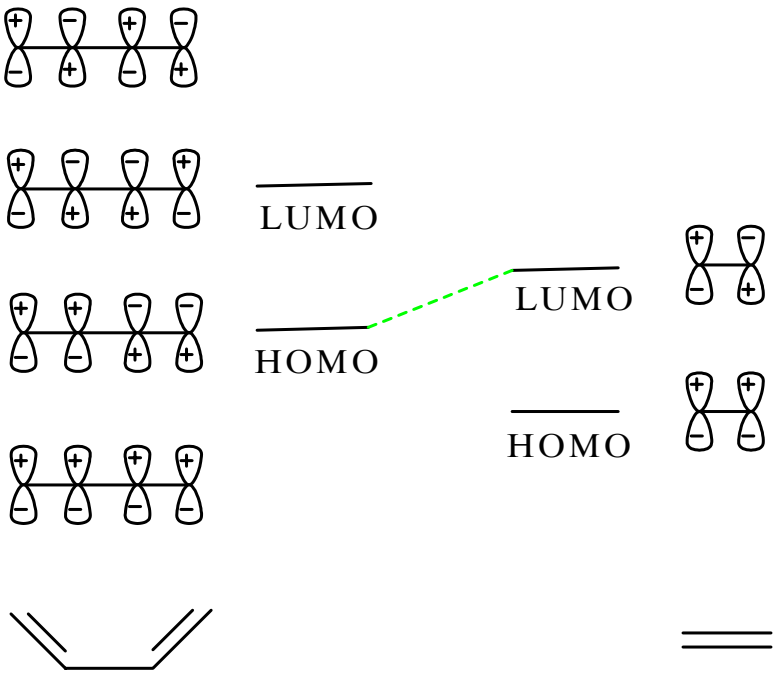
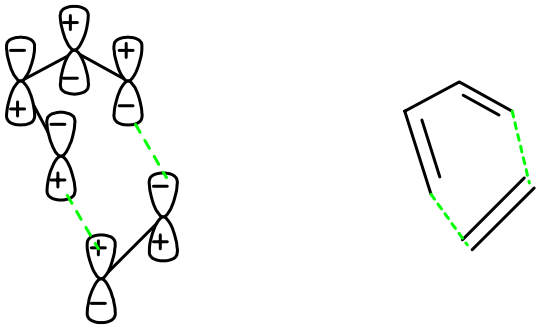
CIKLOADICIJE

Diels-Alder-ova reakcija (4+2)

dien dienofil



$HOMO_{dien}$ + $LUMO_{dienofil}$



* **4 pravila**:

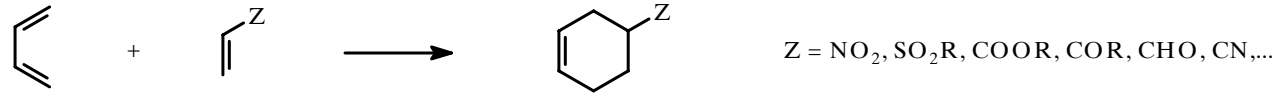
1) elektronska usklađenost diena i dienofila;

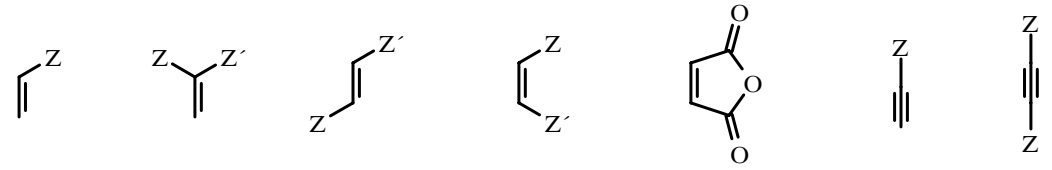
2) *cis*-pravilo;

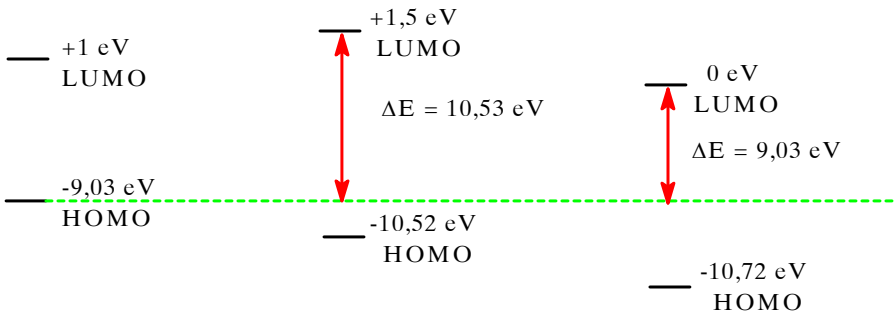
3) *endo*-pravilo;

4) *o, p* - pravilo

1) Elektronska usklađenost



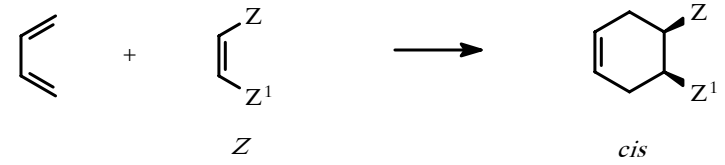




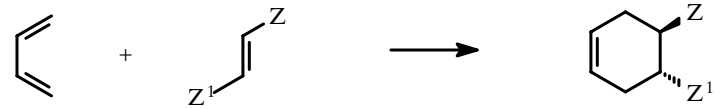
⇒ e-bogati dien + e-deficitarni dienofil

(HOMO↑ + LUMO↓)

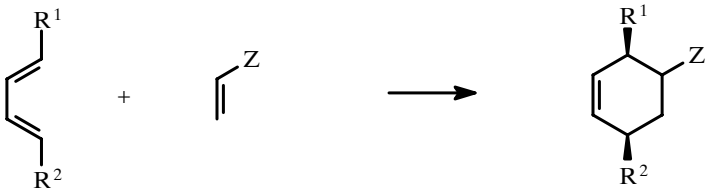
2) *Cis*-pravilo



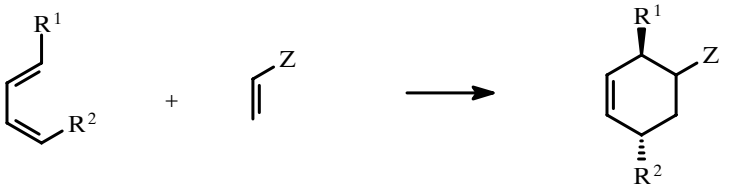
Z *cis*



E *trans*

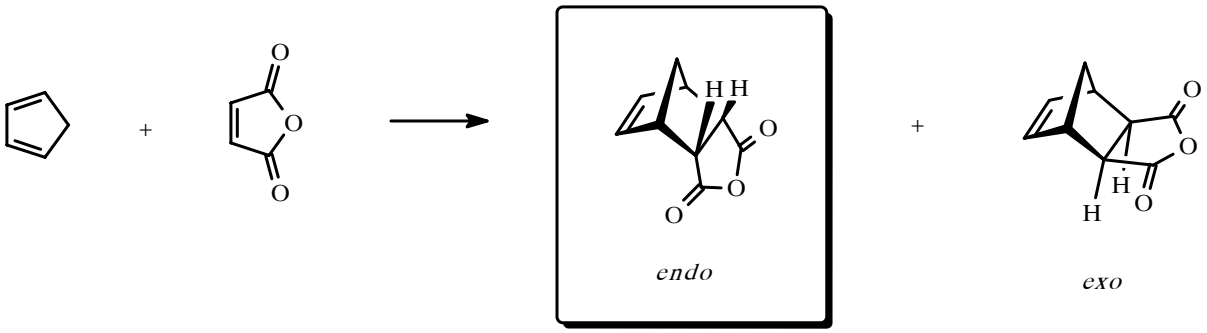


E, E *cis*



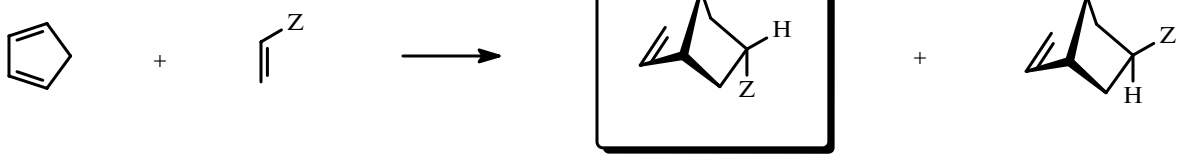
E, Z *trans*

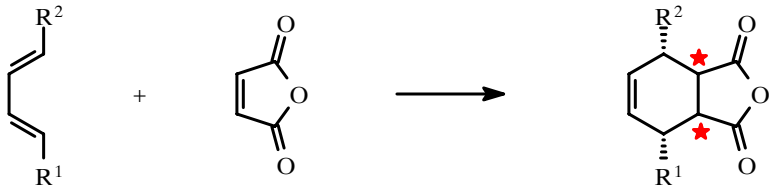
3) *Endo*-pravilo

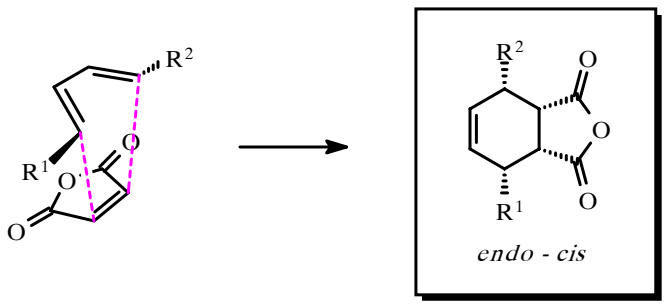


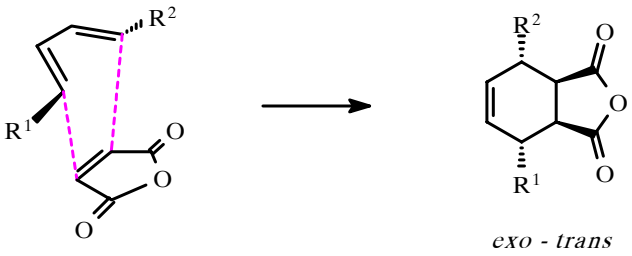
endo *exo*

glavni proizvod



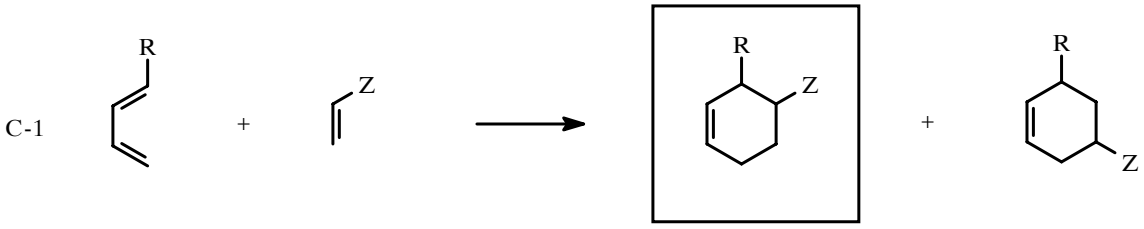


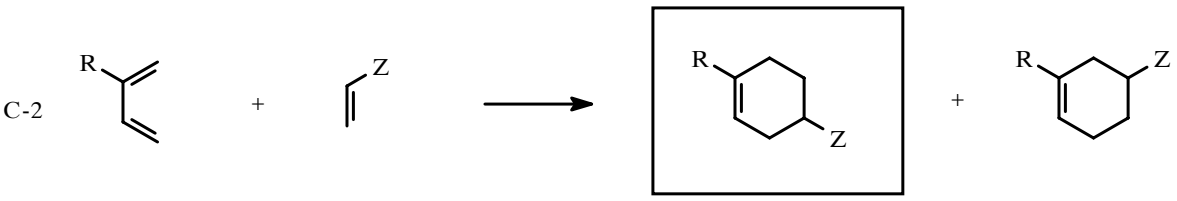




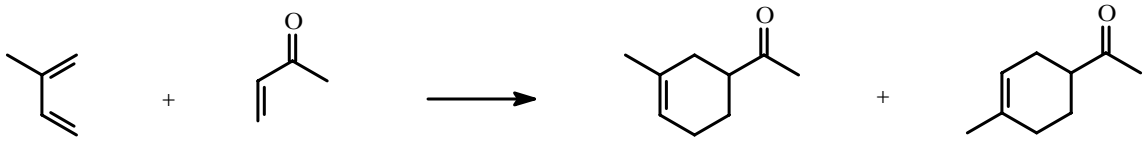
4) *o,p*-pravilo (regioselektivnost cikloadicije)

R = e-donatorska grupa: alkil < TMS < OR < SR



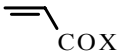


18 : 1

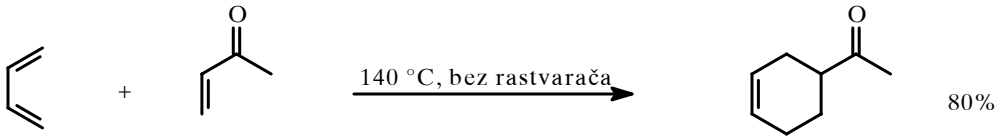


1 : 3

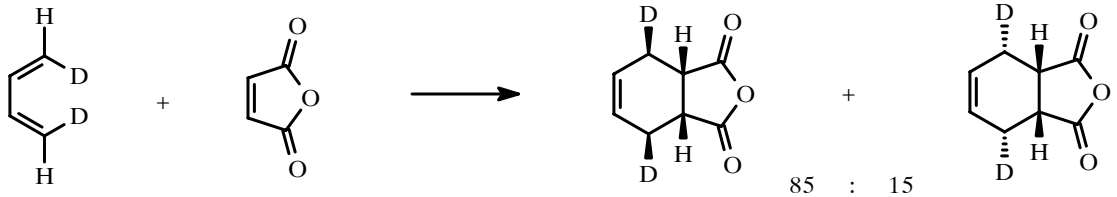
* Dienofili 



X = H, R, OH, OR

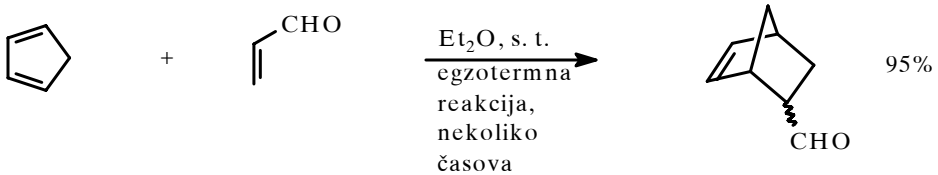


80%

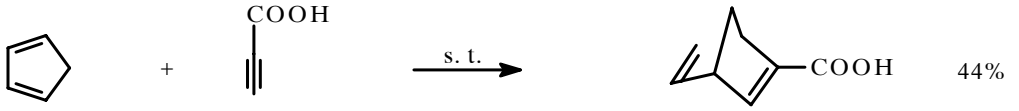


85 : 15

100%

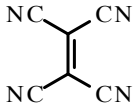
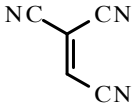
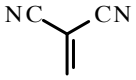


