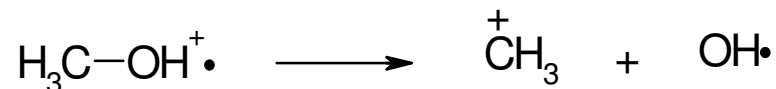
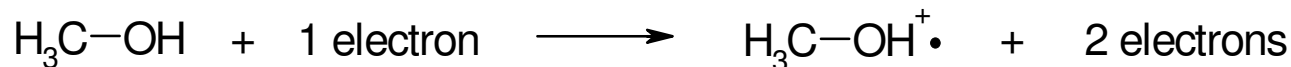

Mass Spec - Fragmentation

An extremely useful result of EI ionization in particular is a phenomenon known as fragmentation.

The radical cation that is produced when an electron is knocked out of a neutral closed-shell molecule in EIMS initially possesses a lot of energy.

Energy sufficient to break chemical bonds: radical cation will usually break into a neutral radical and a cation. It is also possible for a neutral closed shell fragment (such as water) to fall off.



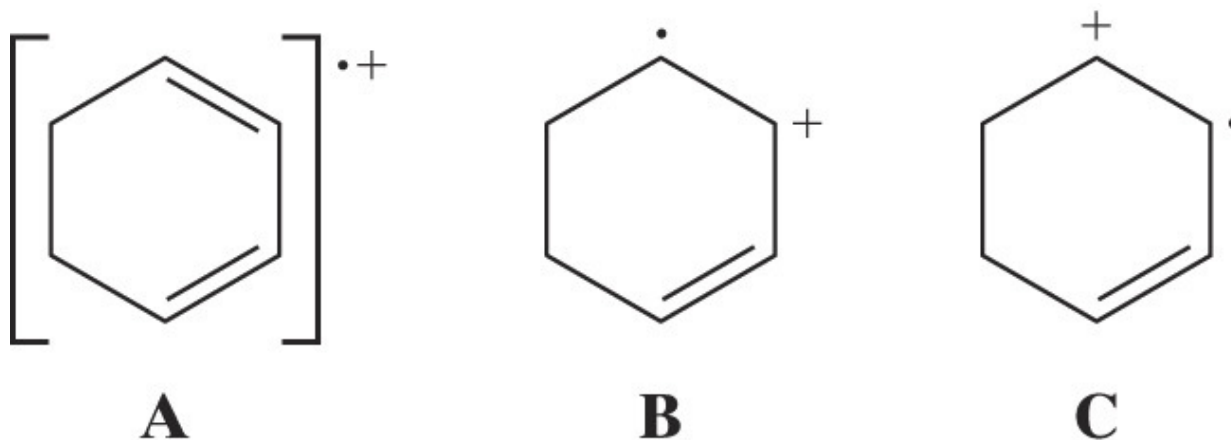
Predicting Fragmentation

A considerable volume of literature regarding the fragmentation reactions of certain molecules is available. Using this knowledge, we can predict how a given molecule might fragment.

But first a few conventions....

Conventions

It is always best to *localize* the cation and radical, obeying the rules of Lewis structures (i.e. don't put more than 8 electrons on carbon).

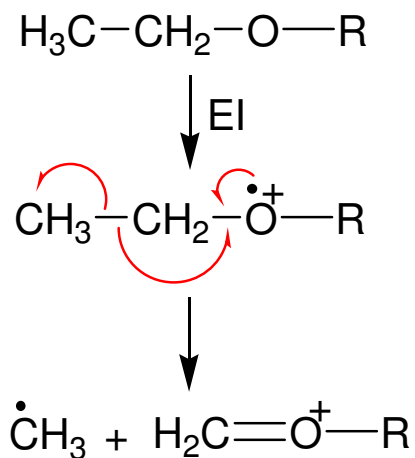
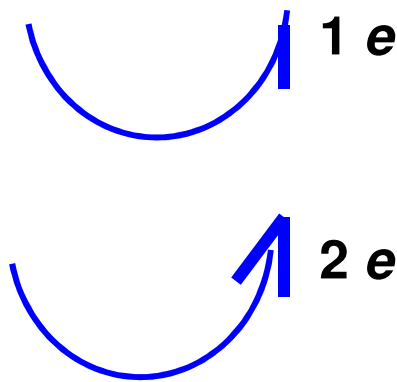


For example, for the three structures above, A is discouraged in favour of B or C. This convention is not always possible to obey (alkanes).

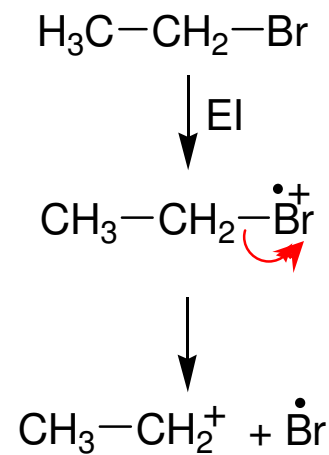
More on Conventions...

When a molecule is ionized by EIMS, must decide which electron to remove. Always best to remove an electron from a π -bond, or from a heteroatom lone pair. It will become more clear which is the better choice when we look at individual examples.

The bond breaking can be done either by homolytic or heterolytic cleavage.



Homolytic



Heterolytic

Fragmentation Notes

- **Most fragments are even-electron cations. These split to make more even-electron cations.**
- **The probability of cleaving a given bond is related to the bond strength, and to the stability of the fragments formed. In particular, cations like to rearrange or decay into more stable cations.**
- **Remember that for a ring system, at least 2 bonds must break for the ring to fragment.**

In addition, there are 10 general rules to keep in mind when predicting the most likely ions to be formed for a given molecule.

Fragmentation Guidelines

- 1. The relative height of the M^+ peak is greatest for straight-chain molecules and decreases as the branching increases.**
- 2. The relative height of the M^+ peak decreases with chain length for a homologous series.**
- 3. Cleavage is favoured at alkyl-substituted carbons, with the probability of cleavage increasing as the substitution increases.**

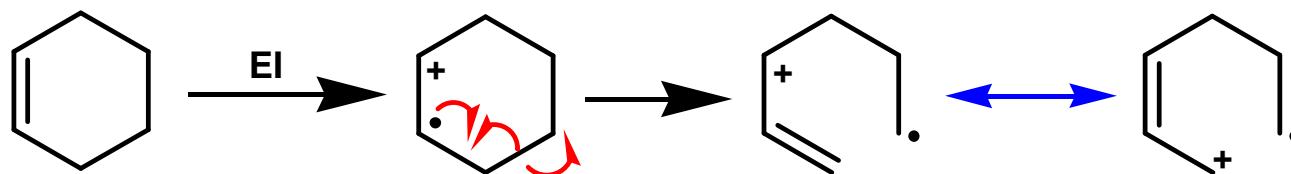
These rules mostly arise from the fact that carbocation and radical stability show the following trend:

Most Stable Benzylic > Allylic > Tertiary > Secondary >> Primary **Least Stable**
“Stevenson’s Rule”

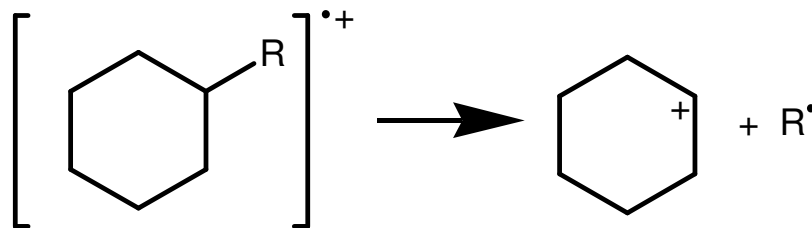
At the point of breakage, the larger fragment usually takes the radical to leave the smaller cation.

Fragmentation Guidelines

- 4. Double bonds, cyclic structures, and especially aromatic rings will stabilize the molecular ion and increase its probability of appearance.**
- 5. Double bonds favor allylic cleavage to give a resonance stabilized allylic carbocation, especially for cycloalkenes.**

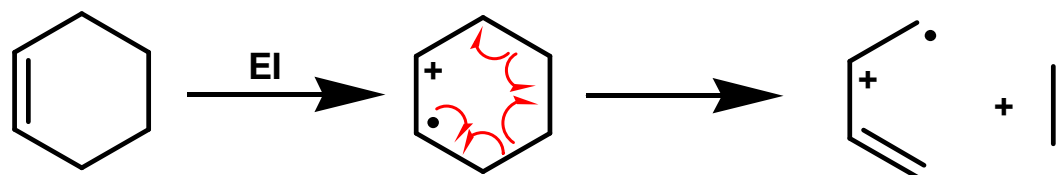


- 6. For saturated rings (like cyclohexanes), the side chains tend to cleave first leaving the positive charge with the ring.**

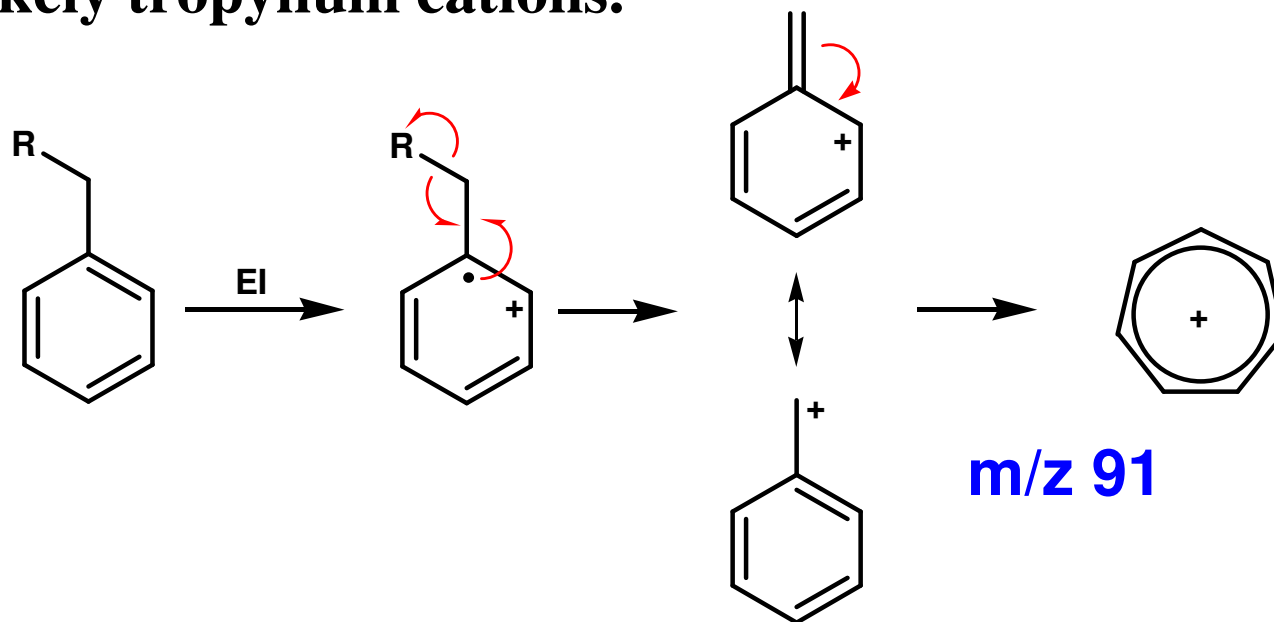


Fragmentation Guidelines

7. Unsaturated rings can also undergo *retro-Diels-Alder* reactions to eliminate a neutral alkene.

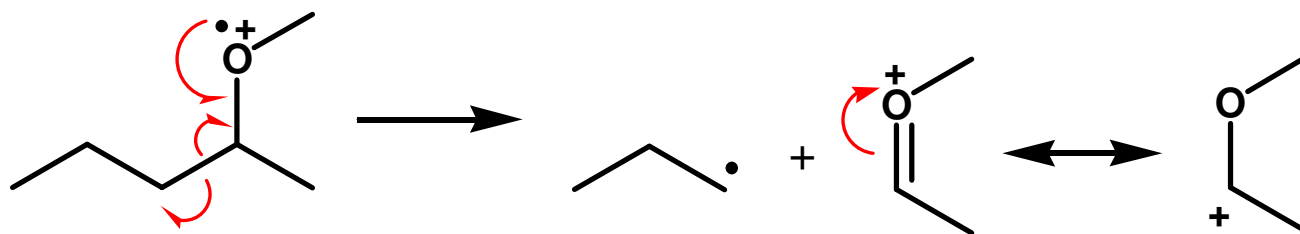


8. Aromatic compounds tend to cleave to give benzylic cations, or more likely tropylium cations.



Fragmentation Guidelines

9. C-C bonds next to heteroatoms often break leaving the positive charge on the carbon with the heteroatom.

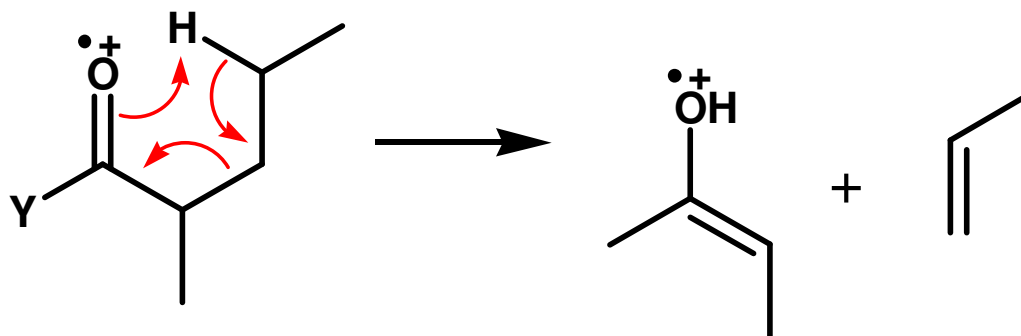


10. Cleavage is often favoured if it can expel small stable molecules like water, CO, NH₃, H₂S, etc.

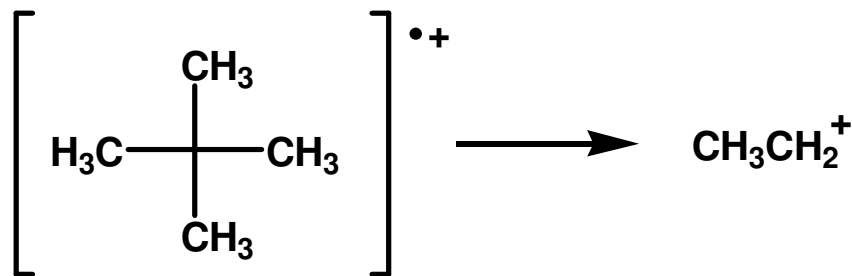
In addition to bond fragmentation, various intramolecular rearrangements can take place to give sometimes unexpected ions.

Rearrangements

One common type of rearrangement in MS is the *McLafferty rearrangement* which takes place in compounds that contain a carbonyl group.



Many other rearrangements are possible, even some that are not well understood and are considered 'random'.



Chem 325

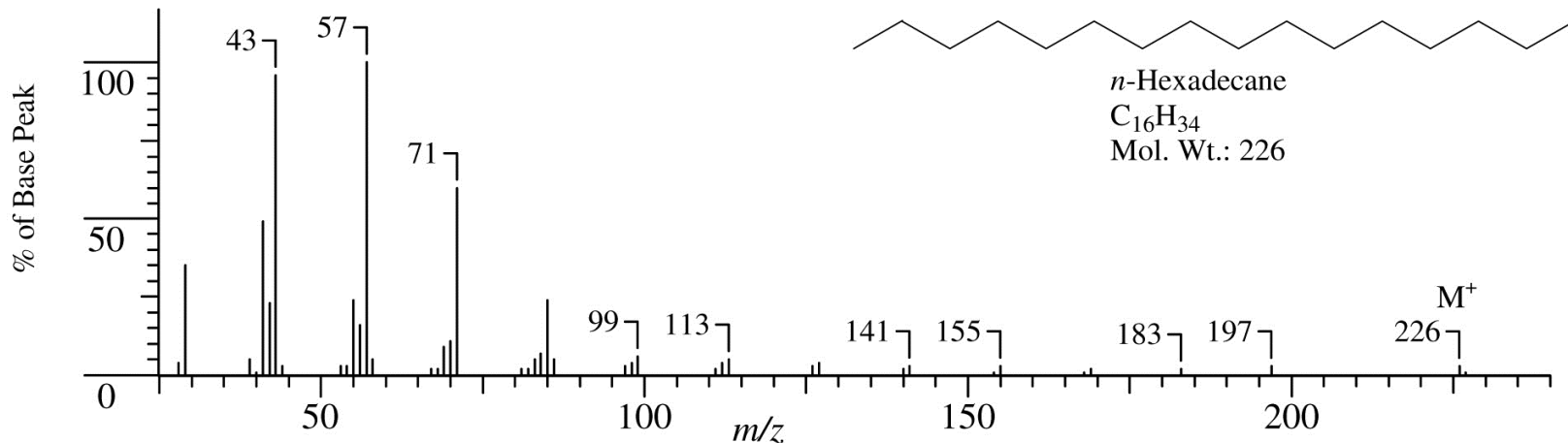
**Mass Spectra
of
Various Classes
of
Organic Compounds**

1. Saturated Hydrocarbons

General rules 1-3 apply well to hydrocarbons.

