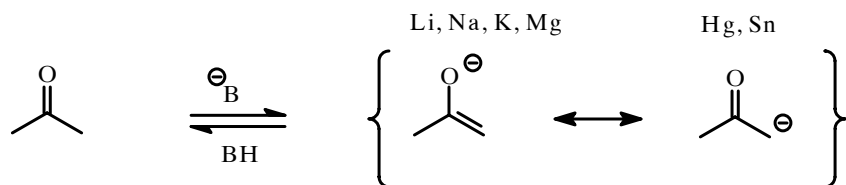
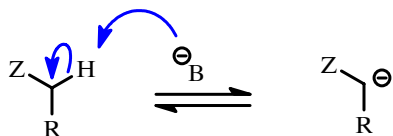
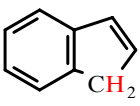

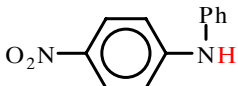


ALKILOVANJE

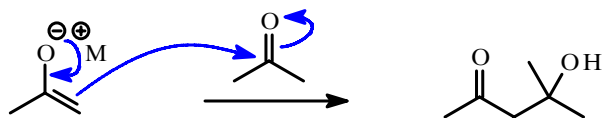
* STVARANJE ENOLATNIH ANJONA



Z : $-\text{NO}_2 > -\text{CR} > -\text{SO}_2\text{R} > -\overset{\text{O}}{\parallel}{\text{C}}-\text{OR} > -\text{CN} > -\text{SOR} > -\text{Ph}$

Jedinjenje	pKa	Jedinjenje	pKa	Jedinjenje	pKa
$\text{CH}_2(\text{NO}_2)_2$	4	$\text{Ph}-\text{CH}_2-\text{CO}-\text{Ph}$	16	$\text{HC}\equiv\text{CH}$	25
CH_3COOH	5	MeOH	16-18	PhNH_2	27
$\text{CH}_2(\text{CN})\text{CO}_2\text{Et}$	9	$\text{CH}_3\text{COCH}_2\text{Cl}$	17	Ph_3CH	28-33
$\text{CH}_2(\text{COCH}_3)_2$	9	EtOH	18	Ph_2CH_2	33-35
$\text{CH}_3\text{CH}_2\text{NO}_2$	9	$i\text{-PrOH}$	18	$\text{CH}_3-\text{SO}-\text{CH}_3$	35
$\text{Me}_3\text{NH}^{\oplus}$	10	$t\text{BuOH}$	19	NH_3	35
PhOH	10	PhCOCH_3	19	Ph_2NH	36
CH_3NO_2	10	CH_3COCH_3	20	PhCH_3	37
$\text{CH}_3\text{COCH}_2\text{CO}_2\text{Et}$	11		21	$\text{H}_2\text{C}=\text{CHCH}_3$	38
$\text{CH}_3\text{CH}(\text{COCH}_3)_2$	11	Et_2NH	21		
$\text{CH}_2(\text{CN})_2$	11	$\text{Me}_3\text{C}-\text{CO}-\text{CH}_3$	21		
$\text{CH}_2(\text{CO}_2\text{Et})_2$	13	$\text{Me}_3\text{C}-\text{CO}-\text{CHMe}_2$	23		
	15	$\text{CH}_3-\text{SO}_2-\text{CH}_3$	23-27		
H_2O	16	$\text{CH}_3\text{CO}_2\text{Et}$	25		
	16	CH_3CN	25		

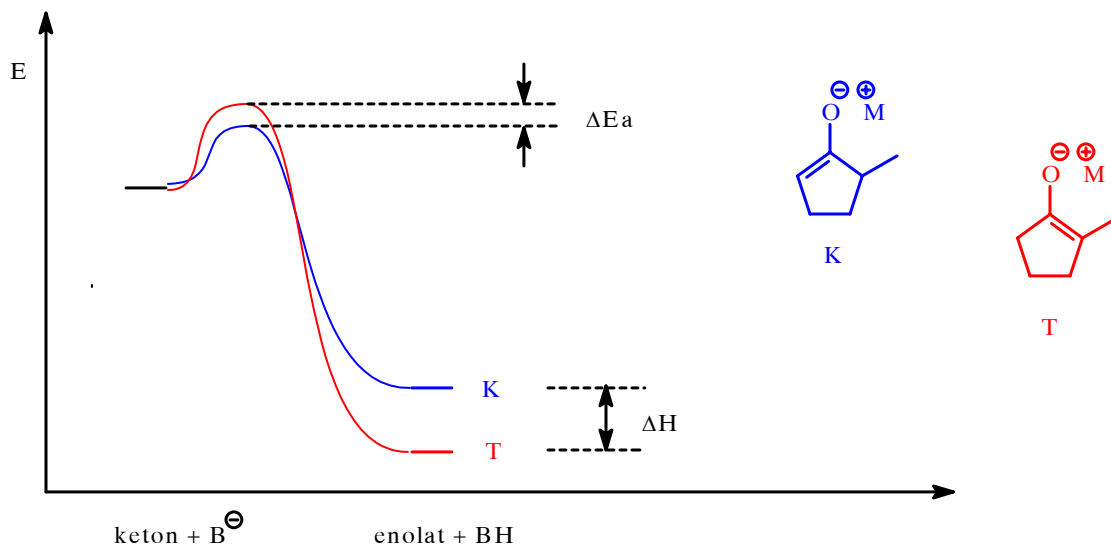
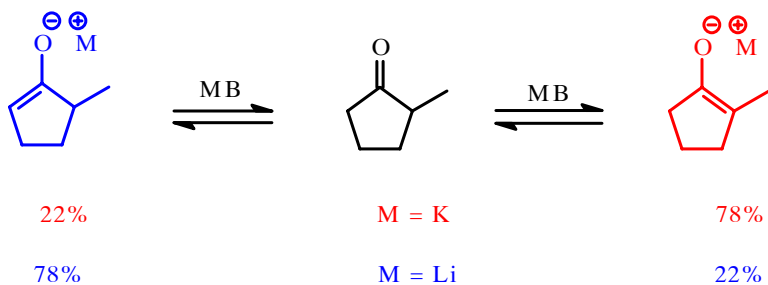
Sporedna reakcija: samokondenzacija



Deprotonovanje nesimetričnih ketona

* Kinetički i termodinamički enolat

* Uticaj metalnog katjona



Kinetički uslovi:

* niska T (-78 °C)

* višak baze

* nema H-donora

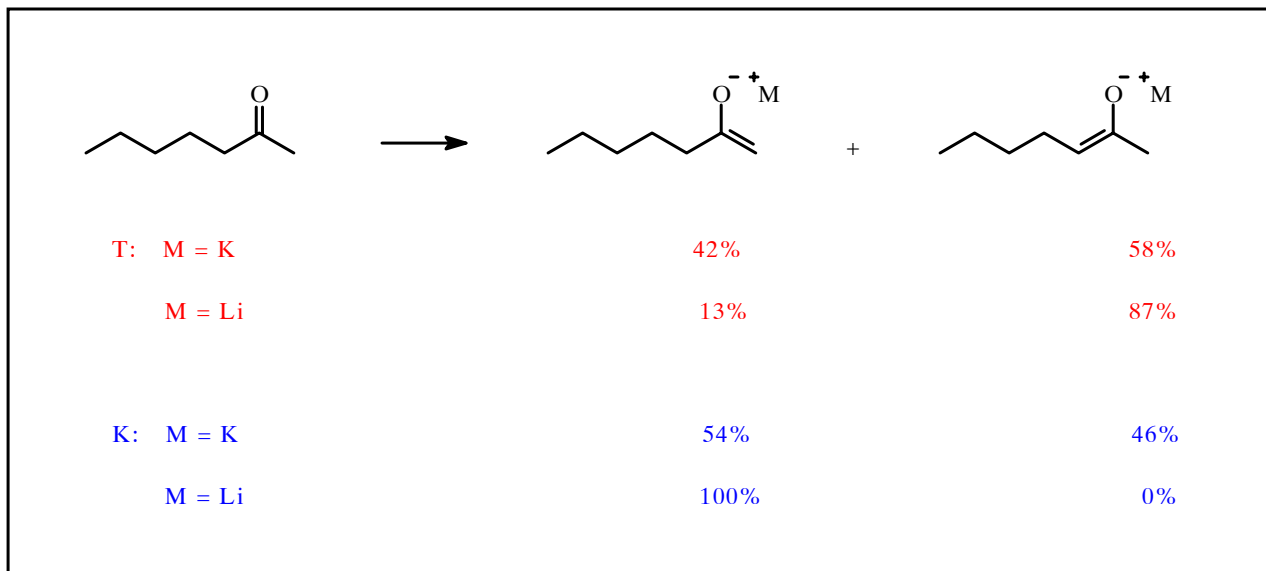
* Li⁺ kao metalni jon

Termodinamički uslovi:

* viša T (s. t.)

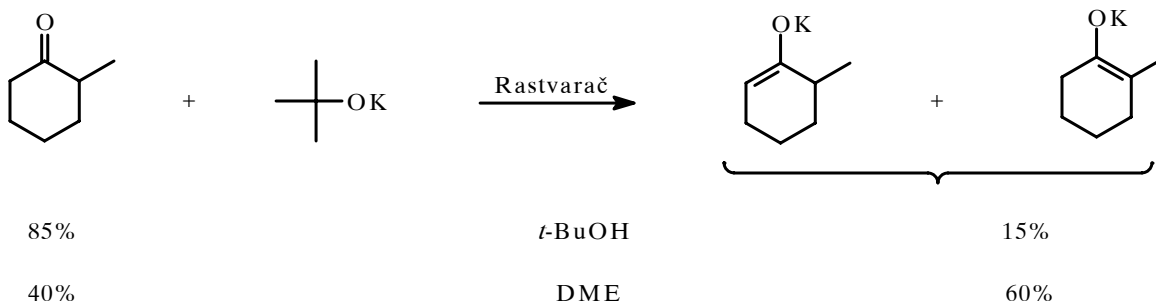
* višak ketona ili prisustvo H-donora

* Na⁺ ili K⁺ kao metalni joni



BAZE

R-OM / R-OH za ketone: OK / OH

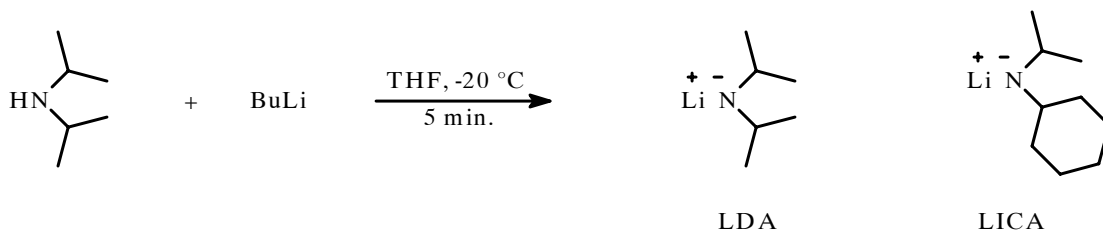


NaH / THF, benzen: Jaka baza, ali nerastvorna

NaNH₂ / NH₃ + Et₂O: Problem rastvorljivosti supstrata u NH₃, moguće sporedne reakcije u NH₃

Ph₃CLi, Ph₃CK

LDA, LICA: Jake, nenukleofilne, rastvorne baze

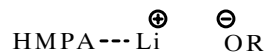
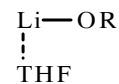
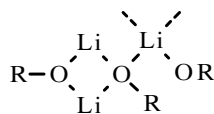


Uticaj rastvarača

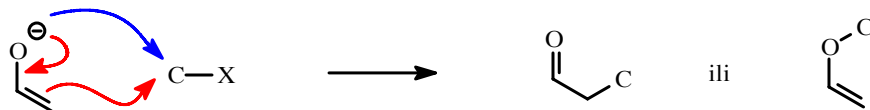
Nepolarni rastvarači: agregacija, polimeri

THF, DME (σ -donori): monomeri, reaktivni enolati

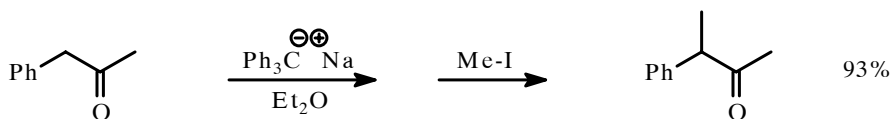
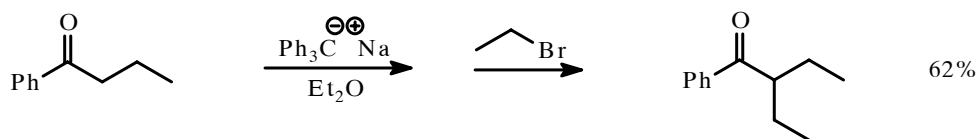
DMF, DMSO, HMPA (π -donori): visoko-reaktivni, razdvojeni jonski parovi



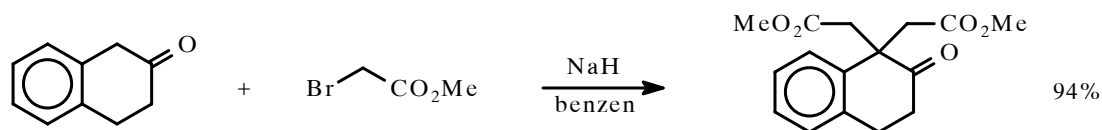
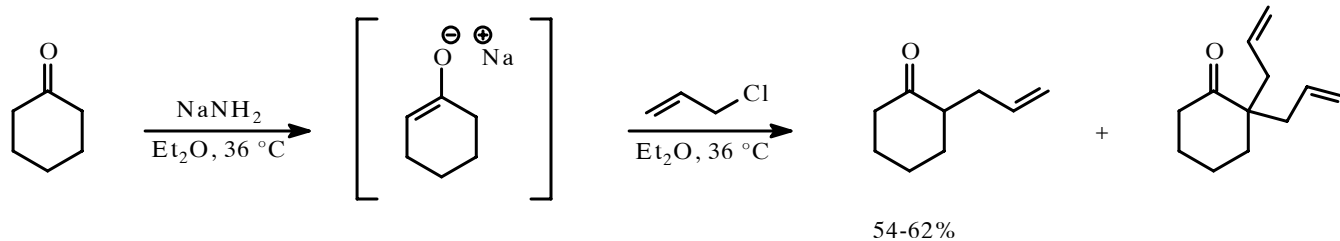
Ambifilan karakter enolata (O- i C-alkilovanje)



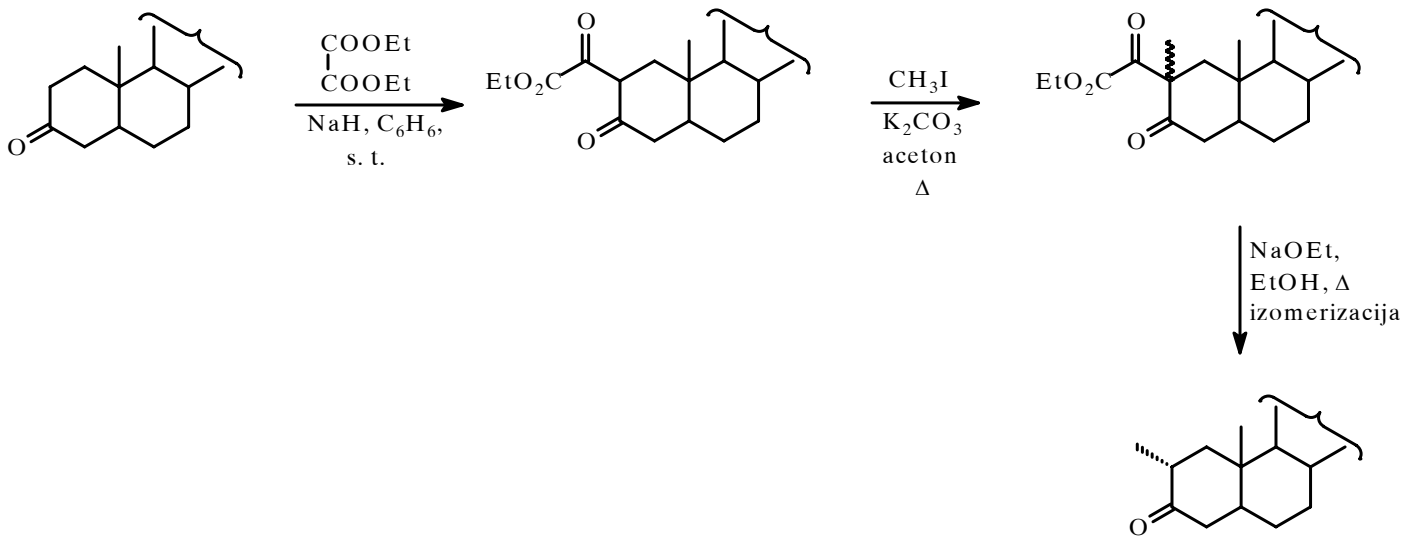
Alkilovanje ketona



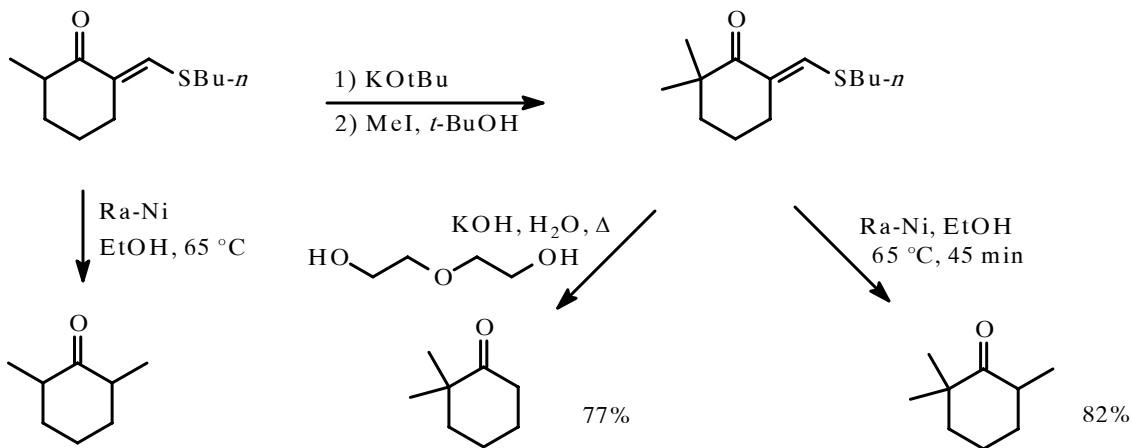
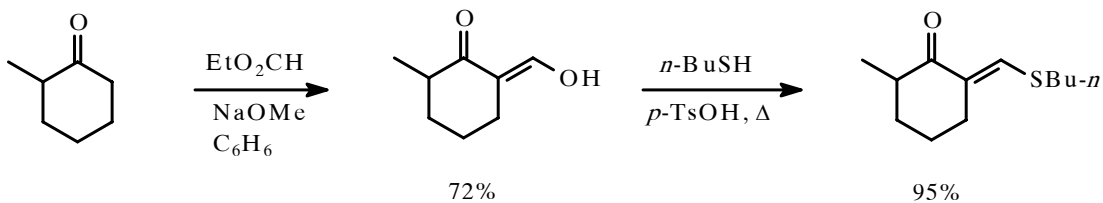
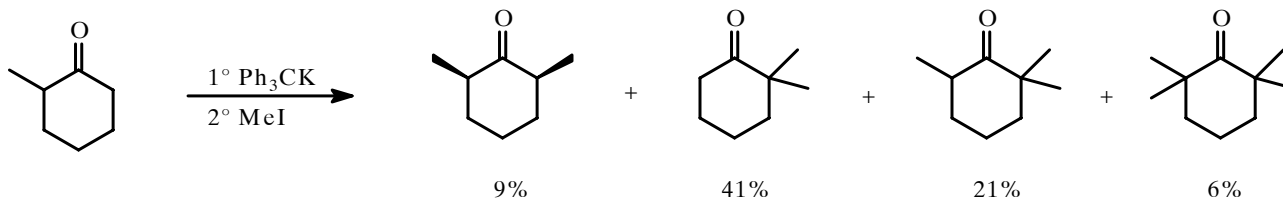
Problem polialkilovanja



