

Lecture 25B • 12/02/11

Difference between a solvent and a nucleophile

In S_N1 reactions, it is often true that the solvent is often the nucleophile. For example, if we had a tertiary substrate that we reacted with something non-basic like ethanol, then that is the nucleophile. Since it's an organic substance [and] it's a liquid, it makes sense to make it the solvent, since it is the reagent. In this case, it is acting as both the solvent and the nucleophile. However, if I had an S_N2 reaction, with a primary alkyl halide, where I was using something like sodium hydroxide, sodium hydroxide is not an aprotic solvent because it's a solid. You just gotta make sure that you're careful about what you identify as solvent and nucleophile. [solvents often not mentioned up to this point]

[exam review : $S_N1/S_N2/E1/E2$ – mechanism, substrate, nucleophile, competing reactions; free radical halogenation; electrophilic additions: plain – HBr, tosic acid and water, catalyst and alcohol order of addition, Markovnikov addition, carbocation rearrangement; cyclic intermediates – oxymercuration/demercuration, halogen, halohydrins, stereochemistry, alkoxymercuration/demercuration; hydroboration/oxidation – anti-Markovnikov addition]

Hydrogenation

Hydrogenation involves an alkene – let me slip back to the same example alkene we've been using – with hydrogen gas and either a platinum or a palladium catalyst. The reaction of an alkene and hydrogen gas is a favorable reaction; it ends up being exothermic, but kinetically it's a difficult reaction, because you have hydrogen, which is a gas. It's reactive, but it's a different phase that usually what the alkenes will be in; most of the time, the alkenes would be in the liquid phase, or even occasionally a solid that then would be dissolved to make a liquid phase. To dramatically increase the reaction rate of this, we add platinum or palladium metal – both of which are able to have platinum adsorbed onto them. There's not a mechanism for this reaction, but let me describe what goes on so at least we can understand the stereochemistry of the reaction. We have hydrogen gas, and then we have the surface of the platinum or palladium metal. Effectively what happens is that hydrogen gets adsorbed onto the metal surface. The alkene then approaches that metal surface, and the hydrogens are added to the alkene. But, in the way that the addition occurs, there's not a chance for one hydrogen to hop on and then suddenly the molecule flips upside down and then the hydrogen hops on onto the [opposite] side; instead, the entire double bond reacts at once – maybe not simultaneously, but it reacts from only one direction, so both of the hydrogens end up adding to the same face of the double bond, which means that this is a syn addition. Hydrogenation is a syn addition, because both hydrogens react on the same face of the alkene as the alkene approaches the catalyst. It's still going to be enantiomeric, because it could yet again add to either face of the double bond. We'll end up with two products; note the same direction that both the hydrogens point in the product.

If we were going to list the six aspects of this reaction: utility is to convert an alkene to an alkane. Reagents – hydrogen gas, then platinum or palladium acting as a catalyst. The conditions – none special that we'll discuss [some other time]. Mechanism – no special classification here, because this is an unusual mechanism, because it involves that metal catalysts. In terms of stereochemistry, because of that metal catalyst, it ends up occurring with sym addition, and you end up with the formation – assuming there's no other stereocenters – of enantiomers. In terms of regiochemistry – there really isn't anything special in terms of stereochemistry, because if you're adding H to each atom, then you're not going to create a secondary versus tertiary ... or there is no concern of whether there is a secondary or tertiary. The least we can say then is there's no rearrangement.

Epoxidation

There's two different reagents that could be used for this. One of them is MCPBA, which stands for meta-chloroperoxybenzoic acid. Benzoic acid – benzene ring with a carboxylic acid group attached, but peroxybenzoic acid means that there's an additional oxygen. Meta is one of those three relative terms for benzene substituents, so meta-chloro means that it is two carbon away from the position of the peroxybenzoic acid. This molecule has unusual reactivity because of the oxygen-oxygen bond. We've already seen some unusual reactivity of oxygen-oxygen single bonds in the hydroboration reaction. Let's see what happens in this case. Because of that weak oxygen-oxygen bond, the alkene ends up being able to attack the oxygen. Why would that happen? Because what's the oxidation state of the oxygen that I'm going to at the moment? Not zero; -1. That's because of the oxygen-oxygen single bond. Most of the time, oxygen want's to have an oxidation state of -2 – unless it's hooked up to oxygen or fluorine; that's because oxygen is equal electronegativity with itself and fluorine's more electronegative. That oxygen currently has an oxidation state of -1; by having this attack occur, it's going to get reduced to an oxidation state of -2.

Let me rewrite this so I can better shown the mechanism that's going to occur. Double bond attacks the oxygen; that oxygen-oxygen bond breaks, and that pair of electrons that used to be in that oxygen-oxygen bond could fall back, kinda like if you were making a resonance structure with the carbonyl that's already there. Of course, if you were to push open that carbonyl, you end up making acetate, which is basic. There's a hydrogen over here that, in response, it could pull off. If that occurs, that bond with oxygen has to go somewhere, so it ends up going back to the alkene. Let me again step through that sequence of steps.

The oxygen-oxygen bond itself is weak, and because reduction occurs if [the] attacks occurs the way that I've shown it, that's the impetus for the reaction. That causes the oxygen-oxygen bond to break, which, once those electrons shift around, cause[s] a hydrogen to be removed. There's a pair of electrons left; that ends up coming back and making another bond with the alkene. What you form is a pair of epoxides.

We [have previously seen] another way of making epoxides. That would be to react with bromine and water to first make a halohydrin; you react with sodium hydride; that deprotonates the alcohol without causing substitution on the bromine. That self-reacts, and you end up with the epoxide. Remember that that bromine and water reacting occurs with anti addition, and because they're anti, that gives you good relative stereochemistry for the oxygen to come back to attack and make that ring. [connection between bond strength and oxidation state?] It does reflect the fact that oxygen doesn't have the maximum number of electrons to itself that it could have if you had something else that was less electronegative for it to be attached to that it could steal the electrons from.

E and Z versus cis versus trans

When can or should you use either of these two systems? First, if we have a molecule like this: 2-methylprop-1-ene, there is no cis versus trans version of this molecule, because if I write in the hydrogens that are there, on one face of the double bond, we have a methyl that's opposite a hydrogen; on the other face of the double bond, we have a methyl versus hydrogen. If you were to swap the hydrogens, those interactions wouldn't change. The only reason that we have cis or trans or E or Z is if, by swapping the substituents, you make a different molecule. In this case, we would say not E or Z or cis or trans since both substituents on one side are the same.

Let's go ahead and put some kind of group on the other side. These we could call cis or trans, and we can also call them E or Z – if we're talking about one individual double bond. Why are the terms useable? Cis and trans can be used because there is exactly one substituent on each side; because the terms cis and trans are relative terms, you can only compare two objects. As soon as we put a third substituent on, we're going to have two cases. This third one is again not cis or trans; that's because two substituents on one side are the same as each other. The last case would be something like this, which cannot be cis or trans, because there's more than one substituent on one side. Another way to put it is this is both cis and trans, because we have two substituents on opposite sides that are on the same face and two substituents on opposite sides that are on opposite faces. Since both terms would need to be used, you can't use either one, so instead, we use E and Z. For E and Z, what you do is determine the most important substituent on each side, then determine whether those most important substituents are on the same or opposite faces.

How do you determine what's the most important substituent? Exactly the same way you'd be determining the substituent order for the purposes of R and S; exactly the same rules apply. In this particular example, it's fairly easy because we have carbon with just hydrogens on it versus a carbon with another carbon on it; the ethyl group is going to be more important than the methyl group. Any of those carbons are more important than hydrogen, so if I were to circle the most important substituents, they would be the ethyl on one side and the methyl on the other. If I were to flip one side versus the other, now, which ones are the most important substituents, they're now opposite faces instead of the same face. When they are on the same face, that is the Z form, and when it's on opposite faces, it's the E form. If we go back up to cis and trans, in those cases where the terms can be used, notice that, still, on either side, there is one more-important substituent. Automatically, in these cases, one of them is hydrogen, so it's whatever alkyl group or whatever else substituted that would make it E or Z; in other words, you could use E and Z there. On this last example, since you have both cis and trans relative configuration, we can't use either of those terms, because we would need to use both, which would not be a very clear use of the terms.

All of this is related to [specifying] one double bond. When naming compound, if they only have one double bond, whether to use cis or trans or E or Z is the same set of decisions: whether or not there's one and only one substituent on either side, or if there's more than one. Fluorine is higher atomic number, so it would take higher priority [than carbon]. If I was to name an alkene like this, where it's a terminal alkene – terminal at the end – neither cis nor trans, so you wouldn't use cis or trans; you'd just name it hex-1-ene. If you have one [internal] double bond – and only one [internal] double bond – then you have an option: you could call it, as in this example, cis-hex-3-ene, or (Z)-hex-3-ene. Why the parentheses for one and not the other? Because cis is just a relative term; E and Z are absolute configurations, so they are expressed differently.

What if we had a methyl group now attached to that double bond? Then it's cis/trans or it's E/Z because only one carbon-carbon double bond. In this case, it cannot be cis or trans, because we have two substituents on one side. If I indicate which are the most important substituents, we see that they're on the same face, so this is going to be (Z)-3-methylhex-3-ene. There's two other cases I should show you: here, there are two double bonds, but we only have one double bond that needs specifying of its configuration. Since there's only one double bond that needs specifying, you're back to the case again where you could have either E or Z or cis or trans, whichever's appropriate. This would be trans-hexa-1,3-diene; the 'a' comes back because we're going to have the 'd' in diene, and we don't say 'hexdiene'. Because it's trans, we could also call this (E)-hexa-1,3-diene. The last kind of case would be if we have two double bonds that need specification of [configuration]. Cis and trans cannot be used correctly, because the word cis [or trans] is supposed to be a comparison of two objects.

We have two double bonds that have that comparison, so if you just use the word 'cis' once, it doesn't show which one it would refer to. Sometimes, you'll see people use numbers with the cis and trans and say 2-cis-3-trans, but it's not a correct use of those terms, so E/Z must be used, since multiple carbon-carbon double bonds have a configuration. It doesn't matter, in this case, which way we number from; the would be (2E, 4E)-hexa-2,4-diene.

What if I had this case; this is a very obscure case, but it's perfectly possible. From one direction versus the other, I could number them the same way, but one of these is E, and one of them is Z. Which one do I number first? E. By default, E is numbered first. R and S, if you ever have that kind of decision that you have to make between, it's R. If you think about the way I always talk about R/S, I always say R/S, R/S, not S/R; it's because R is give more importance than S. I talke about E/Z, E/Z, E/Z ... it's easy to remember that E is more important that Z. This is going to be (2E, 4Z)-hexa-2,4-diene. Again, E has greater importance than Z. These are all of the cases dealing with naming of double bonds. [anticipating incorporating multiple functional groups]

The only reason that there was any choice between E and Z is because the numbering would have been identical. If, in whatever molecule you have, you happen to have an E double bond that could be labeled 4, let's say, and a Z double bond that could be labeled 3, because 3 is lower than four, you'd list the Z first.

There's another aspect of alkene structure that you need to be aware of. It's also connected with nomenclature. What is the name of that compound? This is cyclohexene. That is the correct name for it, but notice there's no '1' used, and no cis or Z used. Why not? The reason that we don't use the '1' is the same reason we didn't use it for cyclohexanol; the '1' is automatically assumed for one of the two carbons of the alkene. How would we determine which one is number one? That would be determined by whatever substituent[s] that you put on. Why is it that there is no cis here? There are [two substituents]; isn't the ring itself a substituent? (That is the way that it is often missed) But still, it is cis; why don't we say it is? Because there's no such thing as trans-cyclohexene. If you tried to make it with a model set, you'd find out that it's physically impossible. The smallest ring that can even be made is 8, but it only exists at sub-zero temperatures, so really the smallest ring that you can get and have a chance of isolating is nine carbons in size. Trans-cyclohexene is impossible to make. This is what it would look like to draw. The double bond would need to be planar, but notice the direction that one of these bonds is pointing; it's pointing with maybe a 60° to the double bond, whereas a normal sp²-hybridized carbon would want to be 120° angle. No matter what you try to do, you can't wiggle those single bonds around enough in order to make the room available to have that trans double bond. That does mean for large enough rings, you would need to specify whether you have E or Z. In this case, the '1' would still not be used with the alkene, cause again it's assumed; by the position of the methyl group, though, we could call it 1, so this is 1-methylcyclohexene. If you did have more than one double bond, now you would need to specify; this would be cyclohexa-1,3-diene. A methyl group with a functional group; an ethyl group with a functional group; or a ring with a functional group: those are the three cases in which you don't use the '1'.

Alkynes

Let's go ahead and see a little bit of nomenclature of alkynes. Alkynes nomenclature is simpler than alkene nomenclature, because what is the geometry of a triple bond? It's hybridization is sp, which means it's geometry is linear. Since it's linear, there's no such thing as cis and trans. It's a very easy type of compound to name. The simplest possible alkyne is ethyne. This is one of those exceptions where, because there are only two carbons and there's no way to have 2-ethyne, we don't even use the '1' when naming ethyne. For alkenes and alkynes, there's even one more exception, because there's no such thing as 2-propyne, either, or 2-propene, because if you put the '2' where the double bond is, it'd be connected to a carbon that that carbon would automatically become '1'. The shortest one that you have to number is for a four-carbon chain, so this would be but-1-yne, versus but-2-yne. If you had multiple [triple bonds], we'd name it like we would with alkenes – of course, without having to worry about cis and trans. This is a seven-carbon compound; we have a triple bond at the 1 position and the 5 position. This would be hepta-1,5-diyne. The one mistake that's often made is how to interpret lines going to or coming from triple bonds. Since I've got this line extending out, that means there is another carbon there; that's why I've numbered this as 1,2.

[mixture of alkenes and alkynes?]

Alkynes can be useful because you can do different kinds of hydrogenations. One way to synthesize alkynes is from vicinal dihalides. If you have a strong base – this compound sodium amide, NaNH₂, is often used as a strong base – it does a double E2 to form the triple bond. In terms of hydrogenation, if we use the same conditions as for alkenes, where we use hydrogen and a catalyst, you'll take it back down to the alkane. But, if instead you use hydrogen with a platform known as Lindlar's catalyst, which is what is known as a 'poisoned' catalysts, it is possible to synthesize just the [cis] alkene. One last possibility is to react the alkyne with sodium metal dissolved in liquid ammonia; when that is done, you're able to form a trans alkene.

Summary of rxns

Hydrogenation is a syn addition because both hydrogens react on the same face of the alkene as the alkene approaches the catalyst

- 1) utility: alkene \rightarrow alkane
- 2) reagents: H_2 (g); Pd or Pt (catalyst)
- 5) stereochemistry: syn addition; enantiomers
- 6) regiochemistry; no rearrangement

Epoxidation

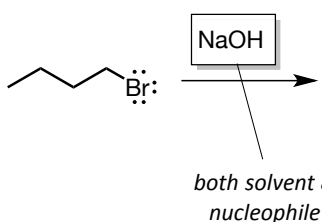
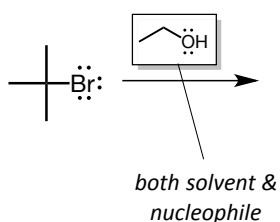
MCPBA – meta-chloroperoxybenzoic acid

For E & Z: determine the most important substituent on each side, then determine whether these substituents are on the same or opposite faces.

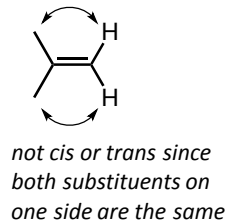
trans-cyclohexene cannot be synthesized due to incredible geometric strain, so “cis” is not needed.

Structures (remaining structures identical to lecture 25A)

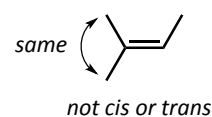
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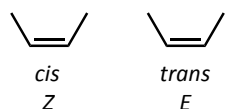
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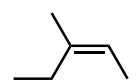


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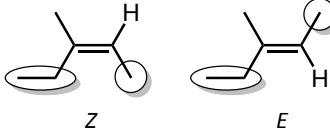
cis & trans can be used because there is exactly one substituent on each side

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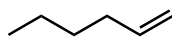


cannot be cis or trans (more than one substituent on one side)

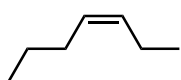
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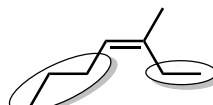
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hex-1-ene
no cis/trans/E/Z



cis-hept-3-ene
(Z)-hept-3-ene
cis/trans or E/Z only one C=C

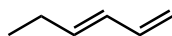


(Z)-3-methylhex-3-ene
no cis/trans (two subs one side)

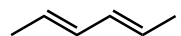
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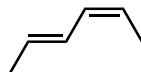
cyclohexene
no cis/Z no 1



trans-hexa-1,3-diene
(E)-hexa-1,3-diene

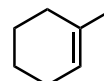


(2E, 4E)-hexa-2,4-diene
E/Z must be used since multiple C=C have a config



(2E, 4Z)-hexa-2,4-diene
E > Z

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1-methylcyclohexene

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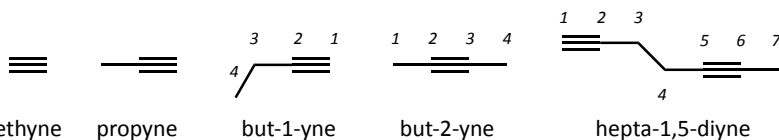


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cyclohexa-1,3-diene

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