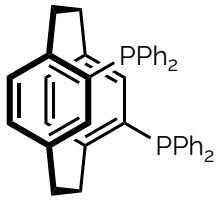
Stereochemical Descriptors for Stereogenic Planes - *Worksheet*

Question 1

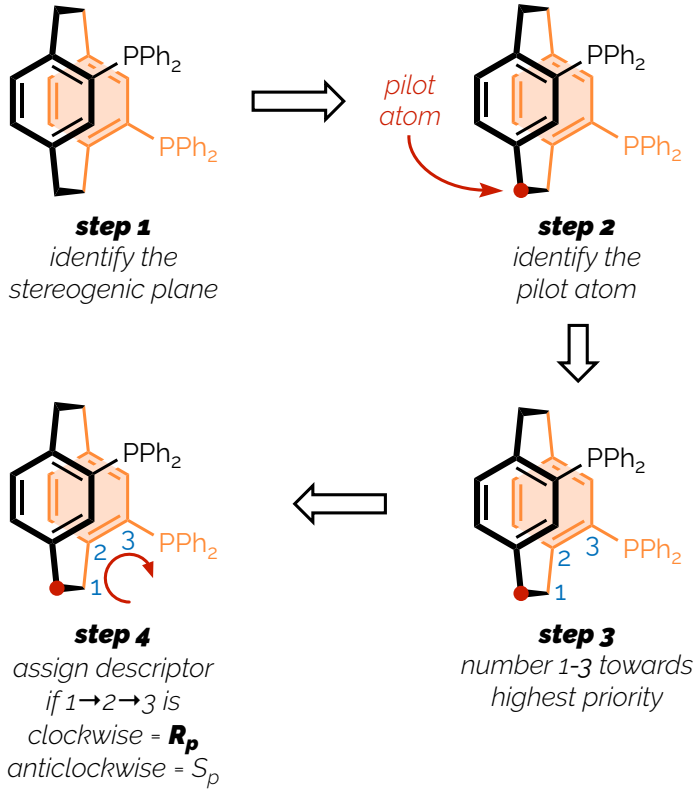
Assign the stereochemical descriptor for PhanePhos, a diphosphine ligand used in hydrogenations:



i) using *R/S* nomenclature;
ii) using the *P/M* nomenclature.

Answer 1i

The steps required to treat a cyclophane as a 'stereogenic centre' are given in the diagram below:



step 1
identify the stereogenic plane

step 2
identify the pilot atom

step 3
number 1-3 towards highest priority

step 4
*assign descriptor if 1→2→3 is clockwise = **R_p***
anticlockwise = S_p

Step 1 - identify the stereogenic plane. This is the plane of the cyclophane with the most atoms in a single plane. PhanePhos is C_2-symmetric so both decks of the cyclophane are identical so it doesn't matter which we chose. As I know what comes next, I've chosen the bottom deck as it will make everything easier.

Step 2 - identify the pilot atom. This is the first atom out of the stereogenic plane but connected directly to the highest priority end of the plane. In English, this means it is the atom closest to the highest priority substituent that is not in the plane. This is shown with a red spot.

Step 3 - number the atoms 1 to 3. Start your numbering with the atom of the plane attached to the pilot atom. Then number the next two atoms moving towards the highest priority group. This means the ipso position of the aromatic ring will be 2 and the carbon attached to the phosphorus is 3.

Step 4 - assign the descriptor. Draw an arrow moving from 1→2→3. If the arrow is clockwise when viewed from the pilot atom the configuration is R_p (as is the case here). If it is anticlockwise, the descriptor is S_p.

*This is **(R_p)-PhanePhos** or **(R_p)-4,12-bis(diphenylphosphino)[2.2]paracyclophane** (or it has a ridiculous 'standardised' name*

Answer 1ii

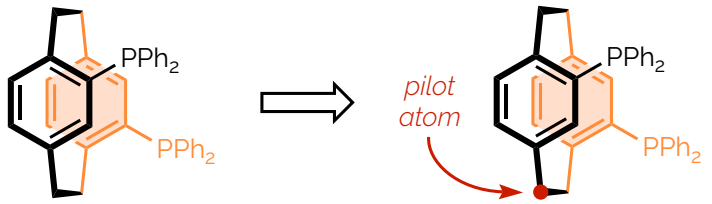
Treating the cyclophane as a helix involves a similar process but requires you to draw a Newman projection.

