MULTIPLE CHOICE. Choose the one alternative that best completes the statement or answers the question.

1) Which of the following is the most reactive carboxylic acid derivative?  
   A) amide  
   B) nitrile  
   C) anhydride  
   D) acid chloride  
   E) ester  

2) \(N\)-Methylacetamide is an example of:  
   A) a secondary amide  
   B) a primary amide  
   C) a tertiary amide  
   D) an imine  
   E) an \(N, N\)-disubstituted amide  

3) Which of the following are strongly hydrogen bonded in the liquid phase?  
   A) secondary amides  
   B) acid chlorides  
   C) esters  
   D) nitriles  
   E) tertiary amides  

4) While the carbonyl stretching frequency for simple aldehydes, ketones, and carboxylic acids is about 1710 cm\(^{-1}\), the carbonyl stretching frequency for esters is about:  
   A) 1800 cm\(^{-1}\)  
   B) 2200 cm\(^{-1}\)  
   C) 1660 cm\(^{-1}\)  
   D) 1735 cm\(^{-1}\)  
   E) 1700 cm\(^{-1}\)  

5) While the carbonyl stretching frequency for simple aldehydes, ketones, and carboxylic acids is about 1710 cm\(^{-1}\), the carbonyl stretching frequency for acid chlorides is about:  
   A) 1800 cm\(^{-1}\)  
   B) 1660 cm\(^{-1}\)  
   C) 2200 cm\(^{-1}\)  
   D) 1735 cm\(^{-1}\)  
   E) 1700 cm\(^{-1}\)  

6) While the carbonyl stretching frequency for simple aldehydes, ketones, and carboxylic acids is about 1710 cm\(^{-1}\), the carbonyl stretching frequency for amides is about?  
   A) 1700 cm\(^{-1}\)  
   B) 2200 cm\(^{-1}\)  
   C) 1660 cm\(^{-1}\)  
   D) 1735 cm\(^{-1}\)  
   E) 1800 cm\(^{-1}\)  

7) The chemical shifts for protons \(\alpha\) to a carbonyl group:  
   A) are similar for all acid derivatives.  
   B) are farthest downfield for carboxylic acids.  
   C) fall between \(\delta\) 3.1 and \(\delta\) 4.2 (ppm).  
   D) fall between \(\delta\) 1.3 and \(\delta\) 1.8 (ppm).  
   E) are farther downfield than those \(\alpha\) to a nitrile.
8) In the proton NMR spectrum of a secondary amide, the amide proton’s signal is:
   A) sharp, around δ 10.0 (ppm).
   B) broad, around δ 9.0 (ppm).
   C) broad, around δ 7.0 (ppm).
   D) usually not observed.
   E) sharp, around δ 5.0 (ppm).

9) In nucleophilic acyl substitution, :
   A) protonation of the carbonyl is followed immediately by loss of the leaving group.
   B) an SN2 reaction occurs.
   C) ester hydrolysis is followed by deprotonation.
   D) loss of the leaving group is followed by rearrangement of the carbocation.
   E) addition to the carbonyl by a nucleophile is followed by loss of the leaving group.

10) A correct order of reactivity of acid derivatives towards nucleophilic attack is:
    A) anhydrides > amides > carboxylates.
    B) anhydrides > amides > esters.
    C) anhydrides > acids > acid chlorides.
    D) esters > acid anhydrides > amides.
    E) carboxylates > esters > amides.

SHORT ANSWER. Write the word or phrase that best completes each statement or answers the question.

11) Using the two key resonance structures for an ester, show how resonance stabilization is lost when an ester is attacked by a nucleophile.

ESSAY. Write your answer in the space provided or on a separate sheet of paper.

12) Provide a detailed, stepwise mechanism for the reaction of propanoyl chloride with ammonia.

13) Provide a detailed, stepwise mechanism for the reaction of propanoic anhydride with phenol.

14) Using potential energy diagrams, explain why alkoxides act as leaving groups in nucleophilic acyl substitutions but not in SN2 reactions.