95%

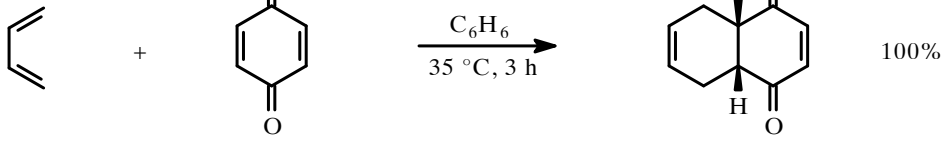


44%

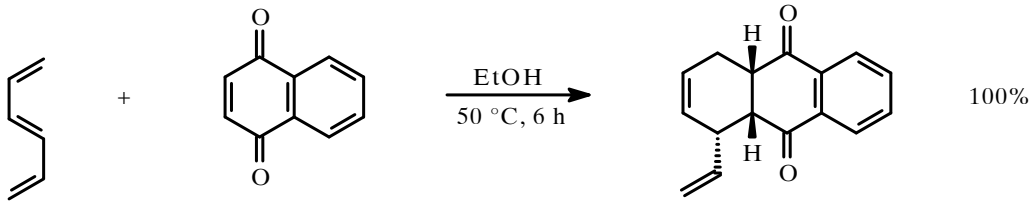
Dienofil:

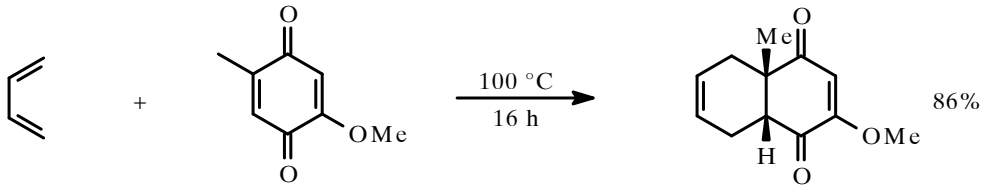

Relativna brzina cikloadicije sa 	$4{,}3 \times 10^7$	$4{,}8 \times 10^5$	$4{,}5 \times 10^4$	1

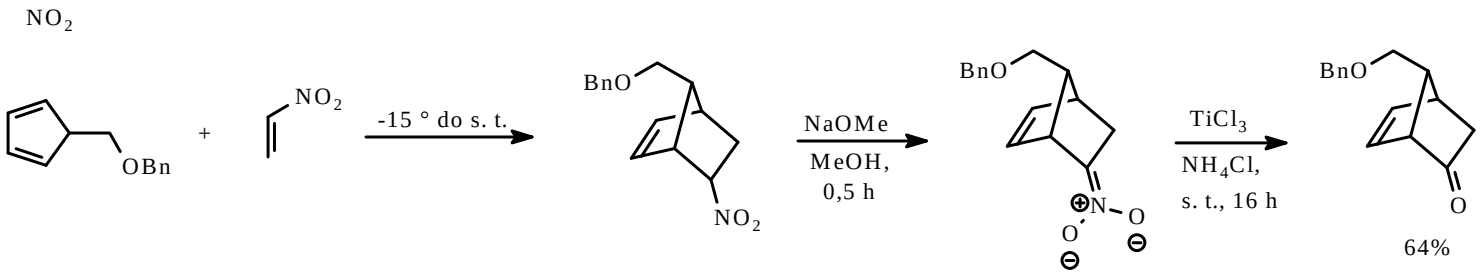


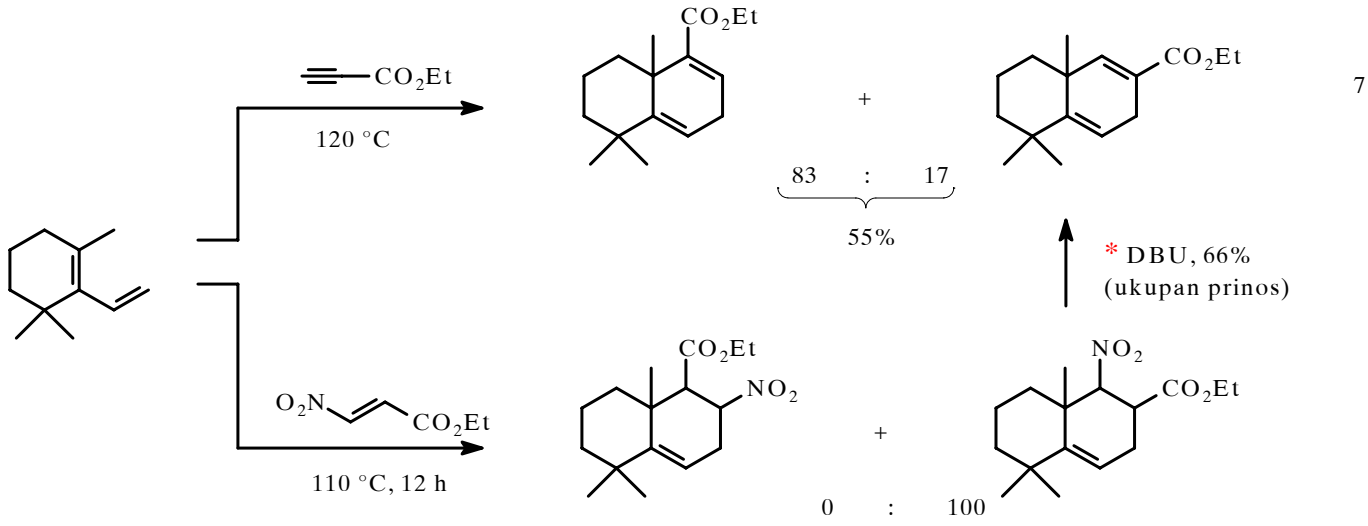
1,1 ekv. 1 ekv.



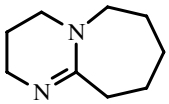
1,5 ekv. 1 ekv.



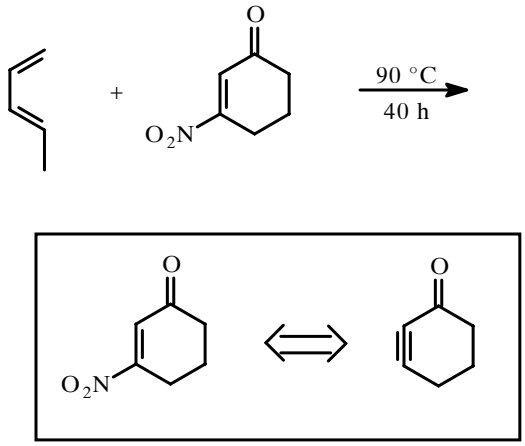




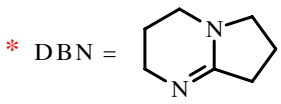
* DBU =



DiazaBiciklоUndecen

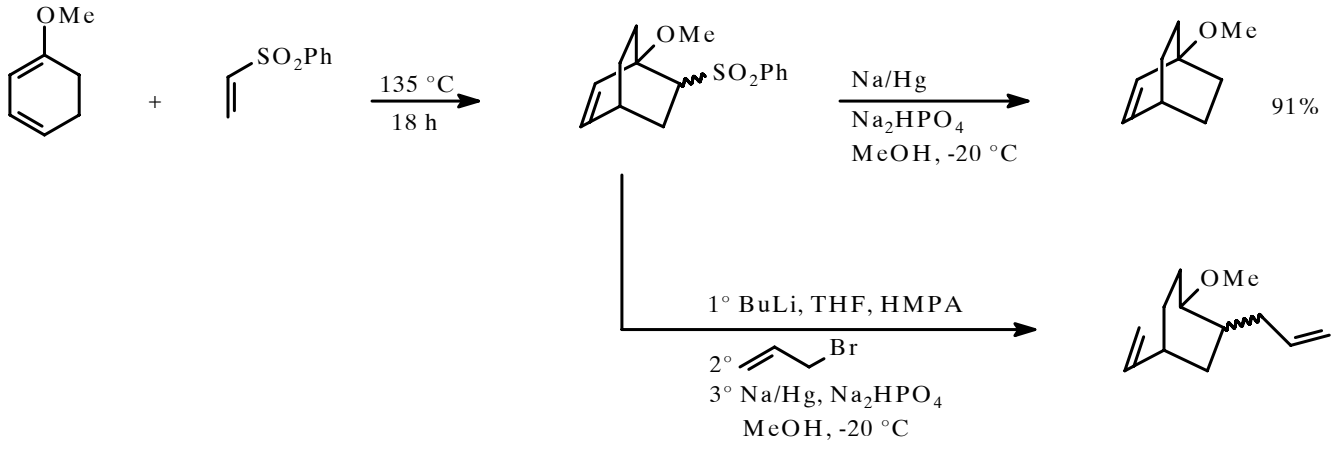


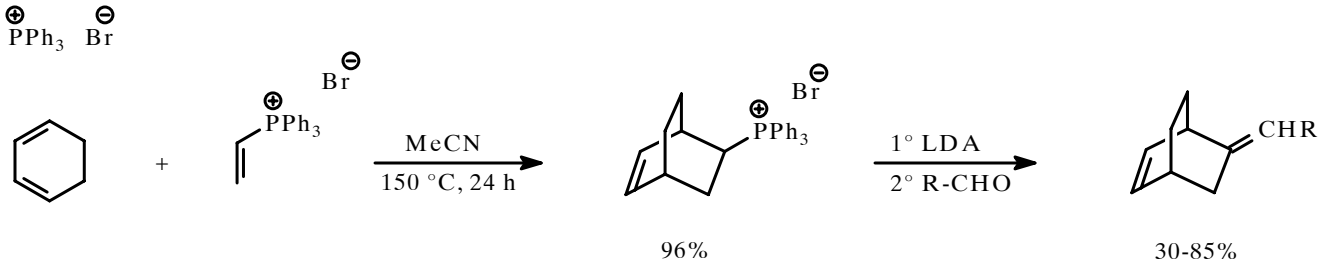
* DBN =



DiazaBiciklоNonen

SO_2R

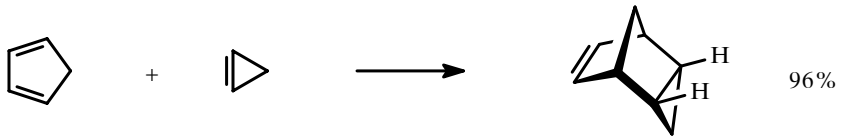




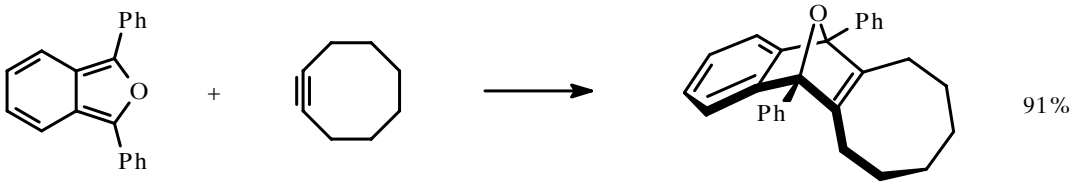
96%

30-85%

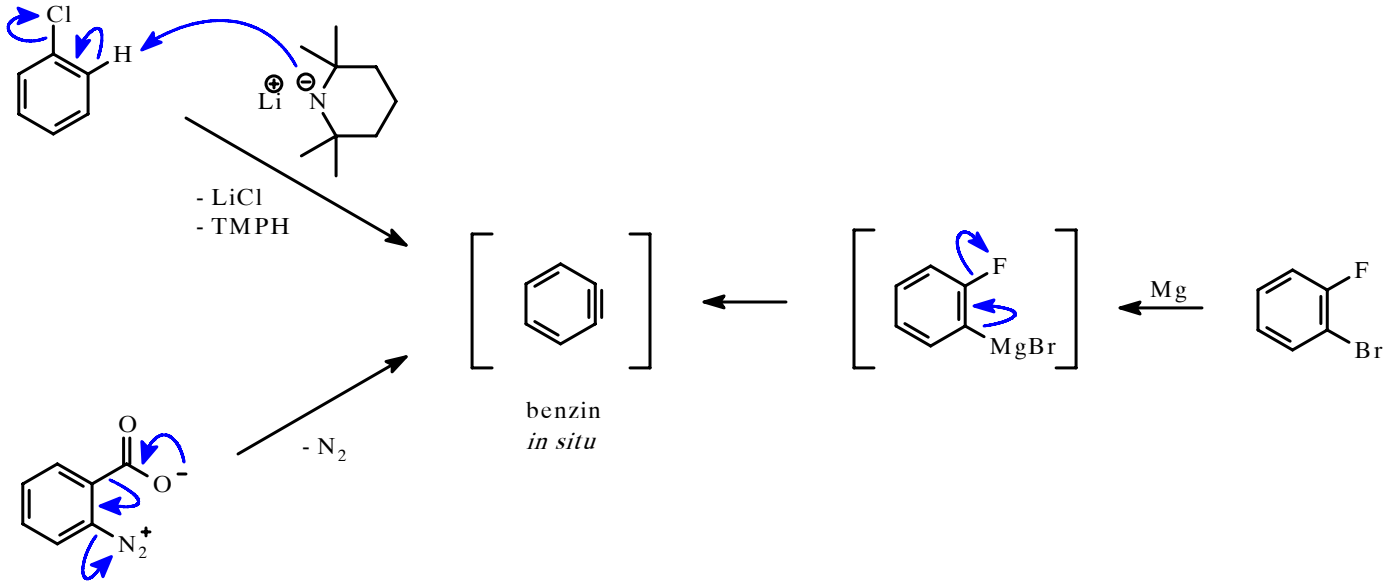
* Ugaono napeti dienofili



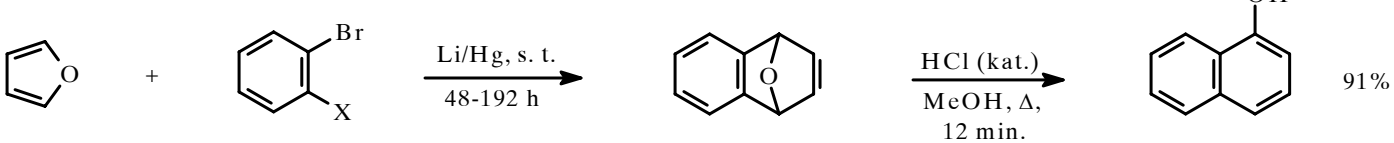
96%



91%



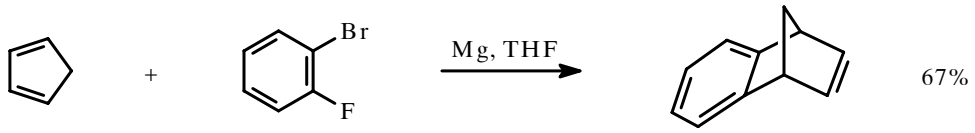
benzin
in situ



X = F, Cl, Br

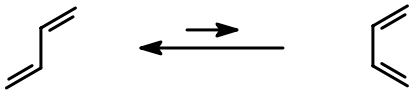
75-88%

91%

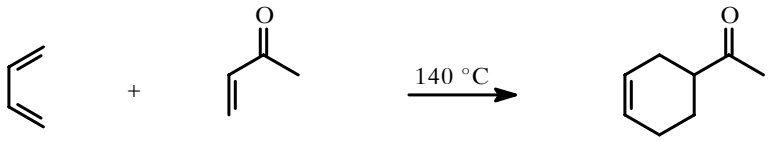


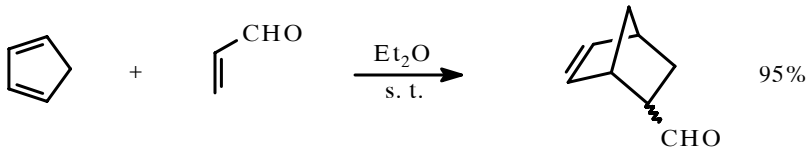
67%

* Dieni



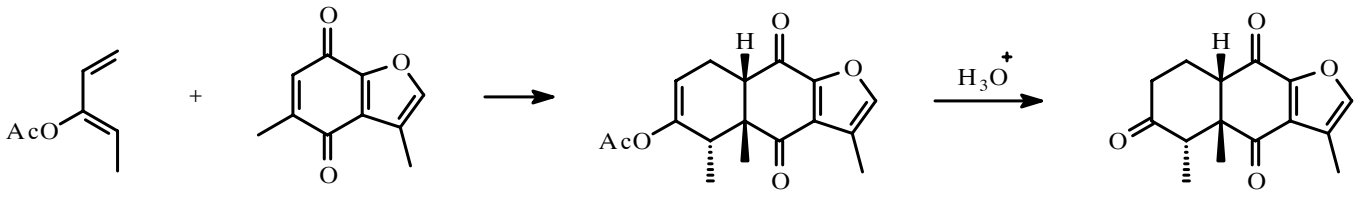
s-trans *s-cis*
(reaktivna konformacija)