Step 1 - identify the stereogenic plane exactly the same as above.

Step 2 - identify the pilot atom as before.

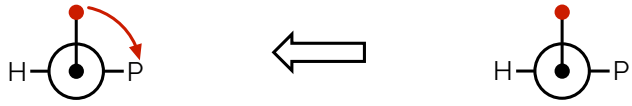
Step 3 - Draw a Newman projection that has the pilot atom at the front and the stereogenic plane behind it.

Step 4 - Assign the descriptor. Rotate the pilot atom so that it it superimposes over the highest priority group of the stereogenic plane. The rotation must be less than 180°. It is the smallest angle required to overlap the two groups. If the rotation was clockwise or plus, the descriptor is P. If it is anticlockwise, it is M or minus.



step 1
identify the stereogenic plane

step 2
identify the pilot atom



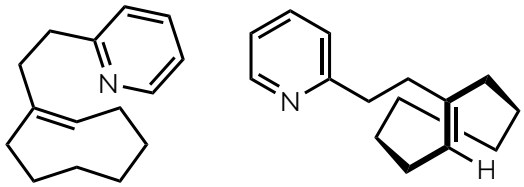
step 4
*assign descriptor rotation of the pilot to highest priority is clockwise = **P***
anticlockwise = M

step 3
draw Newman projection with pilot atom at front

*This means this enantiomer of PhanePhos is **P-PhanePhos**.*

Question 2

Assign both the *R* or *S* and the *P* or *M* descriptors to the chiral alkene ligand below:



Answer 2

It is probably most appropriate to consider this to be a cyclophane and assign the stereochemical descriptors similarly.

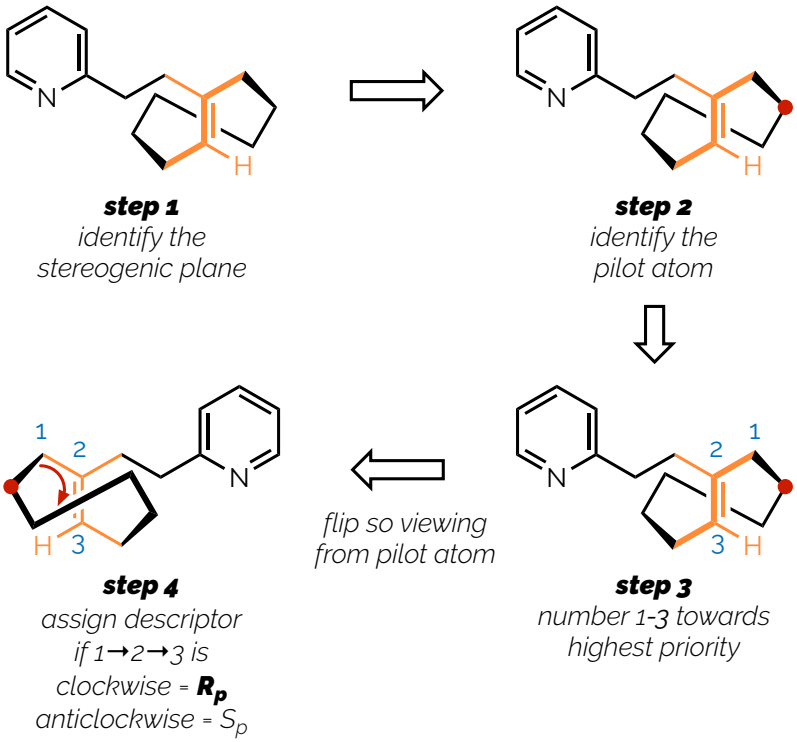
Step 1 - identify the stereogenic plane. This is the alkene and the atoms directly attached (they are not strictly in plane as there is some twisting in the alkene).

Step 2 - identify the pilot atom. This is the atom of the 'cyclophane' that is attached directly to the stereogenic plane but is both out of the plane and at the end highest priority end of the plane. My interpretation of these rules would suggest that it should be an atom of the cyclophane itself and not the ethylpyridine substituent that is attached to the alkene. The carbon indicated by a red spot meets these criteria.

Step 3 - number the atoms 1 to 3 of the . Start your numbering with the atom of the plane attached to the pilot atom. Again, an alkene doesn't fully fit the rules laid out for cyclophanes but I believe the numbering should continue through the plane of cyclophane and not the substituent.

Step 4 - assign the descriptor. You need to view the plane from the pilot atom. This means rotating the molecule so that we look down upon the numbered atoms. If an an arrow moving from 1→2→3 is clockwise the configuration is R_p (as is the case here). If it is anticlockwise, the descriptor is S_p.

*This is **(R_p)-2-(2-(cyclooct-1-en-1-yl)ethyl)pyridine**.*



step 1
identify the stereogenic plane

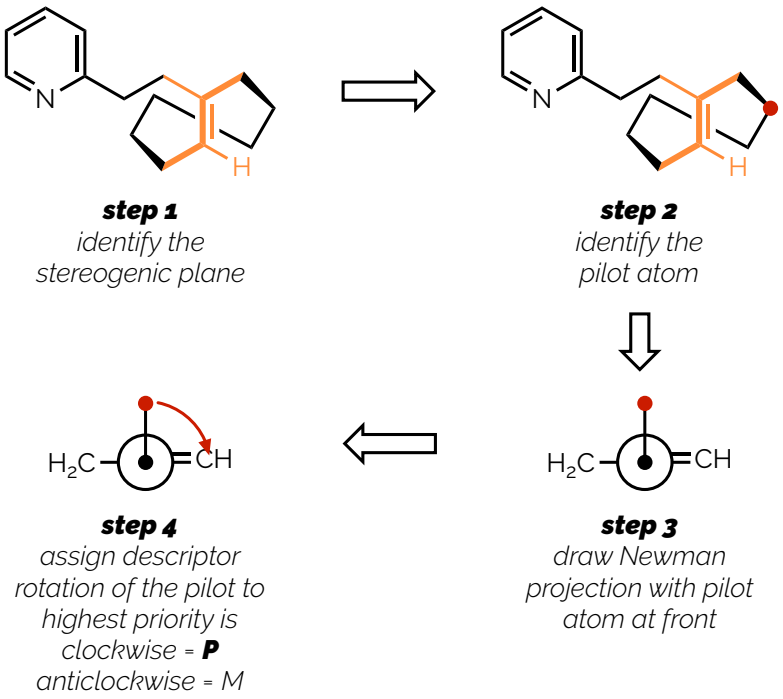
step 2
identify the pilot atom

step 3
number 1-3 towards highest priority

flip so viewing from pilot atom

step 4
assign descriptor
if 1→2→3 is
*clockwise = **R_p***
anticlockwise = S_p

Alternatively, the alkene could be treated as a helix. For once, I think the recommendation to use the helical description makes sense. It is much easier to determine the stereochemical descriptor if you consider this to be a helix.



step 1
identify the stereogenic plane

step 2
identify the pilot atom

step 3
draw Newman projection with pilot atom at front

step 4
assign descriptor
rotation of the pilot to highest priority is
*clockwise = **P***
anticlockwise = M

Step 1 - identify the plane in the same manner as above.

Step 2- identify the pilot atom as above.

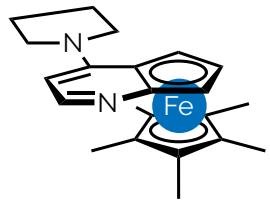
Step 3 - Draw a Newman projection with the pilot atom in front of the stereogenic plane.

