Names of all students (please print) _____

_____

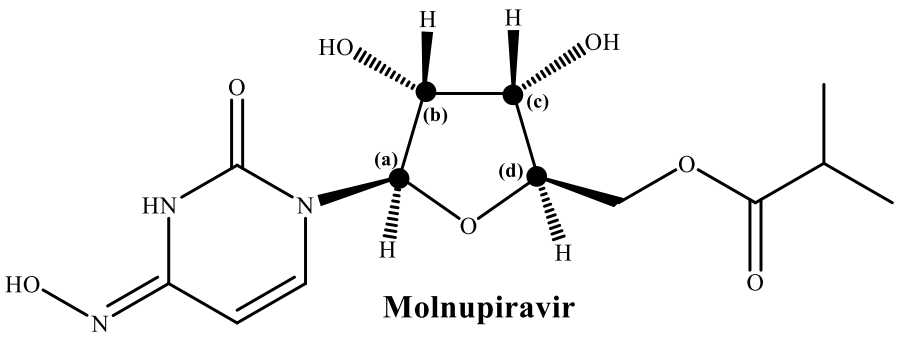
CHEM 243 Organic Chemistry I **Points _____ (10 max)**

Worksheet #12: October 6, 2021. Complete the following worksheet by collaborating with a group of 3-4 students. You can use a text book or your lecture video notes. You must work together, with the names of all students included on **ONE** sheet and turned in for a group grade.

My worksheets are designed with the assumption that you have (1) watched the videos, (2) taken notes, and (3) have your notebook open on your bench.

1) Practical Application of Chirality in Drug Design. News broke last week that Merck & Co. have developed an antiviral drug called **Molnupiravir** that reduces risk of hospitalization and death in patients with mild to moderate COVID-19. Merck has nearly completed Phase 3 clinical trials and will apply to the US FDA for Emergency Use Authorization. The structure of Molnupiravir is drawn below.

The significance is (1) Molnupiravir is an oral antiviral, and (2) it cuts the risk of hospitalization and death from COVID-19 by 50% in people who have mild to moderate forms of the disease. Merck & Co. and Ridgeback Biotherapeutics reported the preliminary data from interim analysis of their Phase 3 trial. This story was reported by Bethany Halford, Laura Howes, and Megha Satyanarayana in Chemical & Engineering News, October 1, 2021.



Molnupiravir

Just pause for a moment and look at the structure of Molnupiravir, and consider how intimidating this structure would have been when you were just starting organic chemistry just five weeks ago! You understand the rings and "zig-zag" carbon chains, you can identify most of the functional groups and the acid/base groups, you can predict what bands you might find in the IR, AND you know that the wedge and dash bonds represent chiral carbons and you can determine their 3D configurations. Not bad for five weeks!

(a) Configuration at Chiral Carbons. A dot (●) has been placed on each of the four chiral carbons, and they are labeled a-d. Determine the R or S configuration at each chiral carbon. **Be careful, its tricky!**

(a) _____ (b) _____ (c) _____ (d) _____

(b) It is a tremendous challenge to synthesize a molecule with just **one** chiral carbon, let alone four! Its also likely that ONLY the stereoisomer drawn above has the desirable anti-viral activity. How many TOTAL stereoisomers are there for Molnupiravir? _____

Another stereoisomer of Molnupiravir had configurations of **(a) S, (b) S, (c) R and (d) S.**

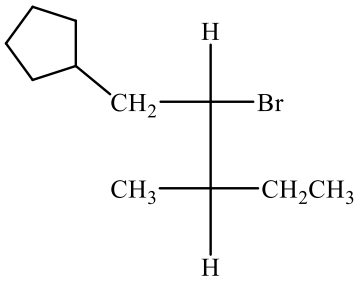
(c) How are these two stereoisomers related to each other _____

(d) Based on your answer to (c), do you expect that these stereoisomers would have the **same** or **different** physical properties? **CIRCLE** your answer.