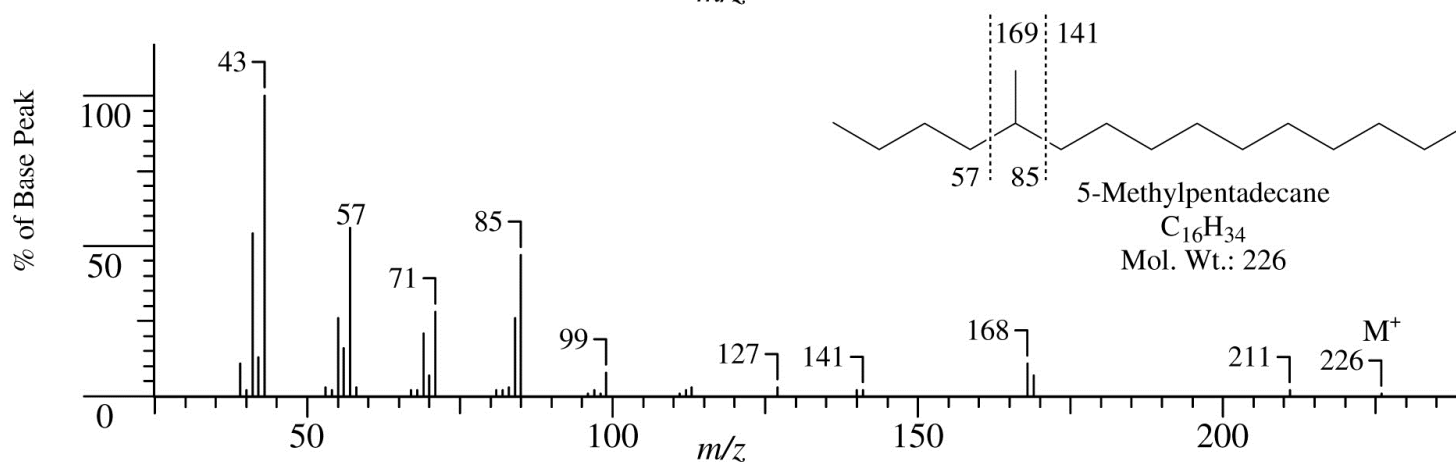
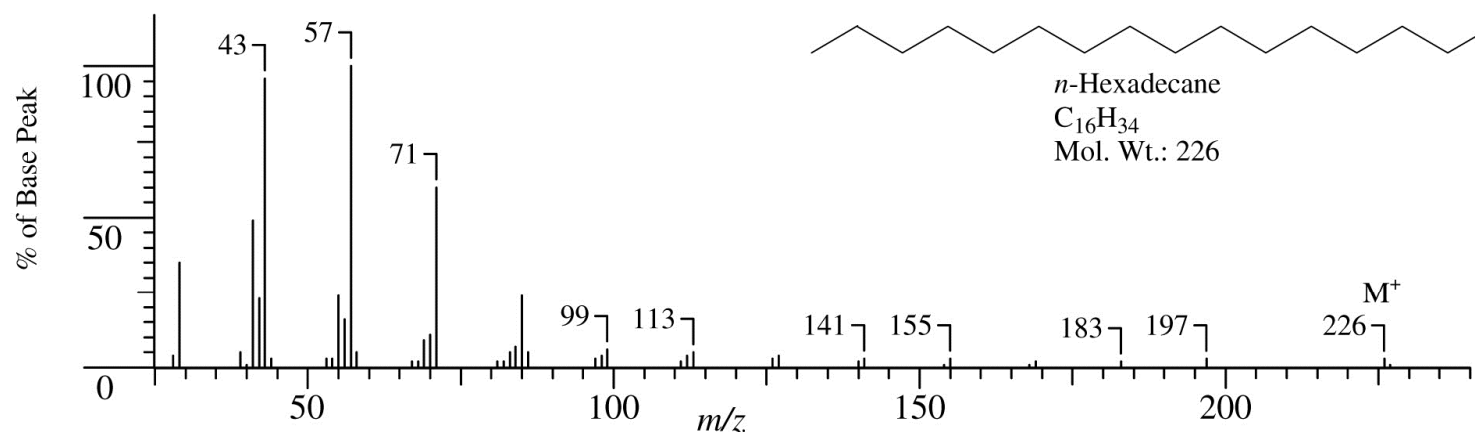
Rearrangements are common but usually do not give intense peaks.

The M^+ peak of a straight-chain hydrocarbon is always visible, but decreases in intensity as the molecule gets larger. The fragmentation pattern is characterized by peaks separated by 14 mass units (a CH_2 group). The most intense peaks are the $\text{C}_3 - \text{C}_5$ fragments.



Branched Hydrocarbons

The MS for branched saturated hydrocarbons are similar, except certain fragments become more prominent.

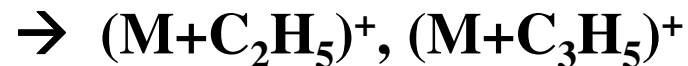


CI-MS

- **For some types of compounds the M^+ peak is very weak or not observable at all!**
- **Due to EI ionization being a ‘hard ionization’: so much internal energy is given to the molecular ion that extensive fragmentation immediately results.**
- **How to measure the molecular mass??**
- **Chemical Ionization (CI).**

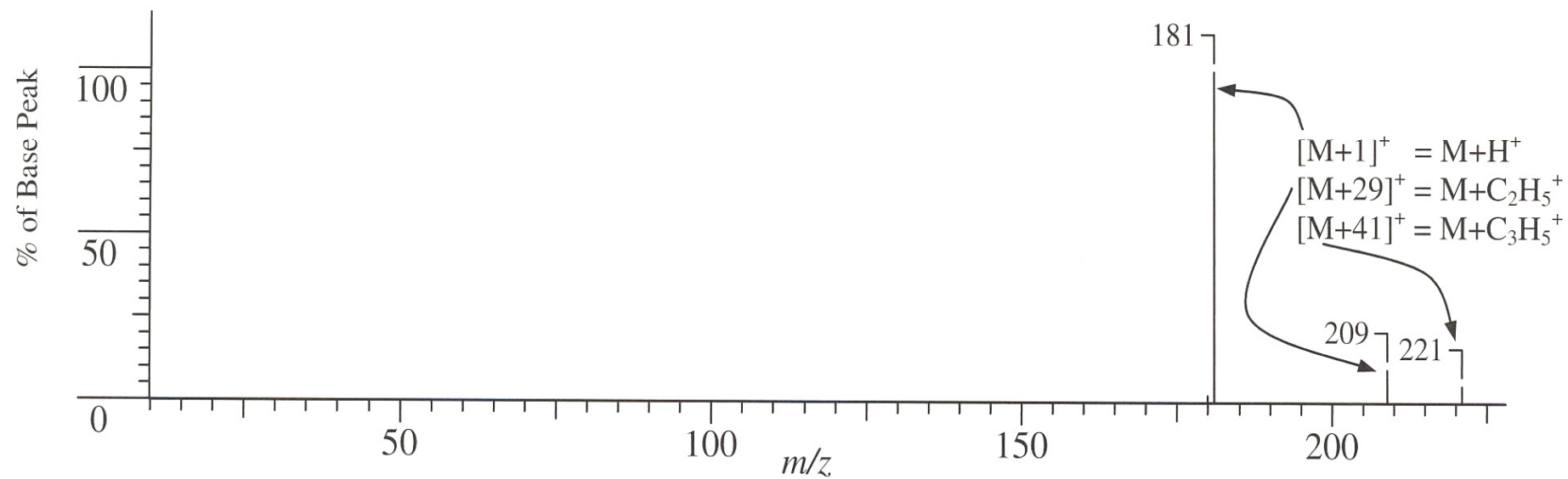
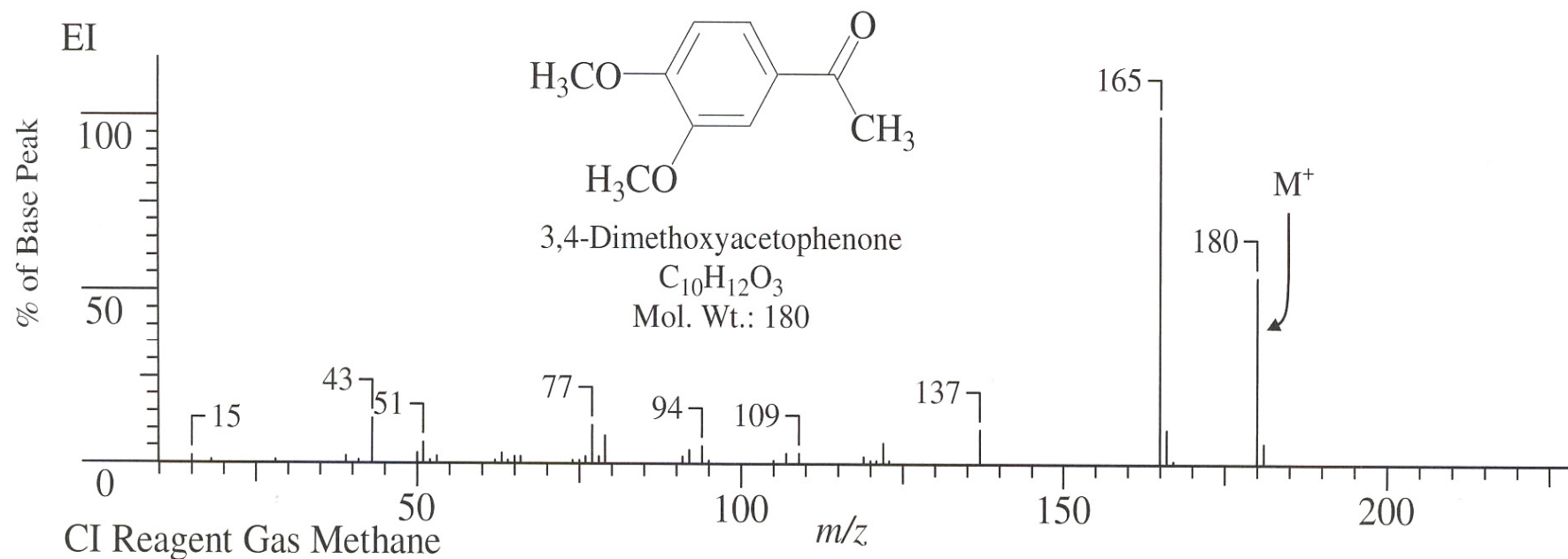
Chemical Ionization

- Ion source filled with relatively high pressure reagent gas, example isobutane $i\text{-C}_4\text{H}_{10}$, ammonia, or methane CH_4
- Electron impact ionizes the CH_4 , high pressure ensures many ion-molecule collisions and reactions to produce CH_5^+ , which acts as a protonating agent when it collides with sample molecule M



Can also use $i\text{-C}_4\text{H}_{10}$, NH_3 , etc.

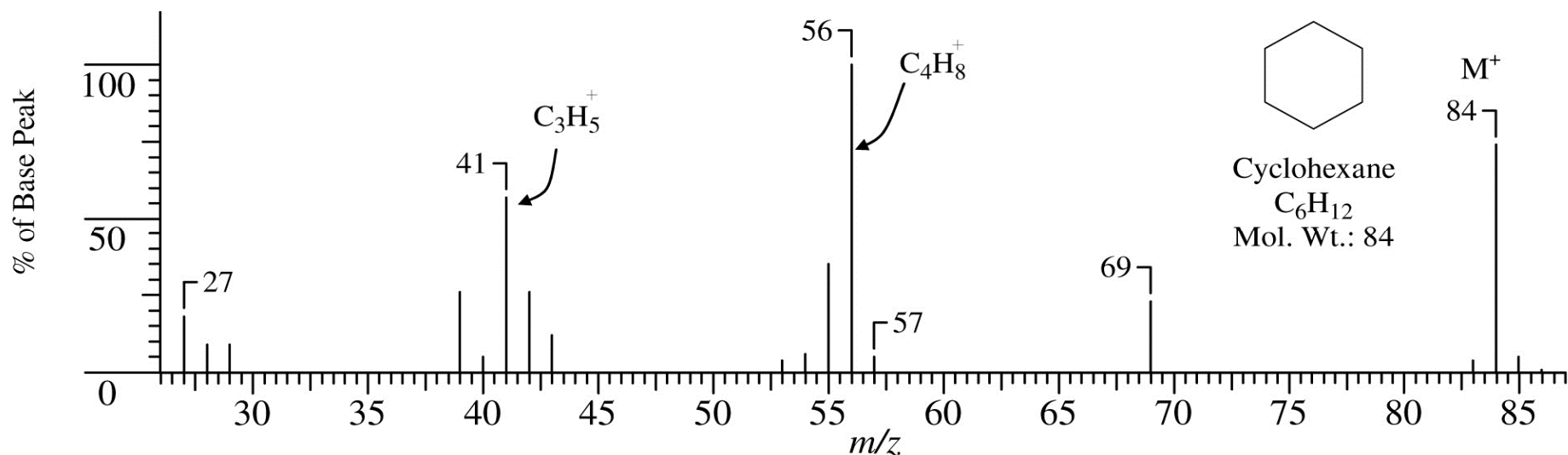
‘soft ionization’: much less fragmentation, can ‘see’ molecular ion



Cyclic Hydrocarbons

Cyclic hydrocarbons show a much more intense M^+ ion (Rule 4)

Two bonds must break to form fragments.

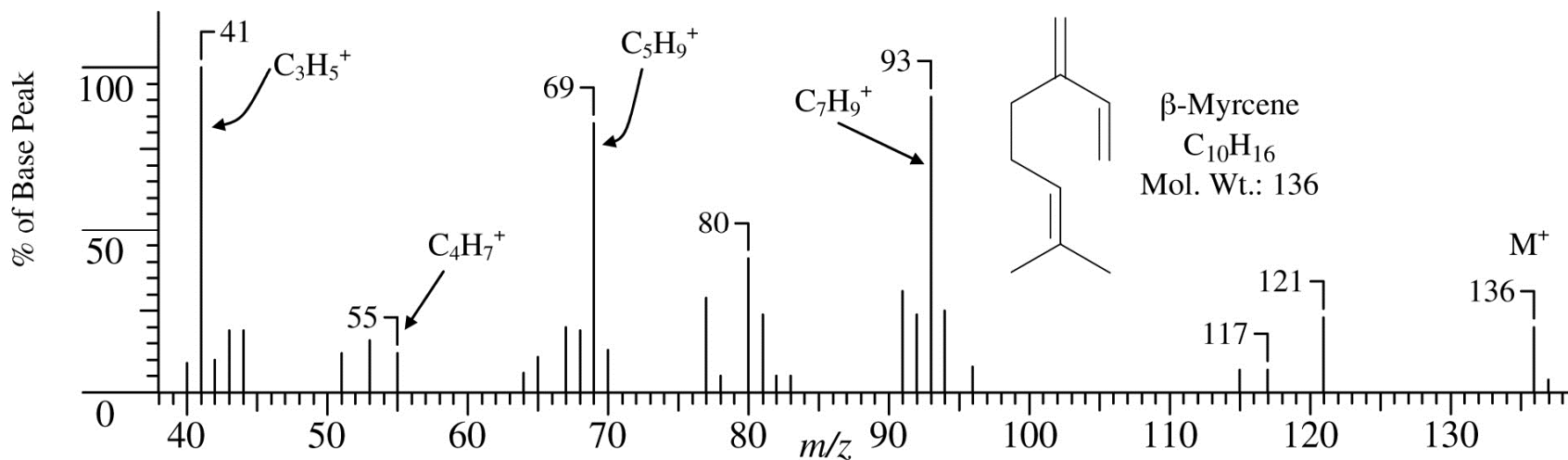


2. Alkenes

It is usually easy to see the M^+ peak of alkenes in EIMS.

