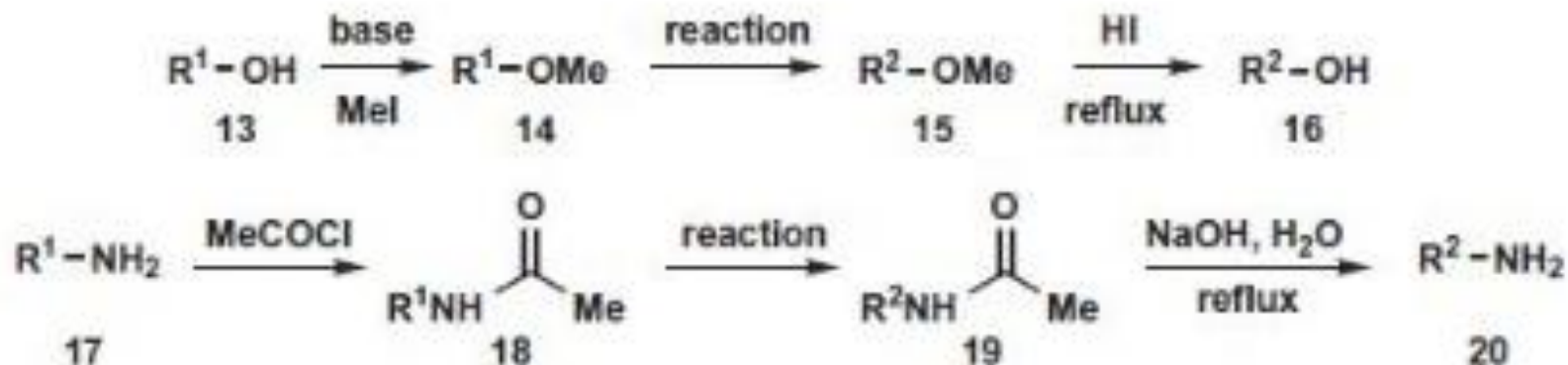


# Grupos de proteção



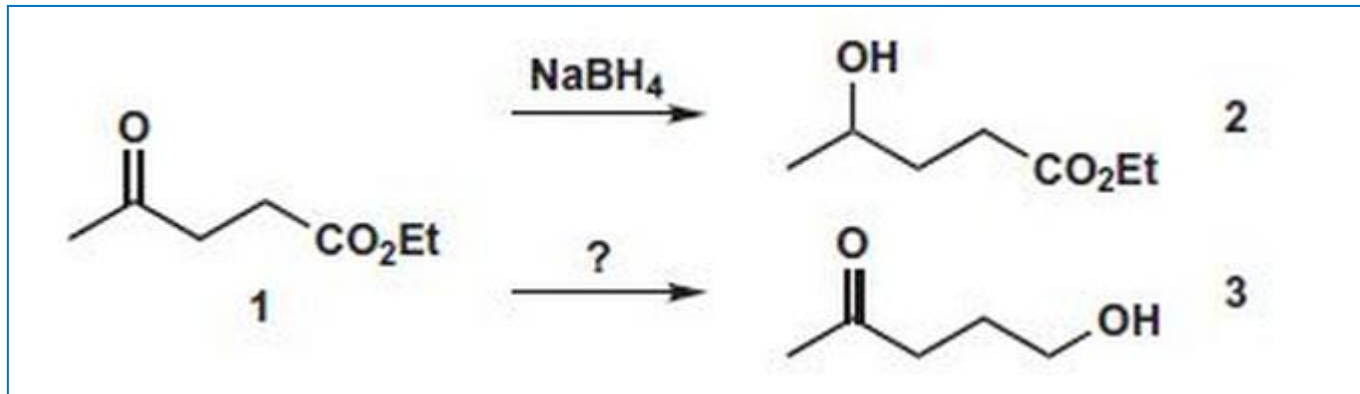
Proteção para moléculas robustas pois a desproteção exige condições drásticas

Grupos protetores devem ser facilmente colocados

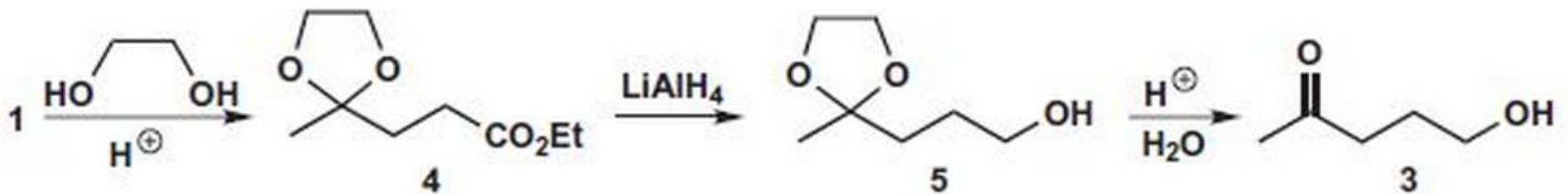
Devem ser resistentes às condições da reação

Devem ser facilmente retirados

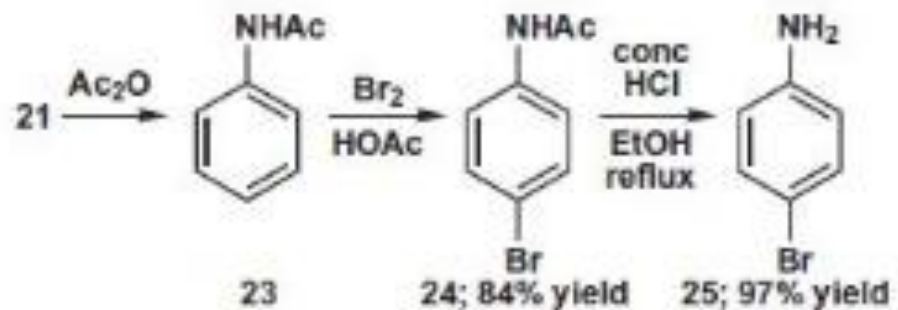
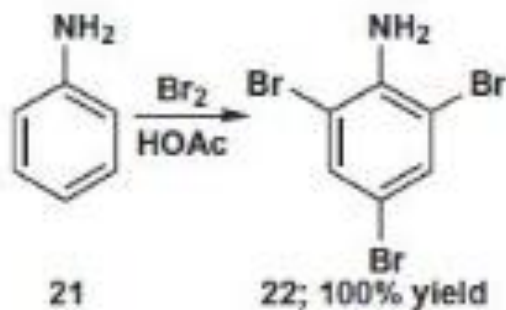
# Como reduzir quimiosseletivamente



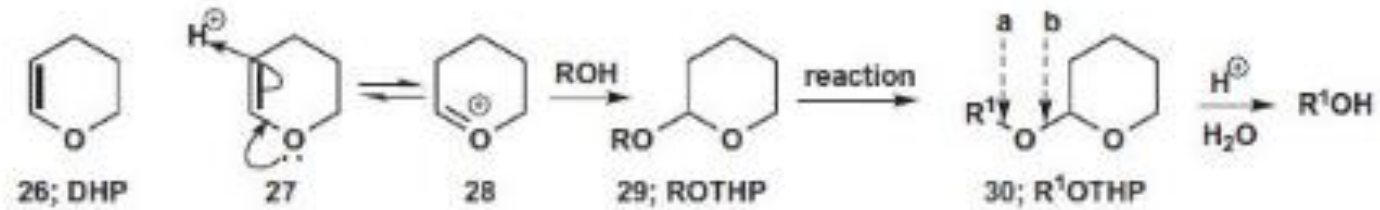
## Grupos protetores devem fáceis de sair



