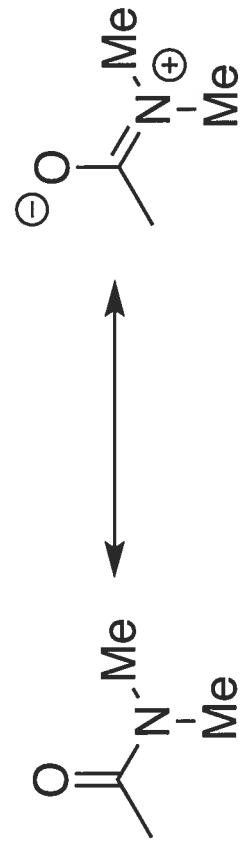


Discussion sections this week!
Quiz A in discussion (1st 5 min)
Full list of discussion and office hours: on the website
Scantron forms now available for purchase from Chemistry
Lab Stockroom

Show your Caper card (or app)
to Kirsten for extra credit. She
is sitting in the back row.

Lecture 5: Organometallic additions to carbonyls, continued

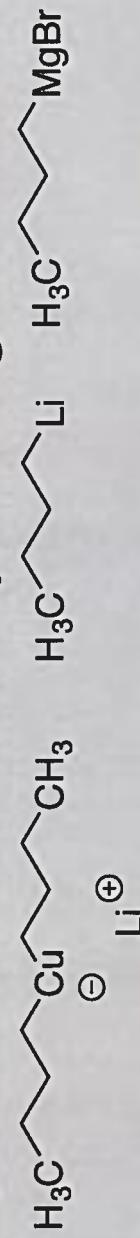


↗ Toto (Africa)

“It’s going to take a lot to take me away from you”

Amides are the least electrophilic carbonyl compounds. They do not react with the organometallic reagents. The only reagent they react with (that you know of so far) is LiAlH_4 .

Capercard question: Most nucleophilic organometallic reagent?



A

B

C

(2)

Monday Tuesday Wednesday Thursday Friday

8 AM

8 AM
DIS Kirst RH 188

9 AM

9 AM
Kirsten OH RH 523

10 AM

10 AM
DIS Kirst RH 188

11 AM

11 AM
Dis Tr SSPA 117

Noon

12 PM
Lecture PSLH 100

1 PM

1 PM
DIS Tr RH 188

2 PM

2 PM
Ayat OH
RH 523

3 PM

3 PM
DIS Tr RH 188

4 PM

4 PM
Elsie OH
RH 523

5 PM

5 PM

Monday Tuesday Wednesday Thursday Friday

8 AM

8 AM
DIS Kirst RH 188

9 AM

9 AM
Mitchel OH RH 523
DIS Kirst RH 188

10 AM

10 AM
Dis Tr SSPA 117

11 AM

11 AM
Tristan OH RH 523
Merrick OH
RH 523

12 PM

12 PM
Lecture PSLH 100

1 PM

1 PM
DIS AI RH 188

2 PM

2 PM
Alissa OH RH 523

3 PM

3 PM
DIS AI RH 188

4 PM

4 PM
Hannah OH
RH 552

5 PM

6 PM

Are you a pre-health student?

A fun NY Times article on why Organic Chemistry is relevant to medical school
https://www.nytimes.com/2013/11/03/education/edlife/how-to-get-an-a-in-organic-chemistry.html?pagewanted=2&_r=0

"You can't memorize all the possible answers — you have to rely on intuition, generalizing from specific examples. This skill, far more than the details of every reaction, may actually be useful for medicine.

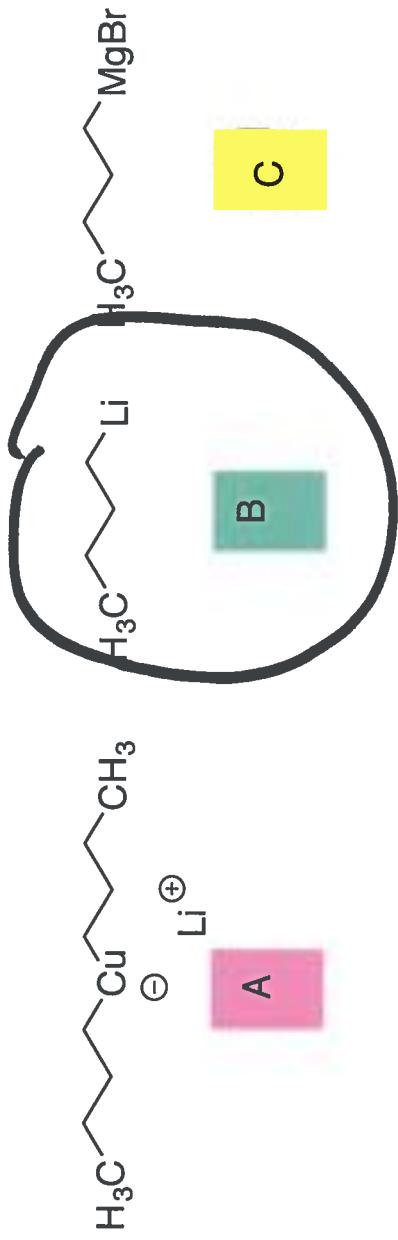
"It seems a lot like diagnosis," said Logan McCarty, Harvard's director of physical sciences education, who taught the second semester. "That cognitive skill — inductive generalization from specific cases to something you've never seen before — that's something you learn in orgo."

