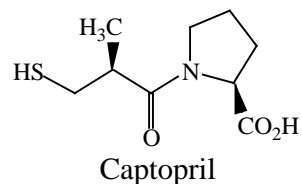


Captopril is a specific competitive inhibitor of angiotensin I-converting enzyme (ACE). The drug enlarges blood vessels slightly, causing a decrease in blood pressure and thus making it easier for the heart to pump blood. Captopril is prescribed to treat high blood pressure and heart failure. Given the stress and poor diet typical of modern Americans, is it surprising that this drug is one of the top-selling drugs currently in use?



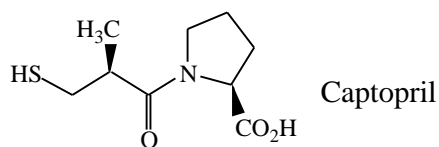
1. (2 points) How many atoms in captopril are sp^2 ? _____
2. (2 points) How many atoms in captopril have open octets? _____
3. (2 points) How many lone pairs are there in captopril? _____
4. (6 points) Lone pairs are important in so many ways. List three significant ways in which lone pairs have obvious influence. **No more than one short sentence each.**

Influence #1:

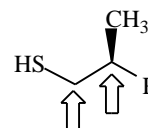
Influence #2:

Influence #3:

5. (2 points) Circle two atoms with the most similar electronegativities: C N H O S
6. (3 points) List the names of all of the functional groups in captopril.
7. (2 points) Name one nitrogen-containing functional group not present in captopril. Illustrate this functional group by drawing any molecule that contains this functional group, a ring, and exactly two carbon atoms.



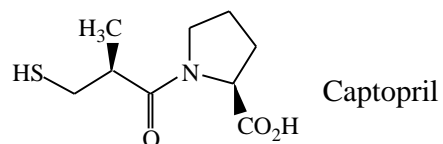
8. (2 points) On the structure above clearly label all stereocenters as R or S.
9. (2 points) In one sentence or less describe the single most important factor that drives any molecule into its lowest energy conformation or geometry.
10. (2 points) Estimate the S-C-C bond angle of captopril: _____ degrees.
11. (8 points) Using Newman projections, draw the most stable and least stable conformations along the bond indicated by the arrows. Use the R abbreviation shown. Put the stereocenter on the front carbon.



Most stable	Least stable
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12. (2 points) Captopril has ring strain (circle one): Yes No Cannot tell
13. (3 points) By adding, subtracting or otherwise changing no more than three atoms, redraw the structure of captopril so that the answer to the previous question is different.
14. (6 points) Draw an enantiomer and a diastereomer of captopril in these boxes.

Enantiomer	Diastereomer
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15. (3 points) By adding, subtracting or otherwise changing at most 8 atoms, redraw captopril in the space below so that it is achiral.
16. (2 points) Of the structures drawn in questions 14 and 15, circle the ones that are optically active: enantiomer diastereomer achiral
17. (2 points) How many captopril stereoisomers are possible? _____
18. (2 points) Captopril is (circle one): dextrorotatory levorotatory cannot tell
19. (12 points) Briefly but precisely define these terms.
- (a) Resolution:
- (b) Racemic mixture:
- (c) Inductive effect:
- (d) Torsional strain:

20. (6 points) For this question, abbreviate captopril as RCO_2H . Draw the three most significant resonance contributors for the conjugate base of RCO_2H . Include all lone pairs and formal charges.

21. (2 points) What is the single most important feature that influences the basicity of *any* base?

22. (1 point) The most acidic hydrogen of captopril is (circle one): SH CO_2H CH_3

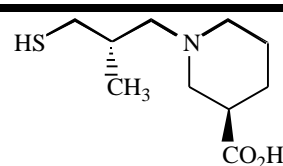
23. (6 points) Very briefly explain your answer to the previous question.

24. (6 points) Illustrate deprotonation of the most acidic group from question 22 using HO^- and curved arrows. Label the nucleophile and electrophile. The R abbreviation may be used.

25. (3 points) By adding, subtracting or otherwise changing no more than three atoms, redraw the structure of captopril so that it is obviously more acidic.

26. (3 points) By adding, subtracting or otherwise changing no more than three atoms, redraw the structure of captopril so that it is obviously less acidic.

Drug structures are often varied in order to improve their effectiveness or decrease side effects. One possible captopril analog is shown at the right.



27. (8 points) Draw the two chair conformations of the most stable stereoisomer of the captopril analog. Assume lone pairs to be smallest. Abbreviate the $\text{CH}_2\text{CH}(\text{CH}_3)\text{CH}_2\text{SH}$ group as R.

Most stable chair

Least stable chair