Application of Spectroscopic Methods in Molecular Structure Determination

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Lecture – 18
Mass Spectrometry

Hello, welcome back to the course on application of spectroscopic methods in molecular structure determination. We are in module 18 now. In this module, we will consider certain fragmentation patterns of organic molecules under electron impact ionization mass spectrometry.

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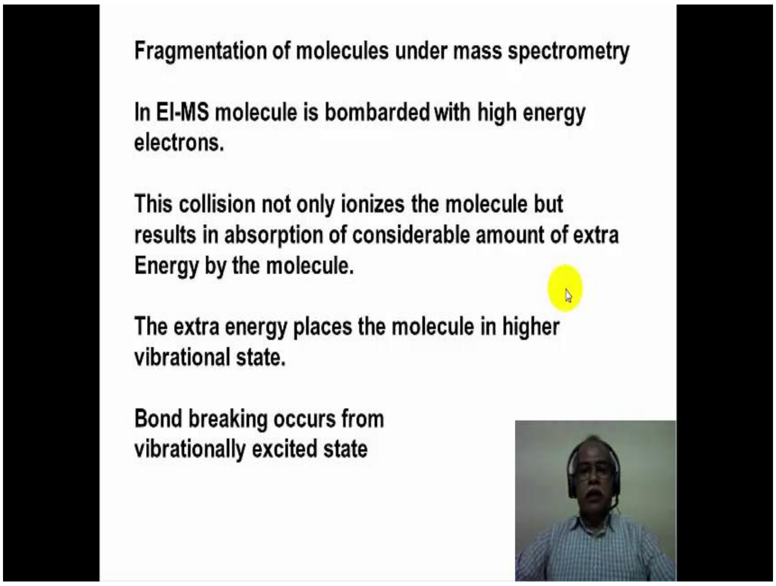

Fragmentation of molecules under mass spectrometry

In EI-MS molecule is bombarded with high energy electrons.

This collision not only ionizes the molecule but results in absorption of considerable amount of extra Energy by the molecule.

The extra energy places the molecule in higher vibrational state.

Bond breaking occurs from vibrationally excited state

Electron impact ionization mass spectrometry, the molecular ion typically undergoes fragmentation pattern which is a very valuable thing in the structural elucidation problems. Now, in the electron impact ionization, molecule is actually bombarded with high energy electron. This collision not only ionizes the molecule, but it results in the absorption of considerable amount of extra energy by the molecule. This extra energy can place this molecule in higher vibrational state. Once, molecules are in the higher vibrational state they can undergo bond breaking from the vibrationally excited state resulting in extensive fragmentation. In fact, the fragmentation pattern is a finger print kind of a signature of an individual molecule and it is reproducible and hence it is extremely valuable in structural elucidation problem.

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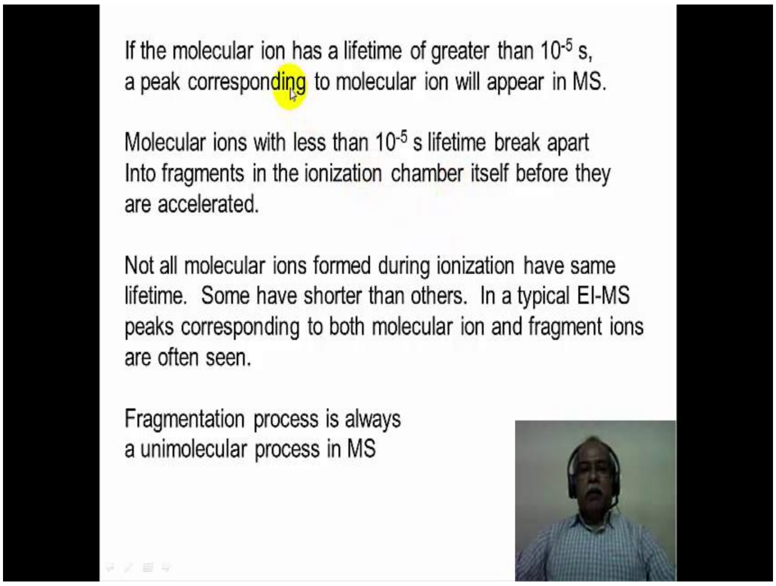

If the molecular ion has a lifetime of greater than 10^{-5} s, a peak corresponding to molecular ion will appear in MS.

Molecular ions with less than 10^{-5} s lifetime break apart Into fragments in the ionization chamber itself before they are accelerated.

Not all molecular ions formed during ionization have same lifetime. Some have shorter than others. In a typical EI-MS peaks corresponding to both molecular ion and fragment ions are often seen.

Fragmentation process is always a unimolecular process in MS

Typically, if a molecular ion has a lifetime more than 10 to the power minus 5 second, the corresponding peak will be registered in the mass spectrum. However, molecular ions which less than 10 to the power minus 5 seconds of lifetime break apart into fragments in the ionization chamber itself before they are accelerated, but then not all molecular ions formed during ionization have the same lifetime. Hence, some of them will be fragmented and some the molecular ions will still get registered as molecular ion in the mass spectrum. Fragmentation process is always a uni molecular process because the concentration of the gas phase ions are so low that collisional intermolecular collision is very unlikely that is the reason one says, the fragmentation process is always a uni molecular process under mass spectrometric conditions.

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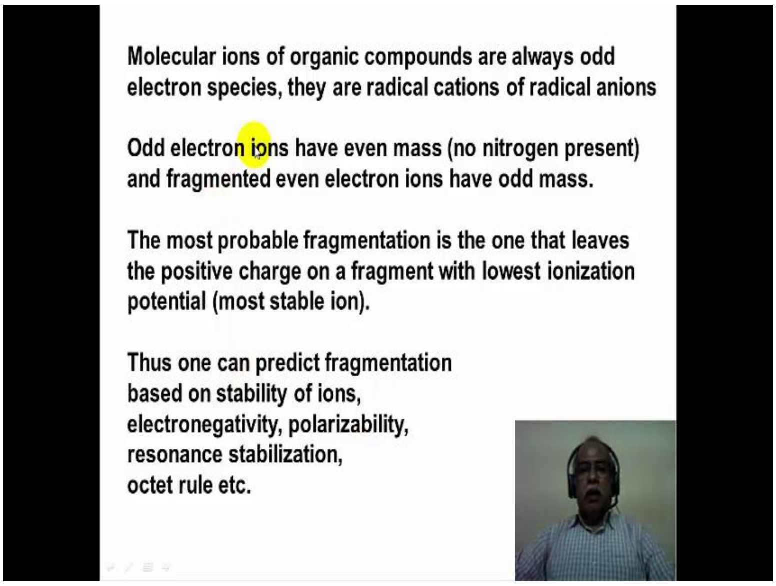

Molecular ions of organic compounds are always odd electron species, they are radical cations of radical anions

Odd electron ions have even mass (no nitrogen present) and fragmented even electron ions have odd mass.

