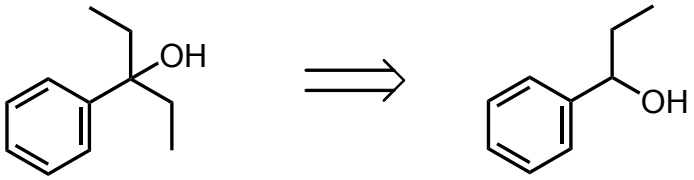
## Retrosynthesis of Carbonyl Derivatives

This Core Concept Sheet covers retrosynthetic analysis using carbonyl addition, substitution, and redox reactions.

*For a more thorough overview of these individual reaction profiles, see the Aldehydes & Ketones, Carbonyl Substitution, and Reduction & Oxidation Core Concept Sheets and accompanying worksheets.*

**Worked Example 1**

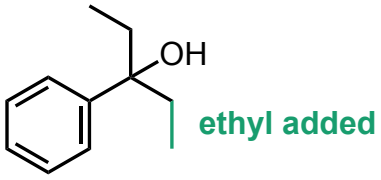



**target product** **starting material**

To begin, let's consider a series of guiding questions:

A. Has the **number of carbon atoms changed**?

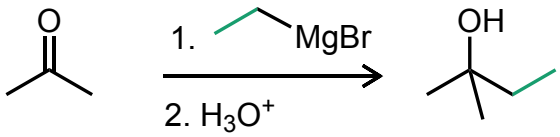
B. Are there any **new functional groups**?




If we consider the first two questions, we see that (A) **two carbon atoms (ethyl group)** have been added; and (B) **no new functional groups** have been added.

C. What types of **precursor(s)** and **reaction(s)** could introduce the new carbon atoms and/or the new functional groups? (e.g. carbonyl addition, carbonyl substitution, reduction/oxidation, etc.…)

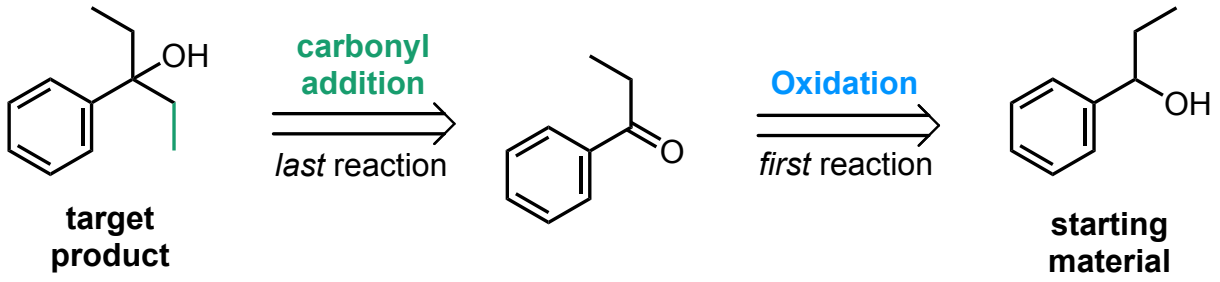
The **ethyl group** can be installed through a grignard addition to a ketone



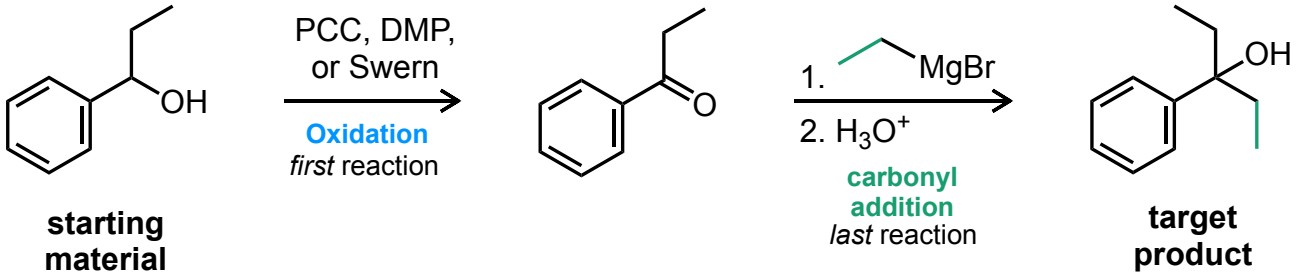

D. Finally, **what order of these reactions** is needed to achieve the target final product?

To set up for the Grignard addition of the ethyl group (nucleophile), we must first have an electrophile. Therefore, **we must first obtain a ketone electrophile** from the alcohol starting material **through an oxidation reaction.**

