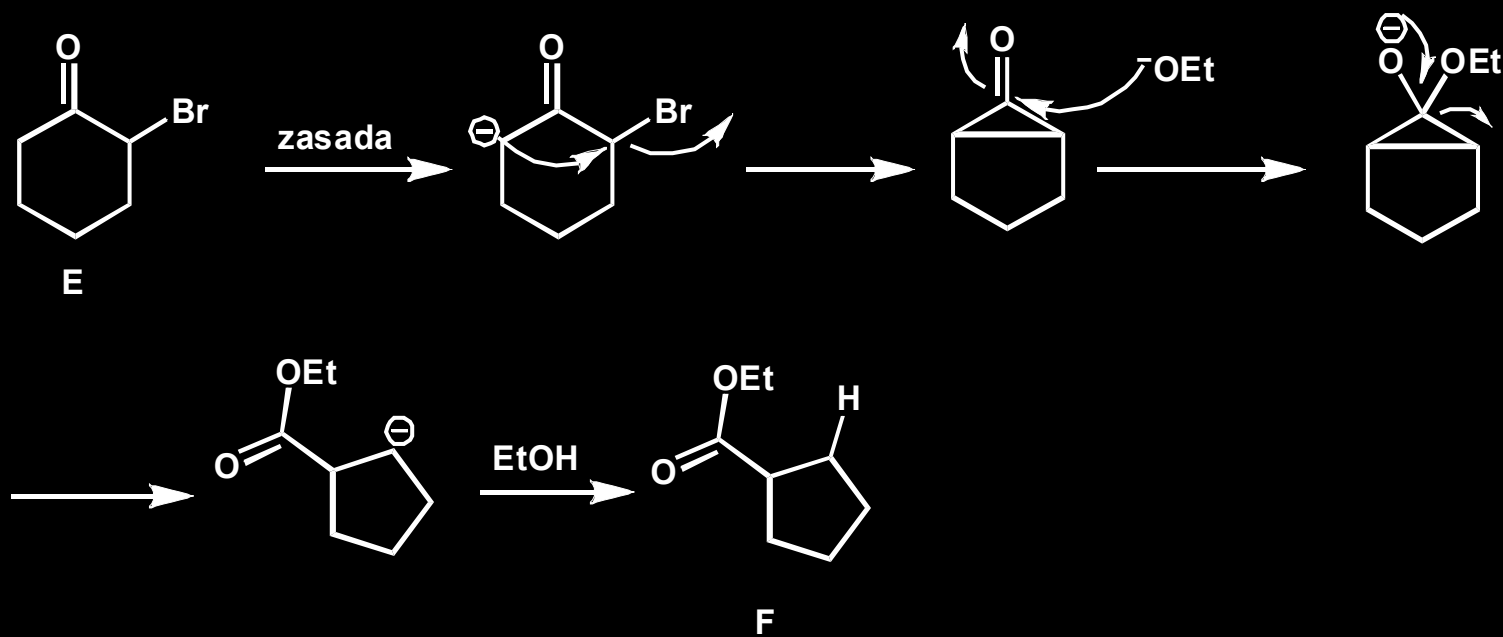
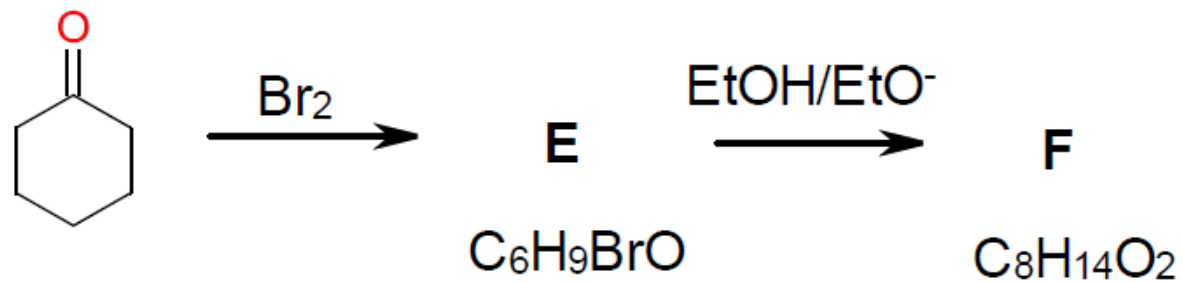
3.89 ppm

Favorskii rearrangement

Transformation of enolizable α -haloketones to esters, carboxylic acids, or amides via alkoxide-, hydroxide-, or amine-catalyzed rearrangements, respectively.



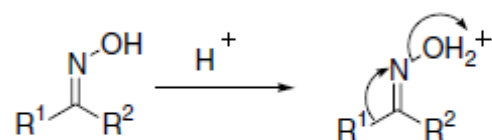
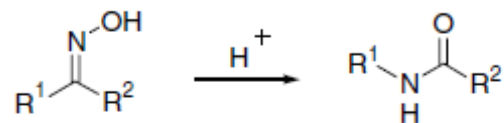
c. podaj struktury związków E i F



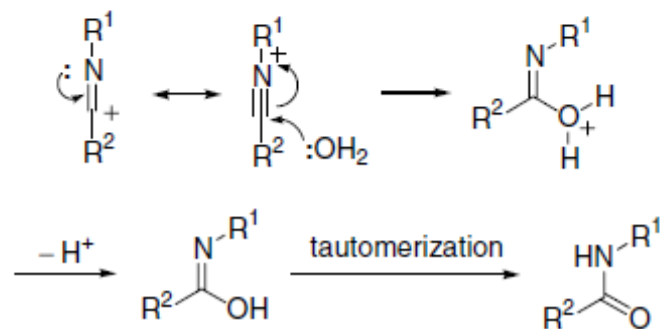
Beckmann rearrangement

Acid-mediated isomerization of oximes to amides.