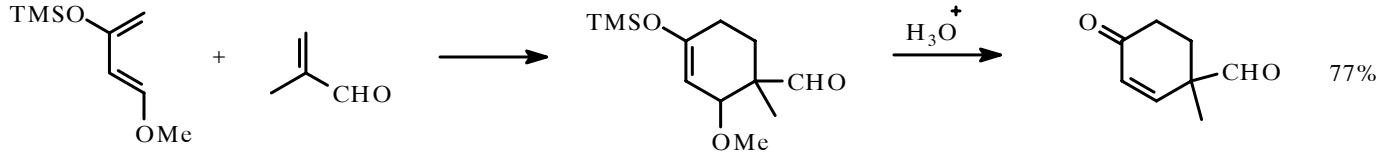


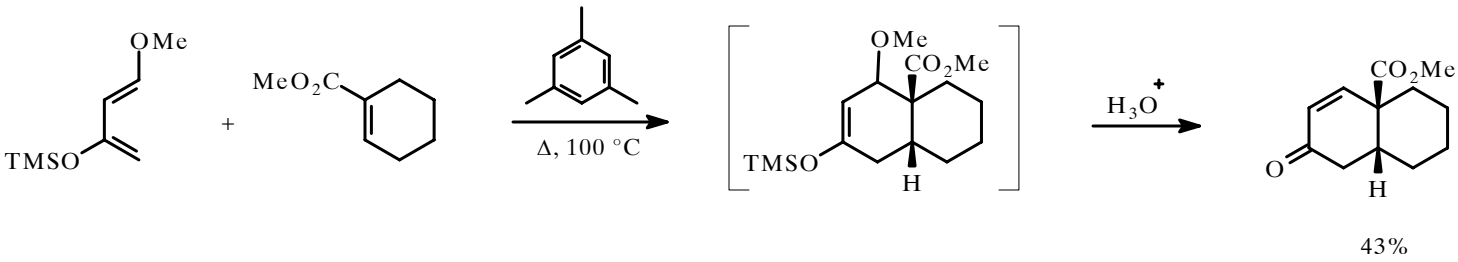
95%

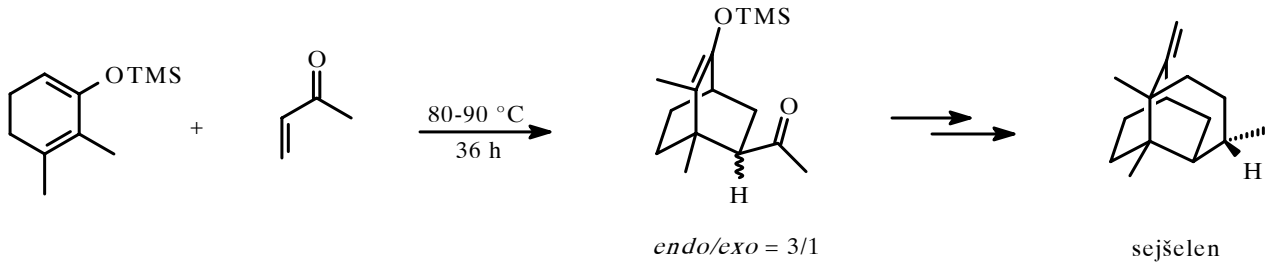
* *O*-supstituisani dieni

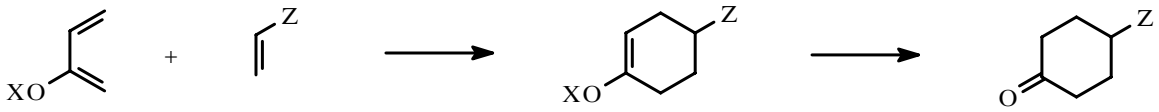


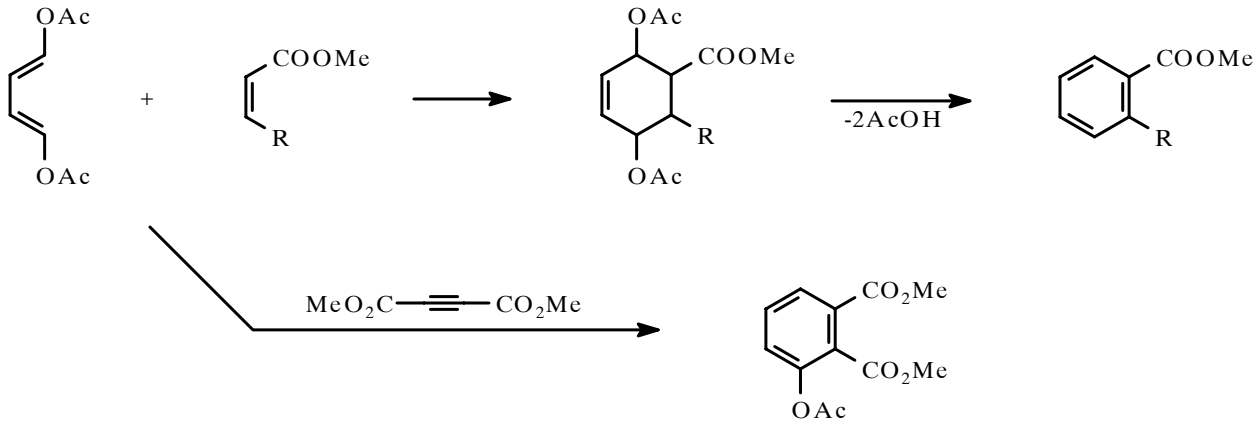

MeOH
H+
LDA
TMSCl
dien Daniševskog
(Danishefsky diene)


77%

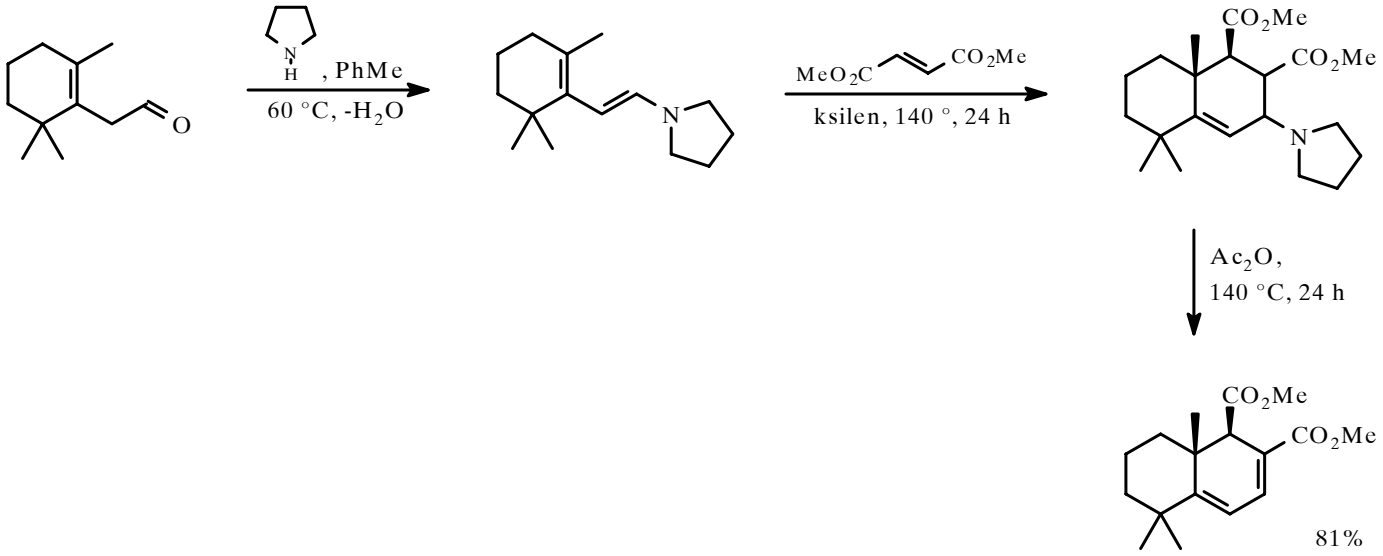

Δ, 100 °C
43%

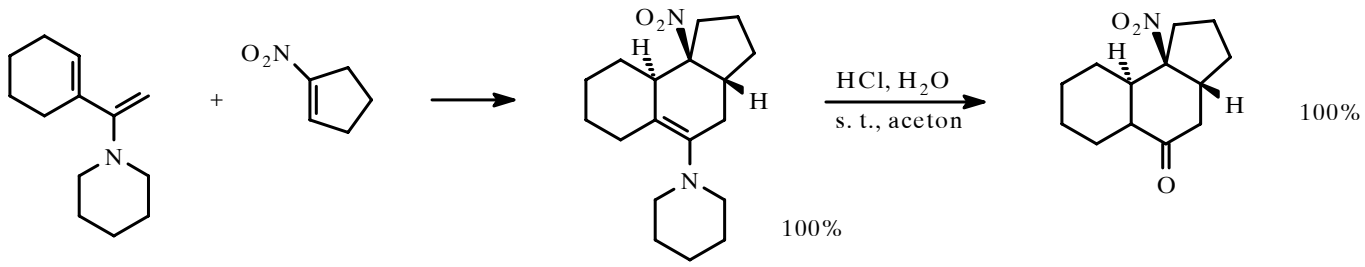

80-90 °C
36 h
endo/exo = 3/1
sejšelen



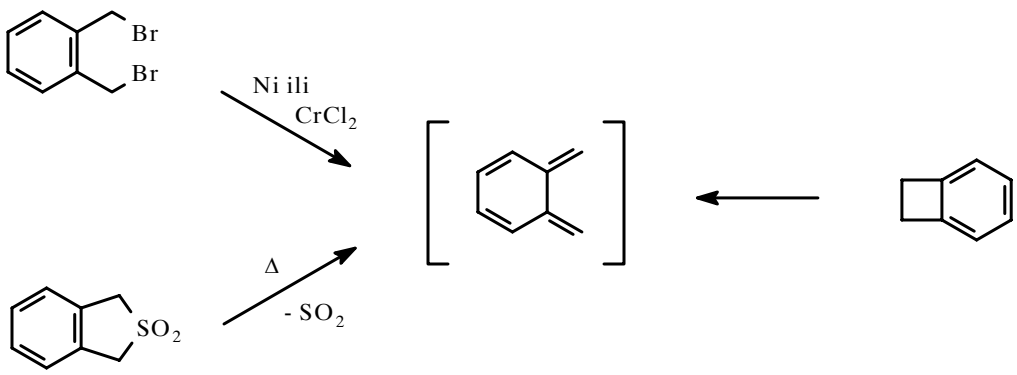


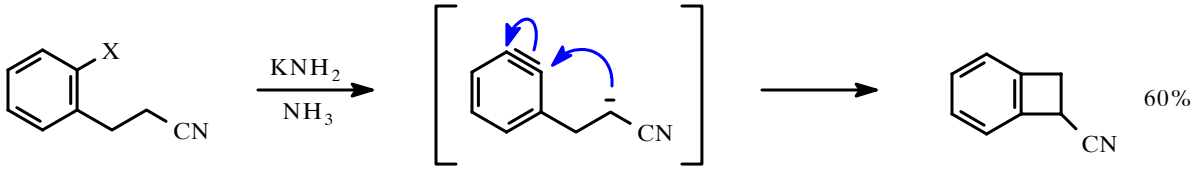
* *N*-supstituisani dieni

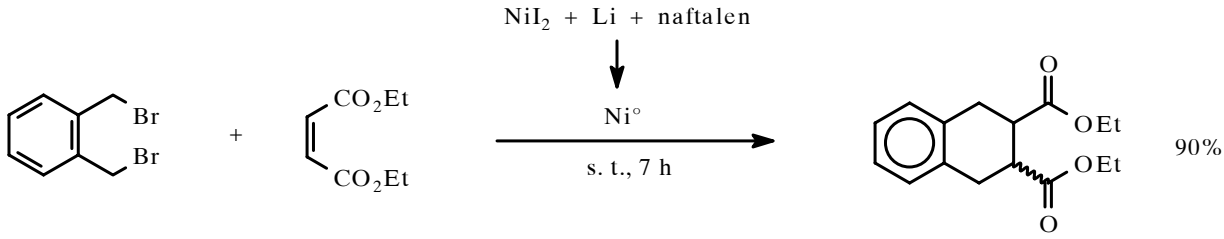


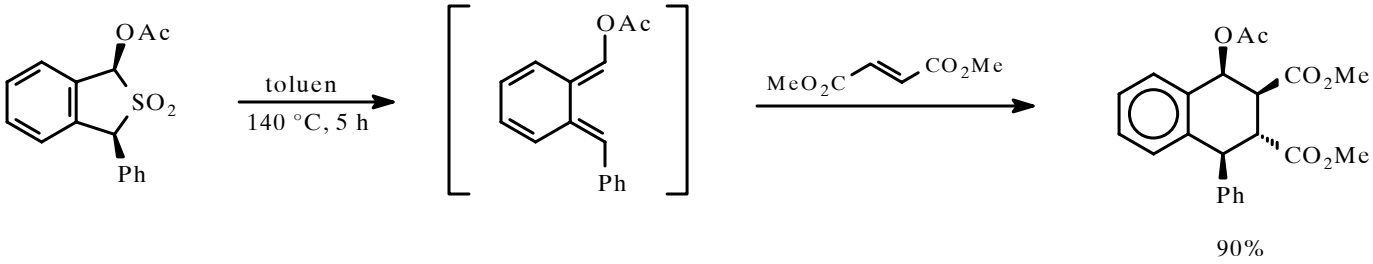


* σ-ksilileni



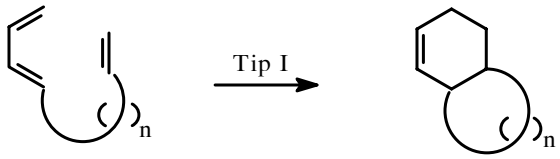


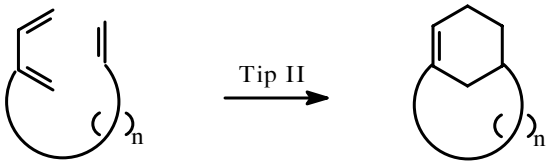


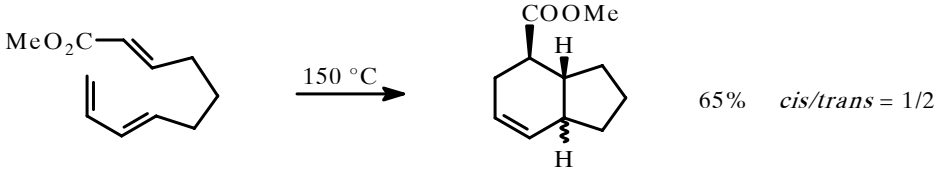


90%

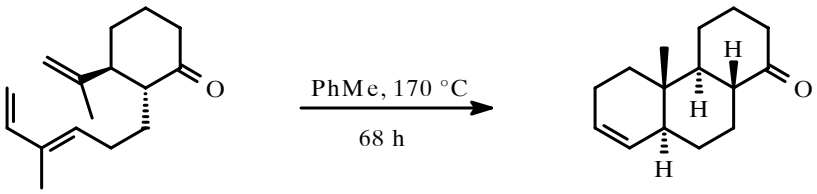
* Intramolekulska Diels-Alder-ova reakcija (IMDA)



