Solutions to Problems - Set 8: Carbonyl compounds (part III)

Problem 1

Write the mechanisms and the structures of the products of the following reactions involving Grignard reagents.

(a) $C_6H_5MgBr + C_6H_5CHO$

(b) $CH_3MgI + CH_3CH_2CO_2C_2H_5$

(c) $(CH_3)_3CMgCl + CO_2$

(d) $CH_3CH_2MgBr + ClCO_2C_2H_5$

(e) $CH_3MgCl + CH_3COCH_2CH_2CO_2C_2H_5$ (1:1)

(f) $C_6H_5MgBr + CH_3OCOOCH_3$

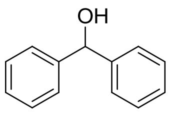
(g) $CH_3MgBr + (CH_3)_2CHCN$

(h) $C_6H_5MgBr + HOCH_2CH_2COCH_3$

Solution

Mechanisms: cf. course ; Products :

a)



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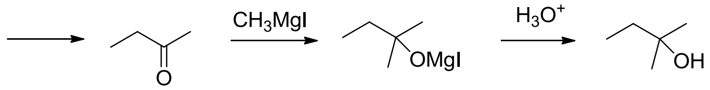
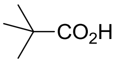


c)



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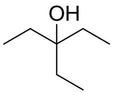

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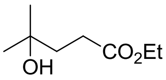

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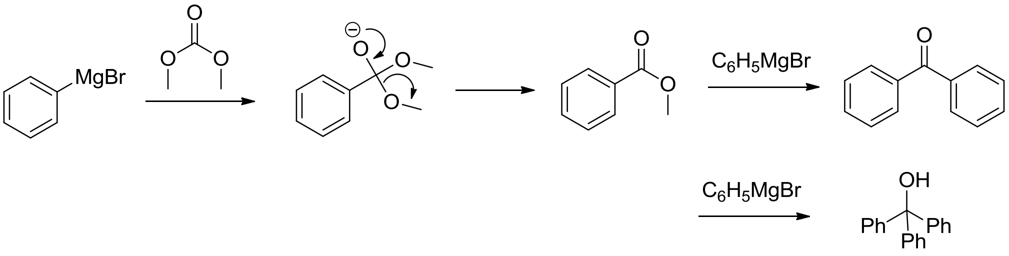

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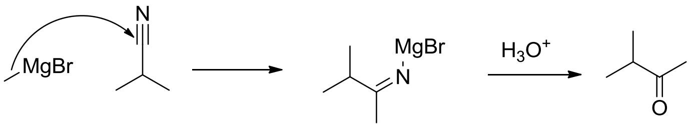

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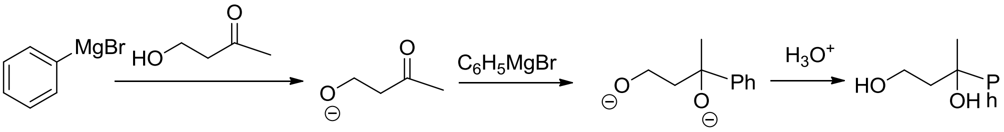
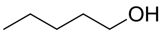
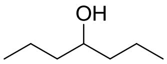
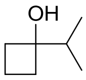


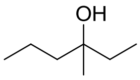
Problem 2

How to make these compounds using Grignard reagents from starting materials that have maximum 4 carbons each :

