

Name: ANSWERS

Please clearly print your name above.

There are 166 points and eight questions on the exam.

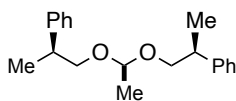
Answer all questions directly in the space provided on the seven exam pages (a diamond lattice has been provided on the eighth page).

You may not use books, notes, phones, etc.

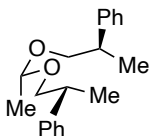
Part I 18 / 18Part II 9 / 9Part III 18 / 18Part IV 15 / 15Part V 18 / 18Part VI 14 / 14Part VII 16 / 16Part VIII 54 / 54Bonus 4 / 4Total 166 / 166

- I. (18 points) For parts a) and b) indicate (circle the word) whether the two structures are the *same*, a pair of *enantiomers*, or a pair of *diastereomers*. If they are diastereomers, indicate the number of stereogenic centers that are different in the two structures. Ignore differences in conformation. For parts c) and d) indicate (circle the word) whether the indicated pairs of atoms, groups, or faces are *homotopic*, *diastereotopic*, or *enantiotopic*.

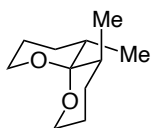
a)



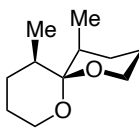
vs.


 same enantiomeric diastereomeric
 (if so, how many
 stereogenic
 centers are different?)

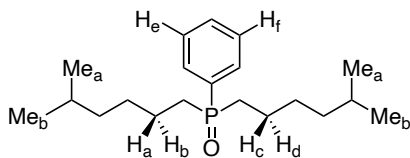
b)



vs.

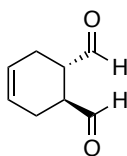

 same enantiomeric diastereomeric
 (if so, how many
 stereogenic
 centers are different?)

c)

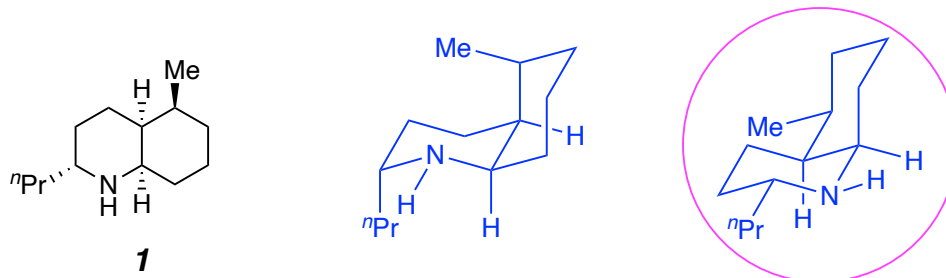


Me _a / Me _b	homotopic	<u>diastereotopic</u>	enantiotopic
H _a / H _b	homotopic	<u>diastereotopic</u>	enantiotopic
H _a / H _c	homotopic	diastereotopic	<u>enantiotopic</u>
H _e / H _f	<u>homotopic</u>	diastereotopic	enantiotopic