Menos reativo

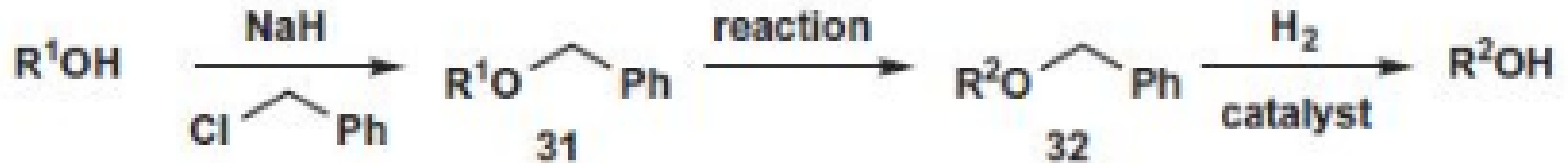


# Éteres e amidas como grupos de proteção



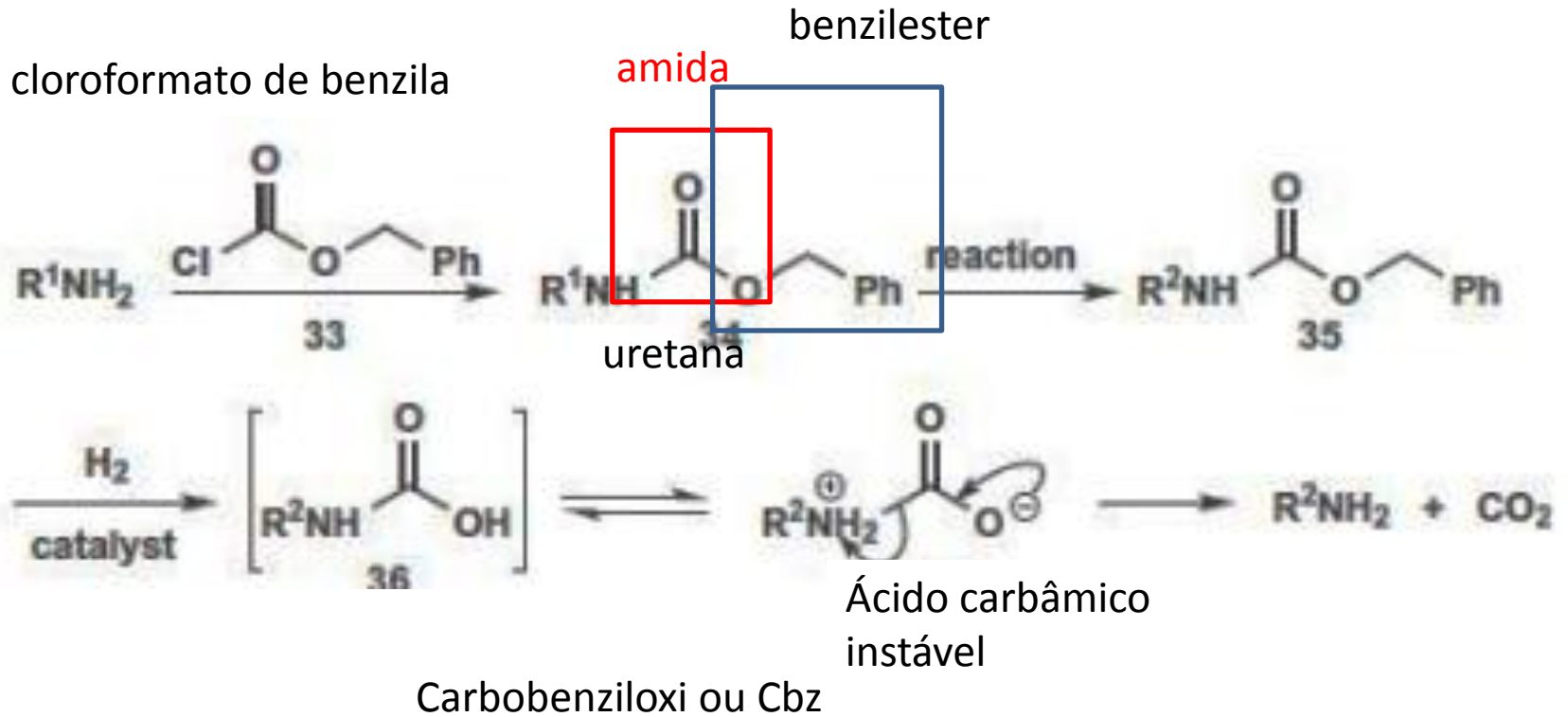
1- Formação de tetrahidropiranos para proteção de álcoois

B é ligação fraca e a ligação forte problema é a formação de outro centro assimétrico



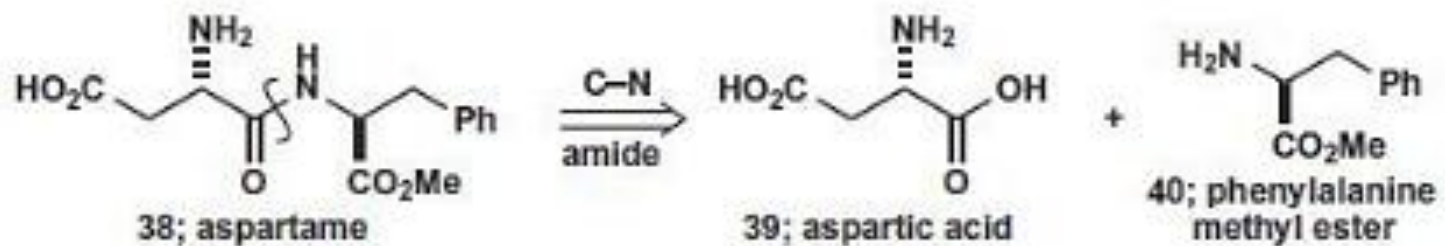
2- Formação de derivados benzílicos de álcoois ,

# Proteção de aminas

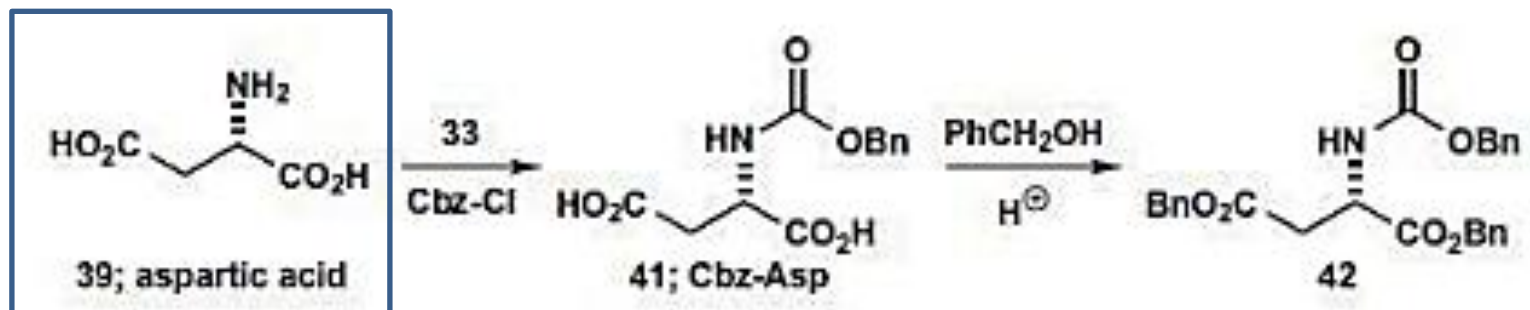


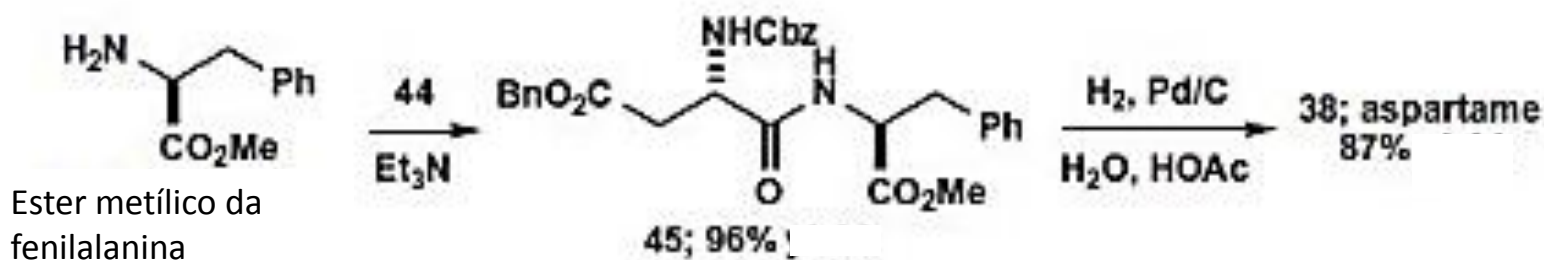
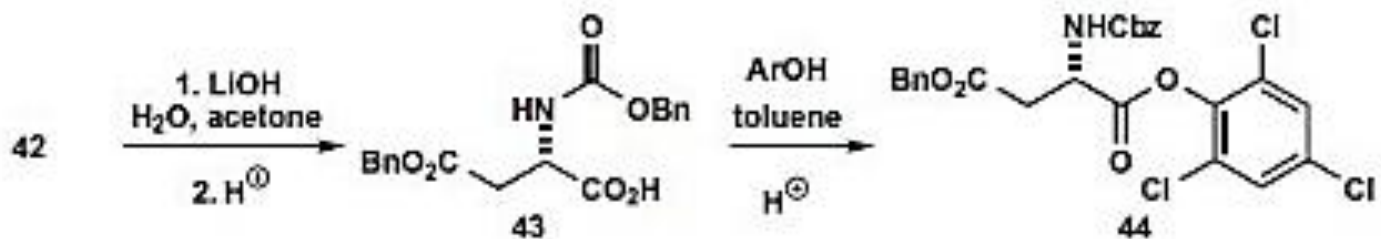
# Síntese do aspartame

