Objectives

You should now be able to:

- recognise the characteristic features of the mass spectrum of a simple phenol;

- explain why phenols typically fragment by loss of CO and CHO rather than OH;

- explain why methyl phenols fragment by loss of H atoms followed by loss of CO and CHO;

- recognise alkyl phenols by the formation of m/z 107 and m/z 108 ions;

- distinguish 2-substituted phenols by the loss of H_2O from M^+;

- identify simple unknown phenols from their mass spectra.

9.5. FRAGMENTATIONS OF CARBONYL COMPOUNDS

The principle cleavage of carbonyl compound is α- to the $C=O$ group, which in most M^+ will carry the positive charge, as described already in Sections 8.2 and 9.1:

$$R-\overset{\overset{+\,\cdot}{O}}{\underset{\|}{C}}\overset{\frown}{X} \longrightarrow R-C\equiv\overset{+}{O} + X^{\cdot}$$
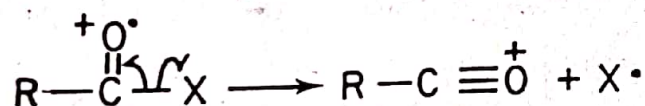
The formation of acylium ions by loss of $H^{\cdot}$, $R^{1\cdot}$, $R^{1}O^{\cdot}$, $HO^{\cdot}$ and $H_2N^{\cdot}$ is an important diagnostic feature of the mass spectra of aldehydes, ketones, esters, acids and amides respectively. There is one other feature which carbonyl compounds have in common which is very useful in identifying them. This is the concerted loss of an alkene from the R group, with H transfer to the carbonyl oxygen. This rearrangement is almost unique to mass spectrometry and is the one fragmentation which is a *named* reaction – the McLafferty Rearrangement. We consider it next.

9.5.1. The McLafferty Rearrangement

In the late 1950's McLafferty was studying the mass spectra of a series of aliphatic methyl esters, in fact all the methyl esters he could get his hands on from simple acids such as ethanoic to long chain fatty acids such as tetraeicosanoic acid, $C_{24}H_{49}COOH$. To his surprise he discovered that from C_6 acids onwards, the base peak of the mass spectrum of each of the methyl esters was always the same ion, m/z 74. A typical example of what he found is shown in Fig. 9.5a.
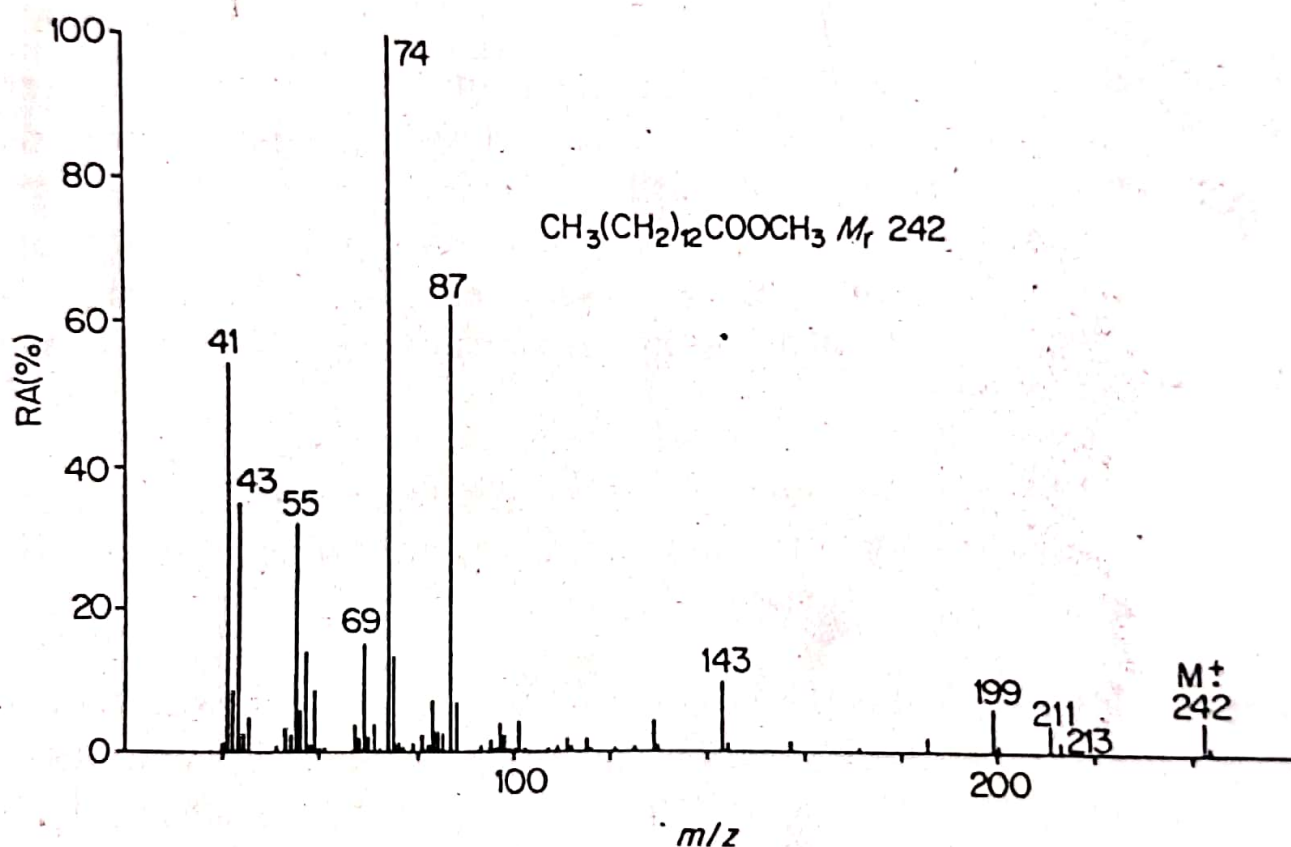

Fig. 9.5a.   *Mass spectrum of methyl tetradecanoate*

∏   What is so surprising about these observations?

Three things should surprise you. One is that such large esters as methyl tetradecanoate would give such a relatively low mass ion as base peak. Secondly that the base peak is of even mass. Most importantly, as you move up a homologous series of compounds you would expect the same fragmentation to occur and to give rise to base peak moving up by a —CH_2— unit each time. McLafferty

was able to show that the formula of his m/z 74 was $C_3H_6O_2$ and he postulated the following mechanism to account for its formation:
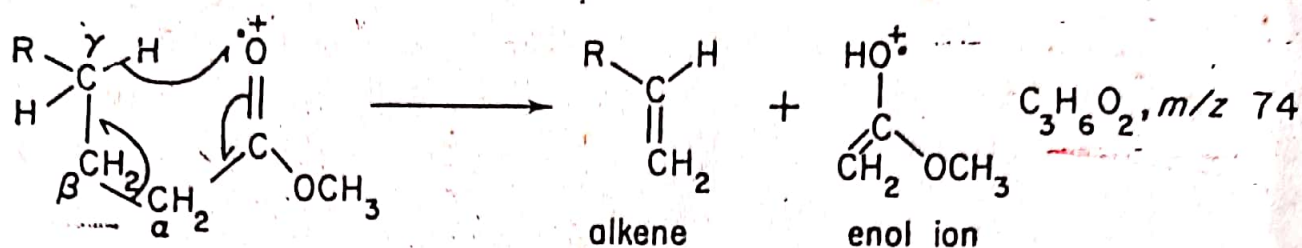

Fig. 9.5b. *McLafferty rearrangement of methyl esters*

You will see that this mechanism can occur in *any* methyl ester possessing a chain of at least three carbon atoms. The compounds McLafferty was examining only differed in the R group. This is eliminated as part of the neutral alkene so variations in the mass of R do not show up in the spectrum. The m/z 74 ion, which is the molecular ion of the enol form of methyl ethanote CH_3COOCH_3, *is the same for all of them.*

