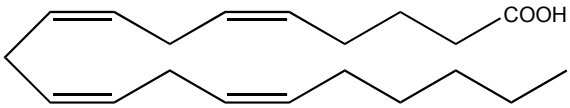
Chem 263 B6 – March 23, 2006

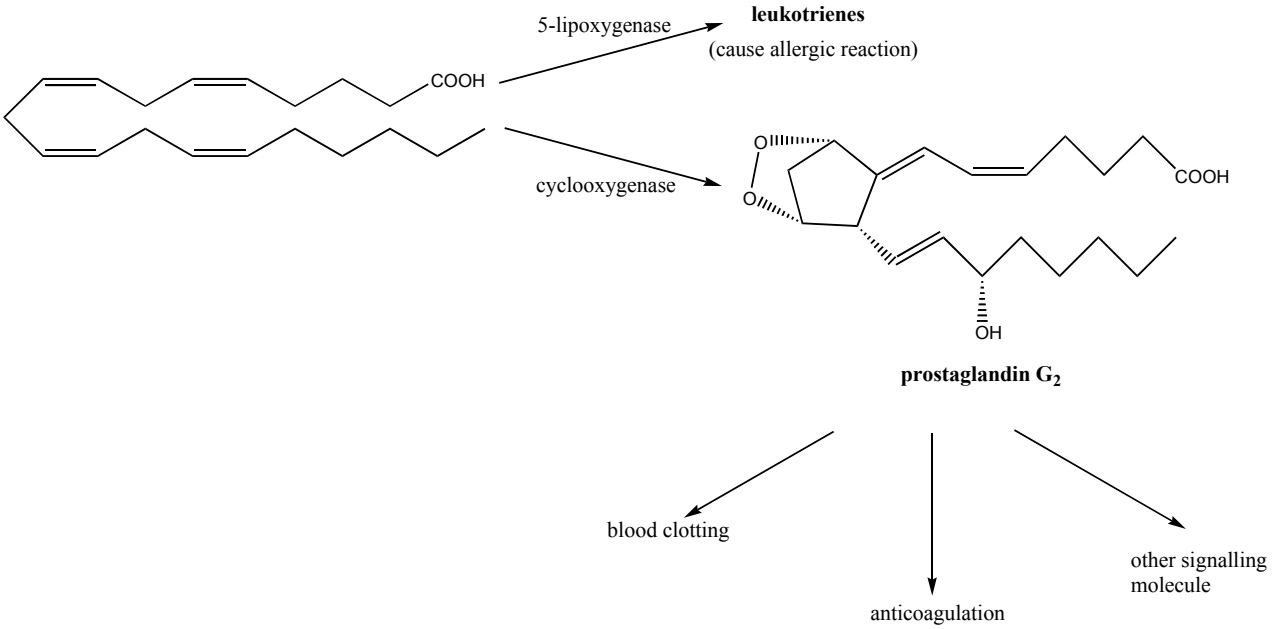
Review of Nomenclature of Carboxylic Acids and Derivatives

Example:



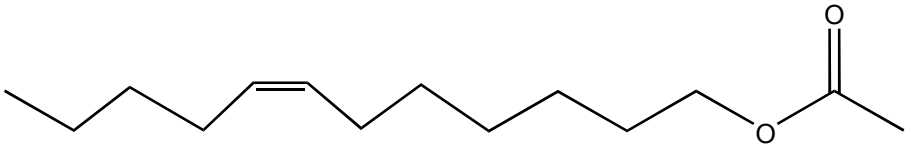
Arachidonic Acid

Arachidonic acid is a polyunsaturated fatty acid, and is one of the essential fatty acids required by most mammals. It is a precursor in the production of eicosanoids: the prostaglandins, thromboxanes, prostacyclin and the leukotrienes (through enzymes including cyclooxygenase, lipoxygenase and peroxidase).



