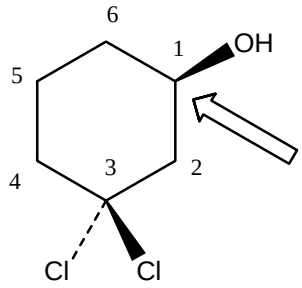
Drawing Conformers of Cyclohexanes and Conformational Analysis ***MAH@ACP***

To determine the energy or relative energy of conformers of cyclohexanes, when you are only provided with the name, follow the steps outlined below.

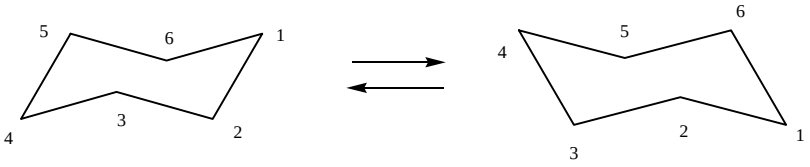
1. Draw the structure of the compound using the "wedge/dotted line" convention to show the proper stereochemistry indicated in the name of the compound. Number the carbon atoms in the cyclohexane structure that you draw.

So for 1R-3,3-dichlorocyclohexanol



C_1 is shown with the proper R configuration

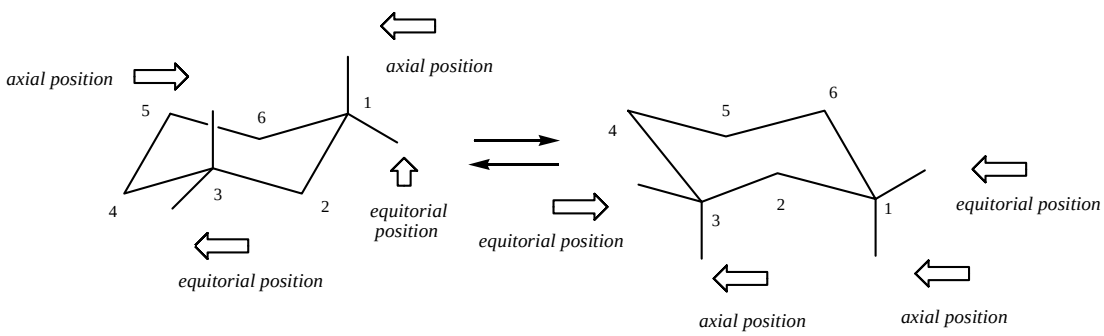
2. Draw two "templates" that represents the two chair conformations of cyclohexane and number the carbon atoms. *All cyclohexanes have <u>two</u> chair conformations.* (Conformer B is the "ring-flipped" conformer of A) Be sure to number the atoms correctly and transpose the numbering properly when going from one structure to the next.



A B

NOTE: Carbon atoms of the cyclohexane chair conformers can be designated as UP carbons of the ring or DOWN carbons of the ring. In conformer A (labeled above) the UP carbons are C_1, C_3 and C_5. ("Pointed" in the upward direction). The DOWN carbons of conformer A are C_2, C_4 and C_6 ("Pointed" in the downward direction.). In conformer B, the UP carbons of the ring are C_2, C_4 and C_6. The DOWN carbons of the ring are C_1, C_3, C_5. All UP carbons in A become DOWN carbons in B and all DOWN carbons in A become UP carbons in B.

3. Fill in lines to represent the axial and equatorial positions at the numbered carbons of the conformation you drew *only for those carbons of the ring that have substituents other than hydrogen.* Axial substituents are drawn straight UP on UP carbons and straight DOWN on DOWN carbons. Equitorial substituents are drawn DOWN 7 OUT on UP carbons and UP & OUT on down carbons. Be sure to clearly show axial and equatorial lines on each carbon. For 1R-3,3-dichlorocyclohexanol, only fill in the axial and equatorial lines on the C_1 and the C_3 carbons.

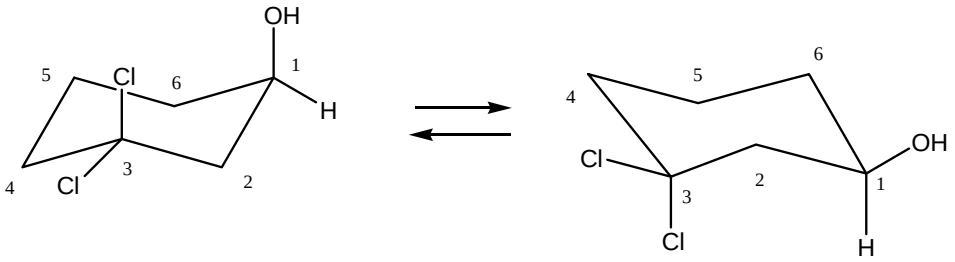


4. Using the numbering scheme in the original structure shown in step 1 and the numbering scheme in the chair conformation templates drawn in step 3, fill in the substituents on the chair conformations. Use the guidelines below place substituents in the proper axial/equatorial orientation.

   Substituents represented on wedges are always positioned UP.
   The UP position on an UP carbon of the ring is AXIAL
   The UP position on a DOWN carbon of the ring is EQUITORIAL

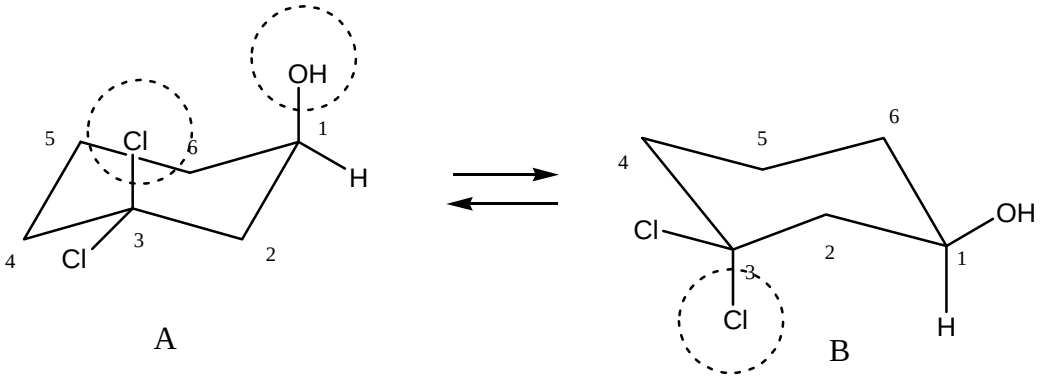
   Substituents on dotted lines are positioned DOWN.
   The DOWN position on a DOWN carbon of the ring is AXIAL
   The DOWN position on an UP carbon of the ring is EQUITORIAL.

   So for 1R-3,3-dichlorocyclohexanol, the two chair conformations are….



   These conformations can then be used to evaluate the absolute or relative steric strain energies.

5. In a chair conformation, (with a few exceptions) only *axial* substituents will give rise to steric strain energy. (This is true for 1R-3,3-dichlorocyclohexanol). In each of the conformations drawn in step 4, circle the axial substituents (other than hydrogen). These substituents will have 1,3-diaxial interactions that give rise to steric strain energy (SSE)

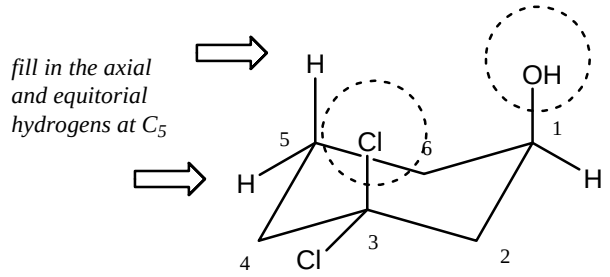


A B

6. Identify and list the 1,3-diaxial interactions present in conformer A. Analyze each axial substituent for 1,3-diaxial interactions.

   For conformer A of 1R-3,3-dichlorocyclohexanol, start with the hydroxyl substituent bonded to C_1. Starting with the carbon atom bonded to the hydroxyl group (i.e., C_1) count over three carbons in the ring *in both directions* (i.e., 1, 2, 3 and in the other direction 1, 6, 5). Fill in axial and equatorial lines at C_3 and C_5 if they are not already shown and fill in the H atoms for these positions.

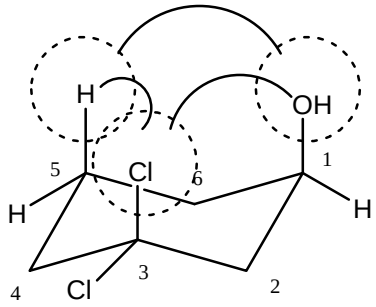
fill in the axial and equitorial hydrogens at C_5



For conformer A of 1R-3,3-dichlorocyclohexanol, the substituents are already filled in for C_3 but they need to be filled in for C_5.

A

The axial ATOM (hydrogen or any other atom or substituent) bonded to the C_3 or C_5 will have a 1,3-diaxial interaction with the axial hydroxyl group at C_1. There is also a 1,3-diaxial interaction between axial groups at C_3 and C_5, since these substituents also have a "1,3-diaxial relative position".

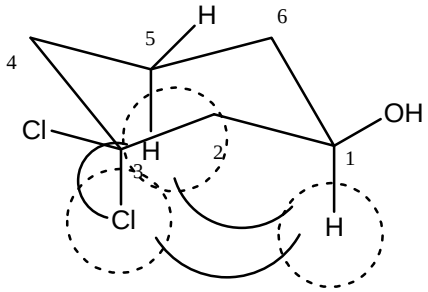


The 1,3-diaxial interactions for conformer A of 1R-3,3-dichlorocyclohexanol are shown by the curved lines in the structure at the left. These 1,3-diaxial interactions are HO-Cl (2 axial groups at C_1 and C_3), HO-H (2 axial groups at C_1 and C_5) and H-Cl (2 axial groups at C_3 and C_5)

A

In this example, the axial Cl substituent is already accounted for. However, in other examples, the process would be repeated for other axial substituents.

Repeat the process for the other conformer (B), drawn in step 4.



The 1,3-diaxial interactions for conformer B of 1R-3,3-dichlorocyclohexanol are shown by the curved lines in the structure at the left. These 1,3-diaxial interactions are H-Cl (2 axial groups at C_1 and C_3) and H-Cl (2 axial groups at C_3 and C_5)

B

7. List the 1,3-diaxial interactions for each conformer and assign energy values to each interaction. The energy values are typically provided in the textbook or will be provided on an exam. The sum of *all* 1.3-diaxial interactions for a given conformer is the total SSE for that conformer.

Conformer A		**Conformer B**	
1,3-diaxial interaction	***Energy****	***1,3-diaxial interaction***	***Energy****
HO-Cl	0.75 kcal/mol	H-Cl	0.25 kcal/mol
HO-H	0.5 kcal/mol	H-Cl	0.25 kcal/mol
H-Cl	0.25 kcal/mol		
Total SSE	1.5 kcal		0.5 kcal

* *Energy values taken from Organic Chemistry, 5th edition by John McMurry, p. 136*

Conformer B for 1R-3.3-dichlorocyclohexanol is lower energy and more stable than conformer A.

The following guidelines can be used to determine the percent distribution of two chair conformers using the Gibbs free energy equation and some simple algebra.

8. The free energy (ΔG°) of the equilibrium process going from one conformer to the other, i.e., from A to B as shown in step 4 or 5 can be calculated from the equation below where the product is conformer B and the reactant is conformer A.

$$\Delta G^\circ = E_{\text{product}} - E_{\text{reactant}}$$

$$\Delta G^\circ = 0.5\text{kcal/mol} - 1.5\text{kcal/mol}$$
$$\Delta G^\circ = -1.0\text{kcal/mol}$$

9. Calculate the K_{eq} for the process using the Gibbs Free-Energy equation. A temperature (in °K) must be given and R, a constant, will be provided. For the two conformers of 1R-3,3-dichlorocyclohexanol, assume the calculation is at 25°C (must be converted to °K by 25°C + 273 = 298°K)

Gibb's Free Energy Equation: $\Delta G^\circ = -RT \ln K_{eq}$
R = 0.002kcal/°Kmol

$$\Delta G^\circ = -RT \ln K_{eq}$$
$$-1.0\text{kcal/mol} = -(0.002\text{kcal/°Kmol})\,(298\text{°K})\,\ln Keq$$
$$-1.0\text{kcal/mol} = -(0.596\text{kcal/mol})\,\ln Keq$$
$$1.677 = \ln Keq$$
$$5.312 = Keq$$

$$Keq = \frac{[\text{Product}]}{[\text{Reactant}]} = \frac{[B]}{[A]} = 5.312$$

10. From the Keq, calculate the percent distribution of products using the two equations: Keq = B/A and 100% =A+B.

$K_{eq} = B/A$	$100\% = A + B$
$5.312 = B/A$	$100\% = A + 5.312A$
$5.312A = B$	$100\% = 6.312A$
	$15.8\% = A$
	$84.2\% = B$