Question I (54 points)

A. Complete the following reaction sequence (in part: Org. Process Res. Dev. 2022, 26, 1960), which begins with an *intramolecular aldol condensation*. You do not need to provide stereochemical information.

\[
\begin{align*}
\text{A.} & \quad \text{CH}_3 \quad \text{NaBH}_4 \quad \text{CH}_3 \text{OH} \\
\text{B.} & \quad \text{HN} \quad \text{SCH}_3 \\
\text{C.} & \quad \text{CH}_3 \quad \text{O} \\
\end{align*}
\]

B. When the epoxide derived from the product in part A, above, is treated with an acid catalyst, a rearrangement to a ketone is observed. Using HB/B as your generic Bronsted acid/base, as needed, provide the complete, curved arrow mechanism for this transformation, in which a carbocation intermediate is anticipated.

\[
\begin{align*}
\text{Catalytic H}_2\text{SO}_4 \\
\end{align*}
\]

C. Complete the following transformation, which is carried out on the aldol condensation intermediate from part A.

\[
\begin{align*}
\text{1) (CH}_3\text{)_2CuLi} \\
\text{2) CH}_3\text{O} \\
\text{3) protonation} \\
\end{align*}
\]
Question II (50 points)

A. Complete the following reaction scheme that was used in a practical synthesis of remdesivir, the first and only FDA-approved antiviral drug for treating COVID-19 ([J. Org. Chem. 2021, 86, 5065]).

Showing stereochemistry is not required.

B. Taken from a synthesis of the osteogenic growth peptide (OGP), present in small concentrations in circulating blood ([Org. Process Res. Dev. 2015, 19, 1257]). Show stereochemistry; no abbreviations.

[Diagram of reaction scheme]
Question III (46 points)

Complete the following transformations.


\[
\begin{array}{c}
\text{Cl} \\
\text{N} \\
\text{O} \\
\text{S} \\
\text{F} \\
\text{F}
\end{array}
\xrightarrow{\text{catalytic mild acid}}
\begin{array}{c}
\text{H}_2\text{O} \\
\text{balance the equation; give the neutral/uncharged product(s)}
\end{array}
\]


\[
\begin{array}{c}
\text{OCH}_3 \\
\text{N} \\
\text{S} \\
\text{O} \\
\text{Cl}
\end{array}
\xrightarrow{1) \text{LiAlH}_4}
\begin{array}{c}
\text{N} \\
\text{H} \\
\text{ClCrO}_3
\end{array}
\xrightarrow{2) \text{H}_2\text{O}}
\begin{array}{c}
\text{protonation}
\end{array}
\xrightarrow{\text{~ pH 6 buffer}}
\begin{array}{c}
\text{+ H}_2\text{O}
\end{array}
\]


\[
\begin{array}{c}
\text{+}
\end{array}
\xrightarrow{\text{~ pH 6 buffer}}
\begin{array}{c}
\text{+ H}_2\text{O}
\end{array}
\]


\[
\begin{array}{c}
\text{210 °C} \\
\text{8 hours}
\end{array}
\xrightarrow{\text{an intramolecular Diels-Alder reaction creates an intermediate that undergoes a retro-Diels-Alder reaction to lose carbon dioxide}}
\begin{array}{c}
\text{+ CO}_2
\end{array}
\]

(e) arabinose is the C2 epimer of ribose

\[
\begin{array}{c}
\text{CH}_3\text{OH} \\
\text{catalytic TsOH}
\end{array}
\xrightarrow{\text{\alpha-L-arabinofuranose}}
\begin{array}{c}
gives the \beta\text{-anomer of the product}
\end{array}
\]
**Question IV (48 points)**

A. The photochemical decomposition of \((\text{NH}_4)_2[\text{Ce(NO}_3]_6\) gives an oxygen atom radical: \(\cdot\text{O}-\text{NO}_2\). The following reaction is observed to occur (Molecules 2004, 9, 480).

![Reaction Scheme]

The mechanistic steps are outlined here: provide the missing intermediates as well as the curved (fish-hook) arrows for each step.

1. **Step 1**: The oxygen atom adds to the triple bond; its regioselectivity can be inferred from the product.

2. **Step 2**: The \(\text{sp}^2\) carbon radical resulting from step 1 removes a hydrogen atom intramolecularly from the benzyl group.

3. **Step 3**: The benzylic carbon radical formed in step 2 undergoes an intramolecular addition reaction to give an oxygen-stabilized radical.

4. **Step 4**: The oxygen-stabilized radical formed in step 3 gives a dissociation reaction resulting in the observed products (drawn above).

B. Complete the following transformations.


(b) *Org. Lett.* 2022, 24, 6722.
Question V (42 points)

(a)  How many exchangeable proton under H/D exchange conditions?

(b)  Number of possible intramolecular aldol condensations?

(c)  Position number of the alcohol group in the IUPAC name?

(d)  Stereochemical configuration (\(\text{R}\) or \(\text{S}\)) for methionine?

(e)  Oxidation number of the shaded atom?

(f)  Relationship of the 2 CH\(_3\) groups in the major product?

(g)  Site (A-F) of reactivity of this compound with an enol under acid conditions?

(h)  Site (A-F) of fastest reactivity with tributyltin radical?

(i)  Most reactive site (A-F) with methyl magnesium bromide?

(j)  Based on the entropy change, the \(K_{\text{eq}}\) for this process is:

(k)  How many chiral diastereomers does L-mannose have?

(l)  The IUPAC name for this compound would include:

(m)  The position of the two groups, “OH” & “Br”, are:

   - endo & endo
   - endo & exo
   - exo & exo

Name: _______________________________

number of correct answers: 1 2 3 4 5 6 7 8 9 10 11 12 13 14

score: 3 6 9 12 15 18 21 24 27 30 33 36 39 42