**Iverson CH 320N KRE Table:** For use in synthesis problems, count carbons in products and starting materials then identify location(s) of new bonds, especially C-C or C=C bonds. With that information, use the following KREs to determine which reactions are appropriate.

KRE: A new C-C bond two carbons away from an -OH group indicates an organometallic reacting with an epoxide.

New C-C bond
1)
2) $H_3O^{\oplus}$ (mild)

KRE: A new C-C bond on the same carbon as a secondary -OH group indicates a Grignard reacting with an aldehyde.

New C-C bond
1)
Racemic
2) $H_3O^{\oplus}$ (mild)

KRE: A new C-C bond on the same carbon as a tertiary -OH group indicates a Grignard reacting with a ketone.

New C-C bond
1)
2) $H_3O^{\oplus}$ (mild)

KRE: A new C-C bond on on a carboxylic acid in which one carbon atom was added indicates a Grignard reacting with $CO_2$

New C-C bond
1) $CO_2$
2) $H_3O^{\oplus}$ (mild)

KRE: A new C-C bond from a CN on the same carbon as an -OH group indicates HCN reacting with a ketone or aldehyde.

New C-C bond
Racemic
HCN

KRE: A new C-C bond from an alkyne on the same carbon as an -OH group indicates an alkyne anion reacting with a ketone or aldehyde.

New C-C bond
Racemic
1)
2) $H_3O^{\oplus}$ (mild)

KRE: A new Z C=C bond indicates an alkyl Wittig reagent was used.

New C=C bond
Z alkene
$P(Ph)_3$

KRE: A new E C=C bond indicates a Wittig reagent with a carbonyl adjacent to the negative charge (enolate Wittig) was used.

New C-C bond
E alkene
$P(Ph)_3$

KRE: An acetal where a carbonyl used to be indicates acetal formation with an alcohol.

New bond   New bond
$H_3CO$   $OCH_3$
$CH_3OH$
$H_2SO_4$ (catalytic)

KRE: A five or six-membered ring cyclic acetal where a carbonyl used to be indicates acetal formation with a two or three carbon diol.

New bond   New bond
HO   OH
$H_2SO_4$ (catalytic)

KRE: A five or six-membered ring cyclic hemiacetal indicates 4 or 5-carbon hydroxyaldehyde starting material.

New bond
Racemic
$H_2SO_4$ (catalytic)
HO

KRE: An imine indicates an aldehyde or ketone reacting with a primary amine or ammonia

New bond   HN
$H_2N$
ph 4.0

KRE: Ester group

New bond
HO   Fischer esterification
$H_2SO_4$ (catalytic)
HO

KRE: This is a lactone (cyclic ester). The six-membered ring indicates a 5-carbon hydroxy acid starting material that undergoes Fischer esterification.

New bond
$H_2SO_4$ (catalytic)
HO   OH

KRE: Amide group

New bond
2 $H_2N$
or
$H_2N$

KRE: Two identical new C-C bonds on the same carbon as a tertiary -OH group indicates two equivalents of a Grignard reacting with an ester.

New C-C bond
New C-C bond
1)
2 MgBr
2) $H_3O^{\oplus}$ (mild)

KRE: A ketone with an new C-C bond adjacent to the carbonyl indicates an acid chloride reacting with a Gilman reagent.

New C-C bond
1)
CuLi
2) $H_3O^{\oplus}$ (mild)

KRE: An β-hydroxy aldehyde with an indicates an aldol reaction with no dehydration.

New C-C bond
α
β   *
Racemic   OH
NaOH (catalytic)

KRE: An α,β-unsaturated aldehyde with an E,Z mixture indicates an aldol reaction followed by dehydration in acid.

New C=C bond
E,Z Mixture
1) NaOH (catalytic)
2) $H_3O^{\oplus}$ (mild) and heat

New C=C bond

KRE: This is an α,β-unsaturated aldehyde that indicates an aldol reaction followed by dehydration. In this case the ring is formed because a 6-carbon dialdehyde is used.

New C-C bond
β   α
1) NaOH (catalytic)
2) $H_3O^{\oplus}$ (mild) and heat

KRE: A β-ketoester indicates a Claisen reaction.

New C-C bond
β   *
α
Racemic
1) 0.5 eq. NaOEt (or LDA)
2) $H_3O^{\oplus}$ (mild)

KRE: This is a cyclic β-ketoester that indicates a Dieckmann reaction starting with a 6-carbon diester. Notice that Dieckman reactions require 1.0 equivalent of base.

New C-C bond
Racemic
1) 1.0 eq. NaOEt (or LDA)
2) $H_3O^{\oplus}$ (mild)

KRE: This is a nucleophile linked to the β-carbon of the amide. This is also a methyl ketone. Putting these together indicates a Michael reaction starting with acetoester

New C-C bond
β   α
$NH_2$
1) 1.0 eq. NaOEt (or LDA)
2) β   α   $NH_2$
3) $H_3O^{\oplus}$ (strong) and heat

KRE: Reaction of a nucleophile (β-diketone) connected to the β-carbon of a carbonyl (the ester)

New C-C bond
β   α
1) 1.0 eq. NaOEt (or LDA)
2)
3) $H_3O^{\oplus}$ (mild)

KRE: alkylated ketone deriving from either an enolate made with LDA or using an enamine

New C-C bond
α   *
Or
1) 1.0 eq. LDA
2) Br
α
Racemic
1)
2) $H_3O^{\oplus}$ (mild)

KRE: A β-diketone indicates reaction of an acid chloride with either an enolate made with LDA or using an enamine

New C-C bond
α   *
Racemic
Or
1) 1.0 eq. LDA
2) Cl
α
1) Cl
2) $H_3O^{\oplus}$ (mild)

KRE: A methyl ketone with substitution at the α-carbon indicates an acetoester synthesis. The second new C-C bond indicates a second alkylation with $CH_3Br$

New C-C bond
α   *
New C-C bond
Racemic
1) 1.0 eq. NaOEt (or LDA)
2) Br
3) 1.0 eq. NaOEt (or LDA)
4) $CH_3Br$
5) $H_3O^{\oplus}$ (strong) and heat

KRE: A carboxylic acid with substitution at the α-carbon indicates a malonic ester synthesis.

New C-C bond
HO   α
1) 1.0 eq. NaOEt (or LDA)
2) Br
3) $H_3O^{\oplus}$ (strong) and heat

KRE: This is a very tricky one. A symmetric ketone indicates a Claisen reaction followed by ester hydrolysis and decarboxylation of the resulting β-keto ester.

New C-C bond
α
1) 0.5 eq. NaOEt (or LDA)
2) $H_3O^{\oplus}$ (strong) and heat

KRE: A new six-membered ring with two new C-C bonds and an α,β-unsaturated ketone indicates a Robinson reaction.

New C-C bond
Racemic
1) 1.0 eq. LDA
2)
3) $H_3O^{\oplus}$ (mild) and heat
New C-C bond