15) Provide a detailed, stepwise mechanism for the acid-catalyzed transesterification of ethyl acetate with n-propanol.

16) Provide a detailed, stepwise mechanism for the base-mediated transesterification of methyl benzoate with sodium ethoxide.

17) Provide a detailed, stepwise mechanism for the reaction of γ-butyrolactone with ammonia.
MULTIPLE CHOICE. Choose the one alternative that best completes the statement or answers the question.

18) The hydrolysis of esters in base is called:
   
   A) transesterification.
   B) the Fischer esterification.
   C) saponification.
   D) the Hunsdieck reaction.
   E) the Dieckmann condensation.

19) Typically, amides will hydrolyze under __________ conditions than esters.
   
   A) milder
   B) stronger
   C) more saline
   D) more dilute
   E) less vigorous

20) The hydrolysis of esters, amides, and nitriles:
   
   A) should be carried out at pH 7.0 for optimum efficiency.
   B) can be carried out under acidic or basic conditions.
   C) is not pH dependent.
   D) must be acid-catalyzed.
   E) must be base-catalyzed.

21) Lithium aluminum hydride reduces carboxylic acids, acid chlorides, and esters to:
   
   A) tertiary alcohols.
   B) primary alcohols.
   C) ketones.
   D) aldehydes.
   E) secondary alcohols.

22) Acids can be reduced to aldehydes by:
   
   A) conversion to the amide followed by treatment with NaBH₄.
   B) conversion to the anhydride followed by treatment with Mg and H₂O⁺.
   C) conversion to the acid chloride followed by treatment with LiAlH₄[OC(CH₃)₃]₃.
   D) treatment with LiAlH₄.
   E) conversion to the ester followed by treatment with LiAlH₄.

23) Acids can be converted to primary amines by:
   
   A) conversion to the nitrile followed by treatment with LiAlH₄.
   B) conversion to the diazonium salt followed by treatment with NaBH₄.
   C) conversion to the primary amide followed by treatment with LiAlH₄.
   D) both A and B.
   E) both A and C.

24) Two equivalents of methyl magnesium bromide will add to:
   
   A) aldehydes.
   B) imines.
   C) secondary amines.
   D) lactones.
   E) ketones.
25) What are the products from the reaction of excess methyl magnesium bromide with ethyl acetate followed by H$_3$O$^+$?

ESSAY. Write your answer in the space provided or on a separate sheet of paper.

26) Show how one might synthesize phenylacetone using toluene, NaCN, and any other necessary reagents.

MULTIPLE CHOICE. Choose the one alternative that best completes the statement or answers the question.

27) Which of the following statements is/are true?
A) LiAIH[OC(CH$_3$)$_3$]$_3$ reacts with acid chlorides to yield primary alcohols after hydrolysis.
B) LiAIH$_4$ reacts with acid chlorides to yield secondary alcohols after hydrolysis.
C) Two equivalents of Grignard reagent react with acid chlorides to yield tertiary alcohols after hydrolysis.
D) both A and B
E) both B and C

28) Phthalic acid produces what acid derivative upon heating?
A) a carboxylate
B) an ester
C) an acid chloride
D) an anhydride
E) an amide

SHORT ANSWER. Write the word or phrase that best completes each statement or answers the question.

29) What are the major organic products when 1 equivalent of acetic formic anhydride reacts with 1 equivalent of methanol?

30) Give two different one-step methods to convert propanoic acid to methyl propanoate.

31) How might one obtain a significant quantity of a lactone even when the formation reaction has a positive $\nu$G?

MULTIPLE CHOICE. Choose the one alternative that best completes the statement or answers the question.

32) A nitrile can be made by dehydrating an amide. However, for this reaction to occur, the amide must be:
A) secondary.
B) primary.
C) part of a lactam.
D) N-methylated.
E) tertiary.

SHORT ANSWER. Write the word or phrase that best completes each statement or answers the question.

33) What reagents are used to dehydrate amides to nitriles?
ESSAY. Write your answer in the space provided or on a separate sheet of paper.

