1. The following questions may have occurred to you: (i) do carbocations occur in living systems? (ii) Can an olefin (a Lewis base) react with a carbocation (a Lewis acid)? To address these questions, consider the following. At this very moment, certain enzymes in your liver are producing cholesterol and related steroids. These enzymes take up an endogenous olefinic compound called squalene and convert it into a carbocation that may be represented with structure $A$ below. The enzymes also keep this carbocation in the rigidly defined conformation shown, protecting it from the action of external nucleophiles and promoting or disfavoring various chemical reactions, including rearrangements. Under such conditions, $A$ is rapidly transformed into lanosterol, which is the precursor of cholesterol and of all other steroids.

![Diagram of squalene and lanosterol conversion]

Answer the above questions by writing a detailed mechanism for the conversion of $A$ into lanosterol.

![Detailed mechanism diagram]
2. Predict the structure of the major product of each of the following reactions and write a detailed mechanism (curved arrows) for its formation.
(as far as we know ...)

1. O₃
2. Zn, H⁺

1. O₃
2. Zn, H⁺
3. Draw a clear skeletal structure of:

(a) an olefin that produces the same alcohol when treated with either H$_2$SO$_4$ / H$_2$O or BH$_3$ followed by H$_2$O$_2$ / NaOH

```latex
\text{H}_2\text{SO}_4 / \text{H}_2\text{O} \\
\text{BH}_3 / \text{H}_2\text{O}_2 / \text{NaOH}
```

(b) an olefin that produces one alcohol when treated with H$_2$SO$_4$ / H$_2$O, but an isomeric alcohol when treated with BH$_3$ followed by H$_2$O$_2$ / NaOH

```latex
\text{BH}_3 / \text{H}_2\text{O}_2 / \text{NaOH}
```

4. Provide all the reagents / catalysts, in the correct order, that are needed to convert vinlycyclopentane (structure below) into compounds a. - h. If a compound appears to be unavailable as the major product of any reaction known to you, answer "inaccessible".
vinylcyclopentane

\[
\begin{align*}
\text{a.} & \quad \text{OCH}_3 \\
\text{b.} & \quad \text{Cl}_2 \\
\text{c.} & \quad \text{O}_2 \text{H}_2 \text{O}_2, \text{acid} \\
\text{d.} & \quad \text{BH}_3, \text{H}_2 \text{O}_2, \text{aq. NaOH} \\
\text{e.} & \quad \text{inaccessible} \quad (\text{why} \ldots ?) \\
\text{f.} & \quad \text{inaccessible} \quad (\text{why} \ldots ?)
\end{align*}
\]
4. Propose a method for the preparation of compounds a. – h. below starting from appropriate alkenes. Draw a clear structure of your proposed starting olefin and list all reagents / catalysts, in the correct order, that are required to induce the desired transformation. Your method must be a good one, i.e., the desired compound must be the major product of your reaction(s). Note: it is understood that chiral compounds will be obtained as racemic mixtures.

- a.
- b.
- c.
- d.
- e.
- f.
- g.
- h.

• this is the anti-diastereomer of a vicinal diol
• the only method known to us for the creation of vicinal diols is the dihydroxylation of alkenes with OsO₄
• to make this compound, one must treat an alkene with OsO₄, followed by aqueous NaHSO₃

**BUT: which alkene do we need to obtain the desired product?**

• A general diagram for the dihydroxylation reaction is:

\[
\text{C} = \text{C} \xrightarrow{1. \text{OsO}_4} \xrightarrow{2. \text{aq. NaHSO}_3} \text{C} = \text{C}
\]

therefore, product a. must result from dihydroxylation of a molecule of 2-pentene:

\[
\text{CH}_3 - \text{CH} = \text{CH} - \text{CH}_2 - \text{CH}_3
\]

**BUT: which isomer of 2-pentene will produce the desired product?**

• The dihydroxylation of alkenes is a *syn*-addition reaction, so the OH groups must enter from the same face of the \( \pi \) bond

• If we were to attempt making a. by dihydroxylation of *trans*-2-pentene, we would get:

\[
\text{syn diastereomer: wrong product}
\]

but if we were to dihydroxylate *cis*-2-pentene . . . :

\[
\text{anti diastereomer: desired product}!
\]
so, the correct answer is:

\[
\text{\underline{cis-2-pentene}}
\]

notice that this molecule is chiral: it will be obtained as the racemate. For simplicity, we draw only one enantiomer, with the understanding that both will actually be formed during the reaction.