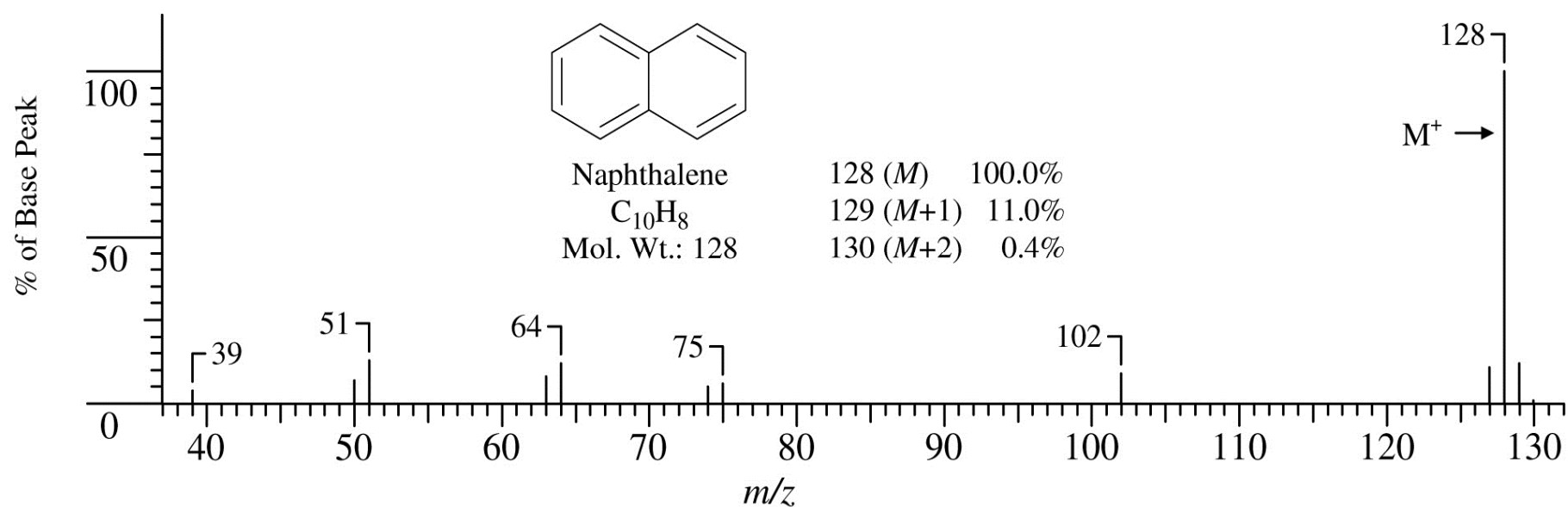
In acyclic alkenes, the double bond freely migrates in the fragments, so it can be difficult to determine the double bond location, but for cyclic alkenes it is easier.

Cleavage usually happens at allylic bonds (Rule 5).



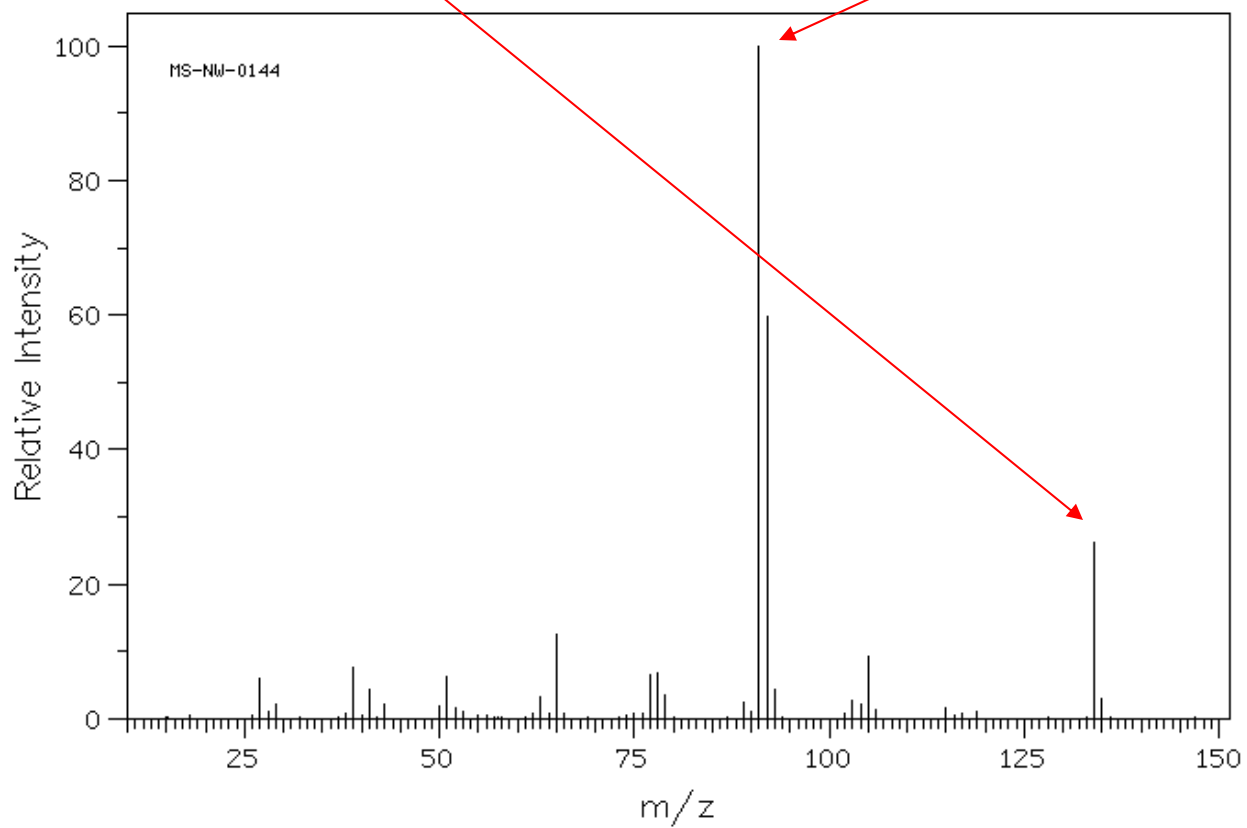
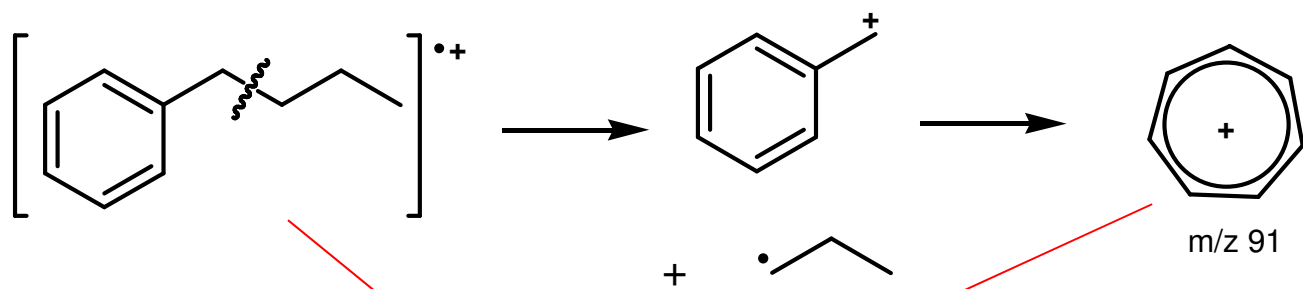
3. Aromatic Hydrocarbons

Aromatic hydrocarbons usually show strong M^+ peaks (Rule 4). Aromatic rings are stable and have a lower tendency to fragment.



Alkyl substituted benzenes often give a strong peak at m/z 91 due to benzylic cleavage (Rule 8).

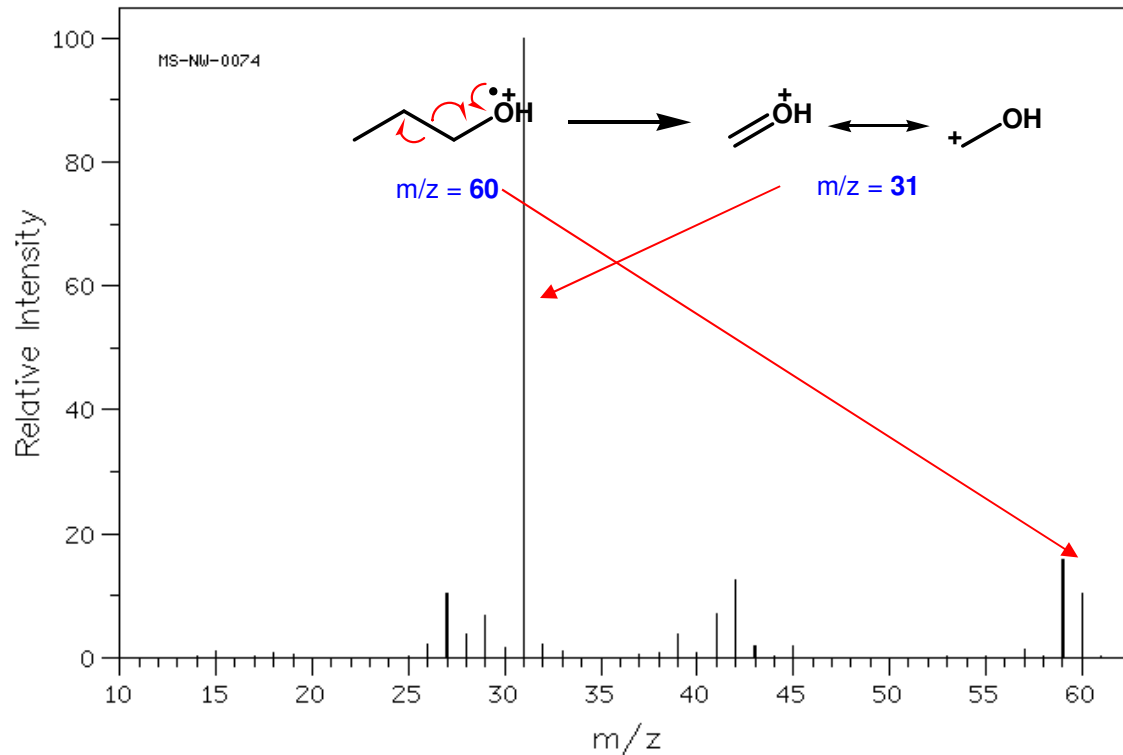
MS of n-butylbenzene



4. Alcohols

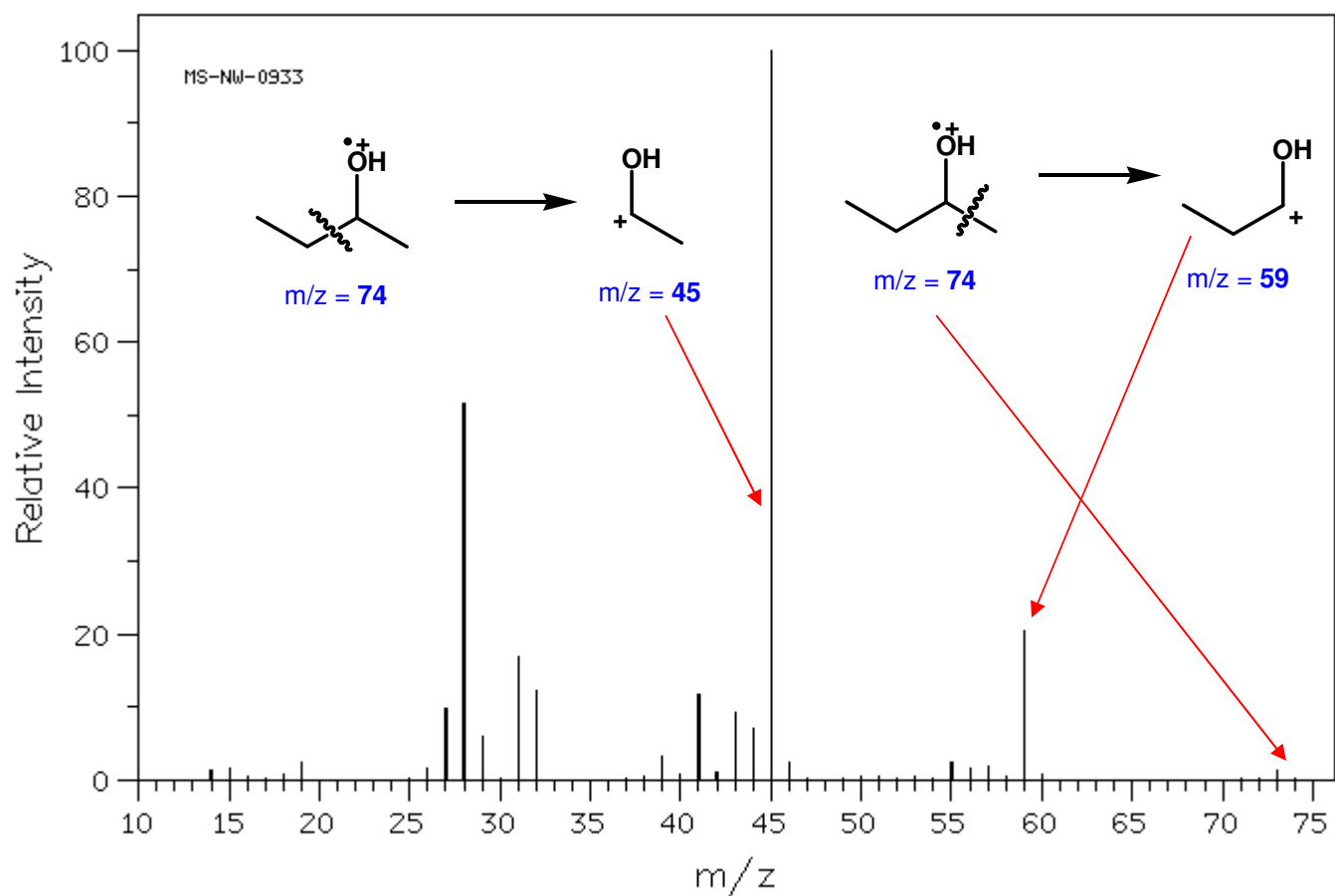
Alcohols fragment very easily – secondary and primary alcohols show very weak M^+ peaks, and tertiary alcohols often do not show M^+ at all. MW is often determined by derivatization or CI-MS.

The C-C bond nearest the OH is frequently the first bond to break. Thus primary alcohols often show a prominent peak at 31 m/z.



