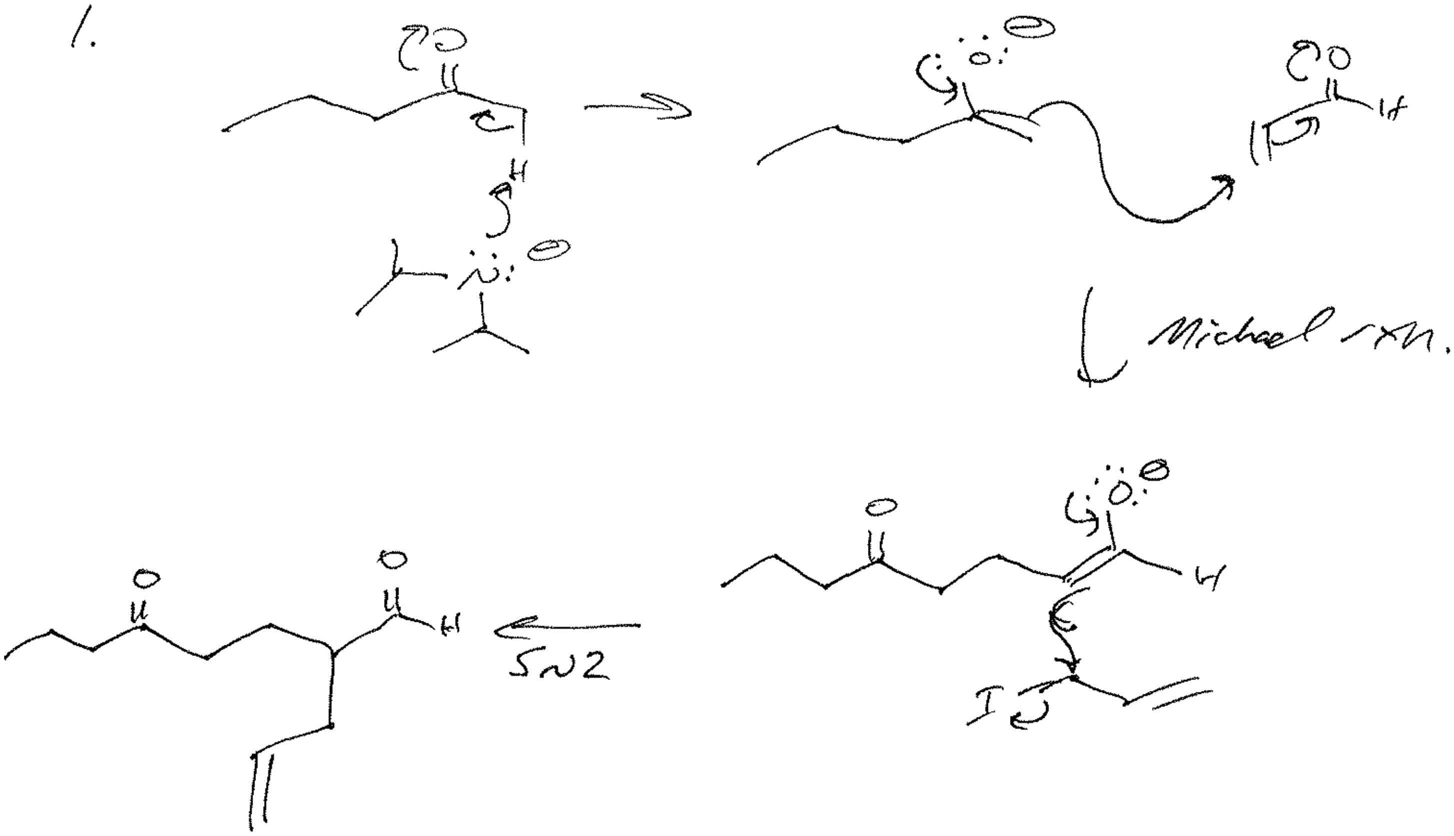
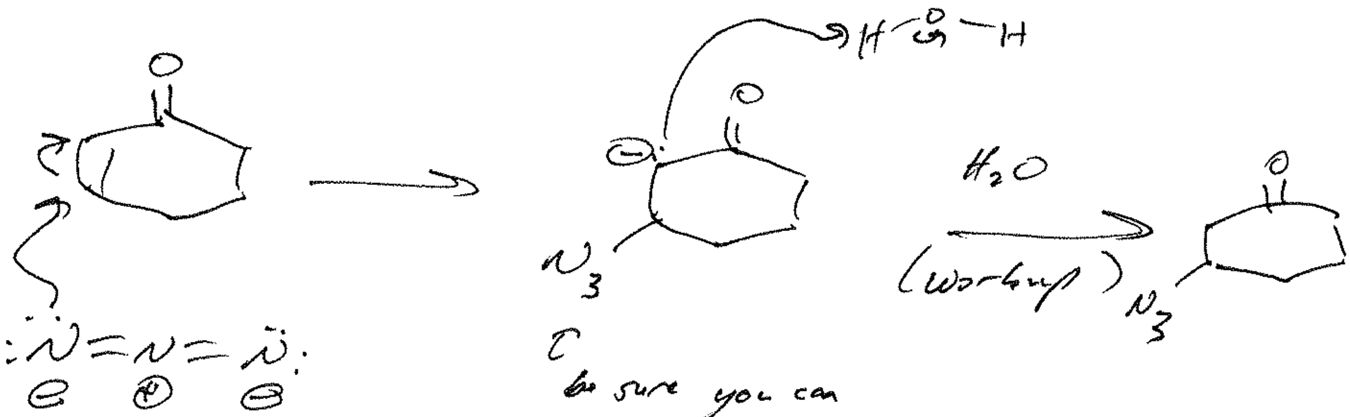
