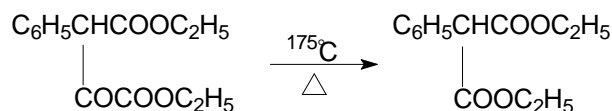
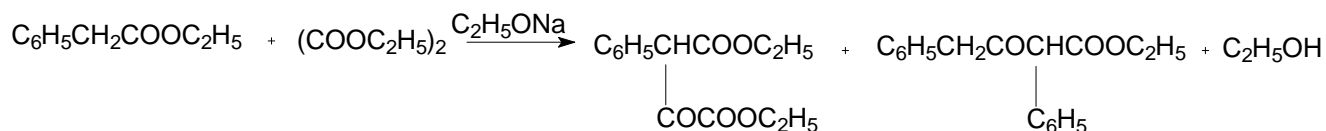


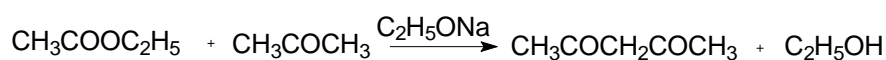
eg.



在酯基 α 位引入醛基

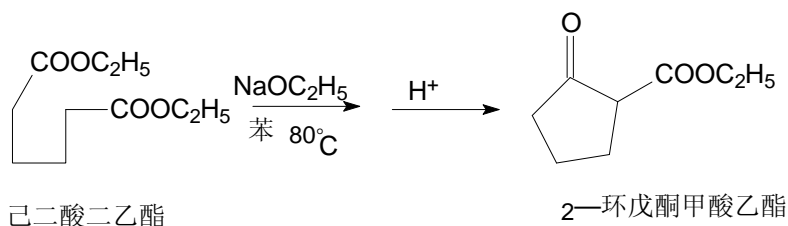


酮的 α 氢比酯活泼。



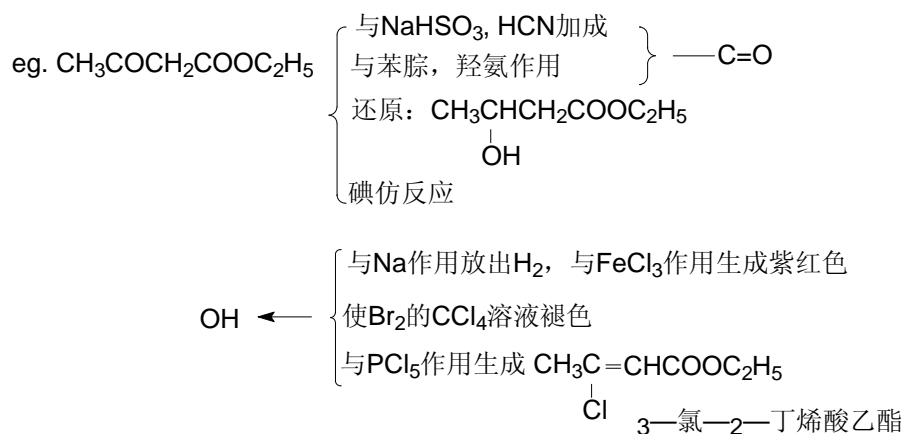
(主)

3. Dieckmann 缩合反应——制备五、六元环状 β ——酮酸酯

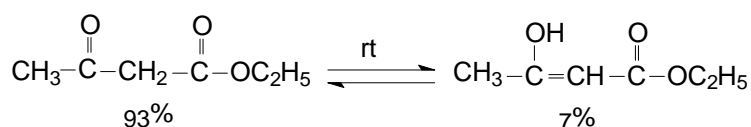


二. 酮-烯醇互变异构 P367

1. 互变异构现象:

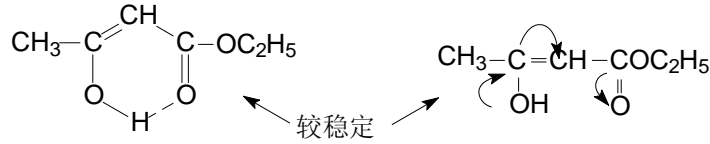


1. 互变异构 (tautomerism)