A great deal of work has been done on this rearrangement (which I will now call the 'McL' for short) and the following points have emerged;
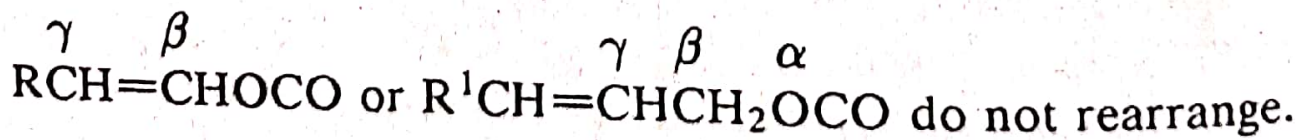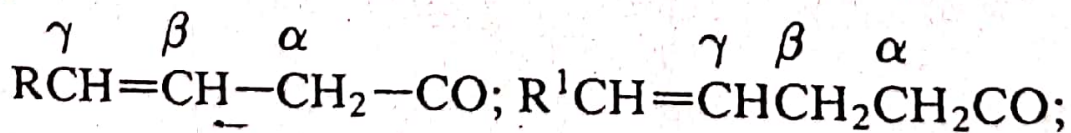
(a) It is very regiospecific. Only the α-, β- and γ-carbons are involved and the hydrogens transferred *must* be from the γ-carbon. This means that the 'McL' process is strictly six-centred.

(b) A very wide variety of C=O compounds with a γ-H will undergo 'McL' rearrangement. It is a most useful diagnostic tool for them.

(c) Other $-Y=X$ groups such as $-S=O$, $-P=O$, $C=C-C=N-$ which ionise to $-Y=X^+$ show 'McL' rearrangements. It is not restricted to C=O compounds.

(d) The α-, β- and γ-atoms need not be carbons. They can be various combinations of C, O, N and S, so long as there is a γ-H present to transfer. For example, an ethyl or higher ester can rearrange using the alcohol moiety:

$$\overset{+\cdot}{O}\cdots H \qquad \longrightarrow \qquad R-C\overset{\overset{+}{O}H}{\underset{O}{=}} \qquad + \; H_2C=CH_2$$
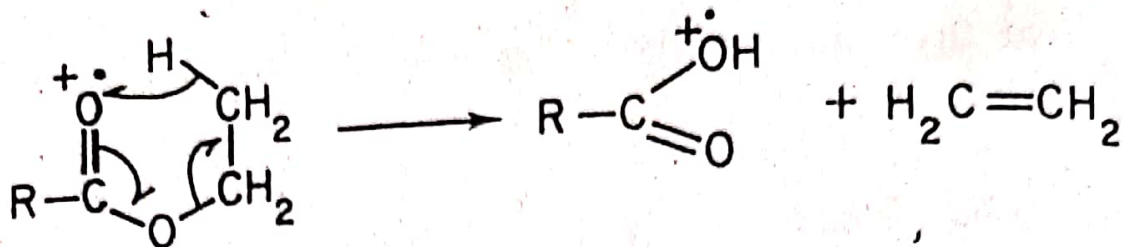
In such a molecule, the α-carbon is replaced by an oxygen but the 'McL' still works, forming the $M\overset{+}{\cdot}$ of the corresponding acid and releasing ethene. What this amounts to is provided a six-membered ring transition state can be formed easily using the flexibility of the side chain(s) a 'McL' rearrangement is likely to be observed.

(e) Since the eliminated group is a neutral molecule (usually an alkene) 'McL' rearrangements give rise to *even* mass ions from C,H,O compounds ie to molecular ions of a smaller molecule. Even-mass ions are unusual in mass spectra of C,H,O compounds, so their presence is usually distinctive even if they are weak. In the case of odd-mass compounds eg amides, the 'McL' rearrangement ions will stand out because they will have *odd* m/z values.
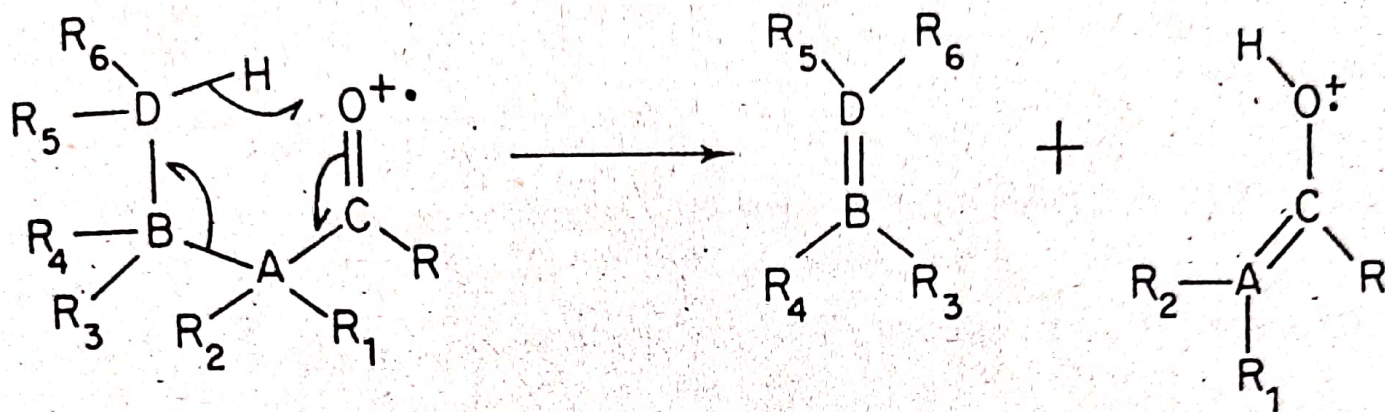
(f) H atoms on double bonds are not transferred in the 'McL' rearrangement eg compounds with side chains such as

$$\overset{\gamma}{R}CH=\overset{\beta}{C}H-\overset{\alpha}{C}H_2-CO; \quad R^1\overset{\gamma}{C}H=\overset{\beta}{C}HCH_2\overset{\alpha}{C}H_2CO;$$

$$\overset{\gamma}{R}CH=\overset{\beta}{C}HOCO \text{ or } R^1\overset{\gamma}{C}H=\overset{\beta}{C}HCH_2\overset{\alpha}{O}CO \text{ do not rearrange.}$$

(g) The 'McL' rearrangement still works if there are a variety of substituents on the α-, β- or γ-atoms.

These points are summarised in Fig. 9.5c as far as C=O compounds are concerned.

Fig. 9.5c. *General representation of the 'McLafferty' rearrangement*

In Fig. 9.5c R will be a typical group found in a carbonyl compound eg R_1—R_6 can be a variety of alkyl, aryl, halo, alkoxy, aryloxy and other groups, and A, B and D could be combinations of carbon, oxygen, nitrogen or sulphur. It is hard to conceive of a system where at least one of A, B or D is not carbon (most likely two of them will be) but you would be wise not to assume too much or the order in which these come in the A—B—D chain. This really is a very general process! So long as double bonds can form B=D and A=C it can work. Fig. 9.5d summarises the common 'McL' peaks found in the spectra of carbonyl compounds.

Compound Type	Substituent R	'McL' Peak (m/z)	Structure*
Aldehyde	H	44	$CH_2{=}C$ with $\overset{\bullet\,+}{O}H$ and H
Methyl ketone	CH_3	58	$CH_2{=}C$ with $\overset{\bullet\,+}{O}H$ and CH_3
Amide	H_2N	59	$CH_2{=}C$ with $\overset{\bullet\,+}{O}H$ and NH_2
Acid	HO	60	$CH_2{=}C$ with $\overset{\bullet\,+}{O}H$ and OH
Ethyl ketone	CH_3CH_2	72	$CH_2{=}C$ with $\overset{\bullet\,+}{O}H$ and CH_2CH_3
Methyl ester	CH_3O	74	$CH_2{=}C$ with $\overset{\bullet\,+}{O}H$ and OCH_3
Propyl ketone	$CH_3CH_2CH_2$	86	$CH_2{=}C$ with $\overset{\bullet\,+}{O}H$ and $CH_2CH_2CH_3$
		58**	$CH_2{=}C$ with $\overset{\bullet\,+}{O}H_2$ and $CH_2^{\bullet}$
Ethyl ester	CH_3CH_2O	88	$CH_2{=}C$ with $\overset{\bullet\,+}{O}H$ and OCH_2CH_3

Compound Type	Substituent R	'McL' Peak (m/z)	Structure*
		$(M-CH_2=CH_2)$***	$R-C\overset{\overset{\cdot\cdot+}{O}H}{\underset{O}{\diagdown}}$
Phenyl ketone	C_6H_5	120	$CH_2=C\overset{\overset{\cdot\cdot+}{O}H}{\underset{C_6H_5}{\diagdown}}$
Phenyl ester	C_6H_5O	136	$CH_2=C\overset{\overset{\cdot\cdot+}{O}H}{\underset{OC_6H_5}{\diagdown}}$

Fig. 9.5d.   *Table of 'McL' peaks commonly observed in the spectra of carbonyl compounds*

* The $H_2C=$ group in any of the ions listed in this column may be substituted either singly or doubly eg $CH_3CH=$ ions would all be 14 amu higher.

** This ion arises because the propyl group itself has a γ-H, and the 'McL' rearrangement can occur *twice* consecutively.

*** This ion arises because the 'McL' rearrangement can utilise γ-H from either the RCO *or* the OCH_2CH_3 giving 'McL' ions of different structures and/or masses.

Now try the examples in SAQ 9.5a. You should not go on until you have attempted these and satisfied yourself that you can identify the relevant γ-H atoms in a molecule and work out the 'McL' ion which will result from the rearrangement.

SAQ 9.5a

In which of the following compounds would you expect to see a 'McL' peak? Give its m/z and structure.

(i) $CH_3COCH_2CH_3$;

(ii) $CH_3COCH_2CH_2CH_3$;

(iii) $CH_3COCH(CH_3)_2$;

(iv) $(CH_3)_2CHCH_2CHO$;

(v) $CH_3CH_2COOCH_2CH_3$;

(vi) $CH_3CH_2CH_2CONHCH_3$;

(vii) $CH_3CH(CH_3)CH_2 CH(CH_3)COOH$;

(viii) $CH_3CH_2CH(CH_3)COC_6H_5$;

(ix) $CH_3CH=CHCH_2COCH_2CH_3$;

(x)

$$(C_6H_5)_2 \overset{\overset{\displaystyle O}{\|}}{P}.SCH_2CH_3$$

If you are now happy you can predict and explain simple 'McL' rearrangements, we will go to explain footnote ** in Fig. 9.5d. This states the ion m/z 86 from a propyl ketone can rearrange again by a 'McL' process to eliminate a second molecule of alkene (ethene in this case) to give another even daughter ion, m/z 58. This is called a *Double McLafferty Rearrangement*. Dipropyl ketone (4-heptanone) is the simplest ketone in which this can occur because both alkyl groups have γ-H atoms:

$$\overset{\gamma\quad\beta\quad\alpha\qquad\alpha\quad\beta\quad\gamma}{CH_3CH_2CH_2COCH_2CH_2CH_3}$$
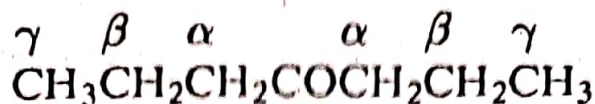
As shown in Fig. 9.5e, the first 'McL' ion, m/z 86, can have two resonance structures. It may fragment again in either of two ways depending on its structure, to give isomeric m/z 58 ions.
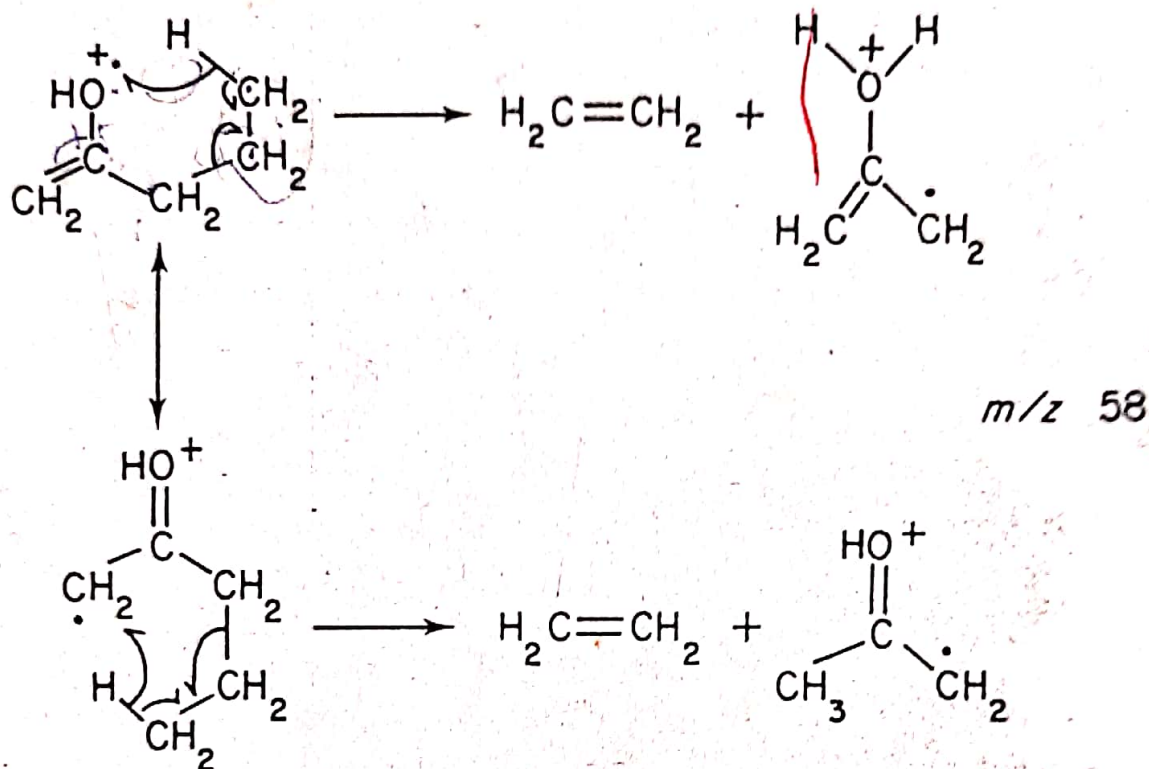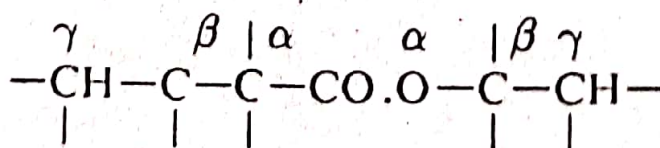

m/z 58

Fig. 9.5e. *Second 'McL' rearrangement of m/z 86*

Ⅱ   Can you suggest another common type of C=O compound which would be capable of Double McLafferty Rearrangement?

The answer is an ester having γ-H in *both* the acid and the alcohol portions of the molecule, that is it must have a partial structure:

$$\overset{\gamma\qquad\beta\ |\ \alpha\qquad\ \alpha\ \ |\ \beta\ \ \gamma}{-CH-C-C-CO.O-C-CH-}$$