retrossíntese

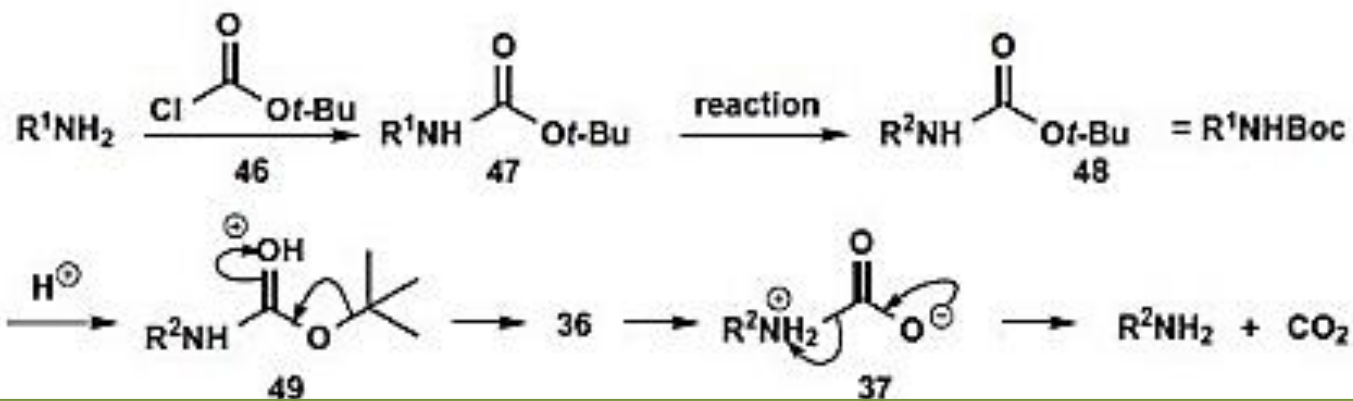


síntese





Outro grupo protetor é o Boc (t-butiloxicarbonyl) é adicionado a um álcool ou amina



O grupo t-butil sai como cátion como SN1 e o mesmo intermediário do CBz

Top Curr Chem (2009) 286: 209–257

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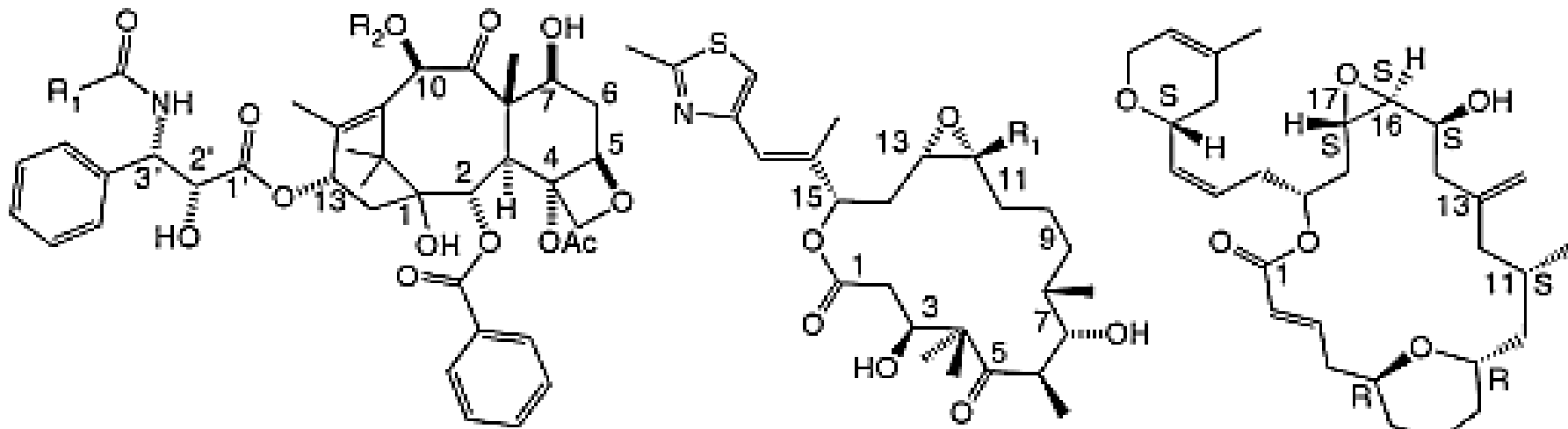
Published online: 31 October 2008

# The Tubulin Binding Mode of Microtubule Stabilizing Agents Studied by Electron Crystallography

**James H. Nettles and Kenneth H. Downing**

**Abstract** Since tubulin was discovered in 1967, drug probes have been used to manipulate mechanisms of microtubule polymerization and disassembly. In parallel, advances in optical imagery, electron microscopy, along with both electron and X-ray diffraction have provided ability to “see” the molecular underpinning of these machines. Nanoscale mapping of different tubulin polymers formed in the presence

# Compostos anticancer inibem, tubulina



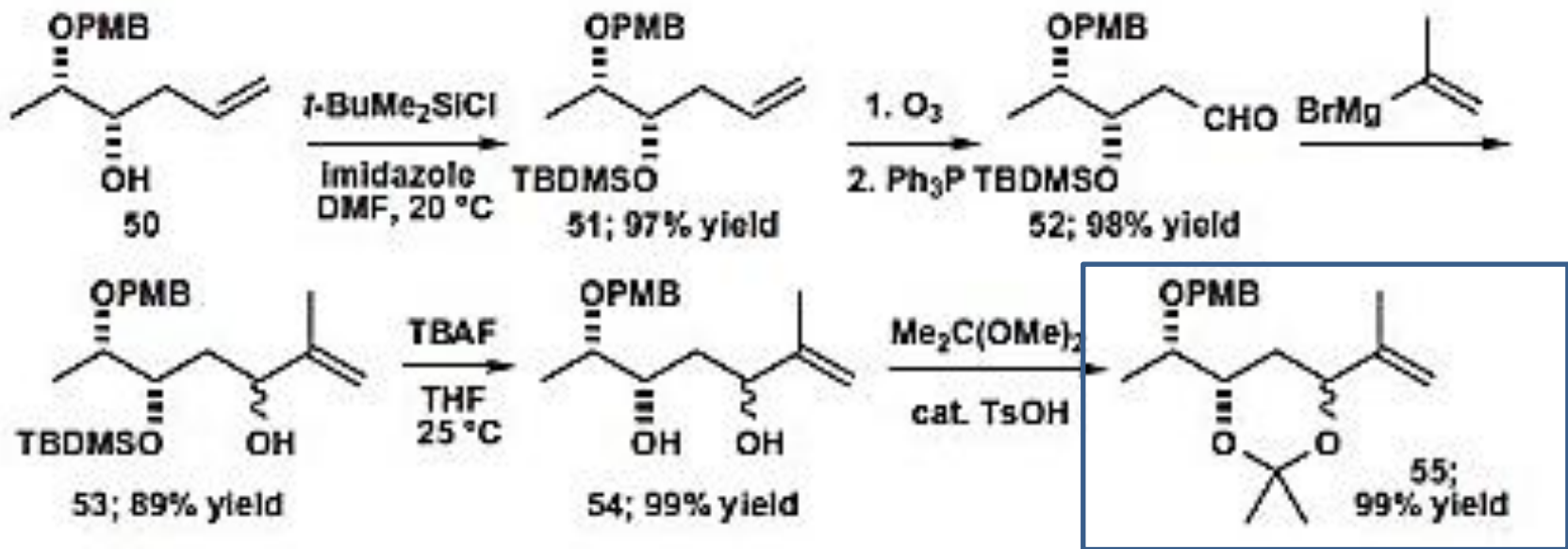
	$R_1$	$R_2$		$R_1$	
<i>paclitaxel</i>	Ph	AC	<i>epothilone A</i>	H	<i>laulimalide</i>
<i>ocetaxel</i>	t-BuO	H	<i>epothilone B</i>	Me	