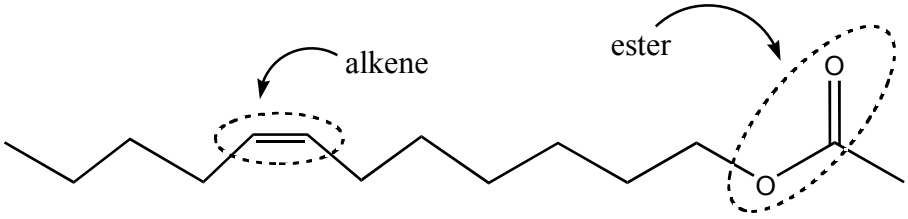
Chemically, arachidonic acid is a carboxylic acid with a 20-carbon chain and four *cis* double bonds. Recall from previous lecture, a 20-carbon alkane is named eicosane.
To name the acid, you would drop '-e", add "oic acid". Since arachidonic acid has 4 double bonds, it would an eicosatetraene. All double bonds are cis, therefore are in Z configuration. Putting everything together, the systematic name is **5Z,8Z,11Z,14Z-eicosatetraenoic acid**.

Example:

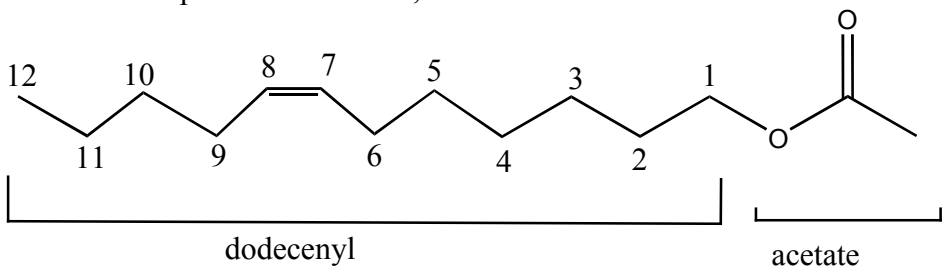


The molecule shown is a sex pheromone for elephants.

What kind of functional group is present in this molecule?



Recall from last lecture, for esters, you name the alkyl part first (drop "e" and add "yl") and then the "ic" of the parent acid is replaced with "ate".
The alkyl group attached to oxygen has 12 carbons. A 12 carbon alkane is named a dodecane, and the corresponding alkene would be dodecene. The parent acid is acetic acid. When replaced with "-ate", it is acetate.

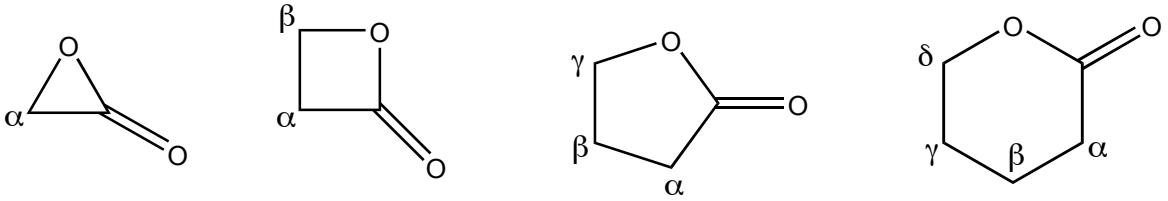


The systematic name for this pheromone is **7Z-dococenyl acetate**.

If any part of this molecule is changed (remove a carbon, or extend by a carbon on the acetate part, or change the configuration of the double bond), it would not work as sex pheromone.

Cyclic esters are called **lactones**

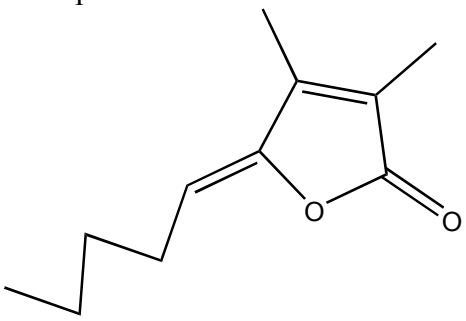
The ring size of the lactone can be described by starting at the carbonyl carbon and designating the other carbons in the ring with Greek letters (shown in figure) until the oxygen atom is reached.



α-lactone **β-lactone** **γ-lactone** **δ-lactone**

You should be able to recognize all four lactones shown above and know that lactones are cyclic esters.