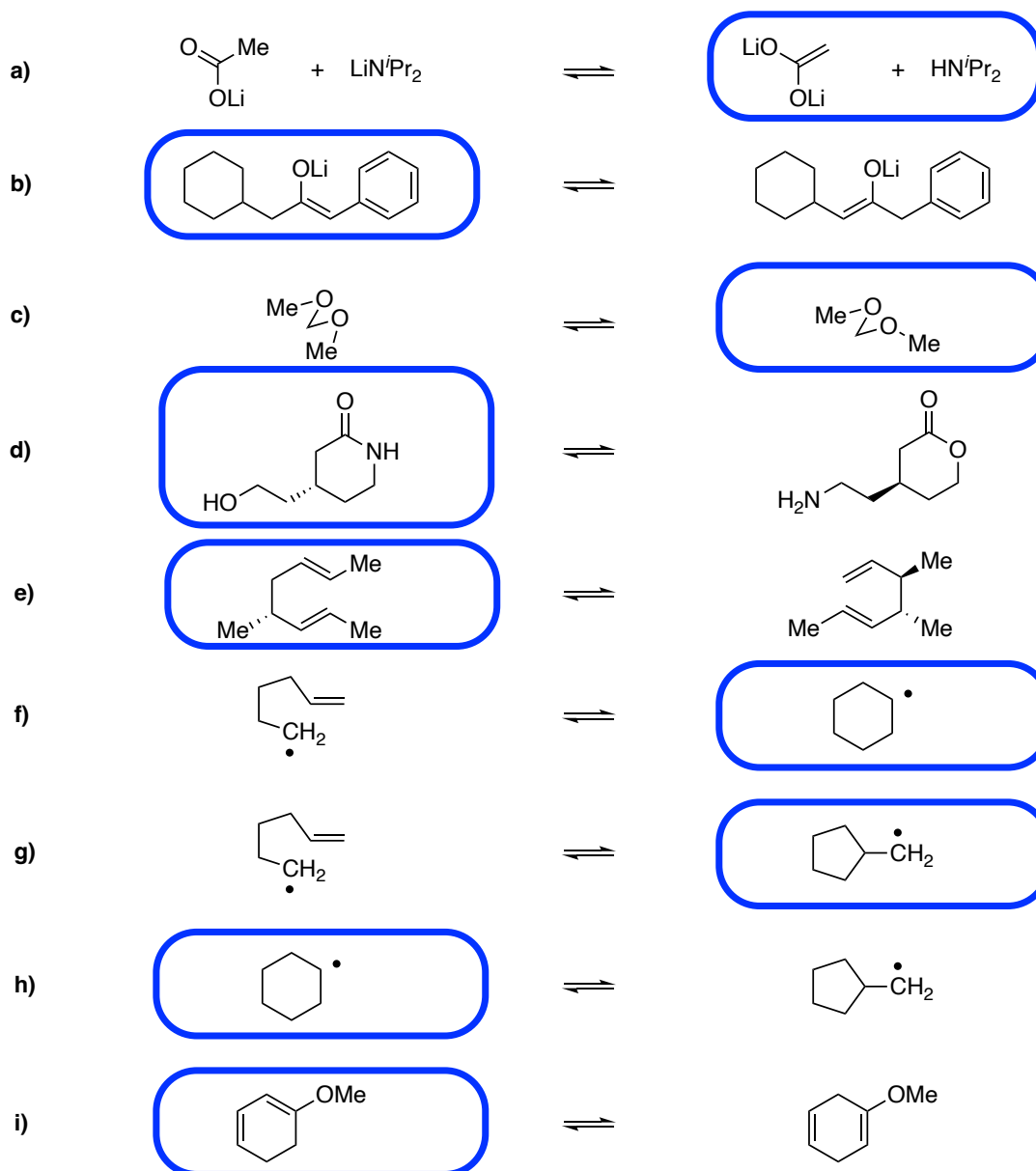
d)

The front vs. back face of the alkene homotopic diastereotopic enantiotopicThe front vs. back face of either one of the aldehydes homotopic diastereotopic enantiotopic

- II. (9 points) Some decahydroquinoline alkaloids have the skeleton shown in **1**. This bicycle can exist in either of two, cis-decalin-like conformations. In each, the two six-membered rings are chair-like. Draw each of these conformations. Circle the more stable of these two conformers.

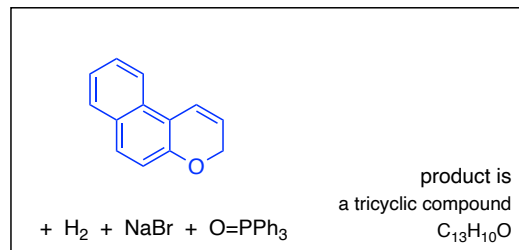
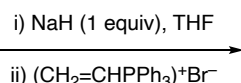
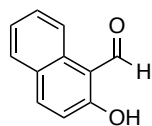


- III. (18 points) Indicate whether each of the following equilibria lies predominantly to the left or to the right by circling the side corresponding to the more stable species.

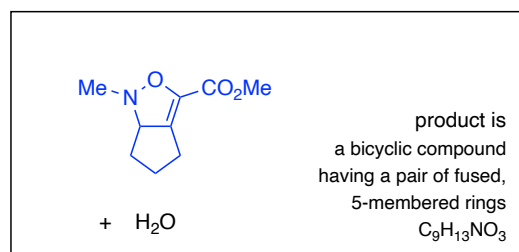
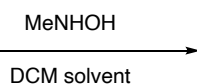
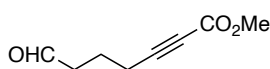


IV. (15 points) Provide the structure of the major product expected from each of the reactions a)-c). The molecular formula of the missing product is given in the lower right corner of each box. [hints: a) the vinylphosphonium ion is electrophilic, b) N-alkyl hydroxylamines react with aldehydes to produce nitrones, and c) a Mislow-Evans rearrangement is involved]

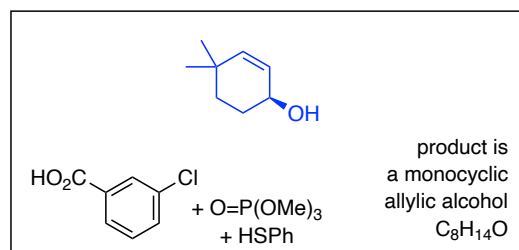
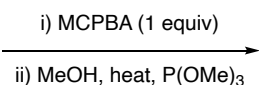
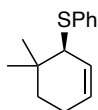
a)



b)

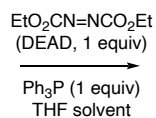
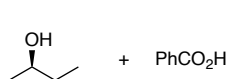


c)



V. (18 points) Provide the structures of the byproducts that, together with the indicated main product, constitute a stoichiometrically and fully balanced reaction equation for each of the following three (a-c) transformations. Ignore any components derived from the catalyst in c) [hint: in each case there are two byproducts]

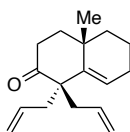
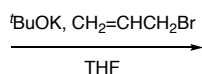
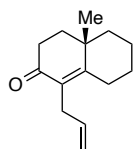
a)



+ ?



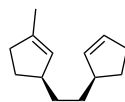
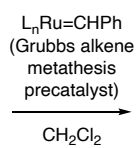
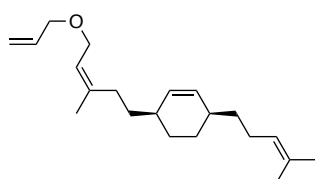
b)



+ ?



c)



+ ?



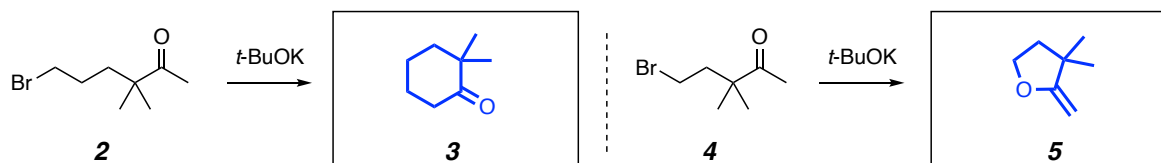
+



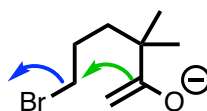
VI. (14 points) Recall that there is an inherent preference for alkylation of simple ketone enolate anions at the carbon atom (to give the α -alkylated ketone product) rather than on the enolate anion oxygen atom (to give an enol ether product).

When each of the bromoketones **2** and **4** is treated with potassium t-butoxide at room temperature under the same conditions, each cyclizes with net loss of the elements of HBr. Ketone **2** gives, principally, a carbocyclic ketone product but **4** gives, principally, a cyclic enol ether as the main product.

a) Provide the structures of products **3** and **5**.



b) Explain why the substrates **2** and **4** give different types of products. Limit your answer to the space within this box. [*hint: you would find the concepts that underlie Baldwin's rules for ring closure useful for guiding your explanation*]



Both C- and O-alkylation processes are energetically favorable events. That is because there is good orbital overlap between the HOMO enolate orbital holding electron density at both carbon and oxygen and the antibonding C–Br orbital (the LUMO). Accordingly, the inherent preference for C-alkylation of the enolate anion from **2** (drawn above) prevails to produce **3**. In Baldwin's classification, both **6-endo-trig** and **6-exo-tet** are favorable processes.



In contrast, the orbital overlap required for C-alkylation of the above enolate (from **4**) with the antibonding C–Br orbital is poor (the tether is too short), which raises the activation barrier for C-alkylation. This poor geometric alignment overrides the inherent preference for C-alkylation. The electron density on the oxygen atom (two sp^2 localized lone pairs and a p-type lone pair that is delocalized into the alkene) "surrounds" that atom and is available to be used in the nucleophilic attack at the sp^3 -carbon bearing the bromine atom. In the transition state leading to the enol ether **5**, there is no loss in bond order at any of the three enolate atoms. In Baldwin's classification, the **5-endo-trig** component of a C-alkylation process is unfavorable whereas the O-alkylation is a favorable **5-exo-tet** process.

VII. (16 points) The Ireland-Claisen rearrangement involves the [3,3]-sigmatropic rearrangement of silylketene acetals. The *E*- or *Z*-silylketene acetal can be made selectively by changing the conditions to favor the initial formation of either the *E*- or *Z*-lithium enolate. This then translates into the relative configuration of the major diastereomer formed from a substrate such as the propanoate ester **6** shown below.

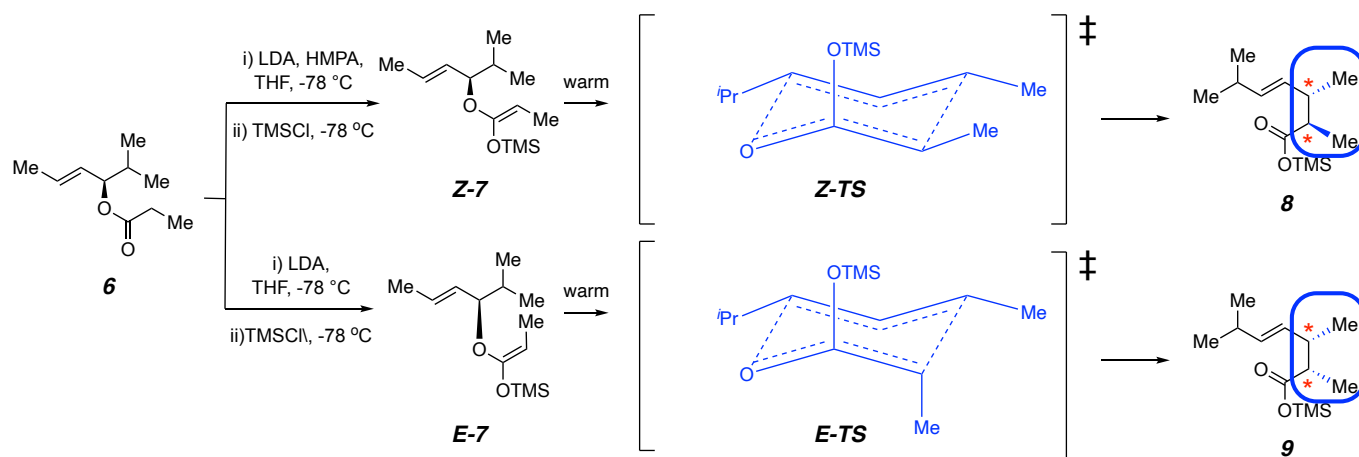
Draw

i) the lowest energy, chair-like transition state structure **Z-TS** for the rearrangement of the silyl ketene acetal isomer **Z-7**,

ii) the lowest energy, chair-like transition state structure **E-TS** for the rearrangement of the silyl ketene acetal isomer **E-7**,

