ORGANIC CHEMISTRY CH 352-02 (Esteb)
Exam #3 Key
March 28, 2002

Question 1 _________ (10)
Question 2 _________ (8)
Question 3 _________ (10)
Question 4 _________ (30)
Question 5 _________ (10)
Question 6 _________ (12)
Question 7 _________ (20)
E. C. _________ (6)

TOTAL _________ (100)
1. Nadolol, a beta-blocking agent is synthesized in 5 steps beginning with 1-napthol. Fill in appropriate reagent (or series of reagents) over each arrow to successfully complete the synthesis (2 pts each)

1) Li, NH₃, CH₃OH (Birch reduction)

2) CH₃COOH, H⁺ or Ac₂O (Fisher esterification)

3) OsO₄, NMO (diol formation)

4) LAH (ester reduction)

5) 1) NaOH 2) 3) H₃O⁺
2. 1-(3-amino-4-benzyloxyphenyl)-ethanone (A) is a synthetic precursor to the bronchodilator carbuterol (B). Propose a synthesis of (A) beginning with p-hydroxyacetophenone (C).
3. Synthesize **1 of the following 2 compounds** starting with benzene, mono-functional groups of 4 carbons or less, 1,3-dithiane, ethylene glycol (for protection), and any inorganic reagent or solvent needed.

Any reasonable synthesis accepted. Come see me with questions.
4. Provide detailed arrow pushing mechanisms for 3 of the following 4 reactions (10 pts each)

a) 

\[
\begin{align*}
\text{OCH}_2\text{CH}=&\text{CH}_2\text{Ph} & \rightarrow & & \text{OH} & \text{Ph} \\
& & & & & \\
\text{C}_{6}\text{H}_{5} & & & & & \rightarrow & & \text{C}_{6}\text{H}_{5}
\end{align*}
\]

\[
\text{C}_{6}\text{H}_{5} & \text{OH} \text{Ph} & & & & & \rightarrow & & \text{C}_{6}\text{H}_{5}
\]

b) 

\[
\begin{align*}
\text{CH}_3 & \text{C}_\text{O} & \rightarrow & & \text{CH}_3 & \text{C}_\text{O} \\
& & & & & \\
\text{C}_\text{O} & \text{CH}_3 & & & & & \rightarrow & & \text{C}_\text{O} & \text{CH}_3
\end{align*}
\]

\[
\text{C}_\text{O} & \text{CH}_3 & & & & & \rightarrow & & \text{C}_\text{O} & \text{CH}_3
\]

c) 1) \text{Hg(OAc)}_2, \text{EtOH} \\
2) \text{NaBH}_4

\[
\begin{align*}
\text{CH}_3\text{CH}_2\text{CHO} & \quad \text{CH}_3\text{CH}_2\text{CH}_2\text{CH(OH)}_2 \\
\text{CH}_3\text{CH} = \text{CH}_2 + \text{Hg(OAc)}_2 & \quad \text{CH}_3\text{CH}_2\text{CH}_2\text{CH} = \text{CH}_2 \\
\text{Hg(OAc)}_2 & \quad \text{CH}_3\text{CH}_2\text{CH}_2\text{CH} = \text{CH}_2 \\
\text{NaBH}_4 & \quad \text{CH}_3\text{CH}_2\text{CH}_2\text{CH(OH)}_2
\end{align*}
\]
5. Provide a detailed arrow pushing mechanism for the following reaction

\[
\text{CO} \quad \xrightarrow{\text{H}_2\text{NNH}_2, \text{KOH}} \quad \text{CH}_3
\]

6. For the following roadmap, give the structure for A, B, and C. (4 pts each)
1) HSCH₂CH₃CH₂SH, H₂SO₄
2) n-ButLi, Et₂O
3) isopentylbromide

A = C₁₂H₂₄S₂

1) HgCl₂, H₂O, CH₃CN
2) CH₃CH=PH₃

B = C₁₁H₂₂

1) BH₃-THF
2) H₂O₂
3) PCC, CH₂Cl₂

C = C₁₁H₂₂O

1) NaCN, Et₂O-H₂O
2) HCl

A = \[ \text{structure of A} \]

B = \[ \text{structure of B} \]

C = \[ \text{structure of C} \]
7. Given the following spectral data, provide a structure for the compound. Stop and think about organization before you begin to write. A correct structure unsupported by a sound proof will lose credit accordingly. The problem is designed to challenge you. Abundant credit will reward partial solutions if they are well reasoned and clearly written. **You do not have to worry about drawing the correct E/Z stereochemistry!**

Elemental composition is \( %C = 63.14 \), \( %H = 8.83 \).
The unknown structure is:

![Structure Image]

The elemental analysis provides an empirical formula of C$_3$H$_5$O.

Examination of the MS shows a M$^+$ of 114. This would then correspond to a molecular formula of 2 x empirical formula or C$_6$H$_{10}$O$_2$.

The IR shows aliphatic C-H stretches, a carbonyl stretch (not an amide or acid), could be an aldehyde (stretches at 2850 and 2750).

The CNMR shows an C=O peak as a doublet at 190 characteristic of an aldehyde.

- There is a d at 168 suggesting an sp$^2$ CH next to an electronegative atom.
- There is a s at 120 suggesting a quarternary sp$^2$ C.
- There is a t at 70 suggesting a CH$_2$ next to an electronegative atom.
- There is a q at 15 suggesting a CH$_3$.
- There is a q at 8 suggesting a CH$_3$.

Upon checking the CNMR with the formula, we see that we have all C’s and H’s accounted for and the electronegative atom must be the extra O.

The HNMR shows a 1H s at 9.5 indicative of an aldehyde

1H s at 7 from a vinylic proton not adjacent to any H bearing atoms and probably connected to an O. Putting C and H NMR info together gives as a partial structure

-O-CH=C<

The 2H quartet at 4 coupled with the 3H triplet at 1.5 is characteristic of an OCH$_2$CH$_3$ group. Therefore an updated partial structure is:

CH$_3$CH$_2$O-CH=C<

Lastly the 3H s is from a CH$_3$ adjacent to atoms that do not bear H’s. Therefore the final structure should be the one shown above.

(3) Extra Credit:

Name one problem with the medicinal route synthesis that was overcome in the scale up synthesis of Viagra - linear synth, toxic intermediates, low yields, high cost, too much waste, etc.

(3) Extra Credit:

Name 5 of the 7 continents on earth. –Asia, Europe, Africa, Australia, Antartica, S. America, N. America