Example:

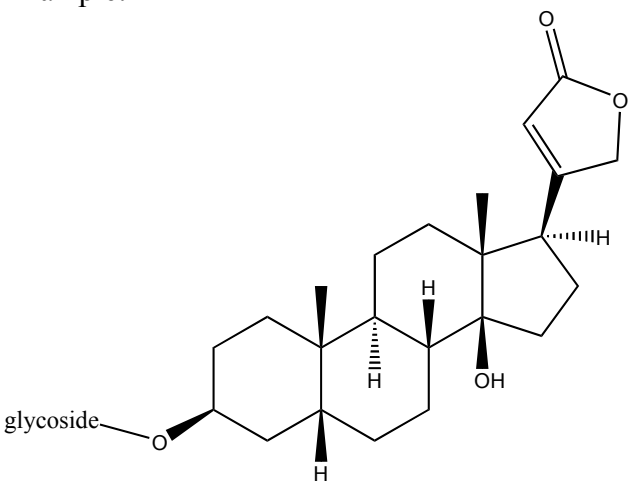


bovolide

Bovolide is responsible for the butter flavor.

What kind of lactone is the above molecule?
Answer: It is a γ-lactone. Specifically, an α,β-unsaturated γ-lactone.

Example:

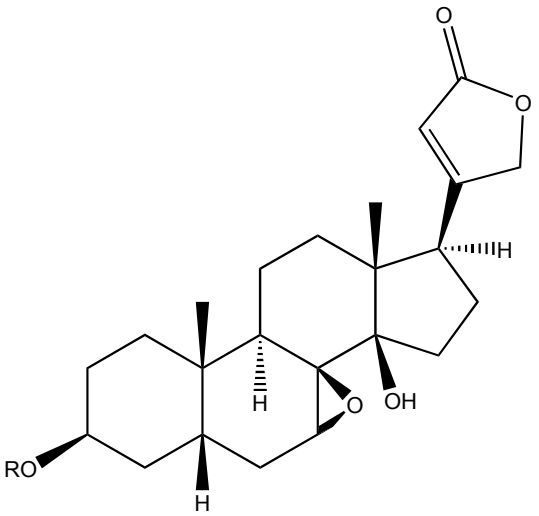


This molecule is digitoxin from plant foxglove. It is a very toxic substance. In small amounts, it is a cardioactive drug. If taken in excess, it is a heart stimulant that can give instant heart attack.

Is the O at position 3 on the A ring α or β substituted?
Answer: it is β.

What kind of lactone does it have?
Answer: it is γ-lactone, since the lactone is 5-member ring.

Example:

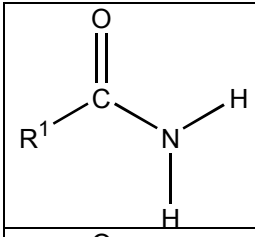
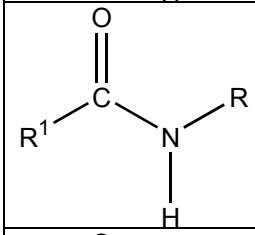
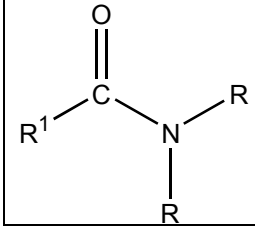


This molecule is Tanghin, and was used at one time to determine if an accused person is innocent or guilty in trial by ordeal. The only difference between this molecule and digitoxin is the epoxide at carbon 7 and 8.

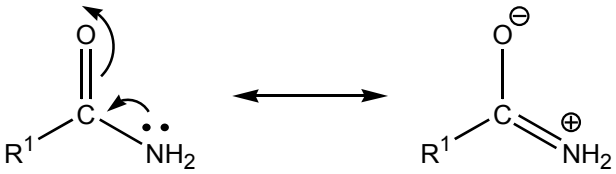
Amide Nomenclature

Name the corresponding acid, drop "-ic acid" or "oic acid", add "amide". If there is alkyl group on the amide nitrogen, then precedes the name with N-alkyl.

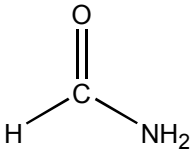
Classification:

	Primary amide where there are two hydrogens attached to amide nitrogen
	Secondary amide where there is one hydrogen attached to amide nitrogen
	Tertiary amide where there is no hydrogen attached to amide nitrogen

Usually amides are planar, because the lone pair on nitrogen can conjugate into the carbonyl.