Ver de onde foram isolados



# Proteção de álcoois são os grupos sili

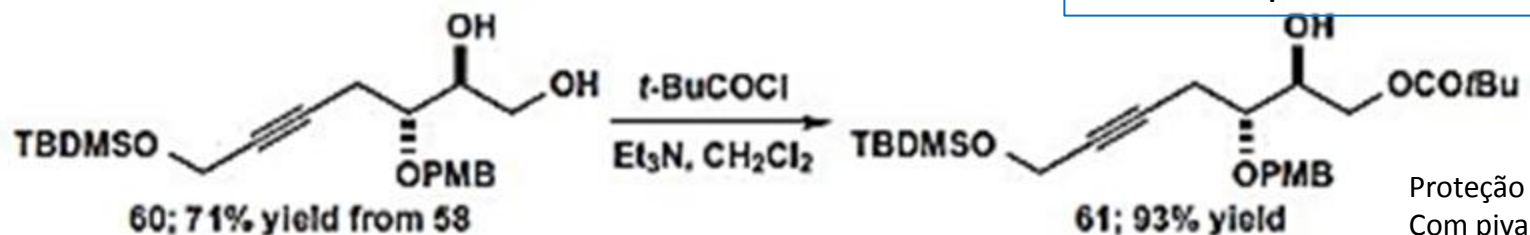
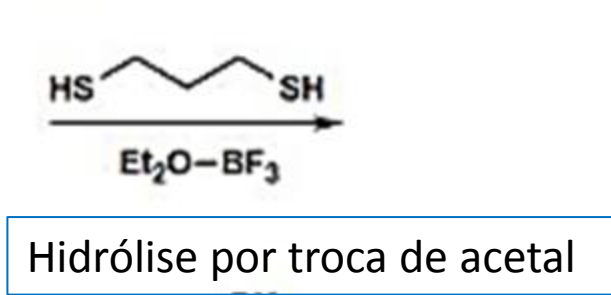
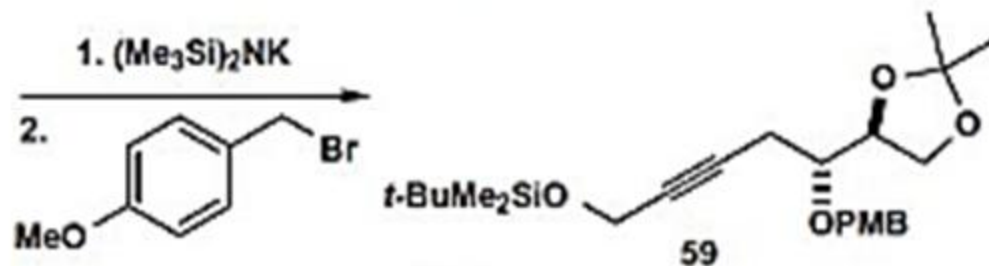
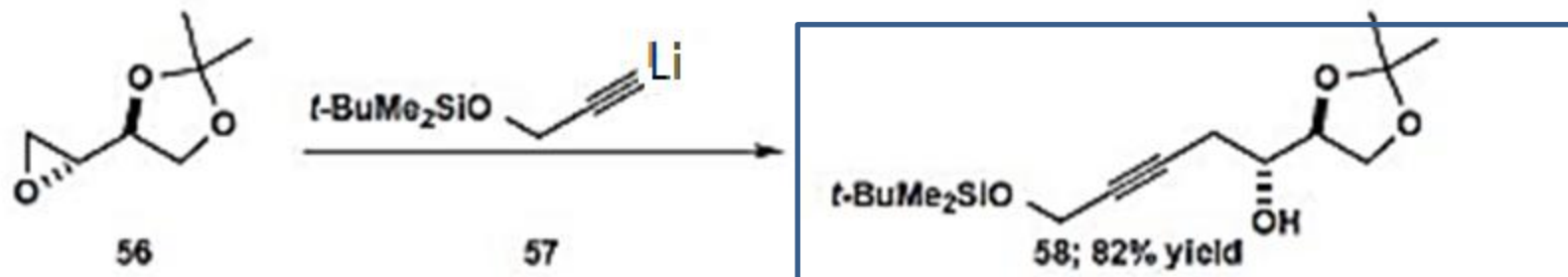
Para a síntese da epothilona B o material de partida foi o composto 50 que possui o para metoxibenil (grupo de proteção) o outro foi protegido com TBDMS é ortogonal ou seja cada grupo é removido em condições diferentes



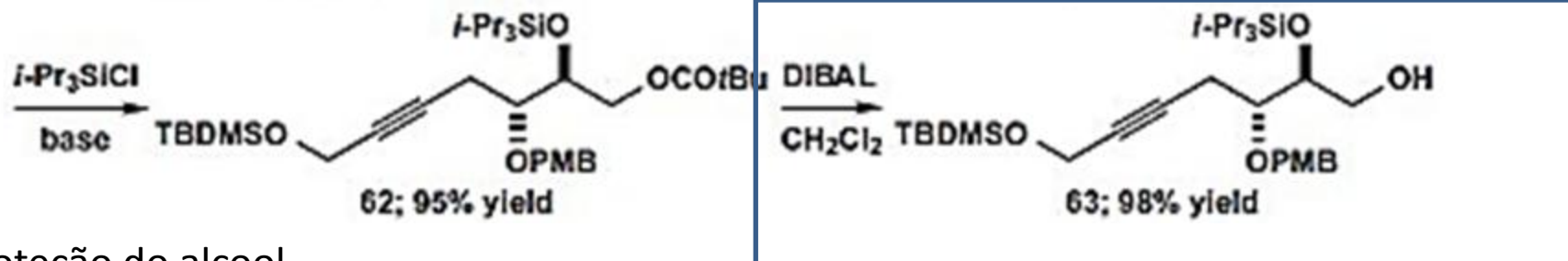
TBAF fluoreto de tetrabutil amonio

O PMB é removido por oxidação com quinona

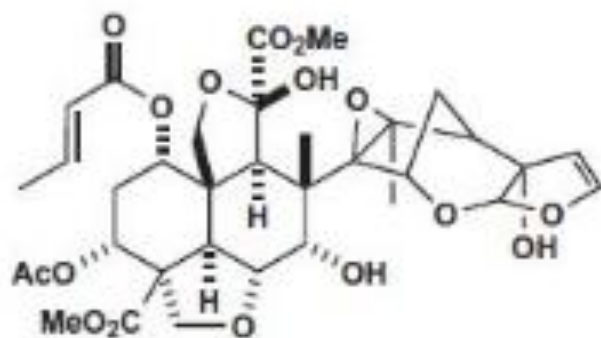
# Síntese de um intermediário da laulimalide