The most probable fragmentation is the one that leaves the positive charge on a fragment with lowest ionization potential (most stable ion).

Thus one can predict fragmentation
based on stability of ions,
electronegativity, polarizability,
resonance stabilization,
octet rule etc.

The molecular ion is actually obtained by knocking of an electron from the organic molecule. Organic molecules typically have even number of electrons therefore, when it is ionized to a cation radical or an anion radical they become odd electron species that is why they are called the radical cations or the radical anions. Odd electron ions have even mass, if there is no nitrogen present. If they have a nitrogen present one nitrogen or odd number of nitrogen present, then it will have odd mass and the fragmented even electron ions will have odd mass. This is something we can see in practical terms when we consider the fragmentation pattern of various molecules.

The most probable fragmentation is the one that leaves the positive charge on a fragment with a lowest ionization potential. This is understandable because the ion will be stable ion; it is the most stable ion that is going to be resulting in the fragmentation pattern. So, one can even predict the fragmentation pattern based on the stability of ions based on the electronegativity, polarizability, resonance stabilization, octet rule. All these can be applied towards the stabilization of a particular ion. So, it is possible to predict the fragmentation of certain class of organic compounds.

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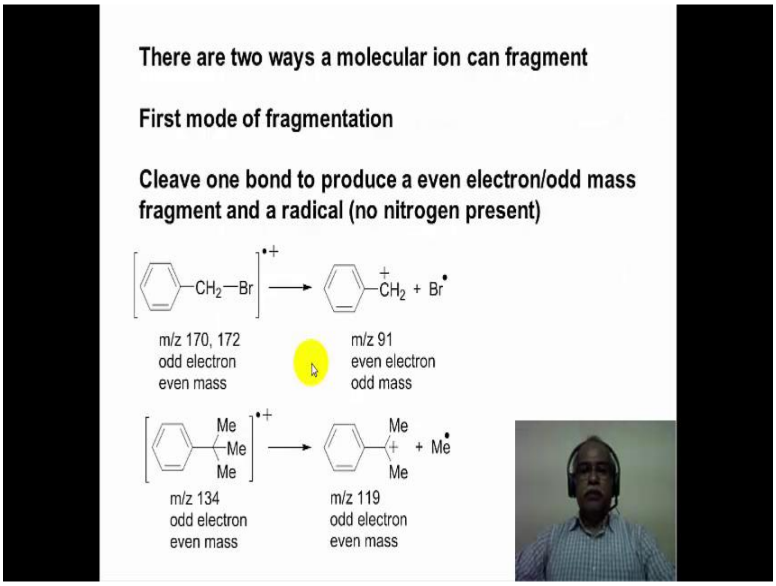

There are two ways a molecular ion can fragment

First mode of fragmentation

Cleave one bond to produce a even electron/odd mass fragment and a radical (no nitrogen present)

There are two ways the molecular ion can fragment. The first mode is essentially cleavage of a single bond to produce even electron, odd mass fragment and the radical. This is illustrated in this example, if you take the benzyl bromide as an example. The radical cation of benzyl bromide will have two molecular ions because of the bromine 170 and 172. This is an odd electron species because it is a cation radical, but the masses are even you can see here. When it undergoes the fragmentation to get rid of the bromine, the bromine radical is produced. The resulting ion is a actually an unbiased value 91, which is an odd mass and it is an even electron species because one of the electron has gone with the bromine. So, the cation radical when it undergoes a fragmentation process in this particular manner, it produces an odd mass and an even electron species. This is what is meant by the statement cleavage of one bond produces the even electron odd mass fragment and a radical.

Let us consider the case of tertiary butyl benzene. Tertiary butyl benzene is one of the methyl carbon methyl bond can be broken resulting in the formation of a tertiary cation which is a stable cation. Similarly, here also the benzyl cation is a stable cation that is one of the reasons why the carbon bromine bond is weakened during the fragmentation process that takes place selectively to get rid of the bromine to get the benzyl cation which is stable cation. This is a di methyl substituted benzyl cation. It should be even more stabled because it is a tertiary cation compared to this one. Once again, if you see you start with the even molecular weight after the fragmentation. To get rid of this methyl radical you get an odd mass which is 119, this is an odd electron species with the even mass and the fragmented molecule is an odd electron species with the even mass this is what is meant by the statement that cleavage can produce and even electron and an odd mass fragment.

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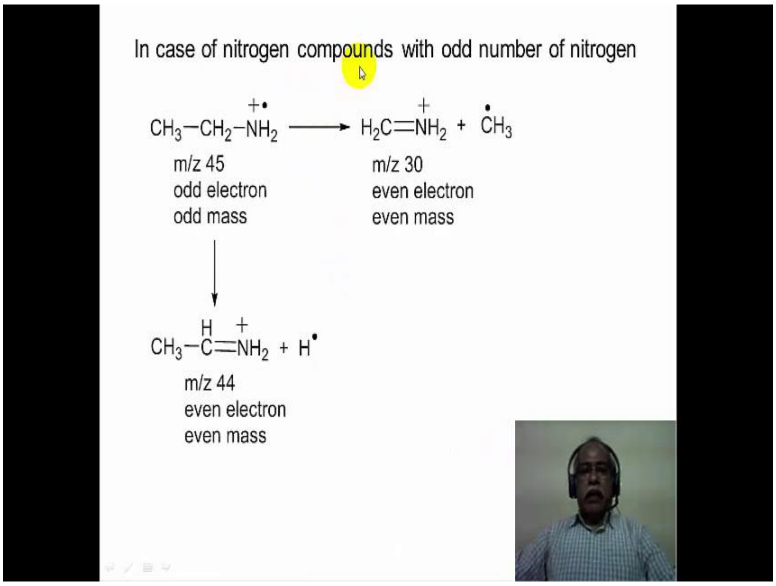

In case of nitrogen compounds with odd number of nitrogen

$$CH_3-CH_2-\overset{+\bullet}{N}H_2 \longrightarrow H_2C=\overset{+}{N}H_2 + \overset{\bullet}{C}H_3$$

m/z 45
odd electron
odd mass

m/z 30
even electron
even mass

$$\downarrow$$

$$CH_3-\overset{H}{C}=\overset{+}{N}H_2 + H^{\bullet}$$

m/z 44
even electron
even mass

Suppose, in case of nitrogenous compound where there is an odd number of nitrogen. Take the example of ethylamine cation radical because of the presence nitrogen the mass is odd, but the molecular ion is also an odd electron molecular ion, so both, the mass as well as the electron count or odd in this particular case when a fragmentation takes place. In this particular case, there are two types of fragmentation that can take place. In the first fragmentation, a methyl can be lost resulting in the formation of an iminium ion which has even number of mass and even electron count also. On the other hand, the alpha hydrogen can be removed as H dot, resulting in the formation of a methyl substituted iminium ion. The difference between this and this is that this is a methyl substituted iminium ion, this is simple iminium ion. This is even electron and even mass species because there is nitrogen present in this particular case.