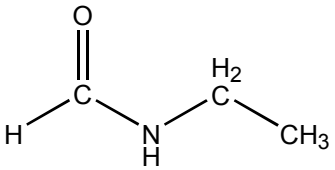


Example:



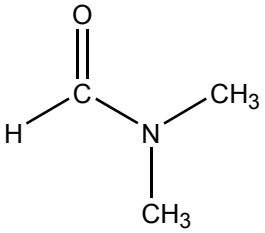
Nomenclature: **Formamide**. The corresponding parent acid is formic acid. Follow the rule above, drop "ic acid" and replace with "amide", this molecule is named as formamide.

Example:



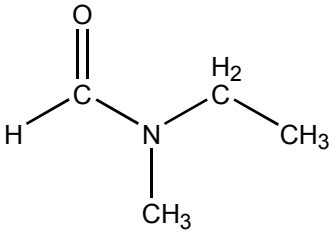
Nomenclature: **N-ethylformamide**. The letter "N" at the beginning of the name indicates that the ethyl group is attached on the nitrogen.

Example:



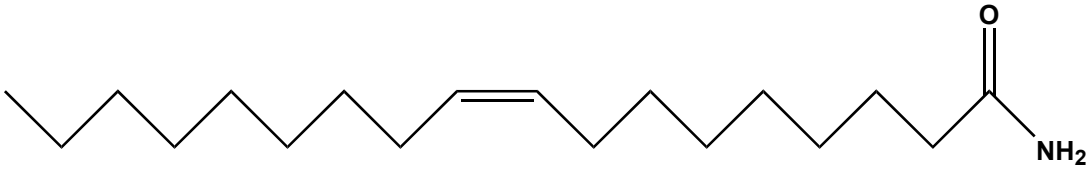
Nomenclature: **N, N-dimethyl formamide** (DMF). This is a very common polar aprotic solvent.

Example:



Nomenclature: **N-ethyl-N-methyl formamide**.

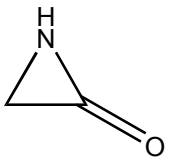
Example:



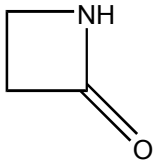
The molecule shown is a sleep hormone Oleamide.
It has 18 carbons. An 18 carbon alkane is called octadecane. The corresponding alkene would be octadecene. The corresponding acid would be 9-octadecenoic acid, for the amide the systematic name is **9Z-octadecenamide**.

Cyclic amides are called **Lactams**

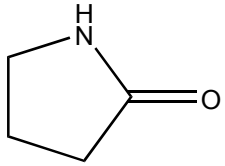
Similar to lactones, the ring size of the lactam is described by starting at the carbonyl carbon and designating the other carbons in the ring with Greek letters until the nitrogen atom is reached.



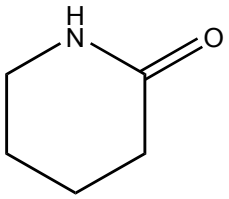
α-lactam



β-lactam



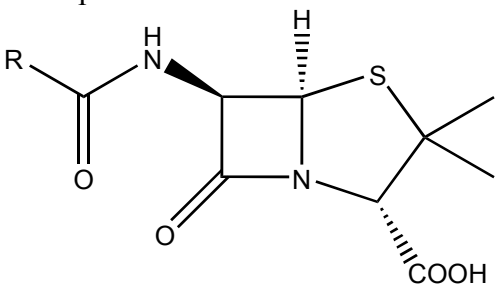
γ-lactam



δ-lactam

The four-, five-, and six-member rings appear frequently in nature.

Example:



penicillin

Penicillin is a broad spectrum antibiotic.