A quicker way to obtain the correct answer:

\[
\begin{align*}
\text{anti diastereomer:} & \quad \text{imagine a rotation} \\
\text{about the internal} & \quad \text{C–C} \sigma \text{ bond} \ldots \\
\text{OH groups now point in} & \quad \text{the same direction, as} \\
\text{required for a \textit{syn} addition.} & \quad \text{Imagine forming a} \pi \text{ bond} \\
\text{between the OH-bearing C} & \quad \text{atoms} \\
\end{align*}
\]

* * *

b.  

- this is an alcohol
- the only methods known to us for the creation of alcohols are the acid-catalyzed hydration of alkenes and the hydroboration-oxidation of alkenes
- A general diagram for either reaction is:

\[
\begin{align*}
\text{C=C} & \rightarrow \text{H–OH} \\
\end{align*}
\]

Therefore, we can make b. starting from:

\[
\begin{align*}
\text{b.} & \quad \text{OH} \\
\end{align*}
\]

BUT: which method will furnish the desired product?

- If we were to hydrate the above alkene under acid-catalyzed conditions, we would obtain:

\[
\begin{align*}
\text{H}_2\text{SO}_4 & \quad \text{H}_2\text{O} \\
\end{align*}
\]

- If we were to subject the above alkene to hydroboration-oxidation, we would obtain:

\[
\begin{align*}
1. & \quad \text{BH}_3 \\
2. \quad \text{aq. NaOH} \\
\end{align*}
\]

so, this is the correct answer

* * *

c.  

- this is a bromohydrin-like compound that — in principle — one can create by treating an alkene with Br₂ and CH₂OH
- A general diagram for either reaction is:

\[
\begin{align*}
\text{C=C} & \rightarrow \text{CH}_3\text{O} \quad \text{Br} \\
\end{align*}
\]

* * *
Therefore, one could make c. starting from:

**BUT:** the above reaction is an *anti* addition, meaning that Br and OCH$_3$ will add from opposite faces of the alkene.

*Will this produce the correct stereoisomer of the product?*

- Because the Br atom and the OCH$_3$ groups in c. are *trans* to each other, one will indeed obtain the desired product from the alkene shown above (1-methylcycloheptene):

so the correct answer is:

* * *

**d.**

- this is a carbonyl compound; a dialdehyde, to be precise.
- the only method known to us to make aldehydes is the ozonolysis of alkenes followed by treatment of the ozonide with Zn and acid

* A general diagram for either reaction is: 

Therefore, one could certainly make d. from an alkene like:

**But there is a better option . . .**

- If the two carbonyl carbons were initially doubly bonded to each other, then ...

so:

- Whereas the first method also yields two additional carbonyl compounds of no interest to us, the second one would produce only the desired d.
- The second method is better, and it represents the best answer

* * *
e. 

- this is an alcohol
- the only methods known to us for the creation of alcohols are the acid-catalyzed hydration of alkenes and the hydroboration-oxidation of alkenes

A general diagram for either reaction is: 

\[
\begin{array}{c}
\text{C=C} \\
\text{H–OH} \\
\text{H}_2\text{SO}_4 \\
\text{H}_2\text{O} \\
\text{C–C}
\end{array}
\]

- If one were to make e. by acid-catalyzed hydration of an alkene, the latter would have to undergo protonation to form the following carbocation:

\[
\text{protonation of either 1-butene, cis-2-butene, or trans-2-butene would afford the above carbocation; therefore, reasonable answers are:}
\]

\[
\begin{array}{c}
\text{H}_2\text{SO}_4 \\
\text{H}_2\text{O} \\
\text{OH} \\
\text{or}
\end{array}
\]

- If one were to make e. by hydroboration-oxidation of an alkene, one could not use 1-butene as the substrate:

\[
\begin{array}{c}
\text{BH}_3 \\
aq. \text{NaOH} \\
\text{OH} \rightarrow \\
\text{OH}
\end{array}
\]

- however, one could employ either cis or trans-2-butene:

\[
\begin{array}{c}
\text{BH}_3 \\
aq. \text{NaOH} \\
\text{OH} \rightarrow \\
\text{OH}
\end{array}
\]

* * *

f. 