34) Why are β-lactams, such as penicillins and cephalosporins, unusually reactive amides?

35) Propose a synthesis of benzonitrile from benzene and any other necessary reagents.

36) Propose a synthesis of 2-phenylethylamine from toluene and any other necessary reagents.

37) Propose a synthesis of methyl thioacetate from one carbon compounds and any other necessary inorganic reagents.

38) Using resonance structures and pictures of orbitals, explain why resonance stabilization of thioesters is less than that of esters.

39) Carbonated beverages typically have pH's below 7.0. What acid is present which lowers the pH? Show the reaction by which it is formed.

40) Ethylene glycol will react with phosgene to produce what organic compound?

41) Provide the proper IUPAC name for the compound below.

\[
\begin{align*}
\text{CO}_2\text{CH(CH}_3)_2
\end{align*}
\]

42) Provide the proper IUPAC name for CICH₂CH₂CONHCH₃.

43) Provide the proper IUPAC name for the compound below.

\[
\begin{align*}
\text{CH}_3\text{CH}_2\text{CH}\text{CH}_2\text{COCl}
\end{align*}
\]

44) Provide the proper IUPAC name for the compound below.

\[
\begin{align*}
\text{CN}
\end{align*}
\]

45) Provide the proper IUPAC name for NCCH₂CH₂CH₂CH₂CO₂CH₃.

46) Provide the structure of N,N-diethylbutanamide.

47) Provide the structure of propanoic anhydride.

48) Provide the structure of 3-oxobutanenitrile.
49) Provide the structure of 2-bromo-2-methylbutanoyl chloride.

MULTIPLE CHOICE. Choose the one alternative that best completes the statement or answers the question.

50) Cyclic amides are called:
   A) lactones.  B) aminals.  C) lactams.  D) imines.  E) animals.  
   50) _______

51) Amides are less basic than amines because:
   A) the carbonyl group donates electrons by resonance.
   B) the nitrogen has a full positive charge.
   C) the carbonyl group withdraws electrons by resonance.
   D) amides do not contain nitrogen.
   E) the nitrogen does not have a lone pair of electrons.  
   51) _______

52) The correct priority of functional groups in IUPAC nomenclature is:
   A) acid > ester > amide > ketone.
   B) amide > acid > ester > ketone.
   C) amide > ester > acid > ketone.
   D) ester > amide > ketone > acid.
   E) ketone > acid > ester > amide.  
   52) _______

53) Cyclic esters are called:
   53) _______

SHORT ANSWER. Write the word or phrase that best completes each statement or answers the question.

54) Provide the major organic product in the reaction of cyclopentanecarbonyl chloride with sodium formate.  
   54) ________________

ESSAY. Write your answer in the space provided or on a separate sheet of paper.

55) Using ethanol as your only source of carbon compounds and using any other necessary inorganic reagents, propose a synthesis of ethyl acetate.

56) Using ethanol as your only source of carbon compounds and using any other necessary inorganic reagents, propose a synthesis of acetonitrile.

57) Propose a synthesis of PhNHCHO from benzene.

58) Provide the major organic product in the reaction of 3-methylpentanoic acid with CH₂N₂.  

59) Provide the major organic product in the reaction of propanoyl chloride with CH₃SH.  

60) Provide the major organic product in the reaction of CH₃CH₂CONH₂ with hot aqueous acid.

61) List the following four carboxylic acid derivatives, ester, anhydride, amide, and acid halide, in order of increasing reactivity in nucleophilic acyl substitution reactions. Start with the least reactive derivative.
62) What compound results when benzoic acid reacts with methylamine, and what compound ultimately results when the initially formed compound is heated at 140°C?

63) Provide the IUPAC name for HCONHCH₂CH₂CH₃.

64) List the following five compounds, ethanamide, 1-propanol, methyl formate, acetic acid, and propanenitrile, in order of increasing boiling point. Start with the lowest boiling compound.

