

Lab 17A • 12/07/11

[lab quiz]

Nomenclature of alkenes

The first molecule that I want to look at is this one, where we have the two methyl groups on one side, two hydrogens on the other side. Would it be appropriate to use cis or trans, or E or Z, or both, or neither? One carbon of the double bond versus the other, those are the two different sides of the double, then the top versus the bottom are the two faces of the double bond. If we notice, on both the top face and the bottom face, we have a methyl group that is pointed the same way as a hydrogen. There is a steric factor as far as what alkene would prefer to form thermodynamically, so there is an importance that there's some interaction there. That methyl group with one hydrogen is exactly the same interaction as you'd have the methyl group and the other hydrogen pointed the opposite way – meaning that if you were to switch the two hydrogens, you'd end up with exactly the same molecule again. The only reason that we use the term cis or trans or E or Z is to describe that it is one configuration versus another, but since there's only one configuration possible, there's therefore no term that should be used. It would, in fact, be wrong to call this cis, trans, E, or Z. When an alkene has two of the same substituent on the same side, there is only one unique configuration of that alkene, and so it cannot be called cis, trans, E, or Z.

So when do we have a cis/trans case? As soon as we put two different substituents on either side of the double bond – cis when they are on the same face, trans is when they're on opposite faces. Let me point out that there is a hydrogen at each [of these] positions, so there are different substituents on each side. But, notice that there's only one alkyl substituent on either side, which means we're only comparing two objects; the hydrogens are effectively being ignored. This is the proper case of using those terms cis and trans because cis and trans are only relative terms. As soon as we put one more substituent on, we can't use the terms cis and trans. The terms cis and trans are appropriate because only two substituents are being compared. Cis means on the same face; trans, the opposite face.

What about these terms E/Z; can they be used here? Yes, cause E and Z are absolute configurations. Here's the way that it works. On each side, you first identify which substituent is the more important of the two substituents. How do we determine that? Using the same priority rules that we had for R and S. In this, it's really simple, because we have a carbon attached versus a hydrogen attached, so automatically, when you only have one substituent on either side, it's going to end up being the same thing as cis and trans. E and Z are absolute – not relative – configurations. Cis and trans are relative configurations, which is why the terms show up in more than one place. We use cis and trans in this case to describe the orientation around an alkene, but we could also talk about substituents pointing the same or opposite ways on a ring [or a transition metal center]; we talked about cis or trans substitution on a cyclohexane ring, for example. E and Z are specifically an only used for double bonds. It's a system in which the configuration's determined by identifying the most important substituent on either side of the double bond, using the Cahn-Ingold-Prelog rules, which are the same ones for R and S.

Let's see some examples, now, where we have multiple substituents. For the cis case, that's going to be the same thing as Z, which comes from *zusammen*, the German word for together; then, *entgegen*, opposite, E, for trans. Now let's come to this case where we have three substituents total. Would this be E or Z? The answer is no, because it's neither, because you have two of the same substituent on one side of the double bond, so again there's only one unique configuration possible [without swapping groups between carbons], so you can't use cis, trans, E, or Z. What about these cases? Now we have two different substituents on either side; we have a methyl and a hydrogen on one side, we have an ethyl and a methyl on the other. The most important substituent on the left side is methyl, cause there's a carbon versus a hydrogen; on the righthand side, it's not automatically because the chain is longer, but it is in this case, because at the end of the methyl group we only have hydrogens, whereas the first carbon out from the double bond, there's another carbon attached on the other one. Carbon outweighs hydrogen, it's more important. The first molecule, that would be E; second molecule would be Z. But you can't use the words cis and trans any longer, because cis and trans are just relative terms. You would have to say there's both a cis and a trans relationship here, which then doesn't tell you which molecule it is, because they both have cis and trans relationships, so you have to use E and Z. What if we had bromine or some other atom? We would follow the same Cahn-Ingold-Prelog rules, where the higher atomic number takes precedence over the lower atomic number. This is just to say whether a double bond is cis or trans or E or Z or none of the above.

What about actually using these terms in nomenclature? There's a slight twist on how you could use these terms when you start naming molecules. Let's name a series of alkenes. Start with a simple one. What would be the name of this compound? How many carbons does it have? Six. I has one double bond, so how would we name that? It's hexene, but we do have to say where the double bond is located, so what would it be then? Hex-1-ene, or 1-hexene if you're following the older style. Do we need cis, trans, E, or Z. No; in fact, we can't use cis, trans, E, or Z. This is a terminal alkene, and if you have a terminal alkene where you have two hydrogens at the end, terminal alkenes never have cis or trans associated with them, so the name is just hex-1-ene. This terminal; it's at the end.

Let's see an internal one. Once we have an internal double bond – a double bond – we're going to have two possibilities. Can we use the terms cis and trans here? Yes, because only two things are being compared – one substituent on one side versus the other substituent on the other side. Can I use the terms E [or] Z here? Yes, because any time you can use cis/trans, you can use E/Z, but not the other way around. You could use cis/trans, you could use E/Z, so this would be either cis-hex-2-ene or (Z)-hex-2-ene. Notice that you don't use parentheses with the word cis; that's because it's a relative time. Notice you do use parentheses with E/Z because it is an absolute configuration. With absolute configurations, you'd use numbers, but only if there's more than one of them. Just as before, where if we only had on R or S in a molecule you didn't use the number, same thing here. Let me put [the trans] up there for comparison. Again, I could use either cis or trans – cause there's only two things being compared – and any time you can use cis and trans, you can use E or Z, so this is trans-hex-2-ene or (E)-hex-2-ene.

What about a case like this? Would I use cis or trans, or E or Z? No, because I'm back again to the case where I've got two of the same thing on one side of the double bond. How would this be named? 2-methylhex-2-ene.

What if I had this case? Which end would get the two: the alkene or the methyl group? The alkene, cause it's the functional group. When you have different functional groups on a molecule, the highest-priority functional group determines the number position. Since the alkene could be numbered by the 2, we start from the right, versus the methyl group could be the two, the alkene wins out. We now have, though, a cis alkene, so we do have to specify that. This could be cis-5-methylhex-2-ene or (Z)-5-methylhex-2-ene. That's because the alkene is more important than alkyl.

Next example: can we call this cis or trans? No, because we'd have to call it cis and trans. We have two things that are on the same face of the double bond, and we have two things that are on opposite faces. The cis and trans words don't have incorporated into them which of these is the most important functional group; that's why I'm saying you can't use the cis and trans there, you have to use E or Z. The only name that would be acceptable in this case would be – is it E or Z? Z, because the propyl group is the most important thing on one side, the methyl group is the most important thing on the other, so that is (Z)-3-methylhex-2-ene.

What about a case like this? Can we use the word cis or trans? Can for either of the double bonds we use the cis or trans term. The one on the right side. Can we use them for the one on the left? No. That means we can use it for this whole molecule, because there's only two things being compared on the one double bond. Cis and trans are still fine, because only one double bond needs specifying. But, it's now a diene, so we do need to reflect that in the stem. Notice so far it's been hexene; why? Because ene immediately follows hex. We're now going to have a diene, and we don't say hexdiene; the rule is: you put an 'a' in, so now it turns into hexadiene. Which way do we number it? From the left, the lowest number would be 1, from the right, the lowest number would be 2, so we're going to number it from the left, so this is either going to be trans-hexa-1,4-diene or (E)-hexa-1,4-diene.

Two more example. Can we use the word cis [or] trans for either double bond? Can we use them for both double bonds? Then we can't use the term, because you're only supposed to compare two objects total; this molecule has two points of comparison, so you can't use cis and trans. You'll see it done sometime, but it's not proper usage of the term. Instead, we have to use E or Z. That becomes just like the R and S, where now we're going to put numbers with it, because we have more than one configuration that needs to be named. We just list it in numerical order; we don't worry about which one's E or Z, except in the next case I'll show you. Curiously, though, would we number this from the left or the right? Doesn't matter, cause you get exactly the same results. Are these E or Z, these double bonds? They're still E, cause they're still opposite, they're still trans. So this will be (2E, 4E)-hexa-2,4-diene.

The last case is this one. Another hexene, but how would I number it, from the left or the right? It still would be 2 from either direction, but before it didn't matter which way I numbered it; I had E versus E. But now, one of them's E and one of them's Z, and that's the only thing different on the molecule. Which one is named with the lower number? E. You can think of it this way: it is E/Z to remember which one is first (easy). So this is (2E, 4Z)-hexa-2,4-diene.

What happens if we have an alkene with an alcohol? I have an alkene at one end; I have an alcohol at the other end. Both of those groups could potentially have the number one. Which one do I call one? The alcohol. Alkenes and alkynes are above alkanes are above halogens; you always name halogens as substituents. Above that, there's alcohols, and then things with carbon-oxygen double bonds – aldehydes and ketones – and above that are the various carboxylic acid[derivative]s. [An] alcohol is more important than an alkene, so this gets the name hex-; where's the alkene located, at the 5 position. Why am I naming the alkene part of it first? Because the letter before the 'n' tells you whether you have a single, a double, or a triple bond – hexane, hexene, hexyne. Following that: hex-5-en-1-ol; you simply add the functional group endings together. If you have two vowels, then due to elision, you drop one.

Let's see one example where I put all of this together. [nomenclature shirt] How many total specifications are we going to have to make? Four: two stereocenters, and two double bonds that need configurations. From right to left, that first double bond is what? Z. R or S? S, cause we have an oxygen; we have a carbon connected to two carbons (remember that there's a virtual atom there cause of the double bond); carbon connected to one carbon.

The next double bond: E. And the next stereocenter: R – oxygen; carbon connected to two carbons; carbon connected to one; it looks S; the hydrogen, the least important group, is pointed towards us, so we have to reverse it, so yes it is R. This molecule, we're going to number from the left, because the most important group – the alcohol – is located at position 1. There are no substituents, so we'll start ... even if we had substituents, we'd put all of the specifications first, so this is (3R, 4E, 6S, 8Z)-deca-4-5-diene-1,3,6-triol. We do need an 'e' because there are two consonants put together.

Alkynes

Alkyne nomenclature [is] very boring, because an alkyne has what kind of geometry at each carbon of the alkyne? Linear; it's sp-hybridized. If it's linear, there's no comparison that you're making, so there's no such thing as cis and trans, so there's no configurations with alkynes. There's this very complicated system of what to do if you have an alkene and an alkyne. [commentary of draft rules]

Here's a typical alkyne – this is but-1-yne. Anything smaller than this, we technically don't need to use numbers with – there's no such molecule as prop-2-yne, because that would mean having carbon #2 connected to carbon #3, but we still have carbon #1 where the triple bond could have been, so it's not numbering it appropriately. Similarly, ethyne – also called acetylene – doesn't need numbers cause there's only one kind of ethyne possible as well. If you had two alkynes in a molecule, pretty straightforward: this would be hexa-2,4-diyne. Just to throw an alcohol example in: this would be [because we have to use a number period?] prop-2-yn-1-ol. This fragment, where you have a position next to a triple bond ... we have this term allyl to describe the position next to a double bond ... next to a triple bond, this is aspargyl [related to asparagus?]

One reaction of alkynes I want to show you. It's a reaction that's only possible with terminal alkynes. You can use very strong bases like sodium amide – NaNH₂ is an ionic compound, it's extremely basic. There's another set of reagents that is sodium ammonia, which is sodium metal in ammonia; in this set of conditions, ammonia is cooled and condensed, so it's liquefied. They are two totally different sets of reagents. If we take that NH₂⁻ ion – think about it, ammonia itself is already a basic compound. We're taking a proton off of it, which means you've got a really basic compound. It'll react with an alkyne, because, remember, one of the physical properties that causes compounds to be more acidic is hybridization of the orbital in which the anion will eventually reside. Because when this gets deprotonated it ends up in an sp[-hybridized] orbital, that's lower in energy than an sp², lower in energy than an sp³, so this is comparatively acidic, so this base will deprotonate it. It makes what's called an acetylide ion – basically, a negatively-charged triple bond.

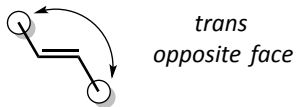
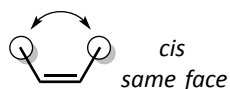
These are useful as a sneaky way of building a carbon-carbon bond. One of the most important types of reactions that you will be learning is how to make carbon-carbon bonds. We already saw a sneaky version of that by using sodium cyanide – technically, that's a carbon that's attacking, making a carbon-carbon bond. This is a very similar reaction, because if you have a primary substrate, the acetylide ion can do an S_N2 reaction. The reason this is important is cause we've now built a larger carbon molecule. If we're trying to do drug design, we have to build carbon frameworks; this is one of the tools that could be used. Note the way that I've written the product: realize that on either side of that triple line, each of those positions counts as a carbon. If I had just taken this molecule and from where the leaving group was, if I wrote the triple bond from there, I just [a] carbon out. This only works for primary substrates because acetylide ions are really basic; even with a hindered primary, you're going to get elimination, or with secondaries, you'd get elimination, and of course tertiaries can't even do S_N2 (only works with primary substrates).

Let me show you a multistep synthesis that's often used to make alkynes. How can we make an alkyne? You can start with an alkene that you react with Br₂. That's going to make a vicinal dihalide. If you throw in sodium amide, this strong base, you can get elimination that occurs. Notice that one elimination occurs, we still have a hydrogen and bromine that, technically, are antiperiplanar to each other. The double bond is flat, so if you look along the double bond along its axis, you'd have a bromine pointing straight up and a hydrogen pointing straight down, so it continues to react, if you have more sodium amide around, to do a double S_N2. If I take an alkene, react it first with bromine and then with two equivalents sodium amide, I can produce an alkyne.

When an alkene has two of the same substituent on the same side, there is only one unique configuration of that alkene, so it cannot be described as cis/trans or E/Z. E & Z are absolute (not relative) configurations. The configuration is determined by identifying the most important substituent on either side of the double bond (using the Cahn-Ingold-Prelog rules).

Structures

12/07/11 lab • 1

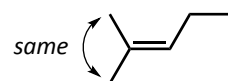


two different substituents on each side (Z)

cis/trans are relative configurations (E)

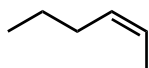
The terms *cis* & *trans* are appropriate because only two substituents are being compared.

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not *cis* or *trans* (even though it has three substituents)

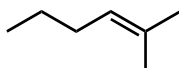
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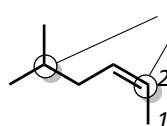
cis-hex-2-ene
(Z)-hex-2-ene



trans-hex-2-ene
(E)-hex-2-ene

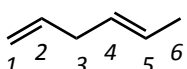


2-methylhex-2-ene
no *cis/trans/E/Z*

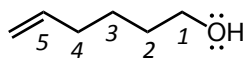


cis-5-methylhex-2-ene
(Z)-5-methylhex-2-ene

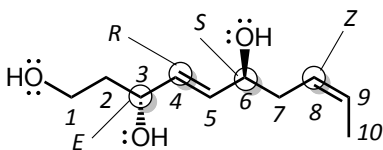
alkene is more important than alkyl



trans-hexa-1,4-diene
(E)-hexa-1,4-diene
only one C=C needs specifying



hex-5-en-1-ol
alcohol > alkene

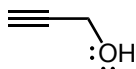


(3R, 4E, 6S, 8Z)-deca-4,8-diene-1,3,6-triol

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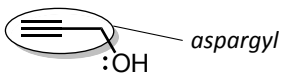


hexa-2,4-diyne



prop-2-yn-1-ol

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12/07/11 lec • 6