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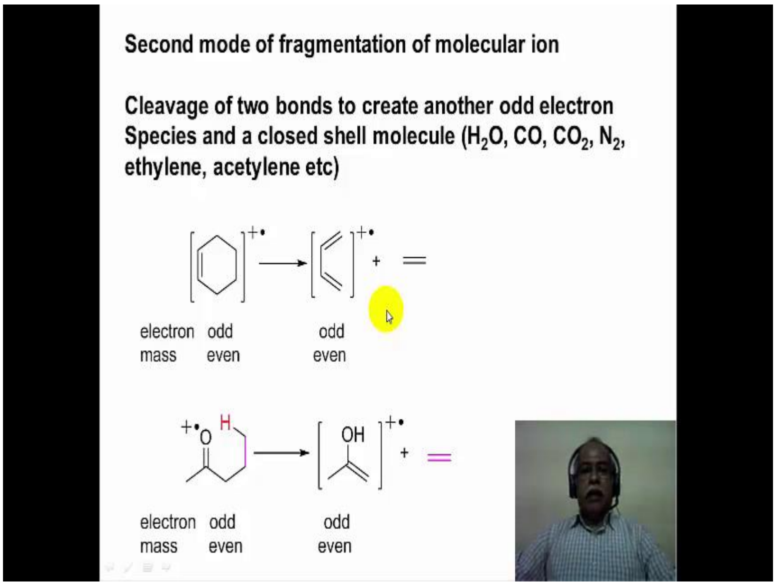

Second mode of fragmentation of molecular ion

Cleavage of two bonds to create another odd electron Species and a closed shell molecule (H_2O, CO, CO_2, N_2, ethylene, acetylene etc)

The second mode of fragmentation of a molecular ion is to cleave two bonds. This typically happens when you have something like a Retro-Diels of reaction taking place or Mclafferty rearrangement kind of a rearrangement that is taking place. In all of these process, a closed shell molecules such as water, carbon monoxide, carbon dioxide or nitrogen, ethylene, acetylene these are simple molecules which are released during the course of fragmentation.

Let us take the example of cyclohexene cation radical. Cyclohexene cation radical one of the fragmentation processes is to lose ethylene to give butadienyl cation radical. Now, you start with an odd electron species and you end up with an odd electron species with the removal of a neutral small molecule like ethylene. In this particular case, the mass is even to start with and end up with even mass also. So, an odd electron even mass species upon a fragmentation to release a neutral molecule like ethylene essentially ends up with an odd electron even mass kind of a species.

This is true in the case, the hydrogen is migrating to the oxygen resulting in the formation of the enol, which is registered as the radical cation and the neutral molecule of ethylene corresponding to this particular fragment is released. We will see the mechanism of the Retro-Diels of the reaction and the Mclafferty rearrangement in a while.

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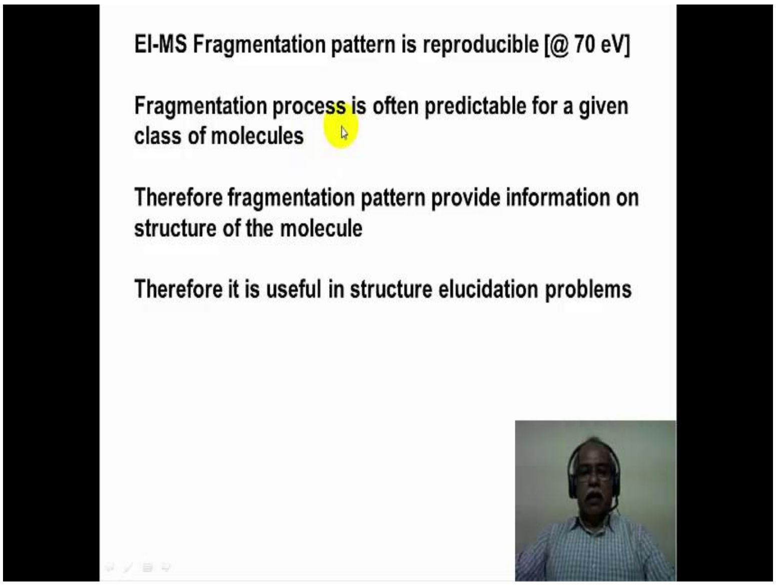

EI-MS Fragmentation pattern is reproducible [@ 70 eV]

Fragmentation process is often predictable for a given class of molecules

Therefore fragmentation pattern provide information on structure of the molecule

Therefore it is useful in structure elucidation problems

As I mentioned earlier, the electron impact ionization mass spectrometry fragmentation pattern is a reproducible one, if it is carried out under controlled condition. Typically, at 70 electron volts of energy of the electron beam which is the excitation beam.

Now, if the molecular fragmentation pattern is reproducible then one can actually create a library of a fragmentation pattern of various types of molecule and this fragmentation pattern being a finger print kind of a system, it is easy to identify molecules or unknown molecules and correlated with the known fragmentation pattern. Fragmentation process is often predictable for a given class of molecule. This is what is meant by the fact that the fragmentation takes place to produce the most stabled cation and so on. Based on this predictability is what is essential for the identification of the organic molecule based on the pattern recognition.

Therefore, this is useful in the structural elucidation problem that is the fragmentation pattern is useful in the structural elucidation problem.

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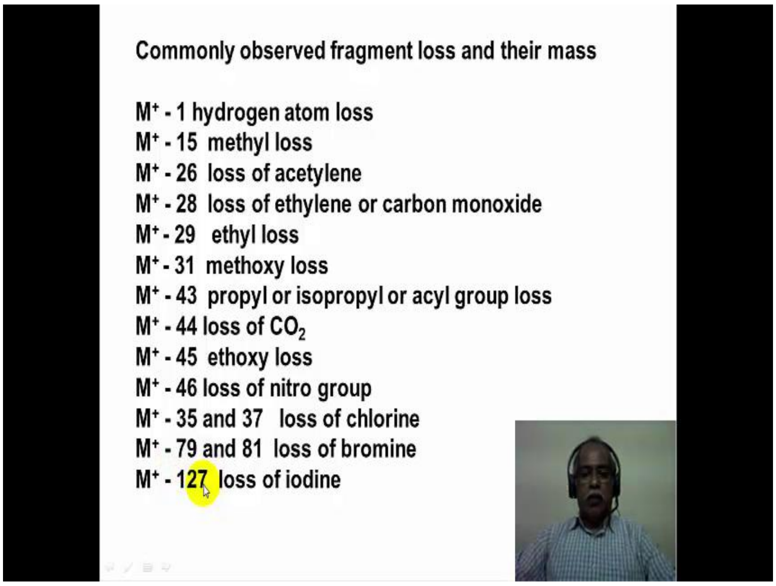

