Interpretative Spectroscopy

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Lecture 38

Introduction to Mass Spectrometry

Hello everyone, I once again welcome you all to MSB lecture series on Interpretative Spectroscopy. Today I shall start discussion on mass spectrometry. In my previous lectures, I started with NMR spectroscopy and then switched over to UV visible spectroscopy and then moved on to IR spectroscopy. So, these three have some resemblance, whereas the present one which I am going to discuss today mass spectrometry is little different from those traditional spectroscopic methods. So why we call it as spectrometry not spectrometer and also, we shall look into it and also always you should say mass spectrometry, not spectrometer as spectroscopy.

It is not mass spectroscopy, it is mass spectrometry. Let us look into some fundamentals on mass spectrometry abbreviated as MS. MS or mass spectrometry analyses or examines ions in gas phase that are produced through hard and soft ionization methods. That means we can ionize using hard methods or we can also use soft ionization methods.

Routinely mass spectrometry is to determine the molecular weight. The sole intention of subjecting a sample, an unknown sample, to mass spectrometry is to determine the molecular weight. However, the ion fragments that are generated can effectively use a fast-exile oxidation. It gives lot of information, the ion fragments, how molecule will fragment out, how it disintegrates. That means how we can reassemble.

All this vital information comes apart from giving information about the molecular weight. The advantage is mass spectrometry can use any state of matter and also it can be coupled with chromatographic methods, so all those operations for mixtures as well. So, this is the main advantage. We can use in gas phase, liquid phase, also in solid phase, but often solid phase; we can use in case of NMR and IR, and solvent we can use. Gas means we have to have a special device, whereas here advantage is no matter in which state the matter is there, we can conveniently use mass spectrometry and also it provides a convenient way to study gas phase reactions.

So, often when we do gas phase reactions, it is very difficult to monitor using other spectroscopic methods, whereas here we can conveniently study and understand the mechanistic pathway and several other related things about kinetics using gas phase reactions. Kinetic and thermodynamic parameters can also be studied using mass spectrometry that is another advantage of mass spectrometry. Since mass spectrometry involves measurement of mass numbers not energy absorption, it is referred to as mass spectrometry and not spectroscopy. I repeat again: since mass spectrometry involves measurement of mass numbers not energy of absorption, it is referred to as mass spectrometry and not spectroscopy.

NMR and IR involve the absorption of energy in the form of appropriate electromagnetic radiation. Just to compare, I have shown this plot here about wavelengths. You can see here the length of one full circle is called wavelength and then the number of cycles per second is referred to as frequency nu, and also, we know the relationship of frequency to wavelength nu equal to c over lambda and c is velocity of light ($\nu = \frac{c}{\lambda}$), 3 into 10 raise to 8 meters per second (3×10^8) or 10 raise to 10 centimeters 10^{10} per second in vacuum. Shorter the wavelength higher the frequency and more energetic the wave is. Lower wavelength means higher frequency. It involves the ionization of compounds, there what happens, the sample identity is retained while measuring, and after measuring, in this case, it involves the ionization of the compound. In order to understand the details about how it ionizes how fragments are coming out and what is molecular weight. We have to destroy the sample here the molecule.

So, it involves the ionization of the compounds and hence is a destructive method of analysis and there is no scope whatsoever for the recovery of the sample, whereas in other spectroscopic methods; in NMR you can measure you can recover the solvent, you can recover the sample and from IR you can recover the sample and also from UV visible you can always recover the sample and also we look for such a condition. So, that sample should not be affected or should not be decomposable or should not be degraded. So, these precautions we take in case of spectroscopic methods, whereas in spectrometry we intentionally destroy the molecule in order to know the information that is required from mass spectrometry. So, this is a destructive method.

Important steps in structural analysis: First of all, the sole intention is to determine the molecular weight and molecular weight can be accurately determined by mass spectrometry, that is the major advantage. While determining the molecular formula, MS can provide the molecular formula. It can identify and provide number of atoms in a

molecule of course, when it gives molecular formula it also tells you the different types of atoms present in it and also in what number are these atoms present. For example, if you have glucose yes $C_6H_{12}O_6$. So, 6 carbon atoms are there, 12 hydrogen atoms are there and 6 oxygen atoms are there. So, we get molecular weight and also the number of atoms and their numbers. In order to publish new results, especially when you are doing PhD or when you are doing research, working in R&D labs, in order to publish new results, elemental analysis data of new compounds is very necessary to prove the purity and similarly molecular weight and mass spectral data is equally important.

So, this information can be obtained by obtaining percentage of constitute elements present in the research sample. So, that means once we know the molecular weight you can subject it to element analyzer and we can know the composition of that sample. This is normally obtained by inductively coupled plasma spectroscopy. As I said, in order to determine the molecular weight, we have to ionize the sample. Then what are the methods that we have at our disposal for ionization. We have two methods: one is called electron impact ionization abbreviated as EI and then the chemical ionization abbreviated as CI.