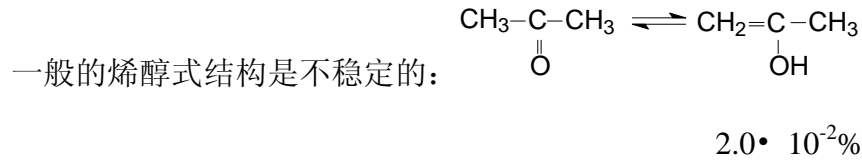


L.Konorr.(1859~1921)发现在低温 (-78°C) 时, 二者可以分开。

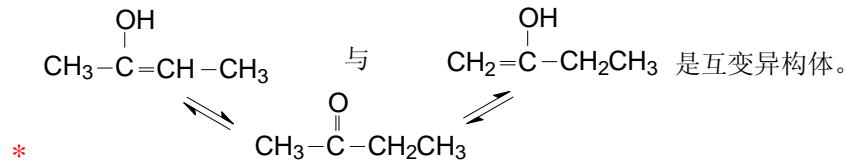
在酸性或痕量碱的作用下, 二者迅速达到平衡, 如用石英设备, 通过蒸馏法可把二者分开。酮式: b.p. 41°C/267Pa; 烯醇: 33°C/267Pa (减压)。由于分子内氢键的存在, 阻碍了分子间氢键的形成, 因此烯醇的沸点小于酮。



原因 { 亚甲基上氢的酸性, 易离开。
共轭。
分子内氢键。

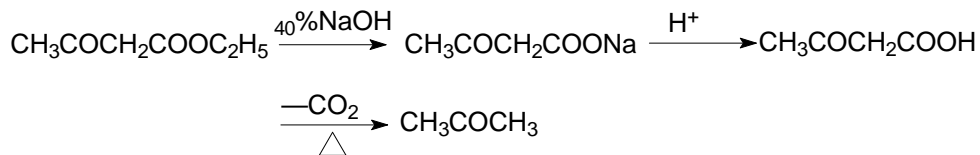
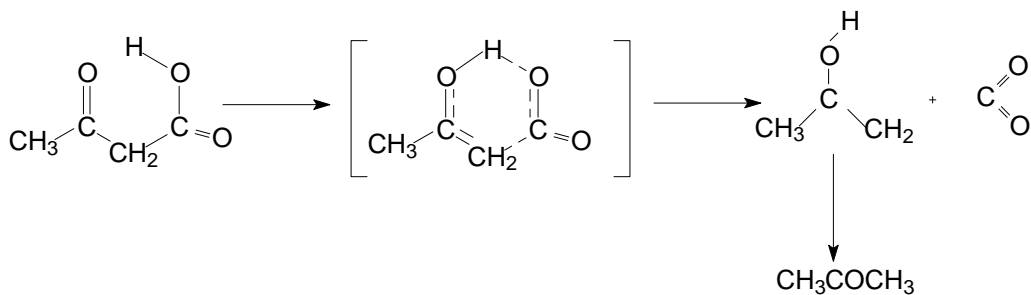


* 互变异构体与共振式的区别:

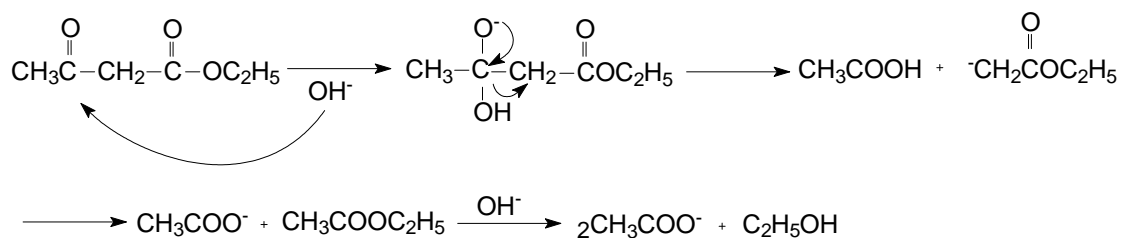
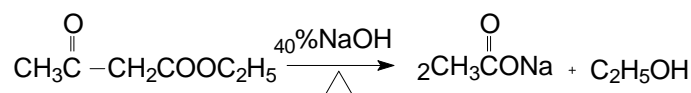


三. 乙酰乙酸乙酯在合成上的应用

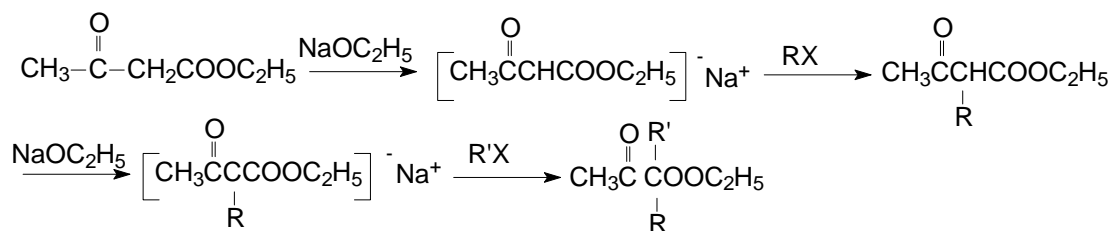
1. 乙酰乙酸乙酯的酮式分解 (稀碱)