Commonly observed fragment loss and their mass

M^+ - 1 hydrogen atom loss
M^+ - 15 methyl loss
M^+ - 26 loss of acetylene
M^+ - 28 loss of ethylene or carbon monoxide
M^+ - 29 ethyl loss
M^+ - 31 methoxy loss
M^+ - 43 propyl or isopropyl or acyl group loss
M^+ - 44 loss of CO_2
M^+ - 45 ethoxy loss
M^+ - 46 loss of nitro group
M^+ - 35 and 37 loss of chlorine
M^+ - 79 and 81 loss of bromine
M^+ - 127 loss of iodine

Now, the commonly observed fragments which are lost during their fragmentation process and their masses are given here. Normally, when there is one mass unit different from the molecular ion, this is typically of hydrogen atom loss. If there is 15 unit of loss, then corresponds to methyl CH3. If it is 26 loss then it is an acetylene molecule, a neutral molecule is lost. In these two cases, these are radicals which are lost hydrogen radical, hydrogen atom and methyl radical whereas, in this case a neutral molecule is lost in the form of acetylene.

Similarly, for the loss of 28, which is an even mass for example, it will be a loss of ethylene or a carbon monoxide molecule. If it is 29, it will be ethyl group loss, C2H5 corresponds to 29. If it is 31 loss, then it will be methoxy. 43 losses can either be a propyl group or an isopropyl group or a CO CH3 group, acetyl group loss can also be 43. 44 is typically carbon dioxide, this is a very characteristic feature of decarboxylation reaction where molecule loses a molecule of carbon dioxide with the loss of 44. Ethoxy corresponds to 45 mass unit losses and nitro group corresponds to 46.

If the halogens are present ,then you will see loss corresponding to 35 and 37 corresponds to the chlorine. 79 and 81 corresponds to bromine and if there is an iodine which is lost from the molecule then a big chunk of the mass is gone, 127 mass loss corresponds to iodine mass loss.

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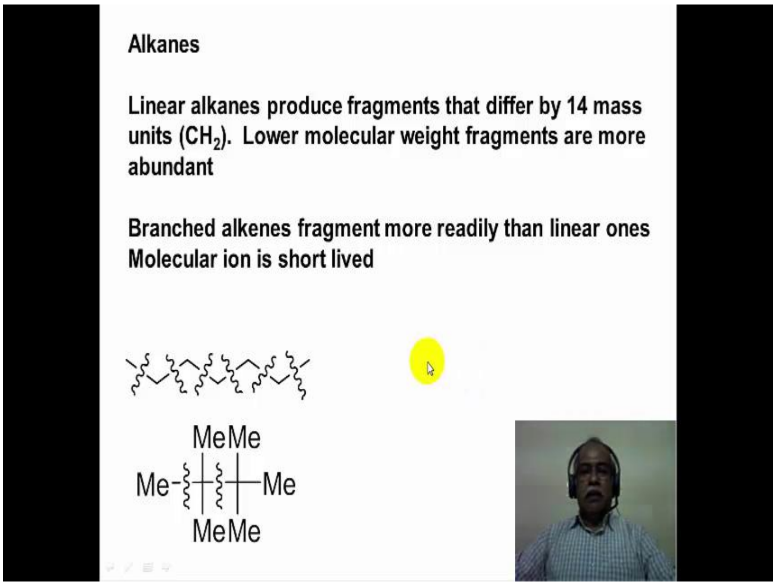

Alkanes

Linear alkanes produce fragments that differ by 14 mass units (CH_2). Lower molecular weight fragments are more abundant

Branched alkenes fragment more readily than linear ones
Molecular ion is short lived

Now, typically in linear alkene, they produce fragments which differ by 14 mass units because let us consider this linear alkene. If you fragment it here, methyl is lost subsequent fragmentations correspond to loss of CH2. CH2 groups which are 14 mass unit difference. So, the lower molecular fragments are more abundant normally compare to high molecular weight fragments. Whereas, in the case of the branched alkene fragmentation takes place more readily because fragmentation of let us say for example, this more branched alkene essentially results in the form of formation of tertiary cations. So, the fragmentation process is much more facile in a branched system and hence the molecular ion is highly short lived. In fact, if we look at the molecular ion peak of the branched system there will be negligible compare to the fragmentation molecular ion of the linear alkenes.

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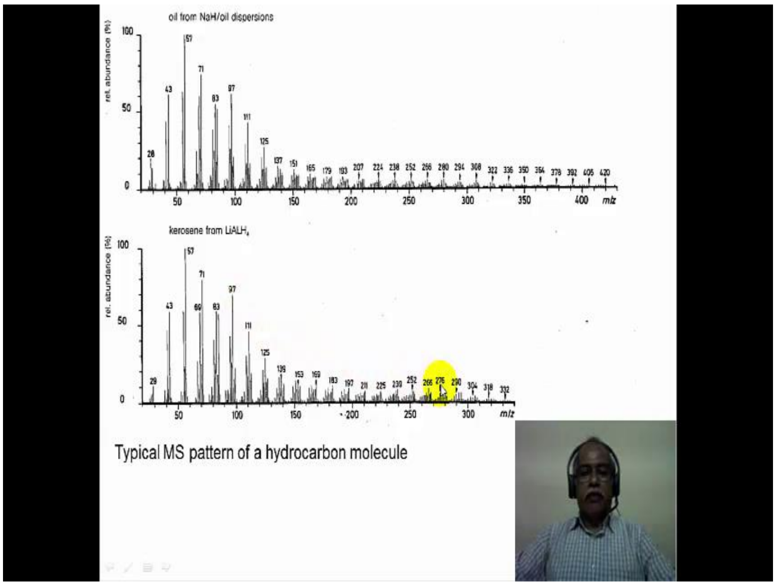

Typical MS pattern of a hydrocarbon molecule

Typically, linear alkenes show a fragmentation pattern like this. This a Gaussian type of a thing, the most probable ions are the low molecular weight ions. If you see each one of them will differ by 14 mass units corresponding to the CH2 unit. This is the oil that is used as dispersion oil for storing sodium hydride. Sodium hydride is typically kept under paraffinic oil and this corresponds to the mass spectrum of such oil being investigated and it gives the peak corresponding to 14 mass unit differences all along up to the point of reaching the lowest molecular weight of 43 or 28 or so. This is the kerosene sampled from lithium aluminum hydride. Lithium aluminum hydride is also stored under kerosene because it is air sensitive, moisture sensitive. So, this is again a typical fragmentation pattern of a linear hydrocarbon molecule kind of thing.