This is mentioned in footnote *** to Fig. 9.5d. The simplest ester which could show this behaviour is ethyl butanoate, Fig. 9.5f.
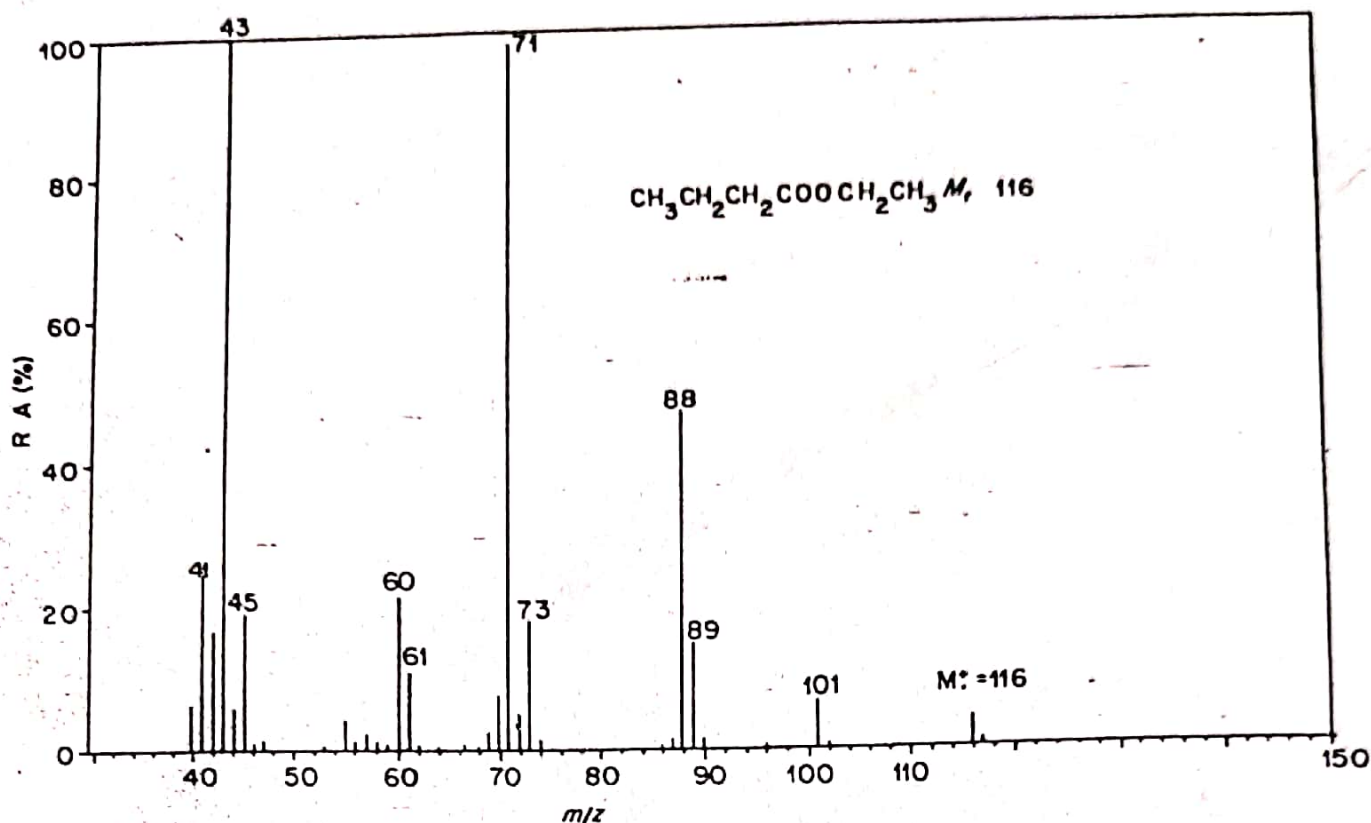
Fig. 9.5f. *Mass spectrum of ethyl butanoate*

∏   Which are the ions in Fig. 9.5f that result from Double McLafferty Rearrangement?

The 'McL' rearrangement ions are m/z 88 and 60. You could have guessed this from the fact that they are the only significant even mass ions in the spectrum, but I hoped you reasoned it out something like this.

Either $\overset{\gamma}{C}H_3\overset{\beta}{C}H_2\overset{\alpha}{C}H_2CO$ or $OCO\overset{\alpha\beta}{C}H_2\overset{\gamma}{C}H_3$

has γ-H atoms so the loss of $CH_2{=}CH_2$ with H transfer would occur from either group, resulting in $(M^{+}{-}28) = m/z$ 88. In the next step of the double rearrangement, the remaining sidechain's γ-H transfers with the loss of a second $H_2C{=}CH_2$ molecule, leading to m/z 60. We will leave discussion of the other ions in the spectrum to the section on esters (Section 9.5.4.).

SAQ 9.5b Give mechanisms for the formation of the two structures for m/z 88 in Fig. 9.5f and show that they both form the same m/z 60 in the second stage of the Double 'McL' Rearrangement.

The answer to SAQ 9.5b makes clear that the rearrangement of hydrogen in six-centred transition states does not necessarily always require a $X=Y^{+}$ terminus, $C-\overset{..}{\overset{+}{O}}-H$ will do for example. Nowadays, the tendency is to call any six-centred hydrogen shift a McLafferty rearrangement, even though the compound may be quite remote from the carbonyl systems originally studied 30 years ago. Incidentally, Fred, as he is known, is still active (1986) in organic mass spectrometry research.