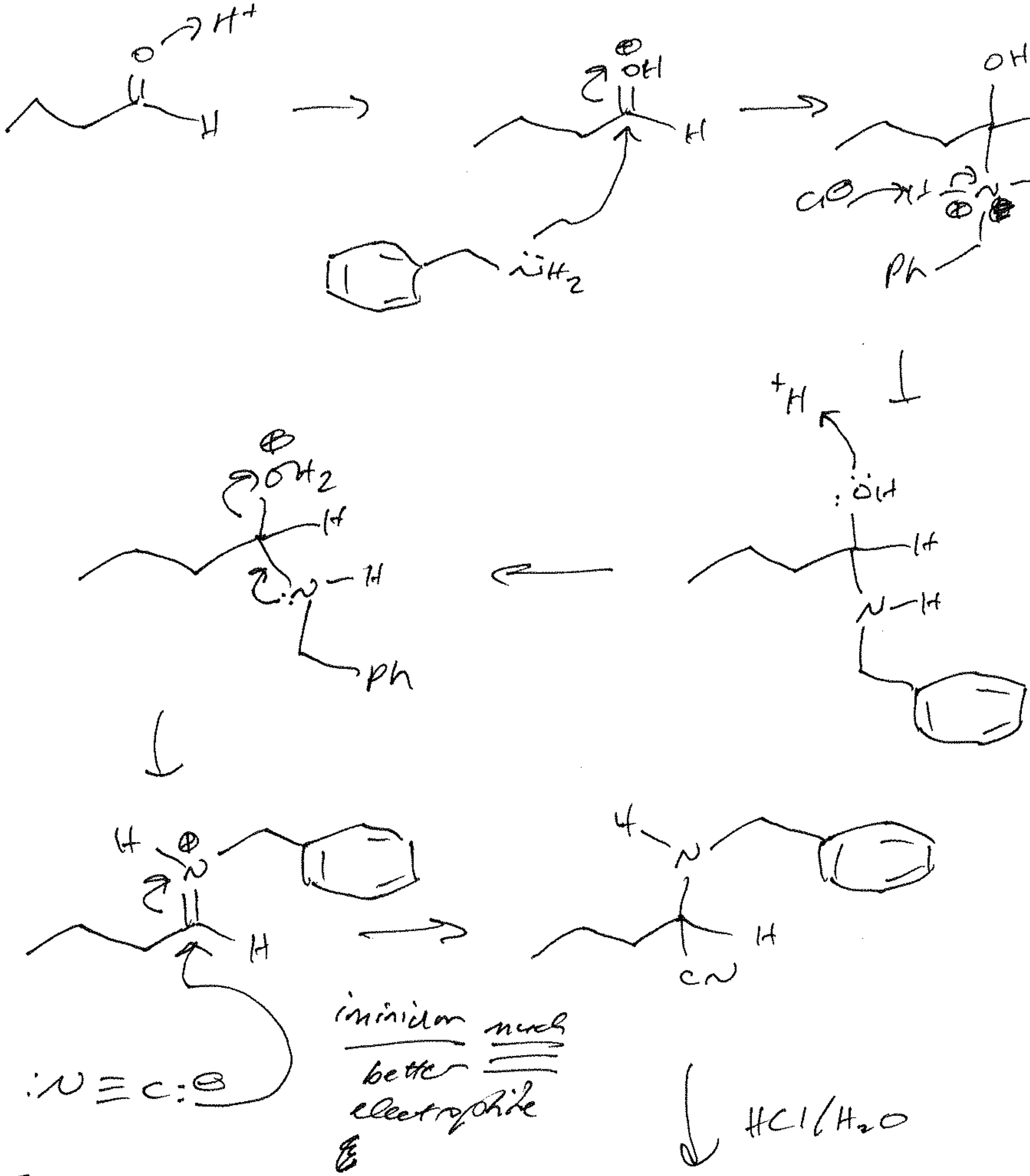
Problem set 9 – Answers