*Step 4 - Assign the stereochemical descriptor by rotating the pilot atom through the smallest possible angle to get it to overlap the highest priority atoms of the plane. If you rotate the pilot atom clockwise the descriptor is P and if you rotate anticlockwise it is M. The alkene above is **P-2-(2-(cyclooct-1-en-1-yl)ethyl)pyridine**.*

P.T.O for metallocenes

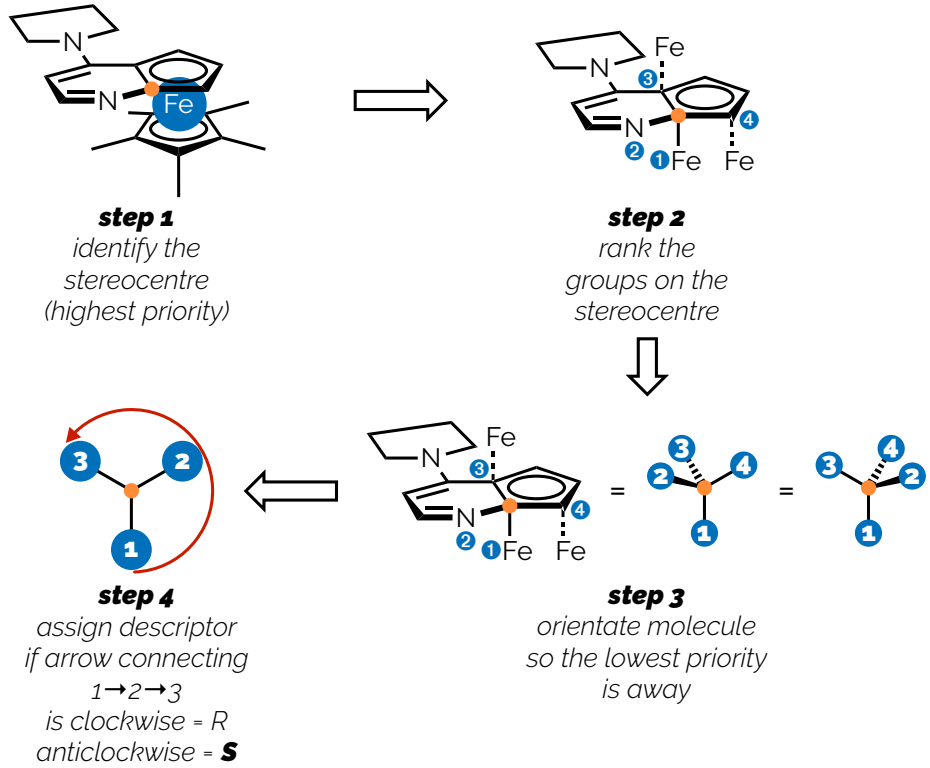
Question 3

Assign the recommended stereochemical descriptor based on a stereocentre for Fu's planar chiral DMAP derivative below. Then (what a surprise) determine its planar chiral descriptor.



Answer 3

Assigning a stereochemical descriptor to a metallocene is very different. The recommended method treats the metallocene as if there were σ bonds between the metal and the arene ring. This results in each carbon of the arene having four bonds and they can be considered to be a stereocentre. After this, the rules for determining the descriptor are the same as those for a 'normal' stereocentre.



step 1
identify the stereocentre (highest priority)

step 2
rank the groups on the stereocentre

step 3
orientate molecule so the lowest priority is away

step 4
assign descriptor if arrow connecting 1→2→3 is clockwise = R anticlockwise = ***S***

Step 1 - identify the stereocentre. This is the highest priority atom of the arene ring as determined using the standard CIP rules. All the atoms are carbon, so they are all same at the first atom so you move along the chain (or around the ring until a difference is located. This example is relatively simple. One carbon is attached to a nitrogen atom, which is a higher priority atom than either carbon or hydrogen, This is the highest priority atom.

Step 2 - Rank the substituents on the stereocentre as for a typical stereogenic centre. The only trick is to remember that the iron is connected to the arene ring atoms so these would have a higher priority than an 'exo-cyclic' carbon. In the case of this DMAP derivative, the two highest ranked groups are determined by the atoms attached directly to the stereocentre. The highest atomic number is the iron atom so this is priority 1, then priority 2 is the nitrogen atom. The remaining two groups both have a carbon attached directly to the stereocentre. Moving to the second atom and one of the groups (furthest away from us in the drawing above) is attached to iron and two carbons while the other is attached to iron, a carbon atom and a hydrogen atom. The group furthest away takes priority 3.

Step 3 - orientate the lowest priority group so that it points away.

Step 4 - assign the descriptor by drawing an arrow through ranks 1→2→3. If this arrow is clockwise the ferrocene is said to be R. If it is anticlockwise the ferrocene is S. In this example it is ***S****.*

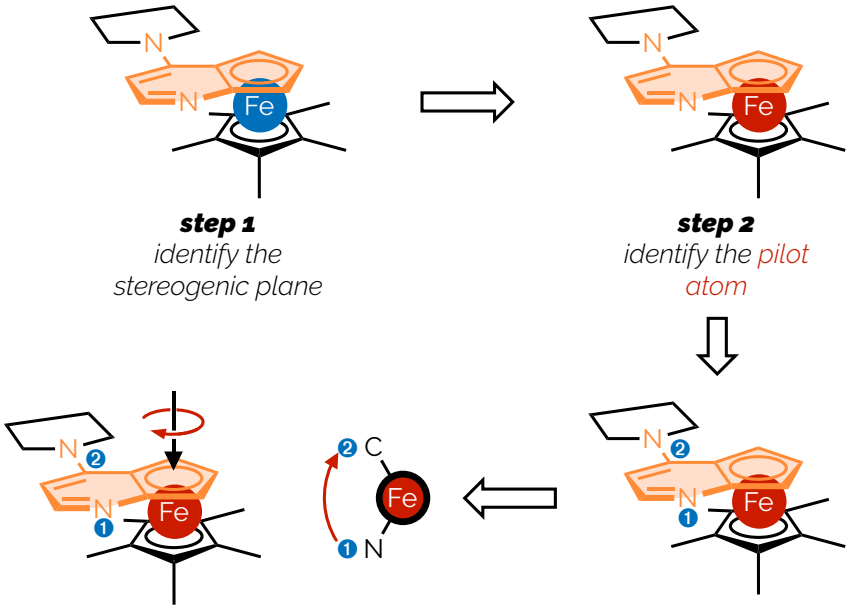
The alternative descriptor treats the ferrocene as planar chiral and normally uses the descriptors R_p or S_p although I have seen the use of R_{Fe} and S_{Fe}.

Step 1 - identify the stereogenic plane. This is the arene fused to the pyridine ring as it has the most atoms.

Step 2 - identify the pilot atom. This is the highest priority atom attached directly to the plane. It is frequently the metal atom.

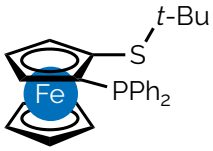
Step 3 - identify the two highest priority groups on the stereogenic plane using the CIP rules. The highest priority will be the nitrogen atom and the next is the carbon atom directly attached to the arene ring.

Step 4 - assign the stereochemical descriptor. View the arene ring from the face opposite *the pilot atom. Draw an arrow connecting the two highest priority groups by the smallest angle. If the arrow from 1→2 is clockwise the molecule is* ***R*****p**, *if it is anticlockwise it is* ***S*****p**. This enantiomer of the DMAP catalyst is ***R*****p**. Frustratingly, this is the opposite designation to the previous method but that is how the two systems work!



Question 4

The last questions asks exactly the same as all the others (that is the nature of practice), use the two different systems to determine the configuration of the following ferrocene derivative:



Answer 4

I'll start with the recommended stereochemical descriptor and treating the molecule as if it had a stereocentre.

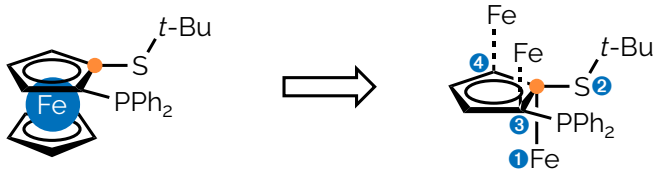
Step 1 - identify the stereocentre. This is the highest priority atom of the arene ring as determined using the standard CIP rules. All the atoms of the ring are carbon so it is necessary to look at the second atom. Again, all the atoms of the ring are bonded to the iron so we can ignore it. Then it is sulfur versus phosphorus versus hydrogen. Sulfur has the highest atomic number so it takes priority..

Step 2 - Rank the substituents on the stereocentre as for a typical stereogenic centre. Iron is ranked higher than the sulfur and carbon atoms attached to the stereocentre. The second ranked substituent is the thiol ether. Third is the carbon attached to the phosphorus ahead of the carbon attached to a hydrogen atom.

Step 3 - orientate the lowest priority group so that it points away. It is already in the correct arrangement.

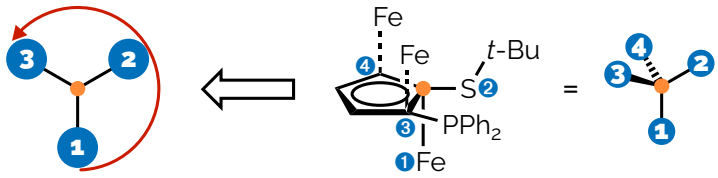
Step 4 - assign the descriptor by drawing an arrow through ranks 1→2→3. If this arrow is clockwise the ferrocene is said to be R. If it is anticlockwise the ferrocene is S. In this example it is ***S***.

The diagram showing this is on the next page:



step 1
identify the stereocentre (highest priority)

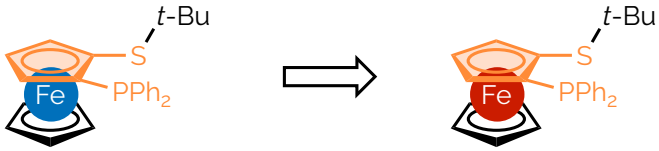
step 2
rank the groups on the stereocentre



step 4
*assign descriptor if arrow connecting 1→2→3 is clockwise = R anticlockwise = **S***

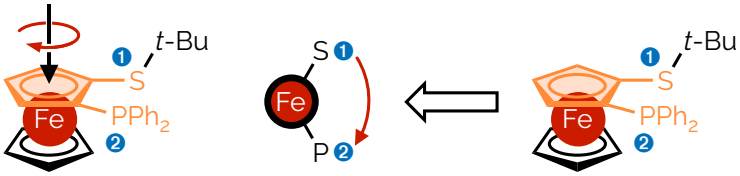
step 3
orientate molecule so the lowest priority is away

The alternative nomenclature will give the opposite descriptor but let's work through it anyway …



step 1
identify the stereogenic plane

step 2
identify the pilot atom



step 4
*assign descriptor viewing from face opposite pilot atom - if 1→2 is clockwise = **R_p** if anticlockwise = S_p*

step 3
identify the two highest ranked groups of arene ring

Step 1 - identify the stereogenic plane. This is the arene fused to the pyridine ring as it has the most atoms.

Step 2 - identify the pilot atom. This is the highest priority atom attached directly to the plane. It is frequently the metal atom.

Step 3 - identify the two highest priority groups on the stereogenic plane using the CIP rules. The sulfur has a higher ranking than the phosphorus as it is one atomic number greater.

*Step 4 - assign the stereochemical descriptor. View the arene ring from the face opposite the pilot atom. Draw an arrow connecting the two highest priority groups by the smallest angle. If the arrow from 1→2 is clockwise the molecule is **R_p**, if it is anticlockwise it is **S_p**.* This enantiomer of ligand is ***R_p***, as stated above, this is the opposite to the other nomenclature.

I hope this has helped.