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Diels Alder Reaction

Transcript

00:00:01:36 - 00:00:09:88
Dr.Jessie Key: Hello again, Dr. Jessie Key here. In this slide show, you'll be examining the Diels-Alder reaction, a type of cycloaddition.

00:00:10:84 - 00:00:47:32
Dr.Jessie Key: The Diels-Alder cycloddition reaction is named after its discoverers, Otto Diels and Kurt Alder, two German chemists who were awarded the Nobel Prize in 1950, recognizing the importance of this reaction. It is one of only a few carbon carbon bond forming reactions taught at the Organic I and II level, and it is an important synthetic tool which has been employed in many syntheses, including the first synthesis of important biological molecules like prostaglandins. The Diels-Alder reaction is an example of a [4+2] cycloaddition, a type of pericyclic reaction.

00:00:47:32 - 00:01:24:28
Dr.Jessie Key: The [4+2] cycloaddition classification is given as it involves two reagents: a 4-carbon conjugated pi system, “the diene”, and a 2-carbon pi system, “the dienophile”, which come together to form a new substituted cyclohexene product. Like all pericyclic reactions, the Diels-Alder proceeds through a concerted single mechanistic step with a cyclic redistribution of bonding electrons. In this example, the pi bond from the dienophile is going to form a new sigma bond between its uppermost vinyl carbon and the uppermost vinyl carbon of the diene.

00:01:24:28 - 00:02:05:94
Dr.Jessie Key: The uppermost pi bond of the diene comes down to form a new pi bond and the lowermost pi bond of the diene goes to form a new sigma bond between the lowermost vinyl carbon of the diene and the lowermost vinyl carbon of the dienophile. Note, when drawing the curved arrow notation mechanism for this reaction or any cycloaddition, the arrows can be drawn going around in a counterclockwise manner as shown or clockwise, the same results will be obtained. Examining a free energy diagram for this reaction with free energy on the y axis and reaction coordinate on the x-axis, we can see this is a single reaction step with a cyclic transition state.

00:02:06:42 - 00:02:29:19

Dr.Jessie Key: The Diels-Alder reaction is in equilibrium with its reverse reaction, the retro Diels-Alder. Lower and moderate temperatures favor the forward reaction, while higher temperatures favor the retro Diels-Alder. The Diels-Alder reaction is entropically unfavorable as the reaction goes from two molecules to one molecule.

00:02:29:19 - 00:03:05:22
Dr.Jessie Key: Furthermore, that one molecule is cyclic which has less freedom. However, breaking the 3 pi bonds and formation of 1 new pi bond and 2 sigma bonds is favourable in terms of enthalpy, since sigma bonds are stronger than pi bonds, resulting in a negative value for the change in enthalpy. We can therefore justify the reactivity observed for the reaction by taking into account the opposing enthalpic and entropic factors with the Gibbs free energy equation: delta G is equal to delta H plus negative T delta S. A lower value for

00:03:05:22 - 00:03:25:11
Dr.Jessie Key: the temperature will give a negative value for delta G, allowing the Diels-Alder reaction to proceed effectively. A higher value for temperature will give a positive value for delta G, favoring the reverse reaction, the Retro Diels-Alder. The structure of the dienophile plays a significant role in the usefulness of the reaction.

00:03:25:11 - 00:03:51:81
Dr.Jessie Key: Reactions using dienophiles with no electron withdrawing group present proceed very slowly due to having a relatively high activation energy. However, addition of an electron withdrawing group greatly reduces the activation energy and allows the reaction to proceed efficiently at lower temperatures. In this slide, the presence of the aldehyde group highlighted in red allows this Diels-Alder reaction to proceed rapidly with approximately 100% yield.

00:03:51:81 - 00:04:12:98
Dr.Jessie Key: To help explain the effect of the electron withdrawing group, we can turn to a Frontier Molecular Orbital Theory explanation. Frontier molecular orbitals were first described by Japanese chemist Kenichi Fukui in 1952. For this important contribution to understanding organic reaction mechanisms, Fukui was later awarded a Nobel Prize in 1981.

