1. The incorporation of cyclic protecting groups at the C3/C5 and C9/C11 hydroxyl groups in erythronolide seco acid derivatives is thought to preorganize these molecules such that their conformation resembles that of the macrolactone. This preorganization has been shown by many researchers to be critical to the success of lactone formation. In his synthesis of (+)-9S-dihydroerythronolide A, Stork identified an additional requirement of the cyclic protecting group, e.g. that when C9/C11 is protected as an acetal, R₂ must be a hydrogen as shown in the examples below. In cases where R₂ = Me, no cyclization is observed. Clearly explain the basis for this observation. Be specific.

![Chemical structures showing cyclization examples](image)

<table>
<thead>
<tr>
<th>R₁</th>
<th>R₂</th>
<th>Macrocyclization</th>
</tr>
</thead>
<tbody>
<tr>
<td>Me</td>
<td>Me</td>
<td>no</td>
</tr>
<tr>
<td>H</td>
<td>Me</td>
<td>no</td>
</tr>
<tr>
<td>Me</td>
<td>H</td>
<td>yes</td>
</tr>
</tbody>
</table>

2. Show how you would carry out the following transformations in the most efficient manner and with the fewest side reactions. Show all intermediate products and reagents. Pay attention to issues of selectivity. Clearly depict any stereochemistry, even if it will later be destroyed.

a. 

![Chemical structures for transformation a](image)

b. 

![Chemical structures for transformation b](image)

c. 

![Chemical structures for transformation c](image)
3. Design a concise, stereoselective synthesis for the following compound:

a. Show two strategically different, but reasonable, retrosyntheses for the compound above that regress back to commercially available starting materials of 8 carbons or less. Your starting materials should cost less than $5/g and should be available from one of the following vendors: Aldrich, Acros, Alfa Aesar, AK Scientific, GFS, Matrix Scientific, Oakwood, Strem, TCI. As part of your answer, list the vendor and price of all starting materials. Your retrosyntheses should show only the C-C bond disconnections.

b. Identify which of the two approaches you would use to make this molecule and clearly explain your reasoning. Be specific.

c. Show your forward synthesis. Show the product of every step in your sequence, as well as the conditions required to complete each transformation in the manner desired (e.g. solvents, reagent equivalents, etc.). Clearly depict any stereochemistry. Justify any issues of selectivity.