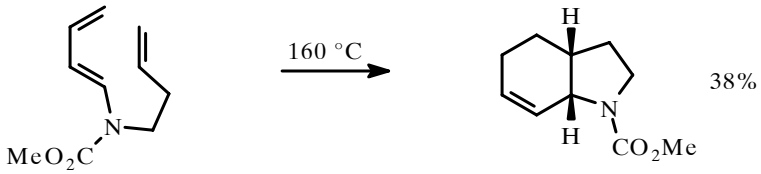


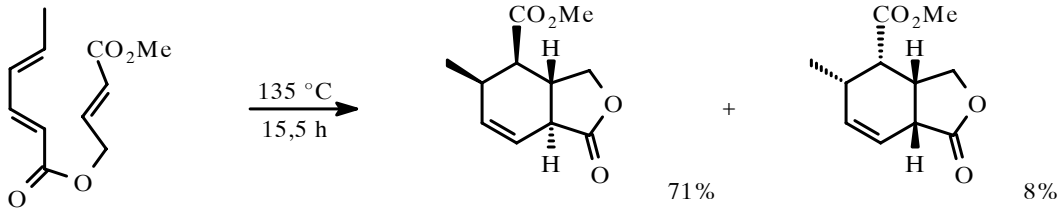


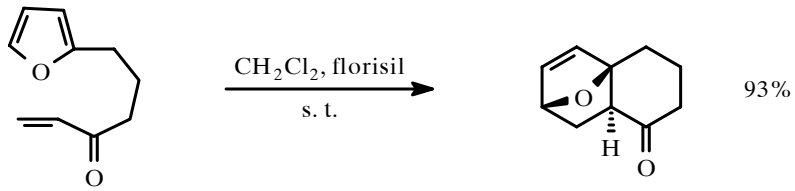
65% *cis/trans* = 1/2

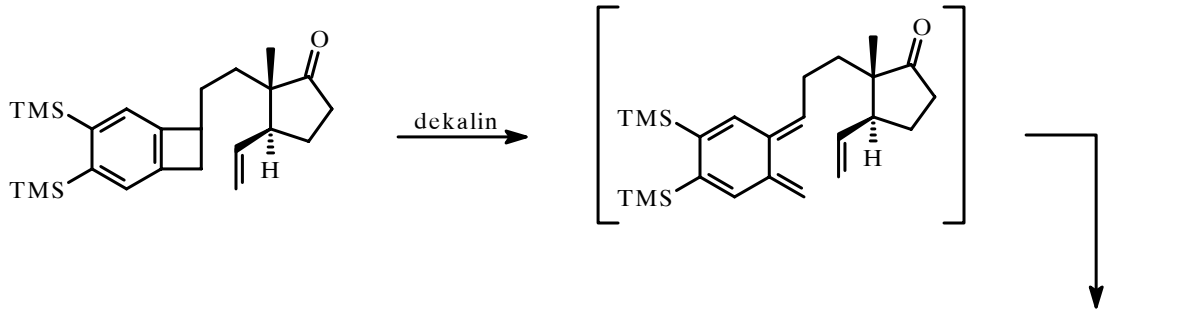


73%


160 °C
38%


135 °C
15,5 h
71%
+
8%


CH2Cl2, florisil
s. t.
93%

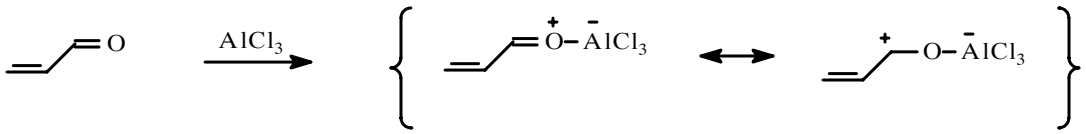

dekalin
1° TFA, CCl4, -30 °C
2° Pb(O2CCF3)4
90%
41%

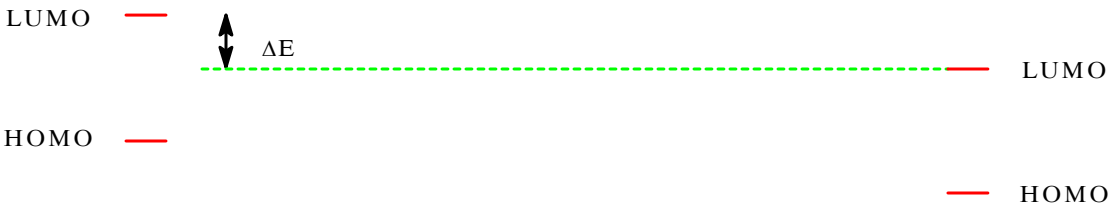
Estron

* Ubrzanje DA-reakcije

* Kataliza Lewis-ovim kiselinama (LA)
* Reakcije pod visokim pritiskom
* Reakcije u vodenoj sredini
* Ultrazvuk

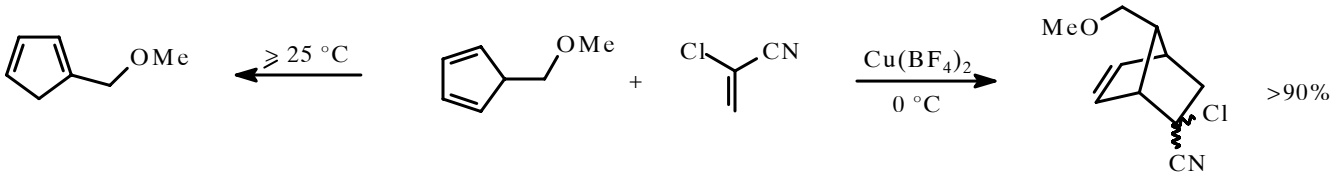
LA

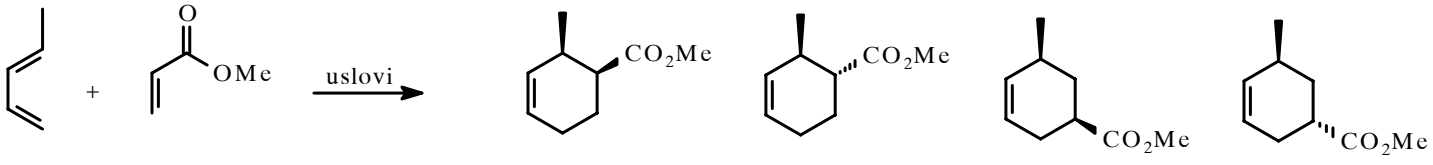




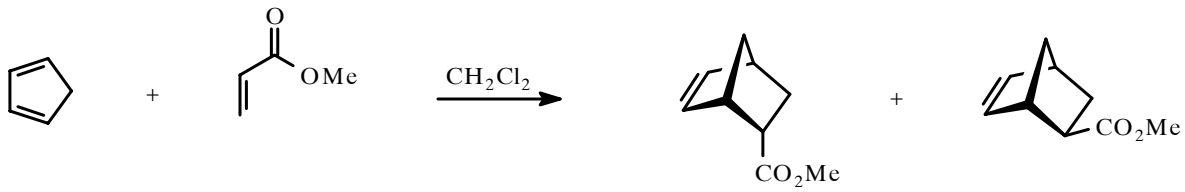
LA: $AlCl_3$, $EtAlCl_2$, Et_2AlCl, BF_3, $TiCl_4$, $Cu(BF_4)_2$, $ZnCl_2$, $SnCl_4$, utd.

* brža reakcija
* viša regioselektivnost (*o, p*)
* viša stereoselektivnost (*endo*)

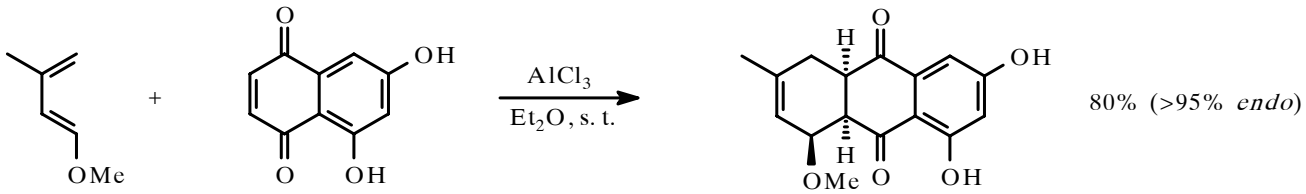




25 °C, 1680 h	53%	[45	39	11	5]
10-20 °C, 3 h, 0,15 ekv $AlCl_3$	50%	[93	5	2	0,1]



Reakcioni uslovi	Prinos			
Bez aditiva	22-51%	82	:	12
$AlCl_3$ x Et_2O (0,1 ekv.), 0 °C	79-91%	96	:	4
$AlCl_3$ x Et_2O (0,1 ekv.), -70 °C	67-72%	99	:	1



80% (>95% *endo*)

Visok pritisak

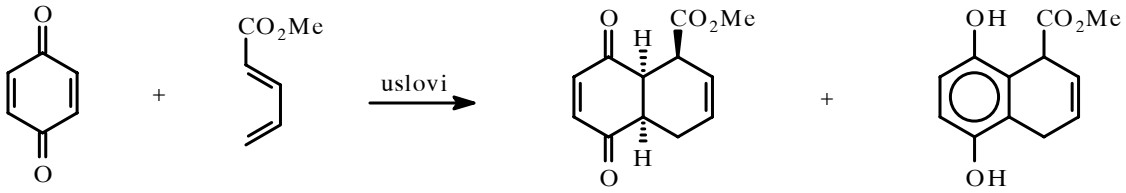
DA: negativna aktivaciona zapremina (ΔV^*)

* Pritisak ubrzava reakciju kada:

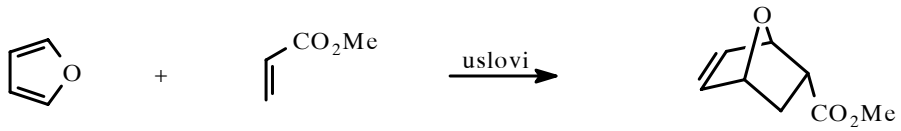
1) opada broj molekula u smeru od reaktanata ka proizvodima (DA)
2) reakcija se odvija preko cikličnog prelaznog stanja (DA)
3) reakcija se odvija preko dipolarnog prelaznog stanja
4) reakcija sa sternim smetnjama

* Pritisci: 5 - 50 kbar

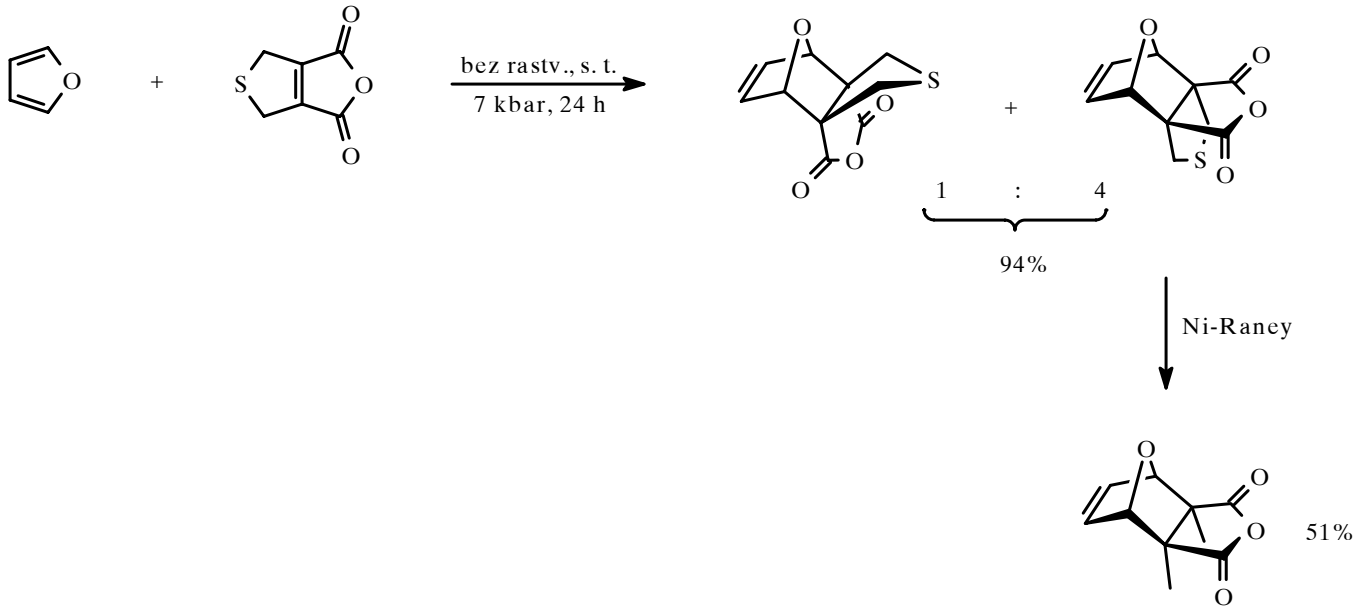
* Rastvarači: CH_2Cl_2, Et_2O, toluen, bez rastvarača (viskozitet, T.t.)