To develop orgo intuition, you solve problems and draw arrow-pushing mechanisms again and again, until they become instinctive. This takes a huge amount of time, for me 20 to 30 hours a week. The class turned me into a bore, a sleep-deprived, orgo-obsessed grind who saw the shapes of molecules in every sidewalk crack and snack cracker."

NOMINATE Songs!

④

Capercard question: Most nucleophilic organometallic reagent?



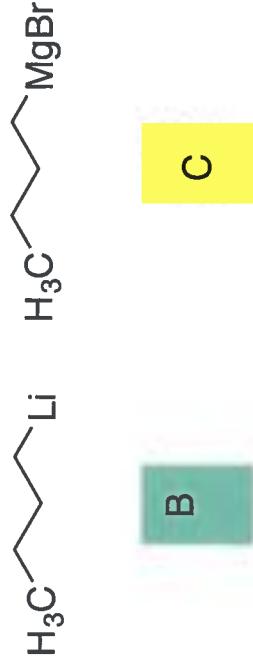
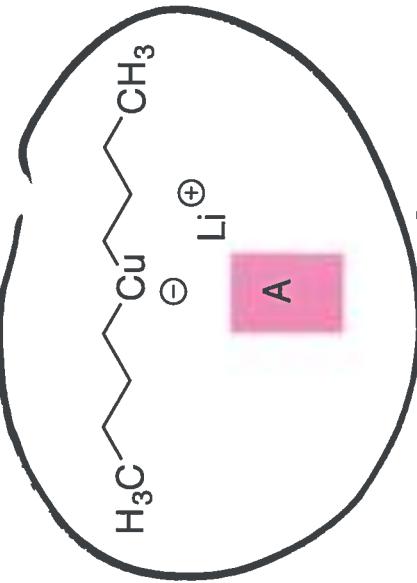
very
reactive!

$n\text{BuLi}$

all

Organolithiums

Capercard question: Least nucleophilic organometallic reagent?



cuprate!

cations we work with:

Li^+ and R_2CuLi

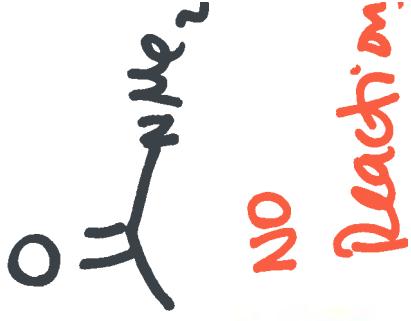
R_2MgBr interchangeable

R_2CuLi is much less reactive
different!

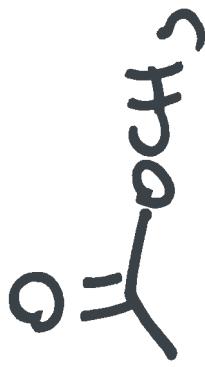
(6)

SONG

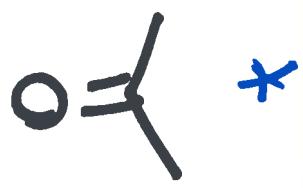
Last day



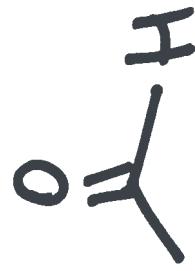
NO
Reaction



*



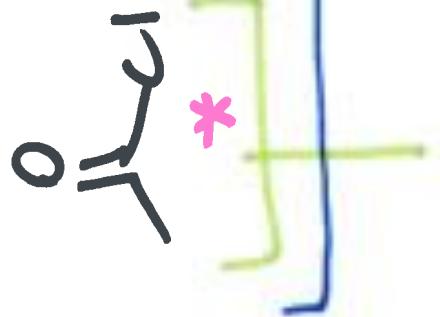
*



*

PdI or Pm₃Br

*



*

Cuprate
* ScCuLi

today!