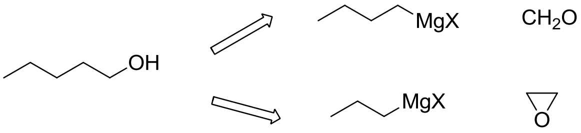


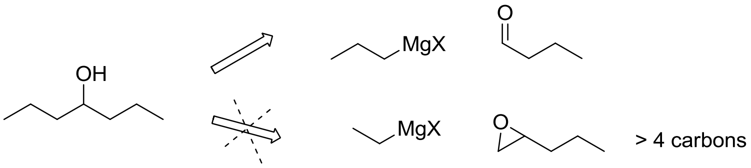


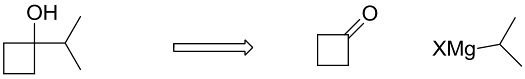


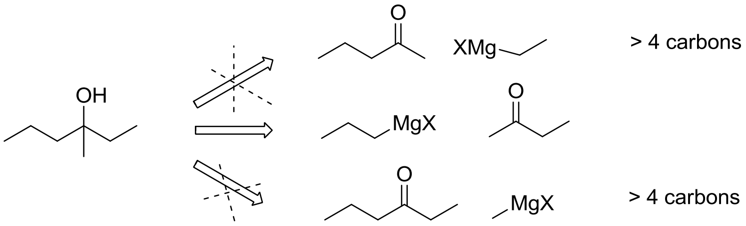


Solution





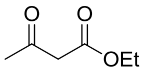




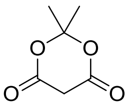
Problem 3

1,3-Dicarbonyl compounds such as A are mostly enolized. Why? Draw the enols of compounds B-E and explain why B prefers the enol form wheras C, D and E prefer the ketone form.

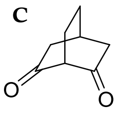
A



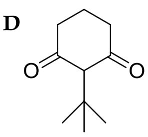
B



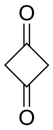
C



D

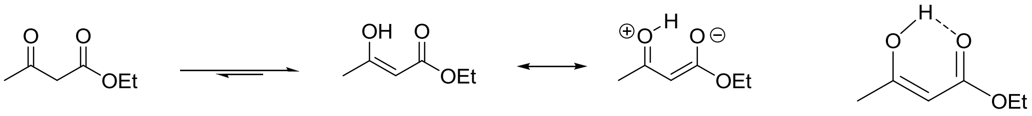


E

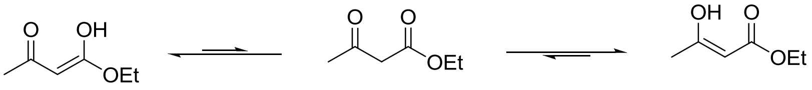


Solution

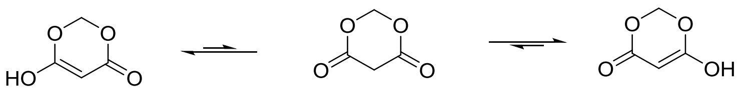
Compound A is mostly enol because the enol is delocalized over five atoms. Also this particular compound has an internal hydrogen bond. The main reason is conjugation.



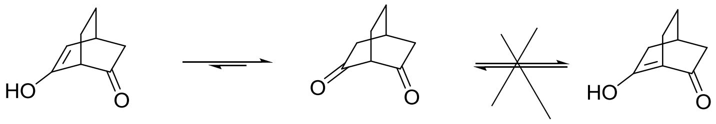
You may also have pointed out that there is an alternative and equally good enol that has the other carbonyl group enolized. These two structures are tautomers of each other and of the keto-ester.



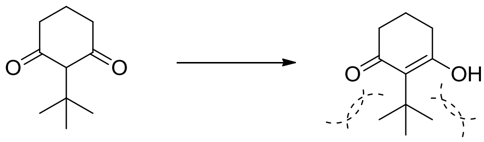
The compound B is totally enolized shows that the conjugation is much more important than the internal hydrogen bond, which is impossible with B.

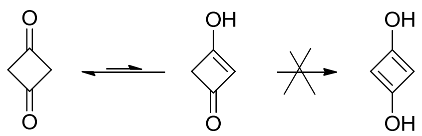


Compound C cannot form an enol between the two carbonyl groups at all as the alkene would be a bridgehead alkene unable to get its p orbitals parallel. It can form an ordinary enol on the other side of the ketone but this has no special stabilization.



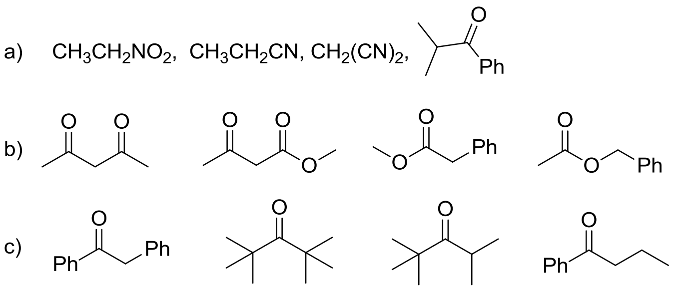
Compound D and E can form enols but the t-Butyl group in D has to move into the plane of all the other atoms and there is a bad steric clash with the adjacent oxygen atoms. The t-butyl group is out of the plane in the keto form. Compound E is strained but the enol is more strained as another sp2 atom has to fit into the four-membered ring. The dienol is worse – even more strained and anti-aromatic (four electrons) to boot.