**MULTIPLE CHOICE. Choose the one alternative that best completes the statement or answers the question.**

65) Which of the following compounds, when reacted with aniline, yield(s) acetanilide?  
   A) acetyl chloride  
   B) acetic anhydride  
   C) methyl butanoate  
   D) both A and B  
   E) both A and C

68) Which of the following compounds is(are) hydrolyzed to butanoic acid upon heating in H₂O, H₂SO₄?  
   A) ethyl butanoate  
   B) butyl acetate  
   C) N-methylbutanamide  
   D) both A and B  
   E) both A and C

69) What compound is produced when N,N-dimethylpropanamide is treated with LiAlH₄?  
   A) CH₃CH₂CH₂NH₂  
   B) CH₃CH₂CONH₂  
   C) CH₃CH₂CH₂OH  
   D) CH₃CH₂CH₂N(CH₃)₂  
   E) CH₃CH₂N(CH₃)₂

**SHORT ANSWER. Write the word or phrase that best completes each statement or answers the question.**

66) Name the compound which results when propyl benzoate is heated in a large excess of ethanol in the presence of catalytic acid.

**ESSAY. Write your answer in the space provided or on a separate sheet of paper.**

67) Name the compound which results when δ-valerolactone is heated in a large excess of methanol in the presence of catalytic acid.

**MULTIPLE CHOICE. Choose the one alternative that best completes the statement or answers the question.**

70) Which of the following reagents convert(s) benzoyl chloride to phenyl propyl ketone?  
   A) CH₃CH₂CH₂MgBr  
   B) CH₃CH₂CH₂Li  
   C) (CH₃CH₂CH₂)₂CuLi  
   D) both A and B  
   E) both A and C
SHORT ANSWER. Write the word or phrase that best completes each statement or answers the question.

71) Provide the structure of cyclohexyl formate. 71)

72) Provide the structure of γ-butyrolactam. 72)

73) Provide the structure of (R)-4-ethoxypentanenitrile. 73)

74) Provide the structure of o-bromobenzoyl chloride. 74)

MULTIPLE CHOICE. Choose the one alternative that best completes the statement or answers the question.

75) What type of compound results from the reaction of an acid chloride and a 2° amine? 75)
   A) carboxylate
   B) 1° amine
   C) ester
   D) nitrile
   E) amide

76) What type of compound results from the reaction of ethyl formate with cyclohexylamine? 76)
   A) carboxylate
   B) amide
   C) nitrile
   D) acid anhydride
   E) 1° amine

SHORT ANSWER. Write the word or phrase that best completes each statement or answers the question.

77) Provide the major organic product of the following reaction. 77)

78) Provide the major organic product of the following reaction. 78)
79) Provide the major organic product of the following reaction.

\[
\text{C}_6\text{H}_{5} + \text{CO}_2\text{C}_6\text{H}_{5} \xrightarrow{\text{AlCl}_3} \]

80) Provide the major organic product of the following reaction.

\[
\text{CH}_3\text{CCH}_2\text{CH}_2\text{CH}_2\text{NH}_2 + \text{O}_2 \xrightarrow{\text{P}_2\text{O}_5} \]

81) Provide the structure of trifluoroacetic anhydride.

82) Provide the IUPAC name of the following compound.

83) Provide the IUPAC name of the following compound.

84) Arrange the following three amides in order of increasing boiling point: propanamide, N-methylacetamide, and N,N-dimethylformamide.

85) Arrange the following compounds in order of increasing boiling point: acetic acid, propanenitrile, butane, and acetamide.
MULTIPLE CHOICE. Choose the one alternative that best completes the statement or answers the question.

86) The most characteristic IR stretch of butanenitrile occurs at approximately what wavenumber? 86) ______
   A) 2600 cm\(^{-1}\)   B) 3100 cm\(^{-1}\)   C) 3500 cm\(^{-1}\)   D) 1750 cm\(^{-1}\)   E) 2200 cm\(^{-1}\)

87) Which compound has a carbonyl stretch in its IR spectrum at the lowest wavenumber? 87) ______
   A) propanoyl chloride
   B) acetic anhydride
   C) formamide
   D) cyclohexanone
   E) ethyl acetate

SHORT ANSWER. Write the word or phrase that best completes each statement or answers the question.