⑦

Reactions of Grignards:

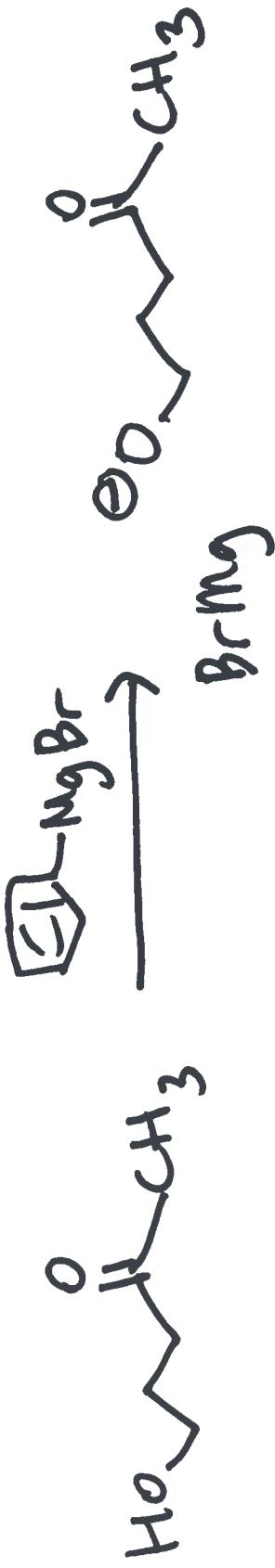
good nucleophiles
and
good bases.

PROTECTING groups

- Sometimes necessary to protect acidic functional groups.



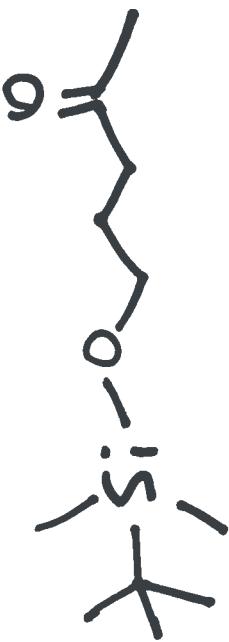
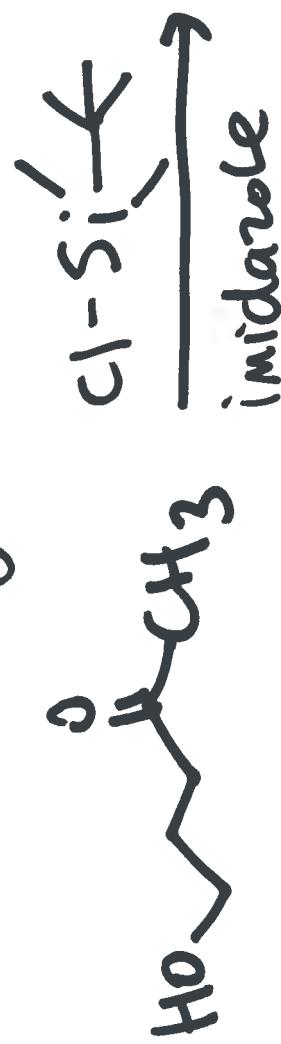
8



AND BASE Reactions
VERY FAST!

Must mask the alcohol: PROTECT IT!