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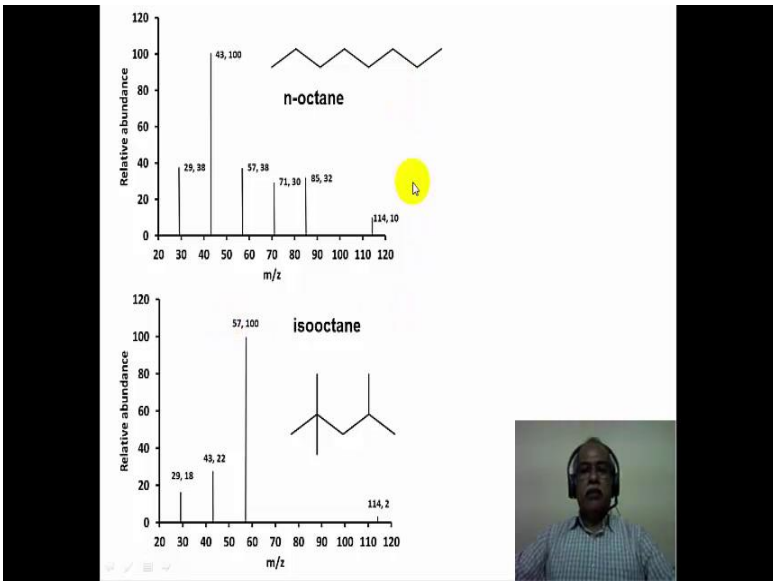

N-octane for example, shows the molecular ion at 114, which is a small one. The most prominent peak is the propyl cation which is 43. So, fragmentation must be happening somewhere around here or somewhere around here, resulting in the formation of the propyl cation as the most abundant cation. On the other hand, if you look at isooctane, which is a highly branched hydrocarbon, the molecular ion which is at 114 is a negligible amount of molecular ion is there in comparison to the n-octane, it is even smaller than n-octane. For example, here the relative abundance is 10 percent, whereas the relative abundance here is only 2 percent and the fragmentation results in the tertiary butyl cation which corresponds to 57, which is the most abundant or the base peak of the mass spectrum.

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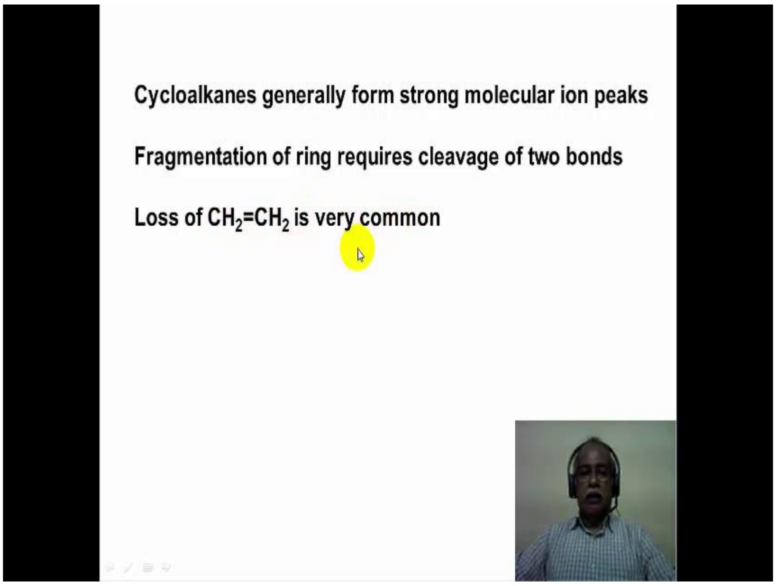

Cycloalkanes generally form strong molecular ion peaks

Fragmentation of ring requires cleavage of two bonds

Loss of $CH_2=CH_2$ is very common

Cycloalkanes generally form strong molecular ion. Fragmentation requires bond cleavage at two different positions. In other words, the Retro-Diels kind of a fragmentation will result in the cleavage of two bonds; therefore, the loss of ethylene is generally very common in the case of cycloalkene.

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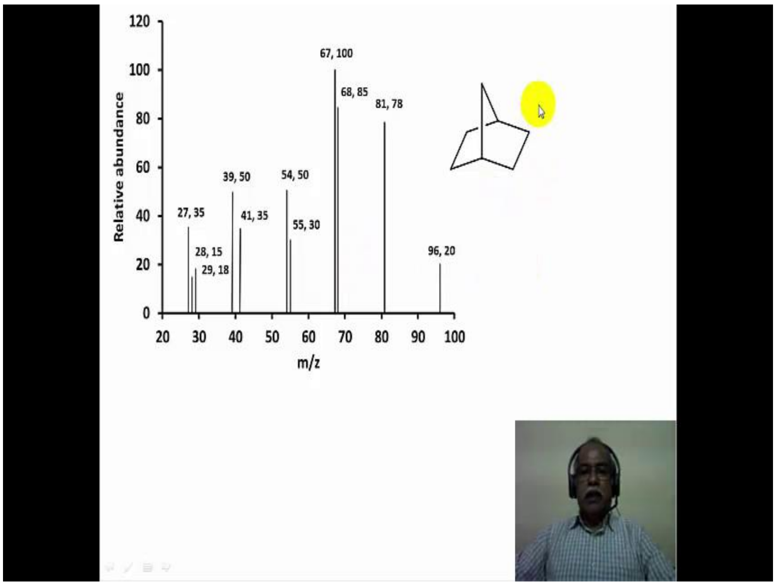

Let us take the example of norbornane. Norbornane molecular ion peak is around 96.2 and if it loses an ethylene molecule 28 mass unit will be lost that would correspond to 67. After that you get the loss of ethylene molecule probably it to produce a cation radial of cyclopentene for example, or cyclopentene cation radical is what will be produced and such a cation radical loses a hydrogen atom to give 67 which is the base peak. So, loss of an ethylene unit followed by loss of a hydrogen atom resulting in the formation of a cyclopentenyl cation is corresponding to the 67 mass units. The subsequent fragmentation produces the smaller peaks at you will see here.

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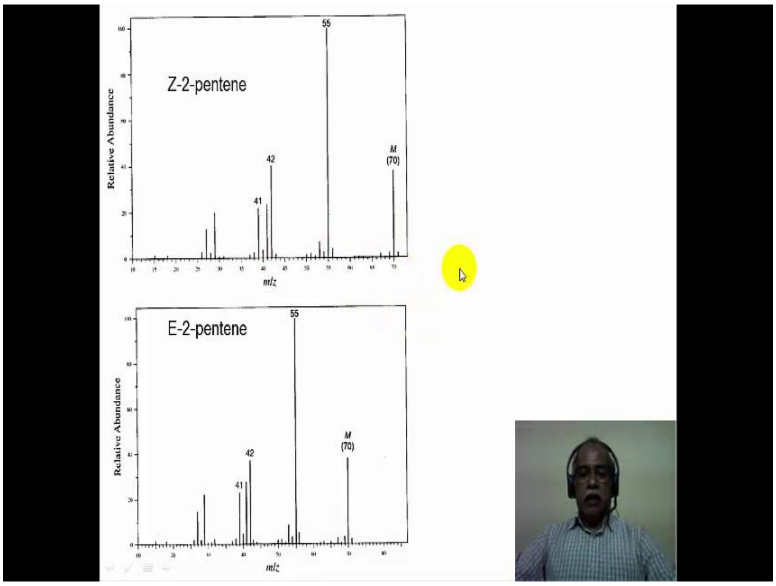

In fact, in the mass spectrum you do not tend to interpret every one of the tiny little peaks that are seen here. The most prominent peaks are generally interpreted with some fragmentation kind of a pattern; the rest of the peaks are generally not valuable in the structural elucidation problem and one does not pay attention to anything less than 20 percent of relative abundance unless it is a molecular ion peak.