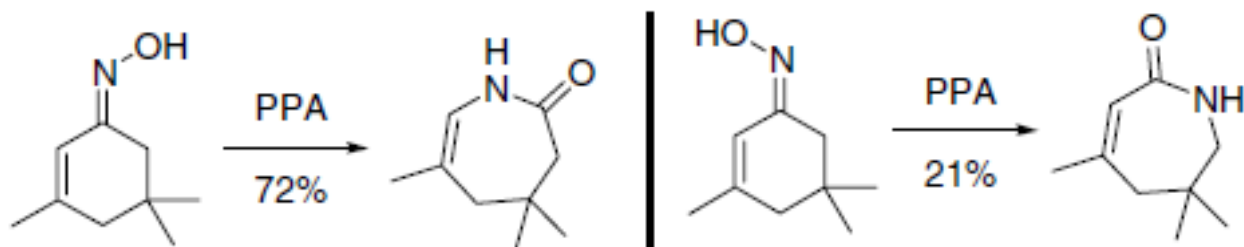
In protic acid:



the substituent *trans* to the leaving group migrates



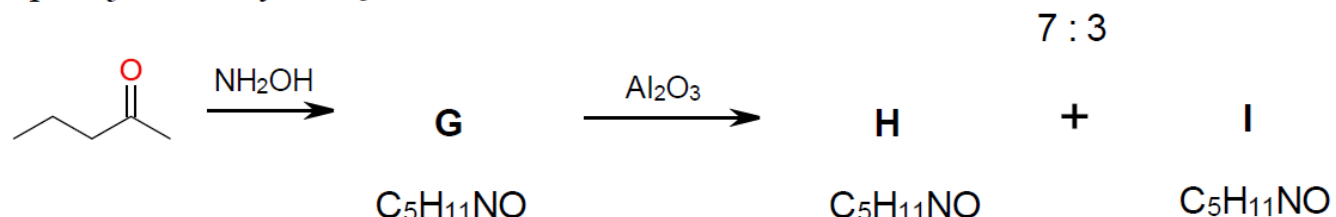
Example 1¹²



PPA = polyphosphoric acid

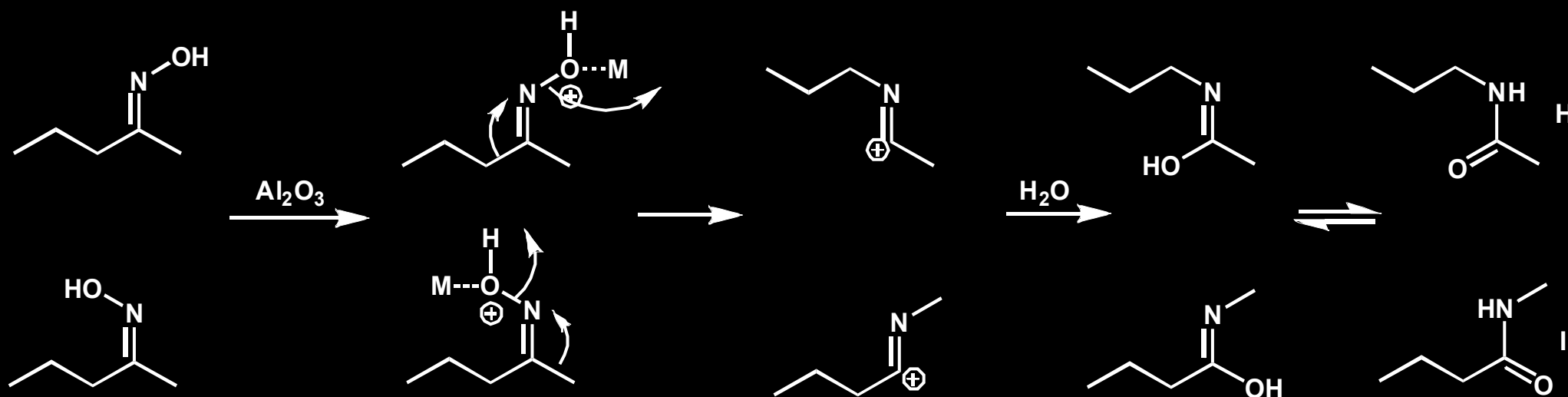
References

d. podaj struktury związków G, H oraz I

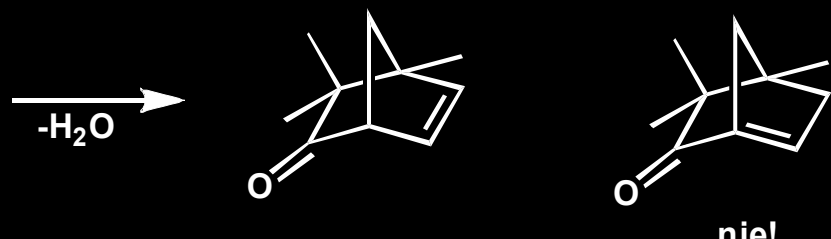