88) Describe, in short phrases, the three step mechanism by which hexanoyl chloride reacts with dimethylamine. 88) ____________

89) What compound results when ethyl benzoate is stirred in methanol containing a trace of HCl and by what name is this process known? 89) ___________

MULTIPLE CHOICE. Choose the one alternative that best completes the statement or answers the question.

90) What reagent is used to convert pentanamide to 1-pentanamine? 90) ______
   A) SOCl\(_2\)   B) CuCN   C) POCl\(_3\)   D) CH\(_3\)MgBr   E) LiAlH\(_4\)

91) Identify the correct IUPAC systematic name for the structure below. 91) ______

\[
\begin{array}{c}
\text{O} \\
\text{N} \text{CH}_3 \\
\text{H}
\end{array}
\]
   A) 2-ethyl-5,N-dimethyloctanamide   B) N-methyl-2-ethyl-5-methyloctanamide
   C) 5,N-dimethyl-2-ethyloctanamide   D) 6,N-dimethylnonane-3-carboxamide

92) What is the common name for the following carboxylic acid derivative? 92) ______

\[
\begin{array}{c}
\text{O} \\
\text{N} \text{CSN} \\
\text{OH}
\end{array}
\]
   A) γ-hydroxyvaleronitrile
   B) 1-cyano-2-butanol
   C) 2-hydroxypentane nitrile
   D) β-hydroxyvaleronitrile
   E) β-hydroxybutyronitrile
93) Which of the following structures are carboxylic acid derivatives?

A) 1, 2 & 3
B) 1 & 3
C) 4
D) 3
E) All are carboxylic acid derivatives

94) Which of the following are intermediates in the acid hydrolysis of an amide?

A) 4
B) 1, 2, & 3
C) 1
D) 2
E) 2 & 3

SHORT ANSWER. Write the word or phrase that best completes each statement or answers the question.

95) Draw the product resulting from the following reaction. Indicate any relevant stereochemistry.

96) Distamycin and derivatives have exhibited antiviral, antibiotic, and antitumor activity by binding to the minor groove of DNA (J. Med. Chem. 2004, 2133). Place a line through each bond of distamycin that would be cleaved by acid hydrolysis.
MULTIPLE CHOICE. Choose the one alternative that best completes the statement or answers the question.

97) Which sequence correctly lists the following structures in order of increasing rate of hydrolysis to a carboxylic acid under basic conditions?

\[
\begin{align*}
1 & \quad 2 & \quad 3 \\
\text{H}_2\text{C} & \overset{\text{O}}{\text{C}} \text{Et} & \text{H}_2\text{C} & \overset{\text{O}}{\text{C}} \text{Et} & \text{H}_2\text{C} & \overset{\text{C}}{\text{≡N}} \\
\text{A)} & \quad \text{1} < \text{2} < \text{3} & \text{B)} & \quad \text{3} < \text{2} < \text{1} & \text{C)} & \quad \text{2} < \text{3} < \text{1} & \text{D)} & \quad \text{3} < \text{1} < \text{2} & \text{E)} & \quad \text{2} < \text{1} < \text{3}
\end{align*}
\]

SHORT ANSWER. Write the word or phrase that best completes each statement or answers the question.

98) Predict the product that results from 2-methylamino-1-ethanol being treated with phosgene.

\[
\begin{align*}
\text{H}_2\text{C} & \overset{\text{N}}{\text{H}} \overset{\text{OH}}{\text{H}} & \xrightarrow{\text{phosgene}} \quad \text{H}_2\text{C} \overset{\text{O}}{\text{C}} \text{Et}
\end{align*}
\]
In nucleophilic acyl substitution, the leaving group is ejected in a separate exothermic step. The Hammond Postulate predicts that the transition state for this step resembles the tetrahedral intermediate. Therefore, in the transition state for this step minimal bond breaking has occurred, and the importance of the nature of the leaving group is diminished.
15) 

16) 

17) 

18) C 
19) B 
20) B 
21) B 
22) C 
23) E 
24) D 
25) t-butanol and ethanol 
26) 1. Br₂, hv or NBS 
   2. NaCN 
   3. CH₃MgBr 
   4. H₃O⁺ 
27) C 
28) D 
29) acetic acid and methyl formate 
30) 1. Fischer esterification with methanol. 
   2. Treatment with diazomethane. 
31) This reaction can be driven by the removal of water as it is formed. Often the water is removed as an azeotrope with benzene. 
32) B 
33) P₂O₅ or POCl₃ 
34) Their enhanced reactivity is due to the considerable ring strain in the four-membered ring.
35) 1. HNO₃, H₂SO₄
  2. Fe, HCl
  3. NaNO₂, HCl, cold
  4. CuCN
36) 1. Br₂, hv or NBS
  2. NaCN
  3. LiAlH₄
  4. H₂O
37) Beginning with CO₂,
   1. CH₃MgBr
   2. H₃O⁺
   3. CH₃SH, H⁺ catalyst, Δ
38) See Figure 21-12 on p.989.
   The overlap between the 2p orbital of carbon and the 3p orbital of sulfur is weak and relatively inefficient.
39) carbonic acid, CO₂ + H₂O → H₂CO₃
40)

41) isopropyl cyclohexanecarboxylate
42) N-methyl-3-chloropropanamide
43) trans-5-octenoyl chloride
44) 3,3-dimethylcyclobutane carbonitrile
45) methyl 5-cyanopentanoate
46) CH₃CH₂CH₂CON(CH₂CH₃)₂
47) (CH₃CH₂CO)₂O
48) CH₃COCH₂CN
49) CH₃CH₂CBr(CH₃)COCl
50) C
51) C
52) A
53) B
54) C₅H₉CO₂CHO
55) Beginning with ethanol,
   1. Na₂Cr₂O₇, H₂SO₄
   2. SOCl₂
   3. CH₃CH₂OH
56) Beginning with ethanol,
   1. Na₂Cr₂O₇, H₂SO₄
   2. SOCl₂
   3. NH₃
   4. P₂O₅
57) 1. HNO₃, H₂SO₄
   2. H₂, Ni
   3. (HCO)₂O
58) CH₃CH₂CH(CH₃)CH₂CO₂CH₃
59) CH₃CH₂COSCH₃
60) CH₃CH₂CO₂H
61) amide < ester < anhydride < acid halide
62) PhCO₂⁻ CH₃NH₃⁺ ; PhCONHCH₃
63) N-propylmethanamide
64) methyl formate < propanenitrile < 1-propanol < acetic acid < ethanamide
65) D
66) ethyl benzoate
67) methyl 5-hydroxypentanoate
68) E
69) D
70) C
71)

\[
\begin{array}{c}
\text{O} \\
\text{O} \\
\text{H}
\end{array}
\]

72)

\[
\begin{array}{c}
\text{O} \\
\text{N} \\
\text{H}
\end{array}
\]

73)

\[
\begin{array}{c}
\text{H₃C} \\
\text{CN} \\
\text{CH₂CH₃}
\end{array}
\]

74)

\[
\begin{array}{c}
\text{Br} \\
\text{Cl}
\end{array}
\]

75) E
76) B
Testname: W_ACID_2

77) (CF₃CO)₂O
78) ethyl hexanoate
79) N,N-diethylformamide
80) N,N-dimethylformamide < N-methylacetamide < propanamide
81) butane < propanenitrile < acetic acid < acetamide
82) E
83) C
84) (i) addition of the nucleophile (dimethylamine) to the carbonyl of the acid chloride
     (ii) elimination of the leaving group (the chloride ion)
     (iii) loss of H⁺
85) methyl benzoate; transesterification
86) E
87) C
88) C
89) D
90) B
91) E
92) D
93) B
94) E
Answer Key
Testname: W_ACID_2

95) [Image of molecular structure]

96) [Image of molecular structure]

97) B

98) [Image of molecular structure]