***Supplement #8: Synthesizing Aldehydes And Ketones:***

***A Summary of the Main Routes***

***CHEMISTRY 4524 ORGANIC CHEMISTRY II***

 The reactions to form either aldehydes or ketones are most easily classified (and remembered)

in terms of the final product created. For either aldehyde or ketone synthesis, products are divisible

into three types: aliphatic chains, simple aromatics, and a `general’ case where the aldehyde or ketone

is a combination of aliphatic and aromatic pieces. Your text covers examples for aliphatic and aromatic

carbonyls, but doesn’t supply the `general’ routes, nor does it provide a specific route to an aldehydic aromatic

like benzaldehyde. We have summarized **all** the main routes in the table below, and provide examples of the

several syntheses not already covered in the text (the starred \* reactions). Because acid chlorides (RCOCl) are required in 3 of the major reactions, we have also appended a A Necessary Side Note on Routes to Acid Chlorides.

Substrate Aldehydes Ketones

ROH oxidation of primary alcohol oxidation of secondary alcohols (aliphatics )

RC≡CH or R’ hydration of RC≡CH or HC≡CH hydration of alkyne (RC≡CR’) or (RC≡CH)

 (Brown BH3/H2O2 +OH-) (HgSO4 /H2SO4 route)

>C=C< ozonolysis of symmetric RHC=CRH ozonolysis of symmetric RR’C=CRR’

ArCH3, Ar oxidize toluene-based aromatics \* Friedel-Krafts acylation w/**R**COCl ( aromatics)

General reduce ***R***COCl (***R*=** aliphatics or aromatics)\* Corey-House reaction with ***R***COCl \*

(***R***=aliphatic or aromatic)

a) SPECIFIC ROUTE TO SUBSTITUTED BENZALDEHYDES (Y-ArCHO, Y= any group): oxidation of methyl group



 Y Y Y

b) GENERAL ROUTE TO ANY ALDEHYDE: Reduction of acid chloride

 R-C-Cl or Ar-C-Cl LiAl(t-butoxide)3  R-C-H or Ar-C-H *Note: t-butoxide= -O-C(CH3)3*

 || || || ||

 O O O O

c) GENERAL ROUTE TO ANY KETONE: Corey-House Syntheses with acid chloride

 **CuI**

 R-Li R-CuLi R-C-R’ or R-C-Ar

 **|| ||**

 R’ or Ar-C-Cl O O

 ||

 O

**Necessary Side Note on Routes to Acid Chlorides**

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Several major synthetic routes to form ketones and aldehydes use an

 acid chloride, RCOCl, as the key ingredient.

 R-C=O

 |

 Cl

 *structural formula of acid chloride*

These syntheses (see below), one to make an aldehyde, and two to make ketones, are of general utility since R in the acid chloride can be either alkyl or aryl (aromatic).

 LiAlH(OBu-t)3

RCOCl --------------> RCHO

 AlCl3/CH2Cl2 R- C=O

RCOCl + -------------->

 Y Y Y C-R

 (activating) || O

RCOCl + R’2 CuLi ------------> R-C=O

 |

 R’

Because of the generality and utility of these reactions, it thus makes sense to ask:

 “....how do we make a specific acid chloride, RCOCl ?”

The simple answer is:

 “.... from its corresponding organic acid parent, RCOOH via:

 **SOCl2  or PCl5**

 **RCOOH -------------------> RCOCl**

 **PCl3**

Notes on *Routes to Acid Chlorides* (continued)

But since the common starting point of synthetic preparations is either alcohols,

simple hydrocarbons or alkyl ha1ides, we must then ask:

 “...okay, wise guy, how do you make the organic parent acid

 from R-H, RX or ROH ?”

Your answer comes in quadruplicate. There are four main ways to make RCOCl.

You are strongly advised to remember them.

1) **oxidation of a primary (1o) alcohol**:

 ....C-C-C-OH + (hot) KMnO4---> ......C-C-C=O

 | OH

**2) Oxidation of substituted alkyl benzenes** (...le vasectomie...)

 + hot KMnO4 ---->

 Y C-C-C... Y

(Y=anything) C=O

 OH

**3) Carbonation of Grignard reagents (R=aliphatic or aromatic)**

 Mg/ether CO2 (g) H2O/H+

 R-X ------------> RMgX -----------> {R-COOMgX} ------> RCOOH

**4) Hydrolysis of nitriles (R=aliphatic or aromatic)**

 NaCN/alcohol acid (or base/then acid)

 R-CH2Cl ---------------> RCH2CN -------------------------------> RCH2COOH

(CN‑ is poisonous….take care !)

Note that the two oxidations are specific to aliphatic alcohols and aromatic starting materials. The Grignard and hydrolysis routes are general and can be used for **any** choice of R, alkyl or aromatic.