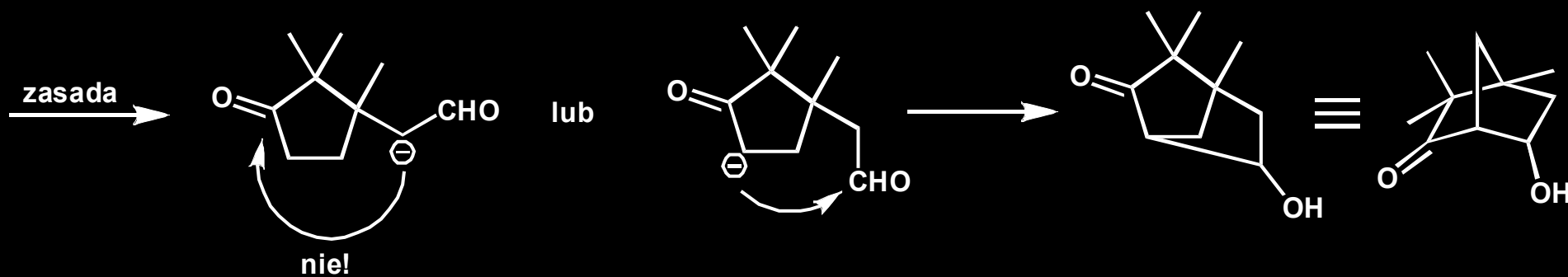
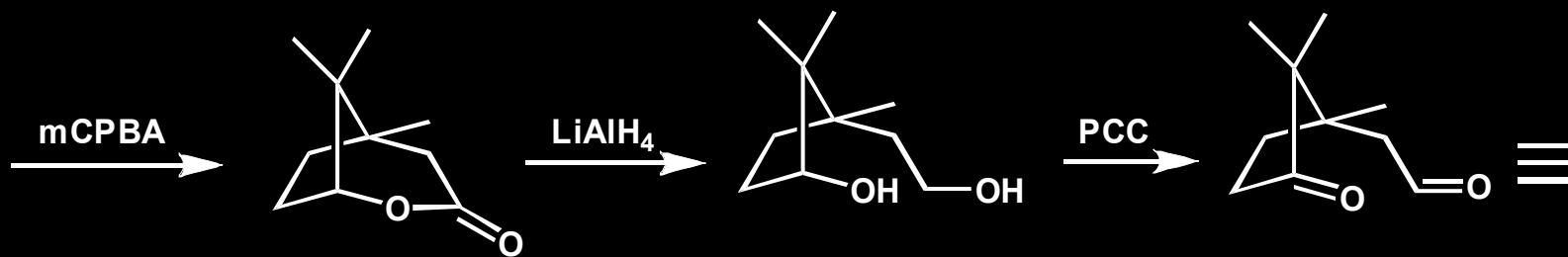
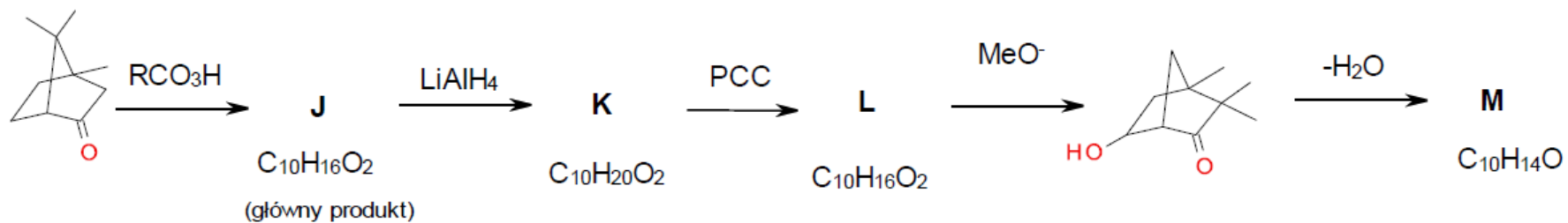


Związek H: ^1H NMR w CDCl_3 , δ ppm: 0,93 (3H, t); 1,53 (2H, m); 2,08 (3H, s); 3,20 (2H, m); 8,02 (1H, t)

Związek I: ^1H NMR w CDCl_3 , δ ppm: 0,92 (3H, t); 1,62 (2H, m); 2,23 (2H, t); 2,78 (3H, s); 5,53 (1H, q)

