NMR -

From ^{1}H NMR, we get:

- Chemical shift data (δ) - This tells us what kinds of protons we have.
- Integration data - This tells us the ratio of each kind of proton in our sample.
- ^{1}H - ^{1}H coupling data - This tells us about protons that are near other protons.

Neighboring protons couple to each other and split each other giving rise to multiple line patterns in NMR spectra.

If a proton is split by n equivalent protons, it will have n+1 lines in its signal, and the intensities of those lines will be given by Pascal's triangle.

BUT, protons that come at the same chemical shift (δ) do not split each other.

Today, we will learn how to determine if protons are equivalent and more about about ^{1}H - ^{1}H couplings.

Topicity

Topicity describes the symmetry relationship of two or more groups (or atoms) in a molecule that have identical connectivities (i.e., they are connected to the molecule in the same way). Two or more groups (or atoms) are:

homotopic if the groups (or atoms) are in identical environments. Homotopic groups are related to each other either by a bond rotation or an axis of rotation in the molecule.

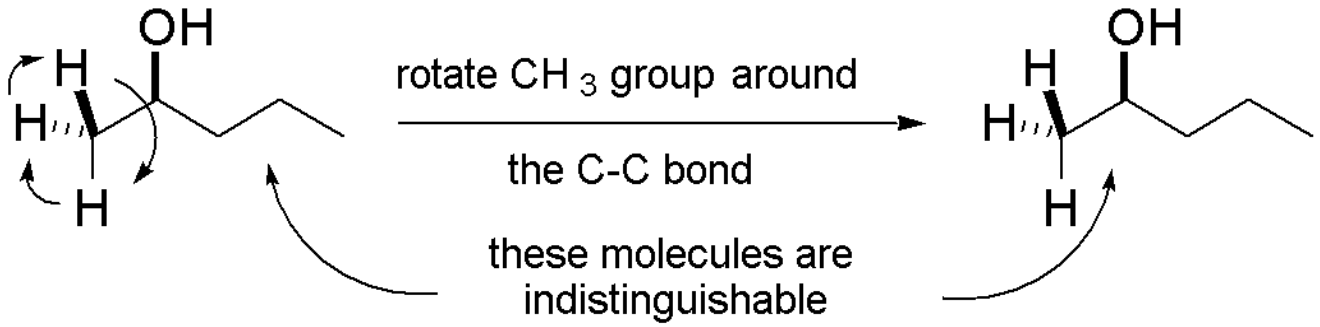
enantiotopic if the groups (or atoms) are in mirror image environments. Enantiotopic groups are related to each other by a reflective symmetry element (the most common being a mirror plane within the molecule).

diastereotopic if the groups (or atoms) are in different environments. Diastereotopic groups are not related by any symmetry elements or bond rotations.

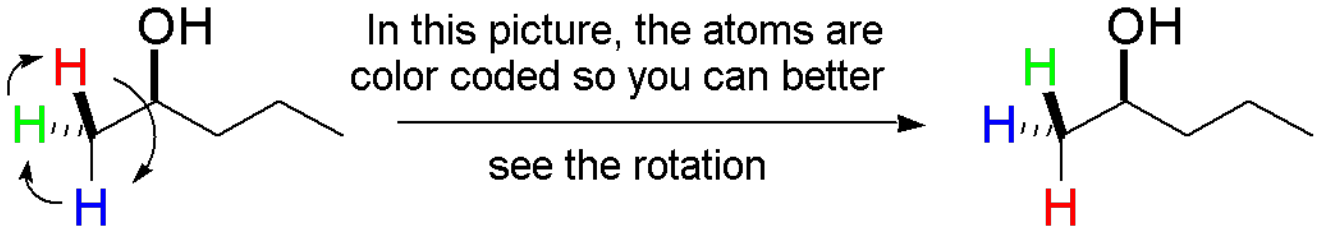
The best way to understand these is by looking at examples, but why do we care about this and why are we learning it in spectroscopy? Because the appearance of protons and groups in NMR spectra depends on whether they are homotopic, enantiotopic, or diastereotopic. **Homotopic and enantiotopic protons always appear at the same δ, but, diastereotopic protons can appear at different δ □□□□□if diastereotopic protons are attached to the same carbon they can split each other (if they appear at different δ).** You can tell that these are important concepts because they are in bold. We will repeat these points on a later slide.

Homotopic Groups

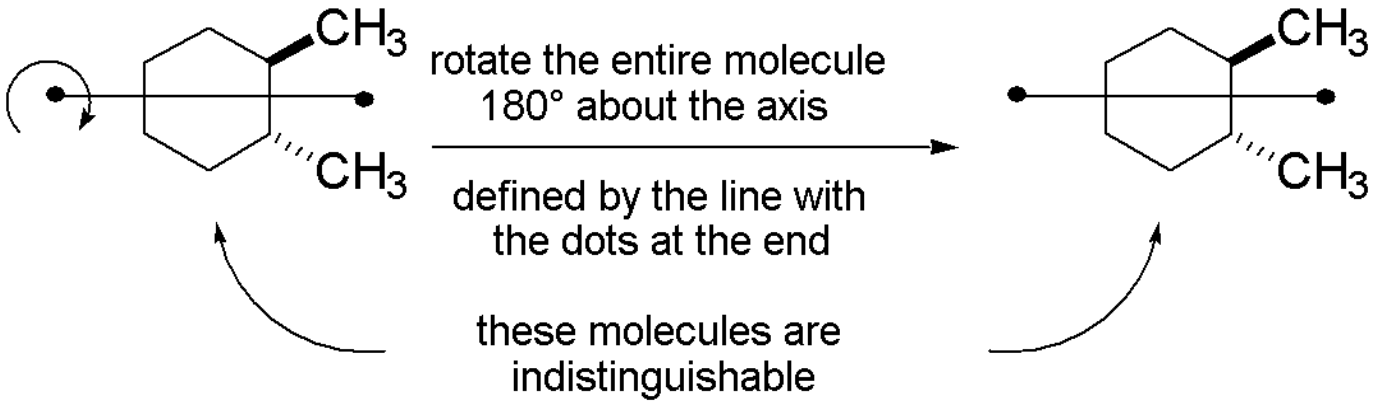
Homotopic groups are in identical environments. They are related to each other either by a bond rotation or an axis of rotation in the molecule. This means that if we can rotate a bond and get an indistinguishable molecule (i.e., if you walk out of the room and someone rotates a bond, when you return, you can't tell that bond has been rotated), or rotate about an axis that runs through the molecule (i.e., if you walk out of the room and someone rotates the entire molecule, when you return, you can't tell that molecule has been rotated), then the groups that change place upon rotation are homotopic. Examples:



Rotation about the CH_3-C bond produces a molecule which is indistinguishable in all respects with the original molecule. All the groups or atoms that change places upon rotation, in this case, the three H's of the methyl group, are homotopic.