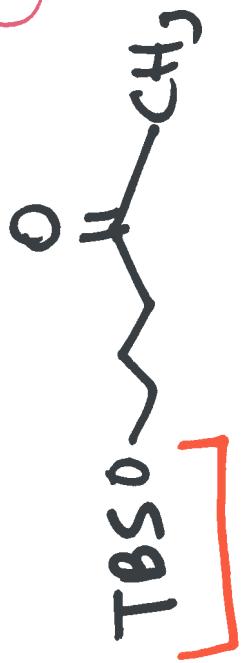
Protecting an alcohol: silyl ethers



Same as

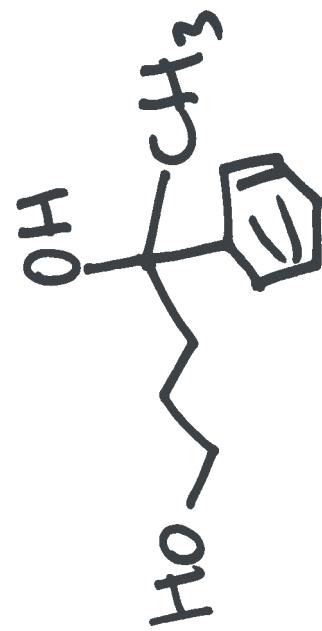
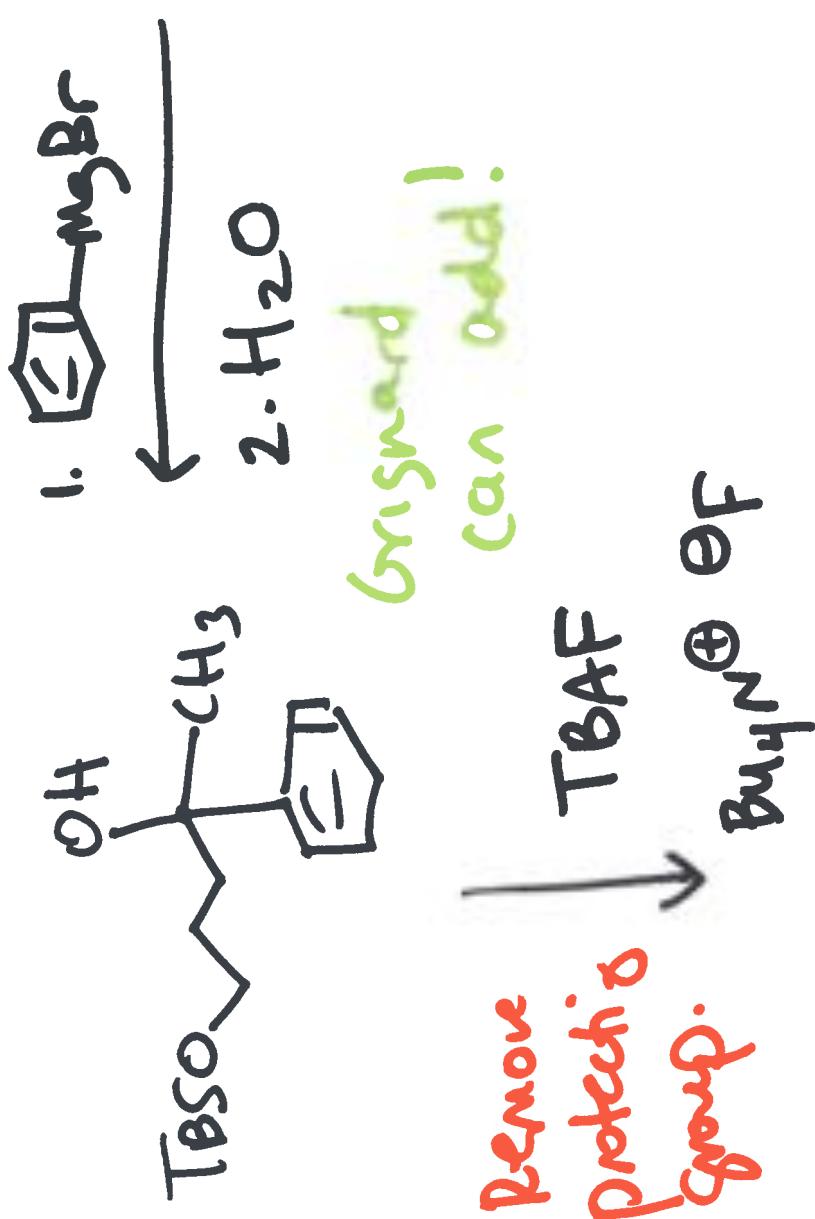
TBS-CH₃ = t-butyl dimethyl silyl chloride

(9)

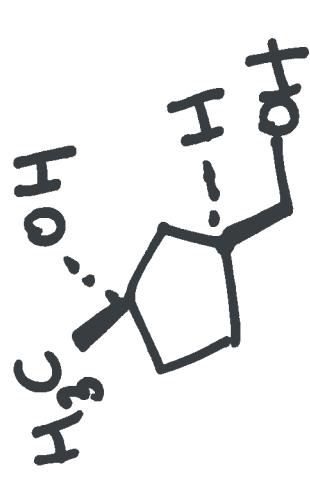
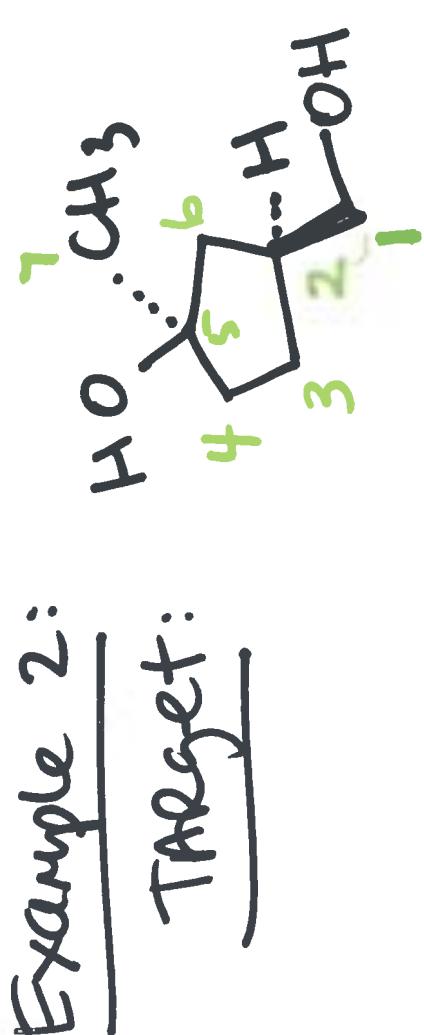


not acidic
just stays
here.

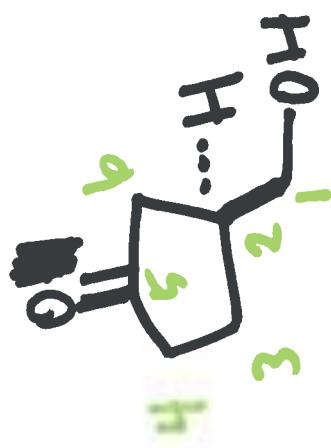
Si-O bond
Strong
Si-F bond
Stranger.



