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.

**Critical feature #1**: methyl ketone +3

**Critical feature #2**: 2° alcohol +4

If both OK, then +1 for the rest

SET methods are OK
SmI$_2$/HOC(CH$_3$)$_3$ 5pt or Ir(III), Bu$_3$N, hv 5pt

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.

Protonation of epoxide mech = 3
Epoxide oxonium ion = 3
Ring opening mech = 3
1,2 hydride shift mech (asst or not) = 3
Carbocation (either/both res form) = 3
Deprotonation mech = 3

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

**Critical feature #1**: dimethyl +3

**Critical feature #2**: methyl ketone +3

If both OK, then +1 for the rest

---

Name: _______________________________
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**: Drawing of reaction schemes with labeled steps and intermediates.

---

**Textual Instructions**

A. 

B. 

---

**Grading**

A: 30

B: 20

---

**Total Points**: 50
Question III (46 points)

Complete the following transformations.


\[
\begin{align*}
\text{Org. Process Res. Dev.} & \quad \text{2022} \quad , \quad 26 \quad , \quad 2337. \\
\text{balance the equation; give the neutral/uncharged product(s)} \\
\text{acetone} & \quad = \quad 2 \\
\text{critical diol in structure} & \quad = \quad 2 \\
\text{if diol OK, +2 for the rest} \\
\end{align*}
\]


\[
\begin{align*}
\text{critical 1' alcohol} & \quad = \quad 4 \\
\text{if OK, rest} & \quad = \quad 2 \\
\end{align*}
\]


\[
\begin{align*}
\text{critical aldehyde} & \quad = \quad 4 \\
\text{if OK, rest} & \quad = \quad 2 \\
\end{align*}
\]


\[
\begin{align*}
\text{an intramolecular} \\
\text{Diels-Alder} \\
\text{reaction creates} \\
\text{an intermediate} \\
\text{that undergoes a} \\
\text{retro-Diels-Alder} \\
\text{reaction to lose} \\
\text{carbon dioxide} \\
\end{align*}
\]

(e) arabinose is the C2 epimer of ribose

\[
\begin{align*}
\text{gives the \( \beta \)-anomer of the product} \\
\end{align*}
\]

\[
\begin{align*}
\text{fundamental} \\
\text{L-furanose} & \quad = \quad 3 \\
\text{if OK:} \\
\text{epi C2} & \quad = \quad 3 \\
\beta\text{-anomer} & \quad = \quad 2 \\
\end{align*}
\]
Question IV (48 points)

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

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

**MUST be fish-hook arrows used throughout for mechanism points**

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

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

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

4. The benzylic carbon radical formed in step 2 undergoes an intramolecular addition reaction to give an oxygen-stabilized radical.

B. Complete the following transformations.

(a) Org. Process Res. Dev. 2022, 26, 10.

(b) Org. Lett. 2022, 24, 6722.

**if enolate not formed, no credit for part 2; -4 if reversed**

other strong bases OK, as well as NaH; but HO-/RO- cannot give enolate alone - reversible bases would be present and react in the next step as \(S_N2\) more effectively!

| A | 1/32 |
| B | 1/16 |
| **Total** | 48 |
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 ([R] or [S]) for methionine?

(e) Oxidation number of the shaded atom?

(f) Relationship of the 2 CH₃ 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_EQ for this process is:

(k) L-mannose is the open chain form of an aldohexose

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

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

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