1.



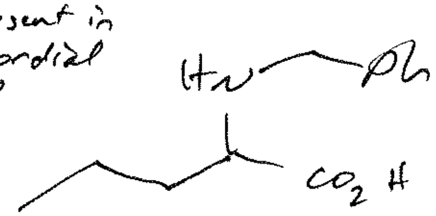


be sure you can draw groups like $-N_3$, $-CN$, $-NO_2$, $-SO_2Me$ etc. for the final!

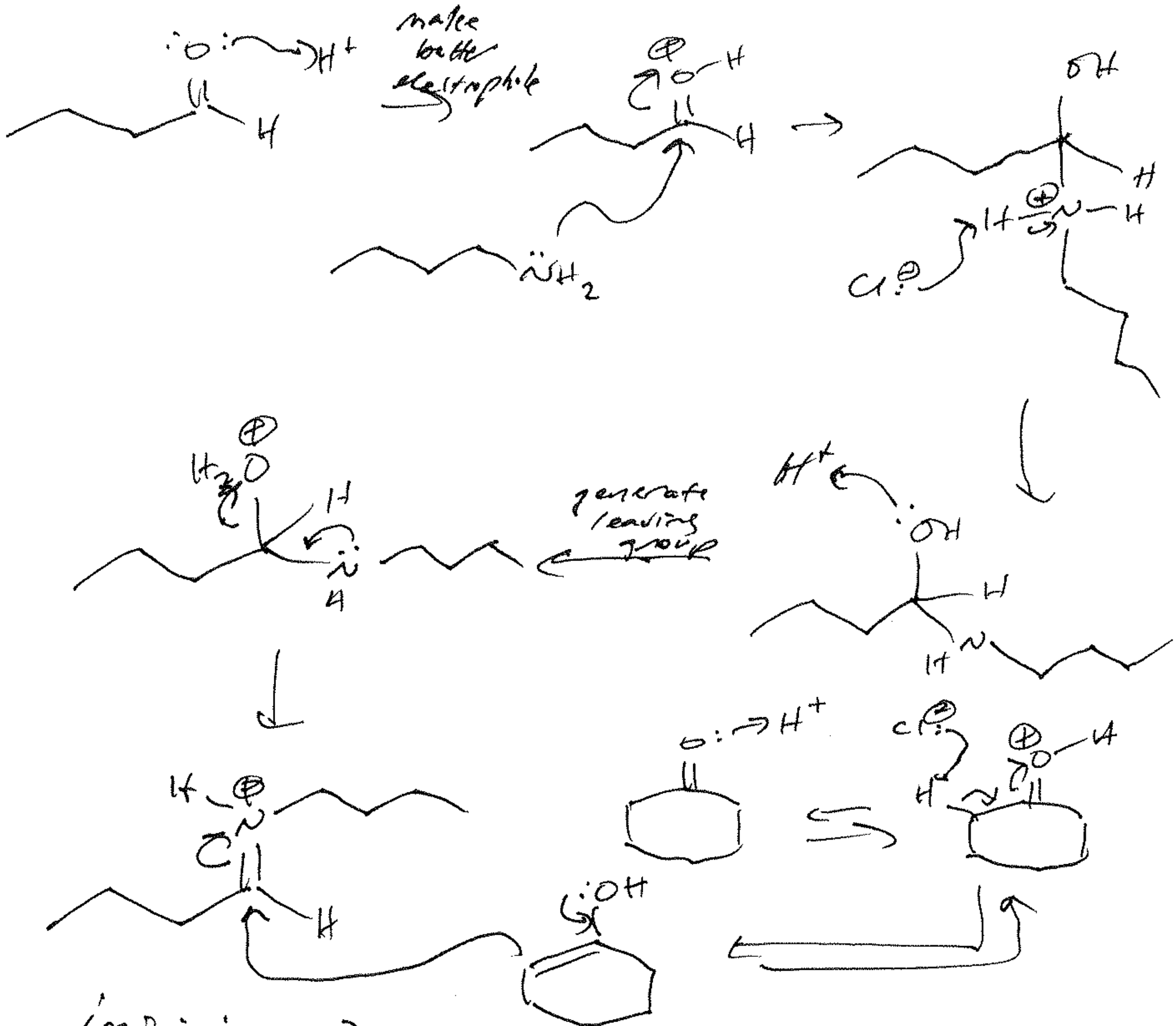


This reaction, the Strecker reaction, (RCHO + NH_3 + HCN) allows ready synthesis of α-amino acids and explains why life on earth uses α-amino acids!

all present in primordial soup



an α-amino acid



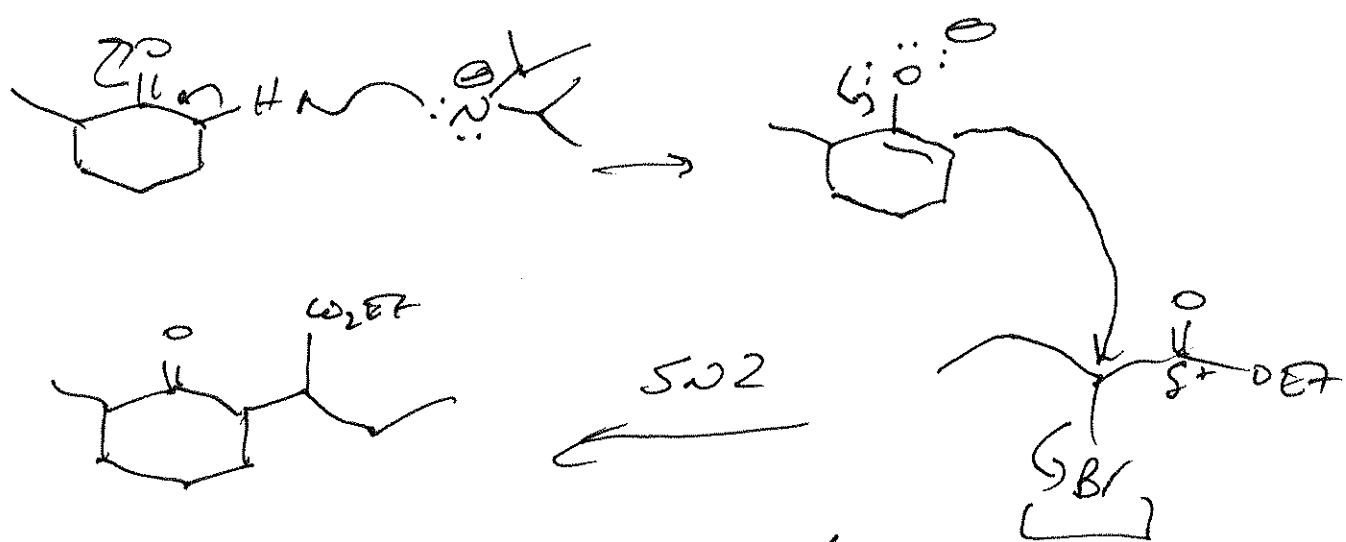
iminium ⇒ excellent electrophile

enol ⇒ nucleophile present under acidic conditions

Note: iminium of aldehyde more stable than that of ketone due to sterics

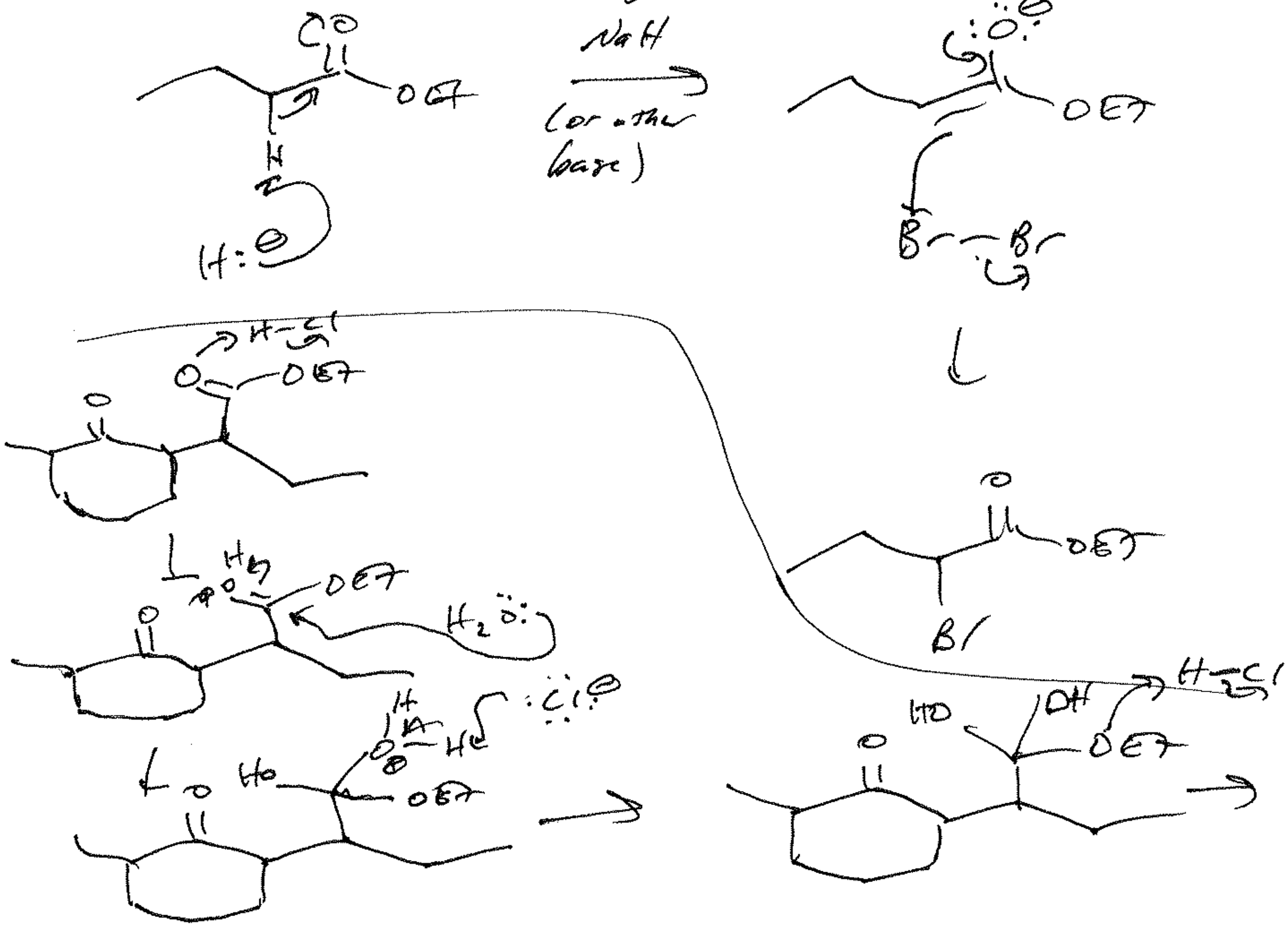
Mannich reaction

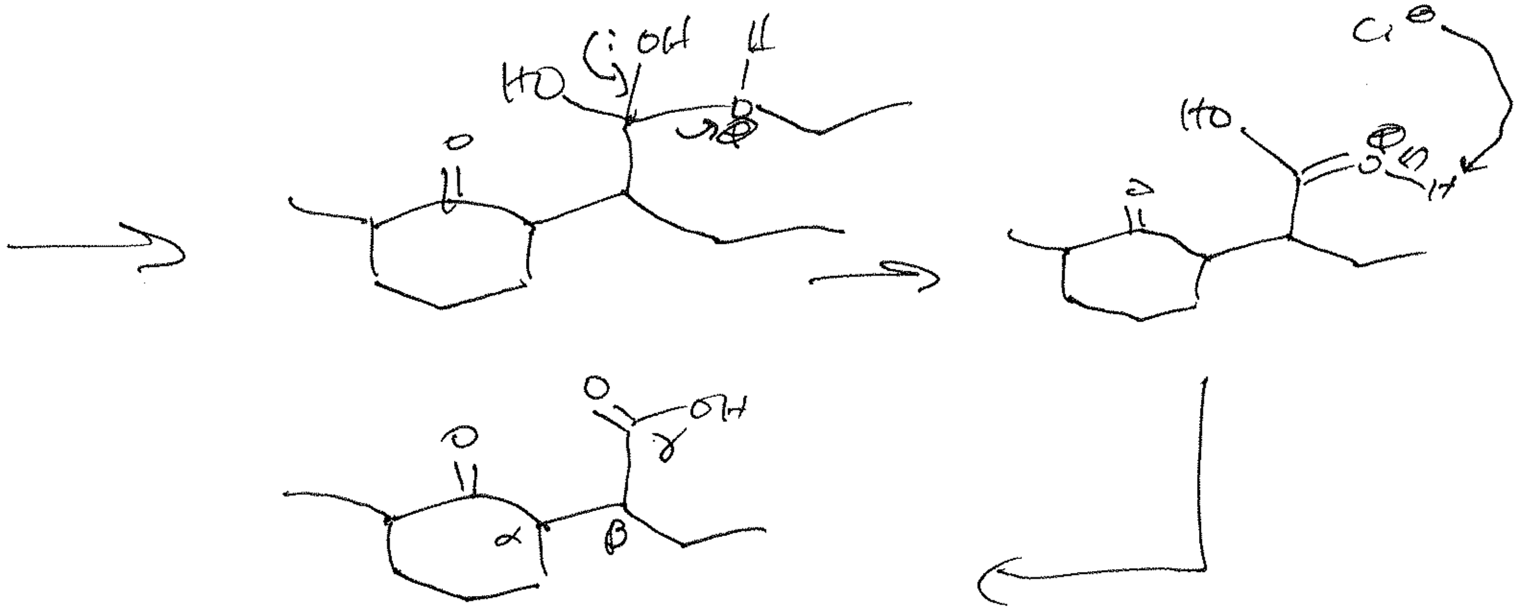
β-amino ketone
(nitrogen analogue of aldol rxn)



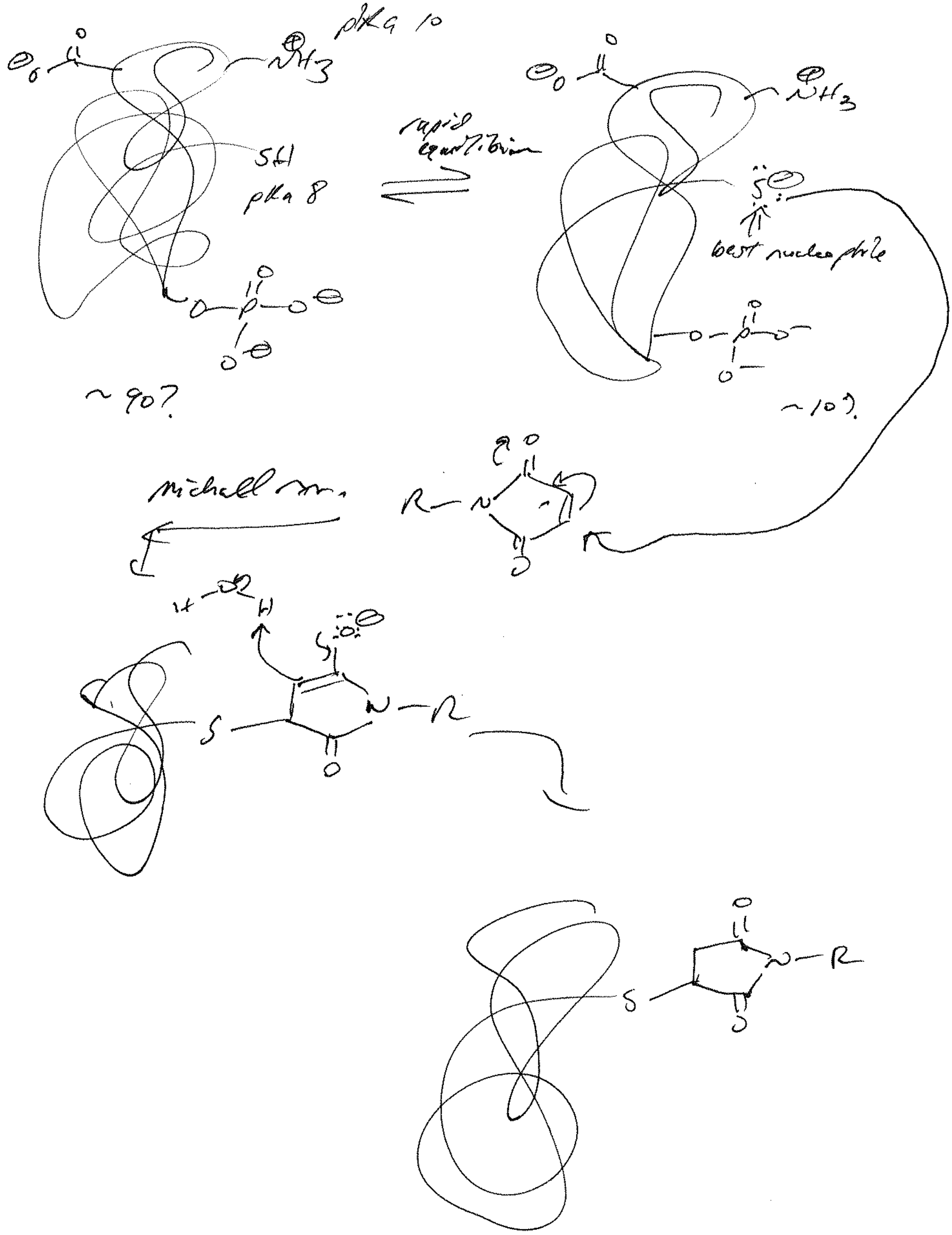
halides α to carbonyl are <u>excellent</u> electrophiles due to adjacent electron-withdrawing groups