00:04:12:98 - 00:04:38:11
Dr.Jessie Key: Frontier Molecular Orbital theory states that the most important molecular orbitals for chemical reactions are the frontier orbitals, the LUMO and HOMO. The lowest unoccupied molecular orbital abbreviated as LUMO is the orbital most capable of accepting electrons. The highest occupied molecular orbital abbreviated as HOMO is the orbital with electrons most able to react.

00:04:38:11 - 00:05:04:29
Dr.Jessie Key: In the case of the Diels-Alder reaction, the HOMO of the diene donates electrons to the LUMO of the dienophile. For a dienophile with no electron withdrawing group, there's a significant energy gap between these two molecular orbitals. However,

when an electron withdrawing group is present on the dienophile, the energy level of the LUMO drops, decreasing the energy gap between the HOMO and LUMO, allowing the reaction to proceed more easily.

00:05:04:29 - 00:05:27:96
Dr.Jessie Key: Common electron withdrawing groups include carboxylic acids, esters, carbonyls, both aldehydes and ketones and nitriles. Carbonyl-based electron withdrawing groups can withdraw electron density by both induction due to their electronegative oxygen and also by resonance. The dienophile can also dictate the stereochemistry of the product obtained.

00:05:27:96 - 00:05:52:99
Dr.Jessie Key: When the dienophile is a Z-disubstituted alkene, the resulting cyclohexene product will have the two substituents arranged cis. However, when the dienophile is an E-disubstituted alkene, a transdisubstituted cyclohexene product will form. The conjugated diene structure also affects the Diels-Alder reactivity.

00:05:52:99 - 00:06:12:75
Dr.Jessie Key: Conjugate dienes can adopt one of two conformations, s-trans and s-cis. This nomenclature refers to the arrangement of the two alkenes relative to the single bond connecting them. It is observed that only alkenes capable of adopting the s-cis conformation undergo a Diels-Alder reaction.

00:06:12:75 - 00:06:45:25
Dr.Jessie Key: This is because only the s-cis conformation diene is capable of adopting the cyclic transition state with the dienophile, whereas the trans conformation carbons are too far apart in space to do this. This means that molecules unable to adopt the s-cis conformation, like the three 3-methylidenecyclohex-1-ene, shown above, cannot participate in a Diels-Alder reaction. Some molecules like cyclopentadiene are always in the s-cis conformation and are more readily able to undergo the Diels-Alder reaction.

00:06:45:25 - 00:07:12:43
Dr.Jessie Key: In fact, cyclopentadiene is so reactive towards the Diels-Alder reaction that even at room temperature, a molecule cyclopentadiene can react with another molecule of itself to form dicyclopentidiine. When cyclopentadiene and some other conjugated dienes are used, they can form bridged bicyclic products, having two possible stereochemical orientations of their substituents. Endo and exo.

00:07:12:43 - 00:07:33:97
Dr.Jessie Key: The terms exo and endo refer to the relative position of the substituents relative to the bridge making the bicyclic system. Substituents which are exo are those which are anti or opposite to the larger of the bicyclic bridges. Substituents which are endo are those which are sin or on the same side as the larger bridge.

00:07:33:97 - 00:07:56:28

Dr.Jessie Key: In this example, there is a larger 2-carbon bridge below a smaller 1-carbon bridge above. So the endosubstituent would be oriented relatively below, and the exo substituent would be oriented relatively above. Generally, the endopduct is favored, often so much that it is the only product observed.

00:07:56:28 - 00:08:30:90
Dr.Jessie Key: This is because in the cyclic transition state, there can be a favorable interaction which occurs between the electron withdrawing groups and the newly developing bonds. Looking at the energy diagram for this reaction with energy shown on the y-axis and reaction progress on the x-axis, the favorable interaction of the endo orientation lowers the energy of the transition state and therefore the activation energy. It is because of this lowered activation energy that the endo product tends to predominate, despite the greater stability seen for the exo substituted final product.