I. (16 points) Indicate whether each of the following equilibria lies predominantly to the left or to the right by circling the side corresponding to the more stable species.

a) $n$-C$_6$H$_{13}$H  $\rightleftharpoons$  $n$-C$_6$H$_{13}$C:  
   i-Pr$_2$NH  $\rightleftharpoons$  i-Pr$_2$NH$_2$

b) 

\[
\begin{align*}
 &\text{Me} &\text{H} \\
 &\text{Me} &\text{O} &\text{OMe} &\text{Me} &\text{Me} &\text{Me} &\text{Me} \\
 &\text{Me} &\text{O} &\text{OMe} &\text{Me} &\text{Me} &\text{Me} &\text{Me}
\end{align*}
\]

\[
\begin{align*}
 &\text{Me} &\text{O} &\text{OMe} &\text{Me} &\text{Me} &\text{Me} &\text{Me} \\
 &\text{Me} &\text{O} &\text{OMe} &\text{Me} &\text{Me} &\text{Me} &\text{Me}
\end{align*}
\]

c) 

\[
\begin{align*}
 &\text{Me} &\text{O} &\text{OMe} &\text{Me} &\text{Me} &\text{Me} &\text{Me} \\
 &\text{Me} &\text{O} &\text{OMe} &\text{Me} &\text{Me} &\text{Me} &\text{Me}
\end{align*}
\]

d) 

\[
\begin{align*}
 &\text{Me} &\text{N} &\text{O} &\text{OMe} \\
 &\text{Me} &\text{N} &\text{O} &\text{OMe}
\end{align*}
\]

e) 

\[
\begin{align*}
 &\text{Me} &\text{N} &\text{N} \\
 &\text{Me} &\text{N} &\text{N}
\end{align*}
\]

f) 

\[
\begin{align*}
 &\text{Me} &\text{O} &\text{OMe} &\text{Me} &\text{Me} &\text{Me} &\text{Me} \\
 &\text{Me} &\text{O} &\text{OMe} &\text{Me} &\text{Me} &\text{Me} &\text{Me}
\end{align*}
\]

g) 

\[
\begin{align*}
 &\text{Me} &\text{O} &\text{OMe} &\text{Me} &\text{Me} &\text{Me} &\text{Me} \\
 &\text{Me} &\text{O} &\text{OMe} &\text{Me} &\text{Me} &\text{Me} &\text{Me}
\end{align*}
\]

h) 

\[
\begin{align*}
 &\text{Me} &\text{N} &\text{N} &\text{H} \\
 &\text{Me} &\text{N} &\text{N} &\text{H}
\end{align*}
\]
Part II (14 points). You will be penalized for any duplicate answers you provide.

a) Draw all possible constitutional and configurational isomers of the dimethylcyclobutanols. Every structure will have two methyl groups and one hydroxy group attached to a cyclobutane ring. Clearly indicate the configuration of any stereogenic centers by using bold and dashed wedges.

b) Circle each of the structures you have drawn that is achiral.

c) Place a rectangular box around any meso compounds; these are, of course, achiral, and hence should already be circled (i.e., some structures can/will carry both a circle and a box).

2,2-dimethyl- and 3,3-dimethylcyclobutanols

2,3-dimethylcyclobutanols

2,4-dimethylcyclobutanols

1,2-dimethylcyclobutanols

1,3-dimethylcyclobutanols
III. (16 points) Provide the structure of the major product in each of the reactions a)-d).