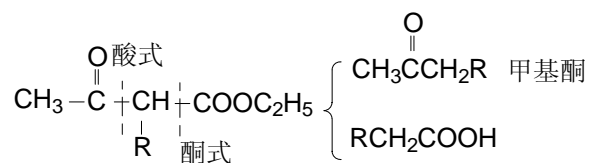
2. 酸式分解: (浓碱)



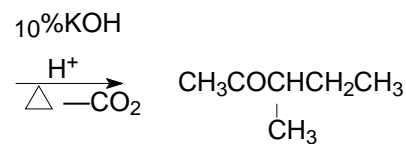
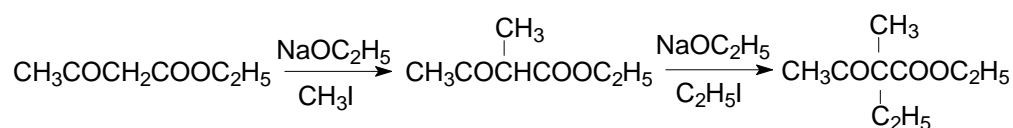
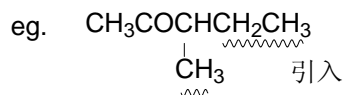
3. 亚甲基上氢的活泼性:



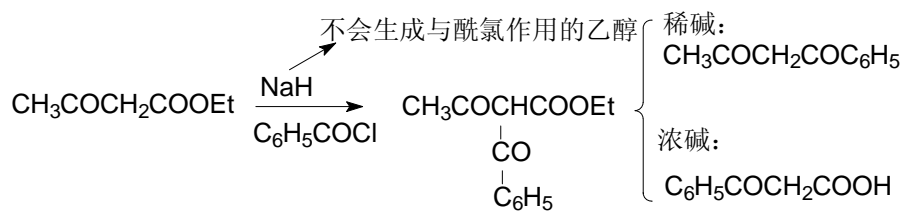
4. 应用



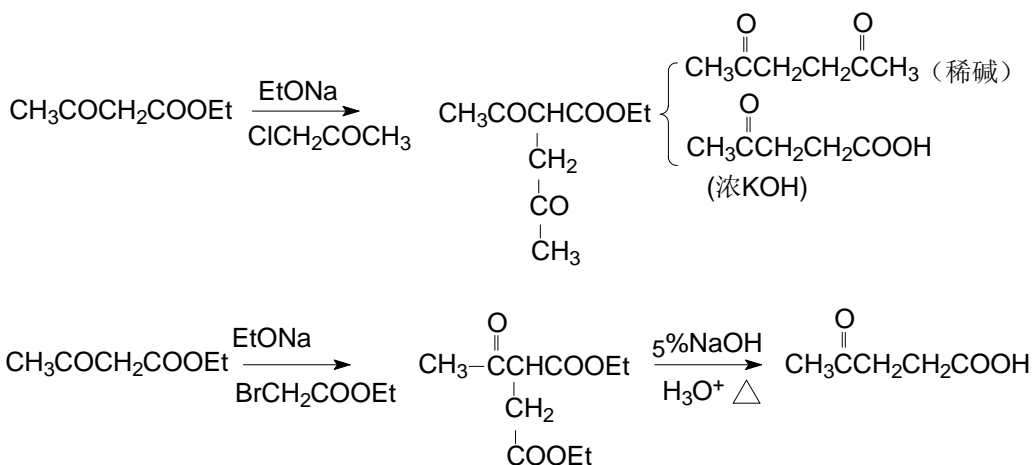
(1) 合成甲基酮



(2) β-二酮、β-酮酸

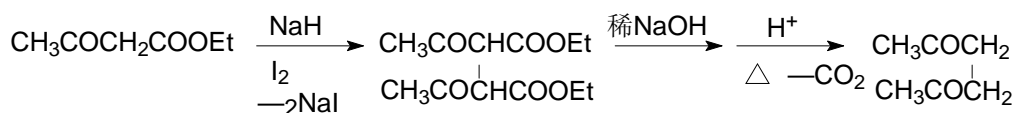


(3) γ-二酮、γ-酮酸



没有副产物 CH_3COOH .