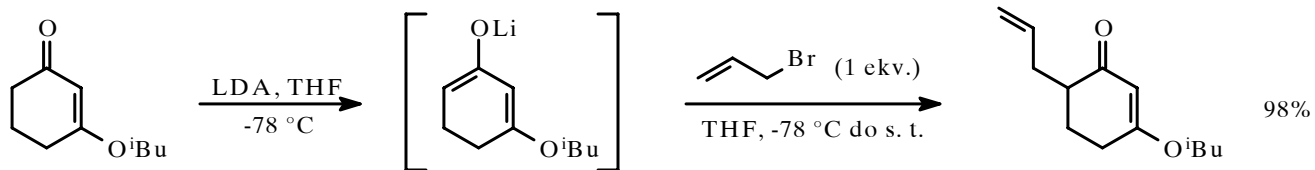
* Aktiviranje α -položaja



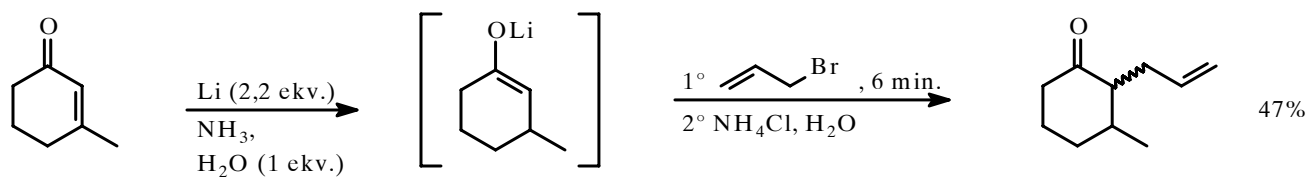
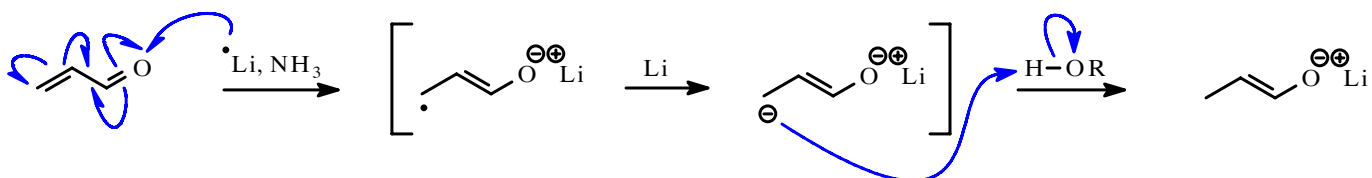
* Blokada α' -položaja



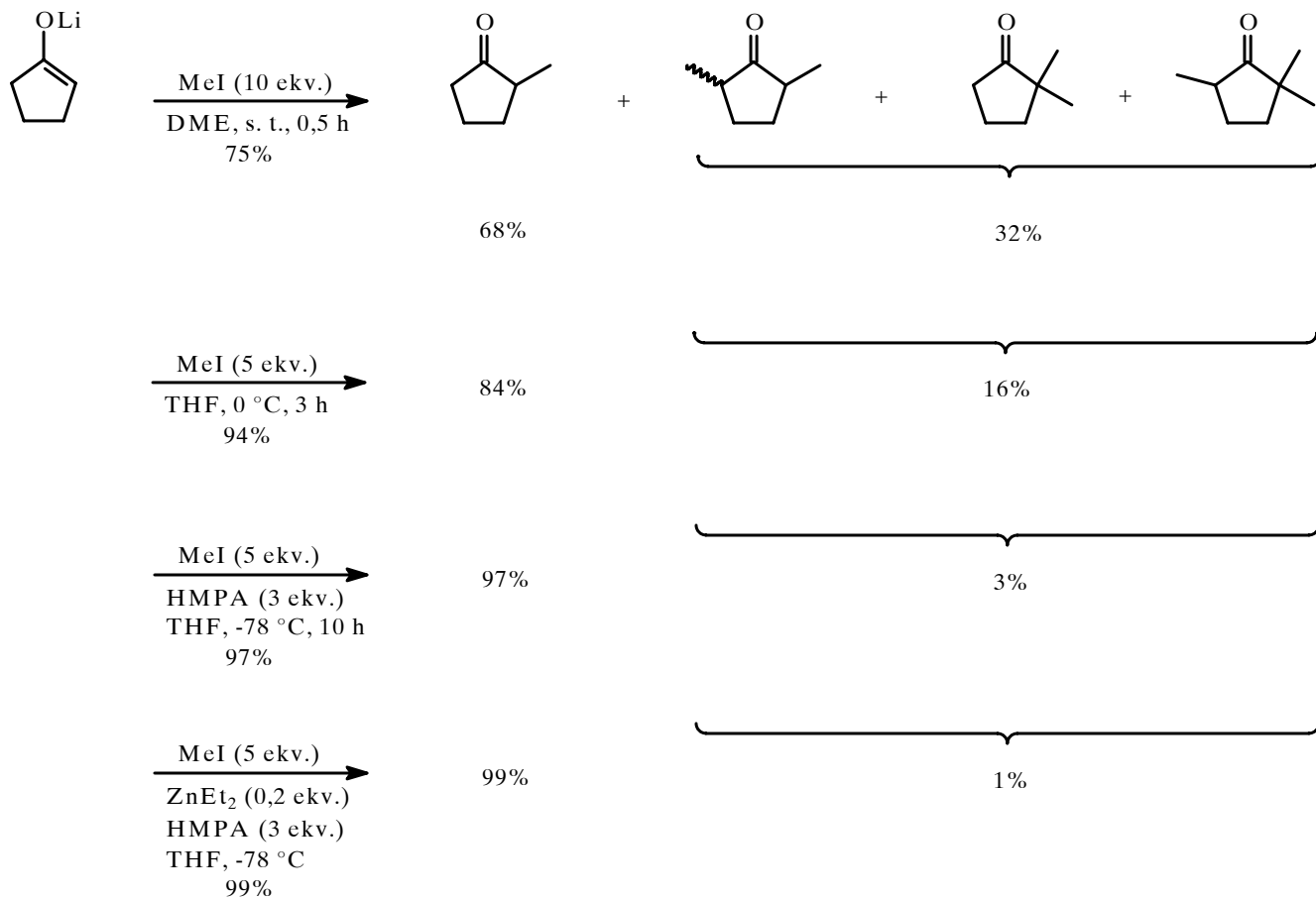
Alkilovanje enona



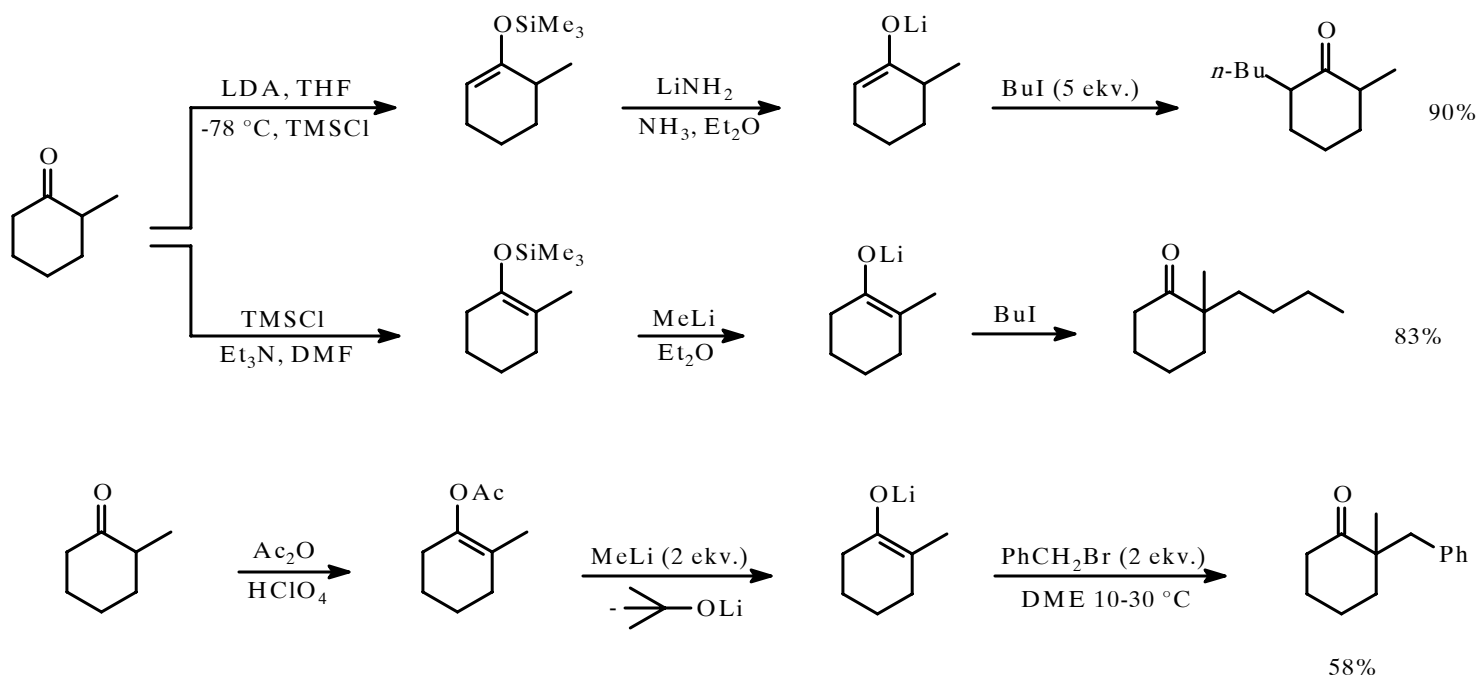
Regioselektivno stvaranje enolata 1,4-redukcijom enona



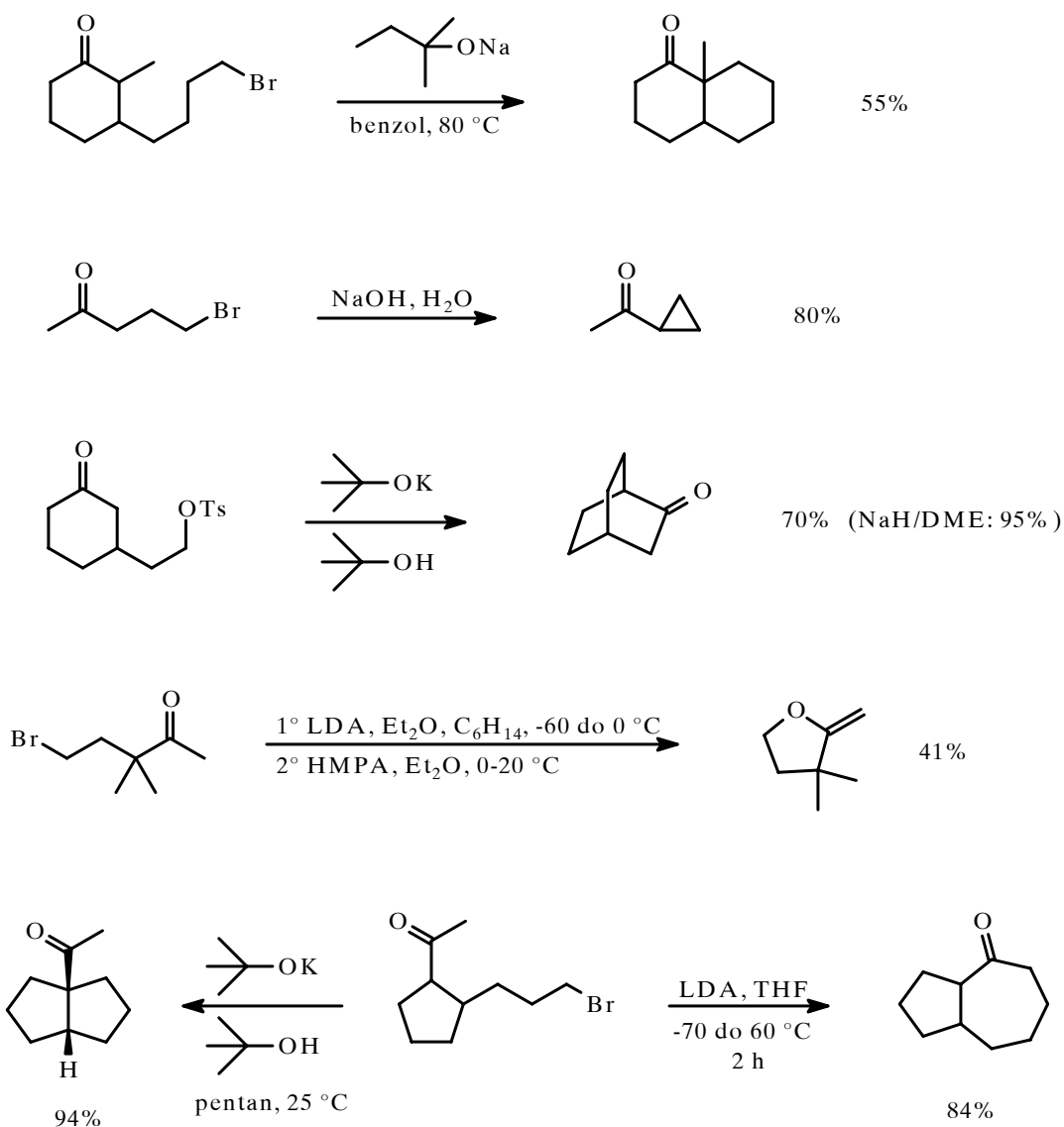
Uticaj reakcionih uslova na reaktivnost kinetičkog enolata



* Selektivno građenje enolata (indirektne metode)



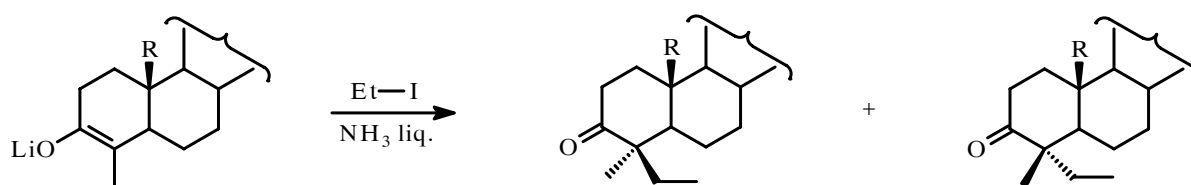
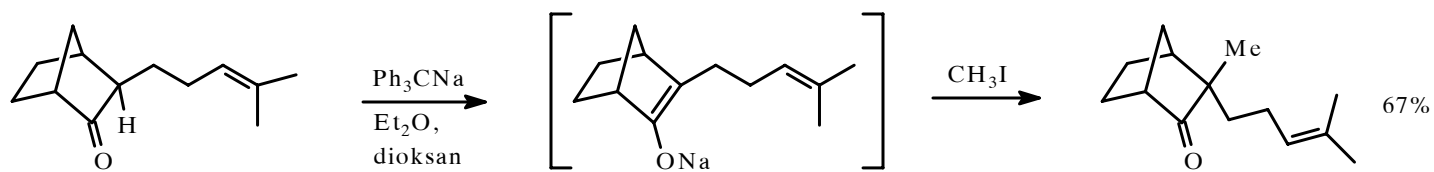
Intramolekulsko alkilovanje



* Stereoselektivnost alkilovanja na cikličnim sistemima

* Napad sa sterno manje zaštićene strane

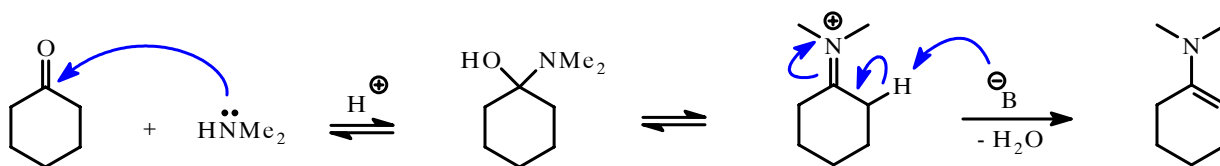
* Na cikloheksanonskim enolatima: aksijalni napad obično pre nego ekvatorijalni