a)

\[
\begin{align*}
\text{EtO} & \quad \text{KOH (cat.), MeOH, reflux} \\
\text{C}_7\text{H}_{10}\text{O} & \quad \text{Et} \\
\text{Me} & \quad \text{pyrrolidine, AcOH reflux} \\
\text{C}_{12}\text{H}_{16}\text{O}_2 & \\
\end{align*}
\]

b)

\[
\begin{align*}
\text{EtO} & \quad \text{LDA} \\
\text{Me} & \quad \text{EtI} \\
\text{Me} & \quad \text{LiAlH}_4 \\
\text{EtO} & \quad \text{H}_2\text{SO}_4 \\
\text{C}_9\text{H}_{14}\text{O} & \quad \text{H}_2\text{O} \\
\end{align*}
\]

c)

\[
\begin{align*}
\text{Me} & \quad \text{H}_2\text{N NH}_2 \\
\text{Me} & \quad \text{AcOH (cat.)} \\
\text{EtOH} & \quad \text{EtOH r.t.} \\
\text{C}_7\text{H}_{12}\text{O} & \\
\end{align*}
\]

d)

\[
\begin{align*}
\text{Me} & \quad \text{TsNHNH}_2 \\
\text{pyridine} & \quad \text{C}_7\text{H}_{10}\text{O} \\
\end{align*}
\]
IV. (12 points) The following synthesis of enone Z from 3,5-dimethoxypyridine (V) makes effective use of the Stork-Danheiser alkylation strategy. Deduce and provide the structures of intermediates W-Y.

![Chemical structure](image)

V. (10 points) There is an inherent preference for alkylation of simple ketone enolate anions at the carbon atom (to give the α-alkylated ketone product) rather than on the enolate anion oxygen atom (to give an enol ether product). When each of the bromoketones A and C is treated with potassium t-butoxide at room temperature under the same conditions, each cyclizes with net loss of the elements of HBr. One of these two substrates gives, principally, a cyclic ketone product but the other gives, principally, a cyclic enol ether as the main product. a) Draw the major product, B and D respectively, arising from each of the bromoketones. b) Explain why these two substrates give different types of products.

![Chemical structure](image)

VI. (8 points) The highly diastereoselective reaction below proceeds through a boron enolate. The β-hydroxyacid product is racemic. Rationalize, by means of a carefully drawn transition state geometry, the step that establishes the relative configuration between the two stereocenters present in the product. Do not use any words in answering this question—provide only the structure of the key transition state structure in which the stereocenters are (simultaneously) being established.
VII. (42 pts) Provide a detailed mechanism to account for each of the following four reactions. Show ALL intermediates, equilibria, and bond-making and -breaking steps.

a) (8) The DEAD/triphenylphosphine-mediated conversion of the indicated, enantiopure cyanohydrin to the enantiopure chloroacetate ester.

\[
\text{NC>Ph} \xrightarrow{\text{Ph}_3\text{P, EtO}_2\text{CN=NCO}_2\text{Et}} \text{ClH}_2\text{C} \xrightarrow{\text{chloroacetic acid}} \text{Ph}_3\text{P} \xrightarrow{\text{OH}} \text{HC=O} \xrightarrow{\text{Ph}} \text{CN}
\]

b) (12) The TMSOTf-catalyzed, low-temperature ketalization of cyclohexenone.

\[
\text{C}=\text{O} \xrightarrow{T\text{MSOTf = Me}_3\text{SiOSO}_2\text{CF}_3 \ (\text{cat.})} \text{DCM, -78 °C} \xrightarrow{\text{TMSOTMS}} \text{C}=\text{O} \xrightarrow{T\text{MSOTMS}} \text{C}=\text{O}
\]
c) (8 pts) The *chain propagation steps* in the reductive cyclization of the following bromoalkyne to the indicated cyclohexanone derivative. Start your mechanism with *n*-Bu₃Sn• (i.e., you do not need to show the initiating steps by which AIBN produces the first copy of the *n*-Bu₃Sn• radical).

![Mechanism Diagram](image)

**d) (14 pts) Production of the sodium carboxylate product. Note that there is *no water* present.**

![Mechanism Diagram](image)
VIII. (42 pts, 7 each) Each of the following known transformations involves a series of thermal cascade reactions. In each case four possible sequences for the individual reaction types (or steps in the cascade) is suggested. Circle the one corresponding to the correct sequence.