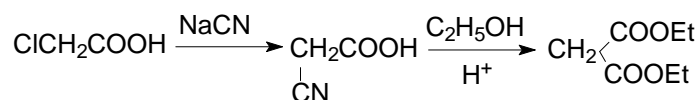
(4) 2,5-己二酮, γ -二酮



在合成羧酸时, 通常不采用乙酰乙酸乙酯法, 而采用丙二酸酯法。因为前者在进行酸式水解时, 常伴有酮式水解产物。

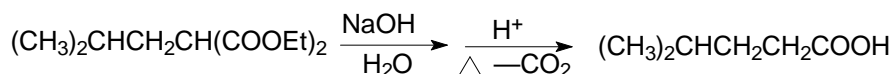
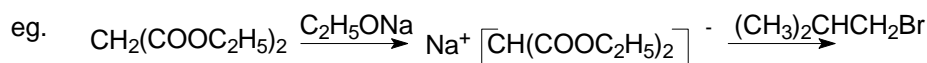
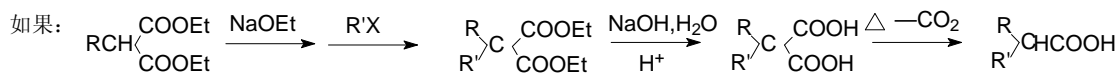
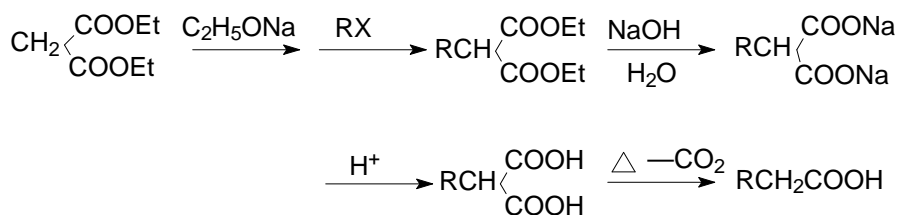
四. 丙二酸二乙酯的合成和应用

1. 制法:

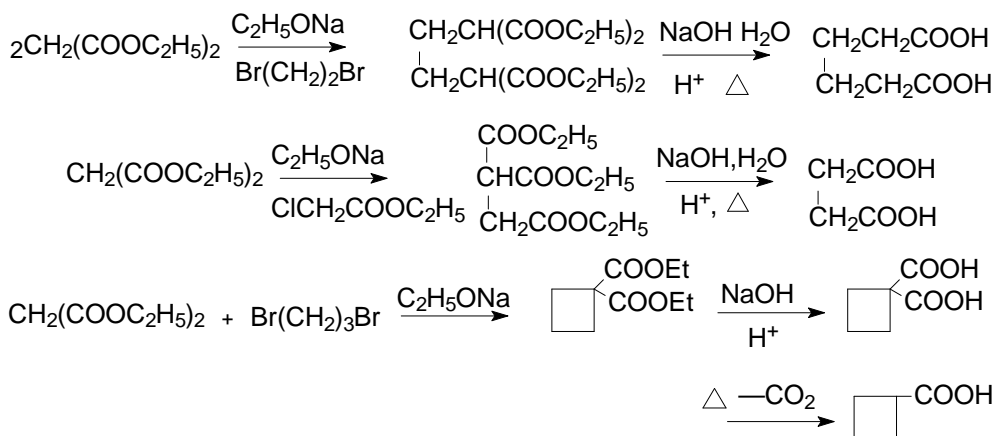


2. 应用:

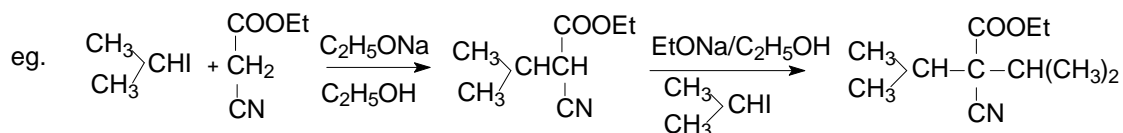
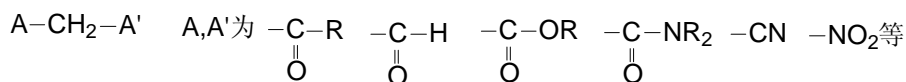
(1) 合成一元羧酸



(2) 合成二元羧酸:

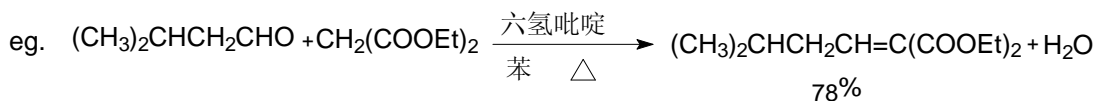


五. 其它含活泼亚甲基的化合物



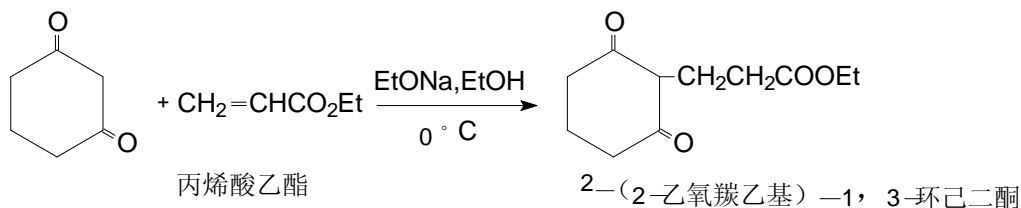
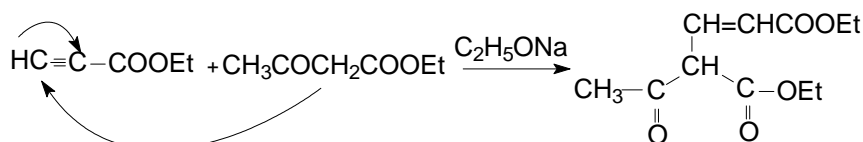
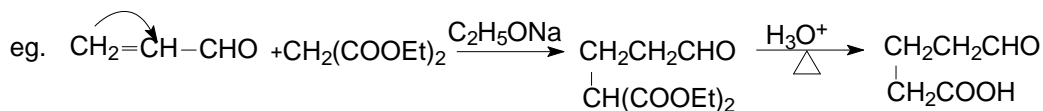
Knoevenagel. 缩合

含活泼氢的亚甲基化合物在碱催化剂存在时, 和醛、酮共热脱水, 生成 α 、 β 不饱和羰基化合物。



六. Michael 加成 (在药物合成中有重要用途)