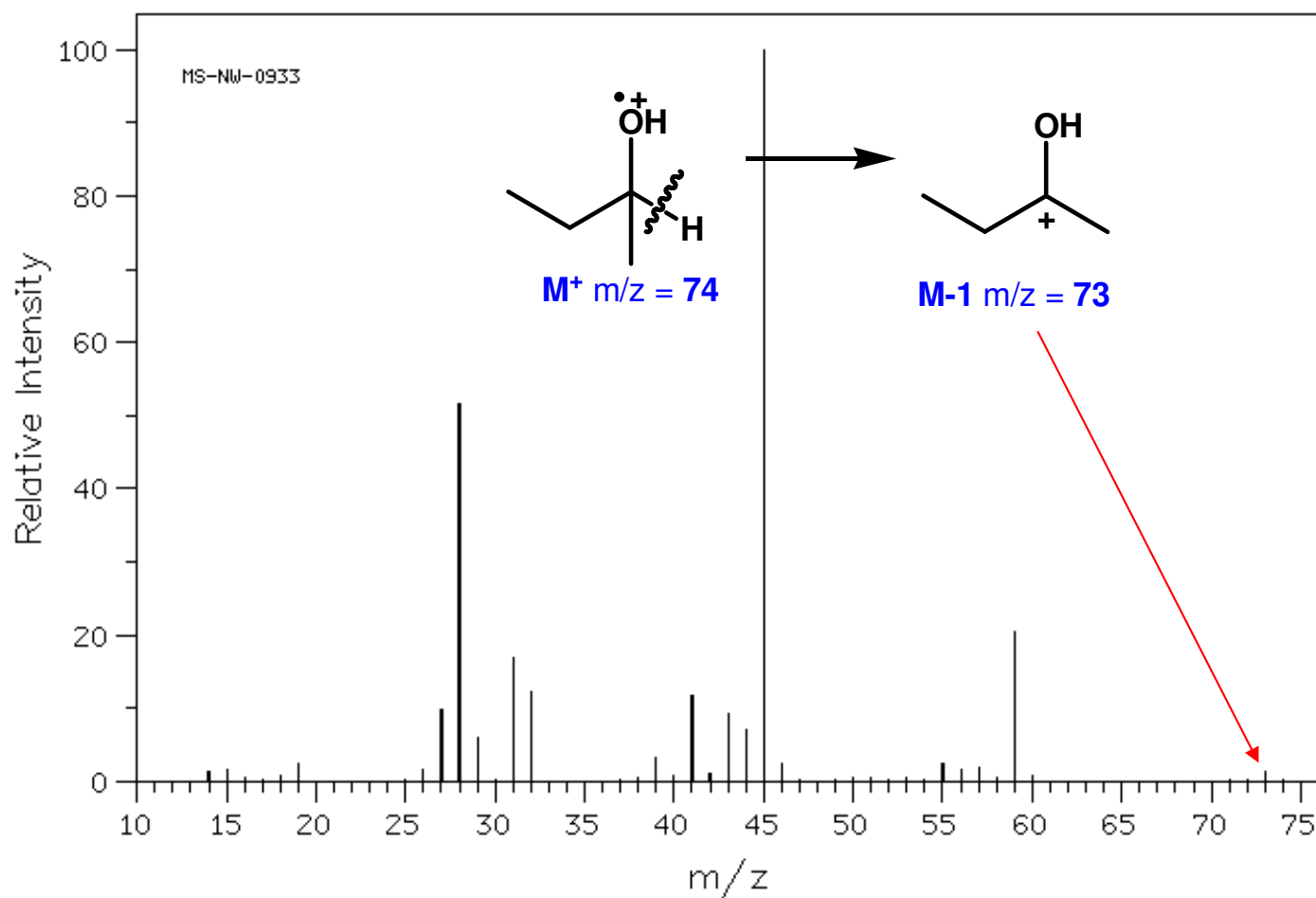
Secondary Alcohols

Secondary alcohols cleave in the same way, often showing a prominent $+CHR-OH$ peak.



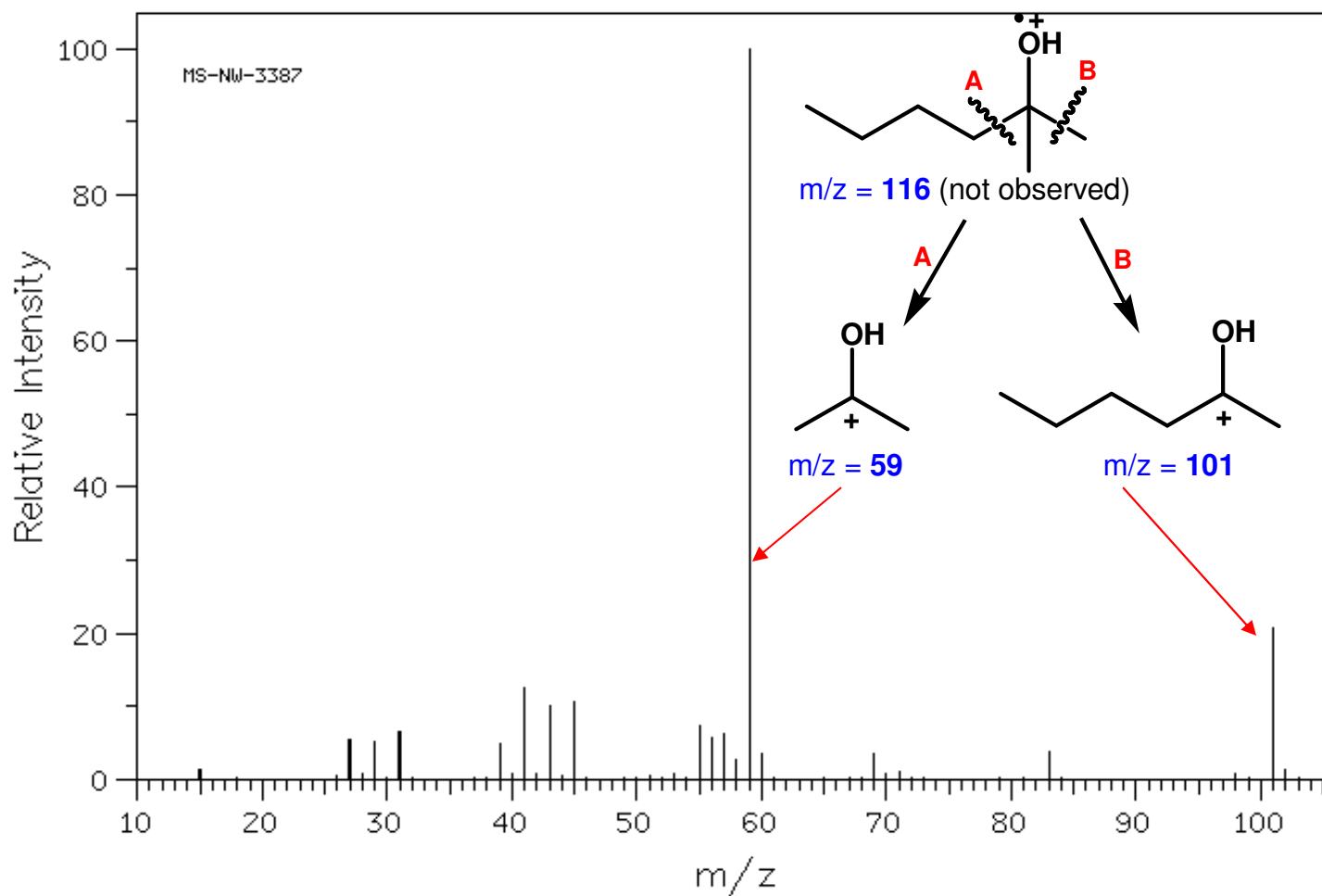
Alcohols

Sometimes the hydrogen R_2CH-OH in 1° and 2° alcohols cleaves rather than an alkyl group. The result is an $M-1$ peak.



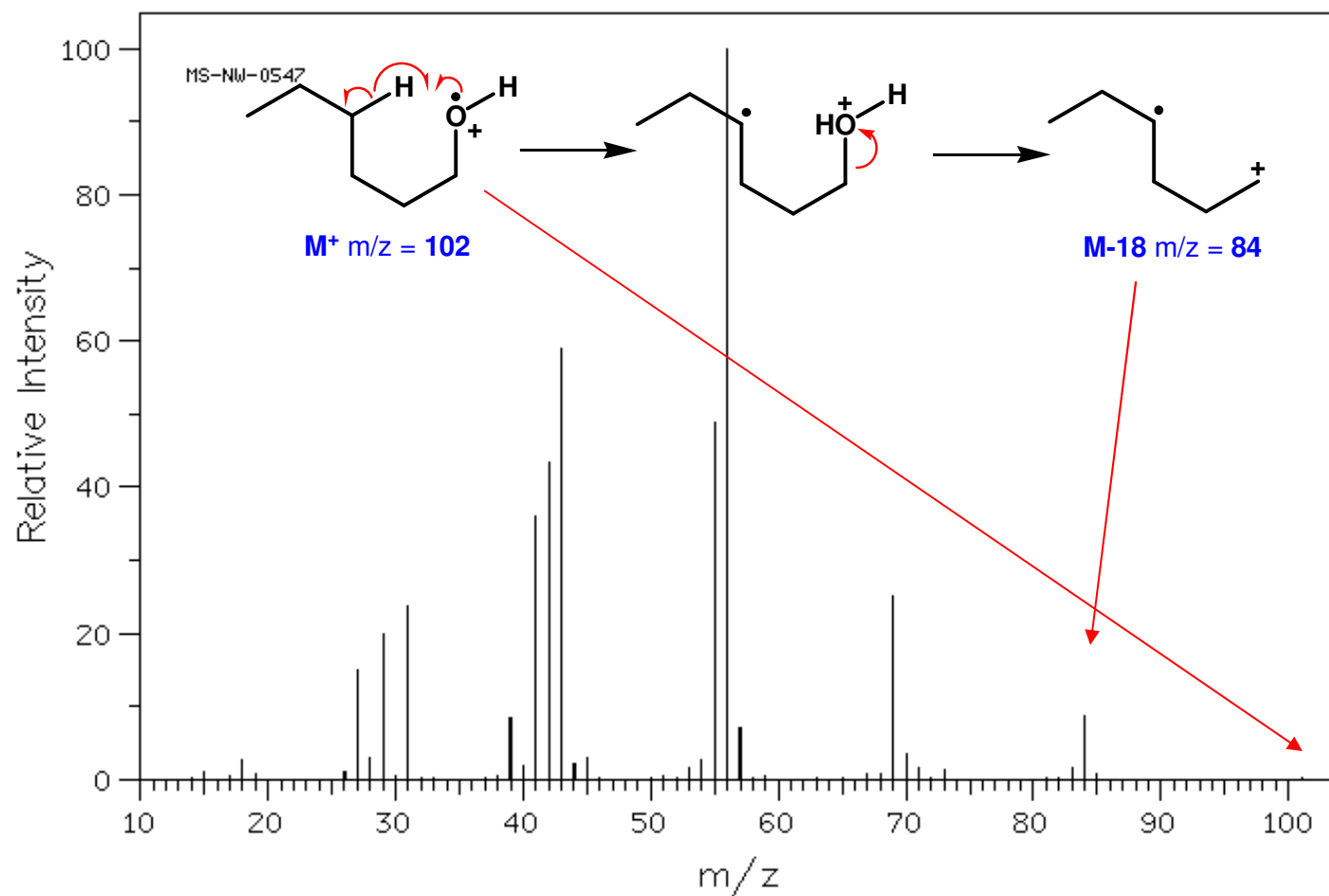
Tertiary Alcohols

Tertiary alcohols cleave in a similar fashion to give $^+\text{CRR-OH}$ fragments.



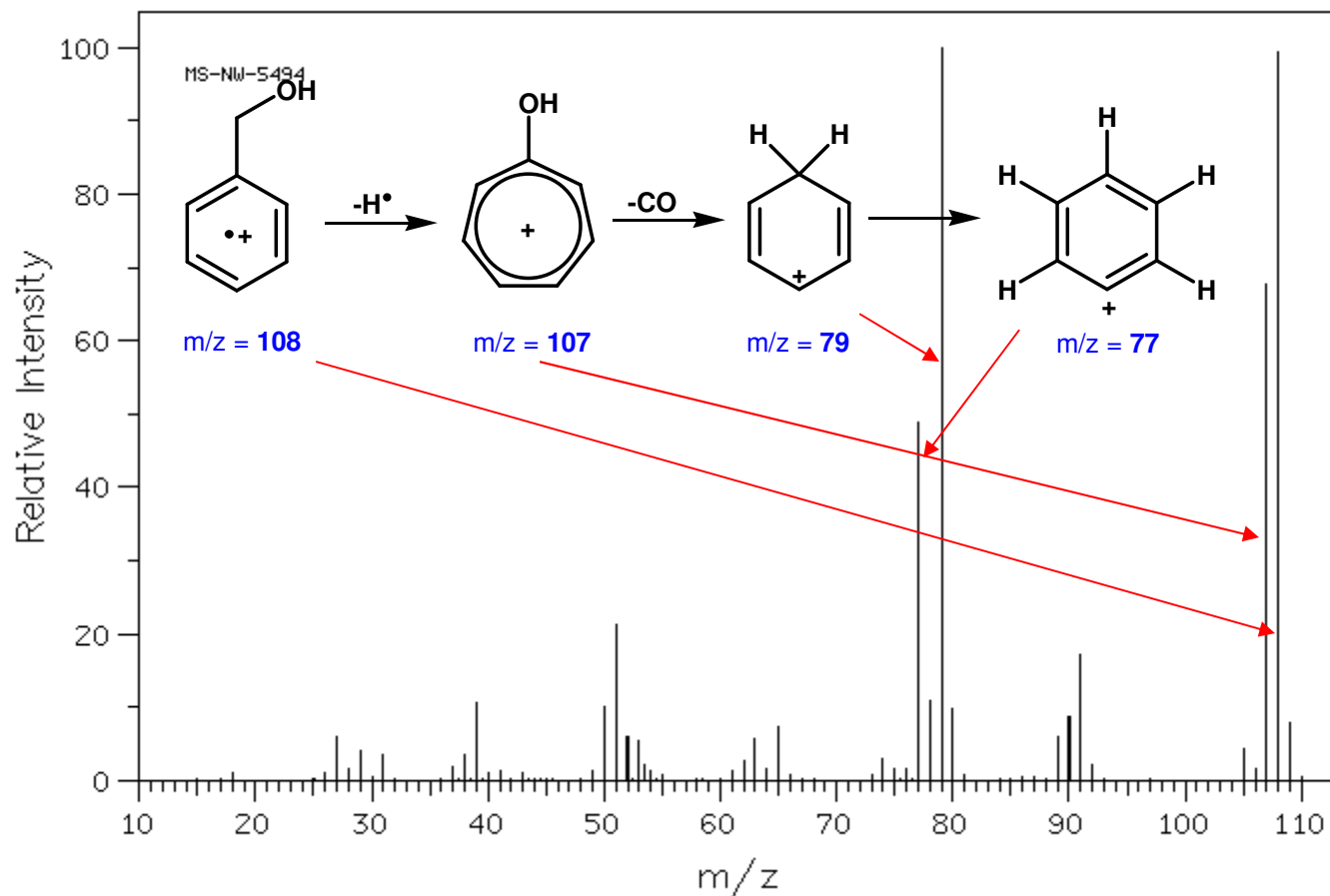
More on Alcohols

Alcohols can lose a molecule of water to show a sometimes prominent M-18 peak. It is especially noticeable for primary alcohols.



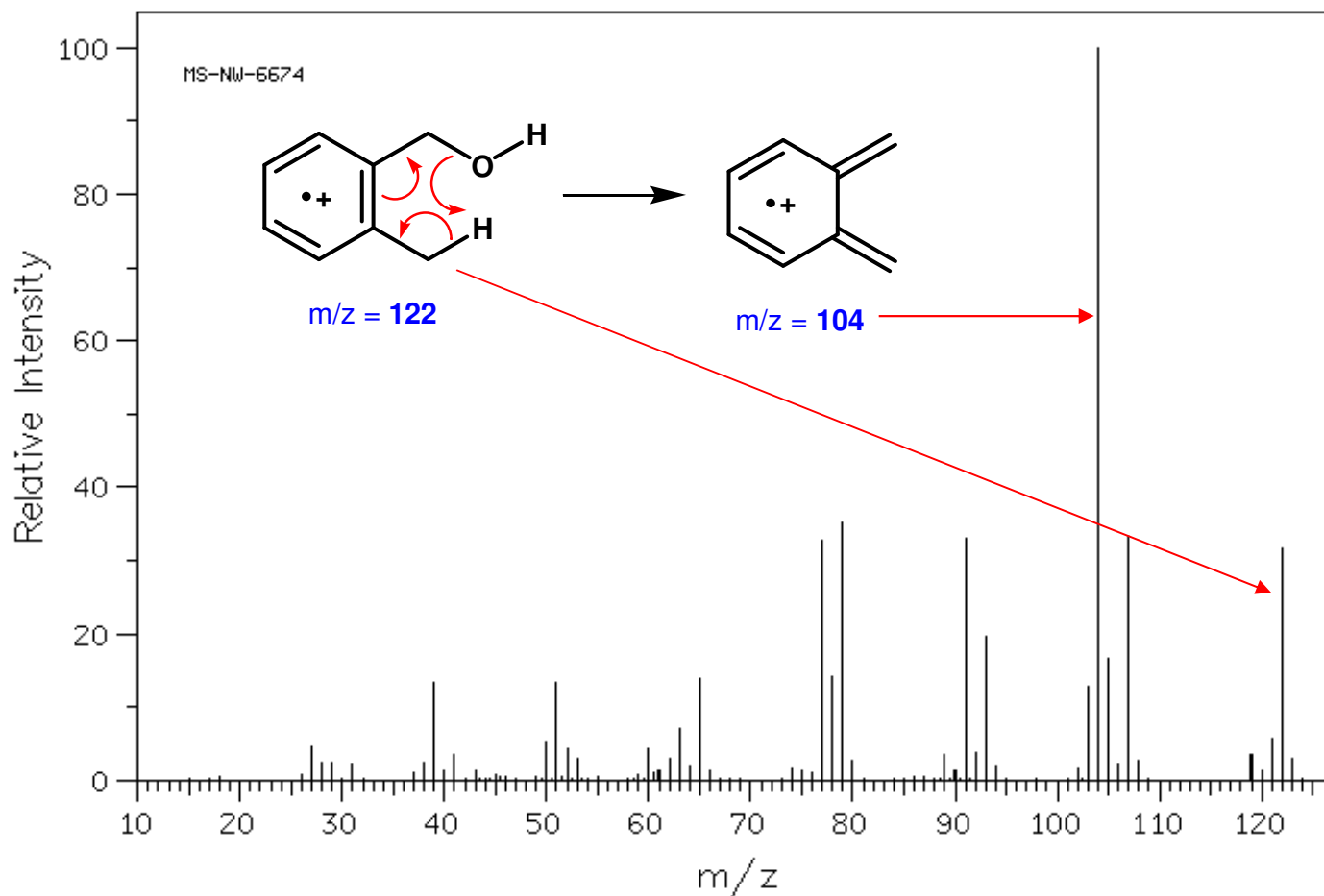
Benzylic Alcohols

Benzylic alcohols fragment much differently from aliphatic alcohols. Benzylic cleavage happens as expected (Rule 8). Benzyl alcohol fragments via the following pathway:



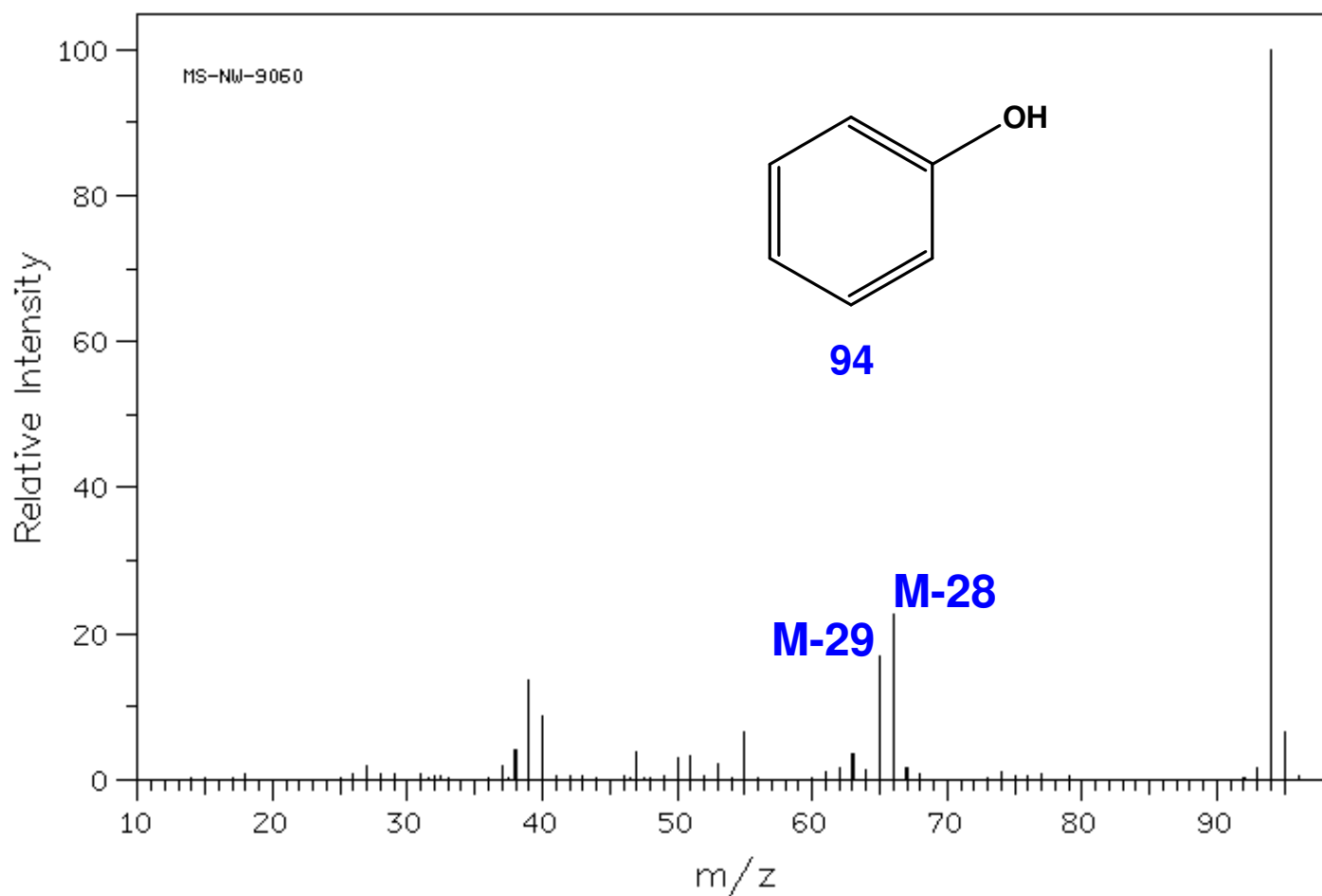
Benzylic Alcohols

Benzylic alcohols will usually lose water (M-18). The M-18 peak is especially strong for molecules for which loss of water is mechanistically straightforward.



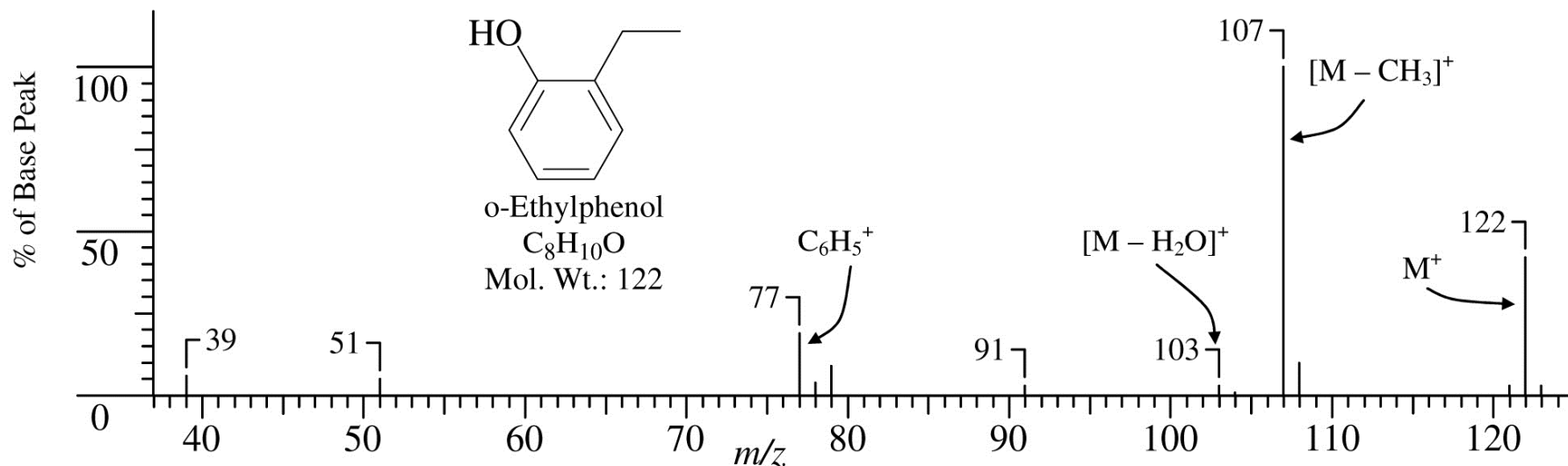
Phenols

Phenols often show peaks at 77 m/z resulting from formation of phenyl cation, and peaks resulting from loss of CO (M-28) and CHO (M-29) are usually found in phenols.



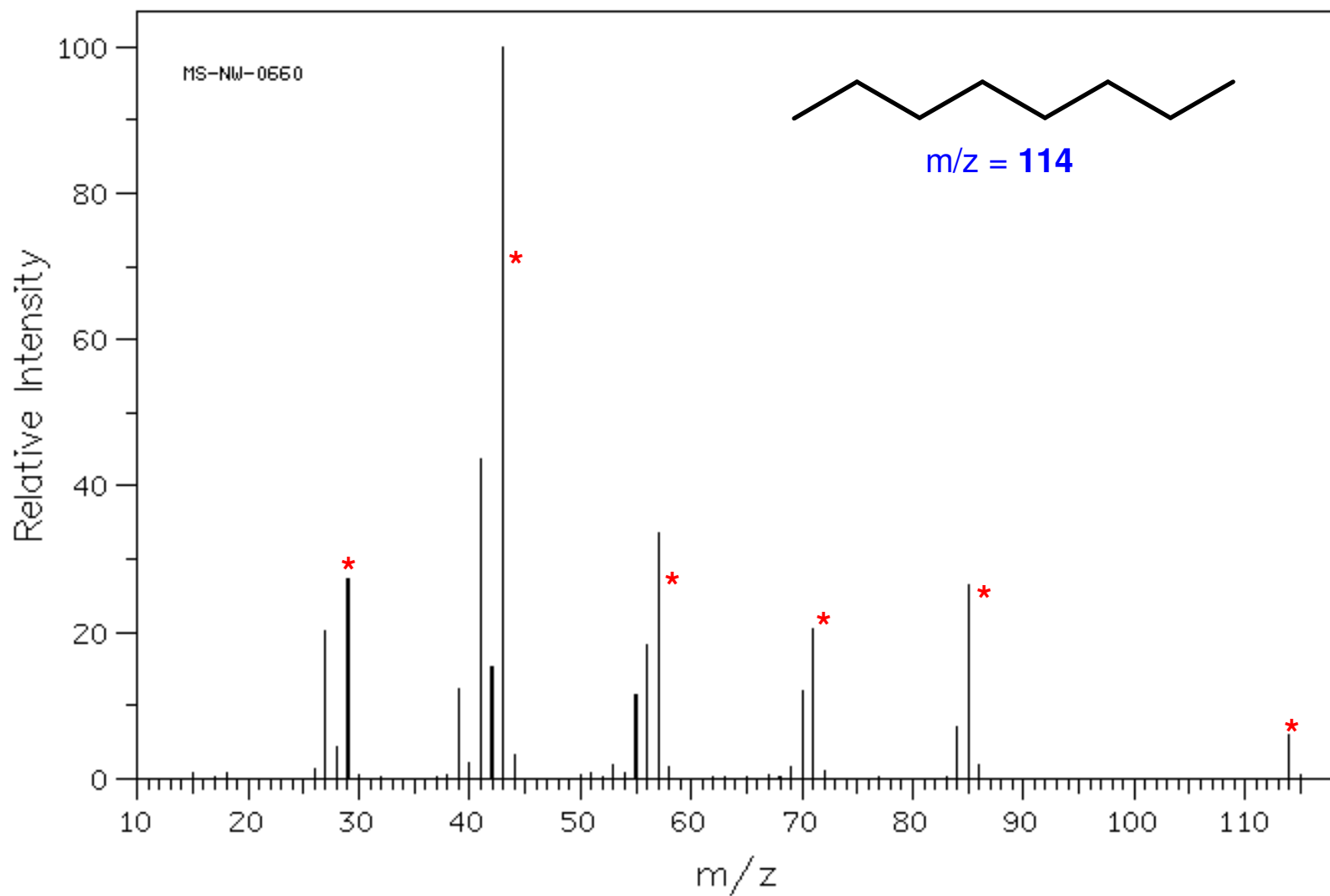
Phenols

If alternative attractive cleavage pathways are available for phenols, the molecule will often take that path.

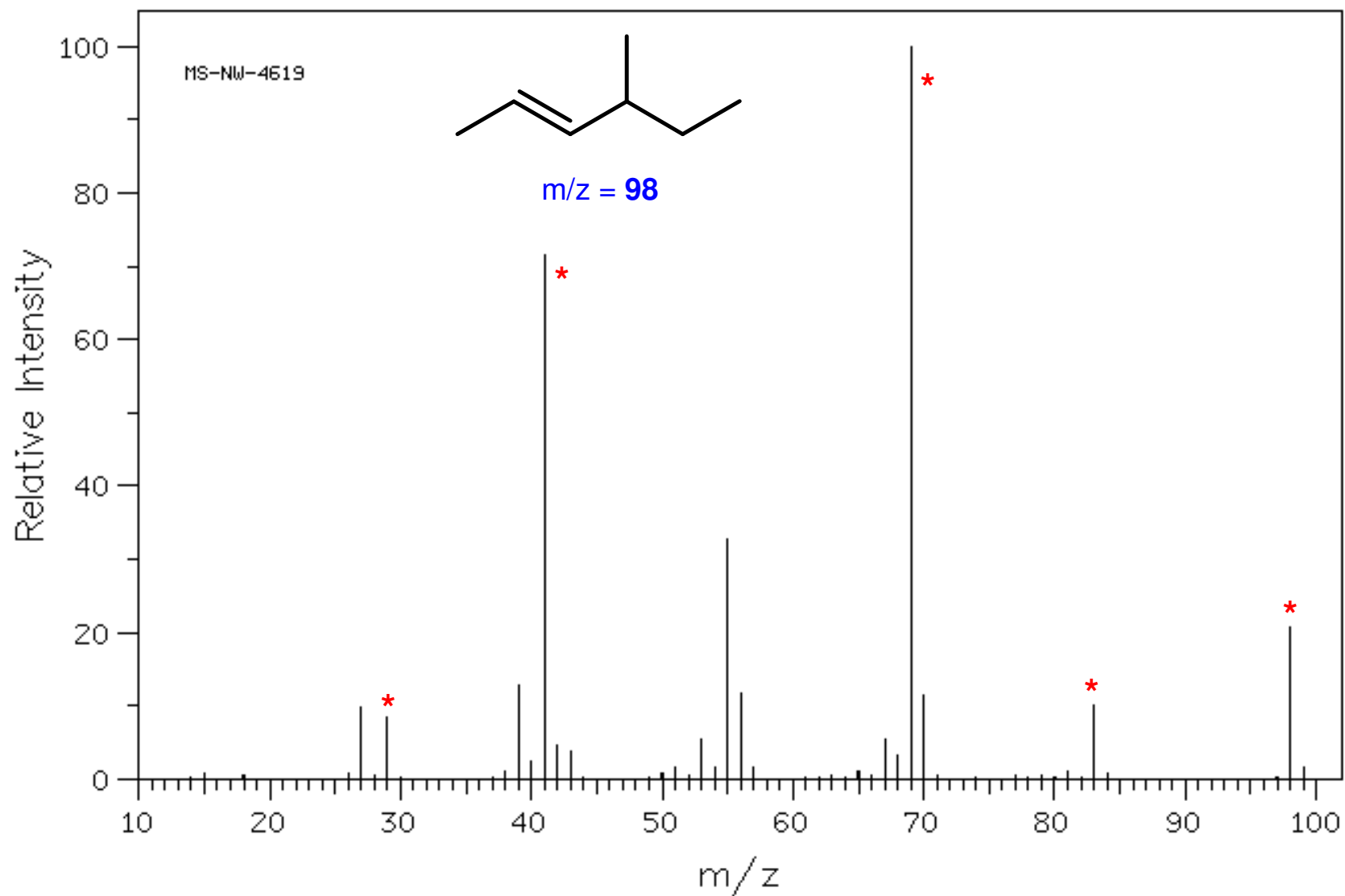


Molecular ions will fragment along the path of least resistance!