Synthesis of α-halo carbonyls:





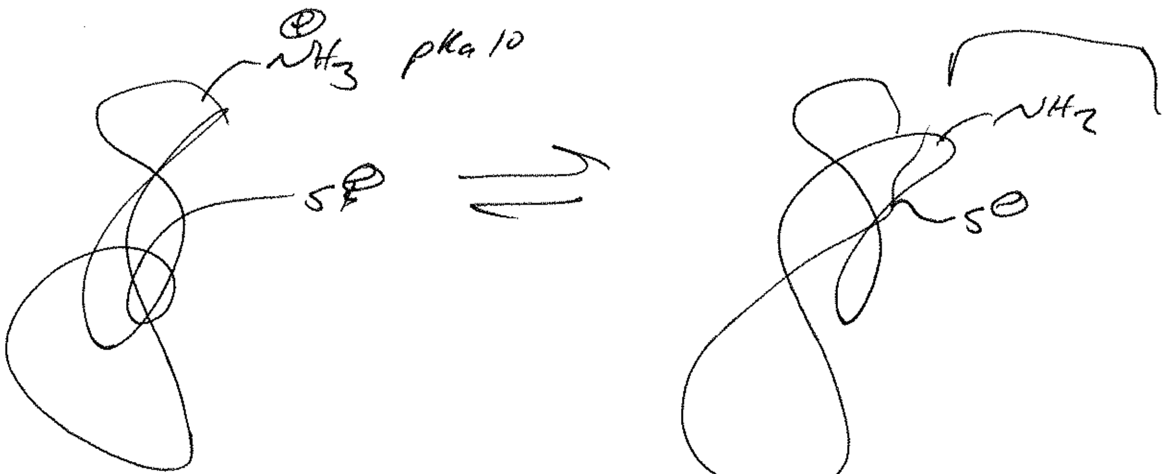
no decarboxylation because γ-keto acid
(7-member ring transition state,
* product would not be enol *.)



pKa 10
SH
pKa 8
rapid equilibrium
best nucleophile
~90%
~10%
michael rxn

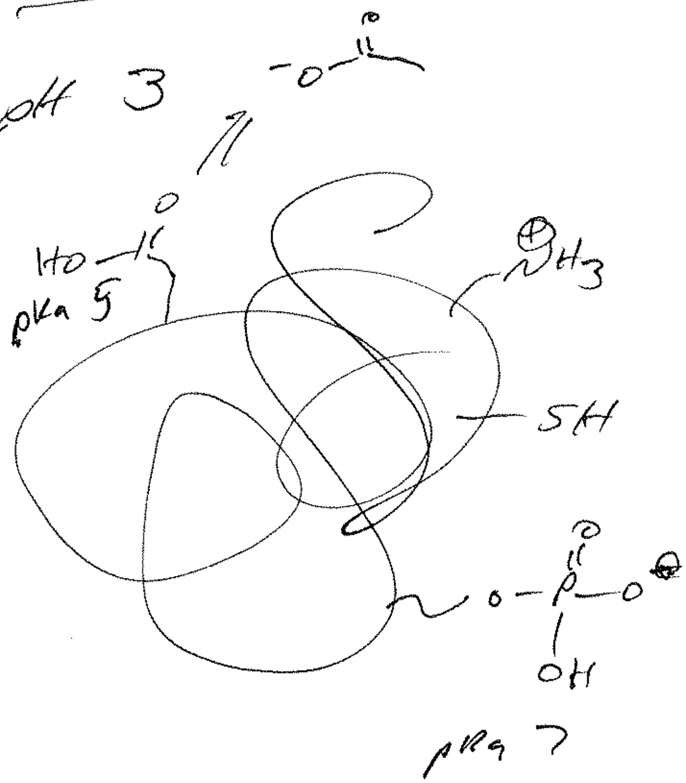
pH 9:

2 excellent nucleophiles



$\Rightarrow$ pdts from Michael rxn. at either

pH 3



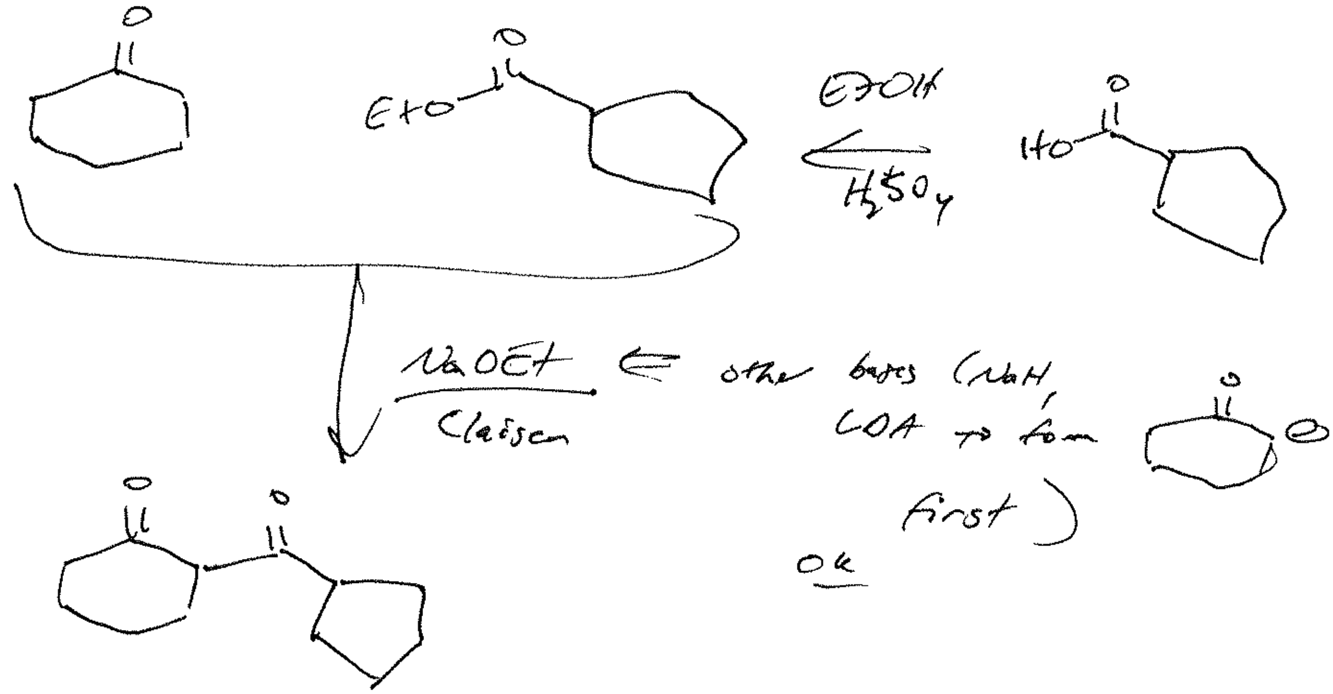
no strong nucleophiles

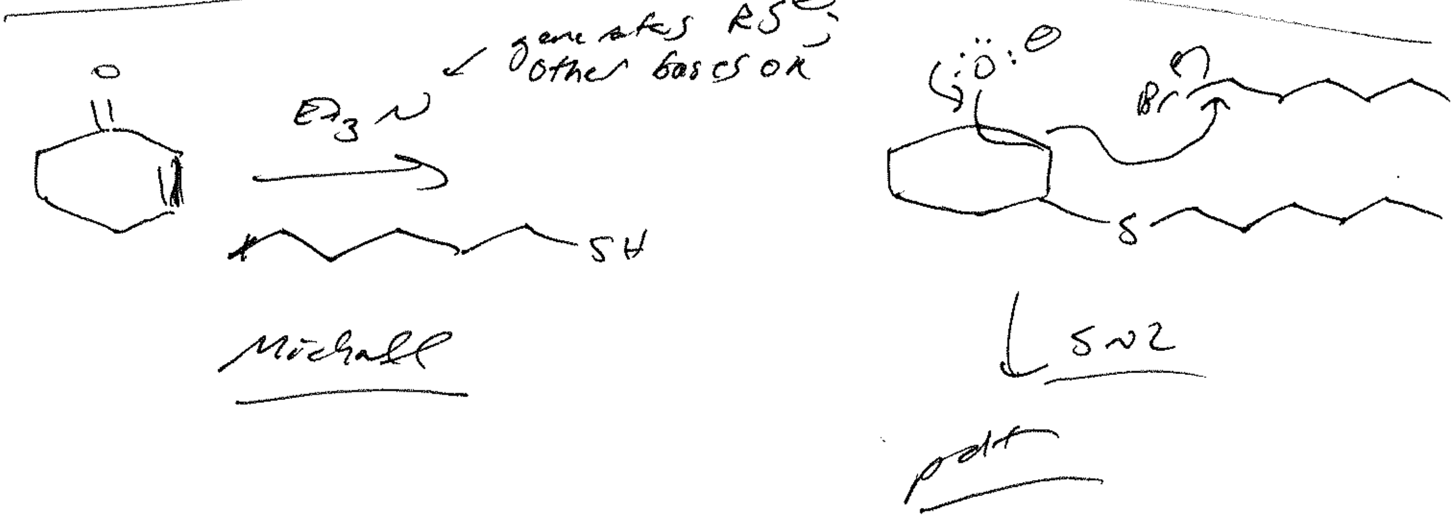
~~[illegible]~~

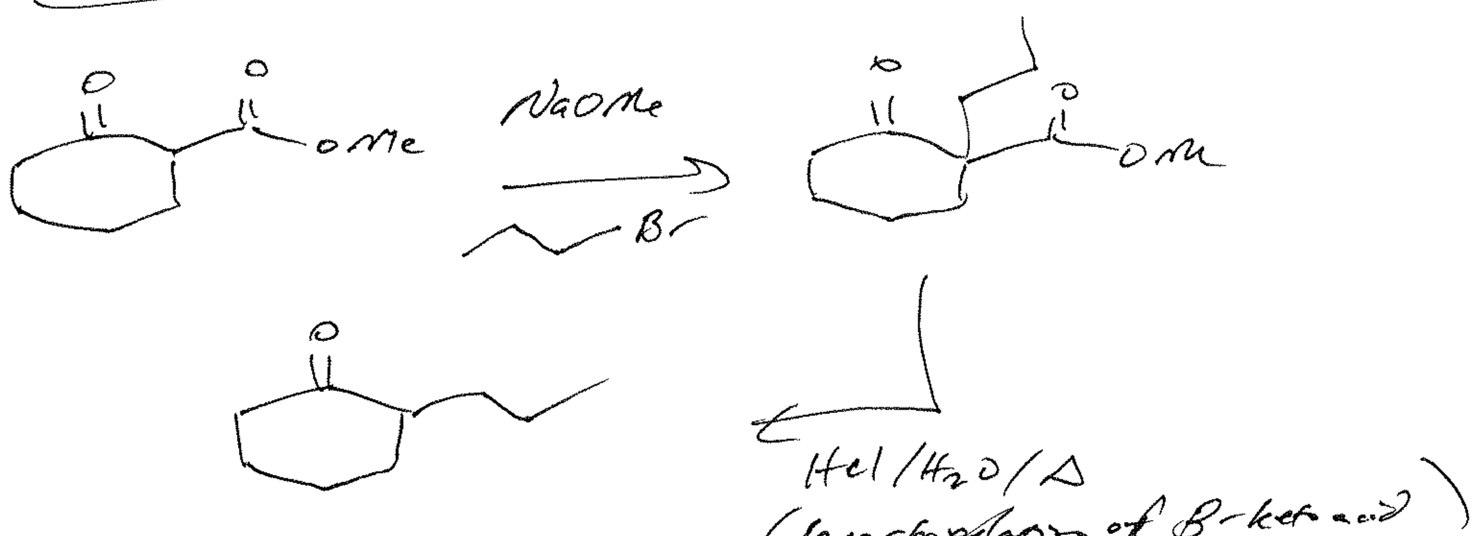
(Also: oxygen nucleophiles react poorly in Michael reaction.)

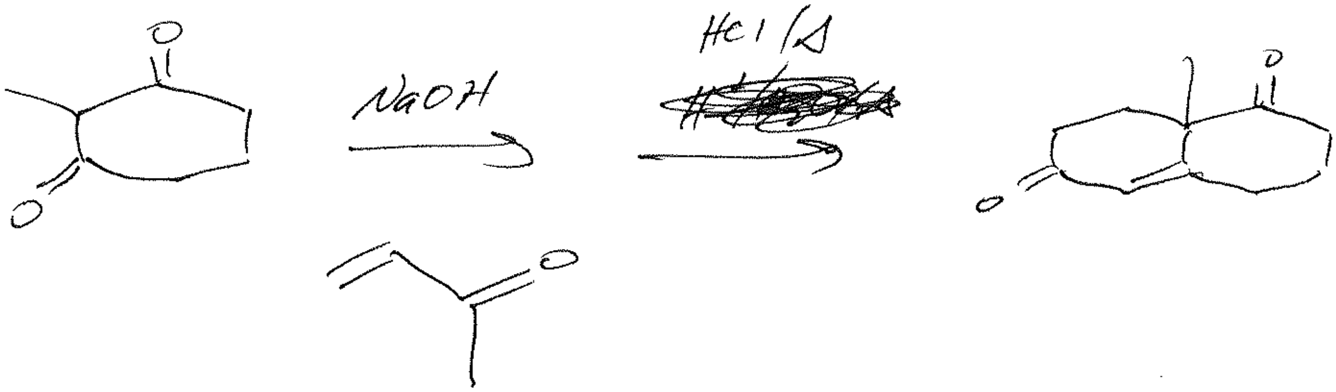
(Me–I would react slowly w/ weaker $RCO_2^\ominus$, $ROPO_3^{2-}$ nucleophiles)

3.


EtO
HO
EtOH
H_2SO_4
NaOEt
Claisen
⇐ other bases (NaH, LDA to form [enolate] first)
ok


Et_3N
SH
generates $RS^{\ominus}$
✓ other bases OK
Br
S
Michael
SN2
pdt


OMe
NaOMe
Br
OMe
HCl / H_2O / Δ
(decarboxylation of β-keto acid)



Robinson annulation

protonation, then deprotonation

(Michael reaction, isomerization of enolate
then aldol reaction,
then dehydration of aldol pdt.)

You should be able to draw the mechanism of this reaction! A good pre-final test!