Now, here the comparison of Z-2 pentene and E-2 pentene are given here and this essentially corresponds to more or less an identical spectrum. You have the molecular ion peak at 70, a fragment peak which is due to the loss of a methyl group for example, comes at 55 and there is a peak at 42, which probably comes from the loss of a ethylene kind of a group because this is 28 mass unit different from the 70 and then loss of a hydrogen from this fragment will essentially give 41.

A similar identical pattern of fragmentation is what is seen. In other words, based on mass spectrometry one cannot distinguish between Z pentene, Cis-pentene from Transpentene, which is the E pentene for example. So, stereo isomers of this nature cannot be distinguished by mass spectrometry, if they have identical fragmentation pattern.

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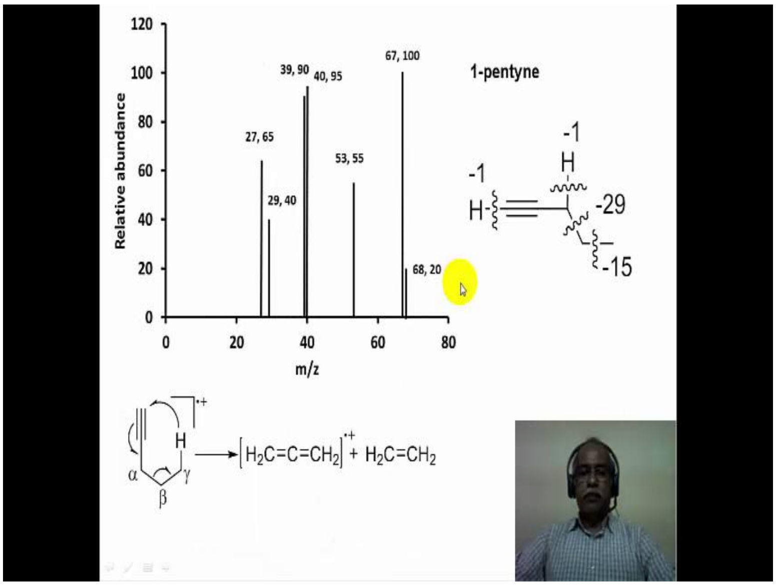

In the case of acetylene, if it is terminal acetylene like in the case of 1-pentyne there are two possible ways hydrogen can be lost. The hydrogen can be lost from the terminal alkane, which is one mass unit less or the propargylic hydrogen can be lost because that will generate a stabled propargylic cation and this is what is registered at 67 one mass unit less than the molecular ion which is 68. So, the base peak is essentially 100 percent abundant peak is loss due to the hydrogen atom either from this position or from this position then comes the loss due to the methyl group which is corresponding to 15 losses corresponding to 29.

For example, if you subtract 29 from this one essentially, you will get the molecular, the fragmented ion somewhere in this particular region for example, and the further fragmentation is the Mclafferty rearrangement, in other words here because of the C triple bond C, it is capable of undergoing a gamma hydrogen abstraction to this position resulting in the formation of an allene, the mechanism is as shown by the fish hook arrows because we are talking about an odd electron species.

We always use fish hook arrows to show the mechanism rather than a regular arrow to show the mechanism. So, the allene is registered as the ion corresponding to let us say 40, I think it is 36 plus 4, 40 is the molecular weight of this particular ion and that is registered and the allene losses one hydrogen to give the alleneyl cation that corresponds to 39 in this case. The ethyl loss can be seen as 29 fragment here in this particular case as a one of the ions that is produced in this case.

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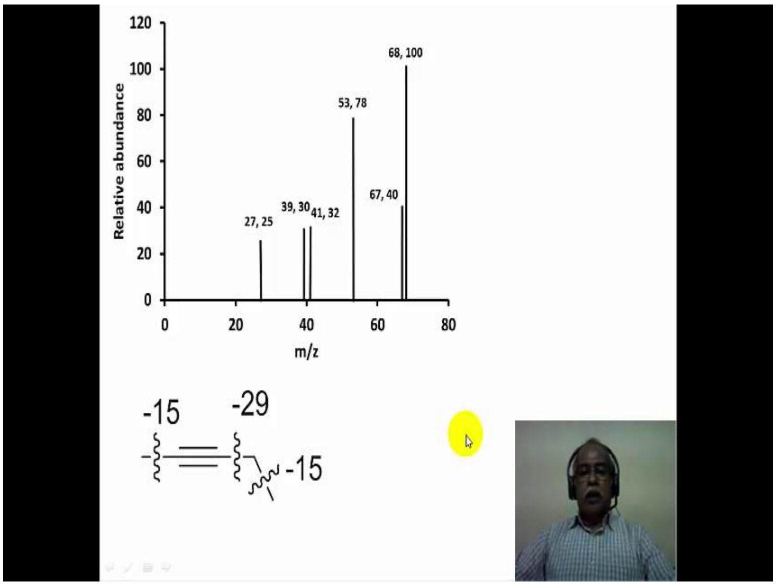

When the alkyne is an internal alkyne, there is no loss here for example, loss of hydrogen is the base peak 68 minus 167 corresponds to the loss of hydrogen, but you see here the base peak itself is the molecular ion peak because the loss of hydrogen from the propargylic position is not so much compared to the terminal acetylene hydrogen, since terminal acetylene hydrogen is missing in an internal alkane as in the case of the two pentyne for example, the molecular ion peak itself is registered as a base peak in this particular case. Subsequently, loss of 29 and 15 essentially gives you the fragmented ions which are seen in the mass spectrum.