The output of ionization either from electron impact ionization or chemical ionization is a plot of relative abundance to mass to charge ratio m/z. That is what we see in case of a typical mass spectrum. This is the typical setup used in electron impact. In electron impact ionization, the chamber is maintained at a pressure of 0.005 torr. The gaseous neutral sample molecules enter into the ion chamber through molecular inlet. This is called as molecular leak. This is the molecular inlet through which sample enters. The gaseous neutral sample is allowed to enter into the ion chamber through the molecular inlet. A tight helical beam of highly energetic accelerated electron beam, approximately 70 electron volts, from a glowing tungsten or rhenium filament pass perpendicular to incoming gas molecules. That means, you can see if it is entering like this here. If it is entering like this here, these are all coming in perpendicular direction. These electrons are drawn off by a positive charged slit called electron trap, which is on the opposite side of the filament. You can see, it is in the opposite side of the filament and then electrons travel across ion chamber.

Ions are generated by the exchange of energy during the collision of the electron beam and sample molecules. So, this happens in the ionization chamber here. As the electron beam is highly energetic with 17 electron volt it provides sufficient energy to gas molecules to have ionization and to cause the characteristic fragmentation of sample molecules either by loss of radicals or by loss of neutral molecules. Under the influence of this high energy electron beam what happens ionization takes place and of course here 70 volt electron volt and it gives m plus (m^+) plus 2 electrons and then m plus(m^+) further. So, the positive ions

formed in the ion chamber are drawn out by a small electrostatic field between the larger repeller plate positively charged one and the first accelerating slit negatively charged one here.

See a strong electrostatic field between first and second accelerating slits of 400 to 4000 volts accelerates the ions of various masses to their final velocities. The ions emerge from the final focusing slit 0 volts as a collimated ion beam with velocities and kinetic energies follows this one. So, we represent with this expression. So, and so on. So, here z is charge of the ion V equals voltage small v equals velocity of various ions and m equals mass of respective ion.

The sample vapor is bombarded by electrons that are perpendicular to the path of the sample that results in ionization in this case. So, that means the advantage with electron impact is it gives reproducible spectra that is very very important no matter how many times you do it the data set looks identical. The disadvantage is it is limited to samples that are thermally stable with molecular weight less than 1000. For example, if you make some molecules having a molecular weight more than 1000 probably electron impact you cannot use it. What happens in the chamber here the initial product is a molecular radical say for example, we have methanol, it will take an electron to generate CH_3OH^+ cationic radical plus two electron comes out. These unstable ions created disintegrate into other species.

What are the other species. For example, these generated positive radicals disintegrate into CH_2OH plus mass to charge ratio is 31 plus H radical and also this can also disintegrate into CH_3 plus here. 15 and then OH radical and also it can disintegrate into CHO plus where MZ value is 29 plus H_2 can come out. So, this kind of tendency to fragment the whole molecule into small fragments is called hard ionization. So, this hard ionization happens invariably in electron impact ionization method.

Now, let us consider two examples one each from an aromatic and another one from non-aromatic cyclic system to understand to what extent fragmentation happens when they are subjected to electron impact ionization. For example, here in case of aromatic group, we will see only the sample is ionized, whereas in case of non-aromatic, extensive fragmentation occurs here.

That means, extensive fragmentation is observed in case of non-aromatic groups, whereas only aromatic group is ionized, both have a molecular weight of 152 and you can see here apart from 152 M plus radical we have a series of lower fragments whereas, in this case very few are there it is only ionized. So, this is a major difference, we are seeing here

between aromatic and non-aromatic compounds. The second method is called chemical ionization. It is more controllable soft ionization method. Electron impact is a hard ionization method, whereas chemical ionization is a soft controllable method, normally gives M+H cationic peaks that gives molecular weight producing little fragmentation. Since it is a soft ionization, it produces very little fragmentation. For chemical ionization, a gas will be introduced into the system which itself ionizes. For example, here we are letting methane gas, while analyzing, into the ionization chamber. CH_4 fragments into CH_4 plus CH_3 plus and CH_2 plus and CH_4 plus can combine with CH_4 to give CH_5 plus CH_3 plus and again various combinations CH_4 plus can combine as well with CH_3 plus to give C_2H_5 plus and H_2.