活泼氢化合物与 α 、 β 不饱和羰基化合物的加成——Michael 加成



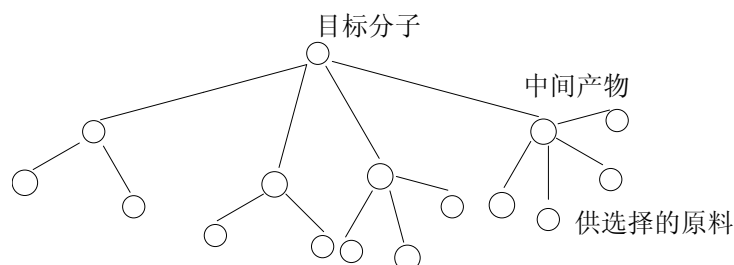
§ 12.4.2 有机合成路线设计

一个好的合成路线，要求：步骤少（一般超过五步以上的反应，实际应用价值不大）；产率高；中间产物与最终产物易提纯；原料易得；价格便宜。

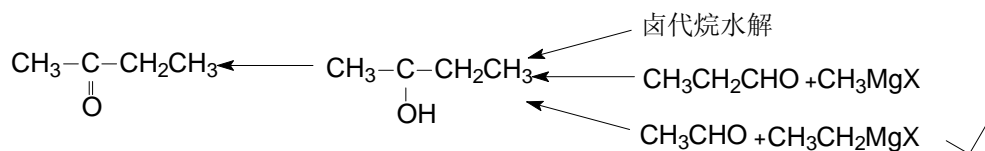
对于目标分子，我们计划要合成的分子结构设计主要包括：

- 1) 碳架的建立；
- 2) 官能团的转化；
- 3) 立体化学选择性和控制。

一. 逆推法

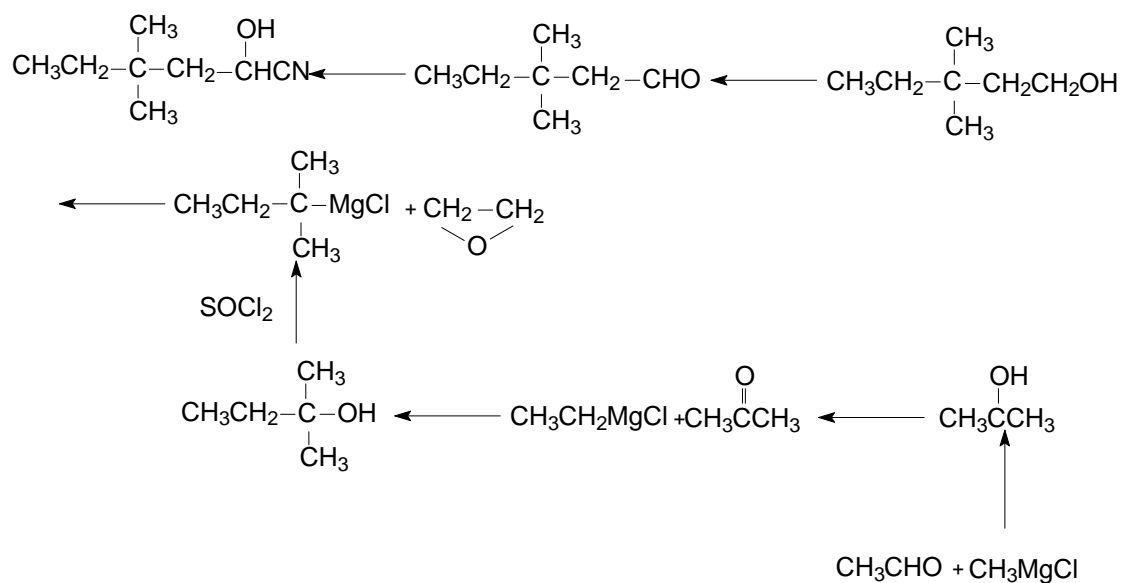


例1. 以少于四个 C 的化合物合成 2-丁酮。



因为乙醛比甲醛易得、便宜，乙基卤代镁比甲基卤代镁易于制备。

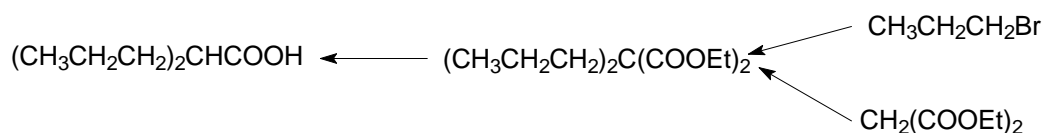
例2. 由 3 个 C 以下的 C 分子合成 $\text{CH}_3\text{CH}_2\text{C}(\text{CH}_3)_2\text{CH}_2\text{CH}(\text{OH})\text{CN}$



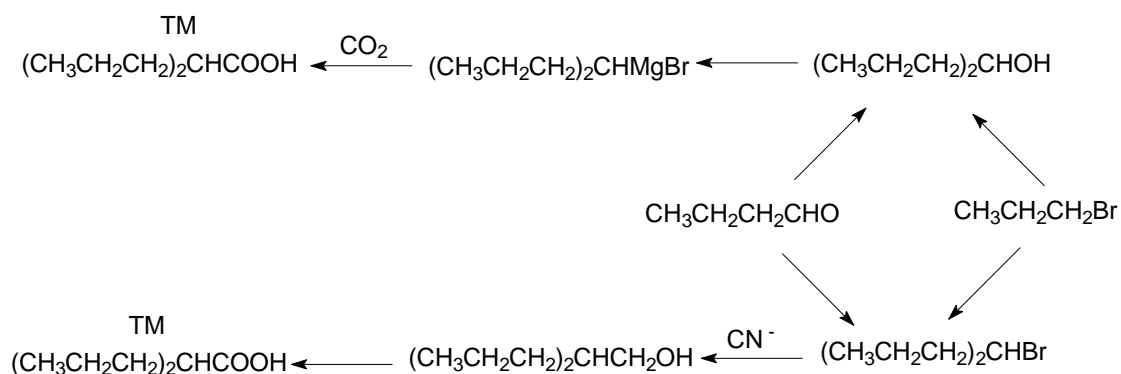
例3. 合成 $(\text{CH}_3\text{CH}_2\text{CH}_2)_2\text{CHCOOH}$ 。(4个C以下)

二丙基乙酸的钠盐是治疗癫痫的药物。

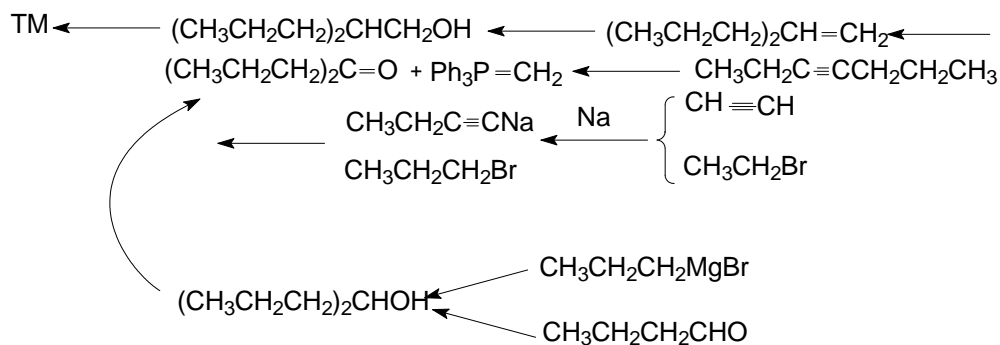
(1)