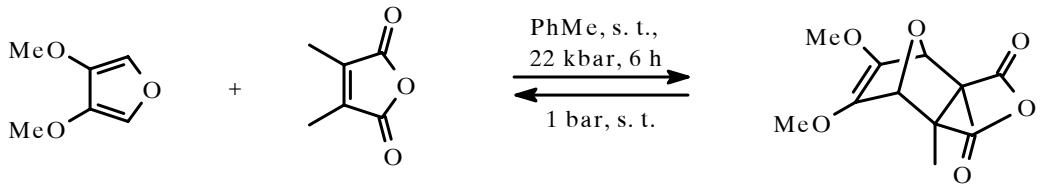
Benzen, Δ, 10 h	18%	izomerizacija →	glavni proizvod
s. t., 15 kbar, 18 h	64%		--



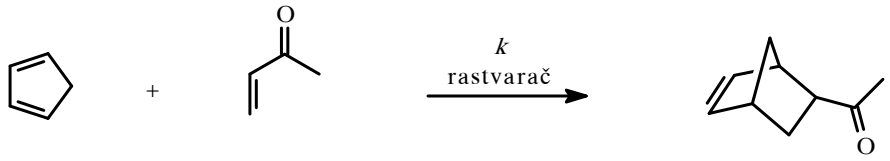
bez rastvarača, 1 at, s. t., 2-3 meseca	50%
bez rastvarača, ZnI_2, 40 °C, 2 dana	55%
CH_2Cl_2, 15000 at s. t., 4 h	62%



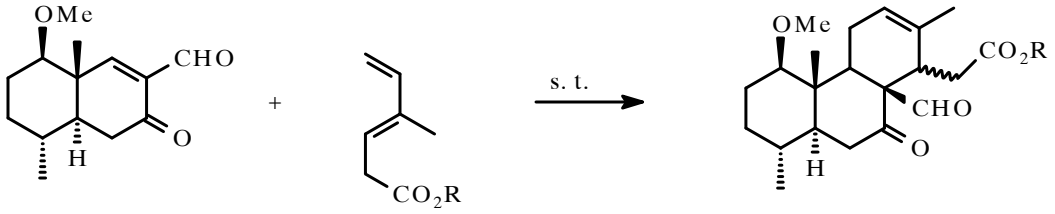
Kantaridin



Hidrofobni efekat



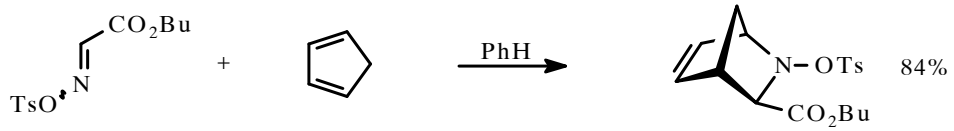
Rastvarač	k / 10^5 [$M^{-1}s^{-1}$]
izo-oktan	5,94
MeOH	75,5
H_2O	4410
H_2O/LiCl	10800

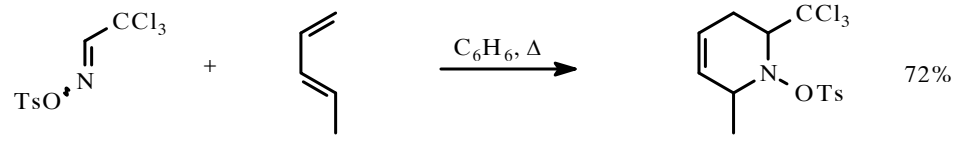


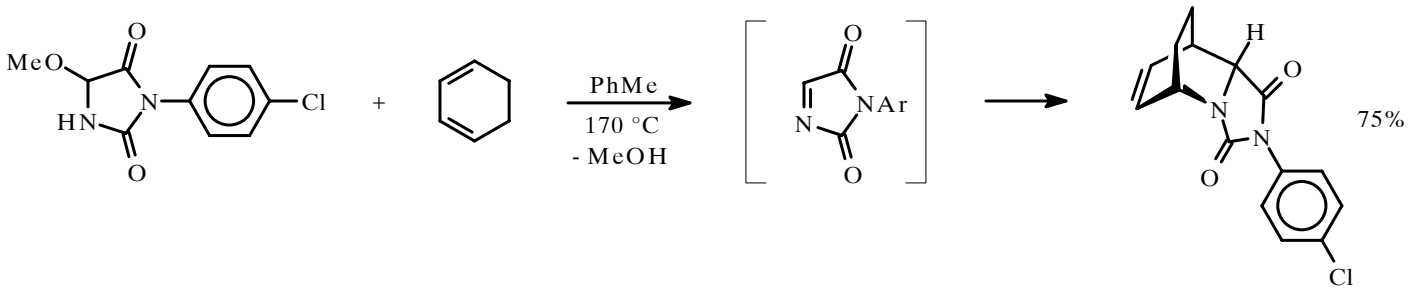
	Rastvarač	vreme	prinos
R = Et	C_6H_6	288 h	52%
R = Et	H_2O	168 h	82%
R = Na	H_2O	5 h	100%

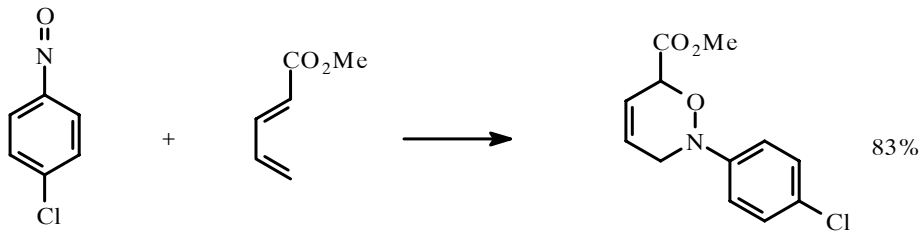
* Hetero-DA

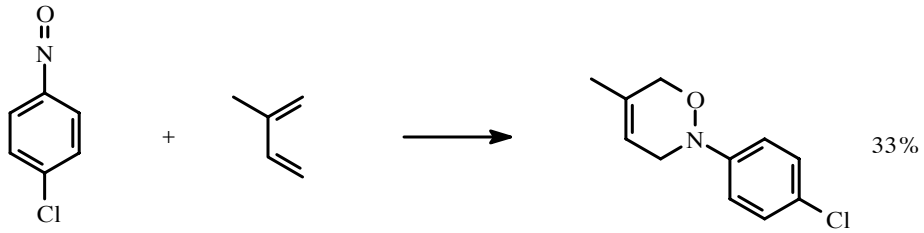
* Heterodienofili

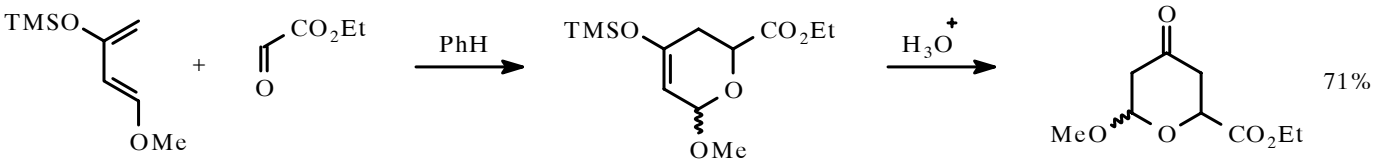


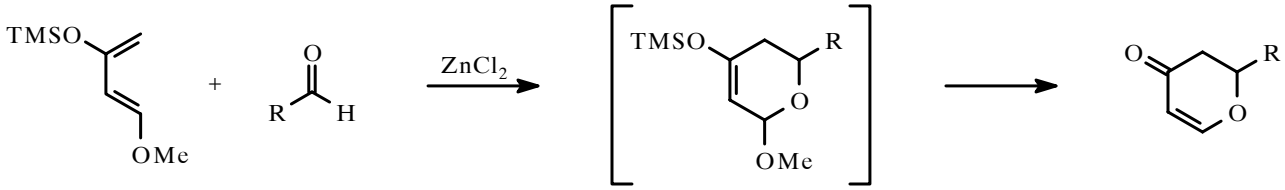










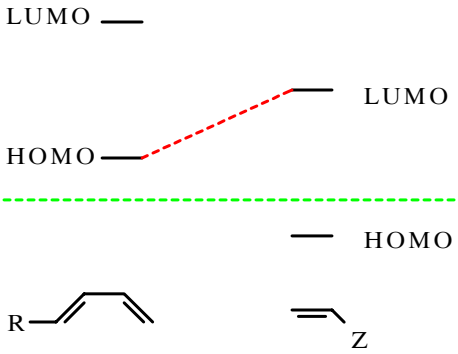


R = H, alkil, alkenil, aril, itd.

* Heterodieni

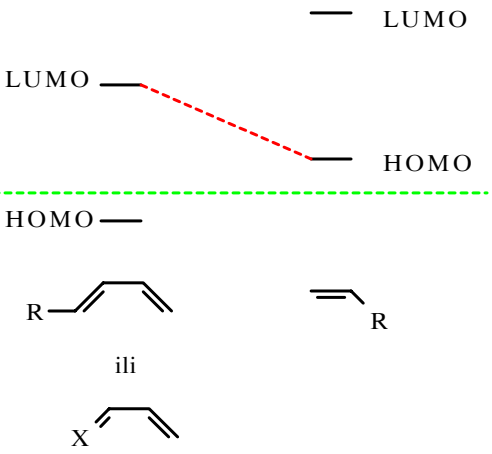
Normalna DA

$HOMO_{diena}$ + $LUMO_{dienofila}$

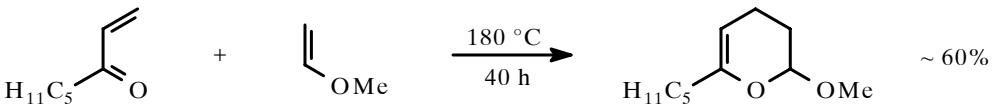


DA sa inverznim elektronskim zahtevima

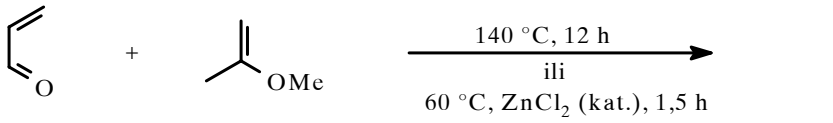
$LUMO_{diena}$ + $HOMO_{dienofila}$



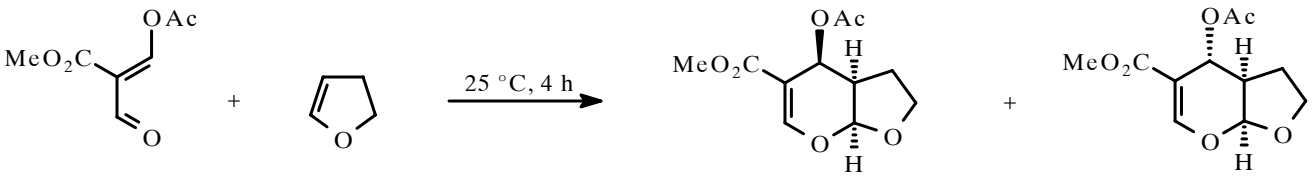
* Intermolekulska hetero-DA



~ 60%

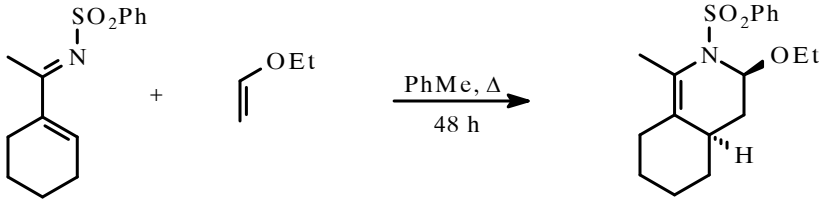


44%
(61% sa $ZnCl_2$)

