Problem Set #14
Solutions

1. Need C1-C10 bond formation
   Need C9-O bond
   Lose -OH from C5
   C=C moves from C1-C6 to C6-C5

[Chemical structures and reaction arrows]
(2) ozonolytic cleavage of $\text{C}_2\text{C}$

a) propanal

\[ \text{H}_3\text{C} - \text{CH}_3 + \text{H}_2\text{C} - \text{CH}_3 \]

pentanal

b) Syn dihydroxylation

\[ \text{H}_3\text{C} - \text{CH}_3 \]

\[ \text{H}_3\text{C} - \text{CH}_3 \]

\[ \text{H}_3\text{C} - \text{CH}_3 \]

\[ \text{H}_3\text{C} - \text{CH}_3 \]

c) Syn deuteration

d) Oxymercuration occurs via Mercurinium Ion
Alkene hydration

\[ \text{CH}_3 + \text{H}_2\text{O}/\text{H}_3\text{O}^+ \rightarrow \text{H}_2\text{O} \text{ from top or bottom} \]

Add

f) Anti Mark. addtn of H\textsubscript{2}O across C=C in SYN fashion
In the second step, the acetylide anion cannot act as a nucleophile with tBuBr as the alkyl halide. The acetylide anion reacts as a base in an E2 rxn, giving back the terminal alkyne plus the elimination product, isobutene.

More...
In (cont'd)

\[
\text{Br}_2 \rightarrow \text{H}_2\text{O}
\]

1,2-Halohydrin formation
an ANTI addition of "OH" and "Br" across C=C

via bromonium ion

\[
\text{H}_2\text{O}^- \rightarrow \text{H} \rightarrow \text{A}^+ \rightarrow \text{Br}^- \rightarrow \text{H} \rightarrow \text{D}^+ \rightarrow \text{Br}^-. \]

intra molecular $S_{N}2$ displacement
to form epoxide
i) Syn dihydroxylation

\[
\begin{align*}
\text{H}_3\text{C} & \rightarrow \text{H} \rightarrow \text{C} \rightarrow \text{CH}_3 \\
\text{HO} & \rightarrow \text{OH}
\end{align*}
\]

j) Ozonolysis

\[
\begin{align*}
\text{C}_4\text{H}_4\text{O}_2\text{CH}_3 & \rightarrow \text{C}_2\text{H}_4\text{O}_2\text{CH}_3 \\
\text{C}_4\text{H}_4\text{O}_2\text{CH}_3 & \rightarrow \text{C}_8\text{H}_{16}\text{O}_2
\end{align*}
\]

k) Catalytic hydrogenation: SYN addn of H-H across C=C

\[
\begin{align*}
\text{CH}_3 & \rightarrow \text{H} \\
3 & \rightarrow \text{H} \\
\text{H} & \rightarrow \text{H} \\
\text{CH}_3 & \rightarrow \text{H}
\end{align*}
\]

l) Ozonolysis

\[
\begin{align*}
\text{C}_8\text{H}_{16}\text{O}_2 & \rightarrow \text{C}_8\text{H}_{16}\text{O}_2 \\
\text{C}_8\text{H}_{16}\text{O}_2 & \rightarrow \text{C}_8\text{H}_{16}\text{O}_2
\end{align*}
\]
m) Alkyne is hydrogenated all the way to alkene unless a poisoned catalyst (e.g., Lindlar catalyst) is used.

\[ \text{H}_3\text{C} = \text{C} \text{H} \]

n) cis-hydrogenation of an alkyne

\[ \text{H}_3\text{C} \text{C} = \text{C} \text{H}_2 \text{H} \]

(3) A retrosynthetic analysis:

\[ \text{CH}_3\text{Br} \]

Note that the problem isn't worried about stereochemistry making things a bit less complicated.
Synthesis

1. BH₃·THF
2. H₂O₂, NaOH

Sodium hydride is useful here. (NaOH would also be OK)

alkylation rxn

\[ \text{Br}^- \text{CH₃} \rightarrow_{SN2} \]

\[ H₃C\begin{array}{cccccc}2&3&4&5&6\end{array}\rightarrow_7 H₃C\begin{array}{cccccc}2&3&4&5&6\end{array}N₃ \]
Synthesis:

\[
\text{H}_3\text{C} - \text{C} - \text{C} \quad \xrightarrow{\text{DBH}_2 \cdot \text{THF}} \quad \text{H}_3\text{C} - \text{C} - \text{C} - \text{OH}
\]

2) \text{NaOH}_2, \quad \text{H}_2\text{O}_2

\[
\text{H}_3\text{C} - \text{C} - \text{C} - \text{C} - \text{N}=\text{N}=\text{N}=\text{N}=\text{O} \quad \xrightarrow{\text{NaN}_3} \quad \text{H}_3\text{C} - \text{C} - \text{C} - \text{C} - \text{O} - \text{SO}_3\text{Na}
\]

Sulfonate ester

Could also use alkyl bromide as R-X.

\( \bigcirc \) Retrosynthesis

\[
\text{CH}_3
\]

Cis alkene suggests alkyne s. mat.

\[
\text{H}_3\text{C} - \text{C} = \text{C} - \text{CH}_3
\]

Note that I'm careful not to lose any carbon.
Synthesis:

\[
\begin{align*}
\text{1. NaNH}_2 & \quad \text{1. NaNH}_2 \\
\text{2. } \text{H}_3\text{C}-\text{Br} & \quad \text{H}_2 \\
\end{align*}
\]

\[
\begin{align*}
\text{C} & \equiv \text{C} - \text{H} \\
\text{C} & \equiv \text{C} - \text{CH}_3 \\
\end{align*}
\]

H \uparrow \\
Lindlar \\
Catalyst

Retrosynthesis

\[
\begin{align*}
\text{H}_3\text{C} & \equiv \text{H}_3\text{C} - \text{CH}_3 \\
\text{Br} & \equiv \text{Br} - \text{Br} \\
\end{align*}
\]

vicinal dibromide suggests addition of \( \text{Br}_2 \) across \( \text{C} = \text{C} \) as a synthetic method. Remembering that alkene bromination proceeds with \text{ANTI} stereospecificity, we can pick correct alkene precursor \( \text{CH}_3 \).
trans alkene
available from
the corresponding alkene via dissolving metal reduction.

Synthesis:

\[ \text{H}_3\text{C} - \text{C\equiv C} - \text{CH}_3 \xrightarrow{\text{Na}^+ \text{ liquid NH}_3} \text{H} - \text{C\equiv C} - \text{CH}_3 \]

\[ \text{H}_3\text{C} - \text{C\equiv C} - \text{CH}_3 \xrightarrow{\text{Br}_2} \text{a meso compound.} \]
4) This looks harder than it really is!

Let's vital to number the carbons. Use the positions of the attached groups (4x CH₃ and CO₂CH₃ groups) to give you in on the numbering in the product.

We're forming two rings (call them A and B):

To form A ring need
C₁-C₆ bond

To form B ring need
C₅-C₁₀ bond

Also, need to make C₈-C₉ double bond.

We know how to start: Make mercurinium ion from C₁-C₂
Redrawn structure

\[ \text{mercuric trifluoroacetate reacts like mercuric acetate, only faster} \]

Open mercurinium ion at non-substituted end. C5-C6 olefin is nucleophile. Make C1-C6 bond and form A ring.

Second cyclization forms B ring by forging C5-C10 bond.