Problem 4

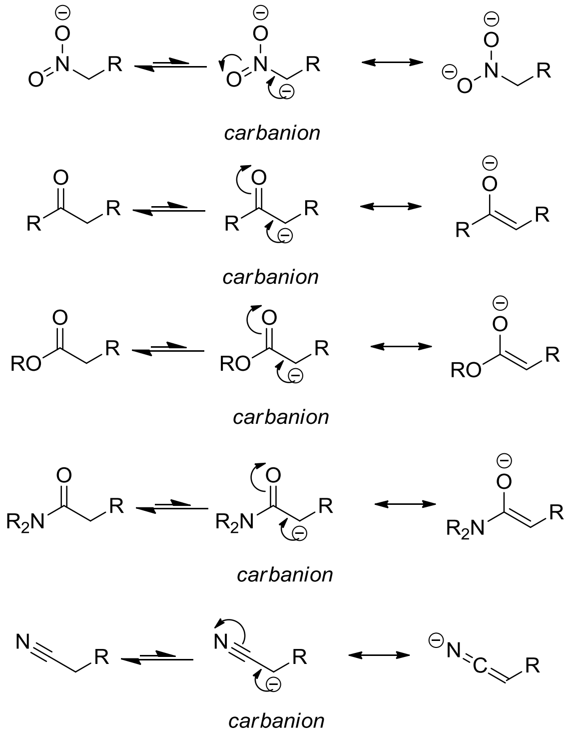
Arrange each series of compounds in order of decreasing acidity at the alpha-position.



Solution

Acidicity of C-H at α possition is dependent on the ability to stabilize carbanion of functional group.

NO2 > COR > CN ~ COOR > SO2R > SOR > Ph ~ SR > H > R



stabilized by conjugation with NO_2 (strong EWG) and induction by nitrogen

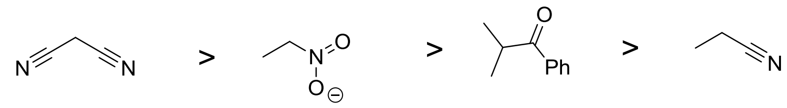
stabilized by conjugation with C=O

stabilized by conjugation with COOR

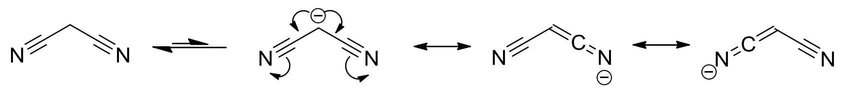
stabilized by conjugation with $CONR_2$

stabilized by conjugation with CN

RO and R_2N, conjugating to C=O as well, can "interfere" the stablization of carbanion. Therefore, acidity of C-H (ketone) > (ester) > (amide) a)

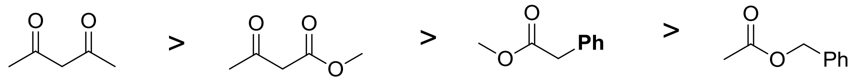


(see above)



strongly stabilized by
2 CN groups

b)



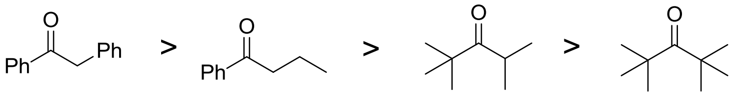
β–diketone

β–ketoester

see above: COR > COOR

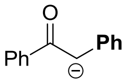
both are esters
Ph group increases stablization of carbanion
see above: Ph > H

c)

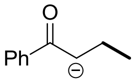


see above: Ph > R

no C-H at
α – position

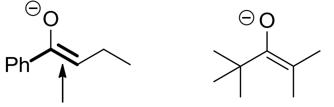


stablizied by Ph ring
(conjugation and EW
inductive effect)



destabilized by ED
inductive effect
of alkyl group

Phenyl ketone > Alkyl keton



enolate conjugates
with Ph ring (stable
resonant structure)