Note: “electrocyclization” here refers to either a ring-opening or a ring-closing event. For example, a “4π-electrocyclization” can refer to either the ring closure of 1,3-butadiene to cyclobutene or the ring opening of cyclobutene to 1,3-butadiene.

a) Conversion of either 2 to 4 or of 3 to 1 (both involve the same sequence).

\[ \text{2} \xrightarrow{} \text{3} \xrightarrow{} \text{1} \xrightarrow{} \text{4} \]

i) Diels-Alder reaction, 6π-electrocyclization, 6π-electrocyclization

ii) 6π-electrocyclization, Diels-Alder reaction, 6π-electrocyclization

iii) 6π-electrocyclization, 6π-electrocyclization, Diels-Alder reaction

b) Conversion of the allyl ether 5 to the decalinol 6.

\[ \text{5} \xrightarrow{220 \text{ °C}} \text{6} \]

i) ene reaction, Cope rearrangement, Claisen rearrangement

ii) Cope rearrangement, Claisen rearrangement, ene reaction

iii) Claisen rearrangement, ene reaction, Cope rearrangement

iv) Cope rearrangement, ene reaction, Claisen rearrangement

c) o-Benzyn (7) plus the enal 8 to the benzopyran derivative 9.

\[ \text{7} + \text{8} \xrightarrow{\text{r.t.}} \text{9} \]

i) [2+2]-cycloaddition, 6π-electrocyclization, 4π-electrocyclization

ii) [4+2]-cycloaddition

iii) [2+2]-cycloaddition, 4π-electrocyclization, 6π-electrocyclization

iv) [4+2]-cycloaddition, 6π-electrocyclization, 4π-electrocyclization
d) Tricyclization of enone 10 to the tricyclic lactam 11.

\[
\text{TBSO} -\text{CHCl}_2\xrightarrow{\text{MeAlCl}_3 (\text{cat.})} \text{CH}_2\text{Cl}_2 , \text{reflux} -\text{H}\]

i) 1,3-dipolar cycloaddition, Diels-Alder cycloaddition, Schmidt rearrangement

ii) Diels-Alder cycloaddition, Schmidt rearrangement

iii) 1,3-dipolar cycloaddition, Schmidt rearrangement, Diels-Alder cycloaddition

iv) Schmidt rearrangement, Diels-Alder cycloaddition

e) Tricyclization of the enediyne 12 to the bis-sulfoxide 13.

\[
\text{PhS}-\text{O} -\text{CO}_2\text{Me} \xrightarrow{\text{heat}} \text{Ph(O)S} -\text{S(O)Ph} -\text{CO}_2\text{Me}
\]

i) [3,2]-sigmatropic rearrangement, Diels-Alder cycloaddition, 6π-electrocyclization

ii) [3,2]-sigmatropic rearrangement, 6π-electrocyclization, Diels-Alder cycloaddition

iii) 6π-electrocyclization, Diels-Alder cycloaddition, [3,2]-sigmatropic rearrangement

iv) Diels-Alder cycloaddition, [3,2]-sigmatropic rearrangement, 6π-electrocyclization

f) Conversion of the oxadiazole 14 to the hexacyclic lactam 15.

\[
\text{CO}_2\text{Me} \xrightarrow{\text{heat}} \text{CO}_2\text{Me}
\]

i) dinitrogen extrusion, hetera-Diels-Alder cycloaddition, 1,3-dipolar cycloaddition

ii) 1,3-dipolar cycloaddition, hetera-Diels-Alder cycloaddition, dinitrogen extrusion

iii) dinitrogen extrusion, 1,3-dipolar cycloaddition, hetera-Diels-Alder cycloaddition

iv) hetera-Diels-Alder cycloaddition, dinitrogen extrusion, 1,3-dipolar cycloaddition

• • • end of exam • • •

You may pick up your graded exam from Sahil Arora (421 Smith) after noon on Monday, May 14.

*** Have a very productive summer of research. ***