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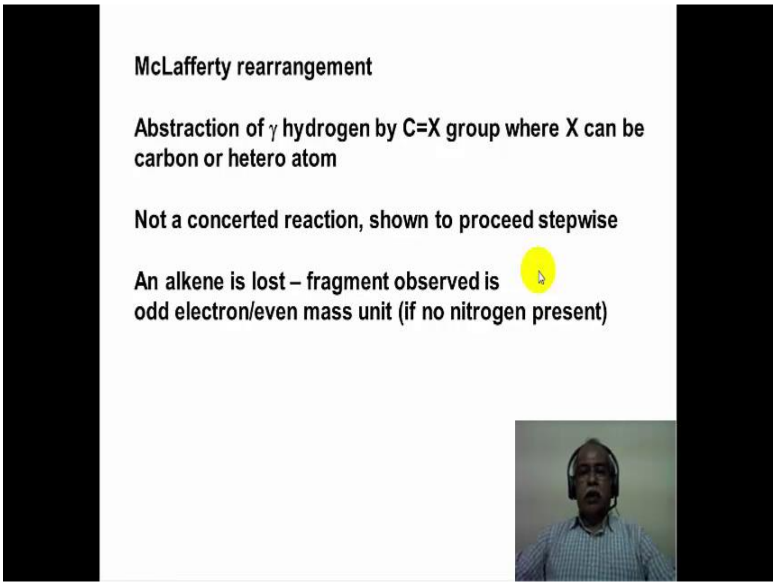

McLafferty rearrangement

Abstraction of γ hydrogen by C=X group where X can be carbon or hetero atom

Not a concerted reaction, shown to proceed stepwise

An alkene is lost – fragment observed is odd electron/even mass unit (if no nitrogen present)

Now, let us have a look at Mclafferty rearrangement. Abstraction of gamma hydrogen by C double bond X or C triple bond X, in other words a cyano group or a carbonyl group will be representation of C double bond X and C triple bond X for example, where x can be a carbon or hetero atom. It could be C double bond C or C triple bond C also is capable of undergoing the Mclafferty rearrangement. It is not a concerted reaction, although the mechanism normally we depict in the mass spectrometry mechanism is concerted mechanism. It has been shown to go via stepwise mechanism. An alkene is generally lost the fragment observed is an odd electron even mass unit if known to a nitrogen is present this is something we have already discussed.

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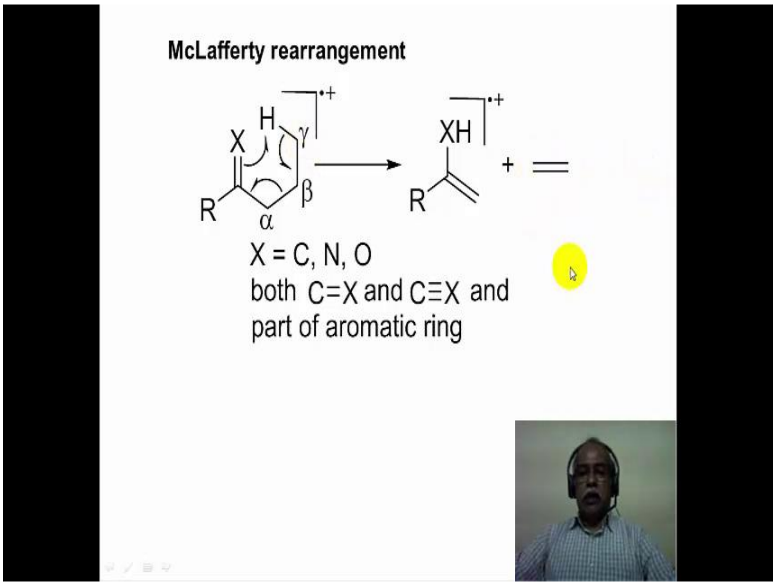

McLafferty rearrangement

X = C, N, O
both C=X and C≡X and
part of aromatic ring

So, this is Mclafferty rearrangement, this is alpha, beta, gamma, hydrogen this is a gamma position hydrogen which is subtracted by the X, resulting in the formation of this kind of een product and one of the ethylene is lost from this beta gamma carbon is lost as a ethylene unit in this particular case. So, typically an alkyne is lost during the Mclafferty rearrangement.

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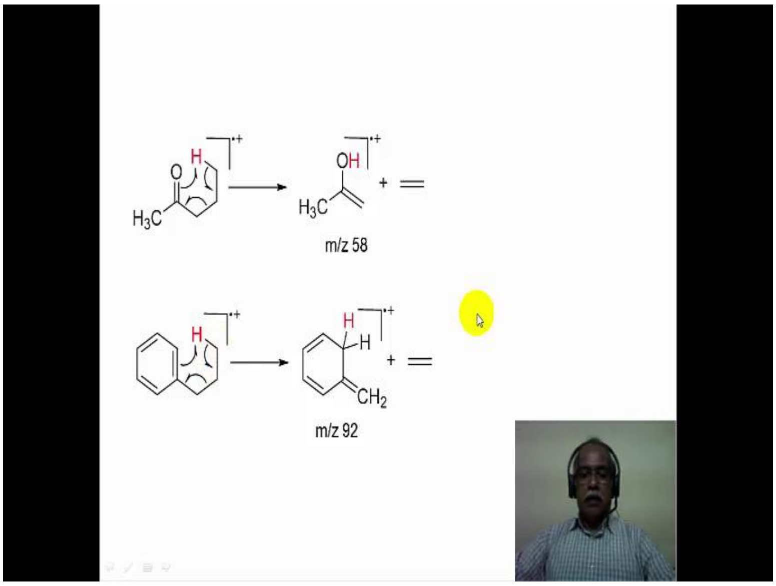

Let us take the example of this particular molecule which is two pentanone I think; two pentanone undergoes Mclafferty rearrangement to produce acetone enol. This is an enolic structure of acetone and loss of ethylene unit corresponds to registering of this particular ion at 58. Between these two fragments that are produced the charged resides with the enol because enol will have a lower ionization potential compared to ethylene. So, you remember that an ion with the lowest ionization potential is what is going to be produced during the fragmentation and this is a good example of that. In the case of butyl benzene, the carbon carbon double bond of the aromatic ring itself acts as the hydrogen acceptor upon hydrogen transfer essentially you produce the tautomer of tolvin, which has the molecular peak at 92 m by z value with the loss of ethylene which is these two carbons are lost as the ethylene in this particular fragmentation pattern.