10



Coumarin
Carboxylic acid



Starting material:

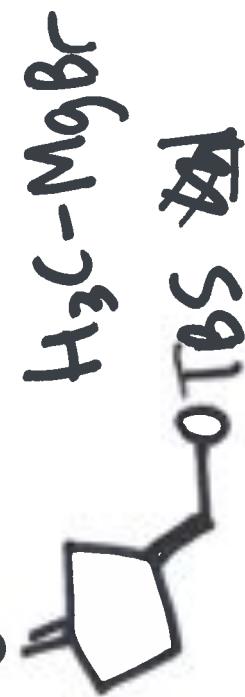
Add " ΘCH_3 " to

carbon 5

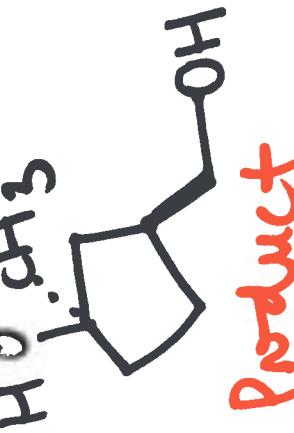
PbCl_2

could use QMgBr on

O



\Rightarrow
reagent



Product

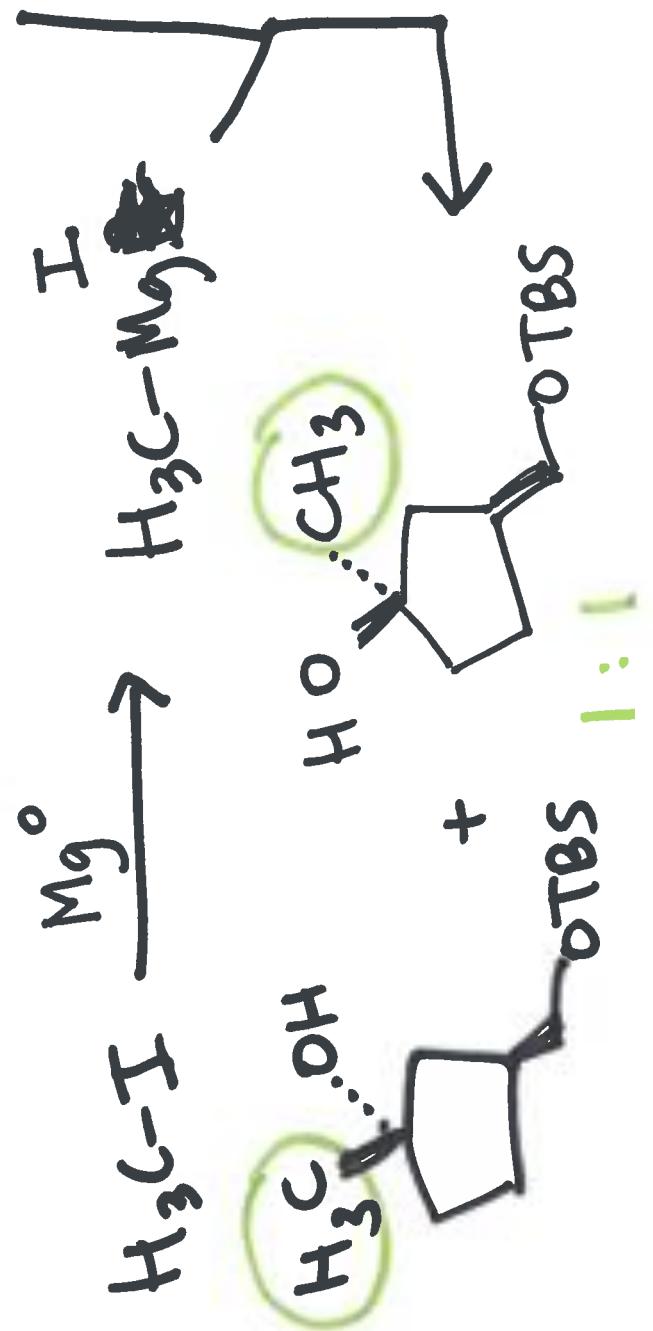
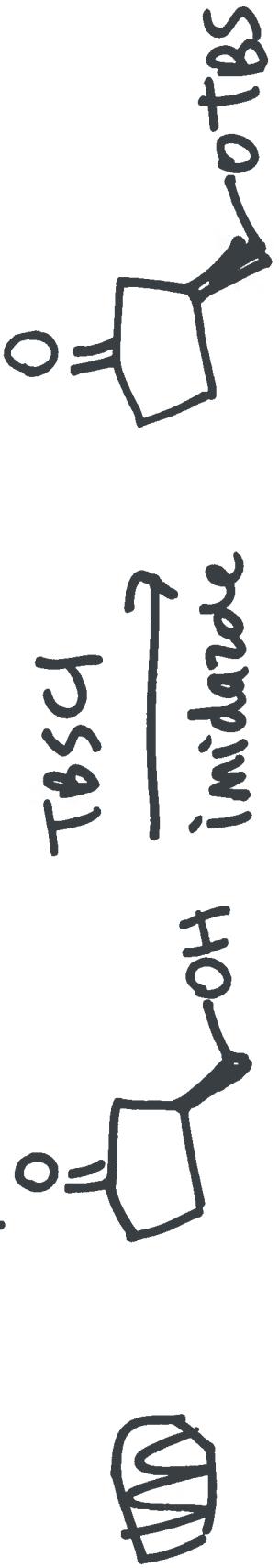
\Rightarrow
Starting material