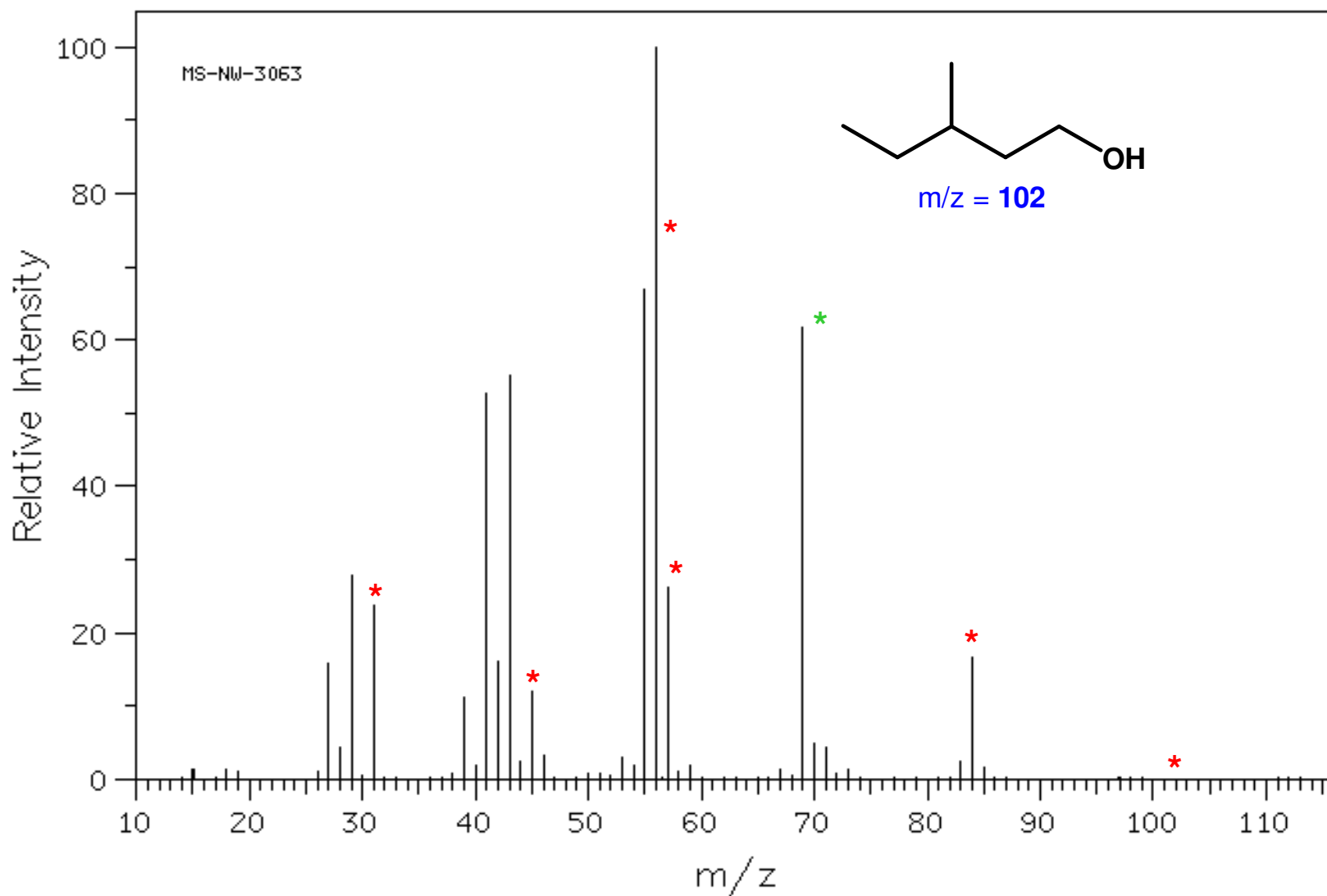
Example: Octane



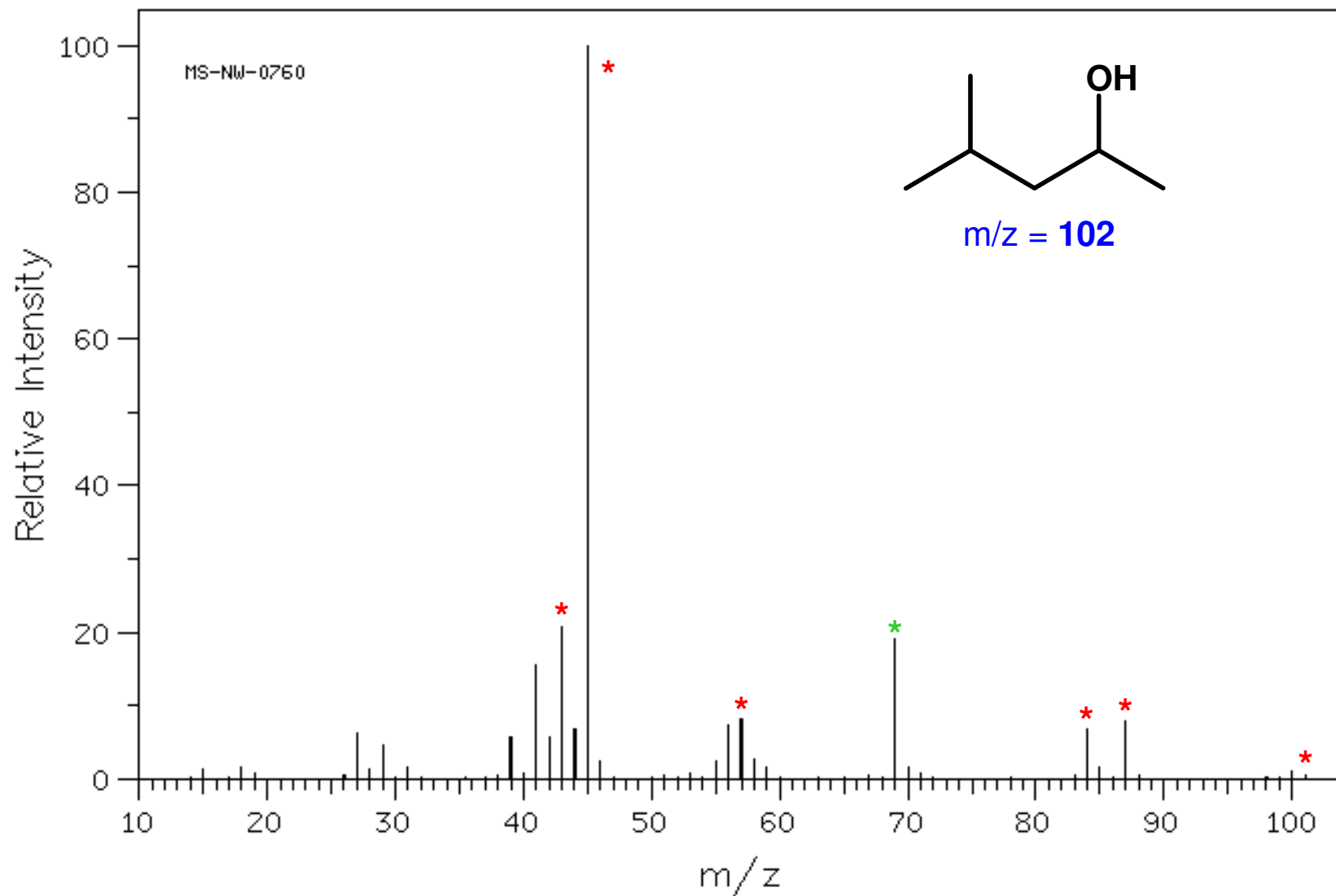
Example: 4-methyl-2-hexene



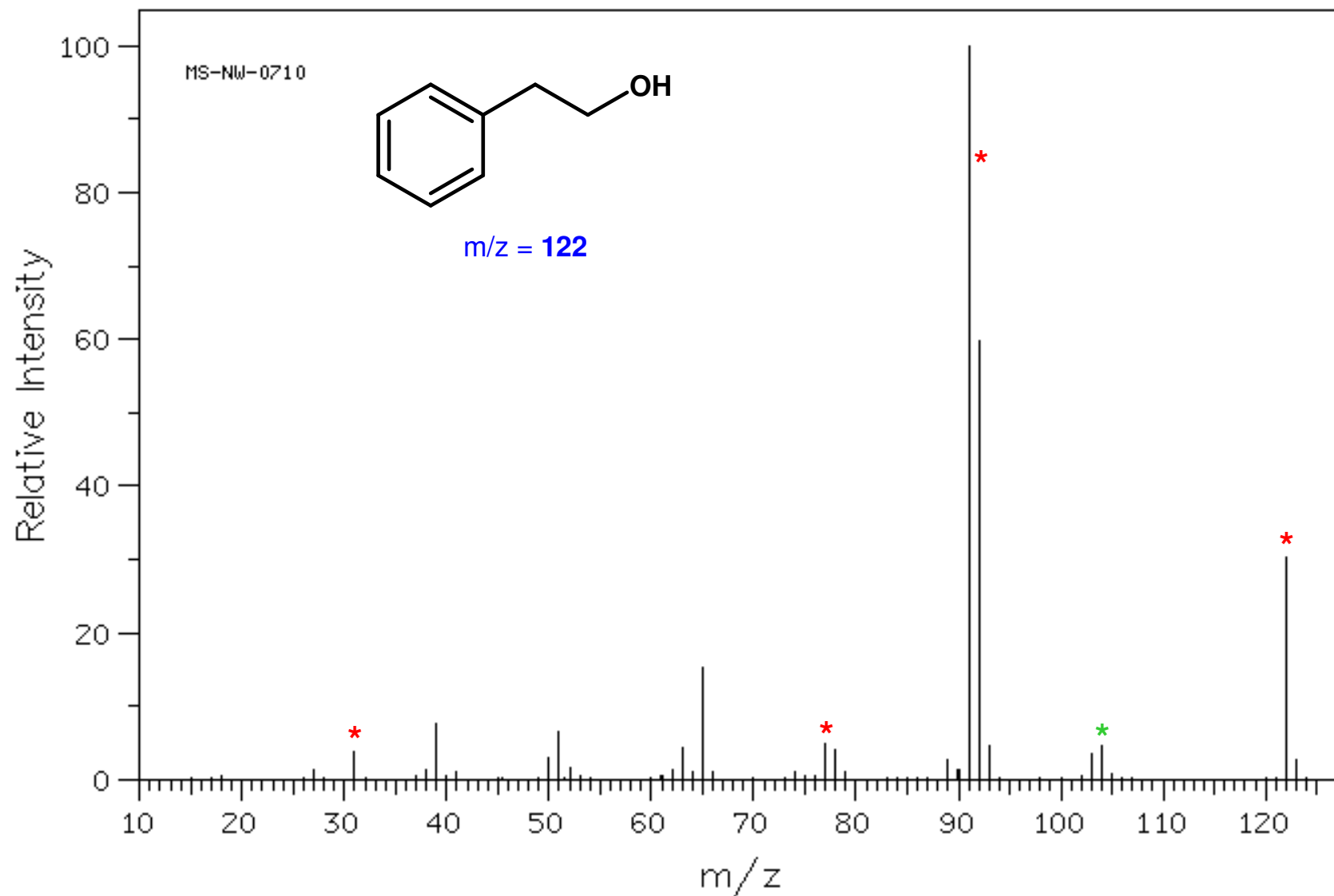
Example: 3-methyl-1-pentanol



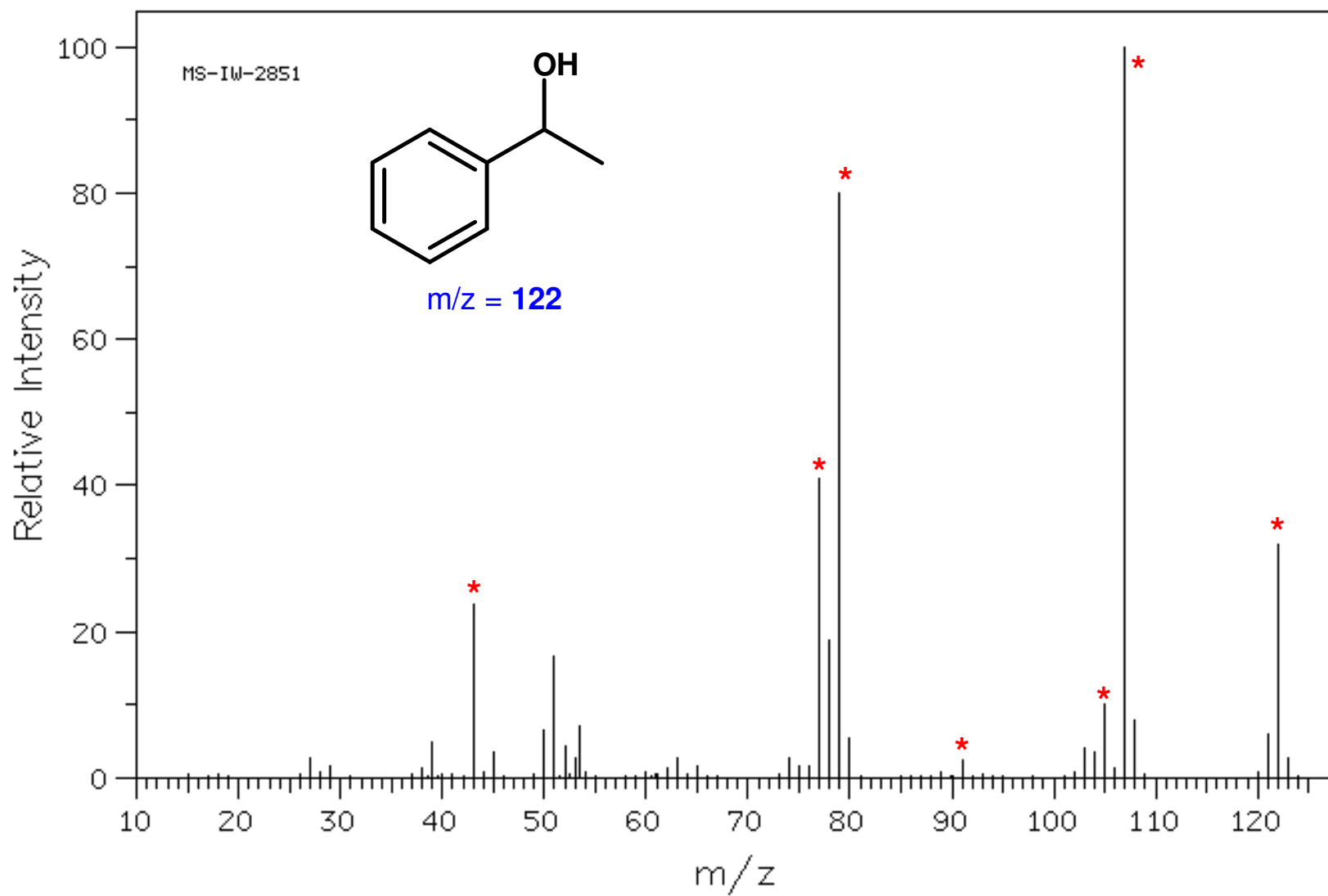
Example: 4-methyl-2-pentanol



Example: 2-phenylethanol



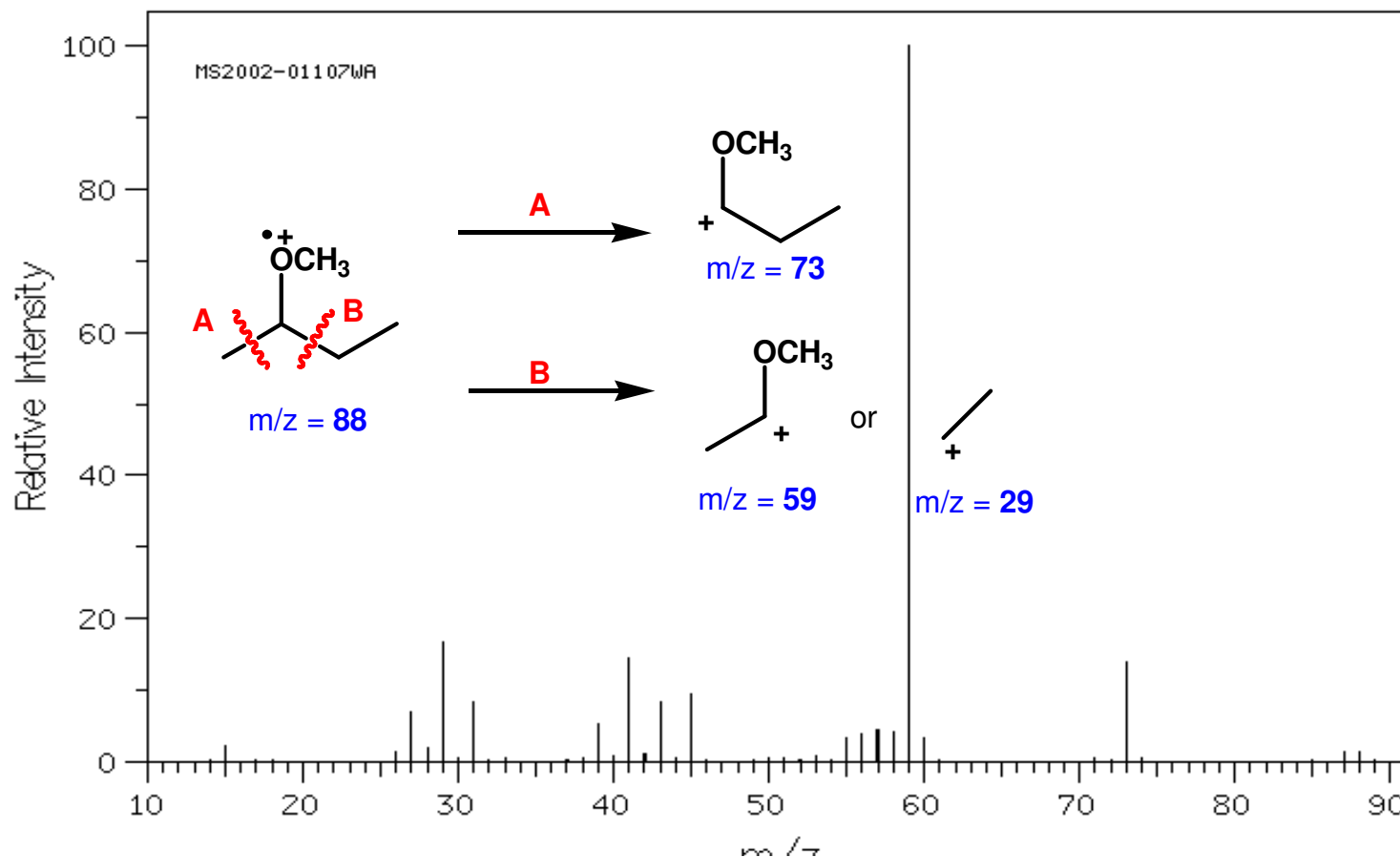
Example: 1-phenylethanol



5. Ethers

Cleavage happens in two main ways:

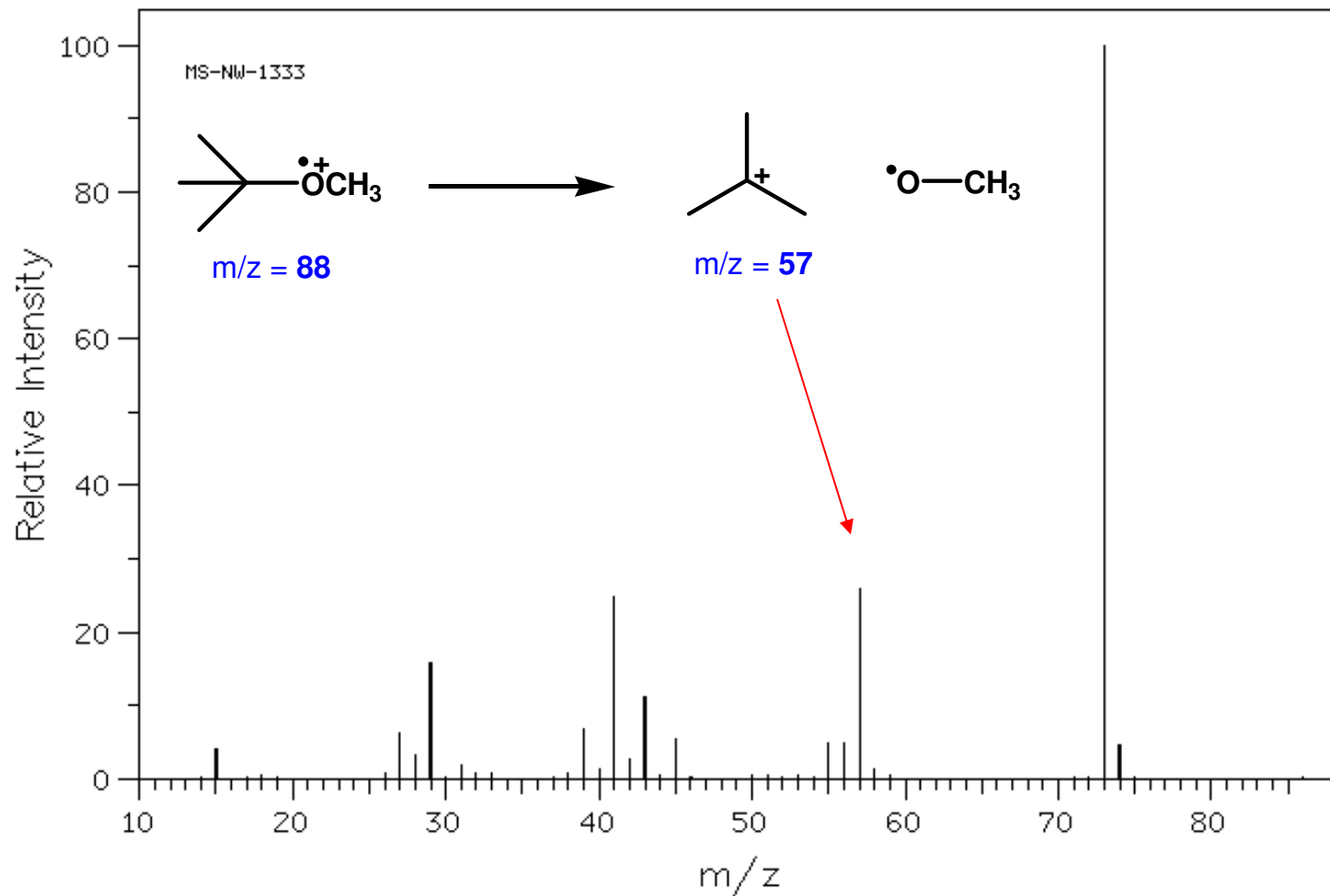
1. Breakage of the C-C bond next to O (like alcohols)



Ethers

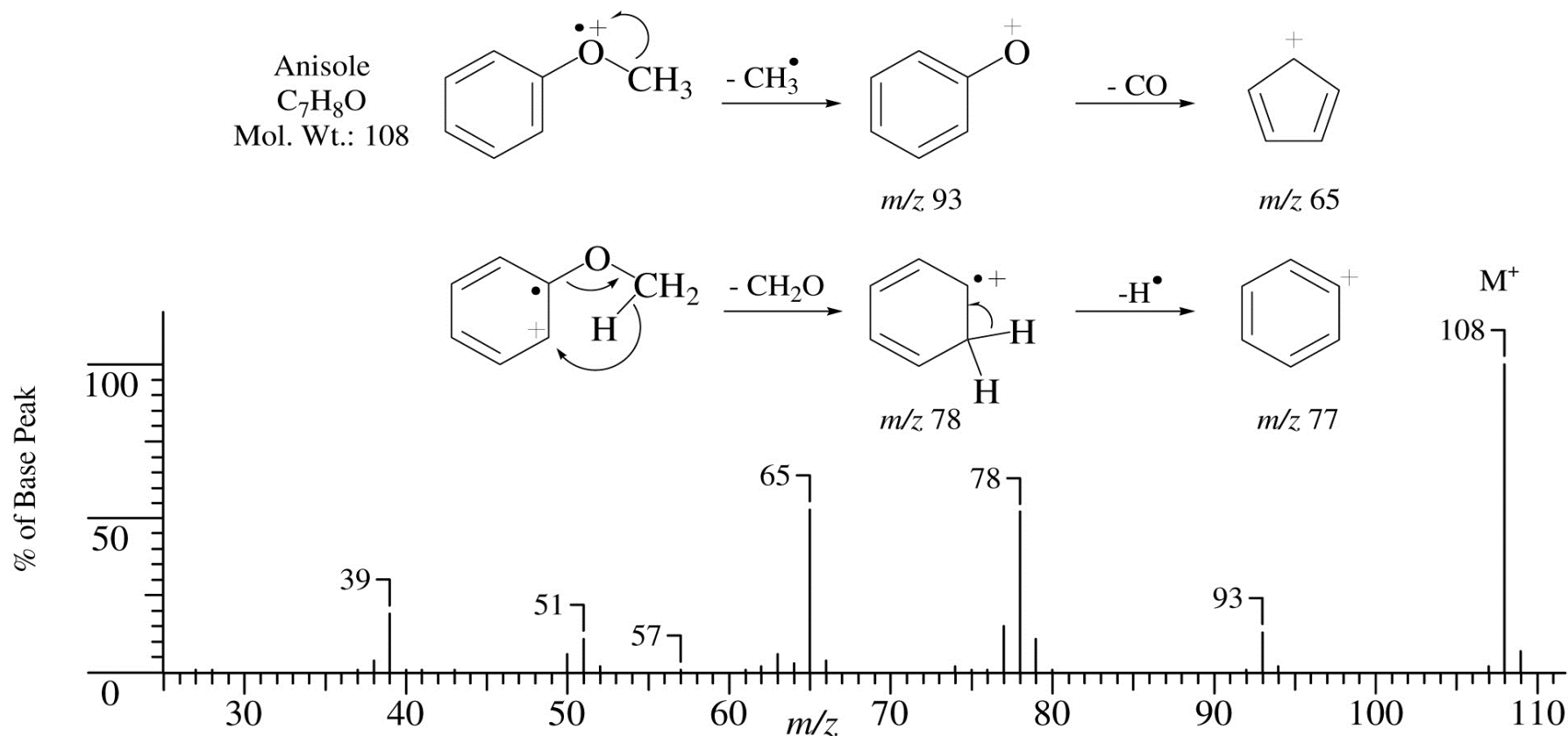
Cleavage happens in two main ways:

2. C-O bond cleavage with the charge on the C fragment.



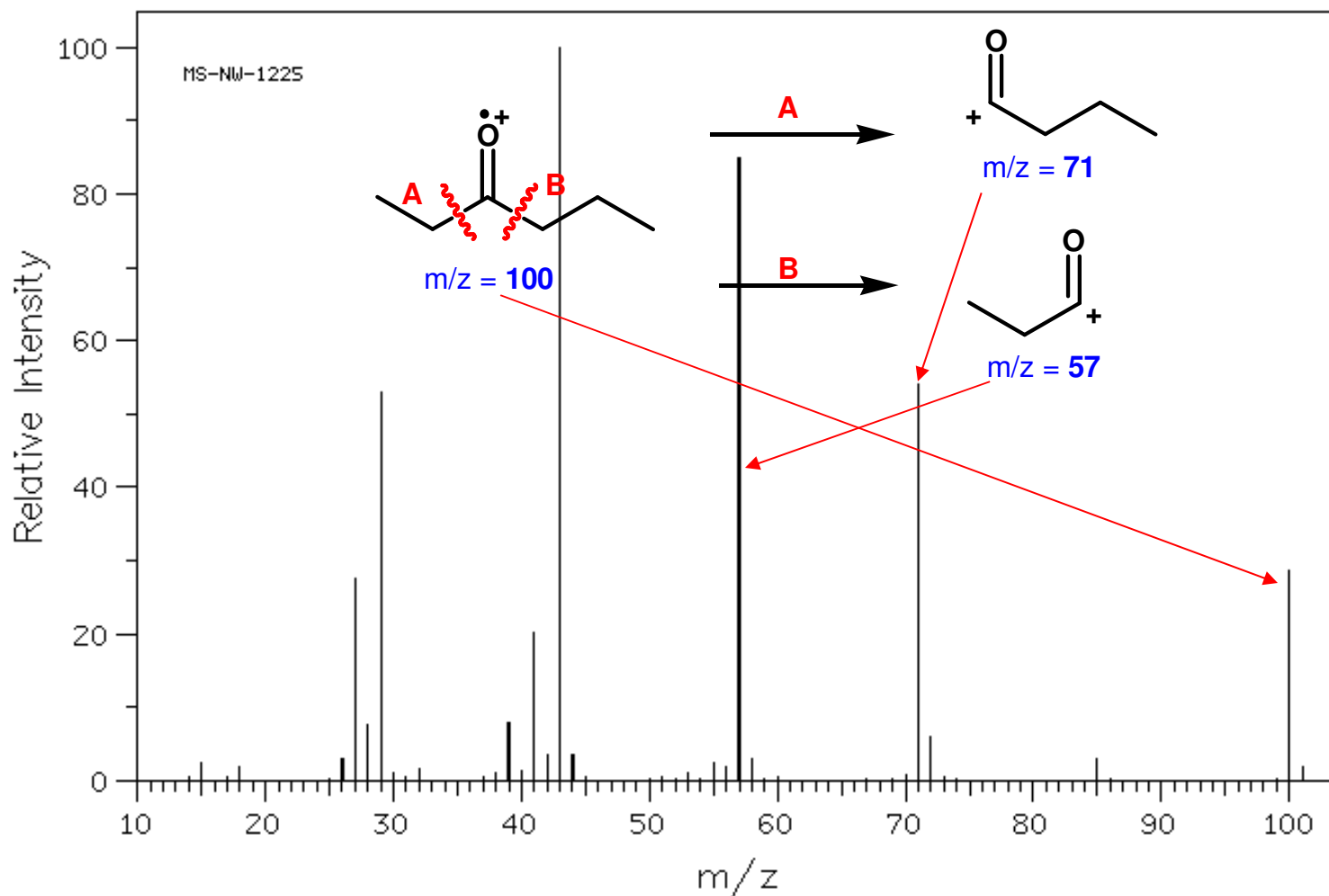
Aromatic Ethers

M⁺ is usually strong. MS is similar to phenols – both form phenoxy cation (m/z 93) and associated daughters.



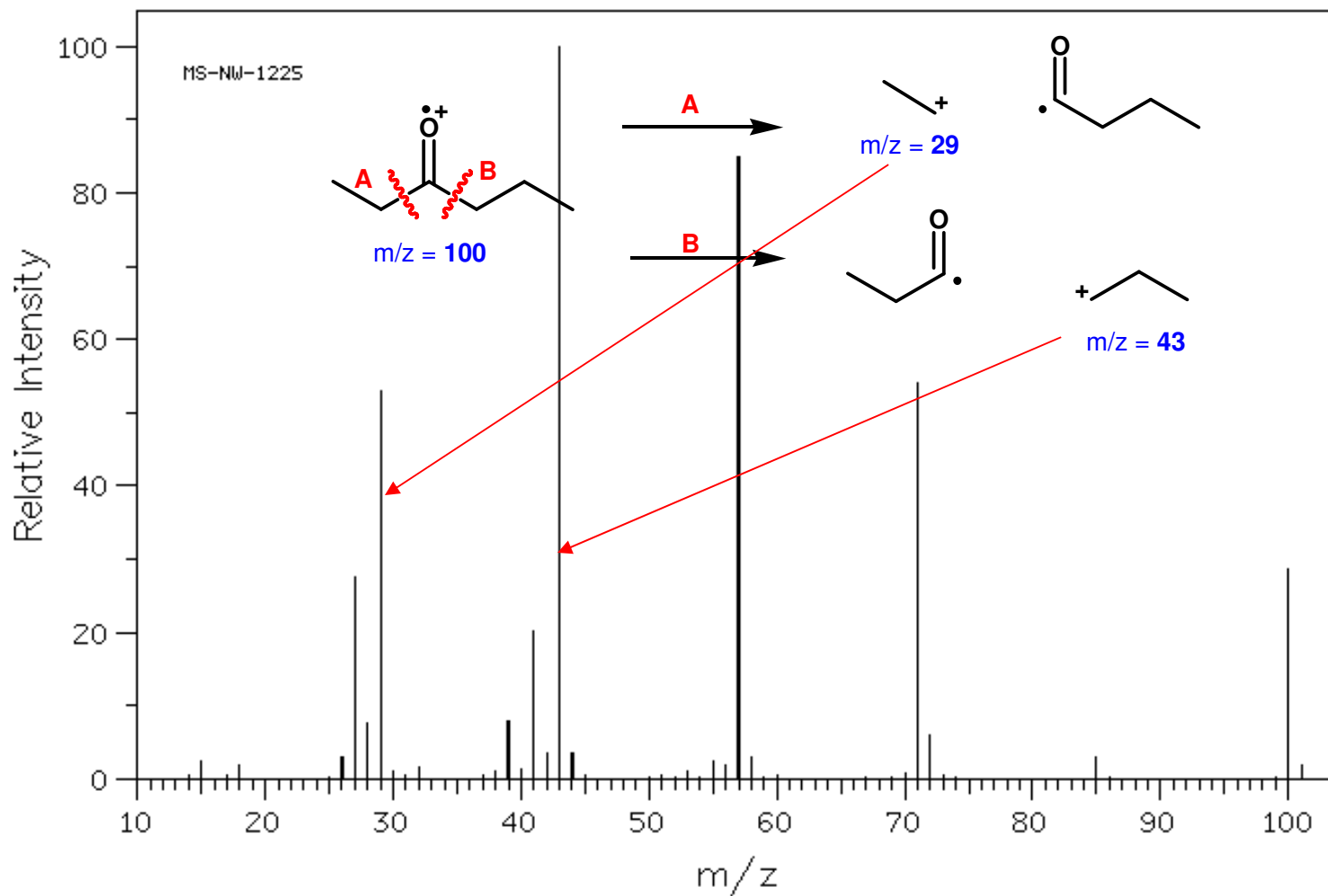
6. Ketones

Ketones usually give strong M^+ peaks. A major fragmentation pathway involves α -cleavage to give an acylium ion.