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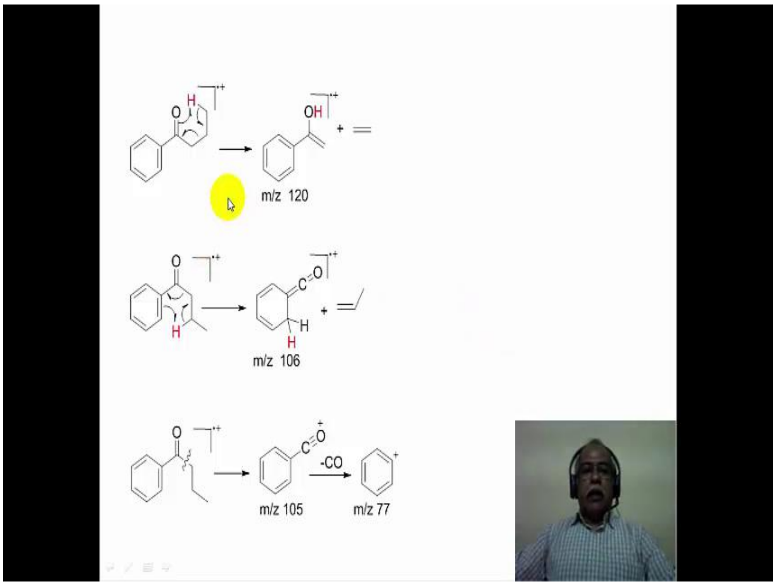

Now, in the case of this particular ketone, which is 1, 2, 3, 4 is butyrophenone. There are two possible ways the Mclafferty rearrangement can happen involving a carbon oxygen bond. The Mclafferty rearrangement is shown to produce an ion at 120 m by z value using the carbon, carbon double bond of the aromatic ring. The Mclafferty rearrangement is shown to produce this particular species which is molecular weight of 106, both of these are essentially even molecular weight ions cation radicals is what is produced. In this particular case, ethylene is lost, whereas, in this particular case the propane the propene is lost as the fragment.

The butyrophenone can also undergo another type of a fragmentation that is by alpha fragmentation which is resulting in a stable assail type of a cation. This is a benzyl cation what is produced with the mass registered at 105 and this can lose a carbon monoxide molecule to produce the phenyl cation which is at 77. So, in the mass spectrum of butyrophenone one should see 105, 106, 120 and 77 as prominent peaks.

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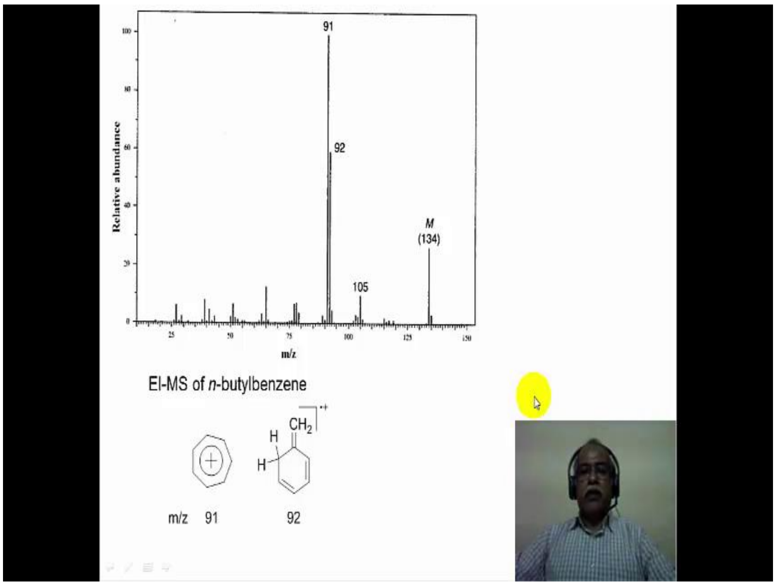

EI-MS of *n*-butylbenzene

m/z 91 92

In fact, you can see this in the mass spectrum of this particular compound. Now, this is the electron impact ionization mass spectrum of n butyl benzene. Remember, we discussed n butyl benzene and said it should register ion at 91, n butyl benzene essentially registers ion at 91, it is fine and this is also producing an ion at 92 because of the Mclafferty rearrangement. 91 is produced by the simple alpha fragmentation, this is n butyl benzene, if you cleave this fragment alpha beta bond here, it produces the benzyl cation. Benzyl cation is 91, whereas this is the tautomer of tolvin which is 92. In fact, you see 91 as well as 92 in addition to that loss of a methyl loss of an ethyl group, which is a 29 fragmentation is also seen which corresponds to the 105 as the registered ion in this particular spectrum.

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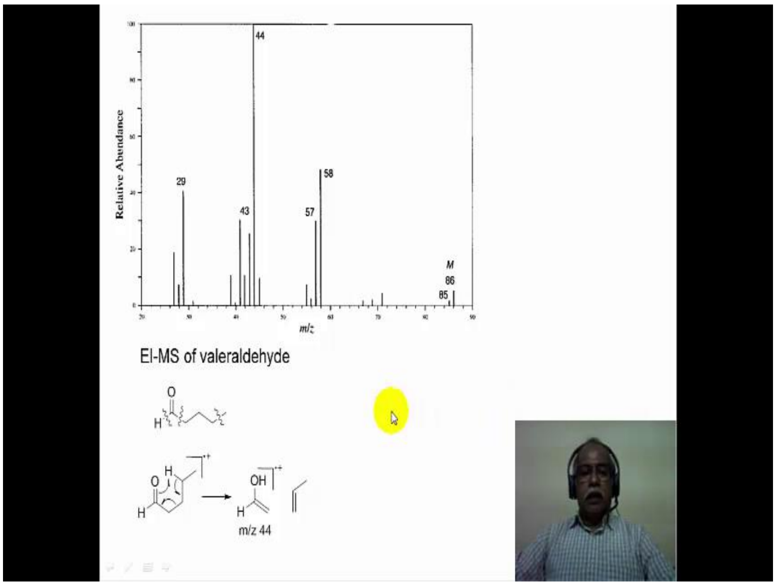

EI-MS of valeraldehyde

This is spectrum electron impact ionization as spectrum of valeraldehyde, which is C5 carbon aldehyde. The formyl loss which is 29 loss should be seen somewhere here. 29 corresponds to the losses corresponding to the 58 peak corresponds to the loss of 29 then the Mclafferty rearrangement peak should come around 44. In fact, that is the base peak in this particular spectrum and 57 corresponds to this is a gamma hydrogen abstraction. One can also have alpha, beta, gamma, delta hydrogen abstraction with the loss of 28 mass units from the molecular ion peak for example, that should result in the formation of the 58 molecular ion peaks. This is the ion peak corresponding to 58 m by z corresponds to the delta hydrogen abstraction, where the hydrogen from this position is subtracted the formyl loss is seen as 29 peak which corresponds to the HCO.

In fact, this alpha fragmentation results in HCO formation as aceline cation in this particular case. So, one can lose a methyl group which is loss of 15, which will be somewhere here 71 corresponds to the 15 loss. One can have a loss of this butyl group here forming the corresponding formyl cation which is 29 for example, the butyl cation itself is registered somewhere here probably and the Mclafferty rearrangement product is registered at 44, these are the fragmentation patterns.

So, what you have seen is the fragmentation pattern of some simple organic molecules. Mclafferty rearrangement and alpha fragmentation, which is a simple fragmentation, is what we have seen. In the next module, we will continue with the desolidar fragmentation and many other functional group fragmentations and consider the electron impact ionization fragmentation pattern further.

Thank you very much for your attention.