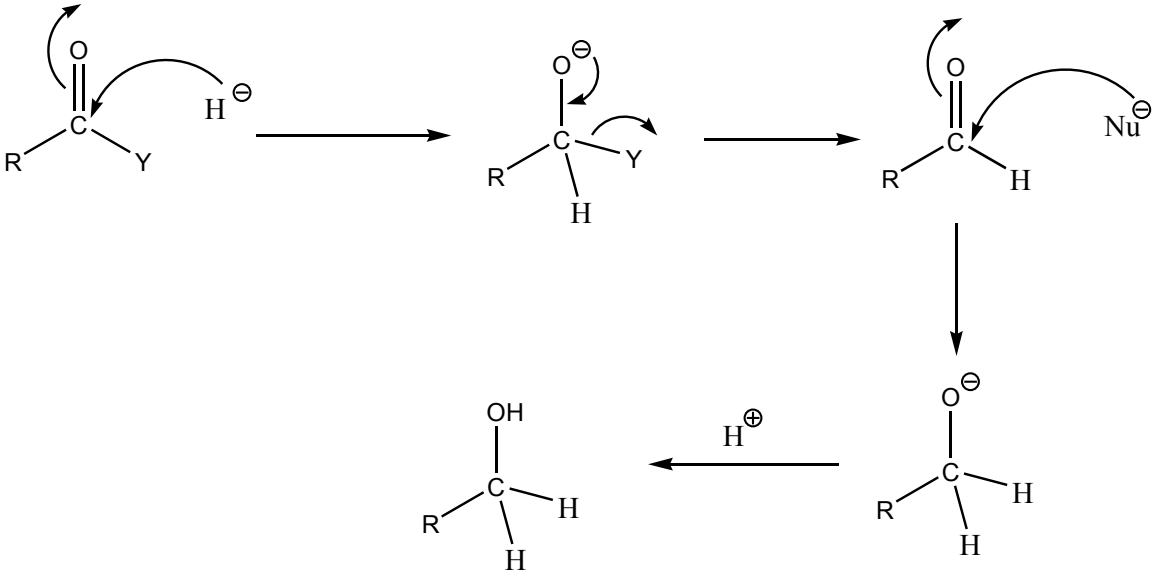
What kind of lactam is penicillin?
Answer: it is a β-lactam since the amide is in a 4-membered ring.

Reactions of Carboxylic Acids and Derivatives: Strong Nucleophiles

The strong nucleophiles (Nu: $^-$) that we have learned in this course are either hydride anion (H^-) or alkyl anion (R^-). As well, remember that attack by strong nucleophiles is not reversible.

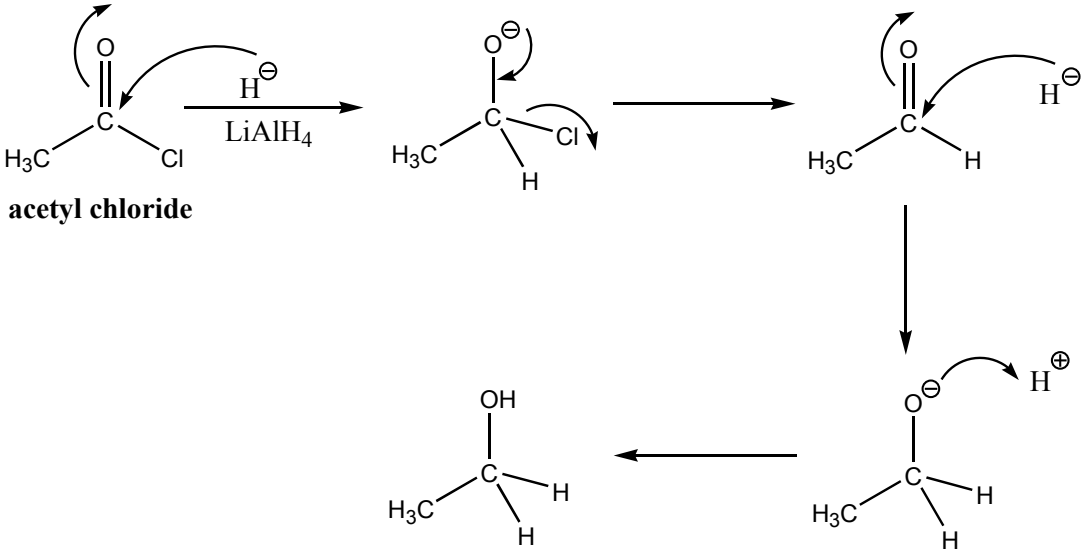
Hydride anion comes from hydride donor such as $LiAlH_4$ or $NaBH_4$ (however, $NaBH_4$ is not strong enough reaction on carboxylic acid derivatives except for acid chlorides). Alkyl anion comes from RM, where R is an alkyl group and M is a metal (these reagents include Grignard reagents (RMgX) and alkyl lithium reagents RLi). Grignard reagents fail with carboxylic acids, but alkyl lithium reagents can be used.

Mechanism for $LiAlH_4$ reduction:



This reaction works for carboxylic acid, acyl chlorides, anhydrides and esters which gives alcohol as product. Amides give amines as product rather than an alcohol.