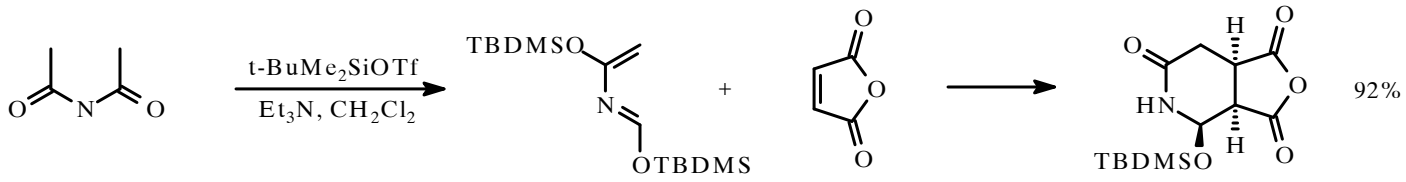


1 : 2

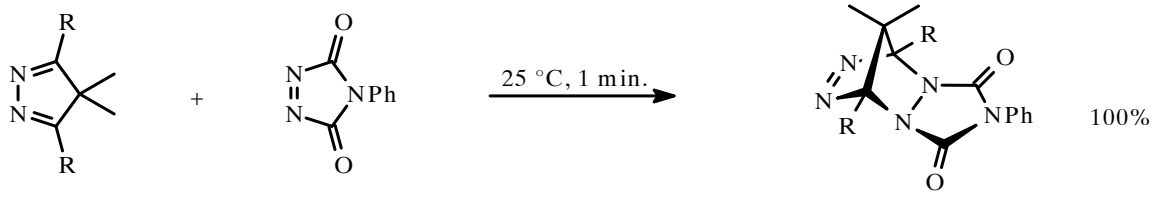
85%



79%
endo : *exo* > 20 : 1

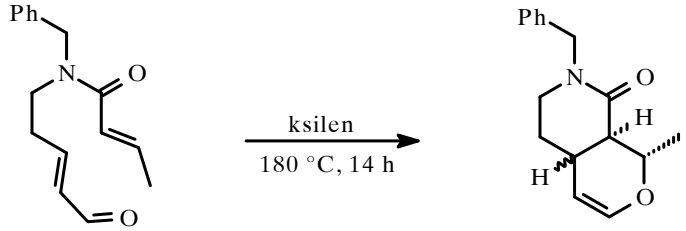


92%

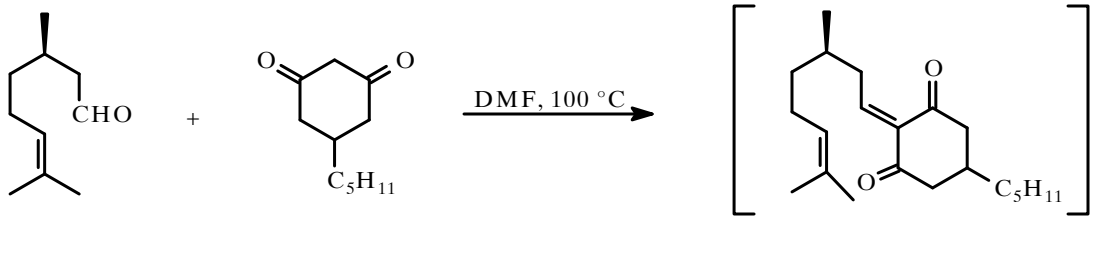


100%

* Intramolekulska hetero-DA

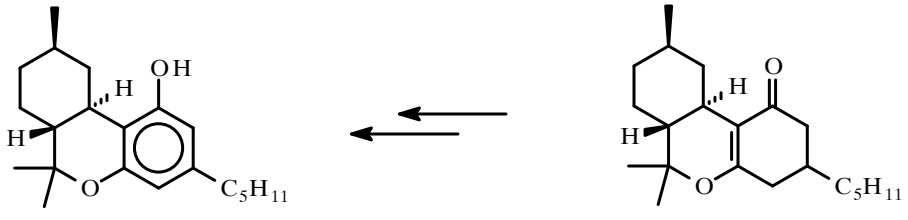


75%
cis : *trans* = 4,5 : 1



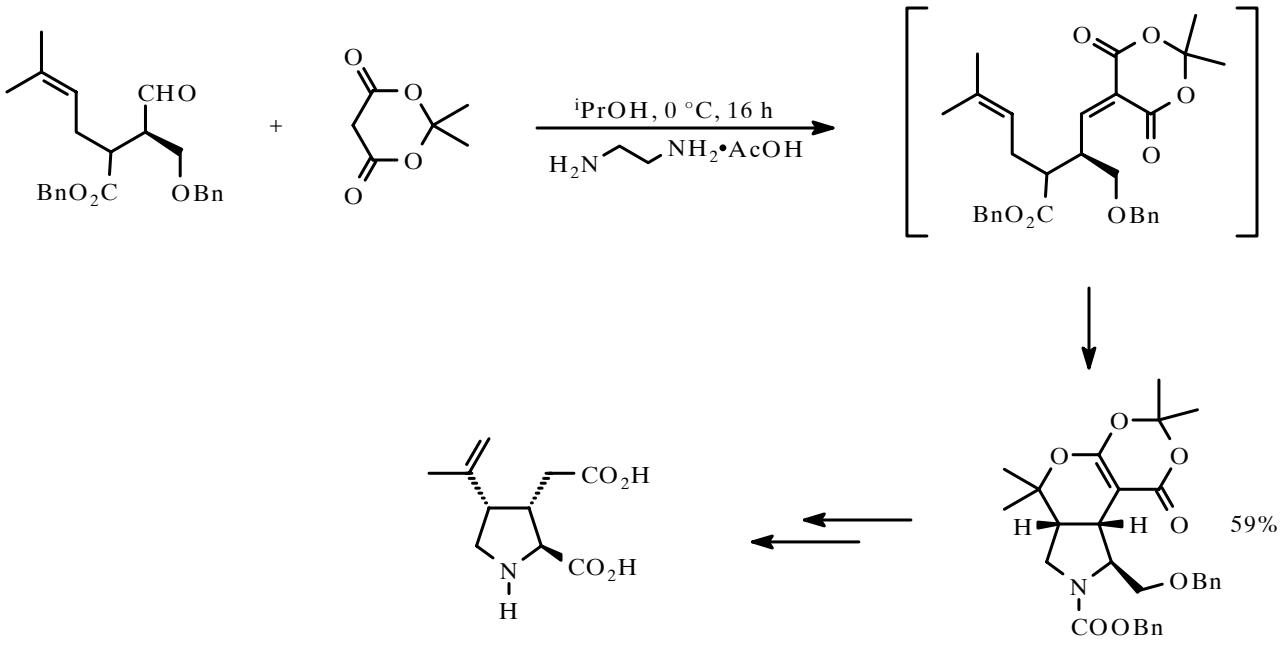
Domino reakcija:

Knoevenagel / DA



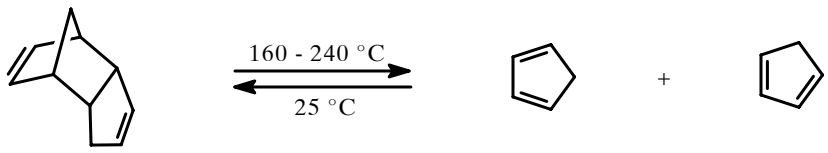
(-)-(3*R*)-Tetrahidrokanabinol

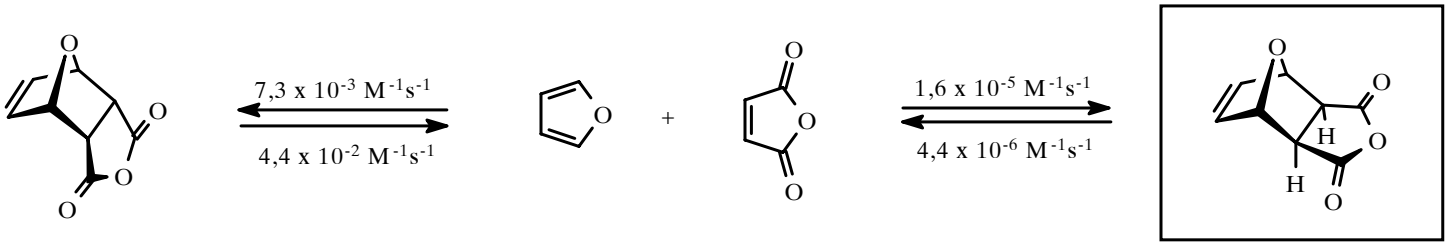
65%

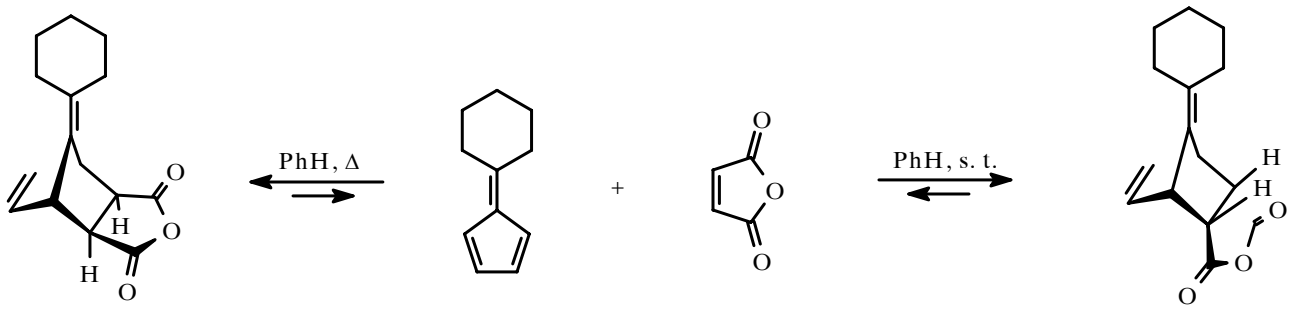


(-)-Kainska kiselina

* Retro-DA

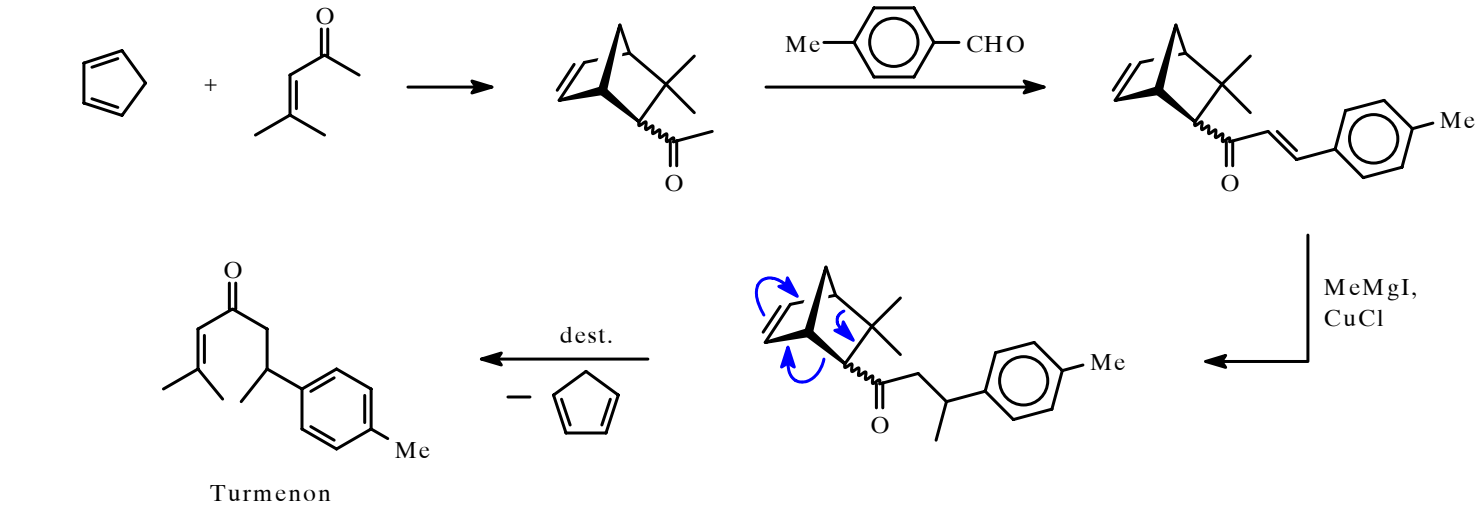


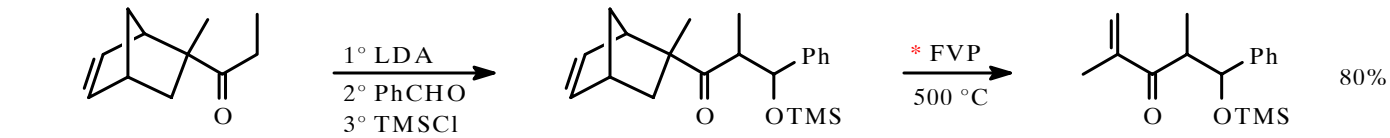




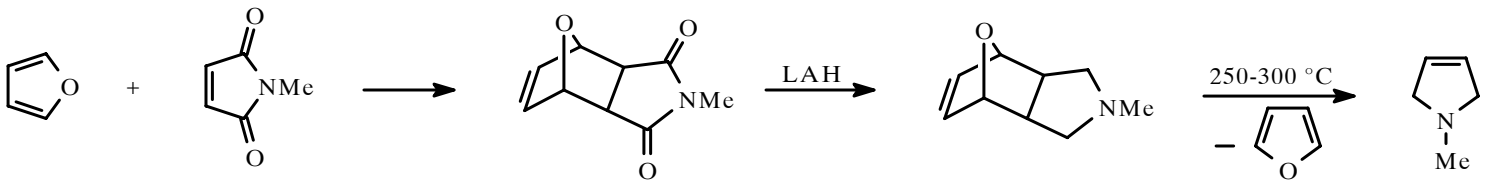
exo *endo*

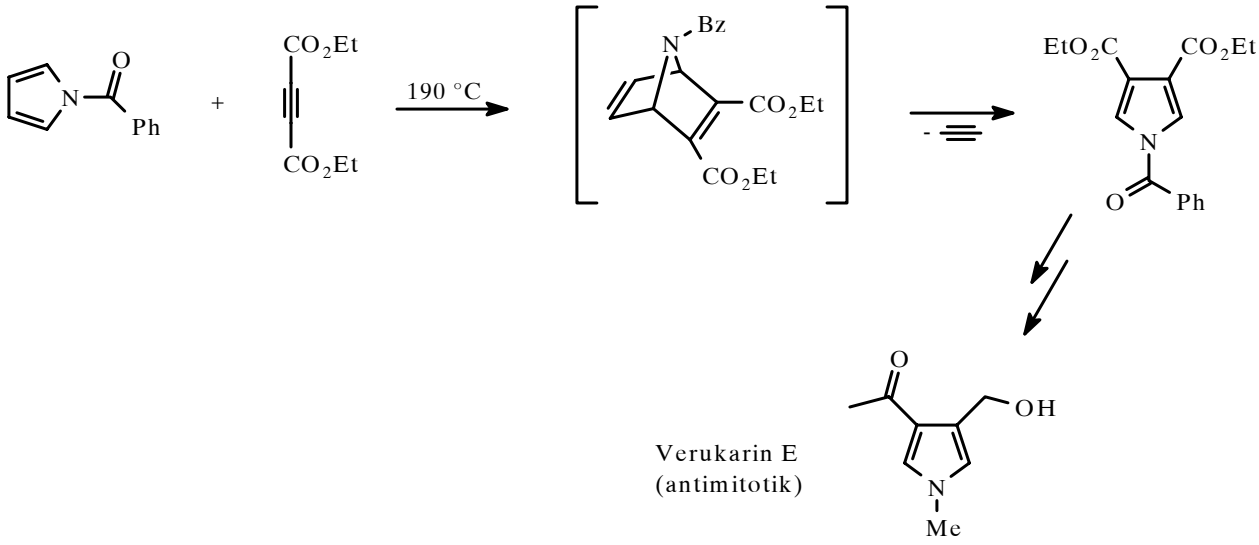
s. t. *endo* : *exo* = 100 : 0
50 °C, 10 min. *endo* : *exo* = 20 : 80
50 °C, 60 min. *endo* : *exo* = 3 : 97





* FVP = flash vacuum pyrolysis

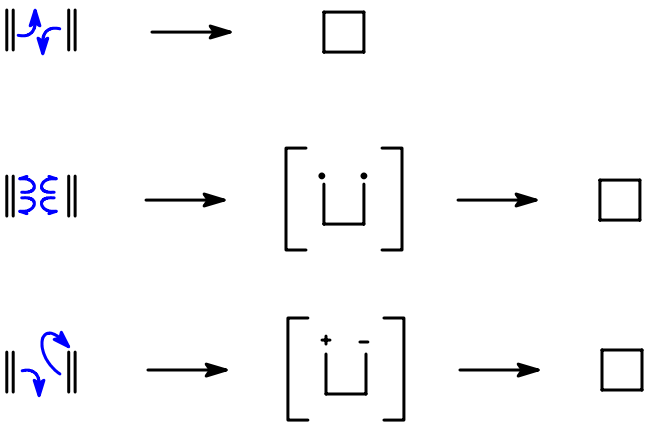




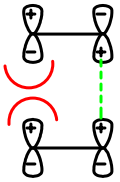
Verukarin E
(antimitotik)

2 + 2 Cikloadicije

* Termičke
* Fotohemijske



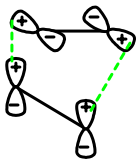
U osnovnom stanju:



LUMO

HOMO

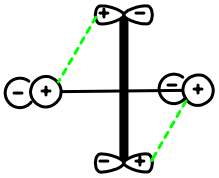
$2\pi_s + 2\pi_s$

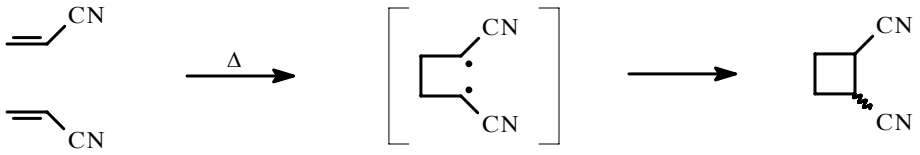


LUMO

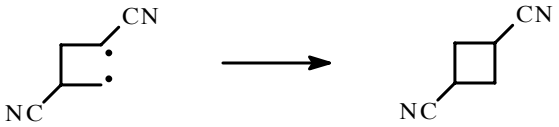
HOMO

$2\pi_s + 2\pi_a$

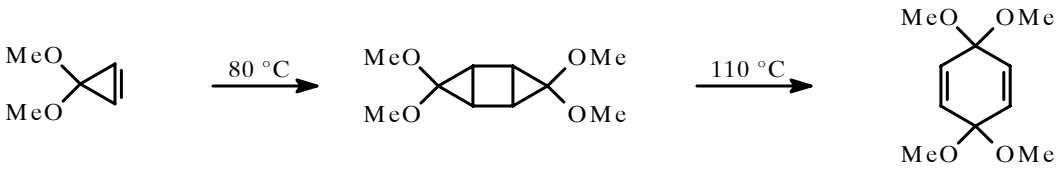


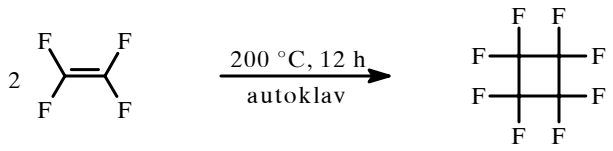


Reakcija NE IDE preko sledećih prelaznih stanja i intermedijera:

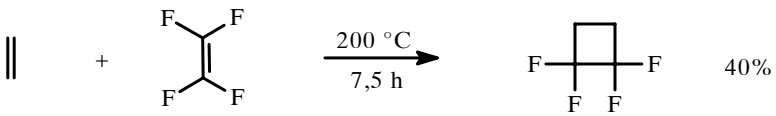


Temperature: 100-225 °C

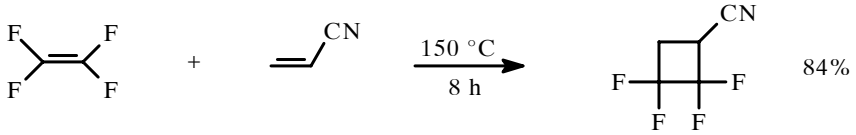




92% (80% konverzija)
T. k. 131-2 °C
T. t. 84,8 °C



40%



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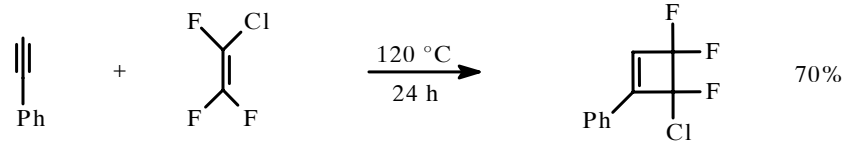

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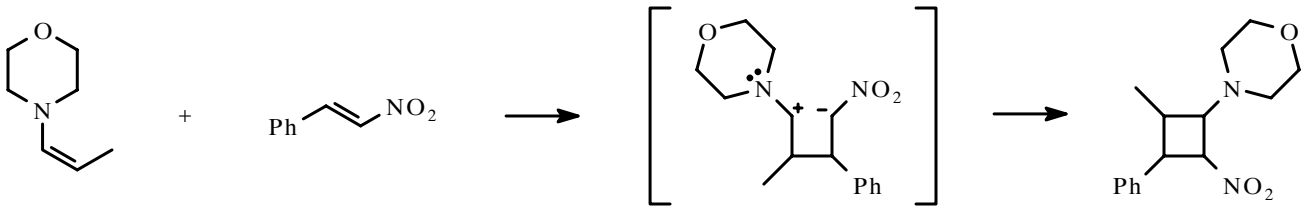
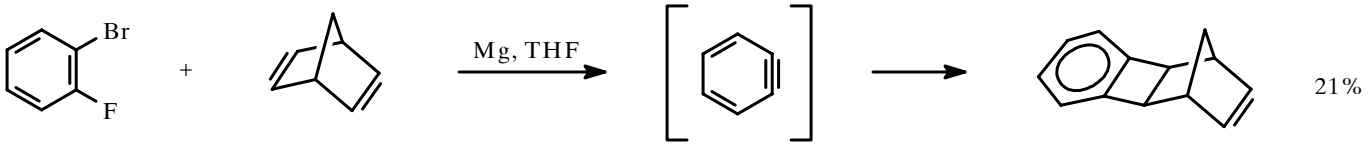
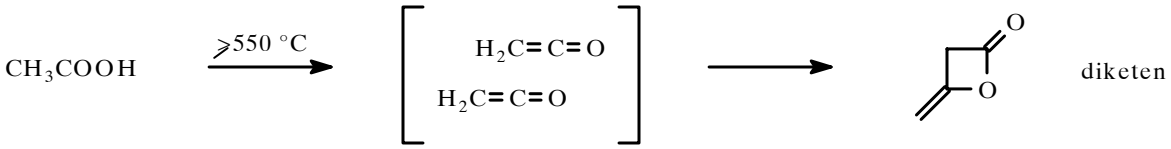
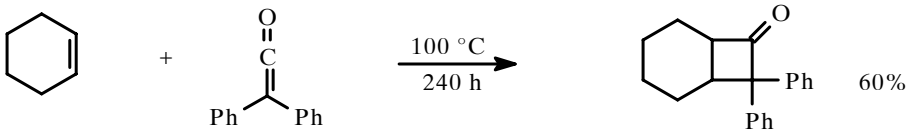
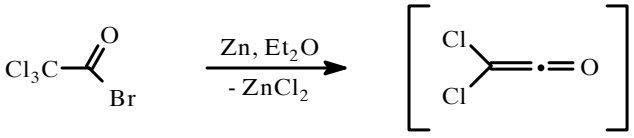


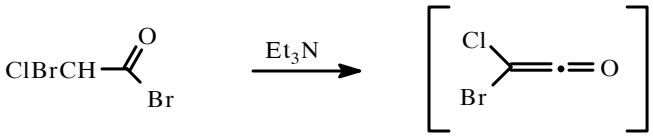


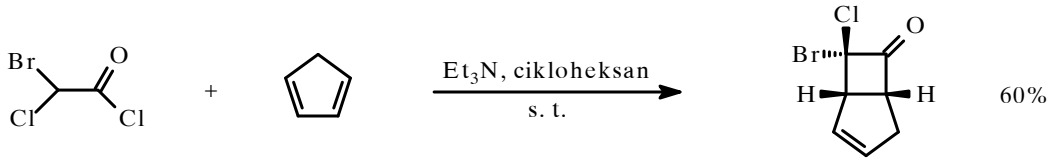
* 2+2 Cikloadicije ketena

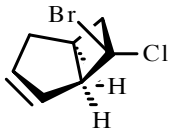






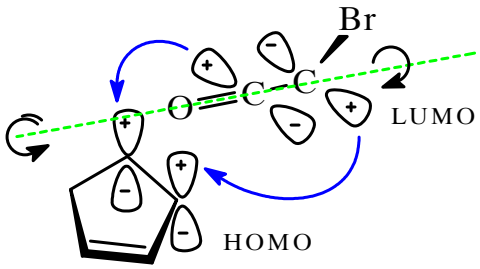


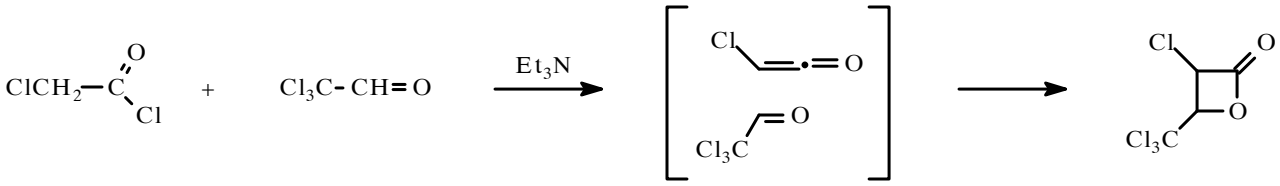


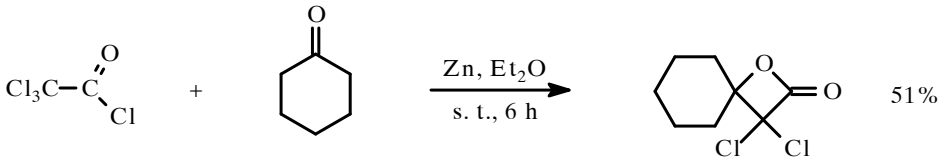


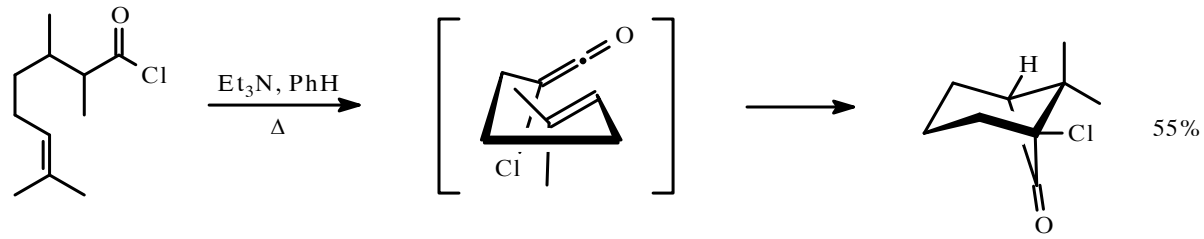
"Mazohistički sterni efekat"

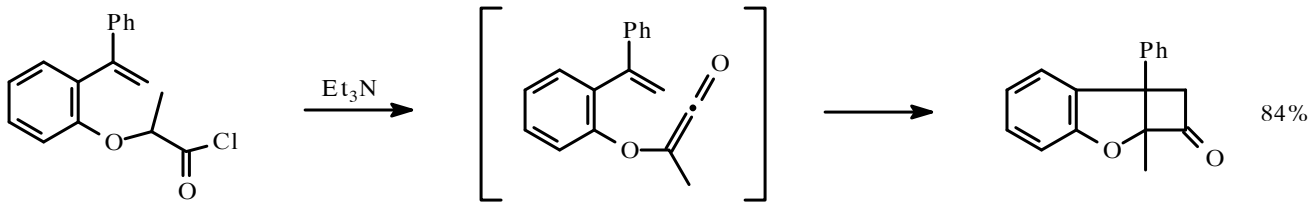
voluminozan supstituent: *endo*



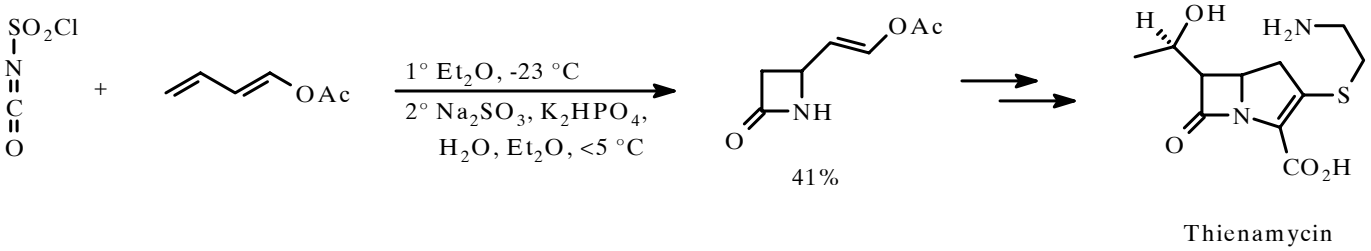




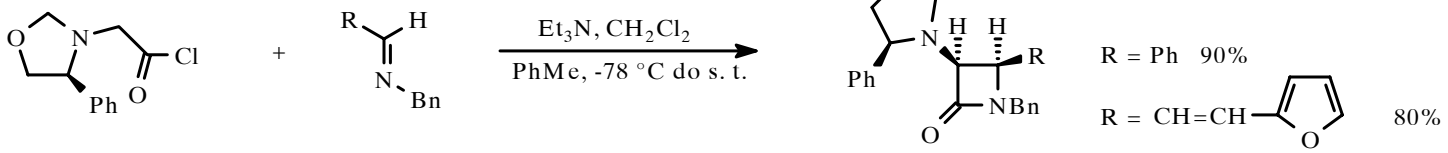


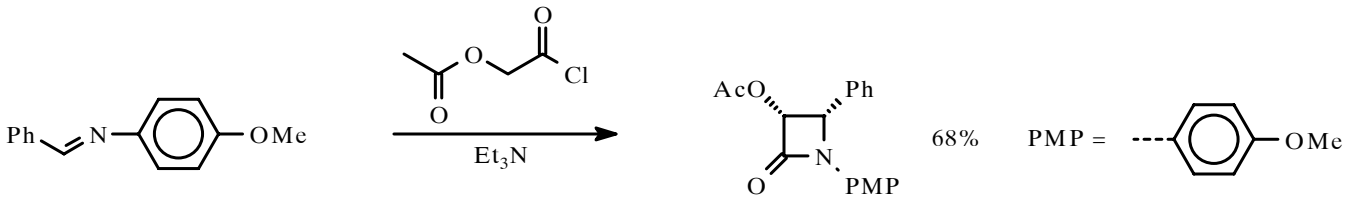


* Sinteze β-laktama

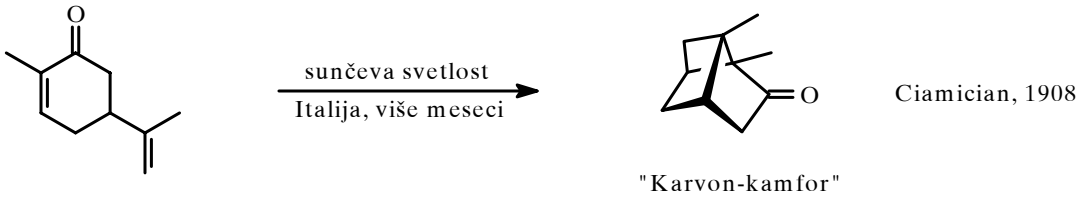


Thienamycin





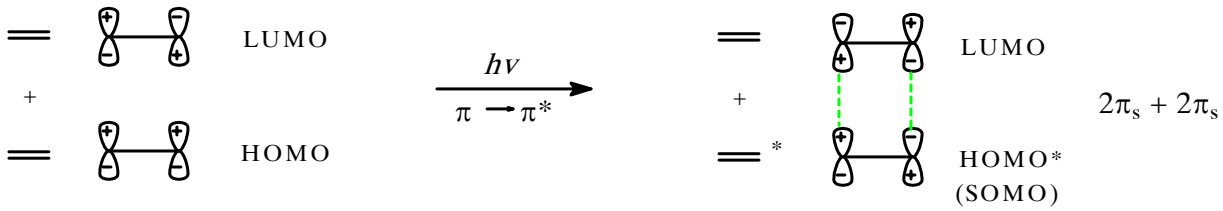
* Fotohemijske 2+2 cikloadicije

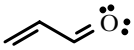


"Karvon-kamfor"

Ciamician, 1908

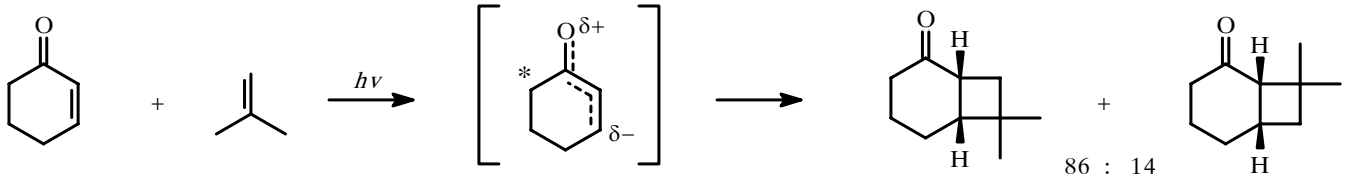
U pobuđenom stanju:

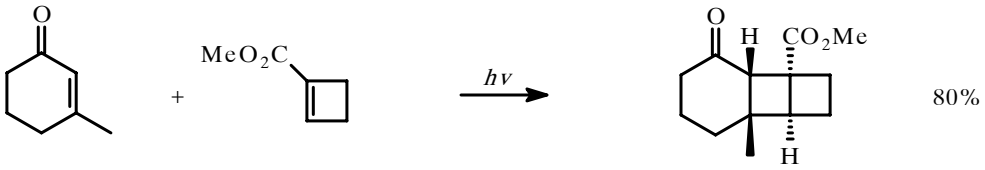


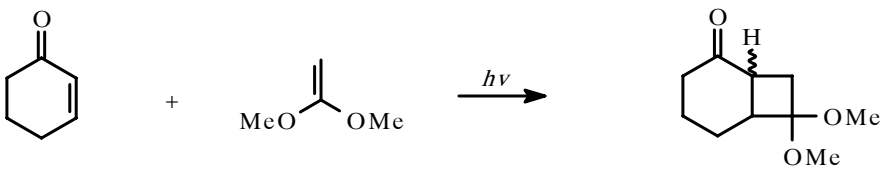


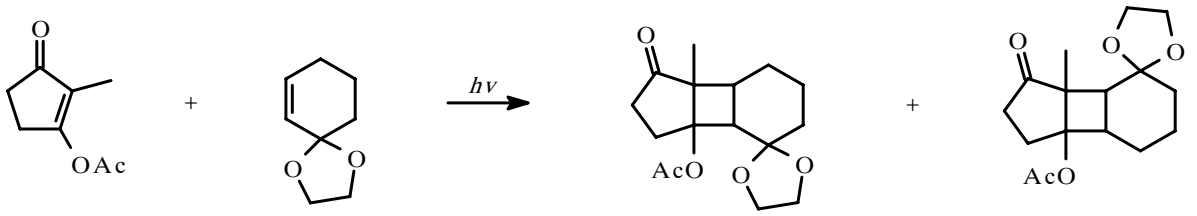
π → π* 210 nm kvarc >200 nm

n → π* 315 nm pyrex >280 nm



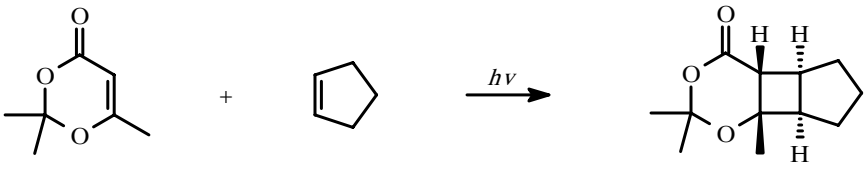


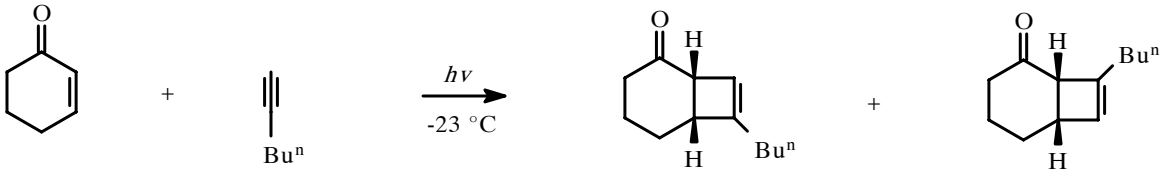




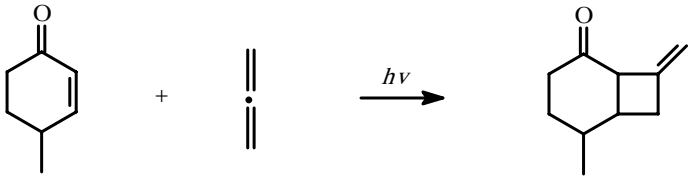
Uticaj rastvarača: cikloheksan 2 : 98

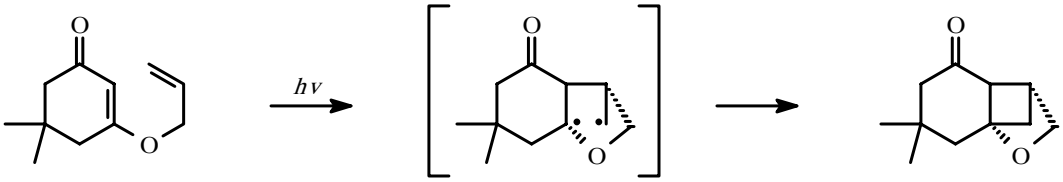
MeOH 55 : 45





1 : 9





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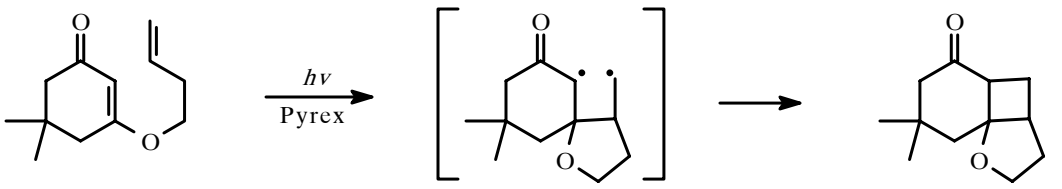
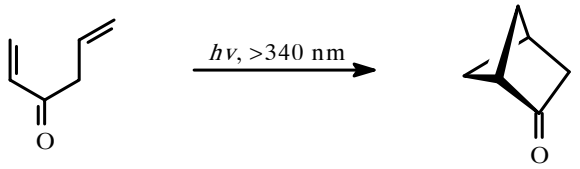
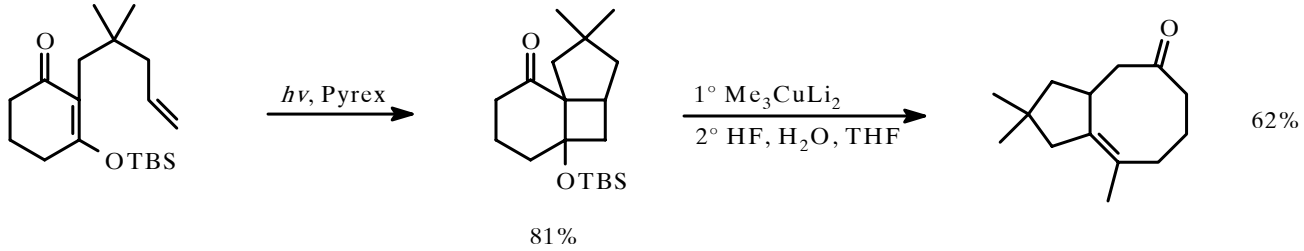
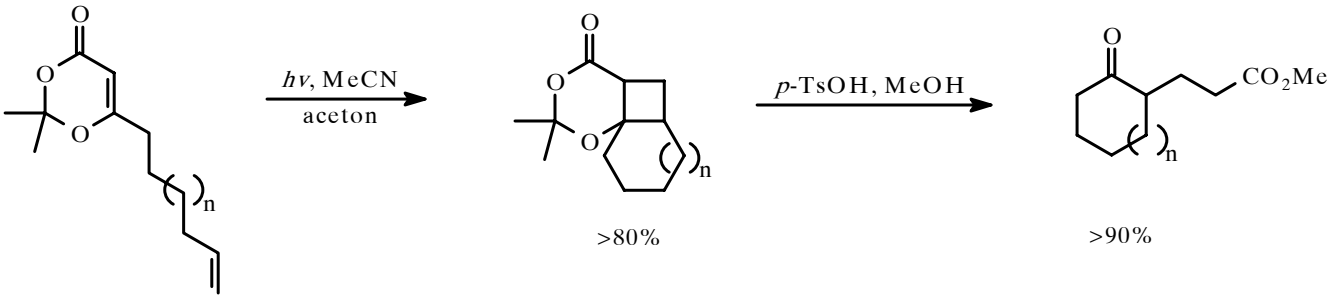
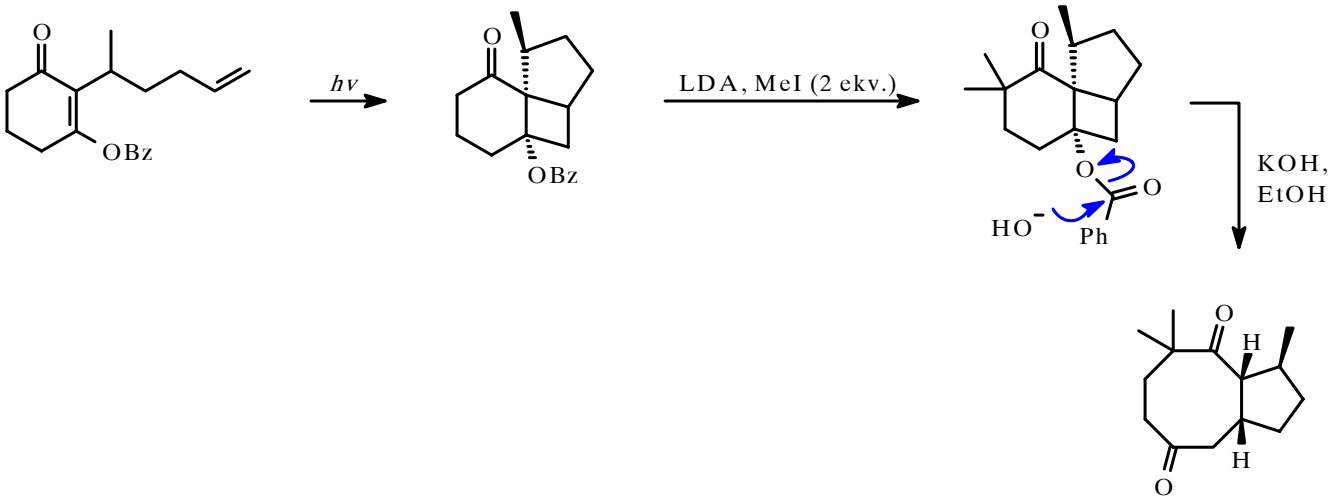


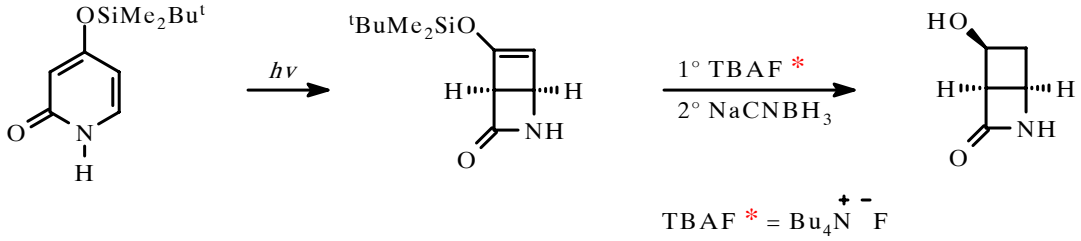
60%


hν, >340 nm
O
O

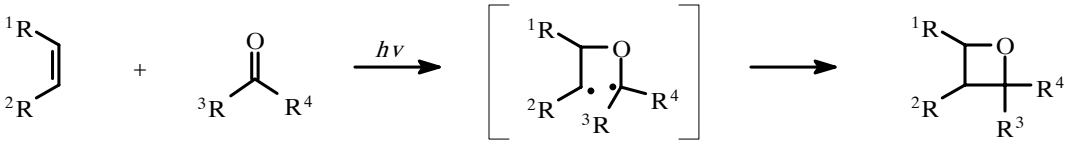

O
OTBS
hν, Pyrex
O
OTBS
81%
1° Me3CuLi2
2° HF, H2O, THF
O
62%

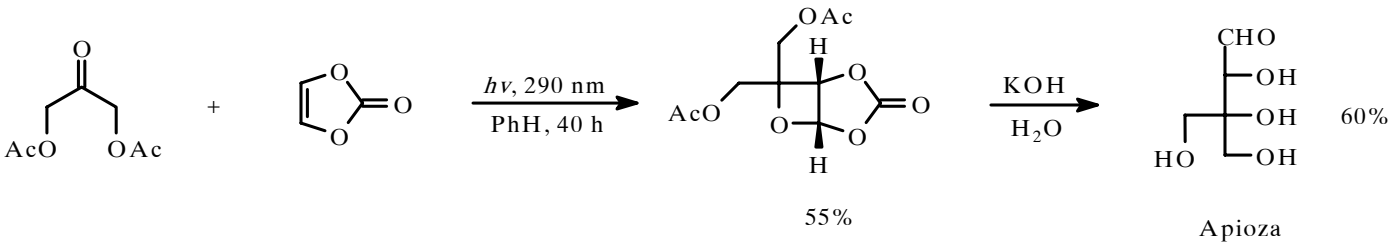

O
O
O
n
hν, MeCN
aceton
O
O
O
n
>80%
p-TsOH, MeOH
O
CO2Me
n
>90%

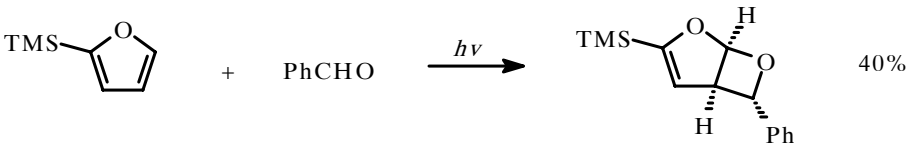

O
OBz
hν
O
OBz
LDA, MeI (2 ekv.)
O
O
O
HO
Ph
KOH,
EtOH
O
H
H
O

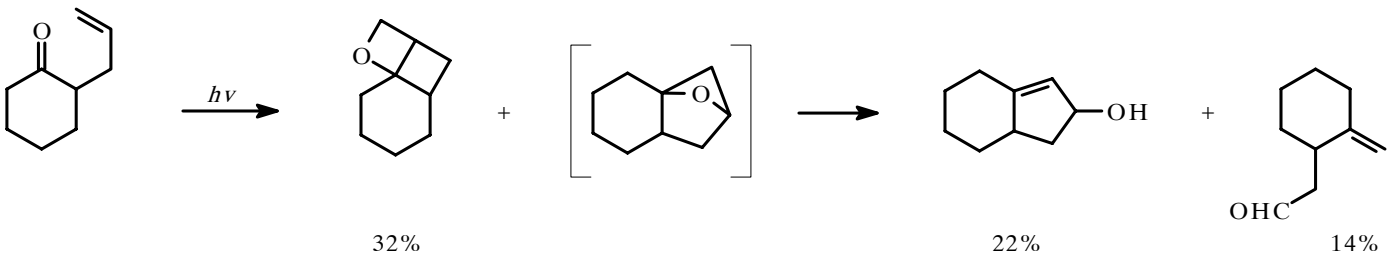

OSiMe2But
O
N
H
hν
tBuMe2SiO
H
H
NH
O
1° TBAF *
2° NaCNBH3
HO
H
H
NH
O

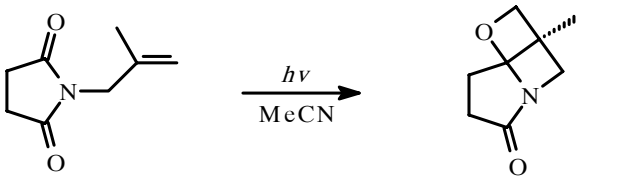
TBAF * = $Bu_4N^+F^-$


1R
2R
+
O
3R
R4
hv
1R
O
2R
3R
R4
1R
O
2R
R4
R3


O
AcO
OAc
+
O
O
O
hv, 290 nm
PhH, 40 h
OAc
H
AcO
O
O
O
O
H
55%
KOH
H2O
CHO
OH
OH
HO
OH
60%
Apioza


TMS
O
+
PhCHO
hv
TMS
O
H
O
H
Ph
40%


O
hv
O
+
O
OH
+
OHC
32%
22%
14%


O
N
O
hv
MeCN
O
N
O
100%