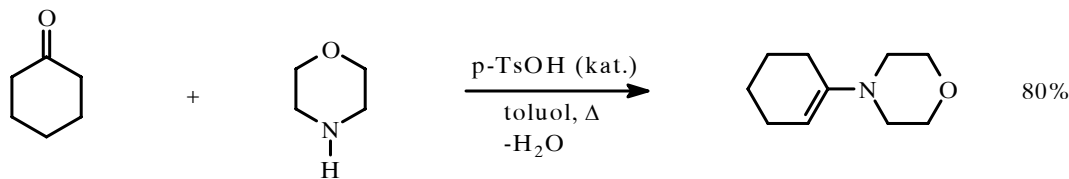
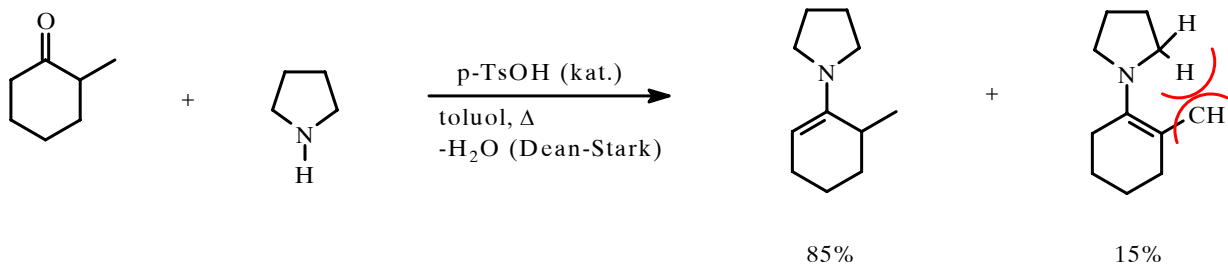
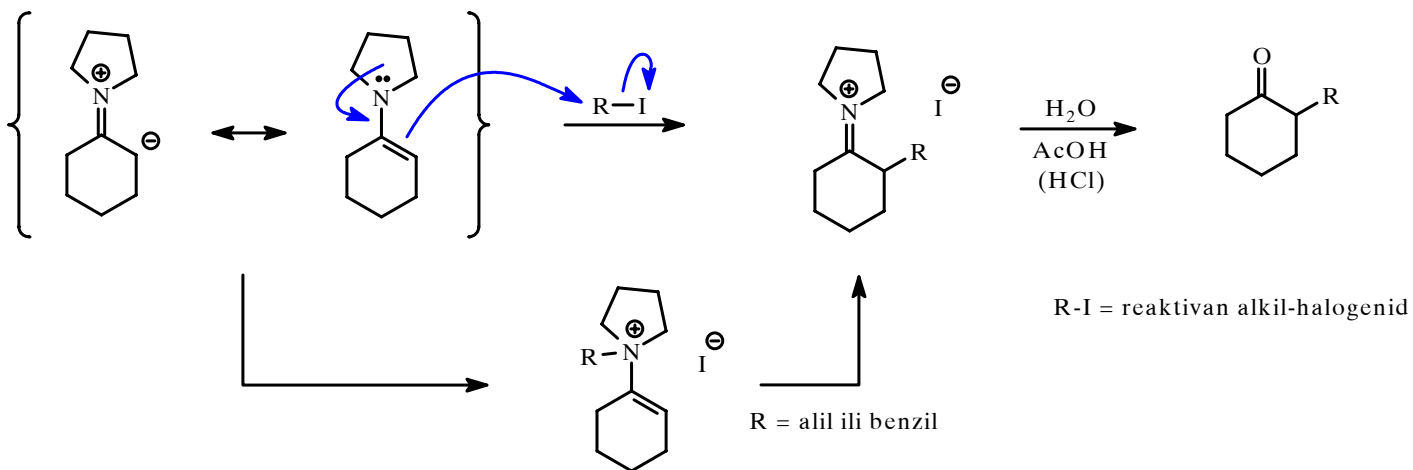
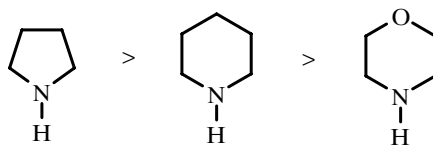
$\text{R} = \text{H}$ 95% 5%

$\text{R} = \text{Me}$ 5% 95%

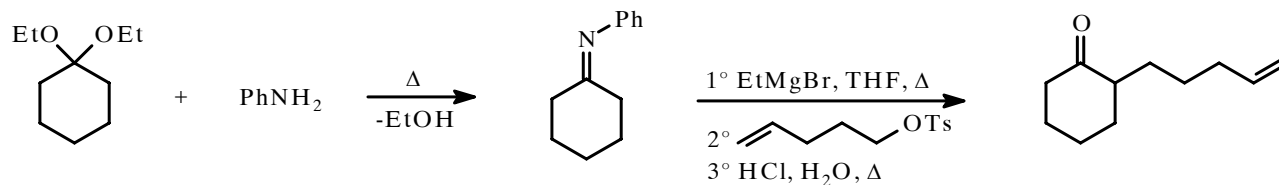
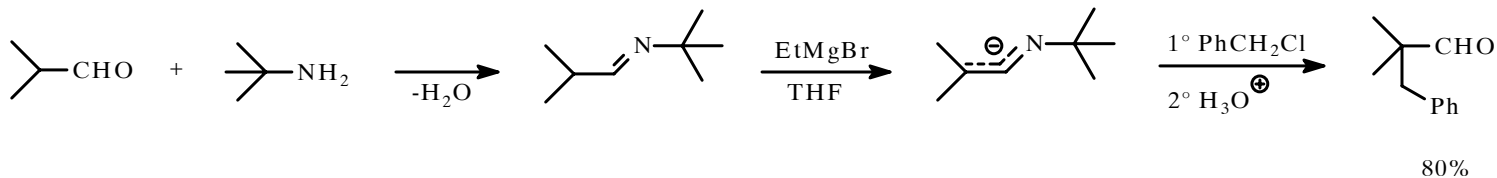
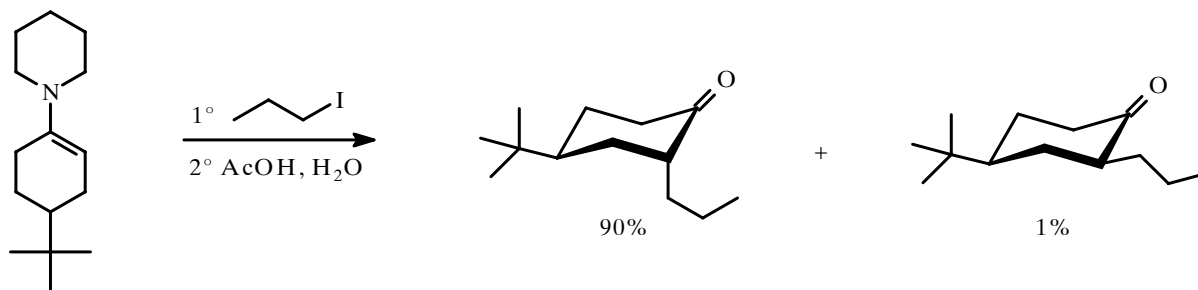
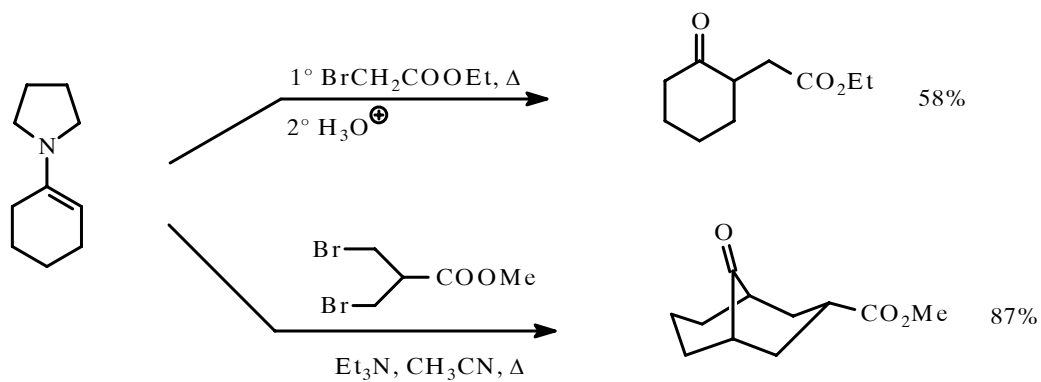
ALKILOVANJE ENAMINA



Najčešće korišćeni amini (poređani po reaktivnosti):

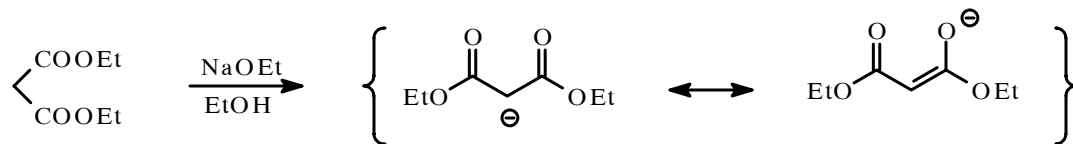


* Rastvarači: toluen, dioksan, acetonitril,....

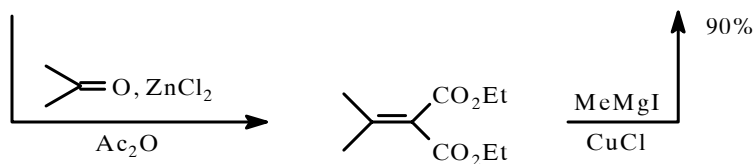
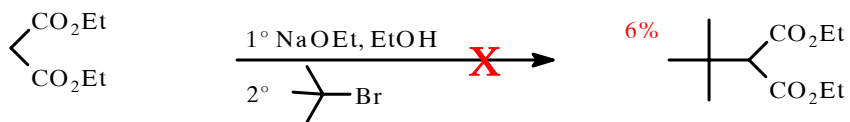
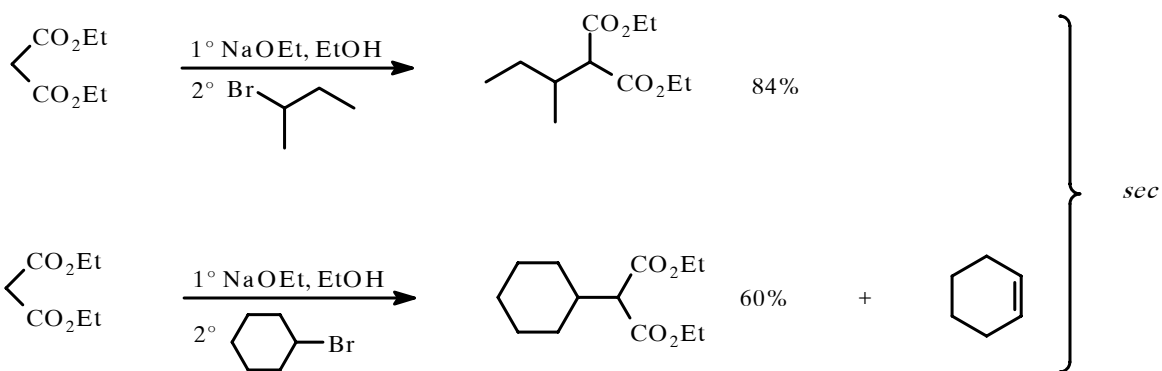
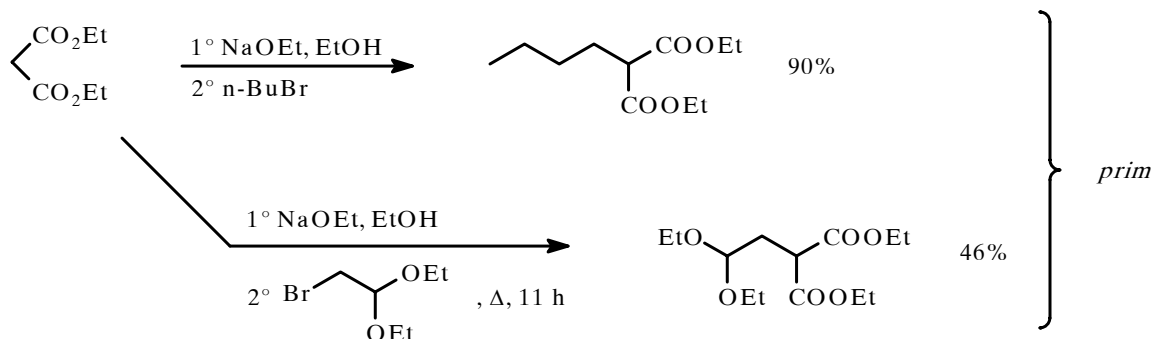


ALKILOVANJE BIFUNKCIONALNIH JEDINJENJA

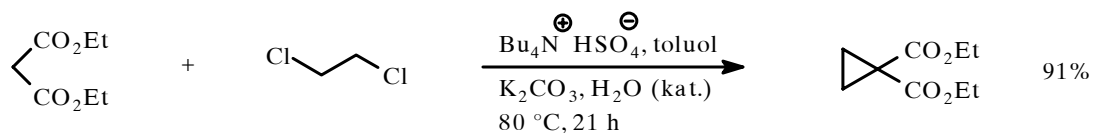
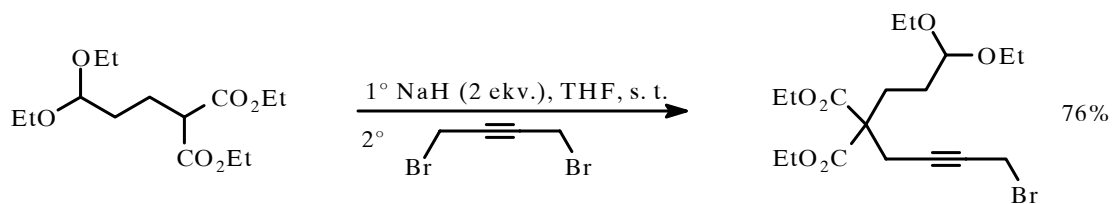
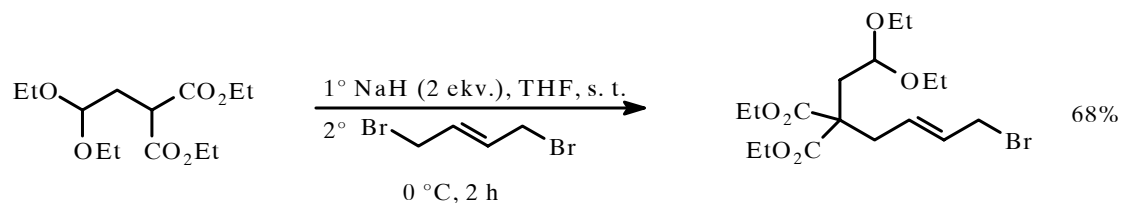
*MALONSKI ESTAR



* Monoalkilovanje

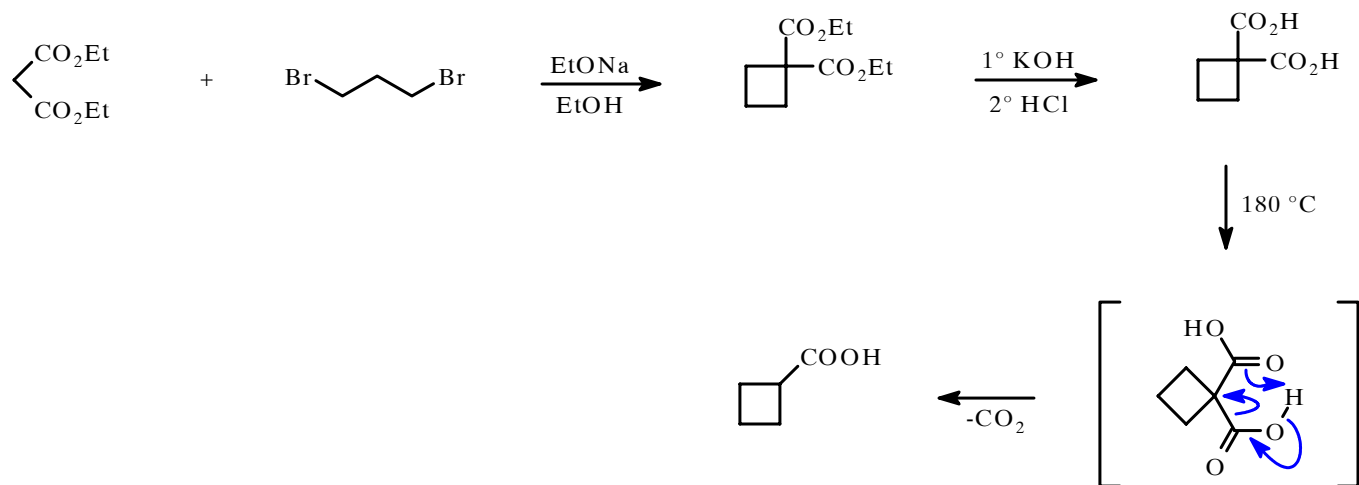


* Dialkiloanje

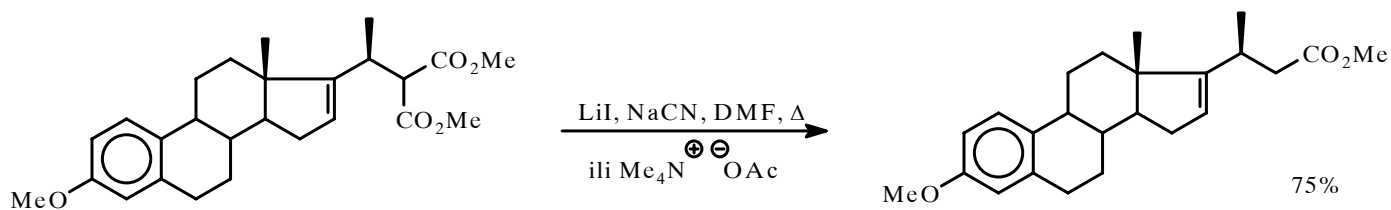
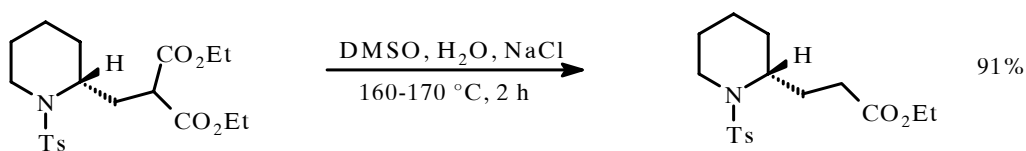
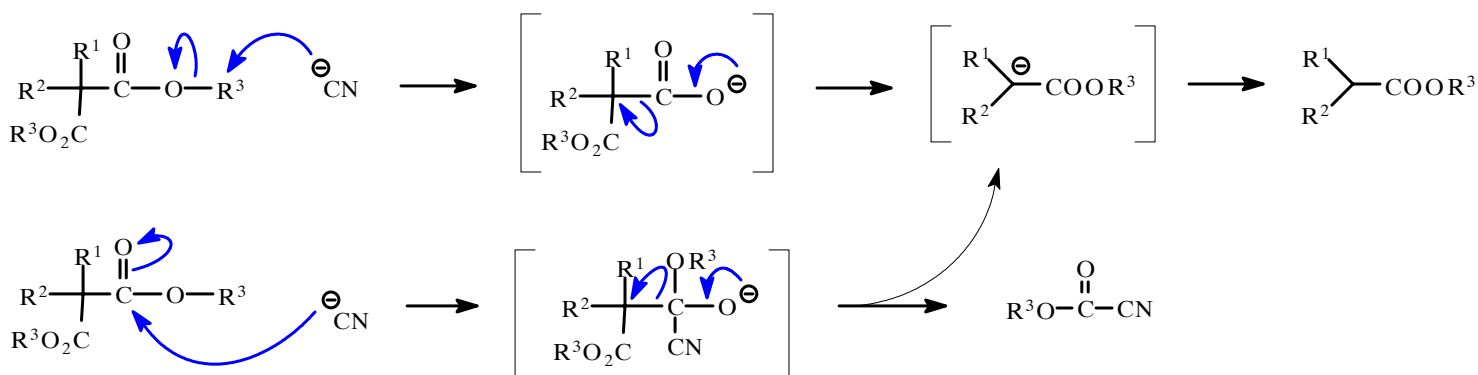
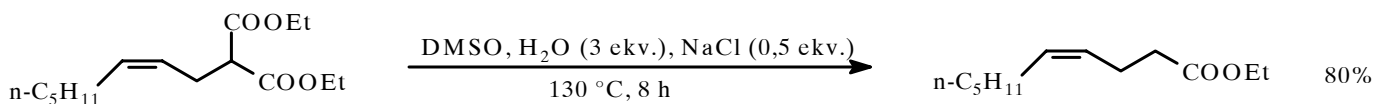
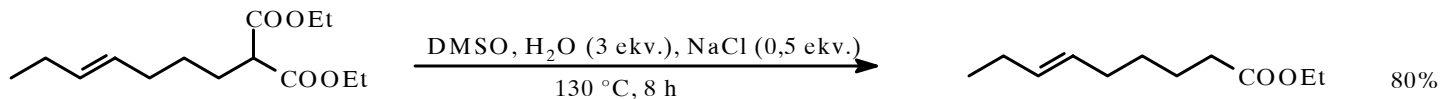