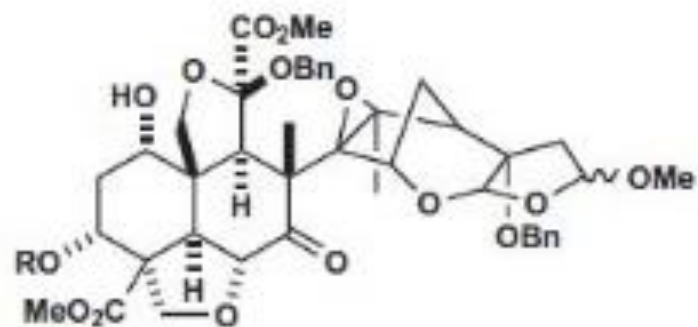
Proteção álcool 1.º  
Com pivaloil



Proteção do álcool  
sec com TIPS



64; azadirachtin



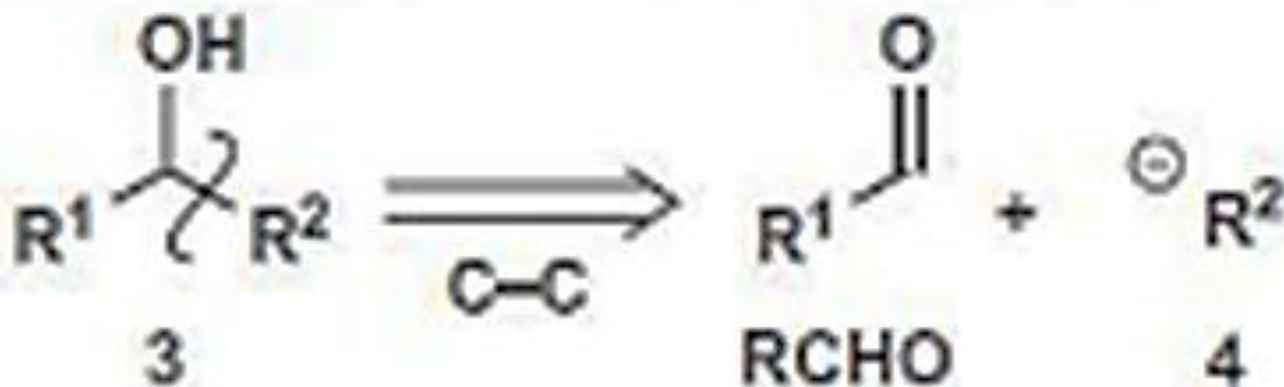
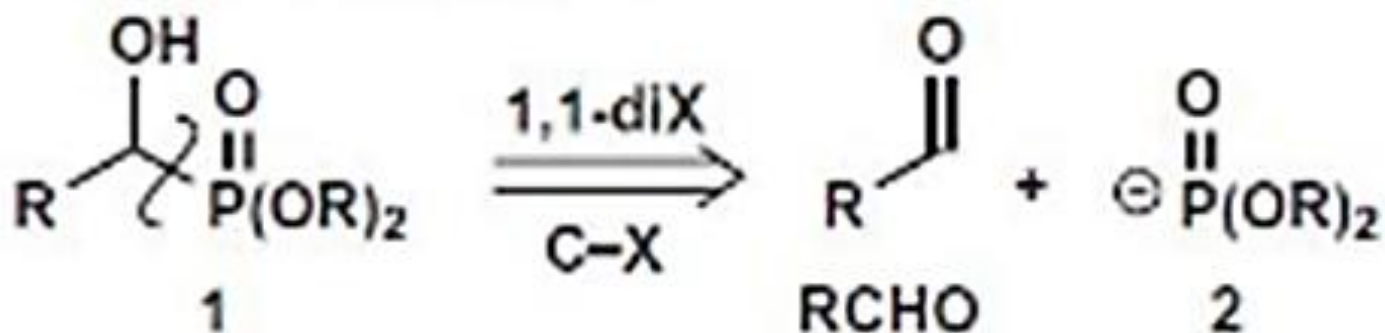
65; R = *t*-BuMe<sub>2</sub>Si

Síntesis con o uso mínimo de grupos protectores

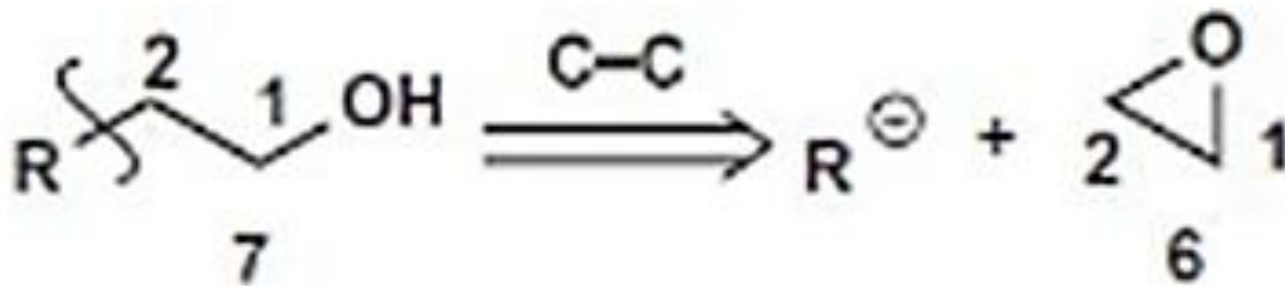
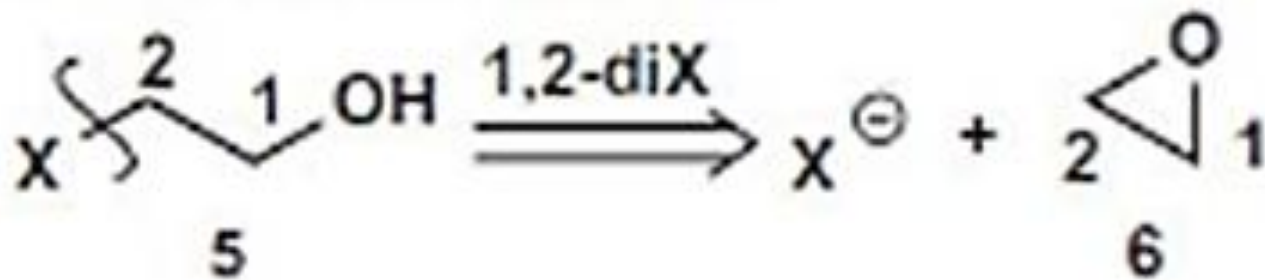
Protecting Group	To Add	To Remove	PG resists	PG reacts with
<b>Protecting Aldehydes RCHO and Ketones R<sub>2</sub>CO</b>				
Acetal (Ketal)	ROH or diol, H <sup>+</sup>	H <sup>+</sup> , H <sub>2</sub> O	nucleophiles, bases, reducing agents	electrophiles, oxidising agents
<b>Protecting Carboxylic Acids RCO<sub>2</sub>H</b>				
Ester: RCO <sub>2</sub> Me	CH <sub>2</sub> N <sub>2</sub>	NaOH, H <sub>2</sub> O	bases elec- trophiles	strong bases nucleophiles
Ester: RCO <sub>2</sub> Et	EtOH, H <sup>+</sup>	NaOH, H <sub>2</sub> O		
Ester: RCO <sub>2</sub> Bn	BnOH, H <sup>+</sup>	H <sub>2</sub> , cat or HBr		
Ester: RCO <sub>2</sub> <i>t</i> -Bu	<i>t</i> -BuOH, H <sup>+</sup>	H <sup>+</sup>	nucleophiles	electrophiles
Anion: RCO <sub>2</sub> <sup>-</sup>	base	acid		
<b>Protecting Alcohols ROH</b>				
Ether: ROBn	PhCH <sub>2</sub> Br, base	H <sub>2</sub> , cat or HBr	see text	nucleophiles
Silyl ether	R <sub>3</sub> SiCl, base	F <sup>-</sup> or H <sup>+</sup> , H <sub>2</sub> O	see text	nucleophiles
Acetal: THP	DHP, H <sup>+</sup>	H <sup>+</sup> , H <sub>2</sub> O	bases	acids
Ester: ROCOR'	R'COCl, pyr	NH <sub>3</sub> , MeOH	electrophiles	nucleophiles
<b>Protecting Phenols ArOH</b>				
Ether: ArOMe	Me <sub>2</sub> CO <sub>3</sub> , K <sub>2</sub> CO <sub>3</sub>	HI, HBr or BBr <sub>3</sub>	bases	electrophiles
ArOCH <sub>2</sub> OMe	MeOCH <sub>2</sub> Cl/ base	HOAc, H <sub>2</sub> O	bases	electrophiles
<b>Protecting Amines RNH<sub>2</sub></b>				
Amides RNHCOR'	RCOCl	NaOH or HCl in water	electrophiles	bases and nucleophiles
Urethanes RNHCO <sub>2</sub> R'	ROCOCl	see text	electrophiles	bases and nucleophiles
<b>Protecting Thiols RSH</b>				
Thioester RSAc	AcCl, base	NaOH, H <sub>2</sub> O	electrophiles	oxidation

# Desconexões de um grupo C-C

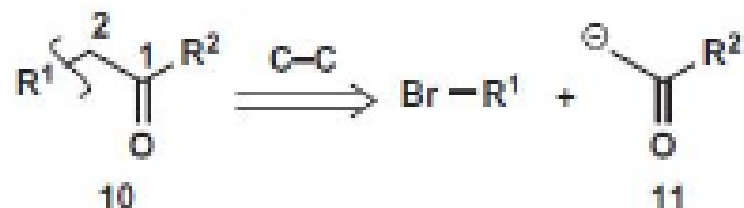
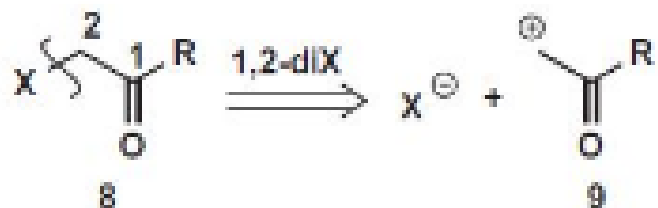
## Tipo I : álcoois rever organometálicos



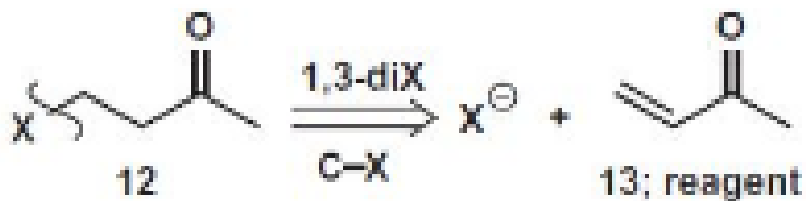
# Correlação entre a desconexão 1,2 di-X e a C-C



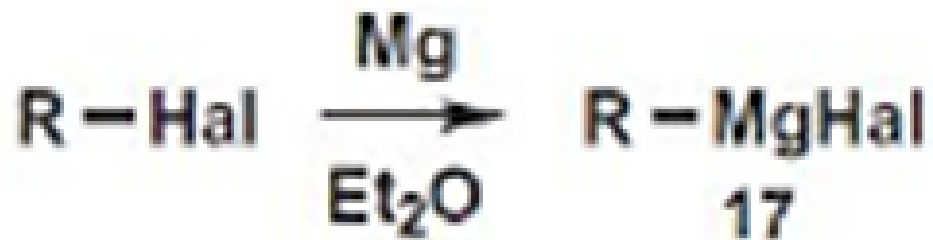
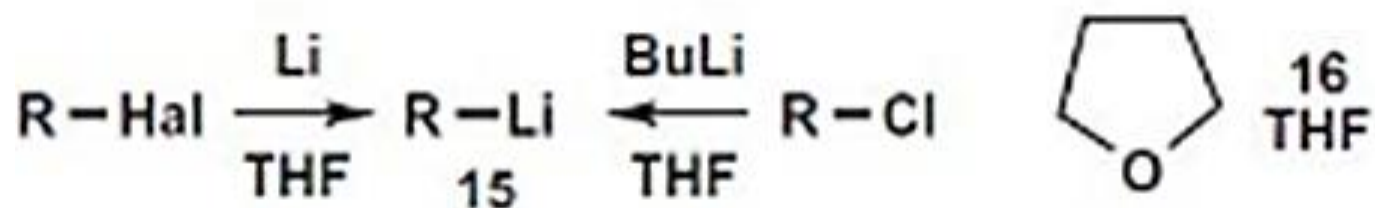
## Correlação entre a desconexão 1,2 di-X e a C-C



## Correlação entre a desconexão 1,3 di-X e a C-C

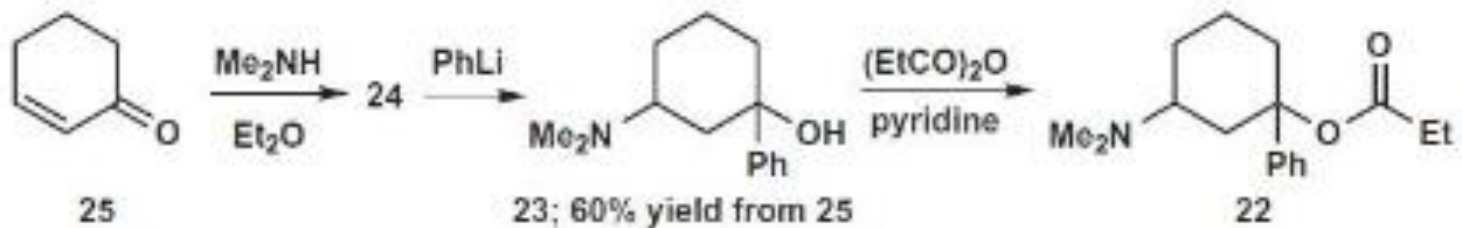
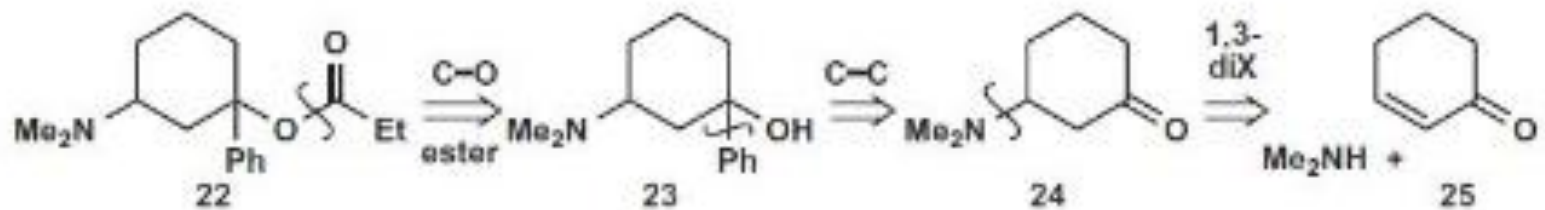
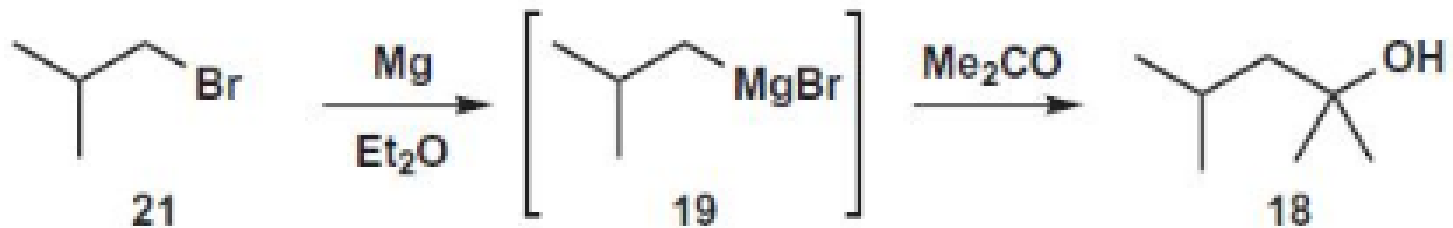


# Reagentes para o Carbono Nucleofílico

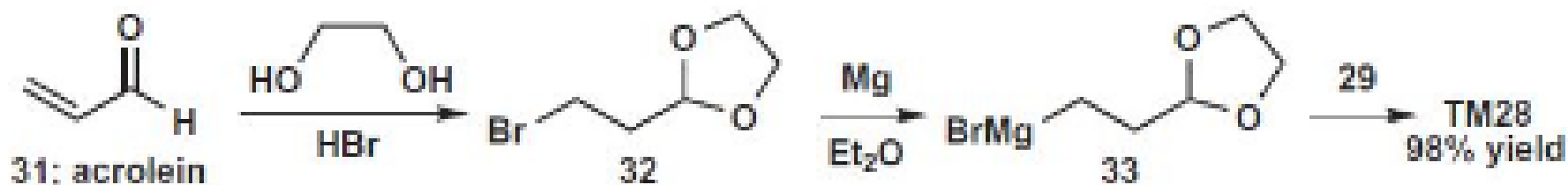
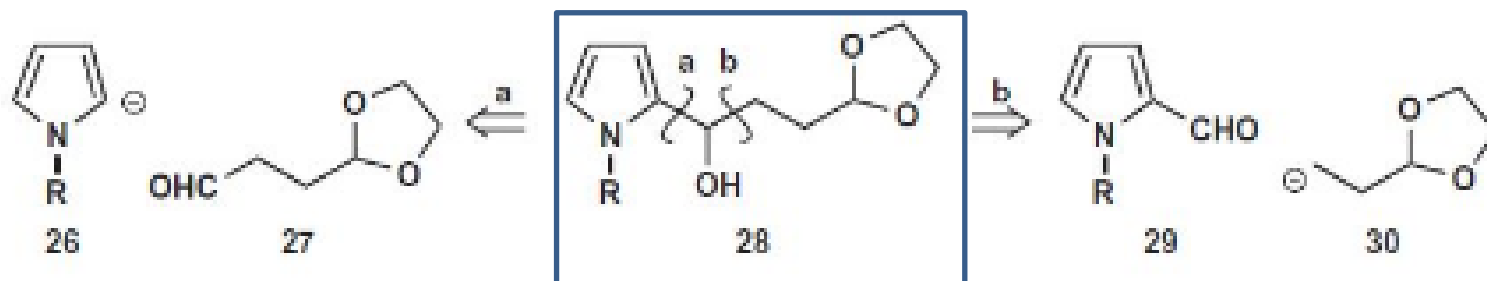