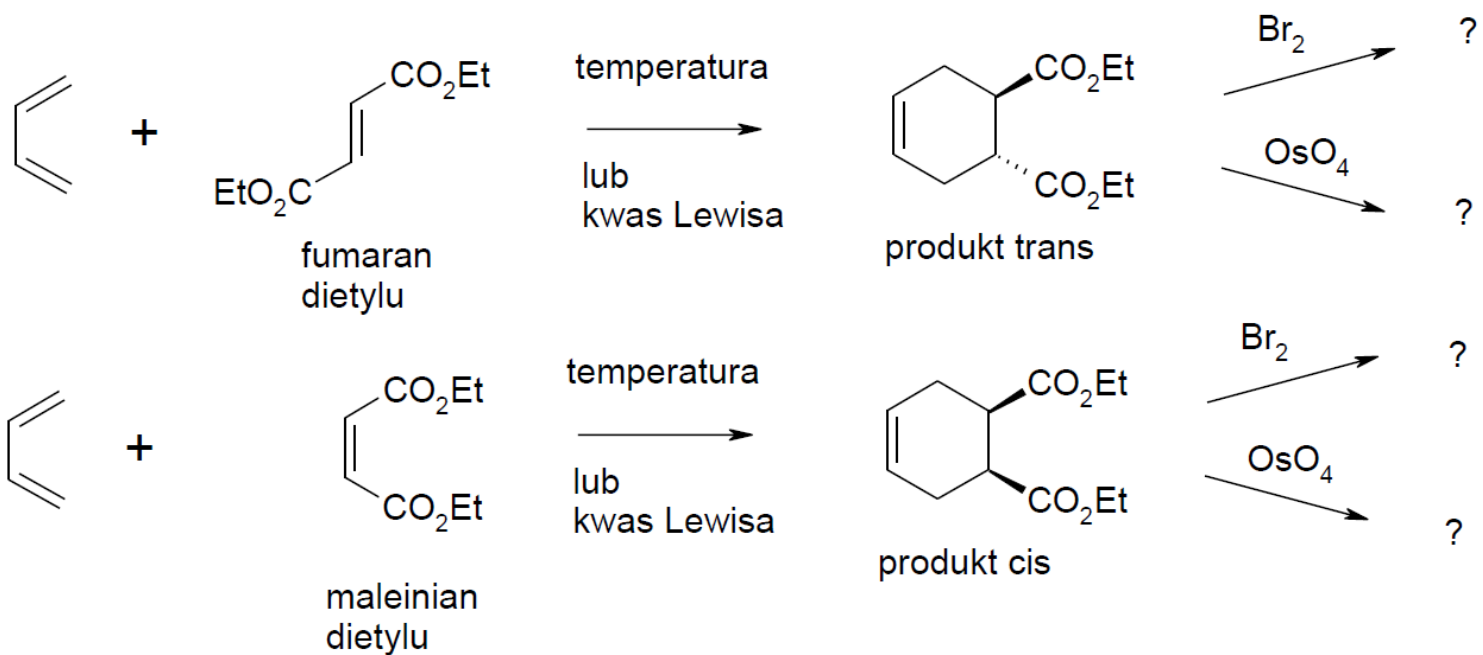


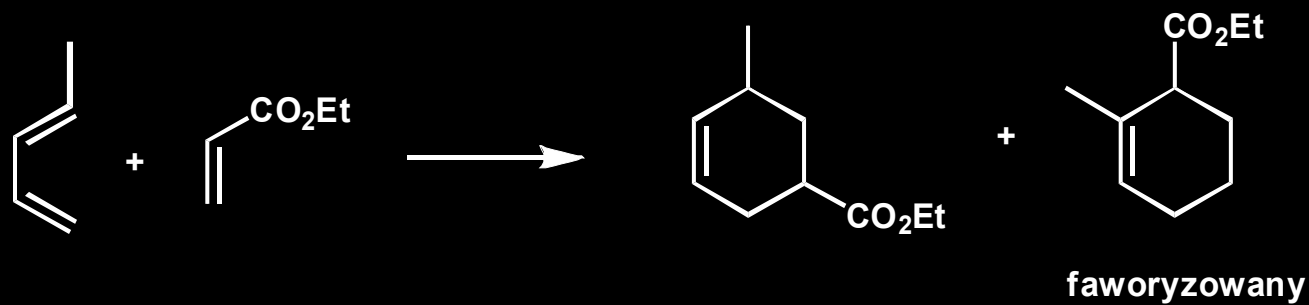
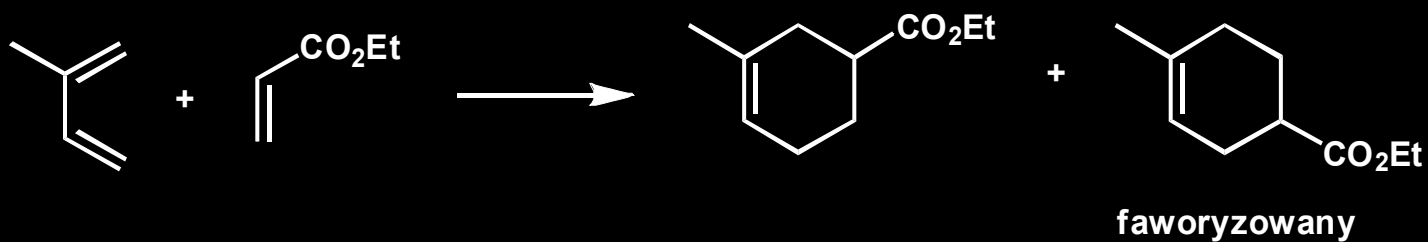
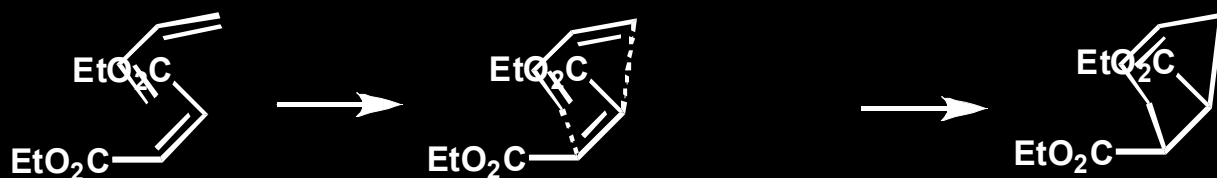
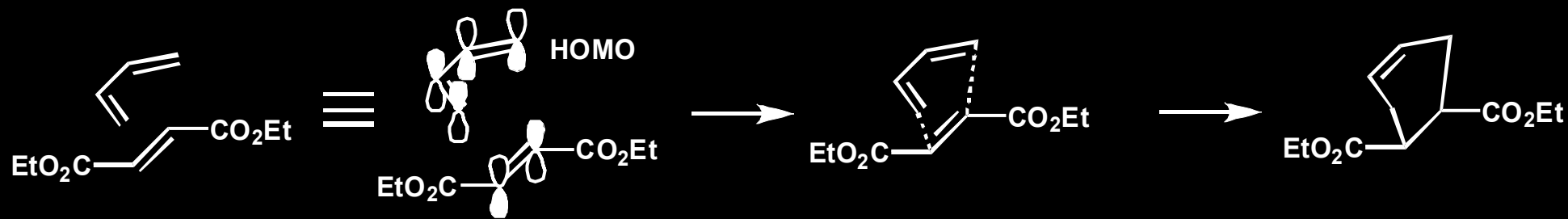
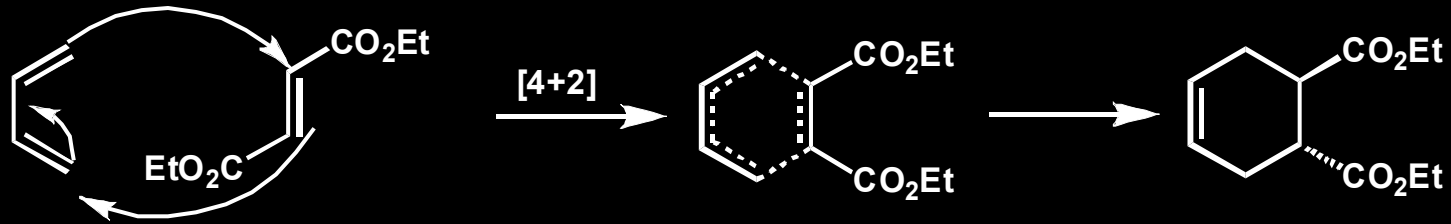
e. podaj struktury związków J, K, L, M

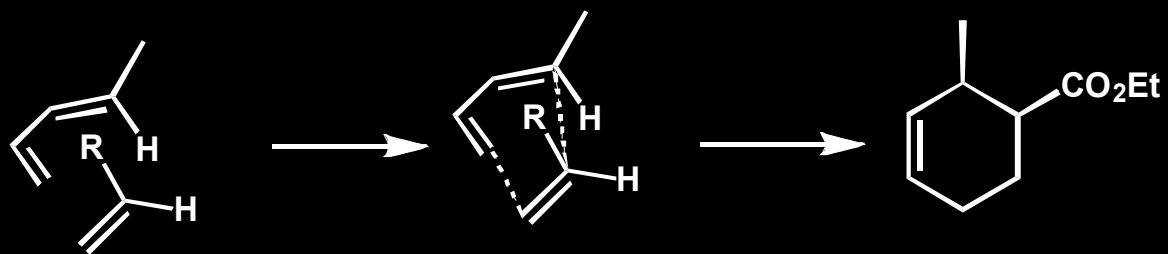
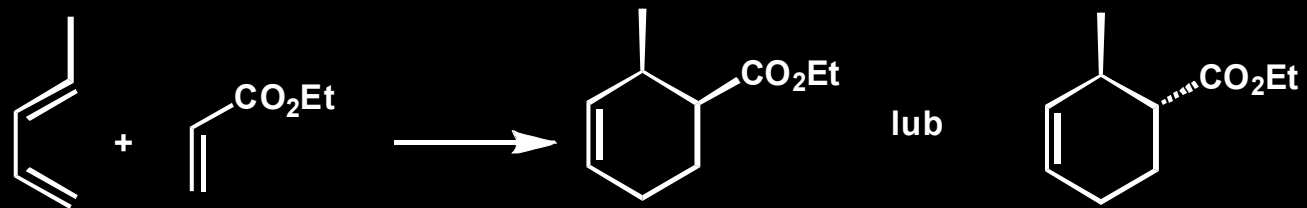


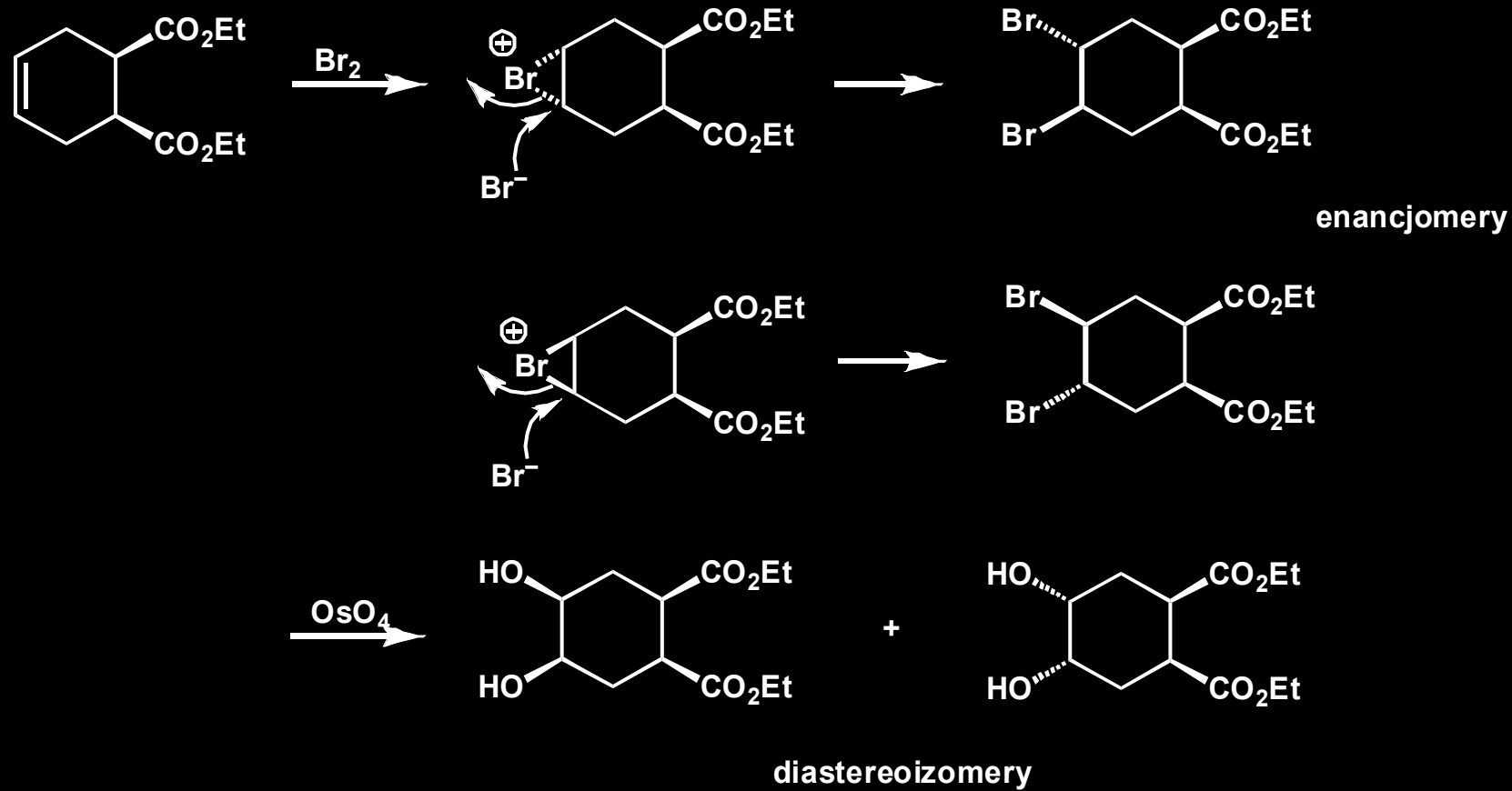
Zadanie B6

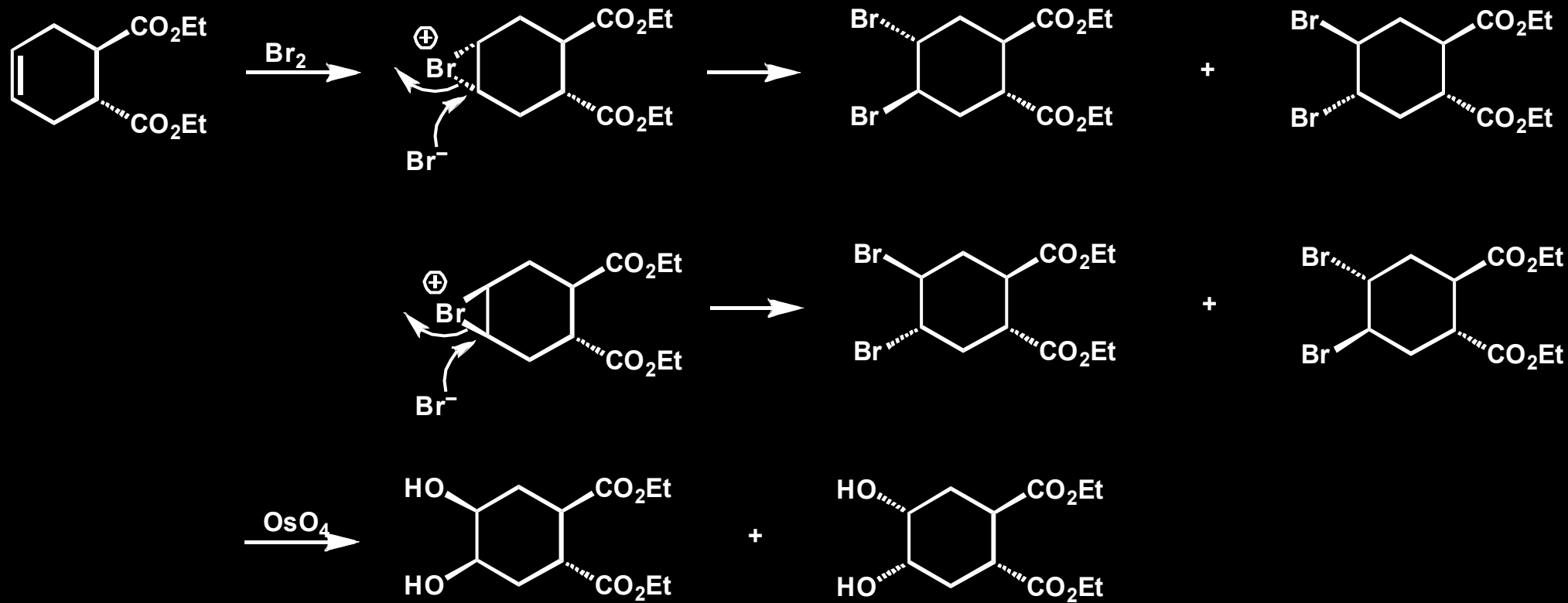
Synteza stereospecyficzna







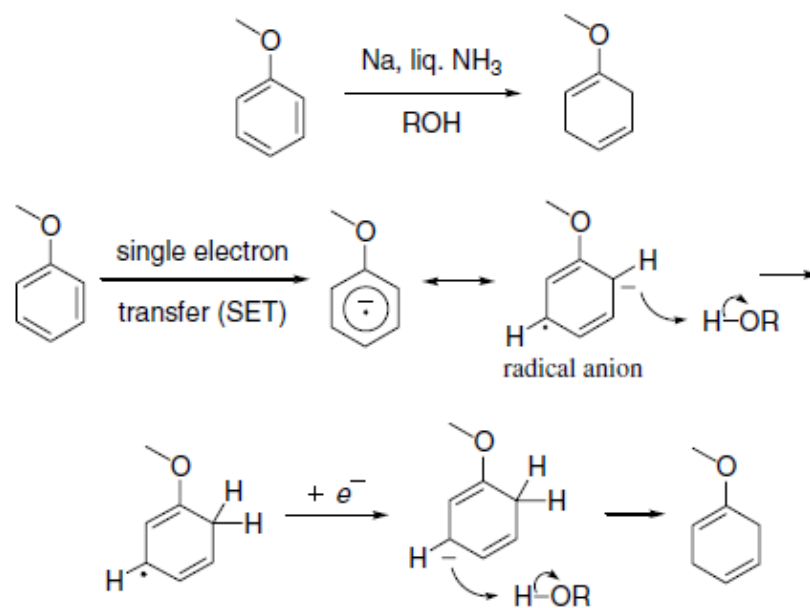




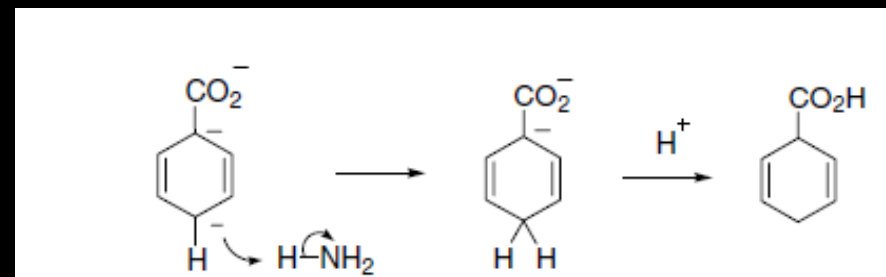
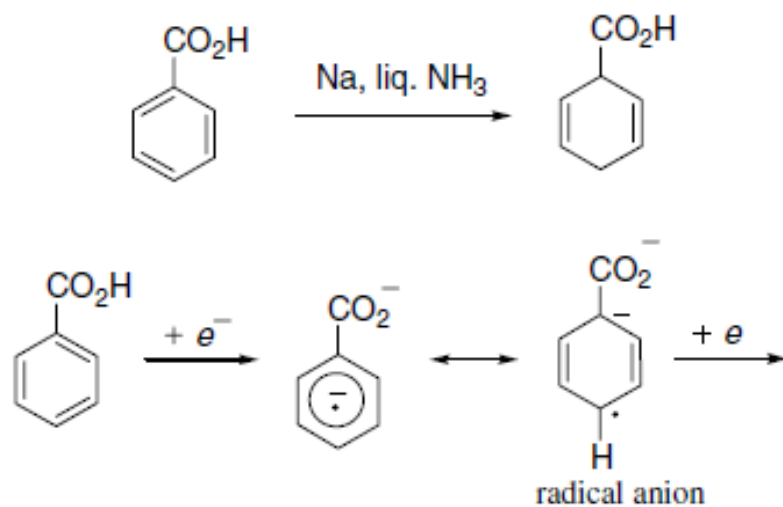
Birch reduction

The Birch reduction is the 1,4-reduction of aromatics to their corresponding cyclohexadienes by alkali metals (Li, K, Na) dissolved in liquid ammonia in the presence of an alcohol.

Benzene ring bearing an electron-donating substituent:

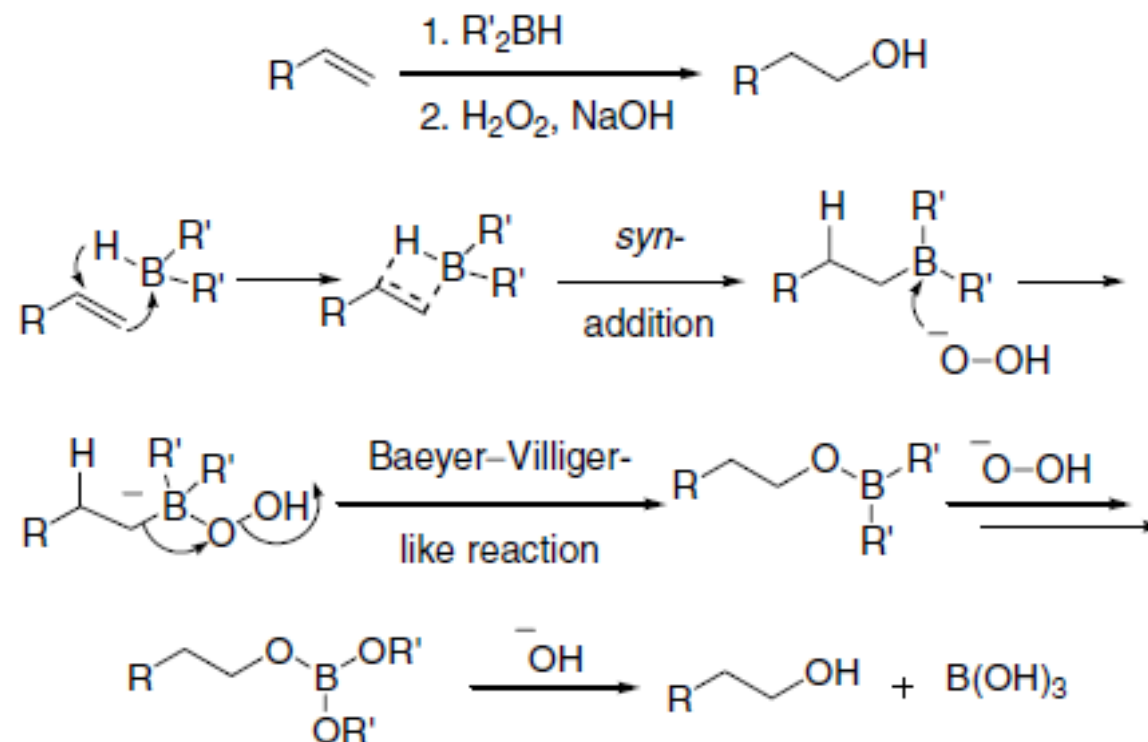


Benzene ring with an electron-withdrawing substituent:

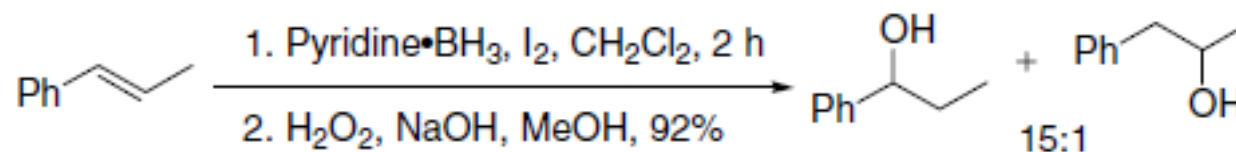


Brown hydroboration

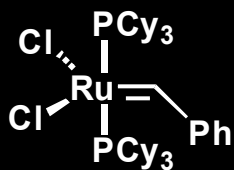
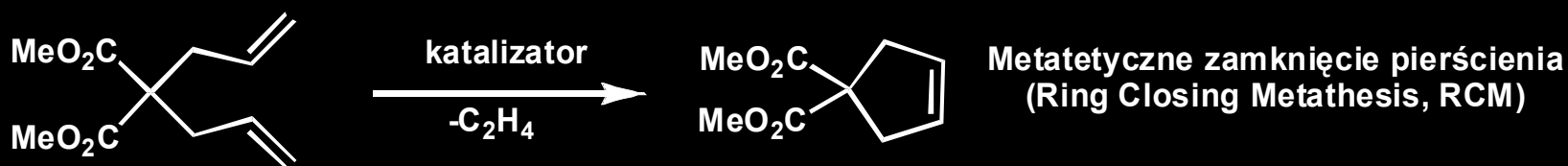
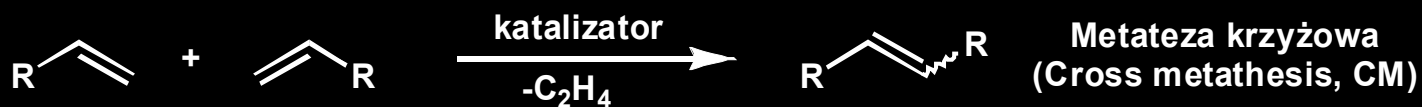
Addition of boranes to olefins, followed by basic oxidation of the organoborane adducts, resulting in alcohols.



Example 3¹⁴

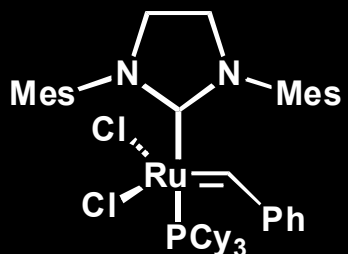


Metateza



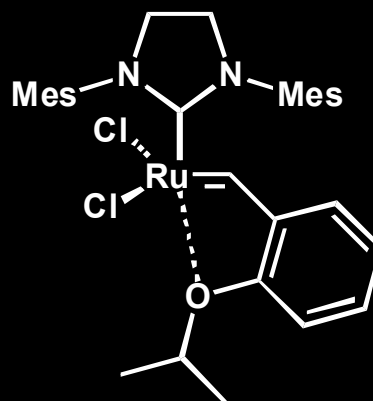
katalizator
Grubbsa I generacji

Cy = cykloheksyl

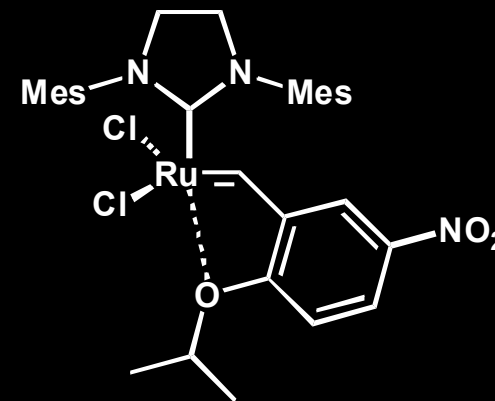


katalizator
Grubbsa II generacji

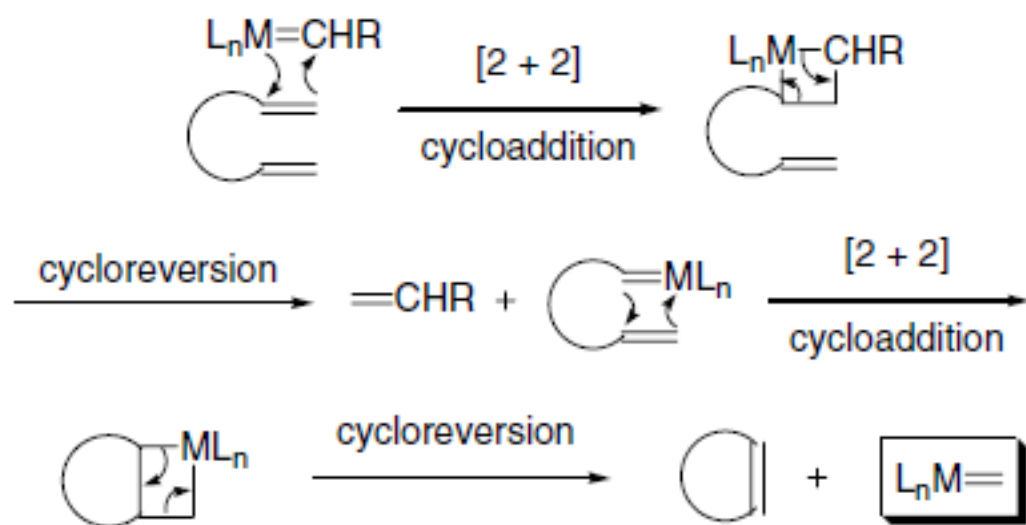
Mes - grupa mezytylowa



katalizator
Hoveydy-Grubbsa II generacji



katalizator
Grelli



Wieloetapowe syntezy – gdzie szukać?

- <http://www.newchemistry.eu/category/synteza-miesiaca/>
- <http://syntheticnature.wordpress.com/>
- <http://totallysynthetic.com/blog/>
- <http://www.chem.wisc.edu/areas/reich/syntheses/syntheses.htm>
- <http://www.organic-chemistry.org/>

Problemy, rozwiązania

- <http://evans.harvard.edu/problems/index.cgi>

Inne

- <http://masterorganicchemistry.com/>

Powodzenia na II etapie!

Tamiflu