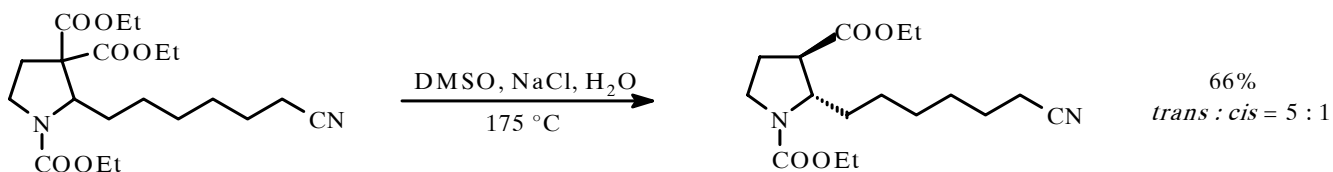
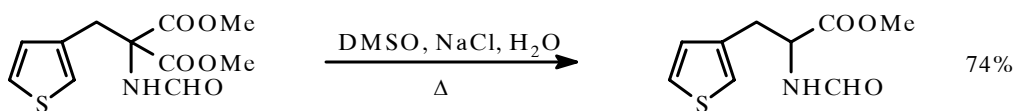
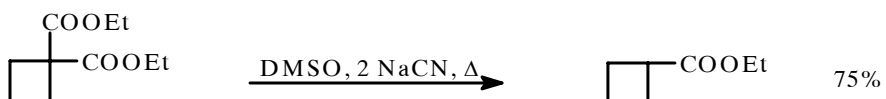
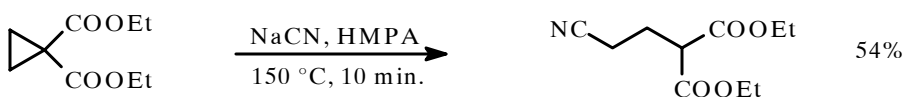
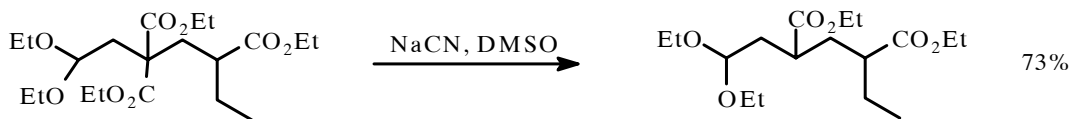
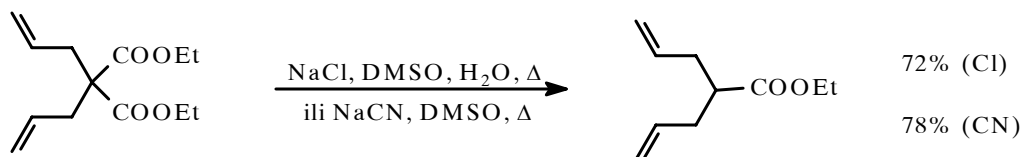
* Transformacije malonskih estara

* Hidroliza/dekarboksilacija

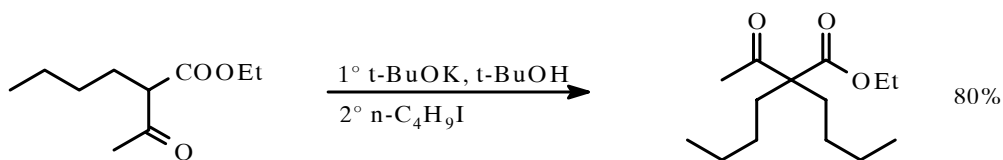
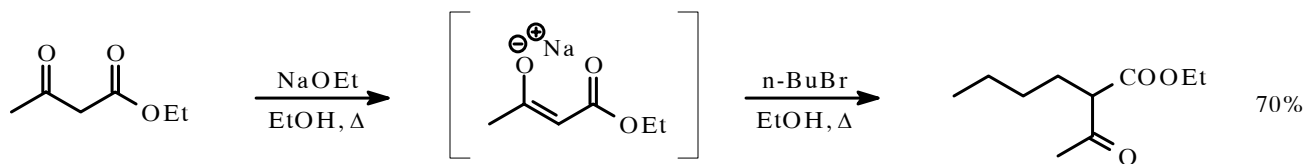


* Dealkoksikarbonilovanje u aprotičnim rastvaračima





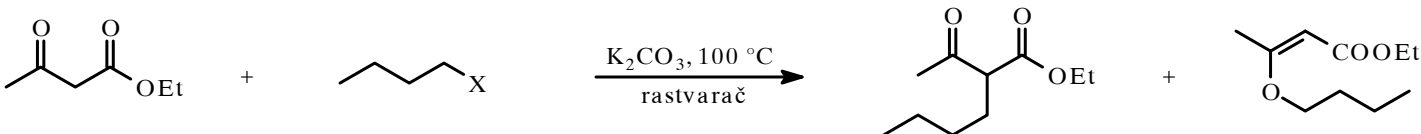
ALKILOVANJE I TRANSFORMACIJE ACETSIRČETNOG ESTRA



Ambifilan karakter acetoacetatnog enolata: *C*-alkilovanje i *O*-alkilovanje

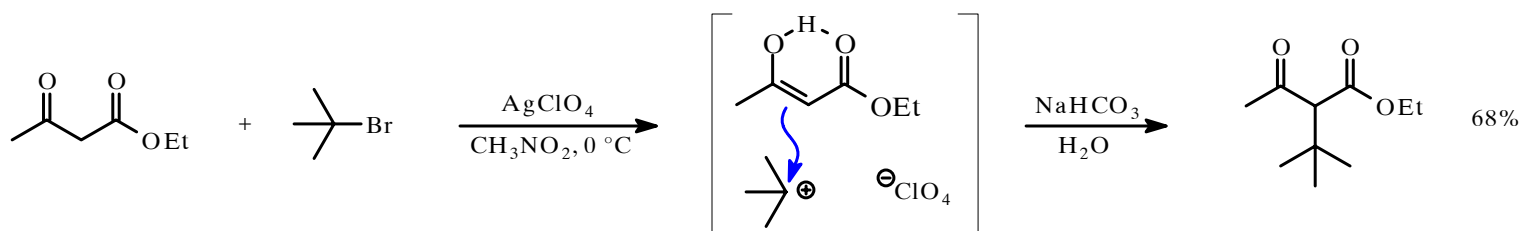
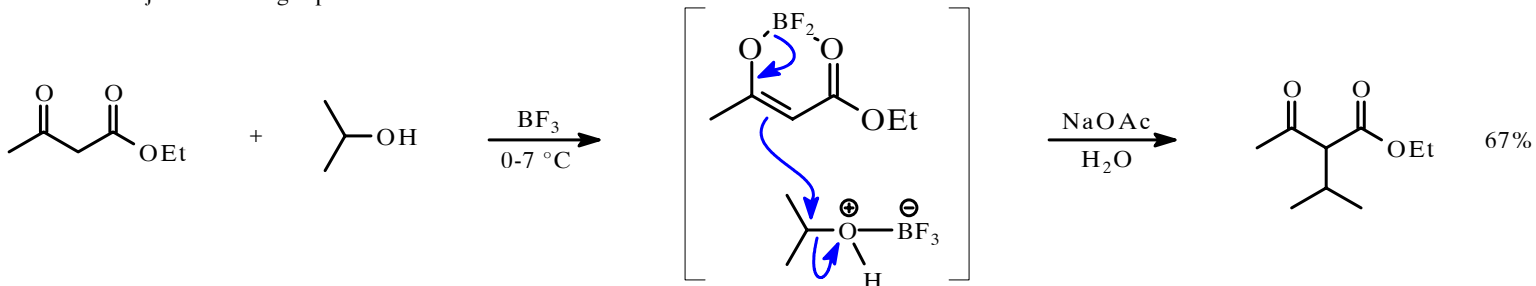
* *O*-alkilovanje: $\text{K} > \text{Na} > \text{Li}$; $\text{Cl} > \text{Br} > \text{I}$; $\text{DMSO, HMPA} > \text{THF}$; voluminozni alkil-halogenidi

* Alilni i benzilni halogenidi obično daju proizvode *C*-alkilovanja

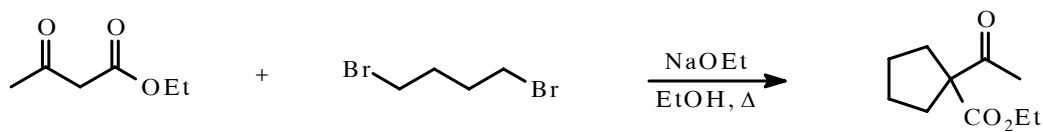


X	Rastvarač	% <i>C</i> -alkil.	:	% <i>O</i> -alkil.
Cl	acetone	90	:	10
Cl	CH ₃ CN	81	:	19
Cl	DMSO	53	:	47
Br	DMF	67	:	33
I	DMF	>99	:	<1

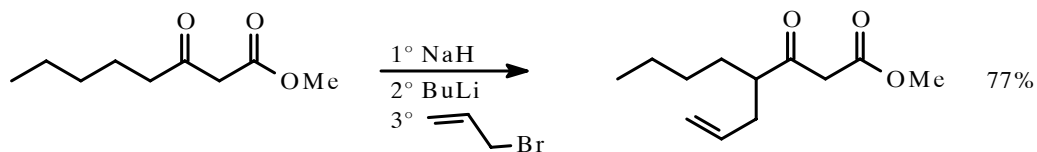
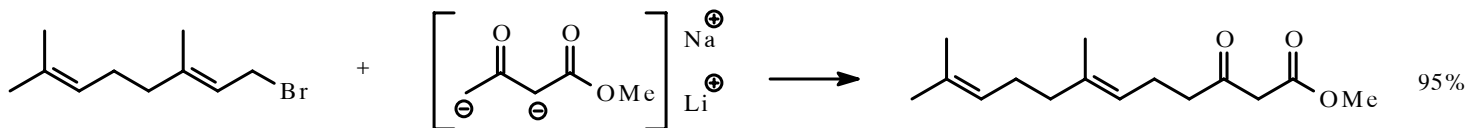
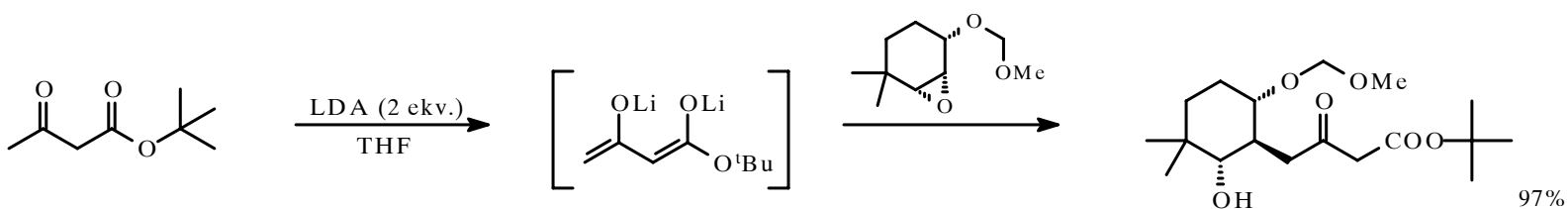
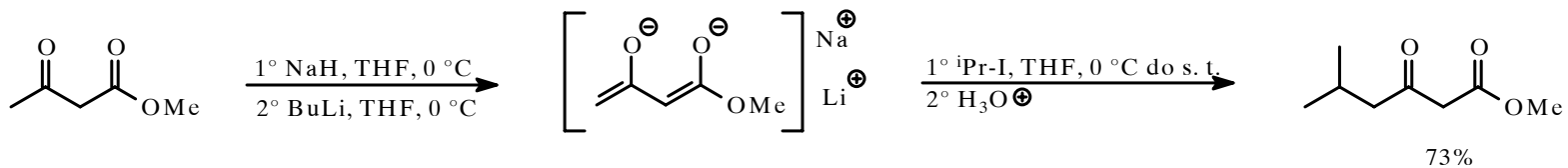
* Alkilovanje *sec* i *tert* grupama u kiselim uslovima



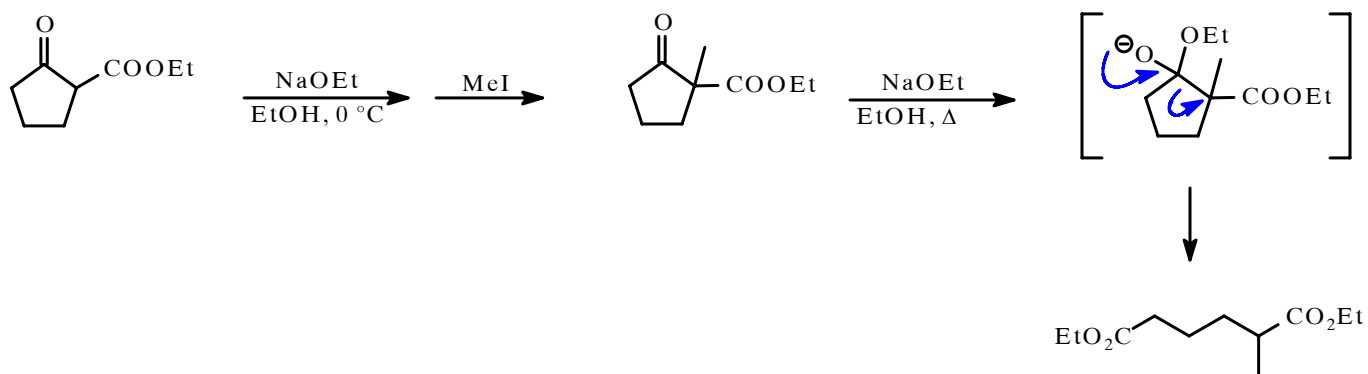
* Intramolekulsko alkilovanje

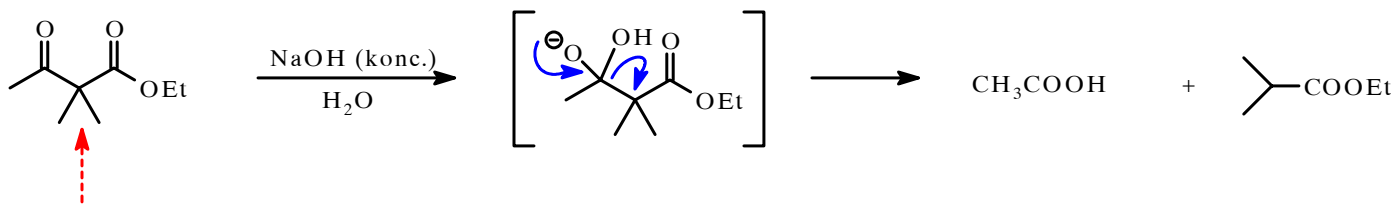


* γ -Alkilovanje dianjona

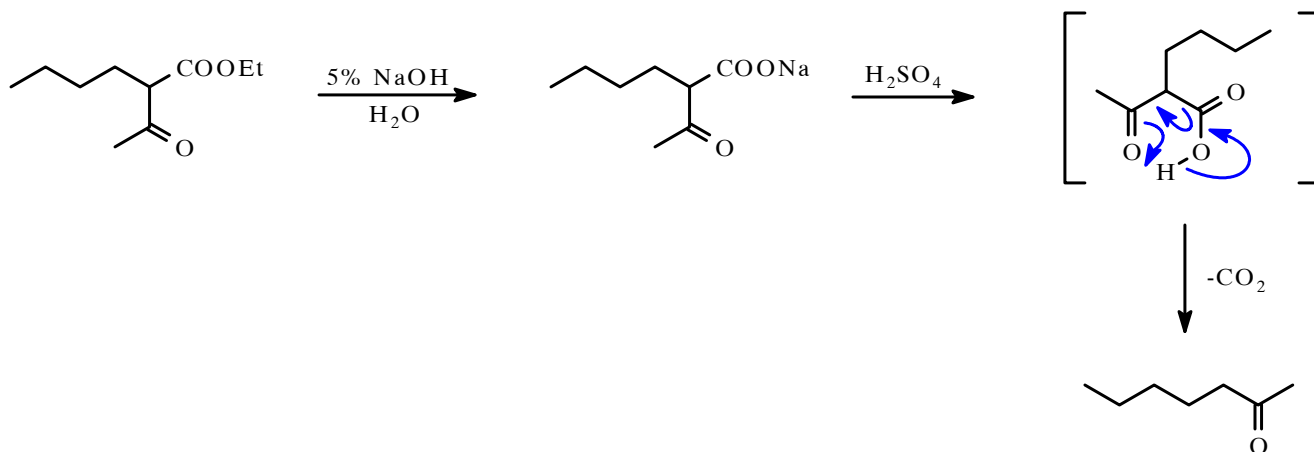


* Transformacije acetoacetatnih estara



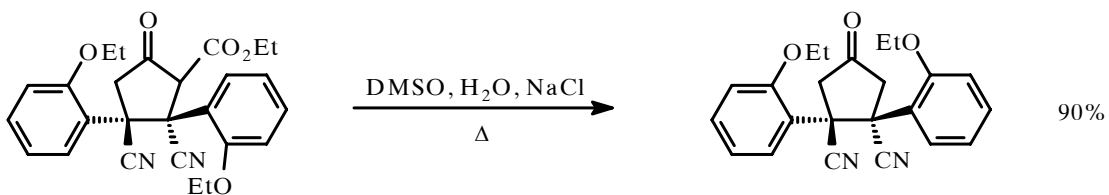
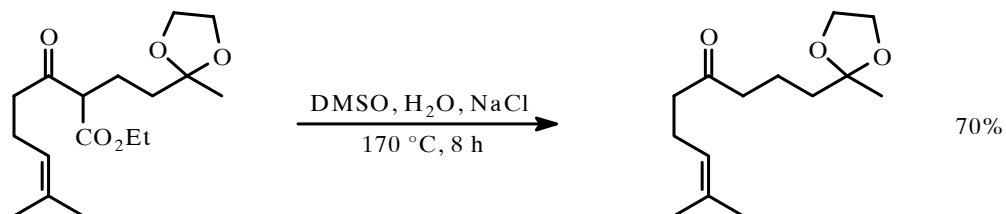
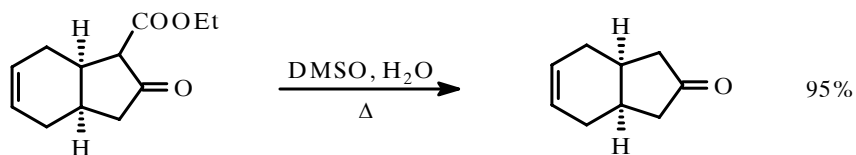