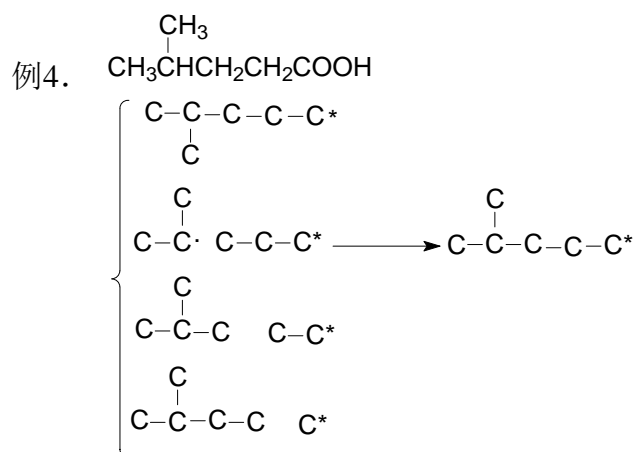
(2) (3)



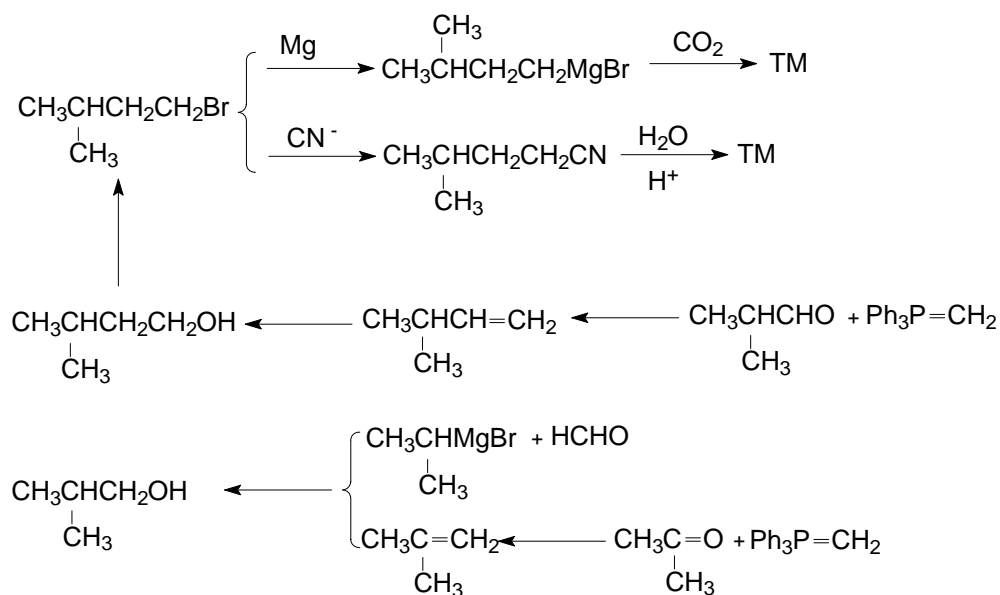
(4)



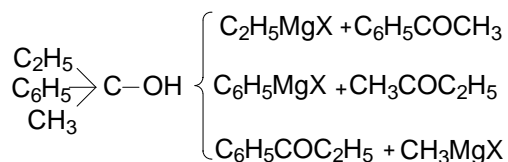
显然, (1), (2) 两种方法较合理.



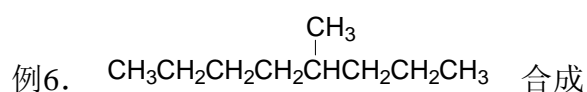
通常尽可能选择靠近官能团的位置, 形成新的碳碳链, 建立 TM 骨架, 以利于合成反应的进行.

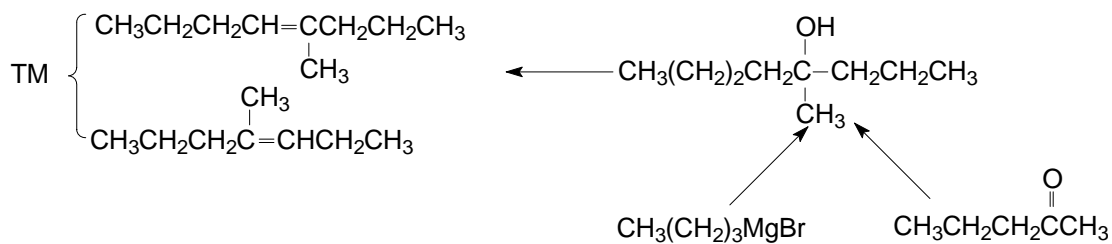


例5.