Therefore, our **full retrosynthesis** is:




And the **forward synthesis**:

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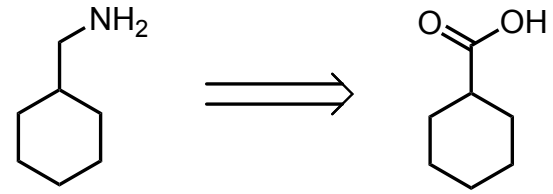
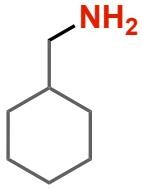
**Worked Example 2**



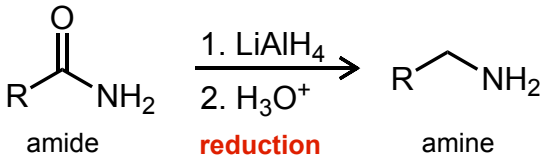

To begin, let's consider the same set of guiding questions.



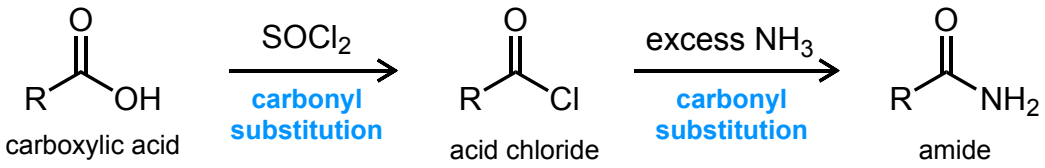

If we consider our first two questions, we see that (A) **no new carbon atoms** have been added nor removed and (B) the **carboxylic acid has been replaced with a 1º amine**.

C. What types of **precursor(s)** and **reaction(s)** could introduce the new carbon atoms and/or the new functional groups? (e.g. carbonyl addition, carbonyl substitution, reduction/oxidation, etc….)

We can obtain a 1º amine from
the **reduction** of a 1º amide



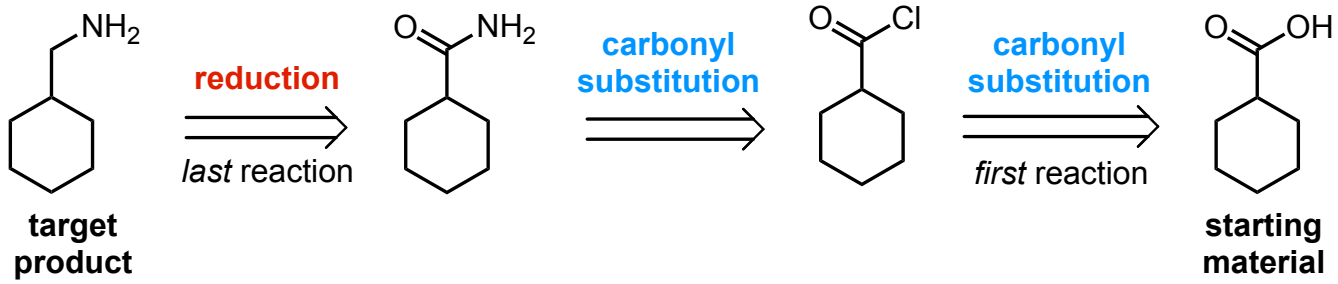

However, **we must first convert our carboxylic acid to an amide**. This is most commonly done through the acid chloride using a series of **carbonyl substitution** reactions.




D. Finally, **what order of these reactions** is needed to achieve the para relationship?

To obtain the amine, we must reduce the amide as our *last* step of the synthesis.

Therefore, our **full retrosynthesis** is:




And the **forward synthesis**: