

Course 345

Day Wed

Notes Taken By Adams

Instructor Gellman

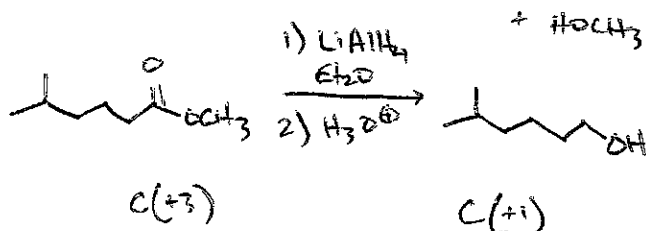
Date 4/02

Total # of Pages 6

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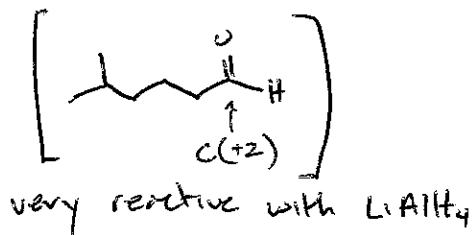
Recall: Reduction of carboxylic acid derivatives

1) Ester \rightarrow 1 $^\circ$ alcohol



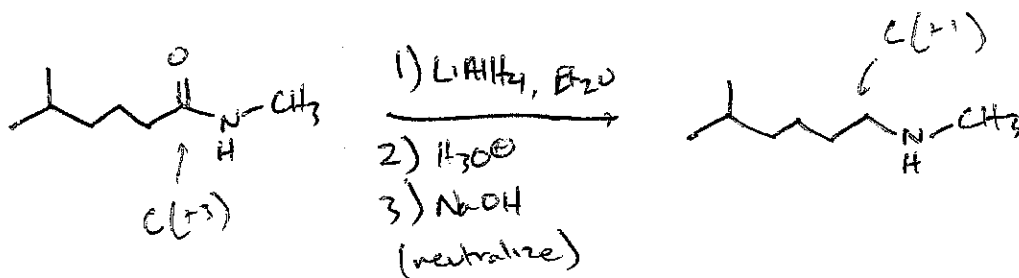
- Reaction proceeds via aldehyde, but cannot stop at this stage.

• NaBH_4 does not reduce esters.

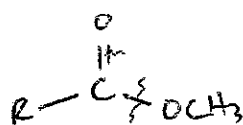


2) Amide \rightarrow amine, via LiAlH_4 (not NaBH_4)

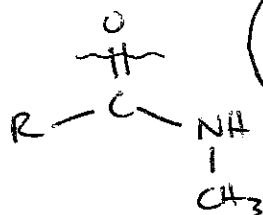
Ex:



Contrast:



vs

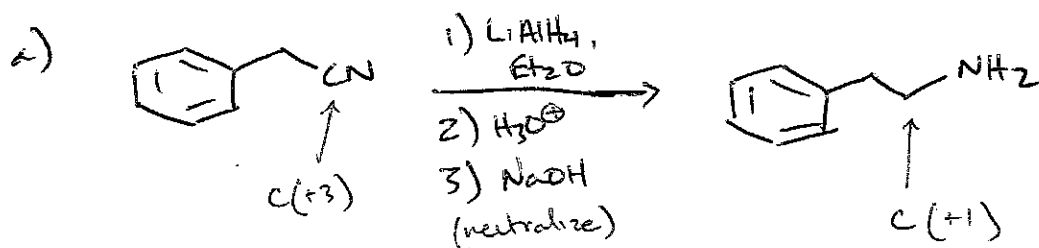


see text

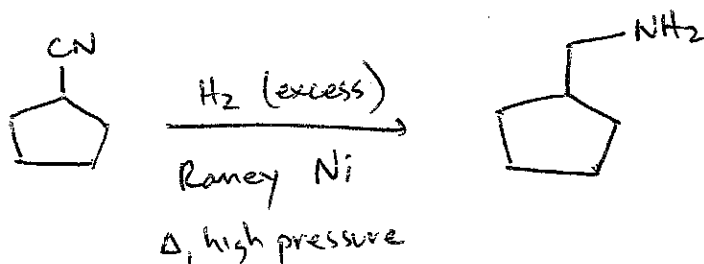
Different bonds broken depending on identity of substrate (i.e., ester vs amide)

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3) Nitrile \longrightarrow amine (2 methods)



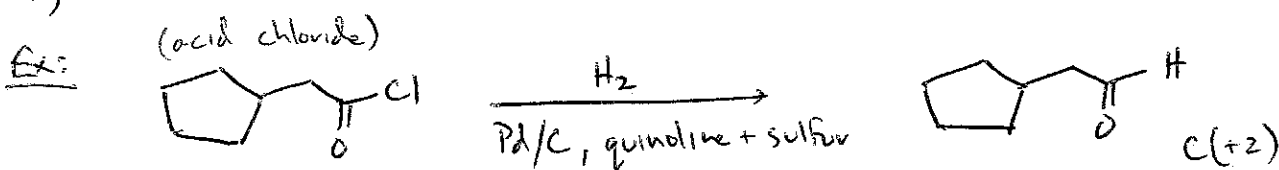
b) catalytic hydrogenation



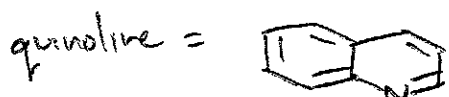
• Is it possible to stop this sort of reduction at the C(+2) stage?