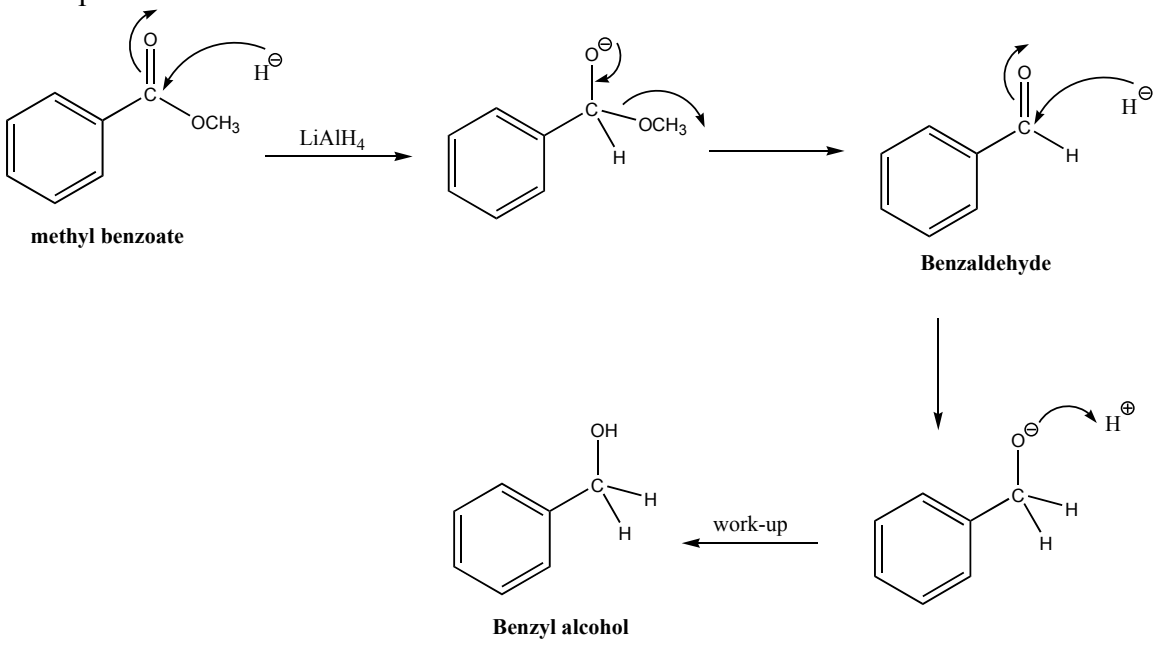
Example:



acetyl chloride

The aldehyde formed is unstable under the condition (since excess hydride ion is present and aldeheyde is very reactive). As a result, the nucleophile (hydride) is added twice to the carbonyl.

Example:

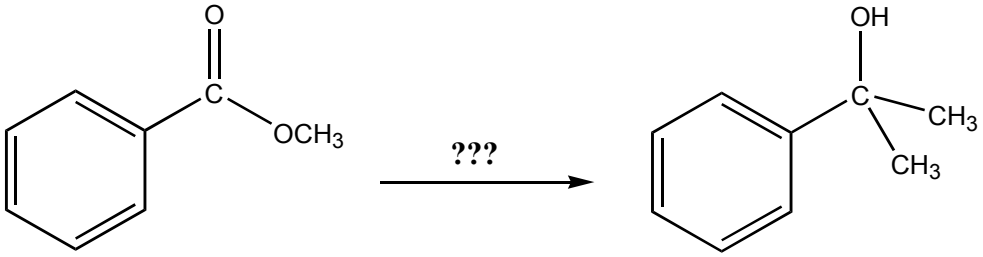


methyl benzoate

Benzaldehyde

Benzyl alcohol

Alkyl Anion addition



What reagent would you use for this reaction?

Let's analyze this: *what has changed between the two molecules?*
The methoxy group has gone, there are two methyl groups attached to the C-O carbon, and the carbonyl oxygen bond is singly bonded on the right side. The mechanism is analogous to hydride anion attack shown above, except that methyl anion attacks.

Analysis of Problem

Add	Reagent	Remove
H+	HCl	
CH_3^-	CH_3Li	
CH_3^-	CH_3Li	
		$^-OCH_3$

Answer: