Carbonyls as Electrophiles

Transcript

00:00:00:28 - 00:00:13:62
Dr.Jessie Key: Hello again, Dr. Jessie Key here. In this slideshow, you will be exploring why nucleophilic attacks can happen at the carbonyl carbon and the general mechanism by which these nucleophilic addition reactions occur.

00:00:13:62 - 00:00:30:19
Dr.Jessie Key: Examples with various nucleophiles will be explored in the remainder of this topic of the unit. The electron-poor carbonyl carbon is a pretty good electrophile because of two reasons. The first reason is induction!

00:00:30:19 - 00:01:09:82
Dr.Jessie Key: The oxygen of the carbonyl is electronegative and withdraws electron density towards itself, making the carbonyl carbon electron-poor. As shown with the bond-line diagram structure of ethanal, commonly called acetaldehyde left side of the slide, we can represent the induction which occurs by drawing a dipole arrow shown in red, where the positive sine tail end of the arrow is at the carbonyl carbon and the arrowhead points towards the more electronegative carbonyl oxygen. Alternatively, this could be represented with partial charge symbols, having the partial positive charge at the carbonyl carbon and the partial negative charge symbol at the carbonyl oxygen.

00:01:10:64 - 00:01:40:92
Dr.Jessie Key: On the right side of the slide, an electrostatic potential map is shown for a ball-and-stick model of the same molecule, ethanal. Electron rich areas are shown with the orange red color and electron poor areas are shown with the blue-purple color. We can see that the black ball representing the carbonyl carbon of ethanal is electron poor with a blue color, while the area around the red ball representing the carbonyl oxygen is an electron rich orangy-red.

00:01:41:09 - 00:02:19:13
Dr.Jessie Key: Carbonyl carbons are also electron poor due to resonance. As shown with propan-2-one, (commonly called acetone), we can draw a second minor but important resonance contributor by moving the pi bond electrons onto the oxygen, giving a formal negative charge on the oxygen and a formal positive charge on the carbon. Again, an

electrostatic potential map shown on the right side of the slide can help us visualize this with the blue electron poor area around the central carbonyl carbon and the orange-red electron rich area around the red ball representing the carbonyl oxygen.

00:02:19:13 - 00:02:48:43
Dr.Jessie Key: Nucleophiles tend to attack the carbonyl carbon from an angle of about 105-107 degrees relative to the plane of the carbonyl. This special attack trajectory is known as the Bürgi-Dunitz angle and has been extensively studied with many different types of nucleophiles. One reason for this specific angle of attack is that it allows for proper orbital overlap of the nuclephile HOMO and the carbonyl LUMO, as shown with the diagram on the right side of the slide.

00:02:48:43 - 00:03:15:79
Dr.Jessie Key: A second reason for this narrow window of nucleophile approach is that the nucleophile must thread the needle between the repulsion from the electron rich oxygen and the steric strain of the rest of the molecule attached to the carbonyl carbon. Which is more reactive towards nucleophilic attack, an aldehyde or a ketone? To answer that, we must think in terms of both sterics and electronics.

00:03:15:79 - 00:03:46:55
Dr.Jessie Key: For sterics: Ketones have two alkyl groups attached to the electrophilic carbonyl carbon, presenting additional steric bulk to get in the way of the nucleophilic attack. Whereas aldehydes have only one alkyl group attached and are therefore more accessible for nucleophilic attack. For electronics: Ketones have two electron donating alkyl groups attached to the electrophilic site, which can help stabilize this electron poor carbonyl carbon, making it less electrophilic.

00:03:46:55 - 00:04:15:67
Dr.Jessie Key: Whereas aldehydes only have one electron donating alkyl group attached, which means that carbonyl carbon is more electrophilic. Nucleophilic addition can occur under both basic and acidic conditions. Under basic conditions, the general two-step mechanism starts with a nucleophilic attack where we start our arrow at the electron source, the lone pair of the nucleophile.

00:04:15:67 - 00:04:40:03
Dr.Jessie Key: The arrow goes to the electrophilic carbonyl carbon, forming the new sigma bond there. The second arrow starts at the pi bond of the carbonyl and finishes on the carbonyl oxygen to form a new lone pair of electrons there. In the second step, proton transfer, the oxygen with the formal negative charge removes a proton from an acid, usually introduced in a workup step.

00:04:40:03 - 00:05:02:02
Dr.Jessie Key: In this example, we start the curved arrow at the lone pair of the oxygen and have it end on the proton of the generic acid H-A. This causes the H-A bond to break and

those electrons travel to the atom that was bearing the proton. This gives the nucleophilic addition product an alcohol with the nucleophile attached at the same carbon.

00:05:02:02 - 00:05:24:01
Dr.Jessie Key: Under acidic conditions, the general nucleophilic addition steps are reversed. First proton transfer occurs where the carbonyl oxygen lone pair acts as a base and abstracts a proton from the generic acid H-A. We can show this with the curved arrow starting at the lone pair of the carbonyl oxygen and ending at the proton of the generic acid H-A.

00:05:24:01 - 00:05:54:76
Dr.Jessie Key: This causes the sigma bond between H and A to break and those electrons move on to the atom that was bearing the proton A. In the next step, nucleophilic attack occurs at the carbonyl carbon, which we can show by having the arrow start at the lone pair of the nucleophile and ending on the carbonyl carbon. The pi electrons then move up to form a new lone pair on the carbonyl oxygen, elimining the formal positive charge on that oxygen and giving the addition product an alcohol bearing nucleophile on the same carbon.

00:05:54:76 - 00:06:14:59
Dr.Jessie Key: You may be wondering why the carbonyl oxygen is protonated first under acidic conditions. In the organic one acid and base unit, carbonyl oxygens were probably never used as a base. Carbonyl oxygens are considered very weak bases and not overly favored in a proton transfer equilibrium.

00:06:14:59 - 00:06:35:45
Dr.Jessie Key: But whatever amount does get protonated reacts quickly. Protonate carbonyls are fantastic electrophiles and readily undergo nucleophilic attack even with weak nucleophiles. Despite the enhanced electrophilicity of the protonate carbonyl, there are some limitations to nucleophilic additions of carbonyls.

00:06:35:45 - 00:06:52:58
Dr.Jessie Key: For example, the addition of halide nucleophiles is not favored. An example of this is shown with a generic ketone electrophile and HBr supplying the nucleophile bromide. This equilibrium strongly favors the reactant side with almost no addition product formation.

00:06:52:58 - 00:07:17:52
Dr.Jessie Key: This can be explained by the good leaving group ability of the halide outweighing its nucleophilicity. Therefore, the starting carbonyl will instead be more favored. In the remainder of this unit, you'll be exploring some common nucleophiles which favor nucleophilic addition to carbonyls, including some very important examples of oxygen nucleophiles, nitrogen nucleophiles, hydrogen nucleophiles and carbon nucleophiles.