- this is the syn-diastereomer of a vicinal dichloride
- the only method known to us for the creation of vicinal dichlorides is the chlorination of alkenes

A general diagram for either reaction is: 

\[
\begin{array}{c}
\text{C=C} \\
\text{Cl} \\
\text{Cl} \\
\text{Cl} \\
\text{CH} \rightarrow \\
\text{CH} \rightarrow \\
\text{CH}_3\text{–CH=CH–CH}_3 \\
\text{CH}_3
\end{array}
\]

- to prepare f. we need the following alkene (4-methyl-2-pentene):

**BUT:** which geometric isomer of the above alkene is required to obtain the desired product?

- The halogenation (chlorination) of alkenes is an anti-addition reaction, so the halogen atoms must enter from opposite faces of the \(\pi\) bond

- If one were to attempt making f. by chlorination of \textit{trans}-4-methyl-2-pentene, one would get:

\[
\begin{array}{c}
\text{Cl} \\
\text{Cl} \\
\text{Cl}
\end{array}
\]
but if one were to chlorinate cis-4-methyl-2-pentene . . . :

\[
\begin{align*}
\text{cis-4-methyl-2-pentene} & \quad \rightarrow \quad \text{Cl} \\
\text{Cl} & \quad \rightarrow \quad \text{Cl}
\end{align*}
\]

so, the correct answer is:

\[
\text{cis-4-methyl-2-pentene}
\]

A quicker way to obtain the correct answer:

\[
\begin{align*}
\text{cis-4-methyl-2-pentene} & \quad \rightarrow \quad \text{Cl} \\
\text{Cl} & \quad \rightarrow \quad \text{Cl}
\end{align*}
\]

* * *

\[
\begin{align*}
g. & \quad \text{this is an alcohol} \\
& \quad \text{the only methods known to us for the creation of alcohols are the acid-catalyzed hydration of alkenes and the hydroboration-oxidation of alkenes}
\end{align*}
\]

* If one were to make g. by acid-catalyzed hydration of an alkene, the latter would have to undergo protonation to form the following carbocation:

\[
\begin{align*}
\text{H} & \quad \rightarrow \quad \text{H} \\
\text{+} & \quad \rightarrow \quad \text{+}
\end{align*}
\]

* the only way to create the above carbocation is to protonate 3-methyl-1-butene:

\[
\begin{align*}
\text{H–OSO}_3\text{H} & \quad \leftrightarrow \quad \text{CH}_3
\end{align*}
\]

* the secondary cation would rapidly rearrange via a H shift to furnish a better stabilized, tertiary one:

\[
\begin{align*}
\text{H} & \quad \rightarrow \quad \text{H} \\
\text{+} & \quad \rightarrow \quad \text{+}
\end{align*}
\]

from which an incorrect product would be obtained:

so, one cannot make g. by acid-catalyzed hydration of an alkene.

* If one were to make g. by hydroboration-oxidation of an alkene — a reaction that produces an "anti-Markownikov" alcohol — the required alkene would be:

\[
\begin{align*}
\text{BH}_3 & \quad \rightarrow \quad \text{R} \quad \quad \text{R} \\
\text{H}_2\text{O}_2 & \quad \rightarrow \quad \text{OH} \\
\text{aq. NaOH} & \quad \rightarrow \quad \text{desired product}
\end{align*}
\]

* Then . . .
h. this is a vicinal diol of cis-configuration
• the only method known to us for the creation of vicinal diols is the dihydroxylation of alkenes with OsO₄

• A general diagram for either reaction is:

• to prepare f. we could dihydroxylate 1-methyl-cyclopentene:

**BUT: will we get the correct diastereomer of the product?**

• The dihydroxylation of alkenes is a syn-addition reaction, so the OH groups must enter from the same face of the π bond

• If one were to dihydroxylate 1-methyl-cyclopentene, one would get:

so, the correct answer is: