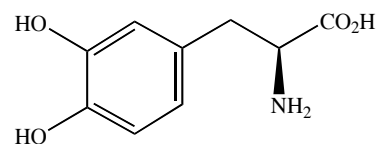


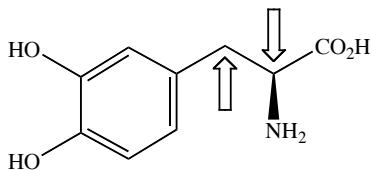
L-dopa is a drug used to supplement low brain levels of dopamine, a critical neurotransmitter. Dopamine deficiency has been linked to a variety of disorders such as Parkinson's disease.



L-dopa

- (3 points) Name the functional groups present in L-dopa.
- (2 points) Give the chemical formula of L-dopa.
- (2 points) L-dopa has (give a number) \_\_\_\_\_ lone pairs.
- (2 points) The best estimate for the H-N-C bond angle of L-dopa is (circle one):  
 $< 109.5^\circ$     Very close to  $109.5^\circ$      $>109.5^\circ$  but  $<120^\circ$     Very close to  $120^\circ$
- (3 points) Define "strain."

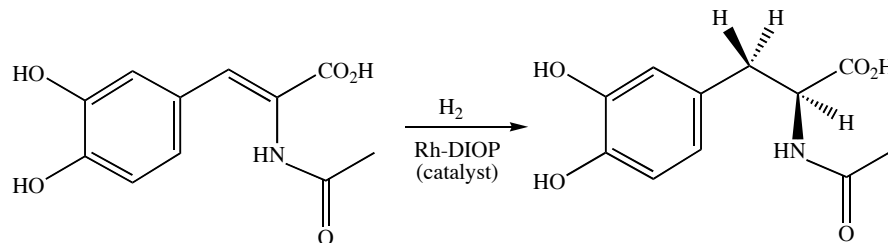
- (6 points) For a drug to be effective, it must be able to adopt a conformation that provides an appropriate fit for the drug's receptor or enzyme target. Use a Newman projection to show the most stable conformation along the carbon-carbon bond indicated by the arrows, with the CH in front. Assume  $\text{NH}_2$  is larger than  $\text{CO}_2\text{H}$ .



On the structure with the arrows, circle the atoms or groups whose gauche interaction cause the greatest strain in the most stable conformation.

- (1 point) Does L-dopa have significant ring strain (circle one)? Yes No Cannot tell

Questions 8-12 refer to this critical step in the industrial scale synthesis of L-dopa:



8. (2 points) Label each stereocenter in the reaction product as R or S.

9. (1 point) Circle the molecule(s) that are chiral:

Starting alkene     $H_2$     Reaction product

10. (1 point) The alkene of the starting material is (circle one): E    Z

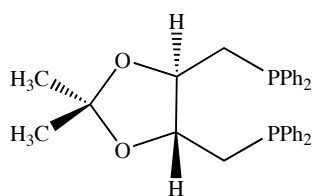
11. (3 points) The effectiveness of a drug depends on various features, which may or may not be the same for both enantiomers. Decide if the properties listed below will differ for L-dopa and its enantiomer (circle the best response).

(a) Solubility in water:                      Same    Different    Cannot determine

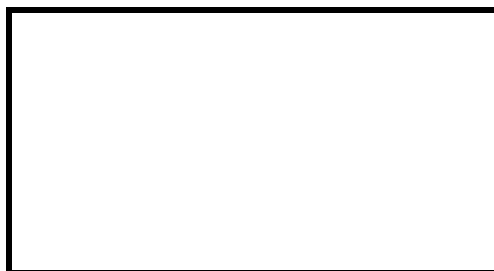
(b) Effectiveness as a drug:                      Same    Different    Cannot determine

(c) Rotation of plane polarized light: Same    Different    Cannot determine

12. (3 points) The hydrogenation catalyst consists of two molecules of DIOP bonded to one Rh atom. If DIOP is not chiral, then the hydrogenation reaction does not give optically active product. By adding, subtracting or otherwise changing at most four atoms, redraw DIOP so that it is achiral. (Ph =  $C_6H_5$ )

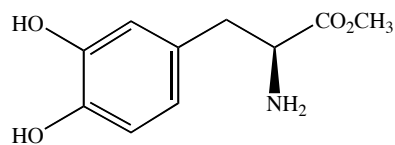


DIOP

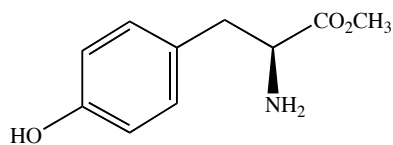


Modified (achiral) DIOP

13. (5 points) In many cases, drug effectiveness is also influenced by the acidity or basicity of the molecule. The OH group of deoxy-L-dopa methyl ester is predicted to be more acidic than either of the HO groups of L-dopa methyl ester. Briefly explain.



L-dopa methyl ester  
*Less acidic*



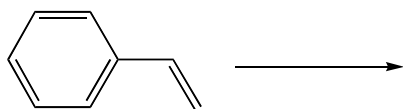
Deoxy-L-dopa methyl ester  
*More acidic*

14. (5 points) By adding, subtracting or otherwise changing at most four atoms, and using a structural feature *not* mentioned in the previous question, redraw the structure of L-dopa methyl ester so that it is obviously more acidic. In one sentence or less explain why the modified molecule is more acidic.

Modified molecule:

Explanation:

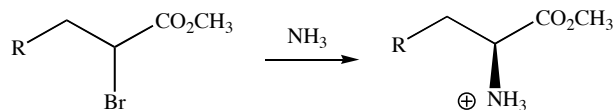
15. (3 points) Using the alkene shown, write an example of an anti-Markovnikov addition reaction. Include all necessary reactants and the major product, but do not include any mechanism details.



16. (3 points) Write a reasonable starting material in the box. If no reasonable starting material can be drawn, write "none" in the box.



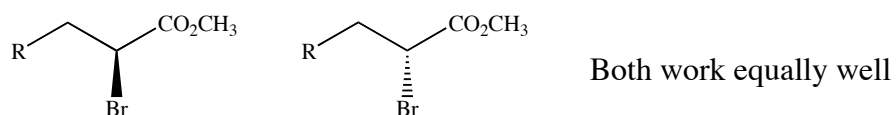
Questions 17-22 refer to this reaction for the synthesis of deoxy-L-dopa methyl ester:



17. (3 points) Define “mechanism.”

18. (2 points) Write the  $S_N2$  mechanism for this reaction.

19. (2 points) Circle the correct  $S_N2$  starting material for this reaction:



20. (2 points) Circle the best solvent choice for this  $S_N2$  reaction:



21. (6 points) What happens to the  $S_N2$  reaction rate if... (circle the best answer in each case):

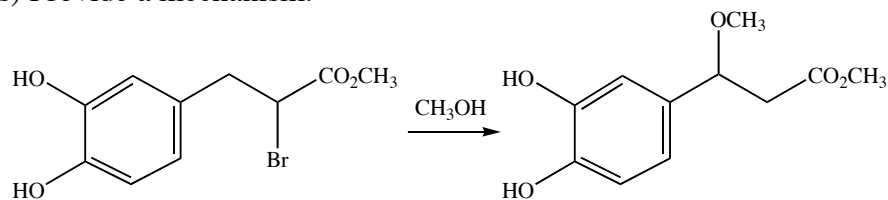
- (a) ...if Br is changed to OH:      Faster    Slower    No significant change
- (b) ...if  $CO_2CH_3$  is changed to H:      Faster    Slower    No significant change
- (c) ...if  $NH_3$  is changed to  $(CF_3)_3N$ :      Faster    Slower    No significant change

22. (7 points) Circle the most probable mechanism for this reaction, and briefly explain your reasoning.

Mechanism:  $S_N2$     $S_N1$

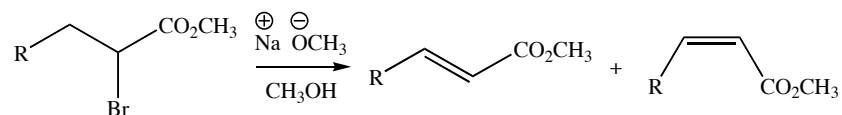
Explanation:

23. (7 points) Provide a mechanism.



The stereochemistry of this product is (circle one): S   R   Both   Cannot determine

When  $\text{NH}_3$  is changed to  $\text{CH}_3\text{O}^-$  elimination is the major reaction pathway. Questions 24-26 refer to the reaction with  $\text{CH}_3\text{O}^-$ .



24. (2 points) Circle the major reaction product.

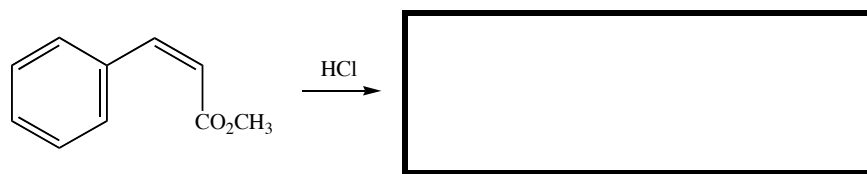
25. (6 points) Write the E2 and E1 mechanisms for the formation of the major product.

E2:

E1:

26. (2 points) Circle the most probable mechanism: E2   E1   Could be either

Questions 27 and 28 refer to this addition reaction:



27. (2 points) Write the major product of this reaction in the box above.

28. (8 points) Provide a mechanism for the formation of the major product.

29. (6 points) Briefly explain your choice of major product.