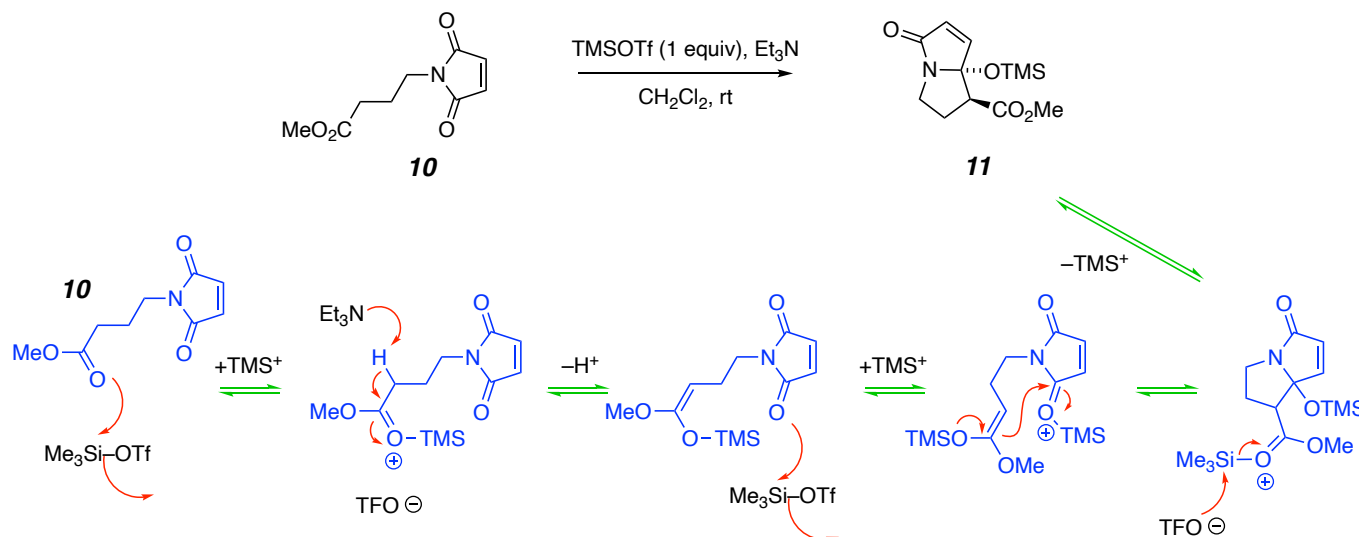
and

iii) the absolute configuration of each of the methyl-bearing stereogenic carbon atoms (starred in red) in **8** and **9**.

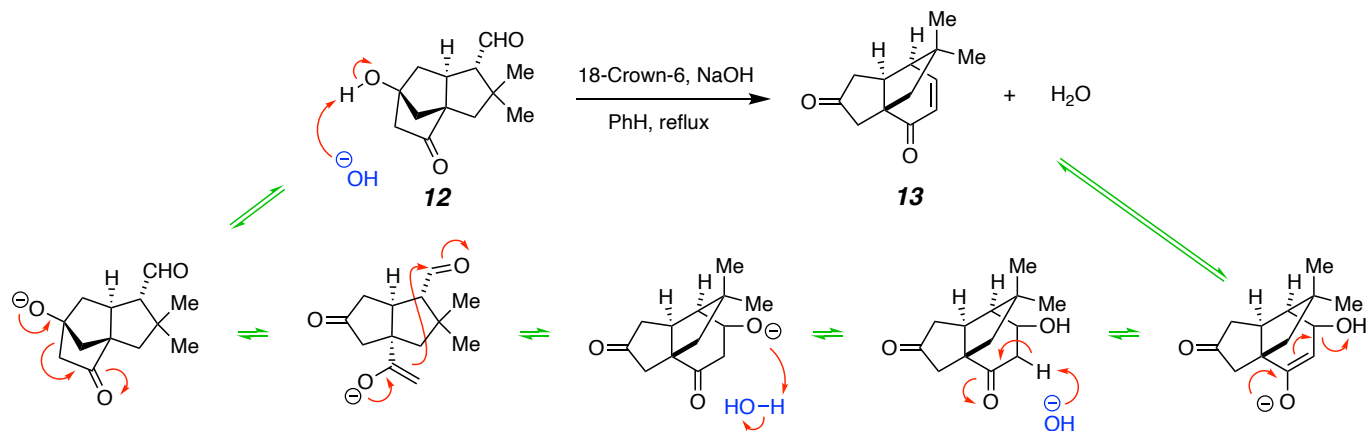


VIII. (54 points) Provide a *detailed mechanism* to account for each of the following four reactions. Show *ALL* intermediates, equilibria, and bond-making and -breaking steps. For species that have more than one significant resonance contributor, you only need to show one of them.

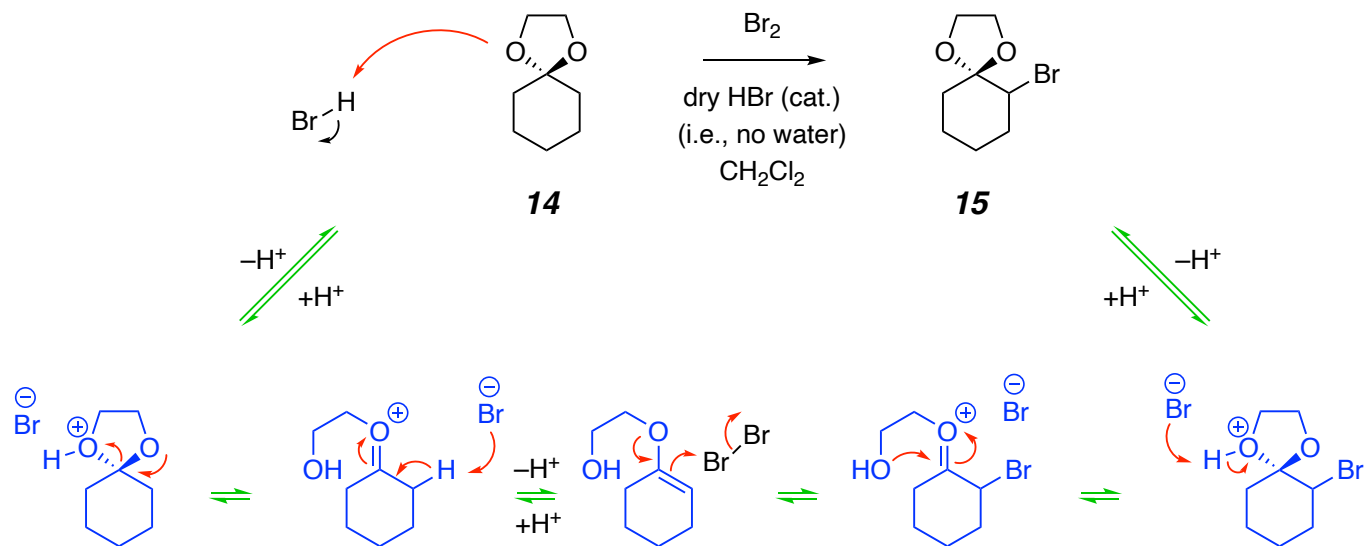
a) (12 points) [hint: "sila-aldol addition"]



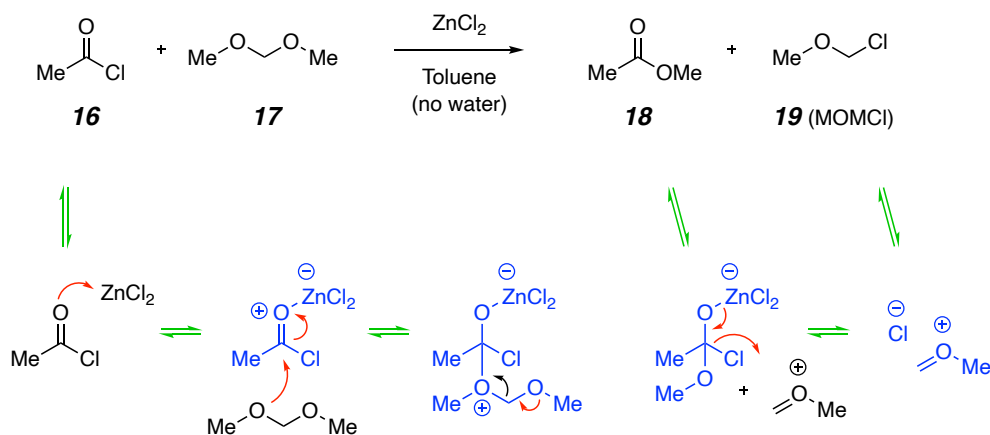
b) (15 points) [hint: "all things (retro)aldol"]



c) (15 points) This reaction is autocatalytic (i.e., it proceeds at a faster rate as the extent of conversion increases) because HBr, a byproduct of the reaction, further catalyzes the transformation.



- d) (12 points) A one pot synthesis of MOMCl (19) from acetyl chloride (16) and methylal (dimethoxymethane, 17), which, incidentally, produces a solution of the reagent that can be used directly for the preparation of MOM ethers.



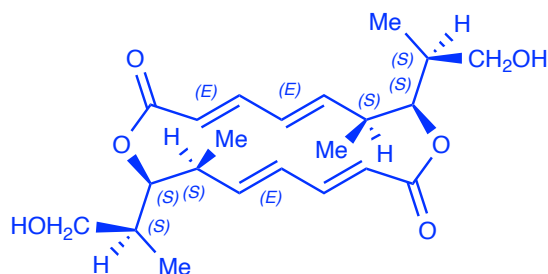
there are variations of the above mechanism that are also reasonable, such as those involving one of the following ion pairs



Bonus (4 pts)

Draw the structure of (3*E*,5*E*,7*S*,8*S*,11*E*,13*E*,15*S*,16*S*)-8,16-bis[(1*S*)-1-Hydroxymethylethyl]-7,15-dimethyl-1,9-dioxacyclohexadeca-3,5,11,13-tetraene-2,10-dione (an intermediate in the Evans synthesis of the elaiophyllin aglycone).

[hint: cyclohexadecane is a sixteen-membered ring; I've started you out by drawing below a 1,9-dioxacyclohexadecane skeleton]



Thank you for all of your hard work this semester. I enjoyed having you in the class. Do not lose sight of all that you have learned. Remember that in your research details matter and that every experiment you ever do is a success if you have learned something from it, no matter how trivial it may seem at the time. Have a relaxing Holiday break and come back renewed for more learning and discovery in the New Year. If you like you may pick up your graded final exam papers from Katharine in 413 Smith.

* * * end of exam * * *