Enolizabilni estri (α -H) reaguju mnogo sporije

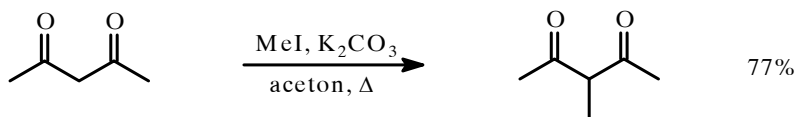


Dealkoksilovanje β -ketoestara u DMSO

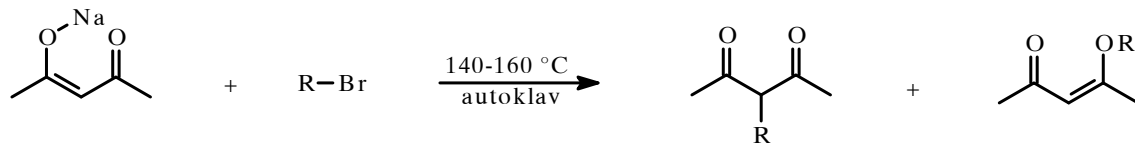
Synthesis **1982**, 893 (2^o deo)



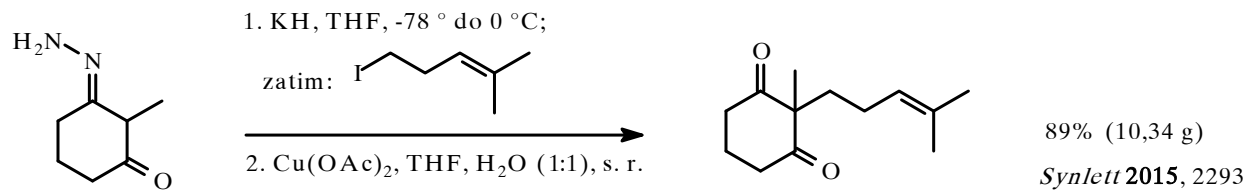
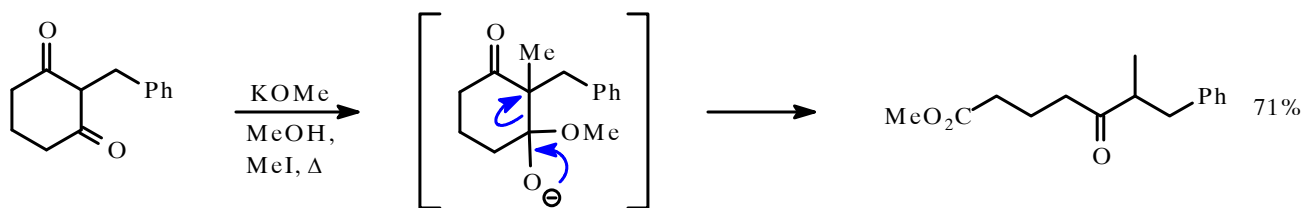
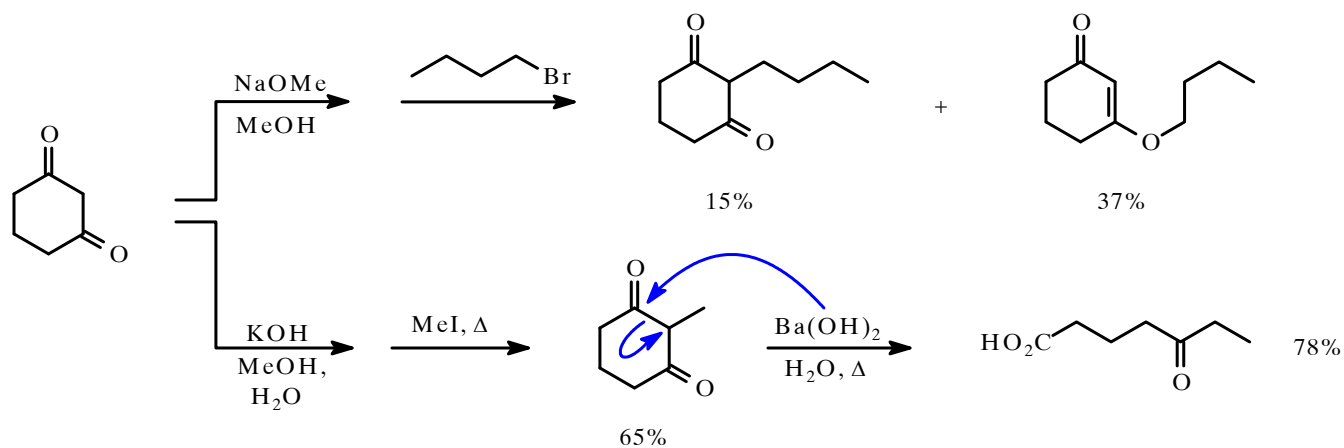
Alkilovanje 1,3-dikarbonilnih jedinjenja



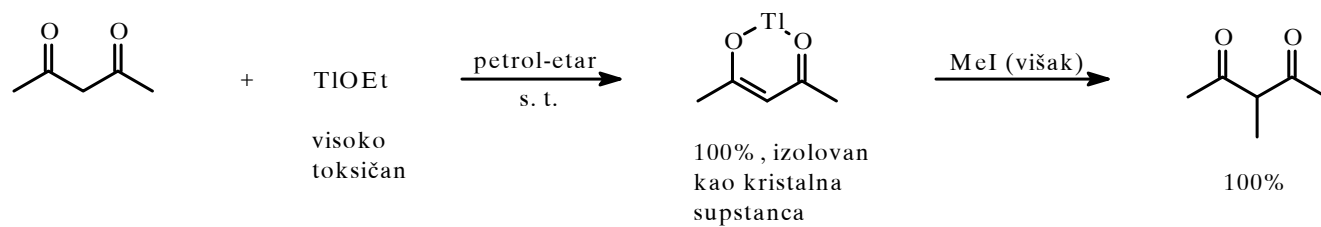
O-alkilovanje (veliki katjon, polaran rastvarač, X = Cl, voluminozan R-X)



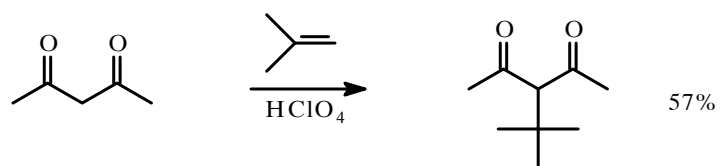
R = *n*-Pr 97 : 3
 R = *i*-Pr 73 : 27



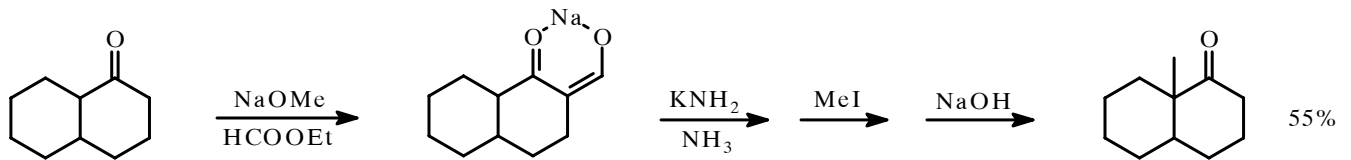
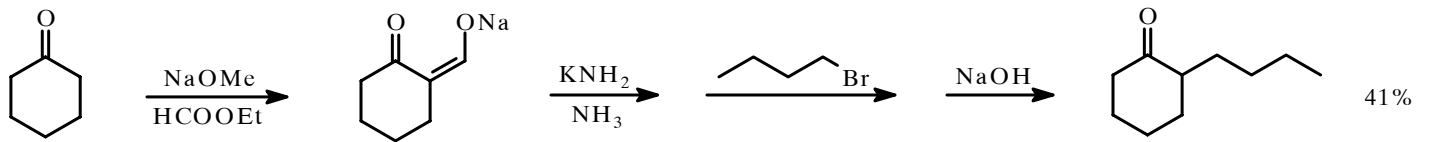
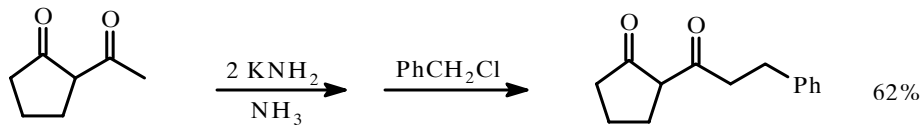
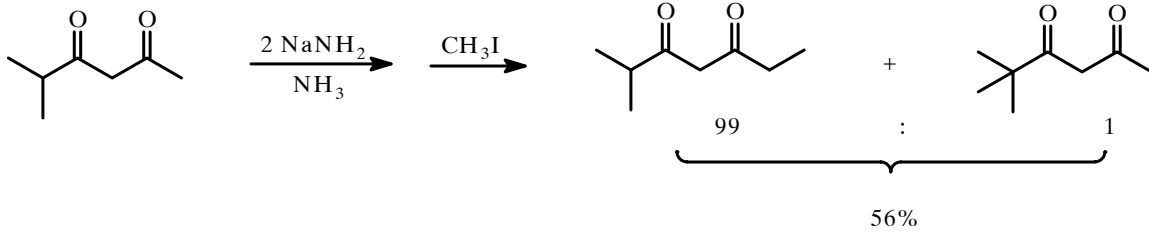
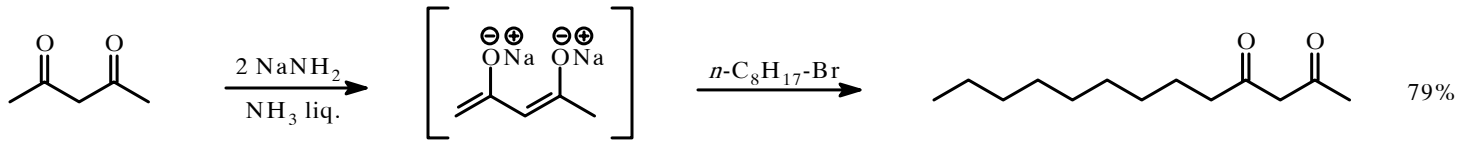
Talijumovi enolati:



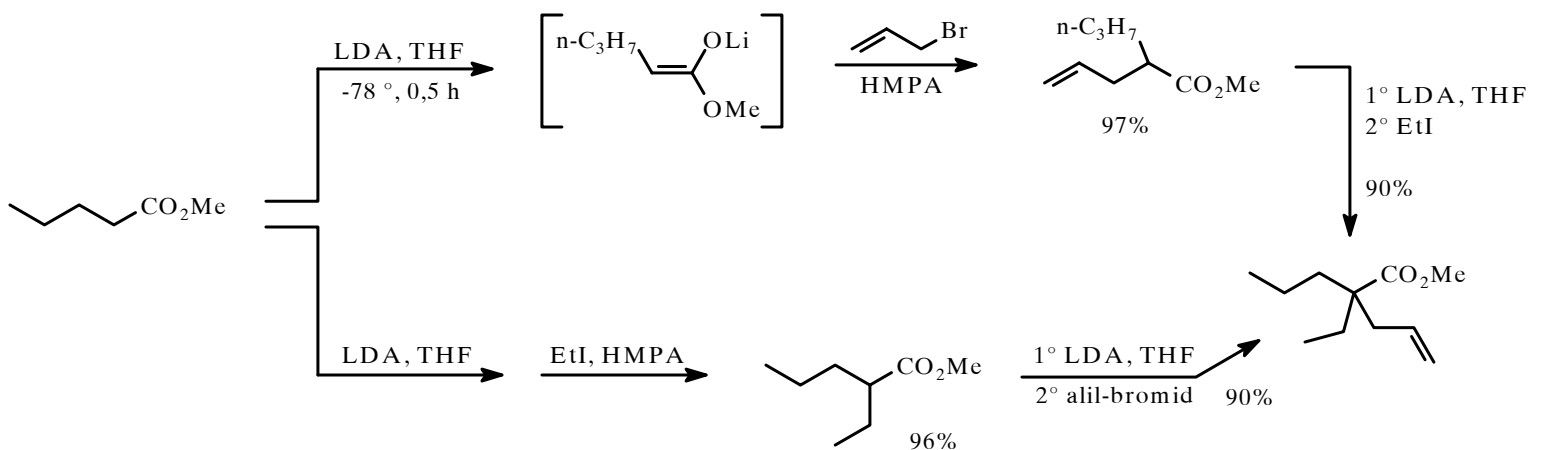
Alkilovanje u kiselim uslovima:

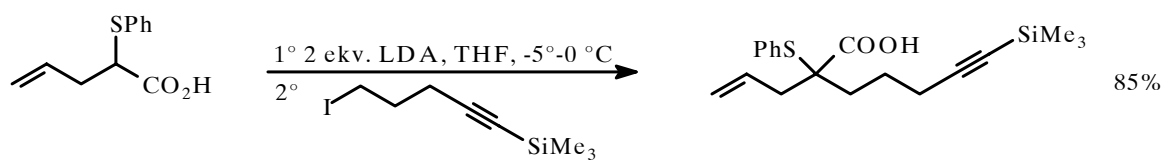
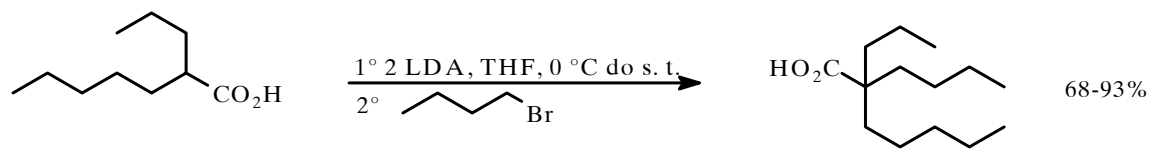
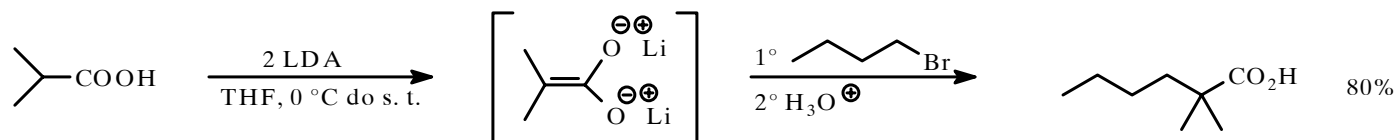
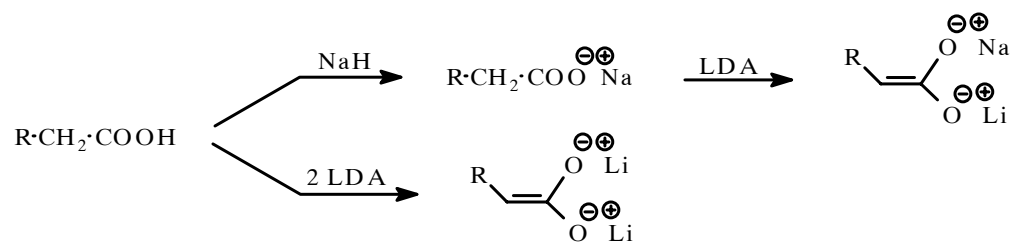
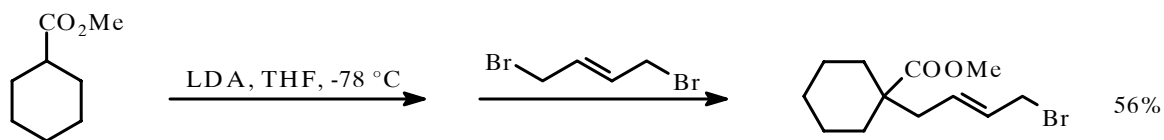
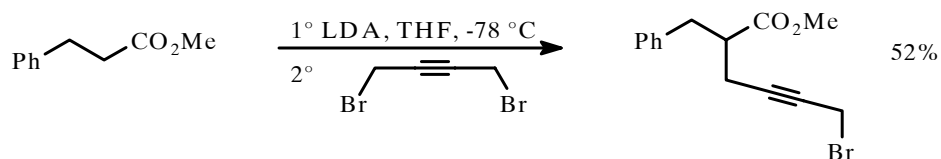


* γ -Alkilovanje dianjona



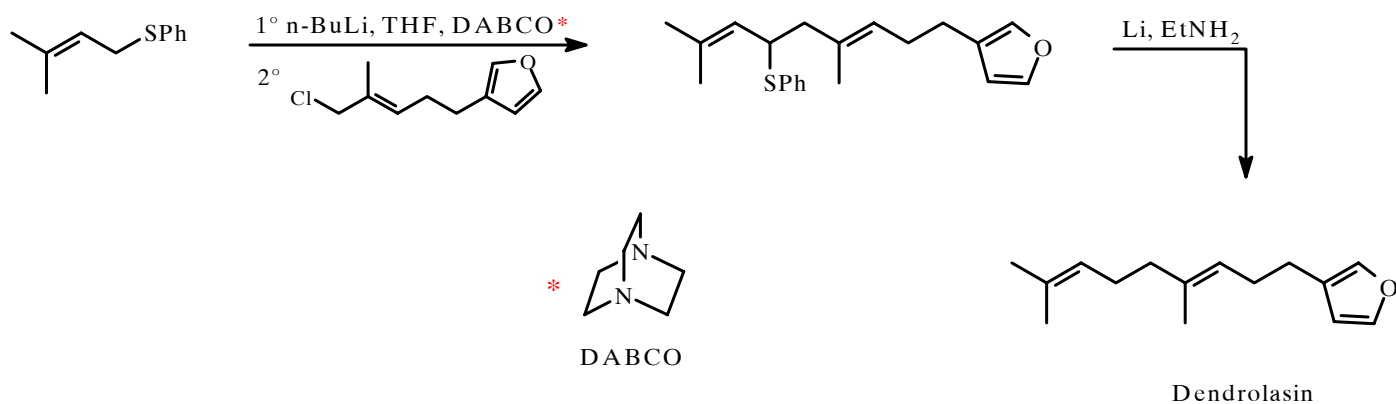
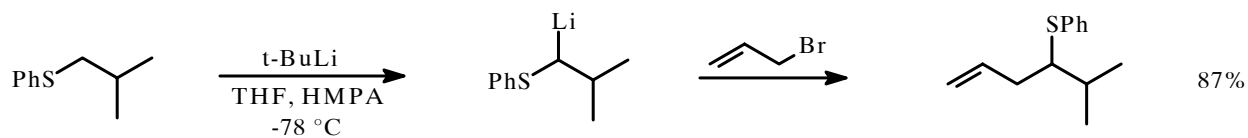
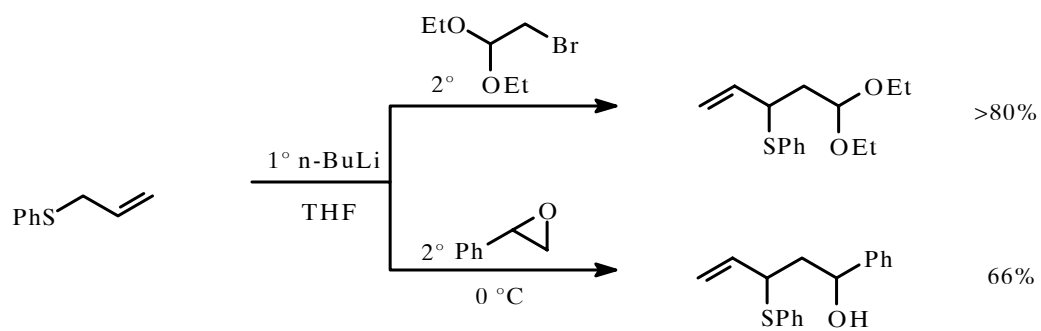
ALKILOVANJE ESTARA I DIANJONA KARBONSKIH KISELINA