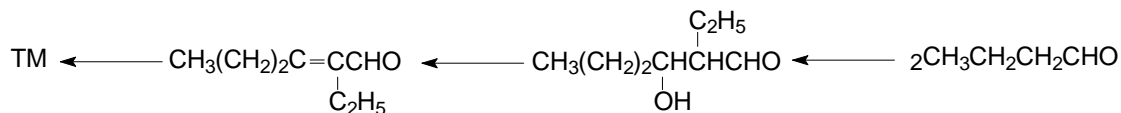


二. 官能团的导入和转化:

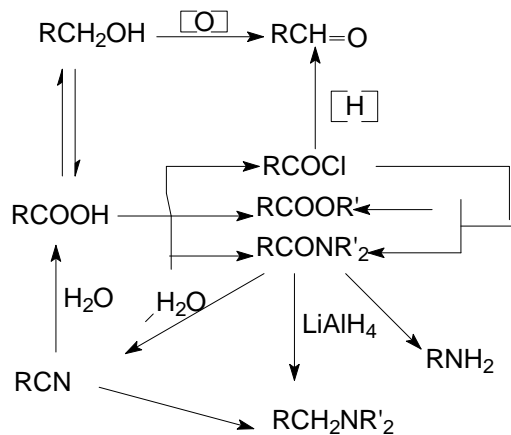
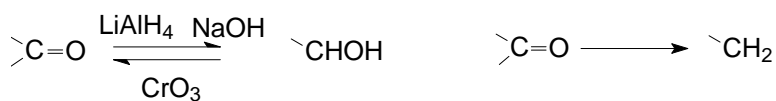
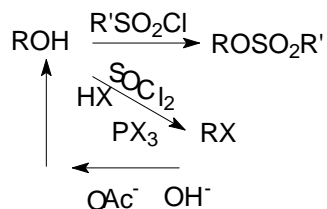




例7. $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\overset{\text{C}_2\text{H}_5}{\text{CH}}\text{CH}_2\text{OH}$ 的合成设计 \longrightarrow 各分一半

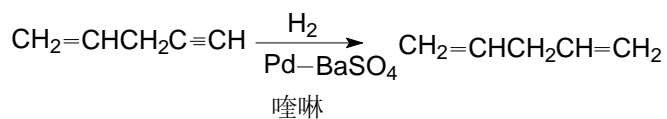
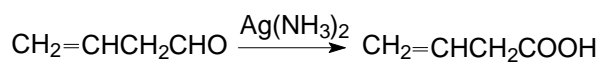


各官能团的相互转化.

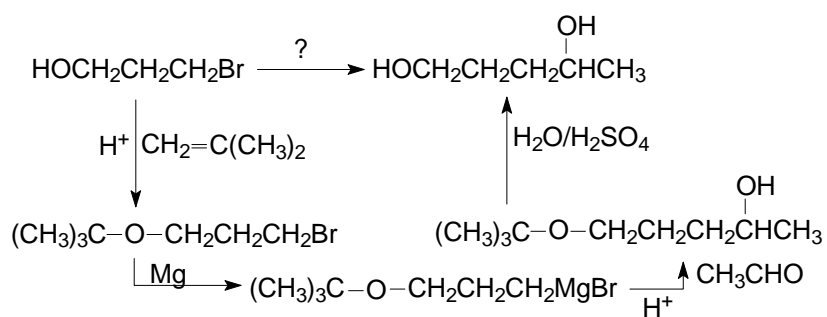


三. 官能团的保护和导向:

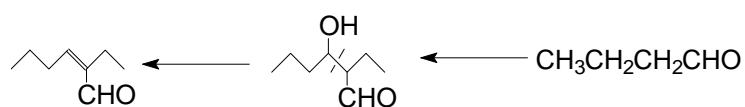
(1) 选择合适的条件:



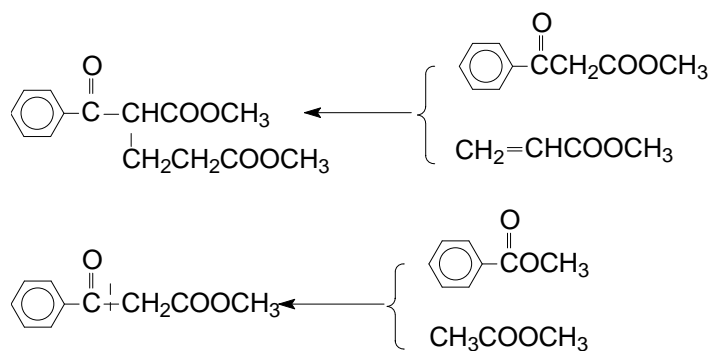
例8.



例9.



例11.



例12.