So, all these happens in chemical ionization with carrier gas, we call it as a carrier gas. The different species generated from carrier gas such as methane reacts with molecules to be analyzed as depicted here. For example, M is the unknown sample. This CH_4 plus reacts to give MH_2 plus, and CH_4, proton transfer method. On the other hand, M can also react with C_2H_5 plus to generate again MH_2 plus, whereas here C_2H_4 comes. This also a typical proton transfer process. M can also react with the same C_2H_5 cation and to generate M cation plus C_2H_6. So, here hydride transfer. That means these are the possible process that we come across in chemical ionization. When we are using a carrier gas such as methane, proton affinity is an enthalpy quantity that determines the binding strength of H plus to a neutral species. For various species, proton affinity in kilo calories per mole is given in this table. Here H_3 plus is 101 kilo calories per mole (kcal/mol). For CH_5 plus it is 130 kilo calories per mole and this for isopropyl plus, it is 192 and for ammonium it is 204 kilo calories per mole. Reaction of cationic species with sample is exothermic in nature. We saw from these values, the interaction of cationic species with the sample always proceeds with in an exothermic manner M^+ RH^+ gives MH plus plus R.

If you look into enthalpy of reaction this is PA, proton affinity for MH plus minus proton. Affinity for RH plus, now see this will give you, typical in case of phenyl propyl ketone, this comes around 208 kilo calories per mole (kcal/mol). So, this indicates this is, exothermic in nature. Let us consider few examples such as ionization of phenyl propyl ketone, I showed you. Proton affinity for this is 208 kilo calories per mole (kcal/mol), that I showed in my previous slide. So, how this happens? Let us look into this one here, when we look into this phenyl propyl ketone, it interacts with C_4H_{11} cation and to generate this cation and then what we get is isopropane comes out and in this one if we try to understand. ΔH involved in it, this is 16 kilo calories per mole (kcal/mol) here minus.

So, it is exothermic and then we look into the same reaction with CH_5 plus. Here also same species we are getting, but here what we get is CH_5. It should be CH_4 here. So, this is

exothermic reaction, the value is minus 78 kilo calories per mole (kcal/mole). So, this indicates that more exothermic the reaction, greater the excess of energy and hence greater fragmentation. So, more exothermic the reaction, greater the excess of energy and hence greater the fragmentation. Now, if you look into this, isopropyl chloride here delta H is minus 16 kilo calories per mole (kcal/mol) and here what we get is CH_5Cl. It is minus 78 kilo calories per mole (kcal/mol).

Of course, here you can see here this is identified in case of both. So, either one can use electron impact ionization method or chemical ionization, but it also depends on what information we are looking into. So, that means, the utility of electron impact or CI method should be clearly spelled out, by knowing what information you want to extract from mass spectral data. To determine the molecular weight, chemical ionization is very ideal because it provides a strong M plus H cationic radical or strong M minus H cation. If more information is required for identification purpose EI is ideal because it will provide finger print.

So, that can be used for identifying the materials. So, if you want much more information other than looking into the molecular weight, EI, electron impact is ideal because the fragmentation is quite rapid and also it provides finger print that can be used for identifying the material and also the constituent species present in that. Normally, M^+ dot is very small and not seen when EI is used when you are using electron impact M plus I is not is very small or sometimes it may not be seen at all. So, usually chemical ionization fragmentation is difficult to predict and rationalize. So, if your molecule say ME is protonated to give MXH plus then two fragments can be anticipated or can be produced E H and M^+ if E is a functional group.

Since EH is a neutral species. It is not detected and hence it is not seen. That means, any neutral species that is formed is not seen in the spectral graph. Now, let us look into the resolution of a mass spectrometry. Resolution of mass spectrometry is given by the term delta M equal to M by R. So, R is resolution which allows to calculate the nearest mass of the sample that is M plus to minus delta M that can be readily distinguished from a given mass by the spectrometer for example, z by m equal to M.

You can readily calculate from the mass spectrometry. The resolution of mass spectrometer: To get more insight, let us look into an example here.

If M equal to say molecular weight is 2000 and R equal to 2000 then delta M equal to 1. M by Z peaks at 19999 or 2001 can be resolved this is called unit resolution if M is say,

200 and R is 2000, then delta M equals 0.1 ratio. So, now, spectrometer will distinguish masses such as 200.1 and 199.9.

So, using HRMS high resolution mass spectrometry, higher resolution can also be achieved. Now, let us consider carbon monoxide and nitrogen molecules. So, exact mass of CO is 27.9949 and the exact mass of N_2 is 28.0062. The difference is 0.0113. So, high resolution mass HRMS containing three decimal places are quite common and capable of distinguishing close masses isoelectronic species such as C1 and N_2. C1 and N_2 are isoelectronic even those in HRMS, we can distinguish. So, resolution can get as low as six decimal places. That means, you can resolve with resolution having up to six decimal places. So, that is a advantage of high-resolution mass spectrometer.

So, let us discuss more information pertinent to mass spectrometry in my next lecture until then have an excellent time. Thank you.