Chemistry 216
First Examination
November 10, 2009
Professor Masato Koreeda
(1 hr 20 min, 80 points)

Please CHECK OFF your lab section.

Tuesday
130 Charles Schuler
131 Benjamin Throesch
132 Rebecca Matz
133 Natalie Vandeven
134 Weng Tham
135 Sameer Phadke
136 Aireen Romu

Wednesday
150 Larissa Kipa
151 Christine Morrison
152 Jiyoung Hong
153 Gabriel Román
154 Sameer Phadke
155 Jonathon Mahlow
156 Anthony Grillo

Thursday
156 Gabriel Román
170 Rebecca Matz
171 Aireen Romu
172 Jiyoung Hong
173 Anthony Grillo
174 Jonathon Mahlow
175 Weng Tham

This exam has 12 pages including this cover page.
The last three pages include a periodic table, tables of characteristic IR frequencies and pKa values for representative acids.
I. (4 points) Arrange the following four compounds in order of their $R_f$ values when analyzed by thin-layer chromatography (TLC) on silica gel-coated plates using $CH_2Cl_2$ as the developing solvent. No partial credit is given to this question.

Answer:

<p>| | | |</p>
<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td>&lt;</td>
<td>&lt;</td>
<td>&lt;</td>
</tr>
<tr>
<td>lowest $R_f$</td>
<td></td>
<td>highest $R_f$</td>
</tr>
</tbody>
</table>

II. (9 points) Silica gel thin layer chromatography (TLC) is often used to monitor the progress of an organic reaction. For the following ester hydrolysis reaction, a solvent system is selected to give the starting material an $R_f$ value of about 0.5. (1) Provide in the box below the structure of the expected product 6. (2) Fill in the spots that would be expected when the reaction is 50% complete and 100% complete, each after acidic work-up. Make sure to assign each spot you draw to the corresponding compound number (5, 6, or 7). Consider only the compounds that can be visualized as a spot on TLC upon exposure of each solvent-dried plate to a 254 nm-UV lamp.

On each TLC plate, a student has placed a sample of the starting material (5) as a reference on the left of the plate, a spot of the reaction mixture (after acidic work-up) on the right, and a co-spot in the center of each. Co-spotting is where some of 5 and some of the reaction mixture are spotted together in order to make better comparisons.
III. (13 points) Ponasterone A (8) is one of the insect molting hormones. As part of my undergraduate research (last century!), I was asked to determine the structure of this hormone. To this end, 46.4 mg of ponasterone A was treated with 2 mol equivalents of HIO$_4$ to provide a mixture of two products, dialdehyde diketone 9 and aldehyde 10. The crude reaction mixture was then subjected to steam distillation by which only one of these two products was distilled over together with water. This distillate mixture was dripped directly into the aqueous acidic solution containing excess 2,4-dinitrophenylhydrazine (11, 2,4-DNP) to immediately produce 21 mg of the yellow-colored 2,4-DNP derivative.

Provide the answer to each of the following questions in the box given.

(1) How many mgs of HIO$_4$ was used in this experiment? The atomic weight of iodine is 127. Show your work.

(2) Draw the structure of the 2,4-DNP derivative formed in this experiment.

(3) What is the theoretical yield of the 2,4-DNP derivative? Show your work.

(4) What is the percent chemical yield of the 2,4-DNP in this experiment? Show your work.
IV. (12 points) A levulinyl group [CH$_3$C(=O)CH$_2$CH$_2$C(=O)-] is an extremely versatile hydroxyl-protecting group. A team of scientists at The Scripps Research Institute in La Jolla, CA, reported that the levulinate group (indicated by a rectangular box) in differentially protected disaccharide 12 can be deprotected selectively to provide alcohol 13 in quantitative yield [Proc. Natl. Acad. Sci., USA 2003, 100, 797].

![Diagram of chemical structures](image)

(1) The methods used to achieve this selective deprotection take advantage of the difference in electrophilicity between aldehyde/ketone and ester carbonyl groups. Among these methods known, the use of NaBH$_4$ is most convenient. In the reaction shown below, the levulinate ester of cyclohexanol, 14, is treated with NaBH$_4$ to afford cyclohexanol (15). The by-product (16) from this reaction has the molecular formula of C$_5$H$_8$O$_2$. Provide in the box below the structure of this compound.

![Diagram of reaction](image)

(2) When a levulinate such as 14 is treated with hydrazine (NH$_2$-NH$_2$) in acetic acid, the levulinate-protected alcohol undergoes facile deprotection (see below). Draw in the box provided the structure of the by-product 14.

![Diagram of reaction](image)

(3) The reaction of levulinate 14 with hydrazine first produces its hydrazone derivative, which further undergoes an intramolecular reaction to produce 17. Draw in the box below the structure of this hydrazone derivative of 14.
V. (16 points) For the following reaction, provide in the boxes below the structure of the expected product and a step by step mechanism through the use of the curved arrow convention.

(1)
\[ \text{benzoic anhydride} + \text{Solvent} \rightarrow \text{Product} \]

(2) Reaction mechanism:

(3) Would you expect the benzylation reaction of 4-nitroaniline using benzoic anhydride to be faster or slower compared with that of aniline? Explain your answer. If any resonance structure(s) of 4-nitroaniline are involved in your answer, make sure to clearly draw pertinent the resonance structure.

Faster or slower (circle one that applies) (2 points)

Explanation (3 points):
VI. (9 points) For each of the following synthetic reactions, draw the structure of the expected organic product in the box provided.

(1)  \[
\begin{array}{c}
\text{C}_3\text{H}_5\text{COO}\text{Na}^+ \quad \text{H}_2\text{SO}_4 \\
\text{CH}_3\text{OH (solvent)} \quad \Delta, \ 2 \text{ h} \\
\text{salt} + \text{H}_2\text{O}
\end{array}
\]

(2)  \[
\begin{array}{c}
\text{CH}_3\text{CH}_2\text{ONa} \quad \text{CH}_3\text{CH}_2\text{OH (solvent)} \quad \Delta, \ 1 \text{ h} \\
\text{H}_2\text{O}
\end{array}
\]

(3)  \[
2 \text{C}_3\text{H}_5\text{COH} + \text{CH}_3\text{CH}_2\text{OH (solvent)} \quad \text{NaOH} \quad \text{room temperature} \quad 2 \text{ h} \\
\text{H}_2\text{O}
\]

VII. (5 points) For each of the following pairs of compounds, match the expected IR frequencies for the C=O bond stretching vibration to the wavenumbers given.

(1) (2 points) 1710 or 1674 cm\(^{-1}\)

\[
\begin{array}{c}
\text{OCH}_3 \quad \text{cm}^{-1} \\
\text{OCH}_3 \quad \text{cm}^{-1}
\end{array}
\]

(2) (3 points) 1760 or 1718 cm\(^{-1}\)

\[
\begin{array}{c}
\text{cm}^{-1} \\
\text{cm}^{-1}
\end{array}
\]
VIII. (12 points). Given below are infrared (IR) spectra of four compounds. The compounds are among those structures given on page 9. Assign each spectrum to its compound by putting the letter corresponding to the compound in the answer box next to the spectrum. The tables of characteristic infrared frequencies appear on pages 10 and 11.

(1) (liquid film) Answer

(2) (liquid film) Answer
VIII. (continued)

(3) (liquid film) Answer

\[
\begin{array}{cccc}
2957 & 11 & 1461 & 35 \\
2930 & 8 & 1413 & 27 \\
2875 & 17 & 1379 & 56 \\
2859 & 13 & 1282 & 30 \\
2873 & 43 & 1232 & 35 \\
1711 & 4 & 1204 & 45 \\
1468 & 36 & 1109 & 66 \\
\end{array}
\]

(4) (KBr disc) Answer

\[
\begin{array}{cccc}
3366 & 12 & 2764 & 84 \\
3179 & 27 & 1642 & 4 \\
2972 & 26 & 1471 & 37 \\
2934 & 62 & 1466 & 60 \\
2910 & 74 & 1430 & 34 \\
2870 & 74 & 1574 & 62 \\
2815 & 81 & 1360 & 68 \\
\end{array}
\]
VIII. (continued)

A

B

C

D

E

F

G

H

I

J
OH absorption broadens and moves to lower $\nu$ when H-bonded:

- non-H-bond: sharp, 3600 cm$^{-1}$
- H-bond alcohol: broad, 3500-3200 cm$^{-1}$
- H-bond acid: very broad, 3300-2800 cm$^{-1}$

Carbonyl absorption frequencies roughly follow observed reactivity trends for carbonyl compounds:

- acid halide $>$ anhydride $>$ ester $>$ aldehyde $>$ ketone, acid $>$ amide

Conjugation lowers $\nu$ by ca. 20 cm$^{-1}$
Table E-1. Molecular vibrations and absorption frequencies in the infrared region.

<table>
<thead>
<tr>
<th>Bond Type</th>
<th>Stretching, cm⁻¹</th>
<th>Bending, cm⁻¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>C–H alkanes</td>
<td>2960–2850 (s)</td>
<td>1470–1350 (s)</td>
</tr>
<tr>
<td>C–H alkenes</td>
<td>3080–3020 (m)</td>
<td>1000–675 (s)</td>
</tr>
<tr>
<td>C–H aromatic</td>
<td>3100–3000 (υ)</td>
<td>870–675 (υ)</td>
</tr>
<tr>
<td>C–H aldehyde</td>
<td>2900, 2700 (m, 2 bands)</td>
<td></td>
</tr>
<tr>
<td>C–H alkyne</td>
<td>3300 (s)</td>
<td></td>
</tr>
<tr>
<td>C=C alkyne</td>
<td>2260–2100 (υ)</td>
<td></td>
</tr>
<tr>
<td>C=N nitrile</td>
<td>2260–2220 (υ)</td>
<td></td>
</tr>
<tr>
<td>C=C alkene</td>
<td>1680–1620 (υ)</td>
<td></td>
</tr>
<tr>
<td>C=C aromatic</td>
<td>1600–1450 (υ)</td>
<td></td>
</tr>
<tr>
<td>C=O ketone</td>
<td>1725–1705 (s)</td>
<td></td>
</tr>
<tr>
<td>C=O aldehyde</td>
<td>1730–1720 (s)</td>
<td></td>
</tr>
<tr>
<td>C=O α, β-unsaturated ketone</td>
<td>1685–1665 (s)</td>
<td></td>
</tr>
<tr>
<td>C=O aryl ketone</td>
<td>1700–1680 (s)</td>
<td></td>
</tr>
<tr>
<td>C=O ester</td>
<td>1750–1740 (s)</td>
<td></td>
</tr>
</tbody>
</table>

C=O acid                  | 1725–1700 (s)    |               |
C=O amide                 | 1680–1650 (s)    |               |
O–H alcohols (not hydrogen bonded) | 3650–3590 (υ) |               |
O–H alcohols (hydrogen bonded) | 3600–3200 (s, broad) | 1620–1590 (υ) |
O–H acids                 | 3000–2500 (s, broad) | 1655–1510 (s) |
N–H amines                | 3500–3300 (m)    |               |
N–H amides                | 3500–3350 (m)    |               |
C–O alcohols, ethers, esters | 1300–1000 (s) |               |
C–N amines, alkyl         | 1220–1020 (υ)    |               |
C–N amines, aromatic      | 1360–1250 (s)    |               |
NO₂ nitro                 | 1560–1515 (s)    | 1385–1345 (s) |

s = strong absorption    w = weak absorption    m = medium absorption    υ = variable absorption

Table E-2. Other double bonds

<table>
<thead>
<tr>
<th>$ν$, cm⁻¹</th>
<th>Chromophore</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>1620–1680</td>
<td>$\text{C=C}$ &lt;br&gt;(vC=C)</td>
<td><strong>Alkenes</strong>&lt;br&gt;The double bond absorption is very weak when symmetrically substituted, but is more intense when terminal. It becomes intense and at relatively smaller wave number in conjugated cases, more so when conjugated with ketones than with other double bonds. Tetrasubstituted double bonds often do not show.</td>
</tr>
<tr>
<td>1400–1600</td>
<td>$\text{O}$ &lt;br&gt;(vC=C)</td>
<td><strong>Aromatics</strong>&lt;br&gt;A series of peaks of variable intensity used principally as a fingerprint.</td>
</tr>
<tr>
<td>1590–1690</td>
<td>$\text{C=N}$ &lt;br&gt;(vC=N)</td>
<td><strong>Imines and oximes</strong>&lt;br&gt;Intensity is usually weak and not much affected by conjugation.</td>
</tr>
<tr>
<td>ACID</td>
<td>pK&lt;sub&gt;a&lt;/sub&gt;</td>
<td>CONJUGATE BASE</td>
</tr>
<tr>
<td>-----------</td>
<td>---------------</td>
<td>----------------</td>
</tr>
<tr>
<td>(Strongest Acid)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>H₂O</td>
<td>-9</td>
<td></td>
</tr>
<tr>
<td>H - I</td>
<td>-9</td>
<td></td>
</tr>
<tr>
<td>H - Cl</td>
<td>-7</td>
<td>CH₃CH₂⁻</td>
</tr>
<tr>
<td>CH₃CH₂OH</td>
<td>-2.4</td>
<td></td>
</tr>
<tr>
<td>H₂O⁻</td>
<td>-1.7</td>
<td></td>
</tr>
<tr>
<td>O₃N⁻</td>
<td>-1.3</td>
<td>O₃N⁻</td>
</tr>
<tr>
<td>CH₃OH</td>
<td>0.64</td>
<td>CH₃OH⁻</td>
</tr>
<tr>
<td>H - F</td>
<td>3.2</td>
<td>O₃N⁻</td>
</tr>
<tr>
<td>O₃N⁻</td>
<td>4.2</td>
<td>CH₃OH⁻</td>
</tr>
<tr>
<td>3H +</td>
<td>4.6</td>
<td>CH₃OH⁻</td>
</tr>
<tr>
<td>CH₃OH</td>
<td>4.8</td>
<td>CH₃OH⁻</td>
</tr>
<tr>
<td>HO₂⁻</td>
<td>6.5</td>
<td>CH₃OH⁻</td>
</tr>
<tr>
<td>CH₃CO₂⁻</td>
<td>9.2</td>
<td>CH₃CO₂⁻</td>
</tr>
<tr>
<td>H - C≡N</td>
<td>9.1</td>
<td>H - C≡N⁻</td>
</tr>
<tr>
<td>H - NH⁻</td>
<td>9.4</td>
<td>H - NH⁻</td>
</tr>
<tr>
<td>H</td>
<td>10.0</td>
<td>H - NH⁻</td>
</tr>
<tr>
<td>(Weakest Acid)</td>
<td></td>
<td></td>
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</tbody>
</table>