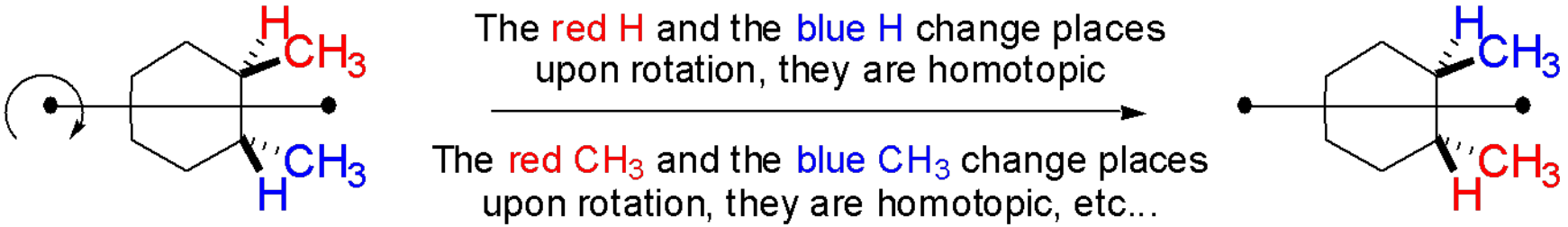
Homotopic Groups, More Examples



This operation is called "rotation about a C_2 axis." This means that we rotated the molecule by 1/2 of 360°. Rotation about a C_3 axis means that we rotated the molecule by 1/3 of 360°. Rotation about a C_4 axis means that we rotated the molecule by 1/4 of 360°. Rotation about a C_5 axis means… you get the picture.

Note that we can draw the molecule in a flat conformation rather than the chair conformation. This is because the molecule is fluxional, and we are interested in its time-averaged properties.

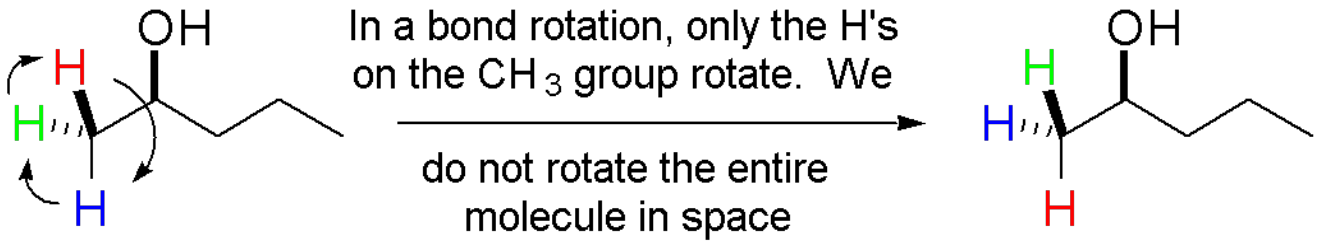
Whenever we rotate about a C_n axis, all the groups that change places are homotopic



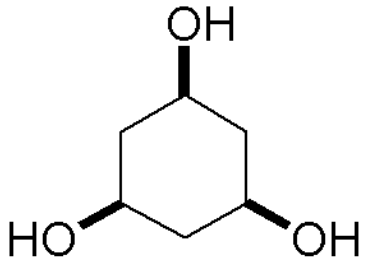
Notes on Rotation About a C_n Ais

Note that rotation about a C_2 axis is akin to flipping a molecule like a hamburger patty on a grill (oops... we're in Boulder. If you're a vegetarian, think of flipping a pancake).

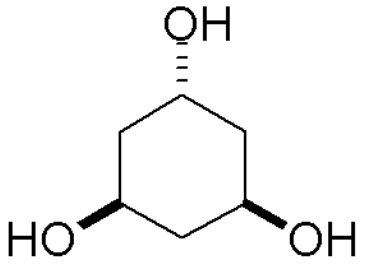
Also, note that rotation about the C-C bond of a CH_3 group is NOT the same as a C_3 axis. In a bond rotation, only the CH_3 group rotates, in a C_3 axis, the entire molecule rotates.



The molecule shown below on the left contains a C_3 axis, and all the OH groups are homotopic to each other. Can you identify the C_3 axis? How about the molecule shown below on the right, does it contain any kind of C_n axis?



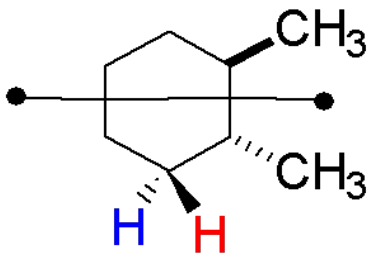
Contains a C_3 axis, find it.



Does this molecule c ontains a C_3 axis? How about a C_2 axis?

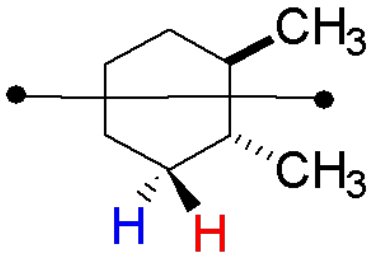
A Question...

As we've seen, the molecule shown below has a C_2 axis. So, are the two H's shown homotopic?

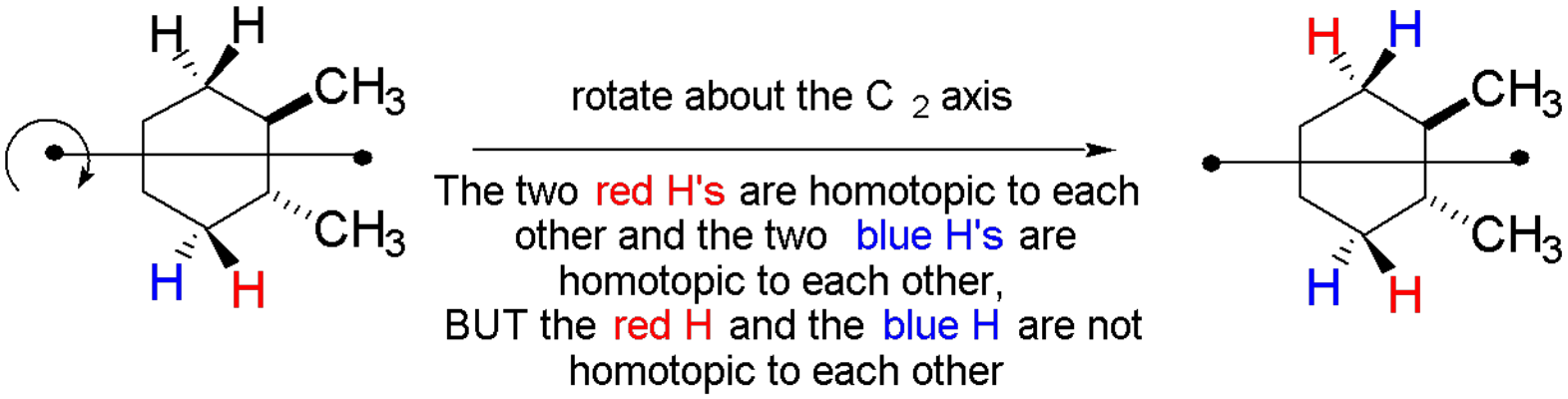


Examples of Groups that are Not Homotopic

As we've seen, the molecule shown below has a C_2 axis. So, are the two H's shown (the red and blue ones) homotopic?

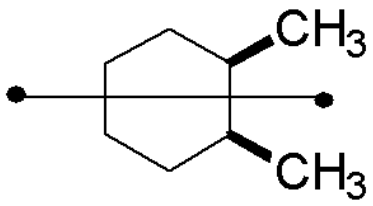


No! In order for two groups to be homotopic, they have to change places with each other upon rotation. These H's do not change places with each other, rather they change places with hydrogens across the ring and are homotopic with respect to those hydrogens, but not to each other.



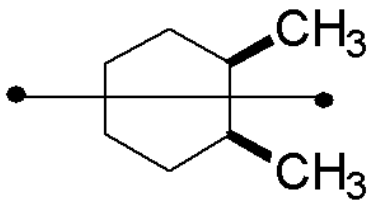
Another Question...

How about the methyl groups in the molecule shown below, are they homotopic?

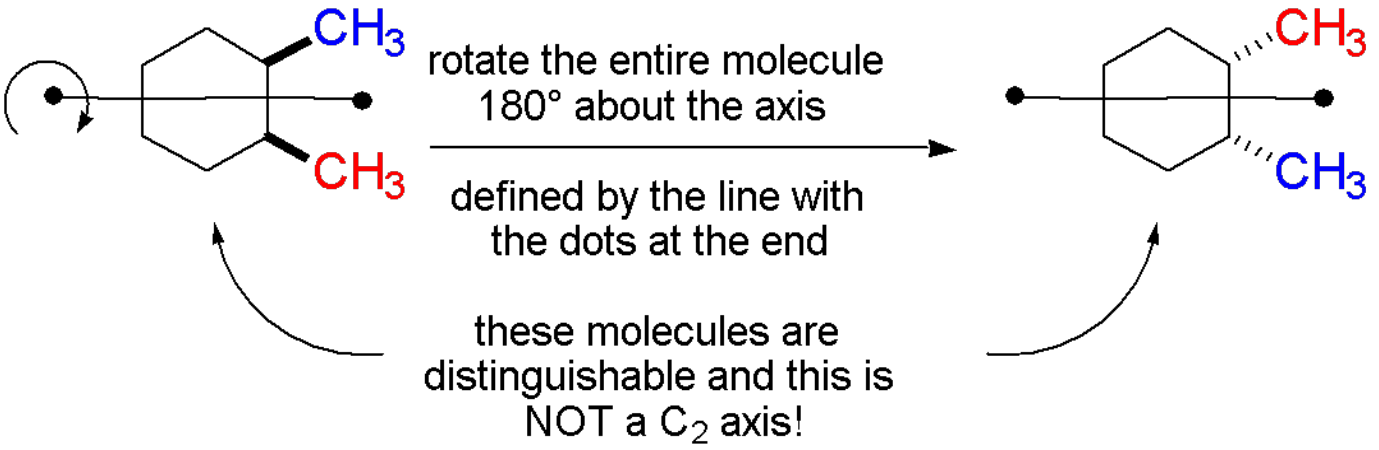


Examples of Groups that are Not Homotopic

How about the methyl groups in the molecule shown below, are they homotopic?

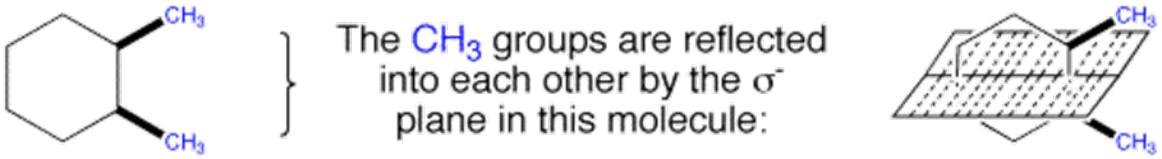


No, they are not homotopic because this molecule does not have a C_2 axis. Rotation about the axis shown produces a molecule which can be distinguished from the starting molecule (if you were to leave the room, have someone apply this rotation, and then return, you'd be able to tell that the molecule was rotated since the methyl groups are now pointing down).

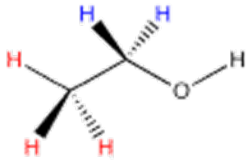


Enantiotopic Groups

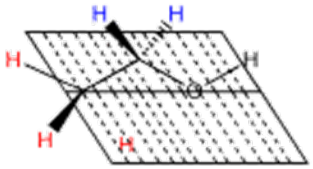
Enantiotopic groups are in mirror image environments. They are related to each other by a reflection within the molecule usually by a mirror (σ) plane (there are other reflections that are more complex, but they are rare and will not be described here). These are the same σ-planes that you used to determine if a molecule is chiral or achiral. So, if we can find a σ-plane in our molecule, the groups that are reflected into each other by that plane are enantiotopic. For example:



The red H's are homotopic because the CH_3 group can undergo rotation, thereby interchanging the H's.



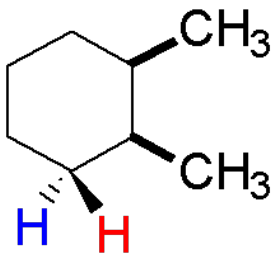
The blue H's are reflected into each other by the σ plane and are enantiotopic



If groups can be designated as either homotopic or enantiotopic, they are homotopic (i.e., homotopic takes precedence).

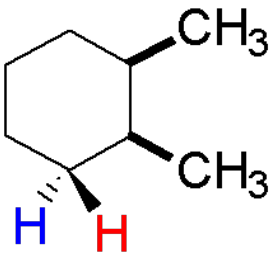
A Question…

As we've seen, the molecule shown below has a σ- plane. So, are the two H's shown enantiotopic?

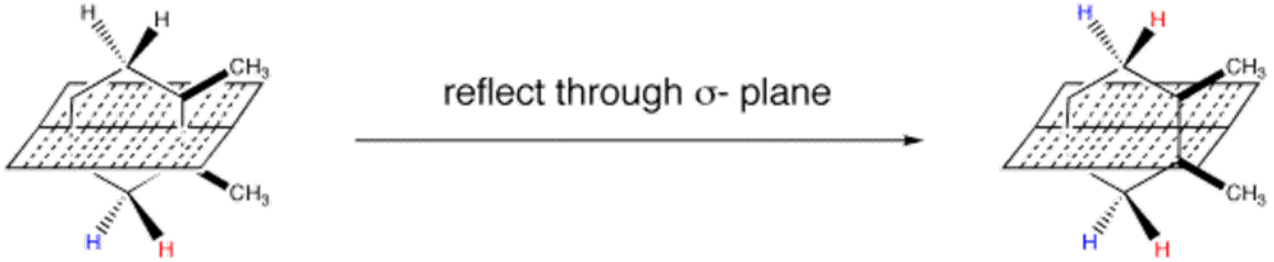


Examples of Groups that are Not Enantiotopic

As we've seen, the molecule shown below has a σ- plane. So, are the two H's shown enantiotopic?



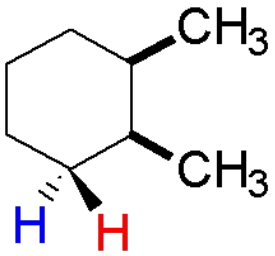
No! In order for two groups to be enantiotopic, they have to change places with each other by the action of the σ- plane. These H's do not change places with each other, rather they change places with hydrogens across the ring and are enantiotopic with respect to those hydrogens, but not to each other.



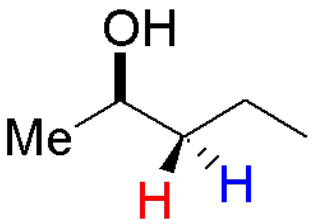
The two red hydrogens are enantiotopic with respect to each other, and the two blue hydrogens are enantiotopic with respect to each other.

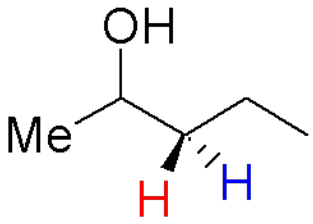
Diastereotopic Groups

Diastereotopic groups are in different environments. They are not related to each other by any symmetry element. For example, the red and blue hydrogens in the molecule shown below are not related to each other by any symmetry element. As we saw in the previous slide, there is a mirror plane in the molecule, but it does not interconvert those hydrogens with each other. Another way to look at it is that the red hydrogen is always *syn*- to the methyl group while the blue hydrogen is always *anti*- to the methyl group.



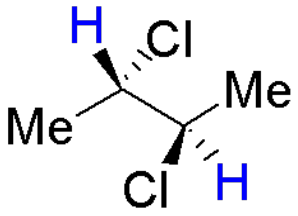
In the molecule shown below, the red and blue H's are also not related by any symmetry element, and are, therefore, diastereotopic. Note that it does not matter if we draw the OH with a bold line (i.e., if we have a single enantiomer) or with a non bold line (if we have a racemic mixture); either way, the carbon bearing that OH is tetrahedral and the carbon cannot be planar, so there are no symmetry elements.



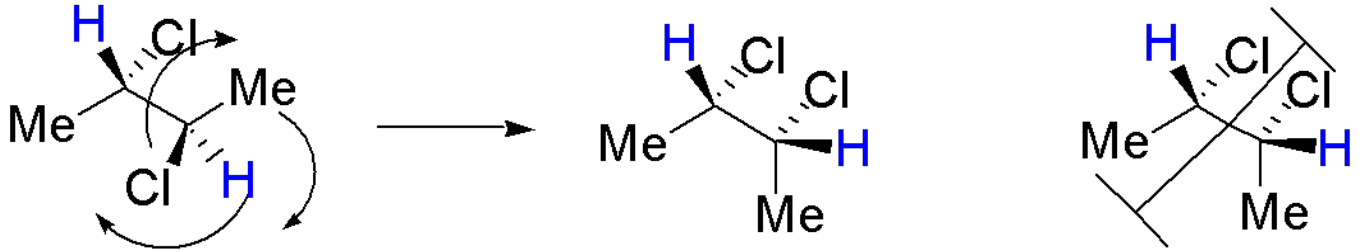


Some Things to Consider

Since molecules are fluxional, we are allowed to rotate about σ- bonds (but not π-bonds) and place the molecule in whatever conformation provides the highest symmetry. For example, the molecule shown in the conformation below has no symmetry elements that we have discussed in that conformation:



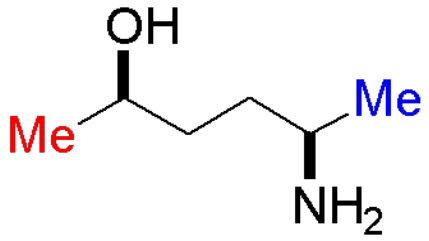
But, we can rotate about the central C-C bond:



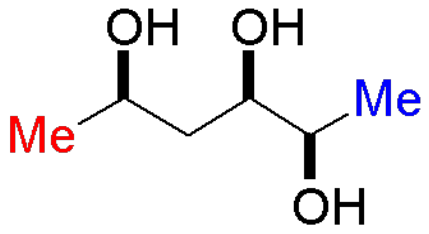
By rotating about the central C-C bond and placing the methyl groups eclipsed, we now have a conformation with a mirror plane running through the central C-C bond which interconverts the blue H's, the Me groups and the Cl's, rendering them all enantiotopic.

And Another Thing...

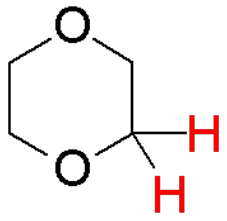
We can only talk about the topicitiy of groups that have identical connectivities. If the groups are connected in the molecule in a fundamentally different way, then they are just plain different, and the concept of topicity does not apply. For example, in the molecule shown below, the methyl groups do not have identical connectivities, one is near the OH, the other near the NH_2, so they are not connected to the molecule in the same way and the concept of topicity does not apply.



In the molecule shown below, both methyl groups are near an OH, but the presence of the third OH renders them not connected to the molecule in the same way, and therefore the concept of topicity does not apply.



Indicate if the Labeled Groups are Homotopic, Enantiotopic, or Diastereotopic, and if They Must Appear at the Same Chemical Shift



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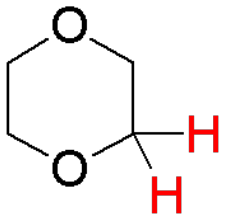
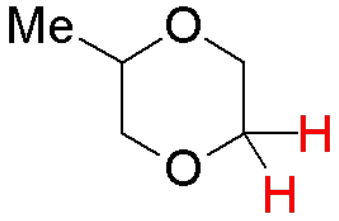


Enantiotopic (mirror plane through the ring in the plane of the screen)

Same δ



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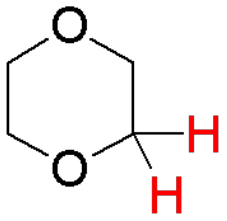
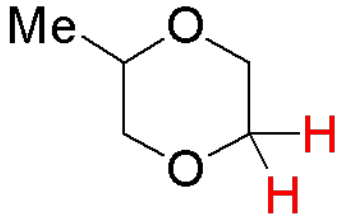


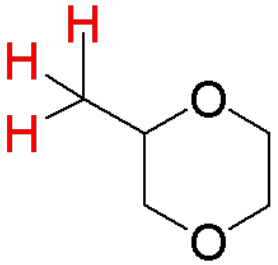
Enantiotopic (mirror plane through the ring in the plane of the screen)

Same δ



Diastereotopic (Me group is NOT in the plane of the screen, disrupts symmetry)

Could be different δ



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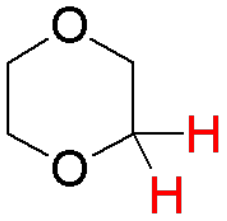
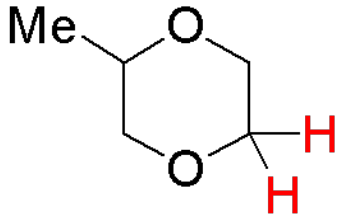


Enantiotopic (mirror plane through the ring in the plane of the screen)

Same δ



Diastereotopic (Me group is NOT in the plane of the screen, disrupts symmetry)

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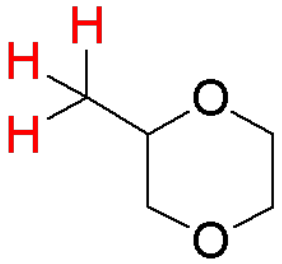
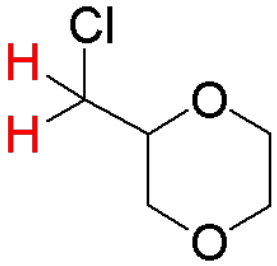


homotopic (H's on methyl groups are always homotopic since they can interconvert by rotation)

Same δ



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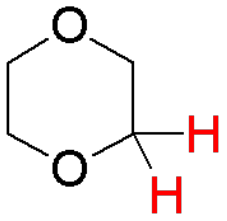
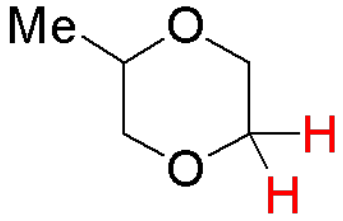


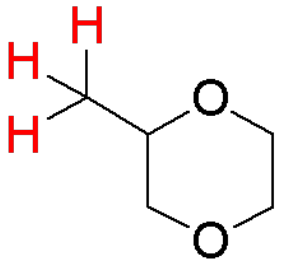
Enantiotopic (mirror plane through the ring in the plane of the screen)

Same δ



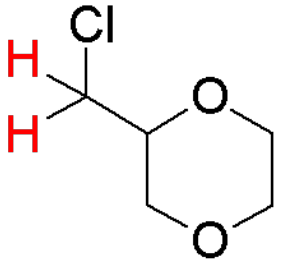
Diastereotopic (Me group is NOT in the plane of the screen, disrupts symmetry)

Could be different δ



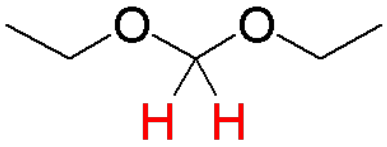
homotopic (H's on methyl groups are always homotopic since they can interconvert by rotation)

Same δ

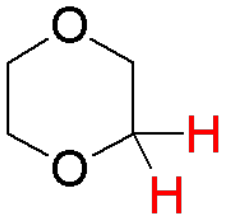


diastereotopic (there is no symmetry element in this molecule)

Could be different δ

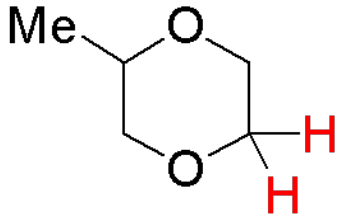


Indicate if the Labeled Groups are Homotopic, Enantiotopic, or Diastereotopic, and if They Must Appear at the Same Chemical Shift



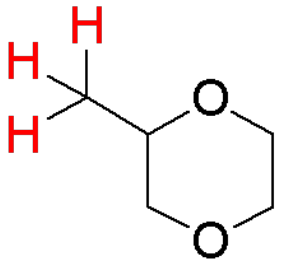
Enantiotopic (mirror plane through the ring in the plane of the screen)

Same δ



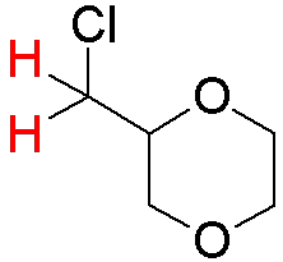
Diastereotopic (Me group is NOT in the plane of the screen, disrupts symmetry)

Could be different δ



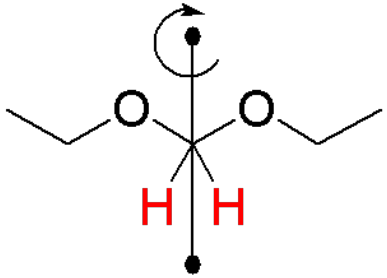
homotopic (H's on methyl groups are always homotopic since they can interconvert by rotation)

Same δ



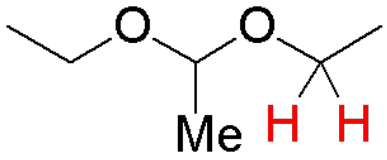
diastereotopic (there is no symmetry element in this molecule)

Could be different δ

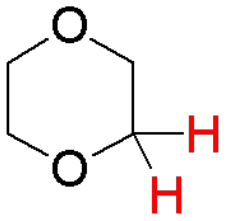


Homotopic (there is a C_2 axis running through the centerof the molecule

Same δ

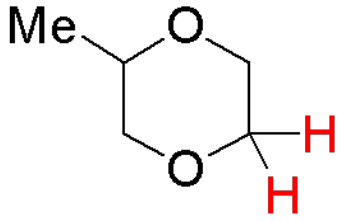


Indicate if the Labeled Groups are Homotopic, Enantiotopic, or Diastereotopic, and if They Must Appear at the Same Chemical Shift



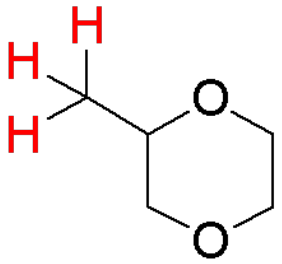
Enantiotopic (mirror plane through the ring in the plane of the screen)

Same δ



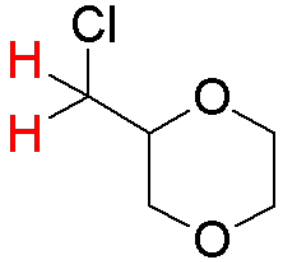
Diastereotopic (Me group is NOT in the plane of the screen, disrupts symmetry)

Could be different δ



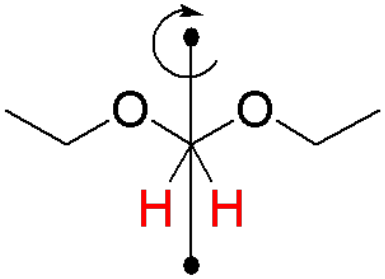
homotopic (H's on methyl groups are always homotopic since they can interconvert by rotation)

Same δ



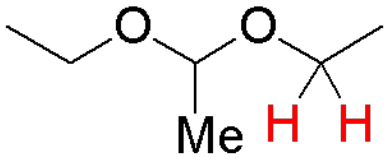
diastereotopic (there is no symmetry element in this molecule)

Could be different δ



Homotopic (there is a C_2 axis running through the centerof the molecule

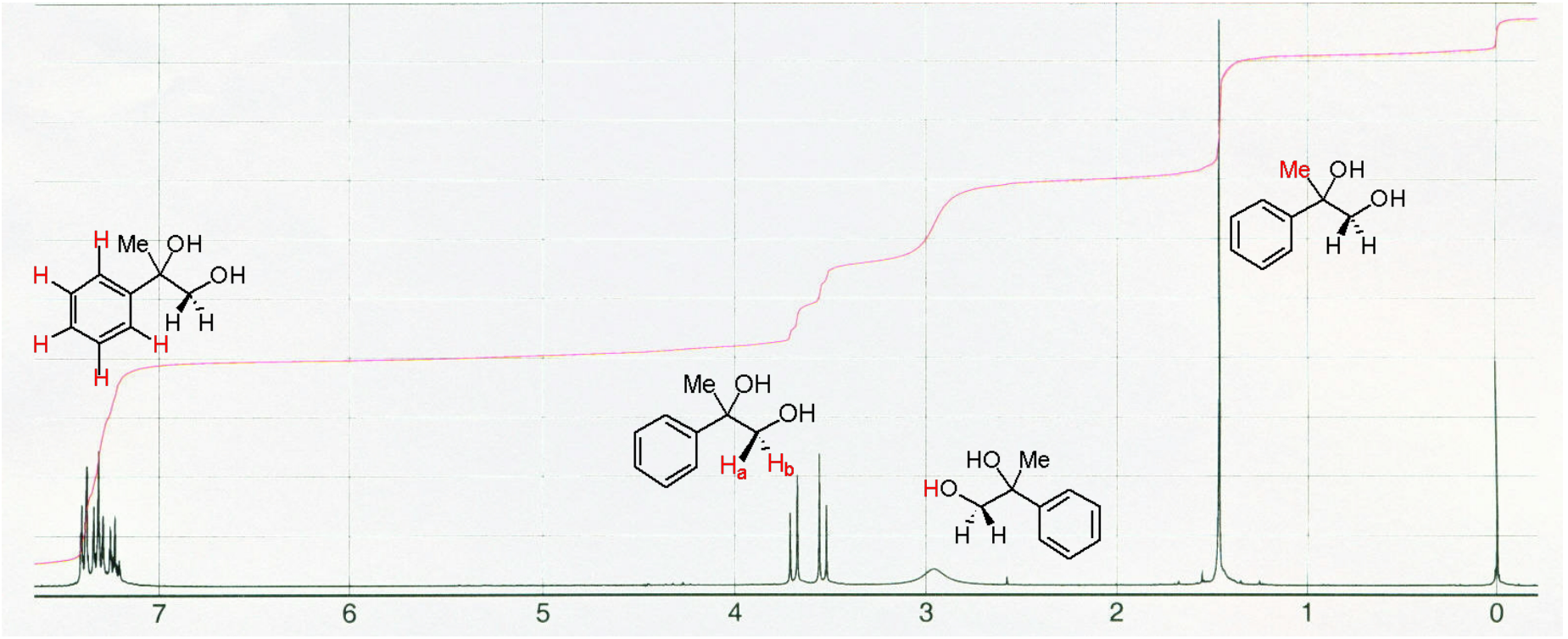
Same δ



Diastereotopic (even though there is a σ-plane running through the centerof the molecule, it does not interchange the two H's

Could be different δ

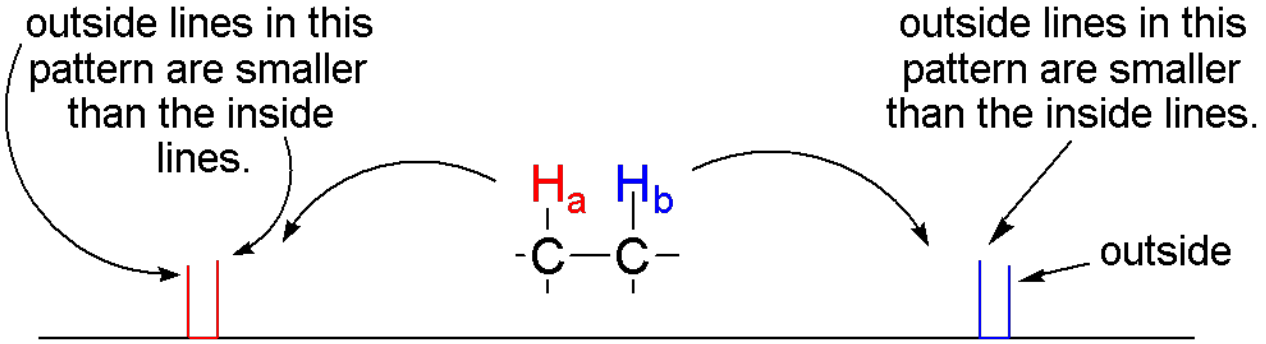
Diastereotopic Protons in an NMR Spectrum



There are several important features to this spectrum. Notice that the protons marked H_a and H_b are diastereotopic and that they appear at different δ. We can't assign which is H_a and which is H_b, but we know they are different. Also, notice that the lines for H_a and H_b are not of equal heights; the outside lines are smaller than the inside lines. Such "leaning" of NMR lines is common and is described on the next slide.

“Leaning” of NMR lines

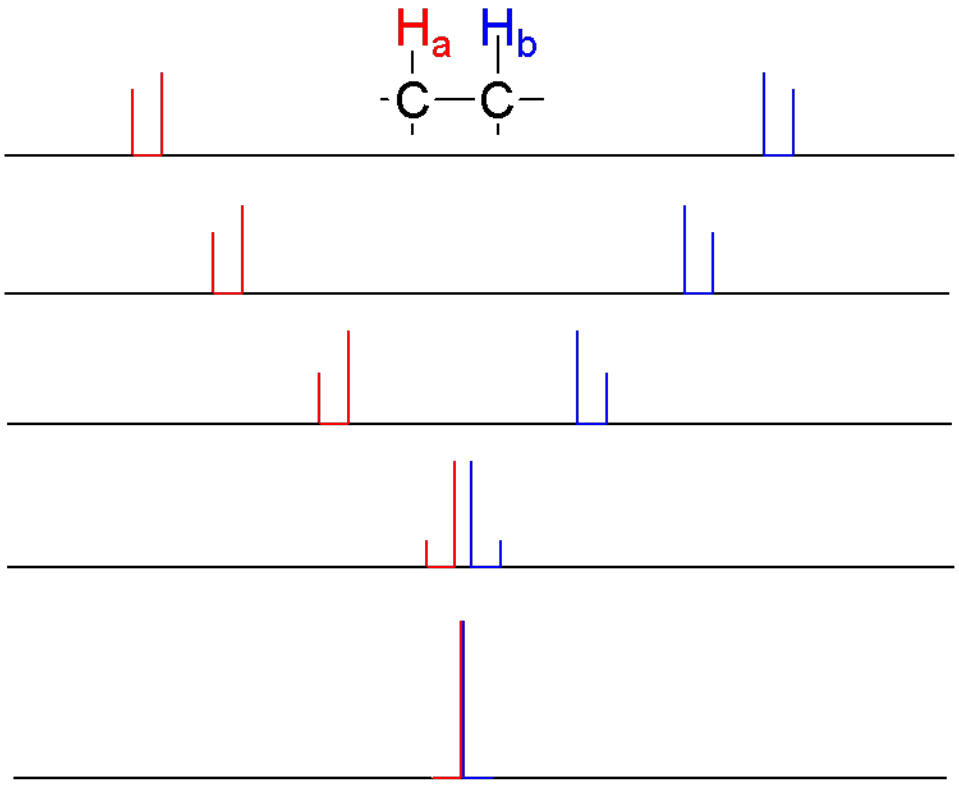
Recall that if we have two protons, H_a and H_b, and they are coupled to each other, H_a will be split into two lines by H_b, and H_b will be split into two lines by H_a. So, we should see a spectrum where there are four lines, two for each proton. But, it turns out that the patterns “lean” towards each other in that the outside lines of the pattern are smaller than the inside:



How much leaning we have depends on how close to each other the signals are in the spectrum, and how strongly they are coupled to each other. The closer they are, the greater the leaning, the stronger the coupling, the greater the leaning as shown on the next slide:

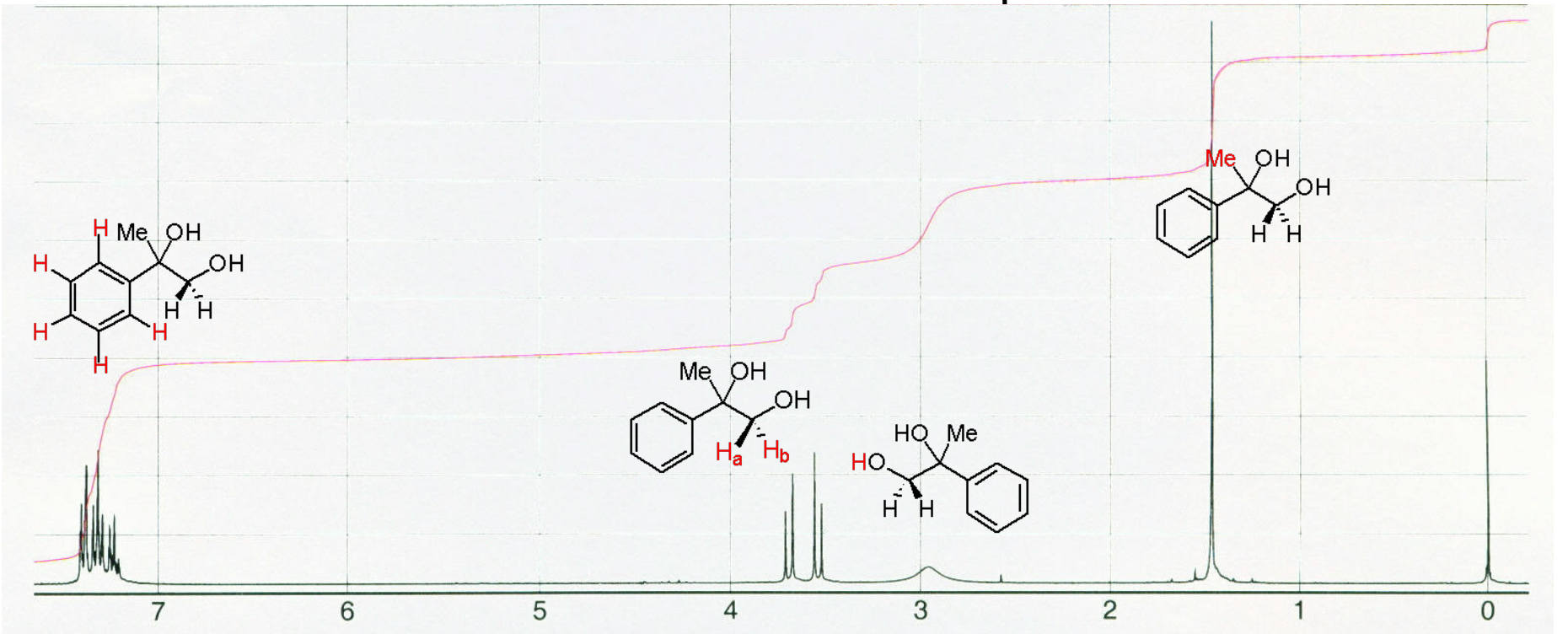
“Leaning” of NMR lines

How much leaning we have depends on how close to each other the signals are in the spectrum, and how strongly they are coupled to each other. The closer they are, the greater the leaning, the stronger the coupling, the greater the leaning:



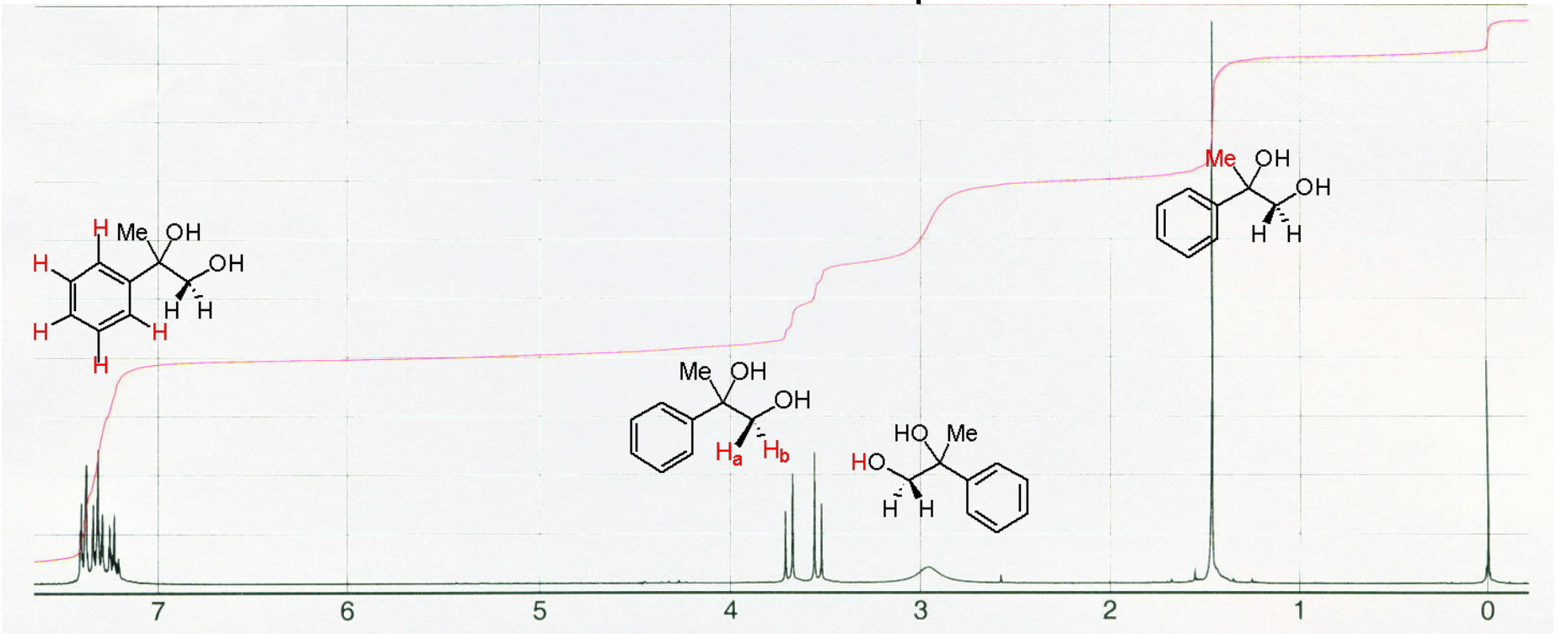
These represent spectra of different molecules where H_a and H_b come at different δ until eventually they come at the same δ. noticehow the inside peaks grow and the outside peaks shrink as the signals get closer to each other. also, notice how once thesignals come at the same δ, the out side peak disappears. So, when protons that come at the same δ they under go extreme "leaning" and don't appear coupled to each other because the outside lines have disappeared.

Back to the Previous NMR Spectrum



Notice the appearance of the OH peak in this spectrum; it's broad and not coupled to its neighbors. This is common with OH peaks. OH peaks are unusual in that their appearance is variable; for the same molecule, sometimes they are coupled sometimes they are not, sometimes they are sharp, sometimes they are broad. In fact, sometimes they are very broad, so broad that you can't even see them! This is due to OH groups undergoing exchange with each other and with traces of water in the solvent. This process is catalyzed by traces of acid or base in the solvent which effects the rate of the exchange and the appearance of the OH.

More on this NMR Spectrum



Now let's consider the appearance of the Ph group. It's a mess! Note that there are more couplings than we would expect based on a nearest neighbor analysis. That's because all the protons come at similar δ, and overlap with each other. In general, whenever there are a lot of signals coupled to each other that are bunched up in a portion of the spectrum, we get complex patterns with extra lines. The reason for this is called virtual coupling, and an explanation of this is beyond the scope of this class, but you should be aware when you are solving spectra that sometimes, this causes the patterns to be more complex than you would initially expect.

Examples of Leaning in Some Spectra We've Already Seen