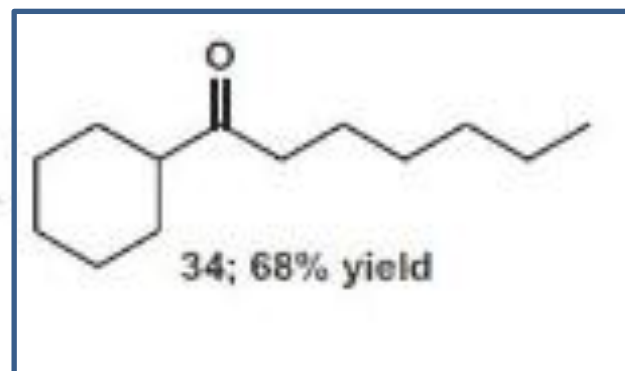
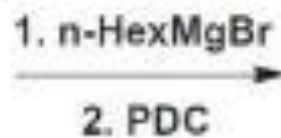
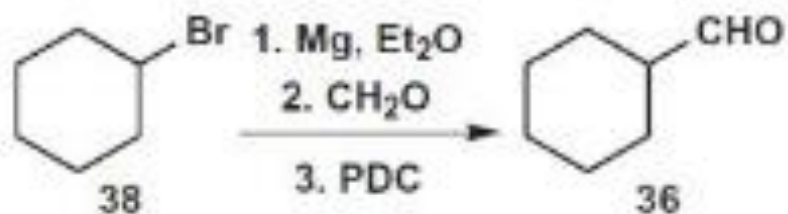
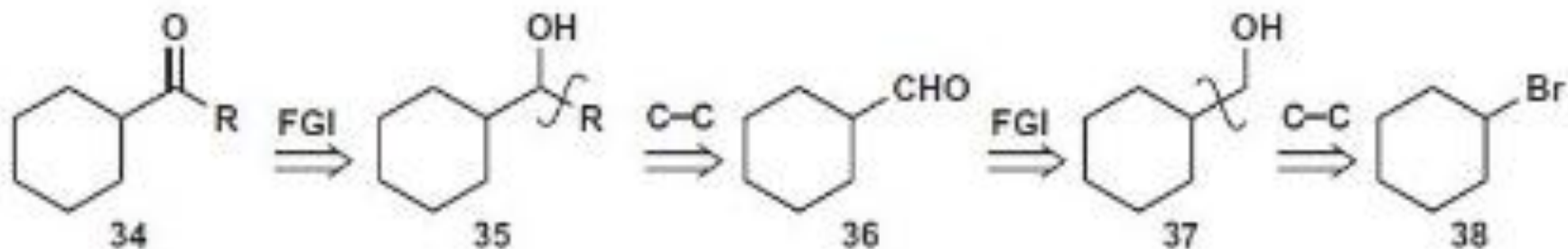
# Desconexão 1,1-C-C álcoois



# Aldeídos e cetonas



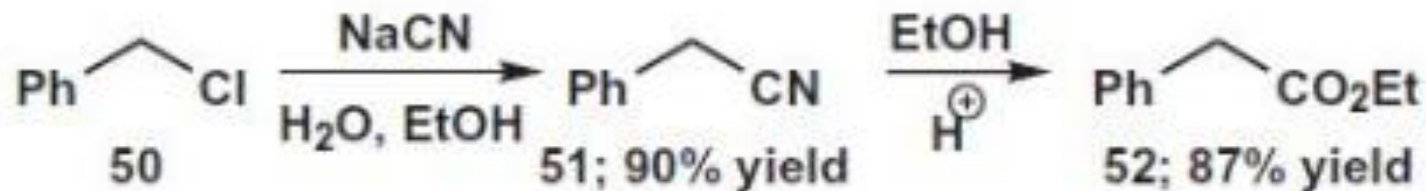
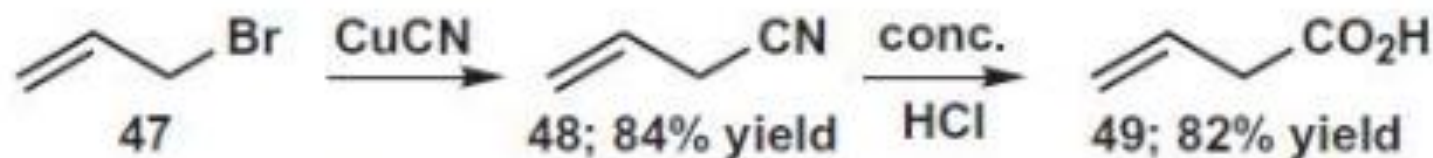
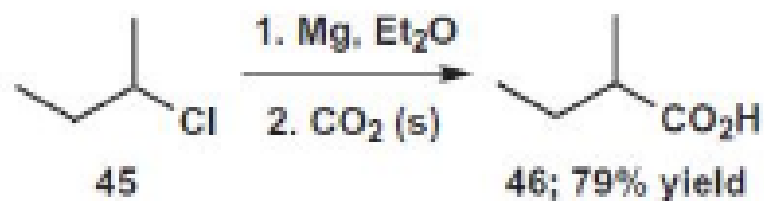
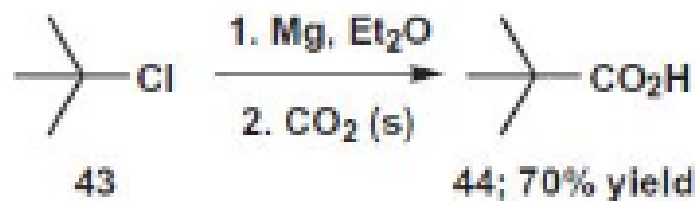
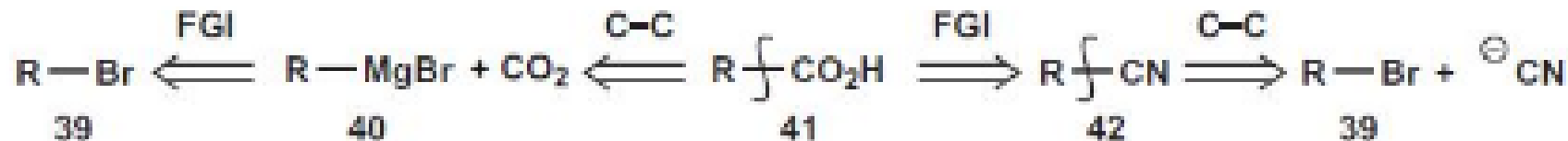
# Outro exemplo



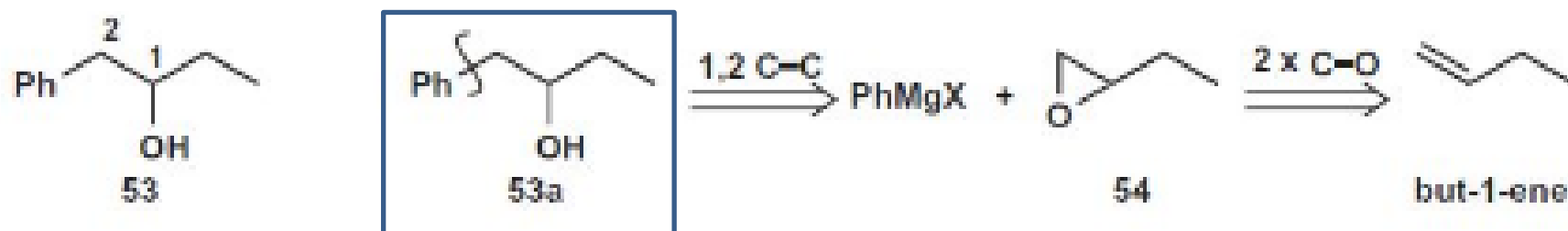
# Agentes oxidantes

## Para ox álcoois a aldeidos

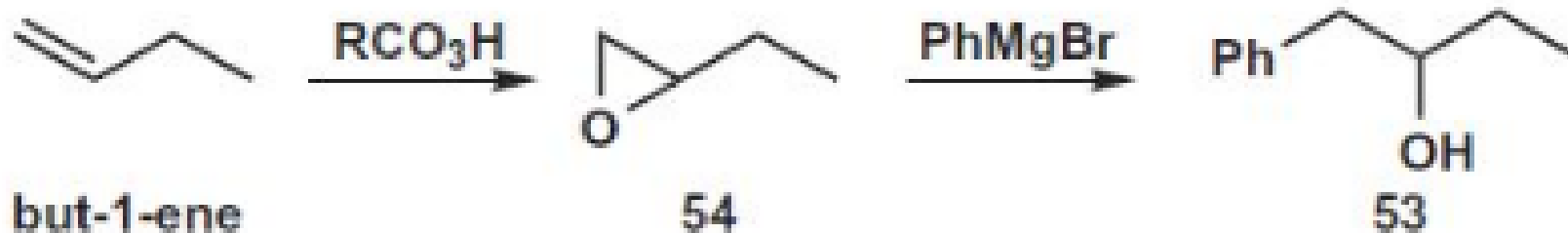
Nome	Reagente	<b>RCH<sub>2</sub>OH to RCHO</b>
–	Na <sub>2</sub> Cr <sub>2</sub> O <sub>7</sub> , H <sup>+</sup>	distil out RCHO as formed
Jones	CrO <sub>3</sub> , H <sub>2</sub> SO <sub>4</sub> , acetone	distil out RCHO as formed
Collins	CrO <sub>3</sub> , pyridine	use in CH <sub>2</sub> Cl <sub>2</sub> solution
PCC	CrO <sub>3</sub> , pyridine.HCl	no modification needed
PDC	(pyridine.H <sup>+</sup> ) <sub>2</sub> Cr <sub>2</sub> O <sub>7</sub>	use in CH <sub>2</sub> Cl <sub>2</sub> solution
Swern	1. (COCl) <sub>2</sub> , DMSO, 2. Et <sub>3</sub> N	no modification needed



# Desconexões 1,2 – síntese de álcoois



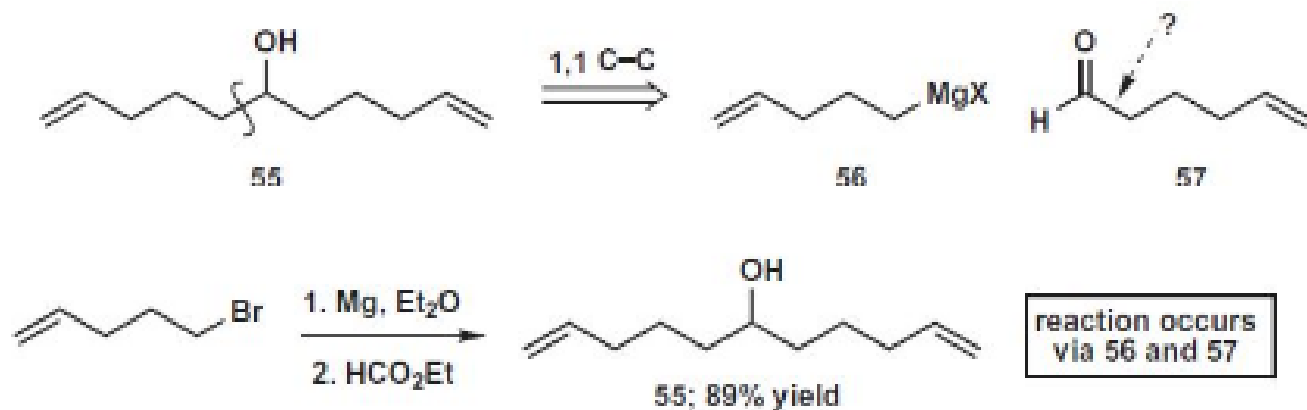
UTILIZADO EM PERFUMARIA

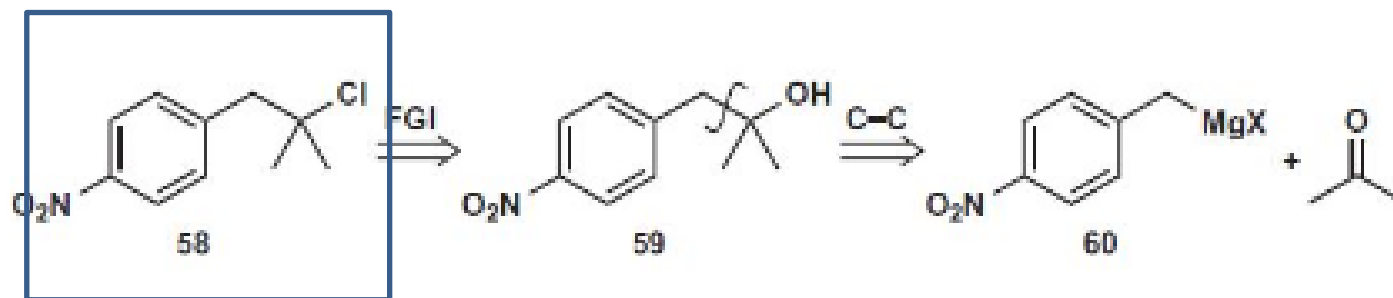


# Compostos Feitos a partir de álcoois

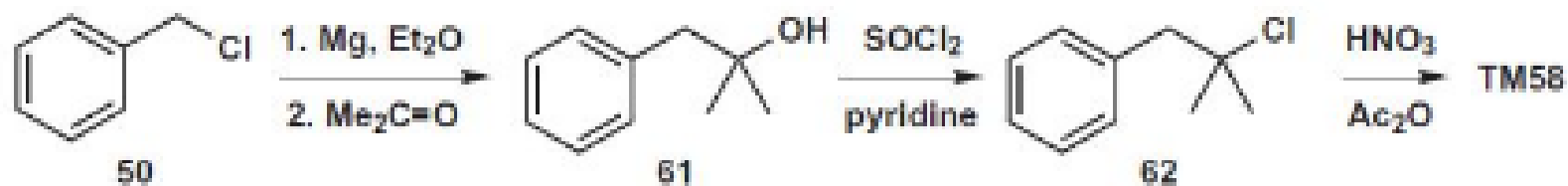
Reaction Type	Product	Chap	Further Products	Chap
Oxidation	aldehydes ketones acids	10	amines by reductive amination or reduction of amides	8
Esterification	esters	4	amines by reduction of amides	8
Tosylation	ROTs	4	other substitutions (see below)	4
HBr or PBr <sub>3</sub>	bromides	4	ethers, sulfides	4
SOCl <sub>2</sub>	chlorides	4	thiols	5
			nitriles	10

## EXEMPLOS





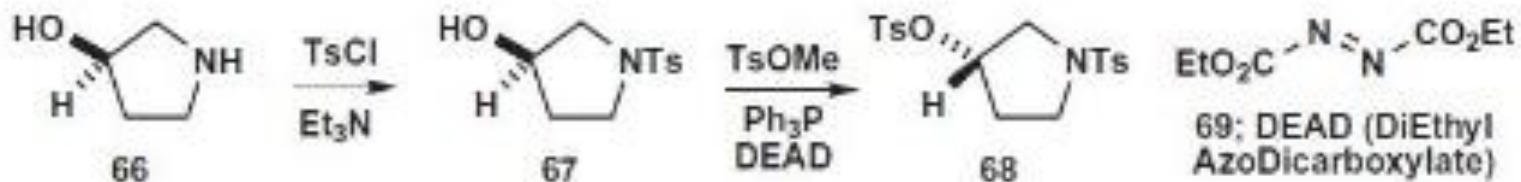
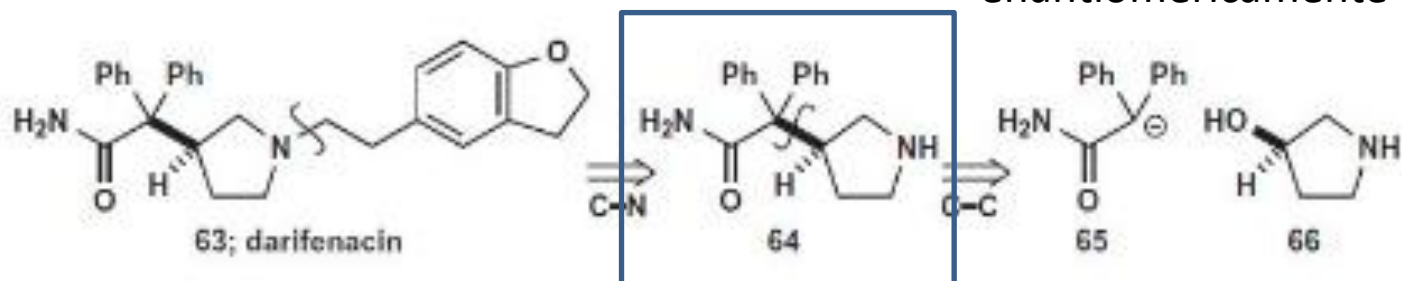
MOLECULA ALVO



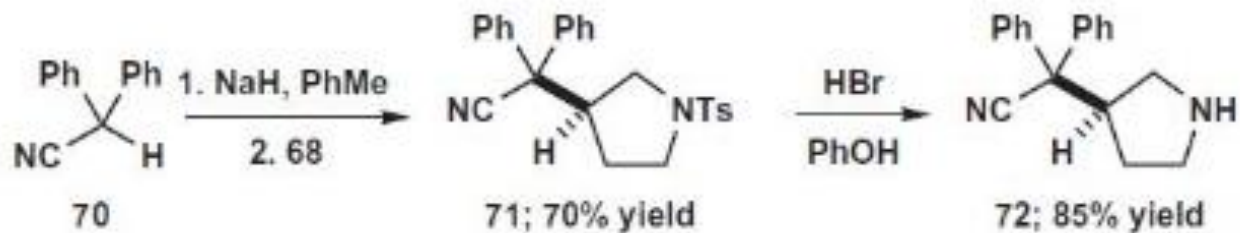


Pfizer para tratar  
incontinencia urinaria

Hidroxi prolina  
enantiomericamente pura



Reação de Mitsunobu



# Mecanismo de inversão de configuração de álcoois pela reação de Mitsunobu