— Yes — one approach involves more reactive C(+3) starting point and special reagents.

1) Rosenmund reduction (H_2 + "poisoned" catalyst)

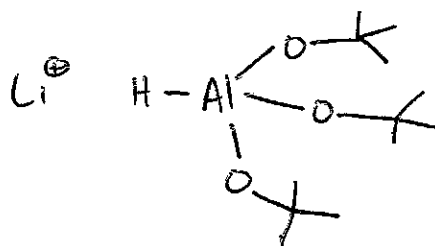
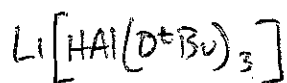


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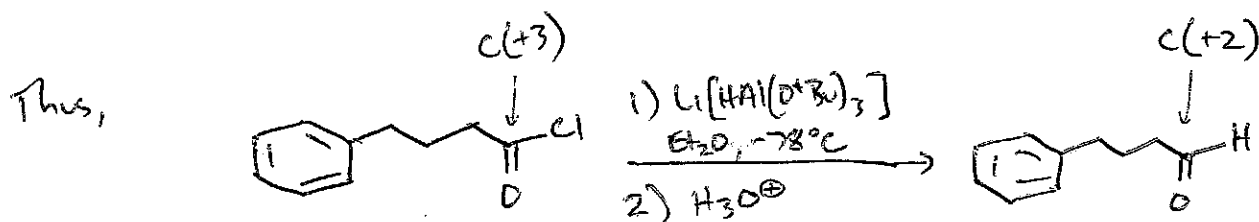


(important thing to remember is
the "poisoned" Pd catalyst)

2) Bulky hydride source

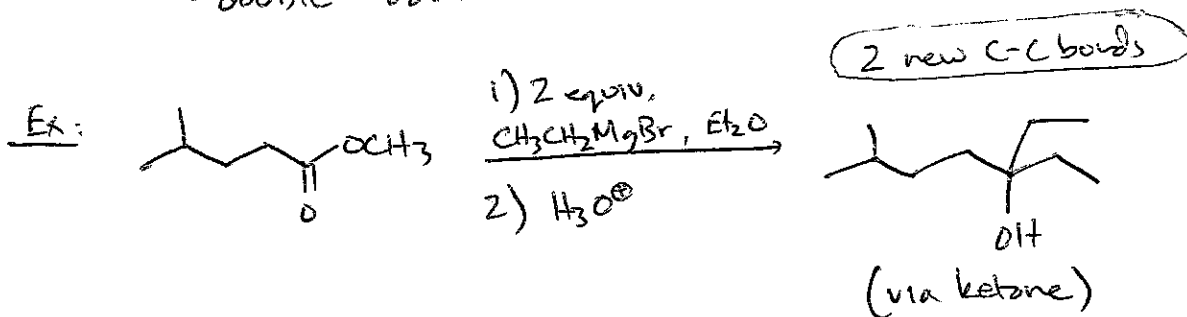


steric bulk surrounding Al-H unit limits reactivity

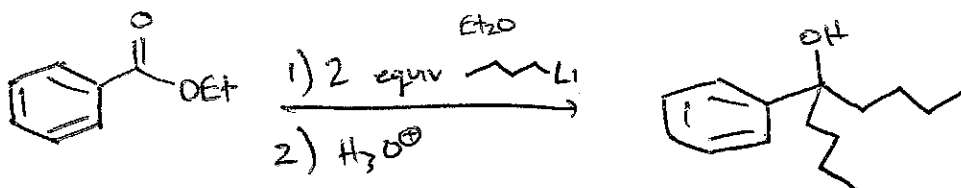


• Rxns of carboxylic acid derivatives w/ organometallic reagents (carbanion-like species)