(2) Stereoisomers: Fisher Projections.

(a) Label each chiral center as R/S for the organic compound represented by the Fisher Projection drawn to the right.

(b) Draw an accurate zig-zag line structure for the organic compound represented by the Fisher Projection. Be sure to show the proper stereochemistry at all chiral centers using wedge and dashed bonds.



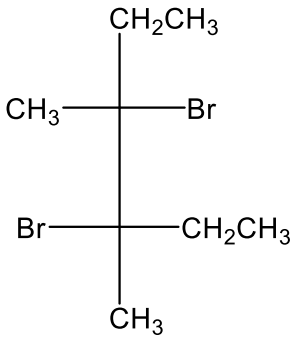
configuration _____

configuration _____

(c) Give an IUPAC name for the structure you drew above, including the correct R/S prefixes.

(3) Meso Compounds.

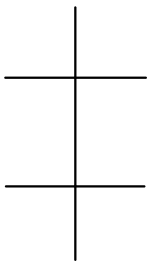
(a) Re-draw the Fisher Projection for Compound A (on the left) using the blank template (on the right), such that the lowest priority groups (**methyl groups)** are on the **vertical axis (top & bottom)**.



Compound A

Configuration _____

Configuration _____



Compound A (each chiral carbon rotated such that the lowest priority methyl groups are both on the vertical axes.

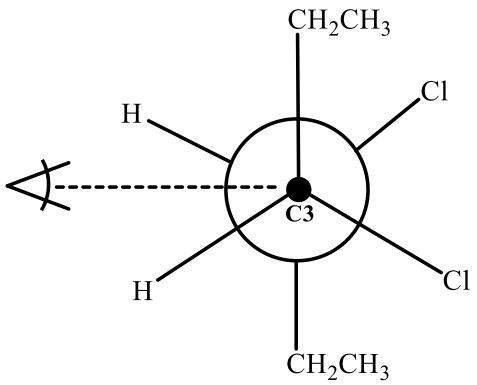
(b) Assign the correct R/S configuration to each chiral center in the Fisher Projection for Compound A.

(c) Is this a Meso compound? EXPLAIN your answer (there are TWO key points).

(4) Converting a Newman Projection into a 3D Zig-Zag drawing and into a Fisher Projection.

(a) Consider the Newman Projection drawn below. Draw a zig-zag structure for this compound in the space at the right. Be sure to show the proper stereochemistry at all chiral centers using wedge and dashed bonds.

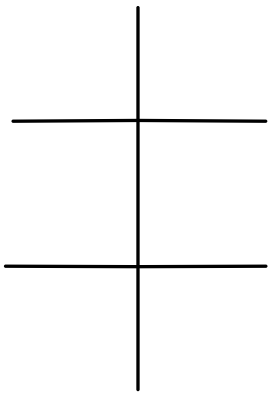
1) In View A your eye is looking at C3 from above, and down the C3-C4 bond.
2) In View B, we have turned the C3-C4 bond 90º to the left.
3) We need to now add 3 bonds to C3 and C4. One bond in the plane of the paper, one wedge bond coming forward, and one dashed bond going back. Lets start with the bonds in the plane of the paper. In the Newman projection the bonds in the plane of the paper are the bonds going up and down.
4) Now for the wedge and dashed bonds. For C3 these will be the -Cl and -H. In the Newman Projection (View A) the -Cl is down and to the right. As you change to View B, the -Cl bond will be down but is it going "back" (dashed bond) or coming "forward" (wedge bond).
5) Do the same analysis for C4 to finish.



VIEW A (looking down at C3)

VIEW B (looking at the C3-C4 bond from left to right)

(b) Now draw a Fisher Projection for this compound using the template at the right. The atoms or groups with the lowest priorities should be on the vertical axes.



(c) Is this a Meso compound?
EXPLAIN your answer (there are TWO key points).