11

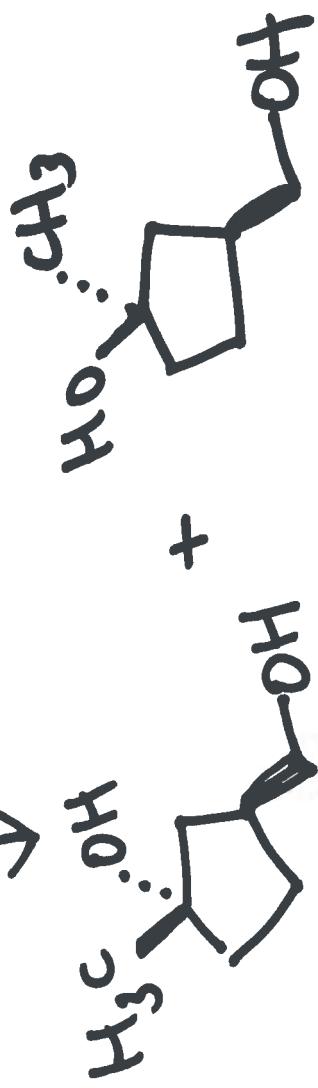


Starting materials

Forward (synthetic direction)



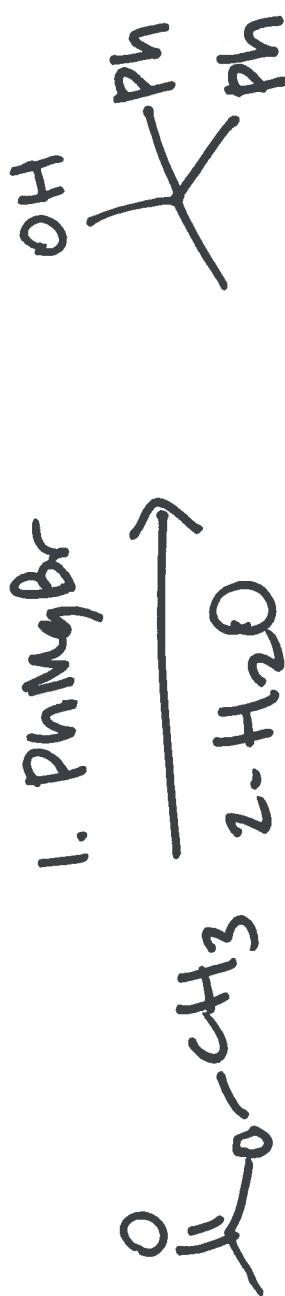
(12)



Do I need to protect something?
more than one functional group?

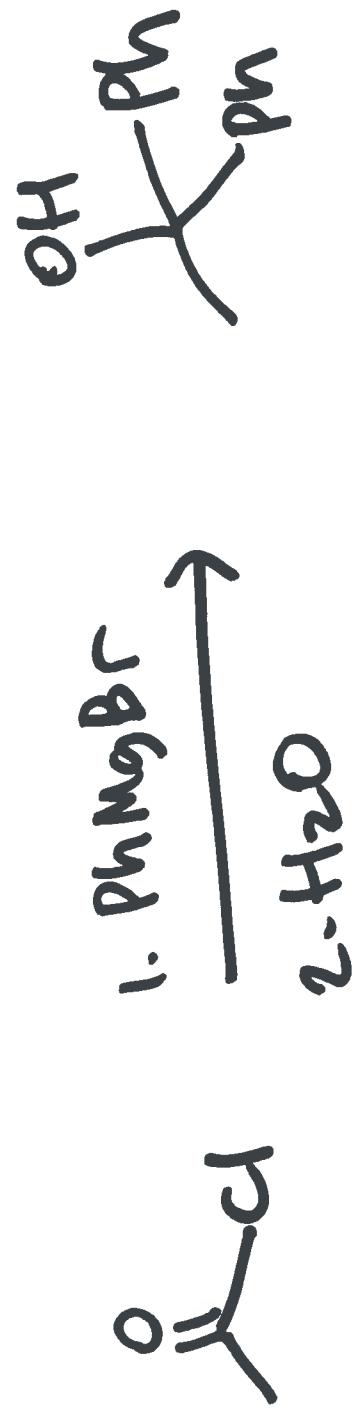
Next: Reacting with esters + acid chlorides

26



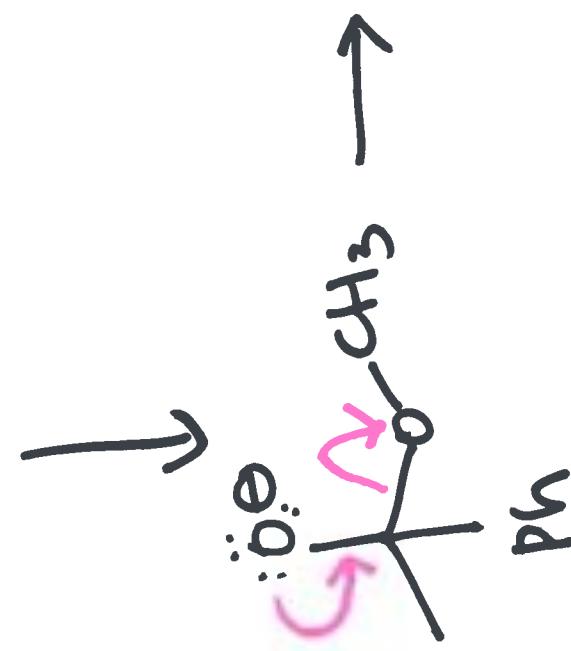
DOUBLE
ADDITION

(PhLi the same!)

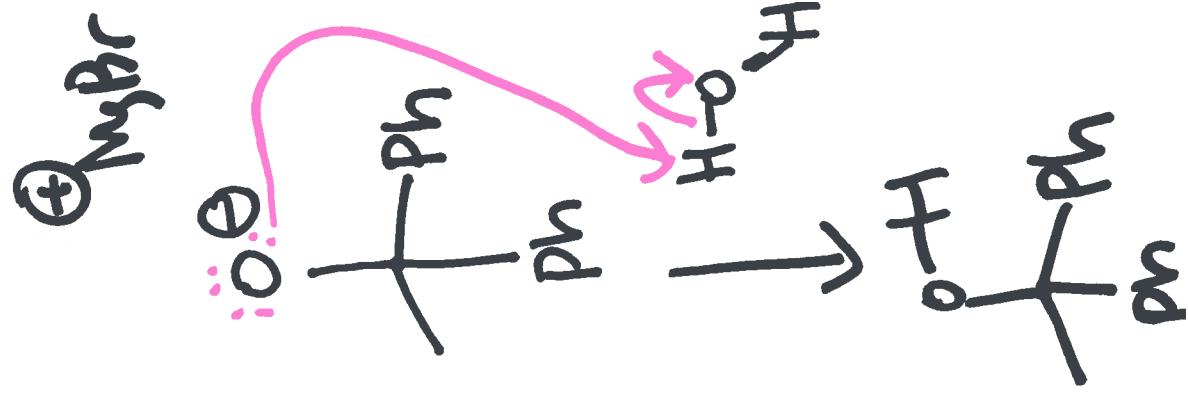


(or PhLi the same)

Mechanism:

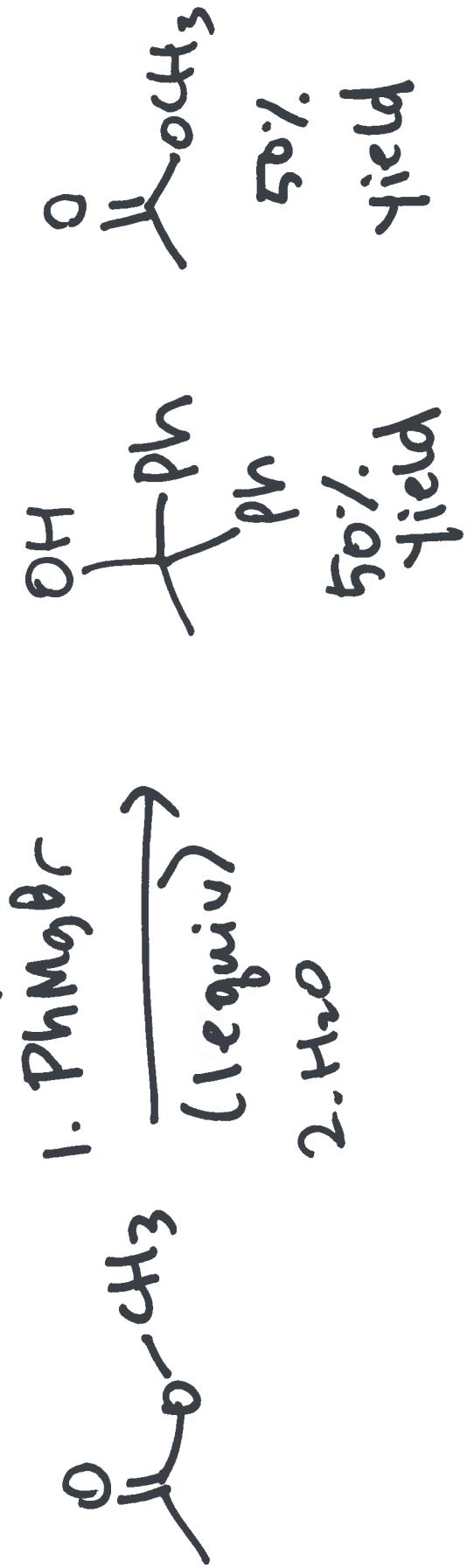


tetrahedral intermediate



One equiv of Grignard?

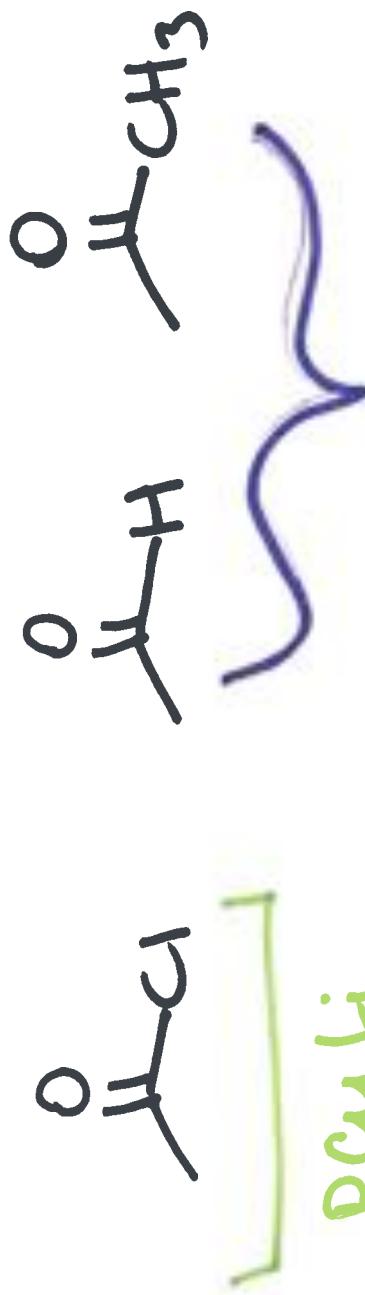
adds twice... because ketone is
MORE electrophilic than ester



Mechanism: Acyl substitution
— SAME as reduction of ester with
 LiAlH_4

16

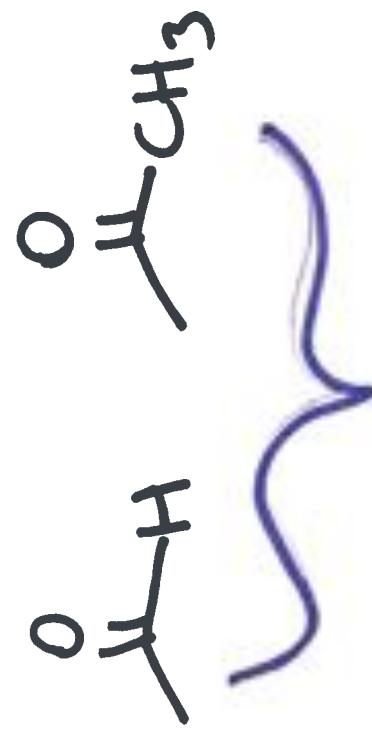
What about cuprates? Special!



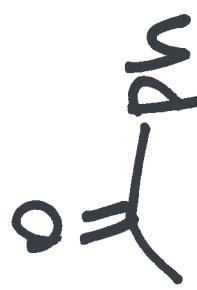
electrophilic

R_2CuLi

can not attack



Ph_2CuLi

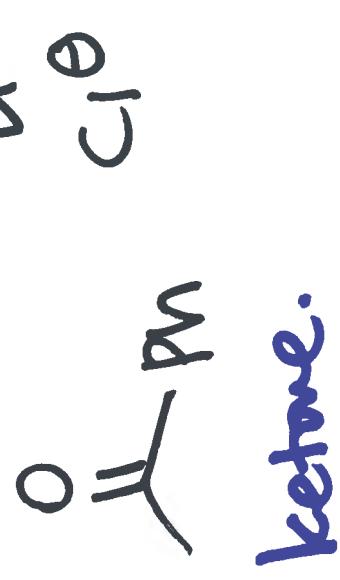


Add one!

Mechanism?



+ tetrahedral intermediate

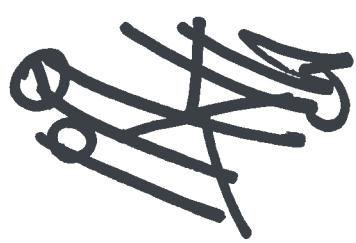


Ketone.

Cuprate
can not
attack!!!

Reaction stops HERE!

DO NOT DO THIS



THIS IS
WRONG!



DO NOT DO $\text{S}_{\text{N}}2$ ON sp^2 CARBONS!