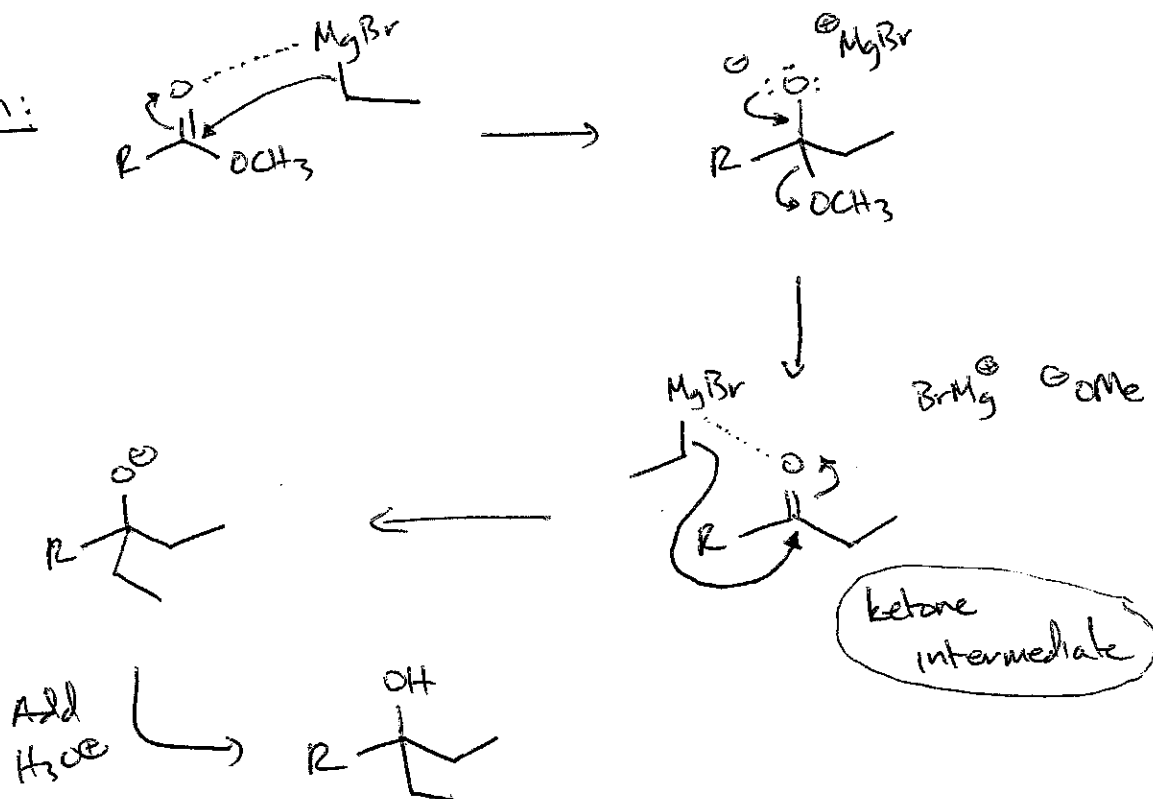
1) Ester + Grignard/organolithium reagents
 - double addition



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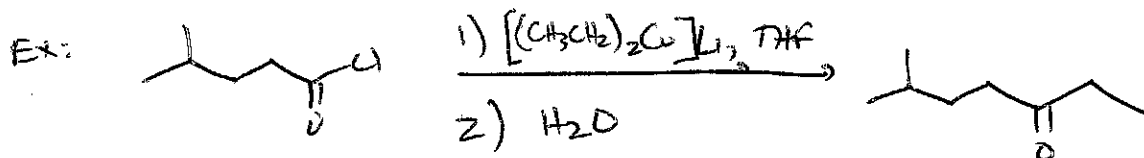
Mech:



2) Acid chloride + lithium diorganocuprate reagents



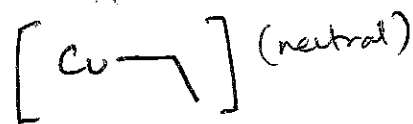
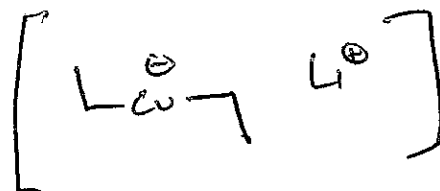
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recall: cuprate reagents

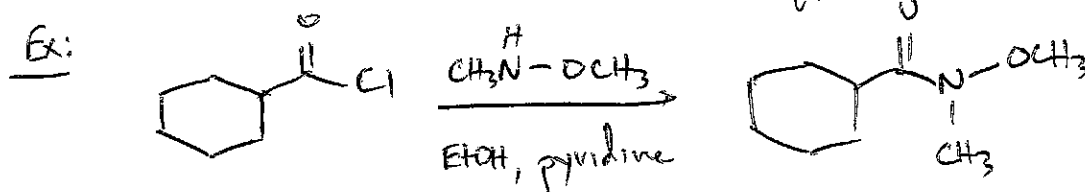


Note: After reaction w/ acid chloride, byproduct is



(not reactive w/ ketone)

Alternative - use of "Weinreb amides"



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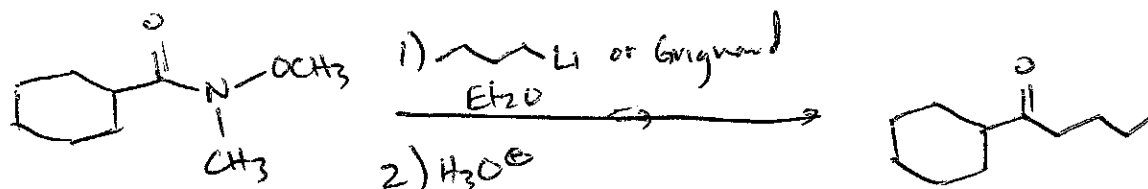
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Key feature - stable tetrahedral intermediate