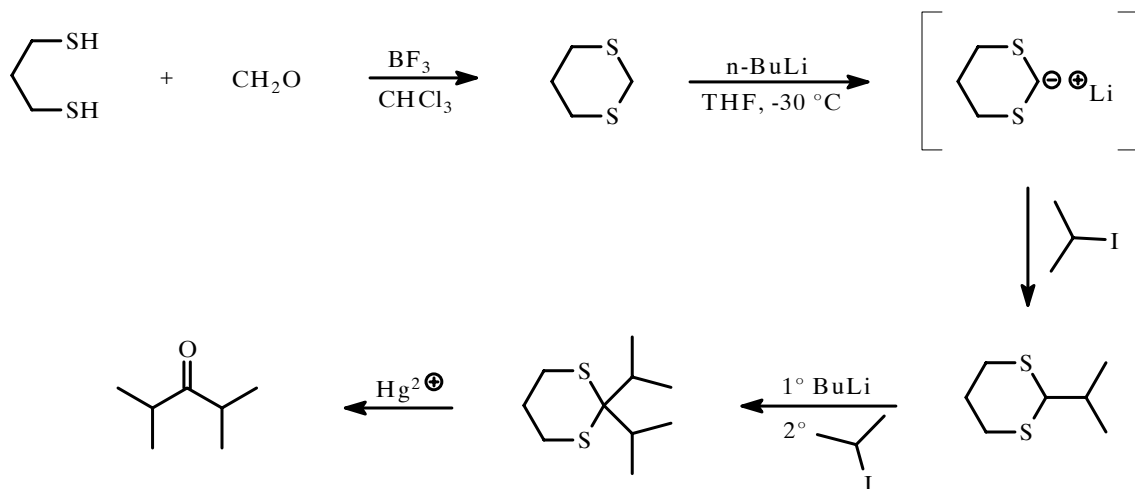


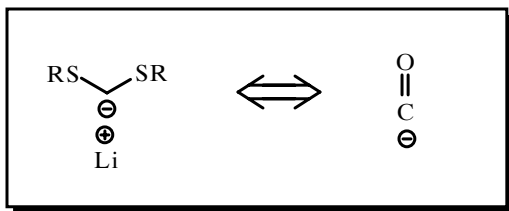
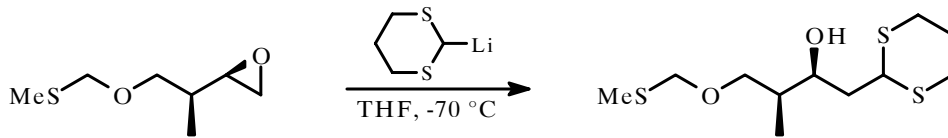
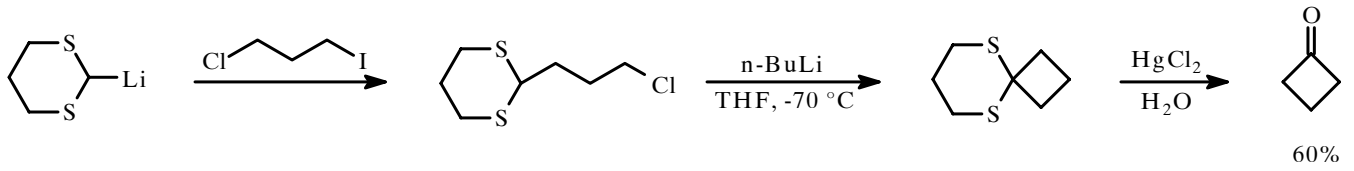
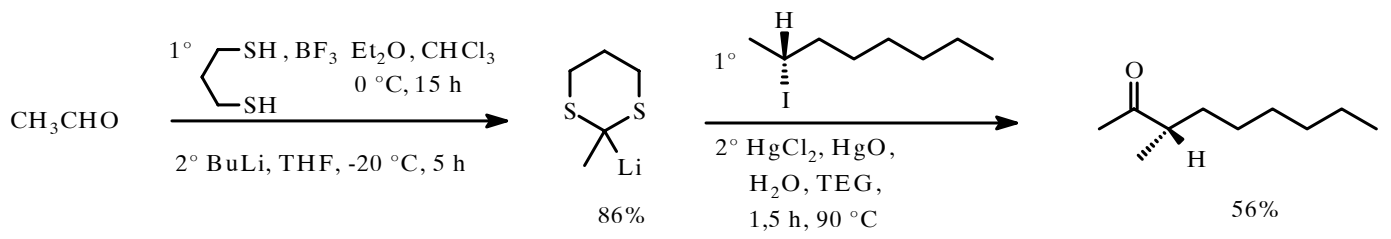
* Pregledni članak o alkilovanjima estarskih enolata i kiselinskih dianjona: Petragani, *Synthesis* **1982**, 521

ALKILOVANJE SUMPOROM STABILIZOVANIH KARBANJONA

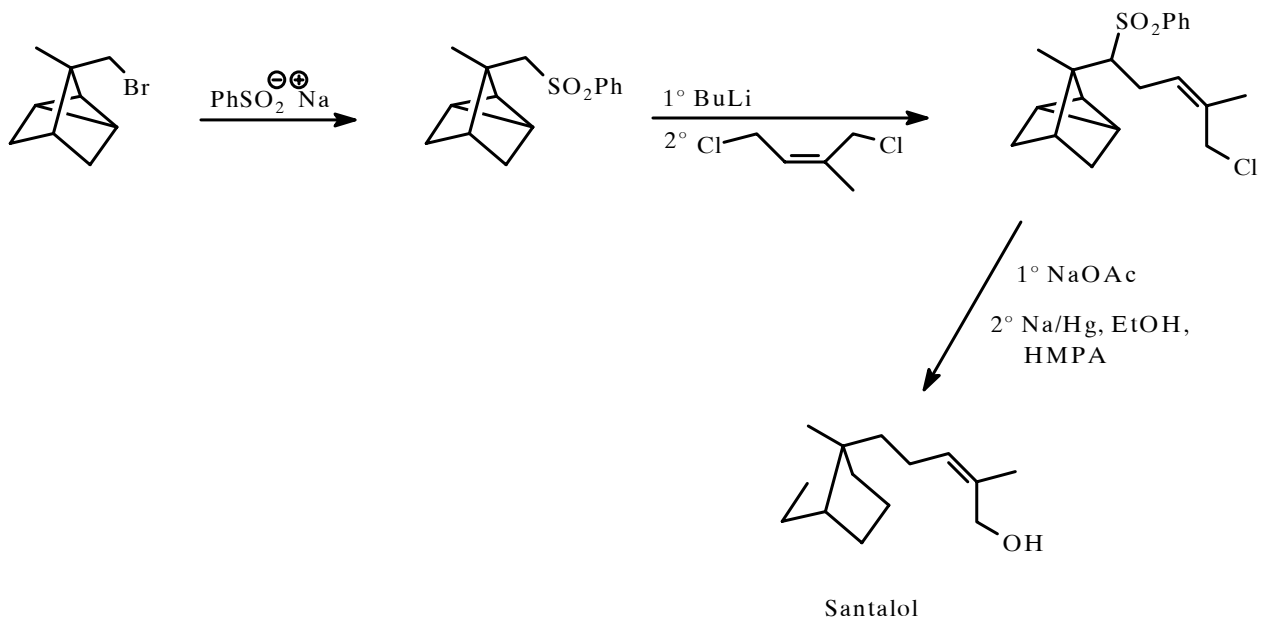


* Alkilovanje ditiana - "UMPOLUNG"

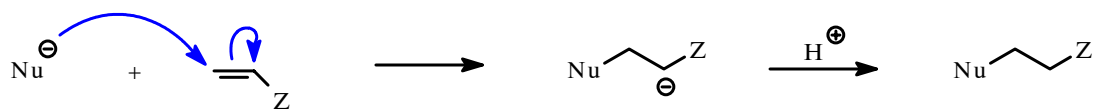




* Alkilovanje sulfona, β-ketosulfoksida i sl.



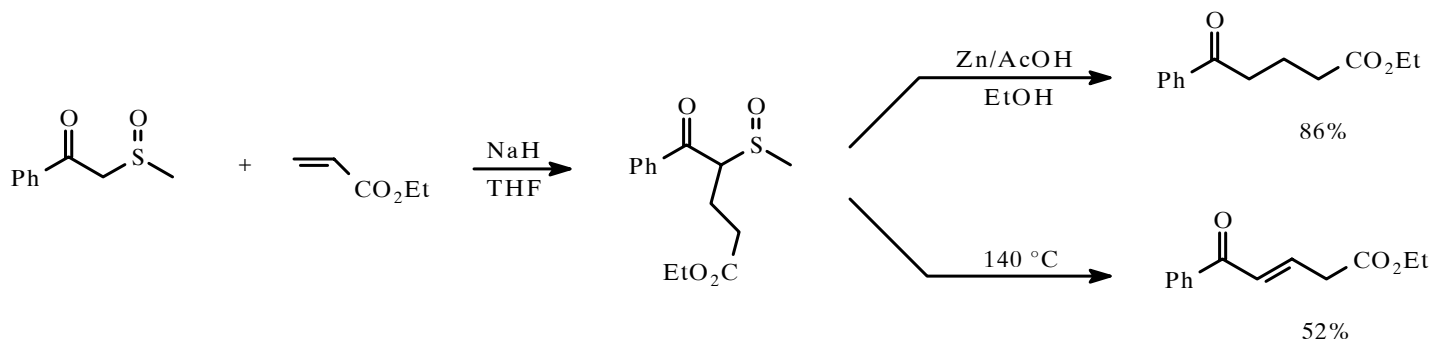
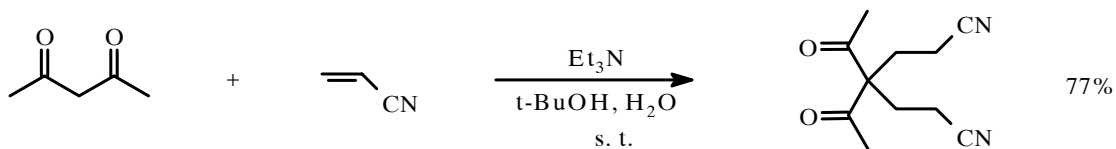
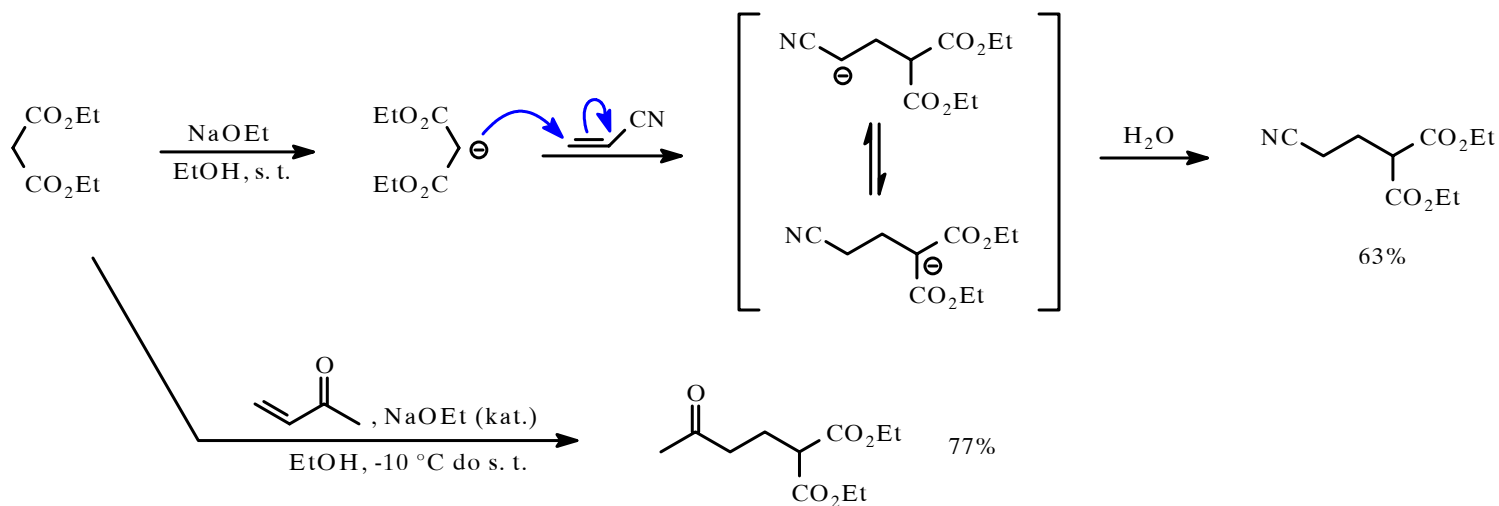
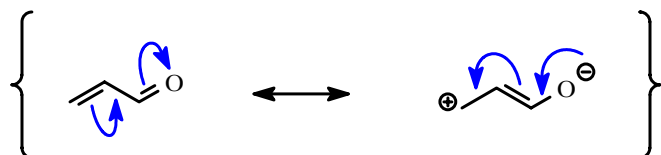
MICHAEL-OVA ADICIJA

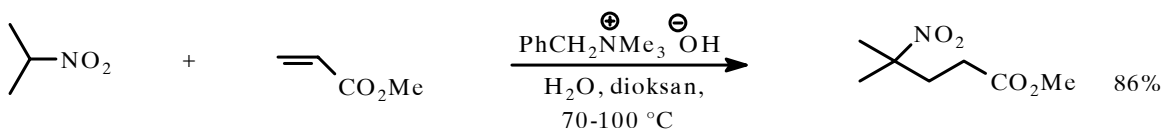
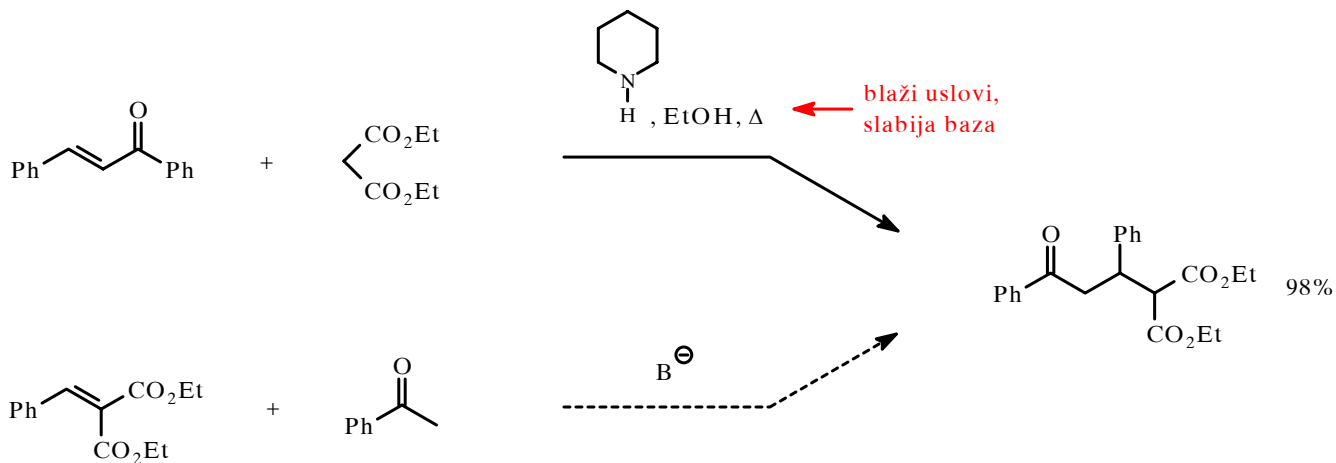


$\text{Z} = \text{NO}_2, \text{COR}, \text{CHO}, \text{COOR}, \text{CN}, \text{SO}_2\text{R}, \dots$

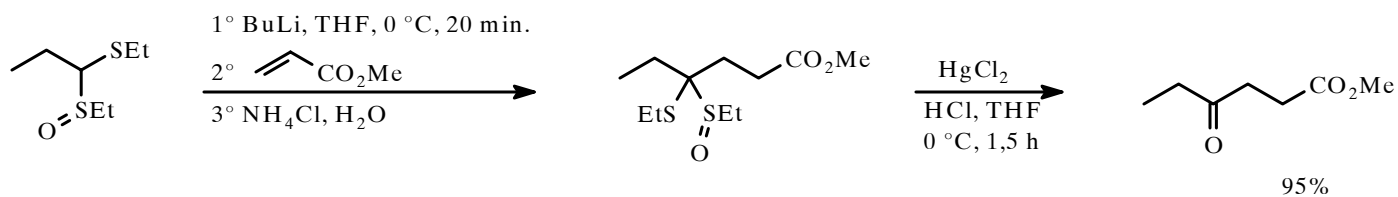
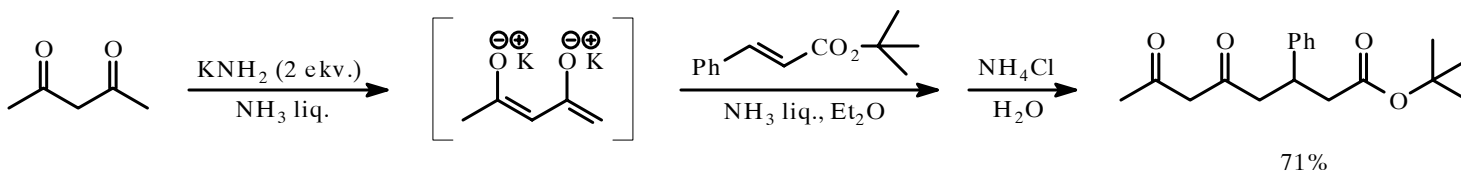
Baze: R_3N , piridin, piperidin, KOH , NaOEt obično katalitičke količine: 0,1-0,3 ekv.

Rastvarači: EtOH , MeOH , etarski rastvarači, $\text{CH}_3\text{CN}, \dots$

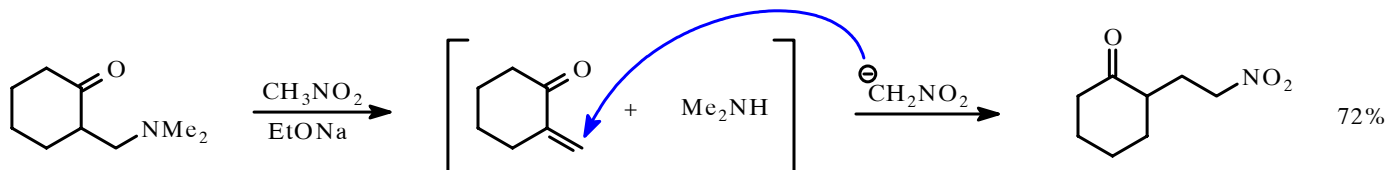
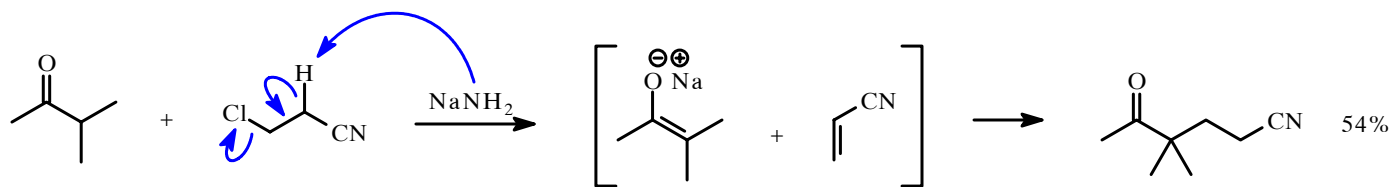




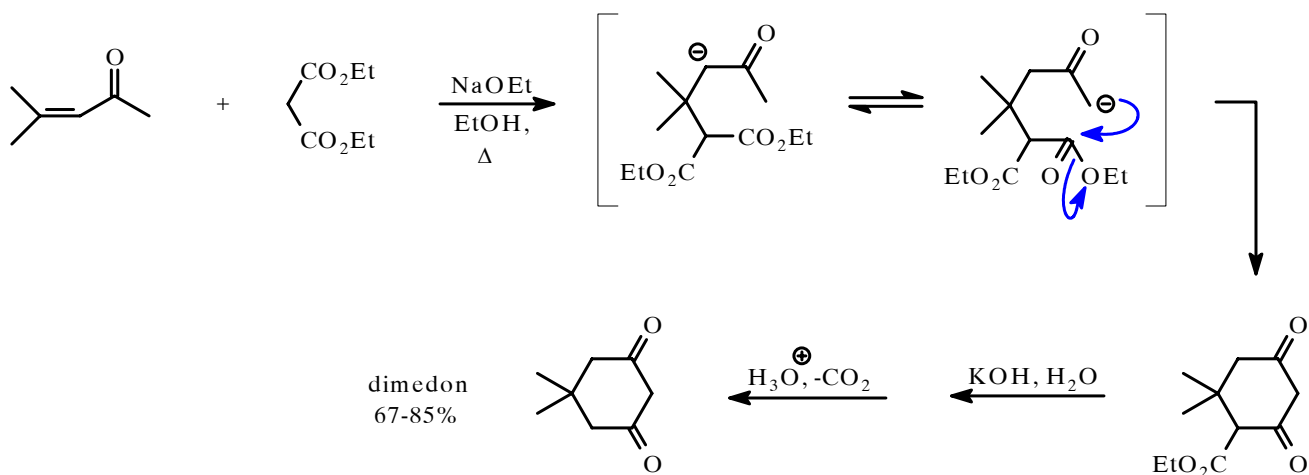
* Adicije preformiranih enolata



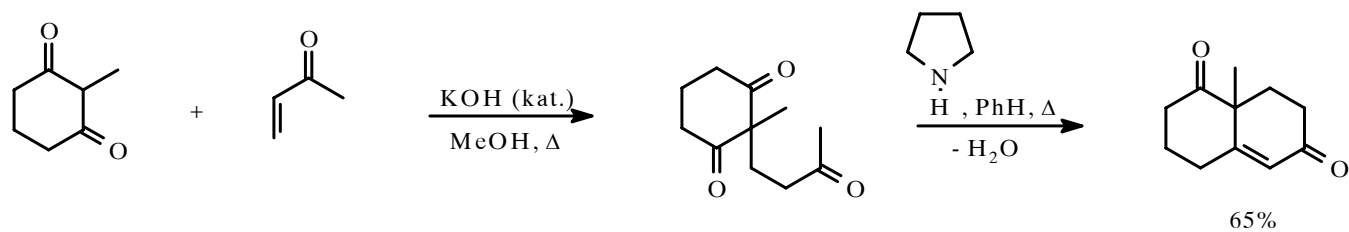
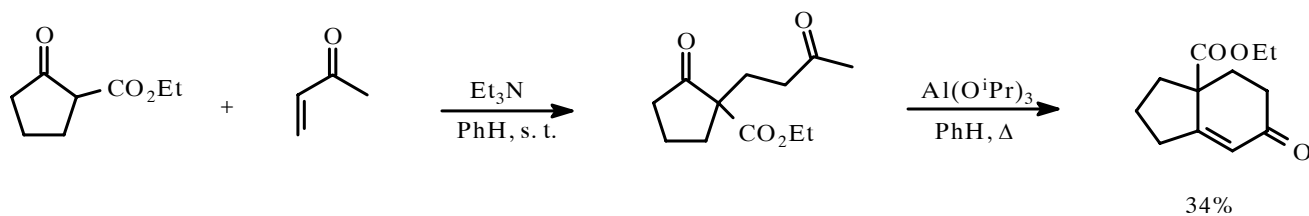
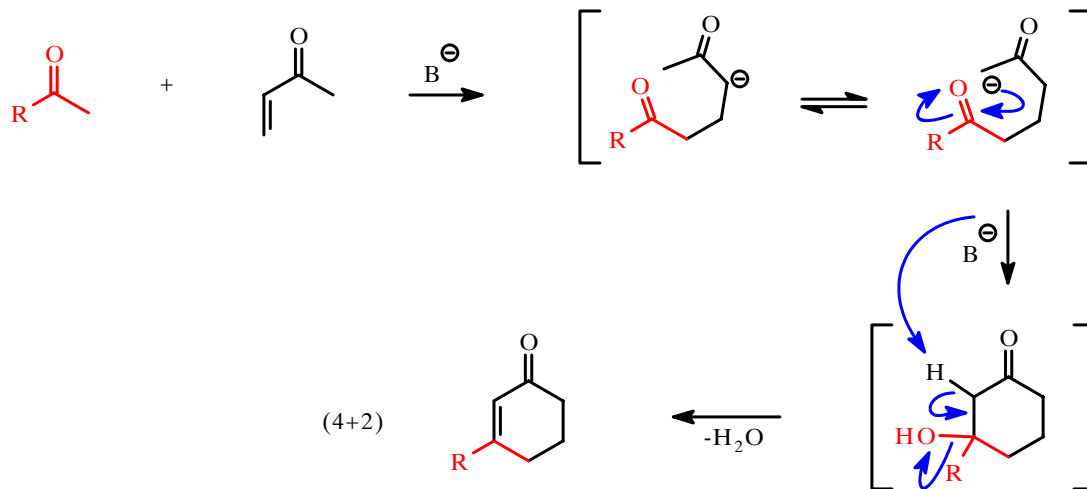
* Akceptori *in situ*

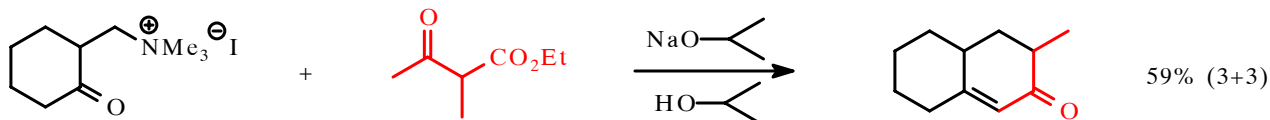
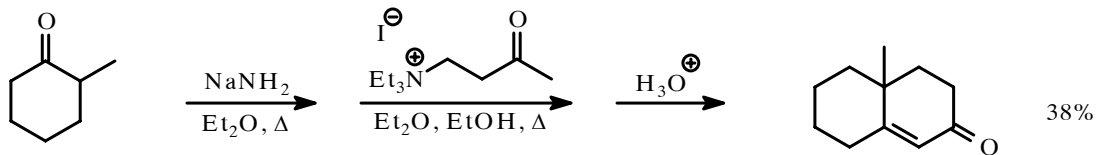


* Domino-reakcije, *Robinson-ova anelacija*,...

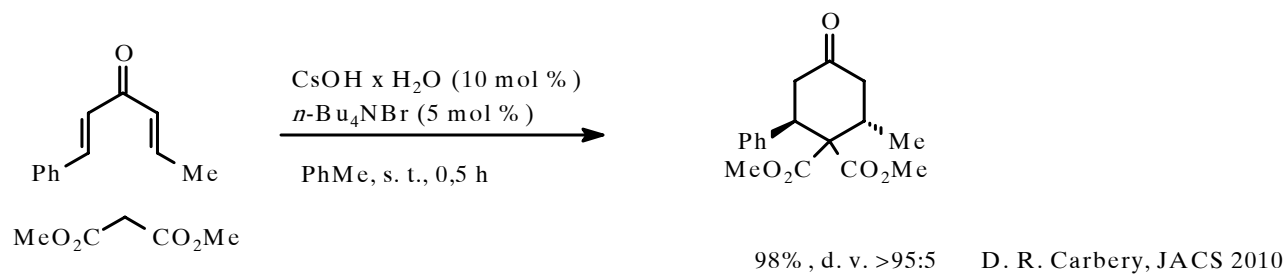


* Robinsonova anelacija:

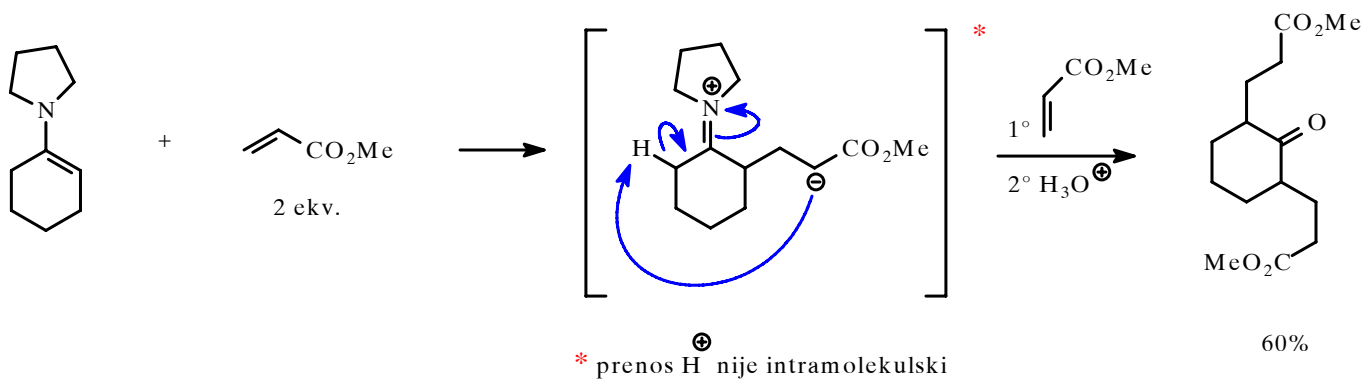
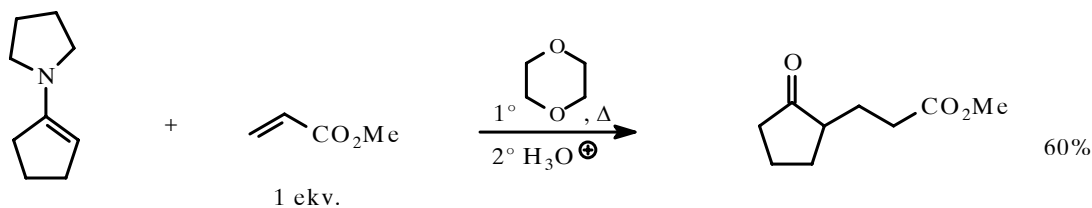
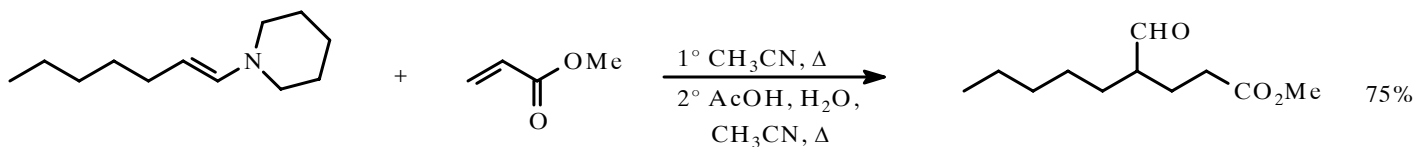


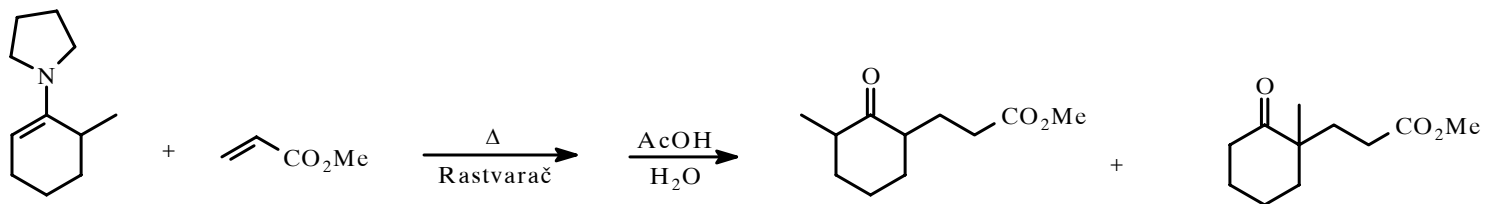


Dvostruka Michael-ova adicija:



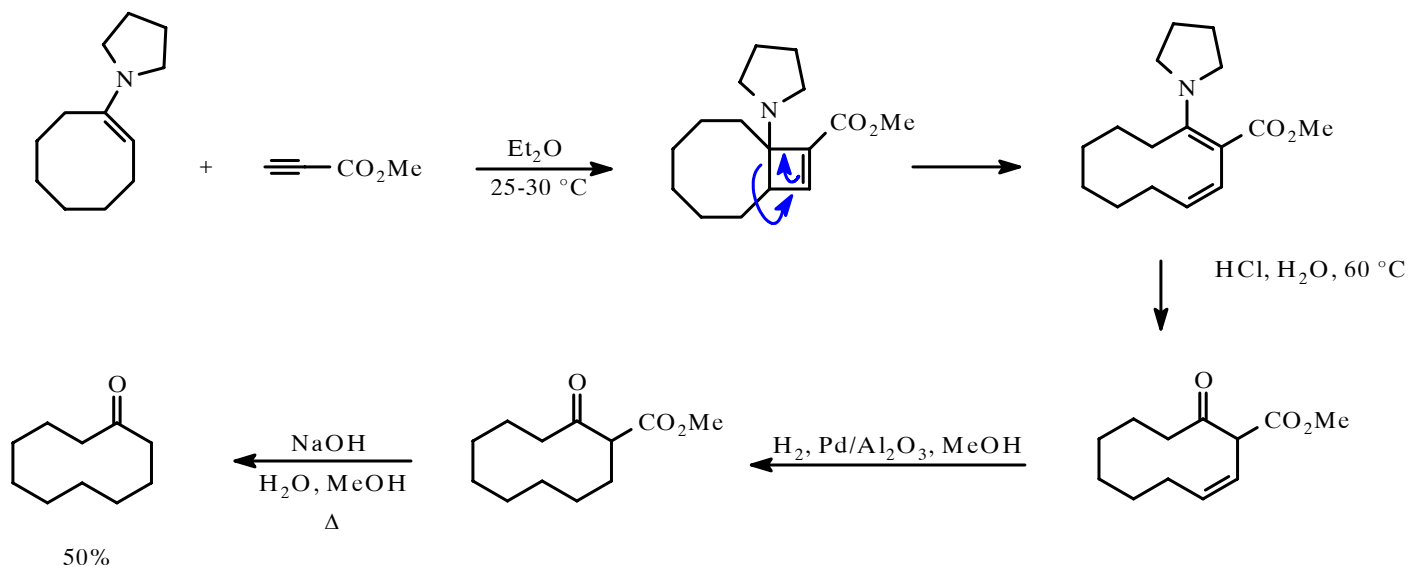
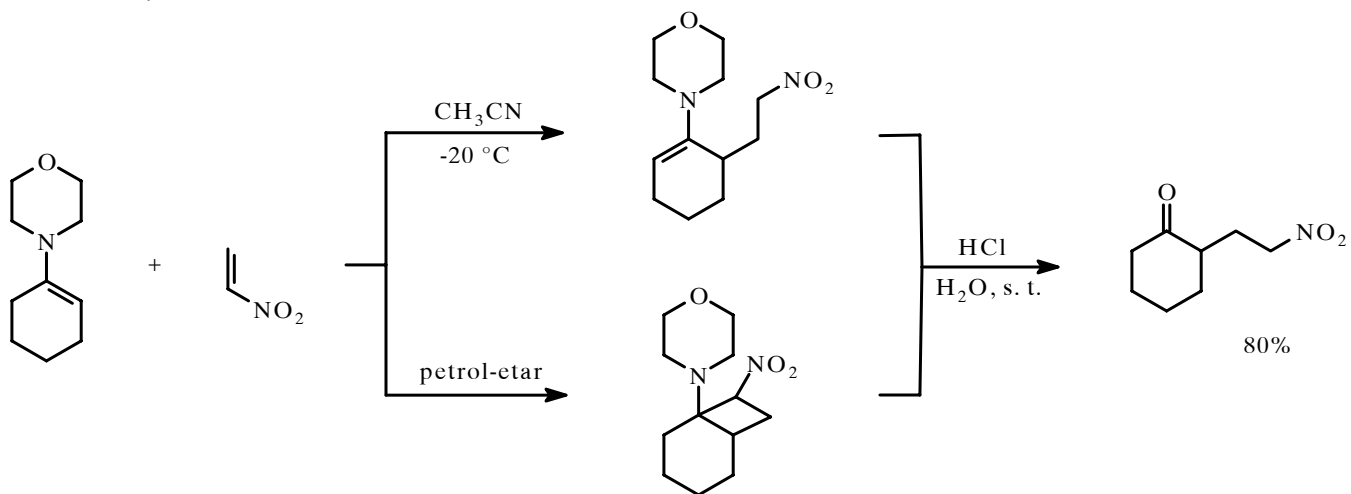
* Adicije enamina



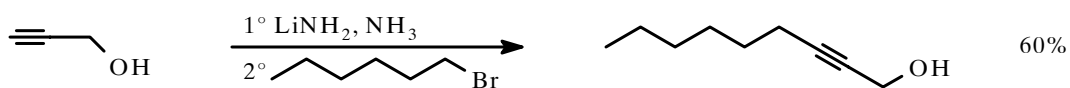
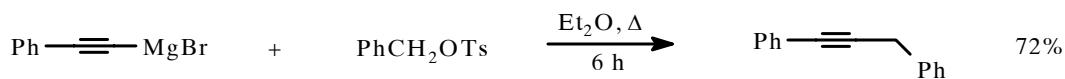
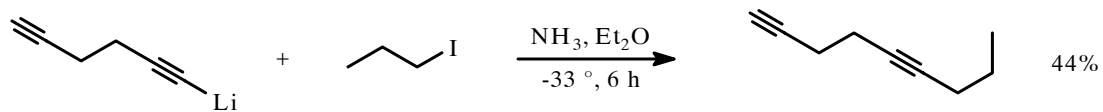
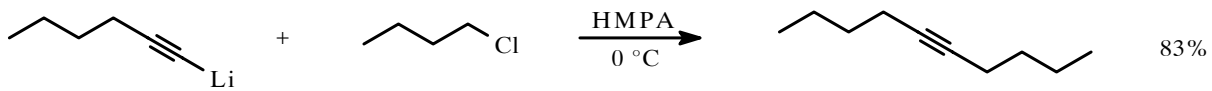
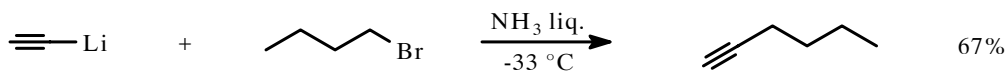
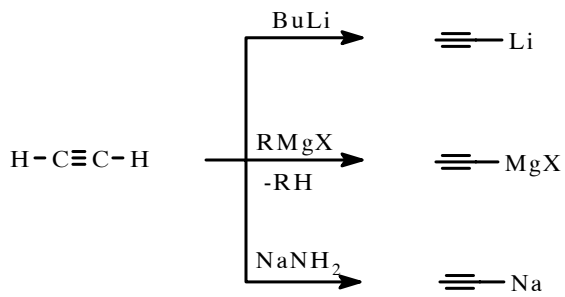
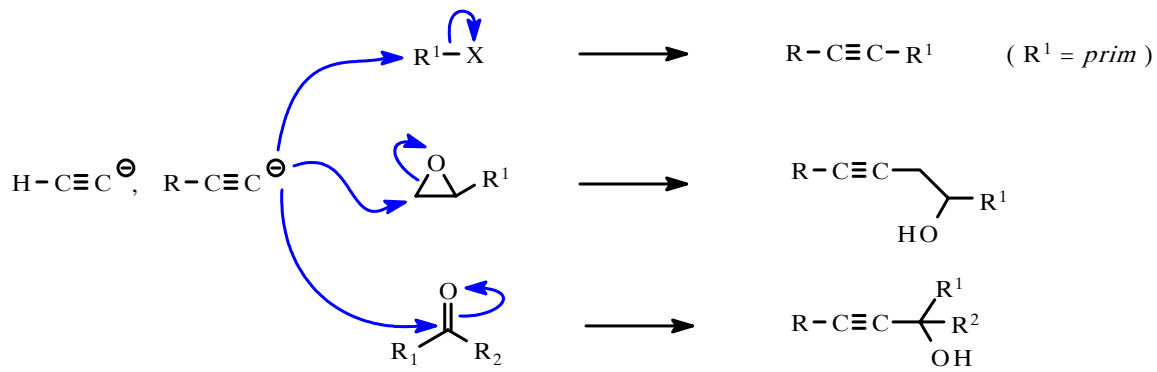


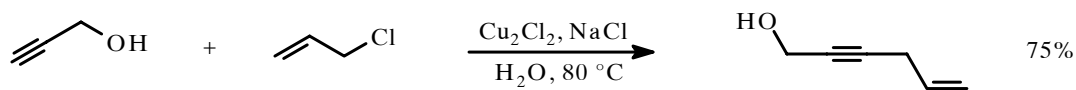
Rastvarač	Prinos	O d n o s i z o m e r a		
MeOH	75%	100	:	0
CH ₃ CN	65%	95	:	5
dioksan	60%	65	:	35
benzol	60%	80	:	20

* Cikloadicije

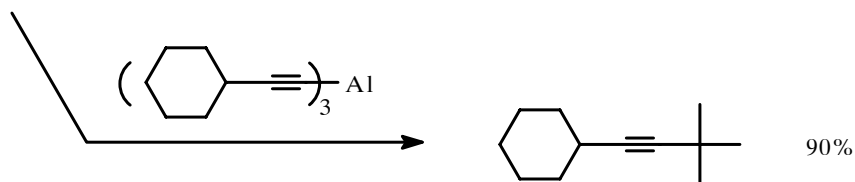
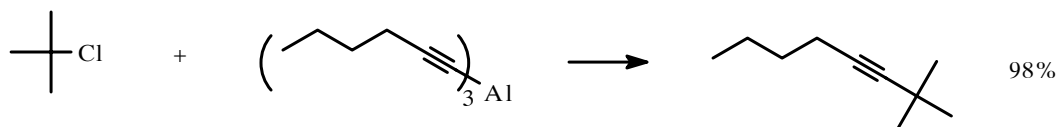
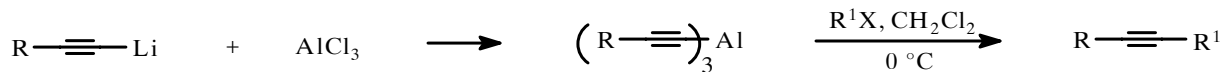


REAKCIJE ACETILIDNOG I CIJANIDNOG JONA

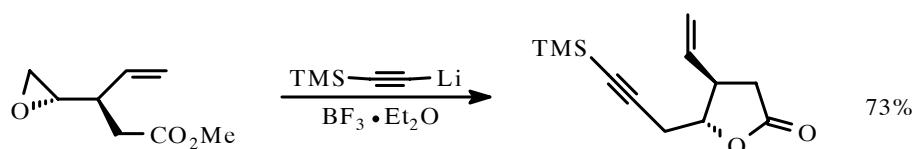
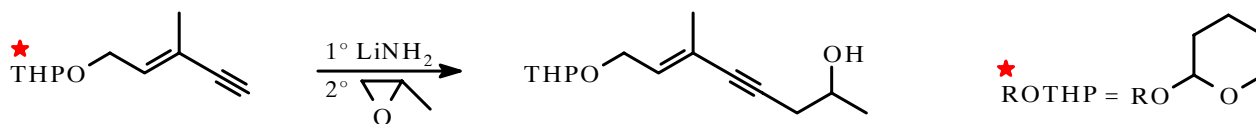
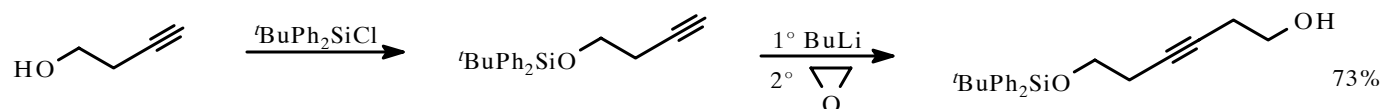


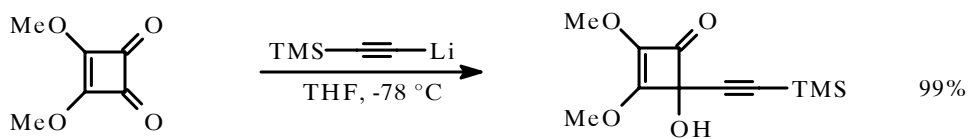
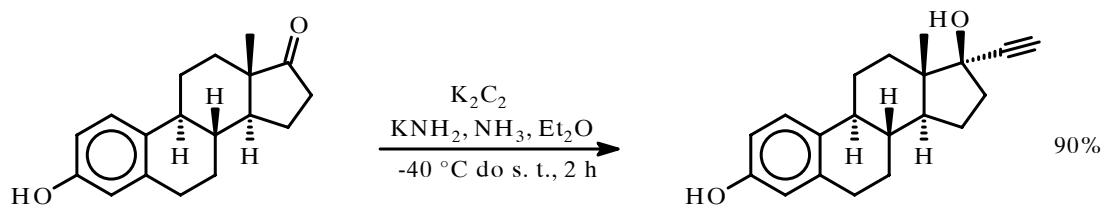
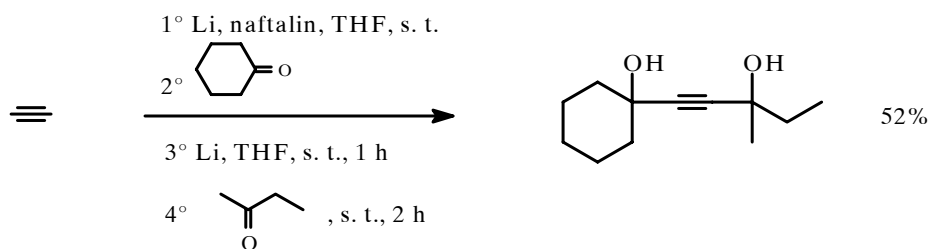
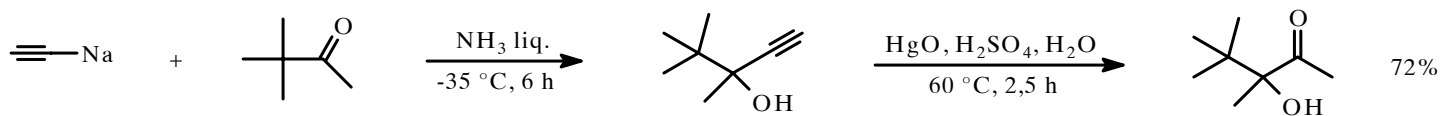
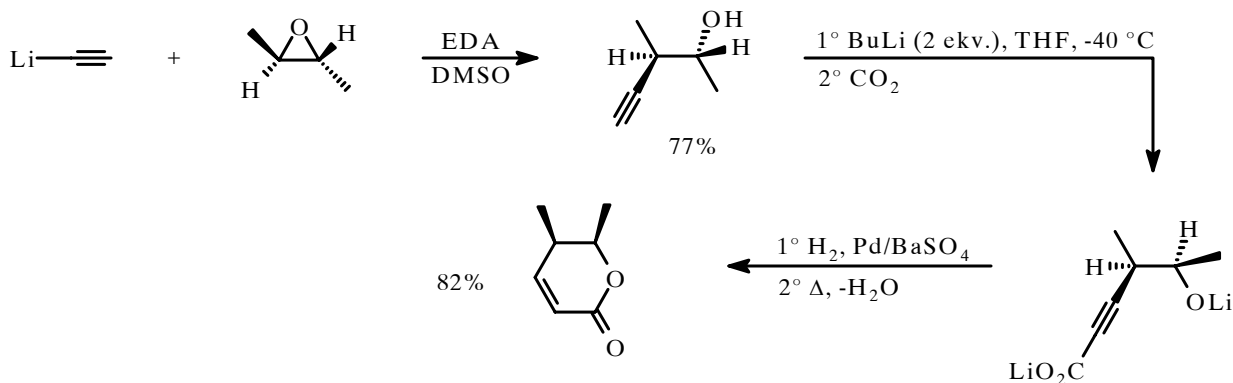
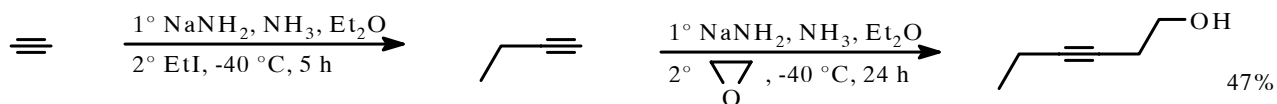


* Za *tert* - RX : Al-acetilidi



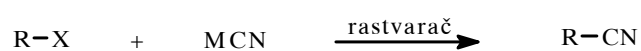
* Reakcije sa epoksidima





REAKCIJE $\ominus \text{C}\equiv\text{N}$

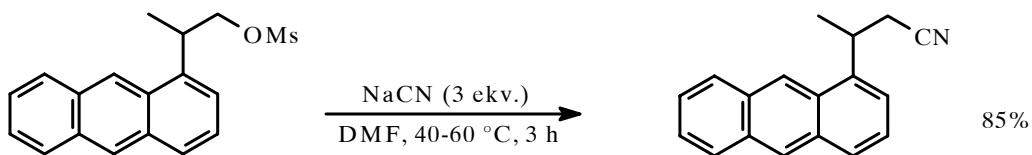
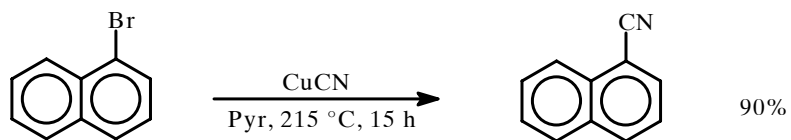
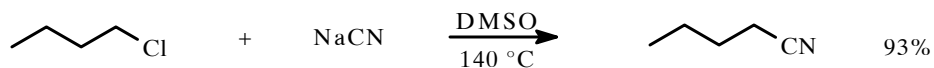
* Nukleofilna supstitucija



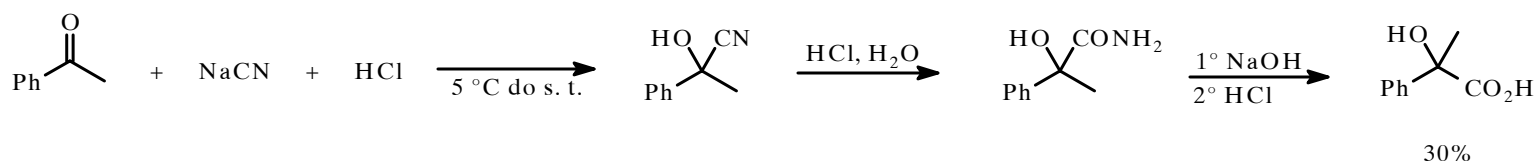
M = Na, Cu

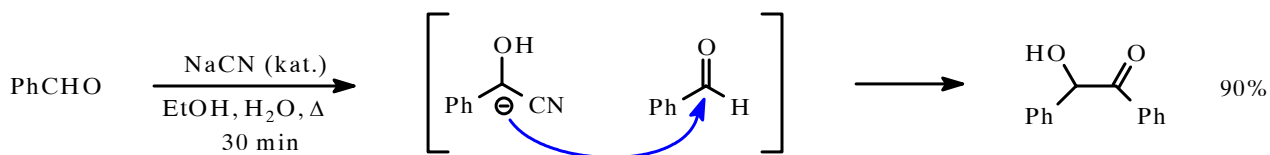
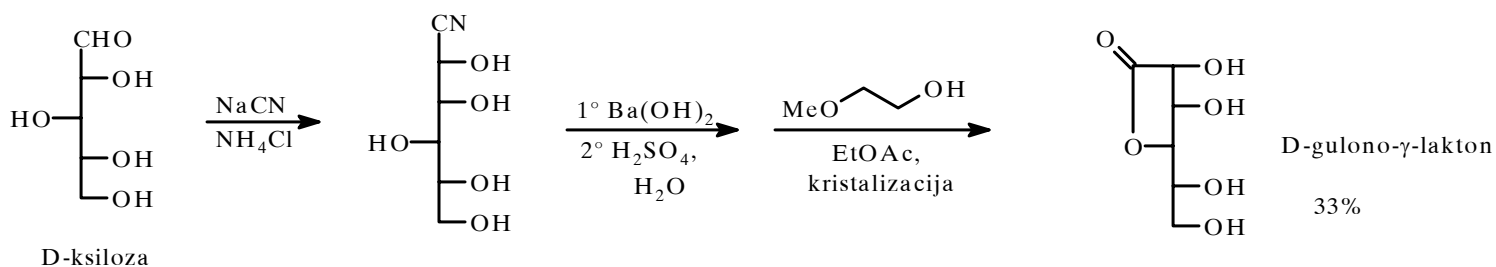
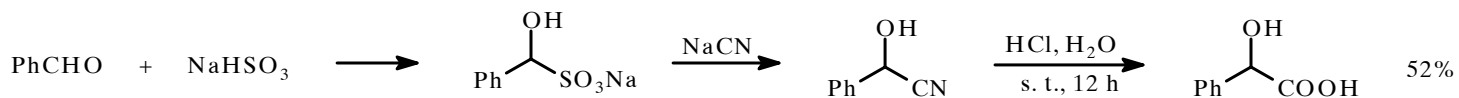
X = Cl, Br, I, OMs, OTs

Rastvarač: EtOH, DMF, DMSO, HO-CH₂-CH₂-OH

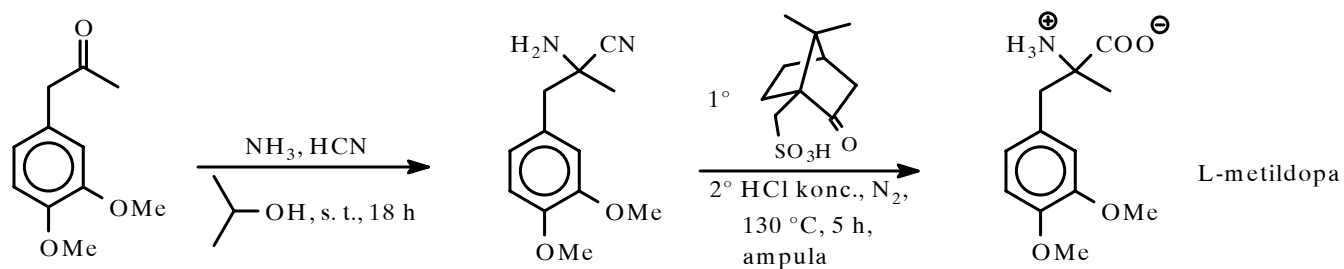
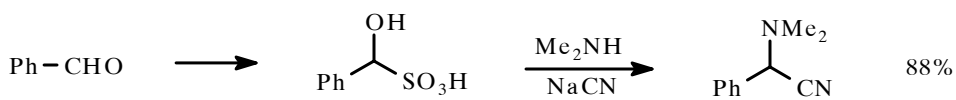
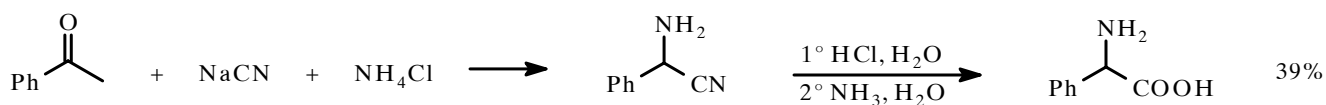


* Cijanhidrijska reakcija

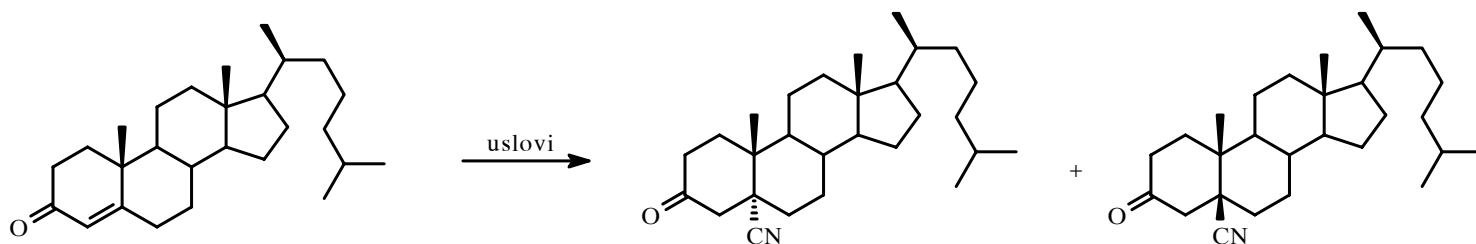
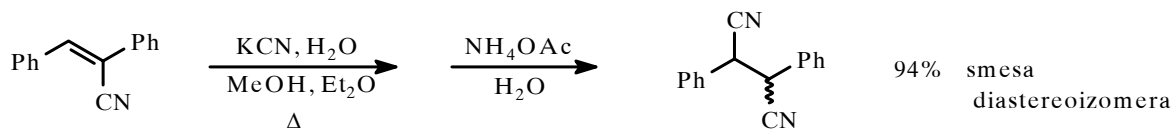




* Strecker-ova sinteza aminokiselina



* Hidrocijanovanje dvostruke veze



uslovi: KCN, NH₄Cl, DMF 1 : 1 (82%)

AlEt₃, HCN 2 : 1 (85%)