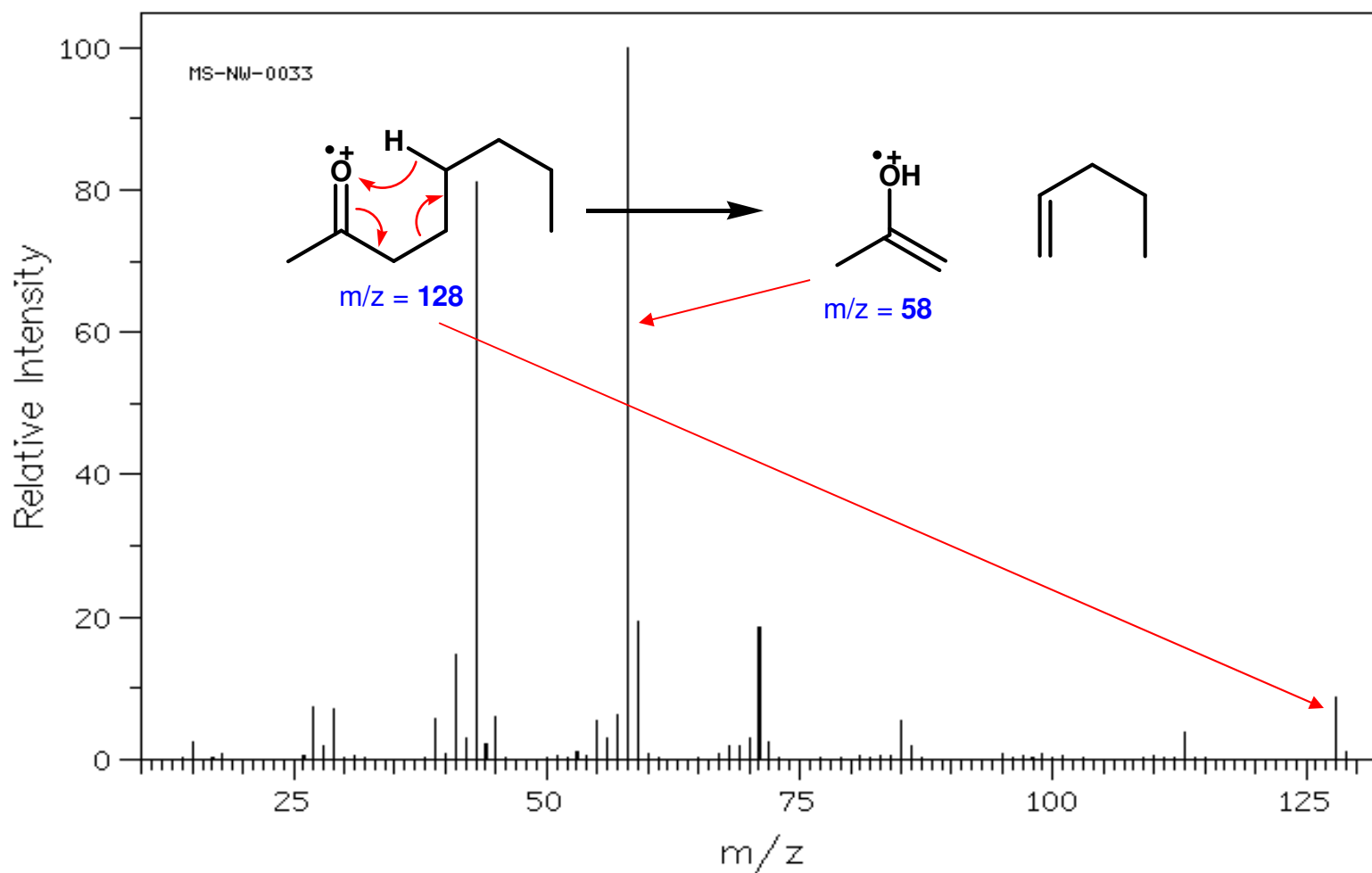
6. Ketones

The carbonyl-containing fragment can also take the radical.



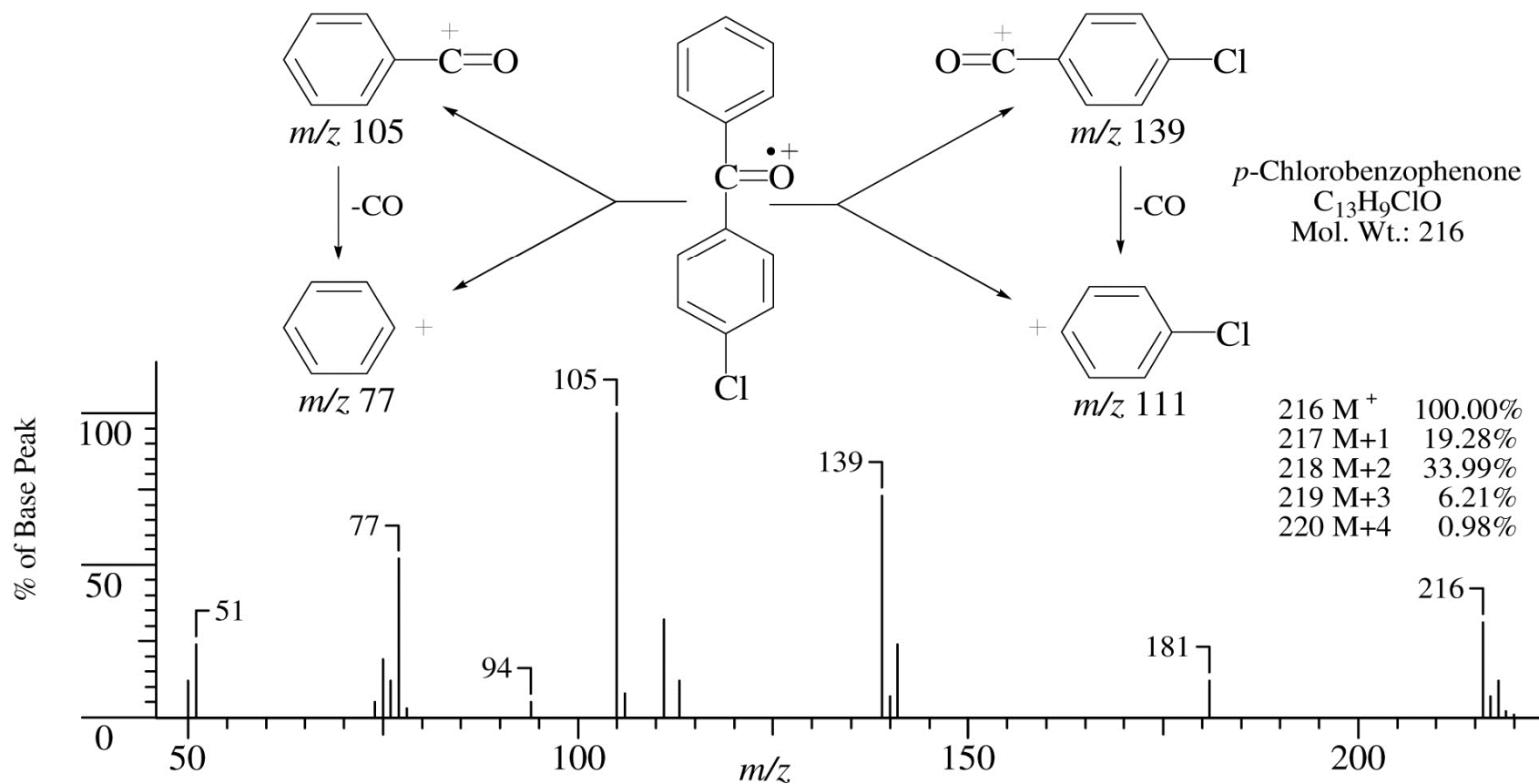
6. Ketones

For ketones with longer chains, the McLafferty rearrangement often leads to strong peaks.



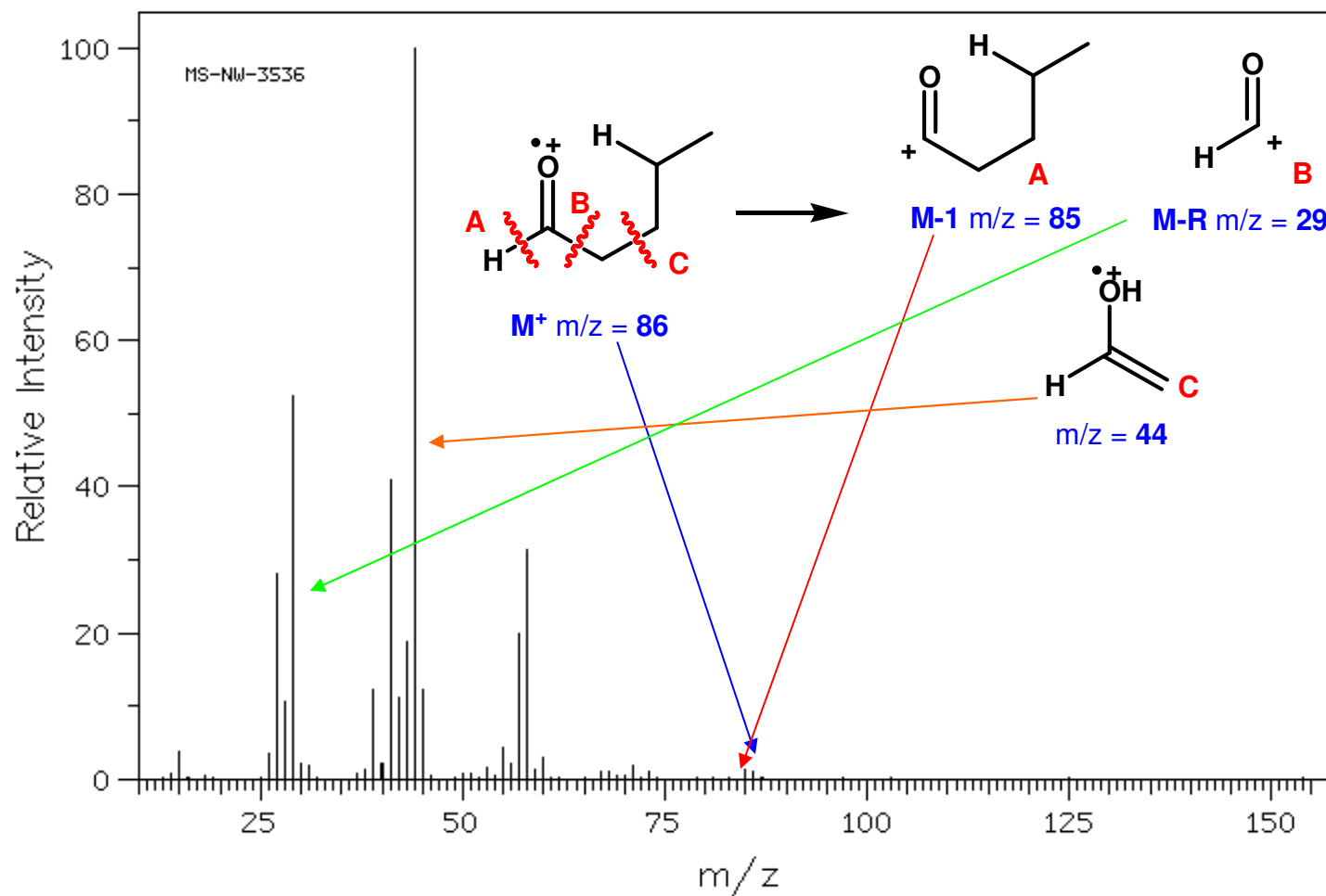
6. Aromatic Ketones

M⁺ is evident. Primary cleavage is α to the carbonyl to give a strong ArCO⁺ peak (m/z 105 when Ar = Ph). This will lose CO to give the phenyl cation (m/z 77).



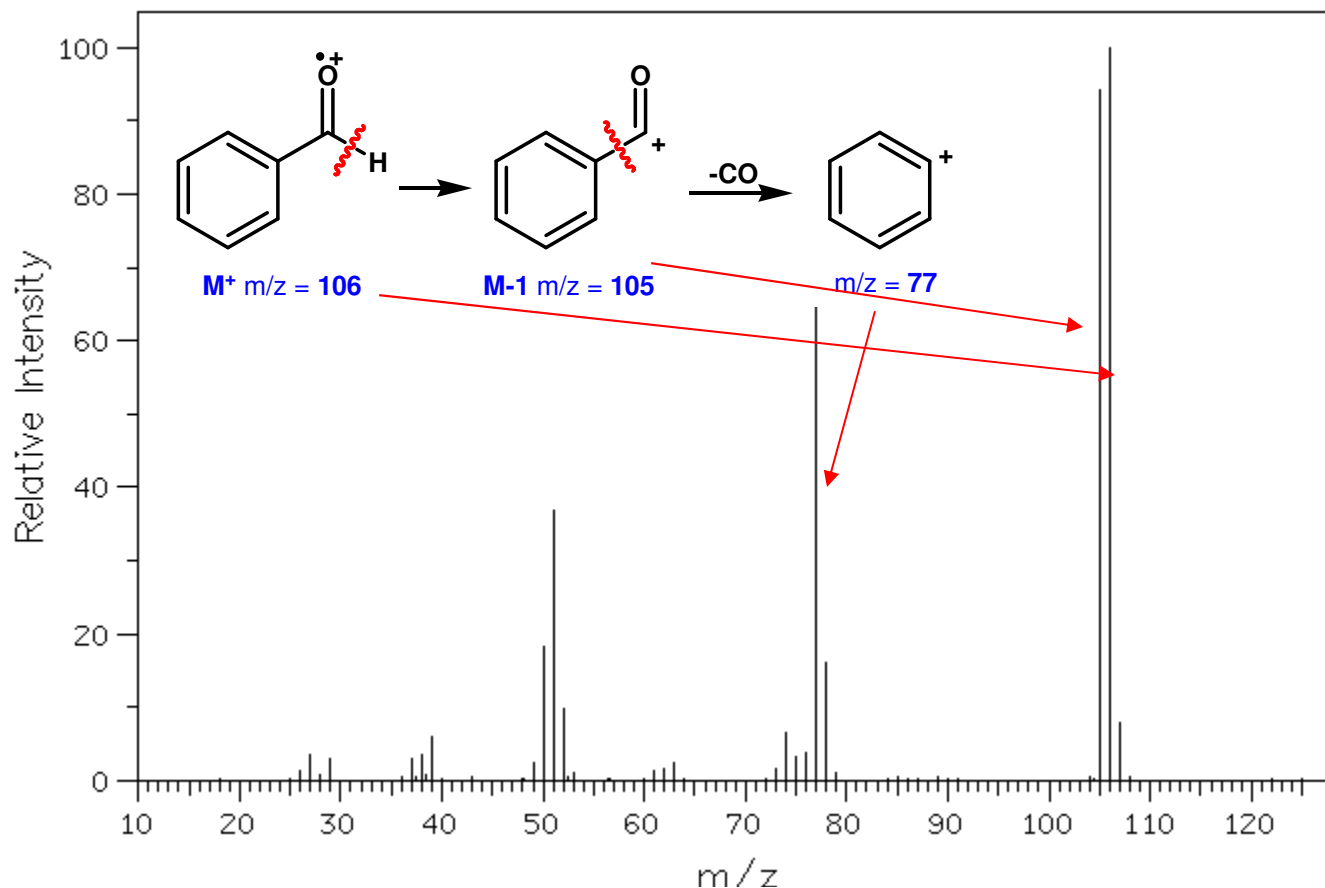
7. Aldehydes

Aldehydes show weak but discernable M^+ peaks. Major pathways are α -cleavage and McLafferty Rearrangement.



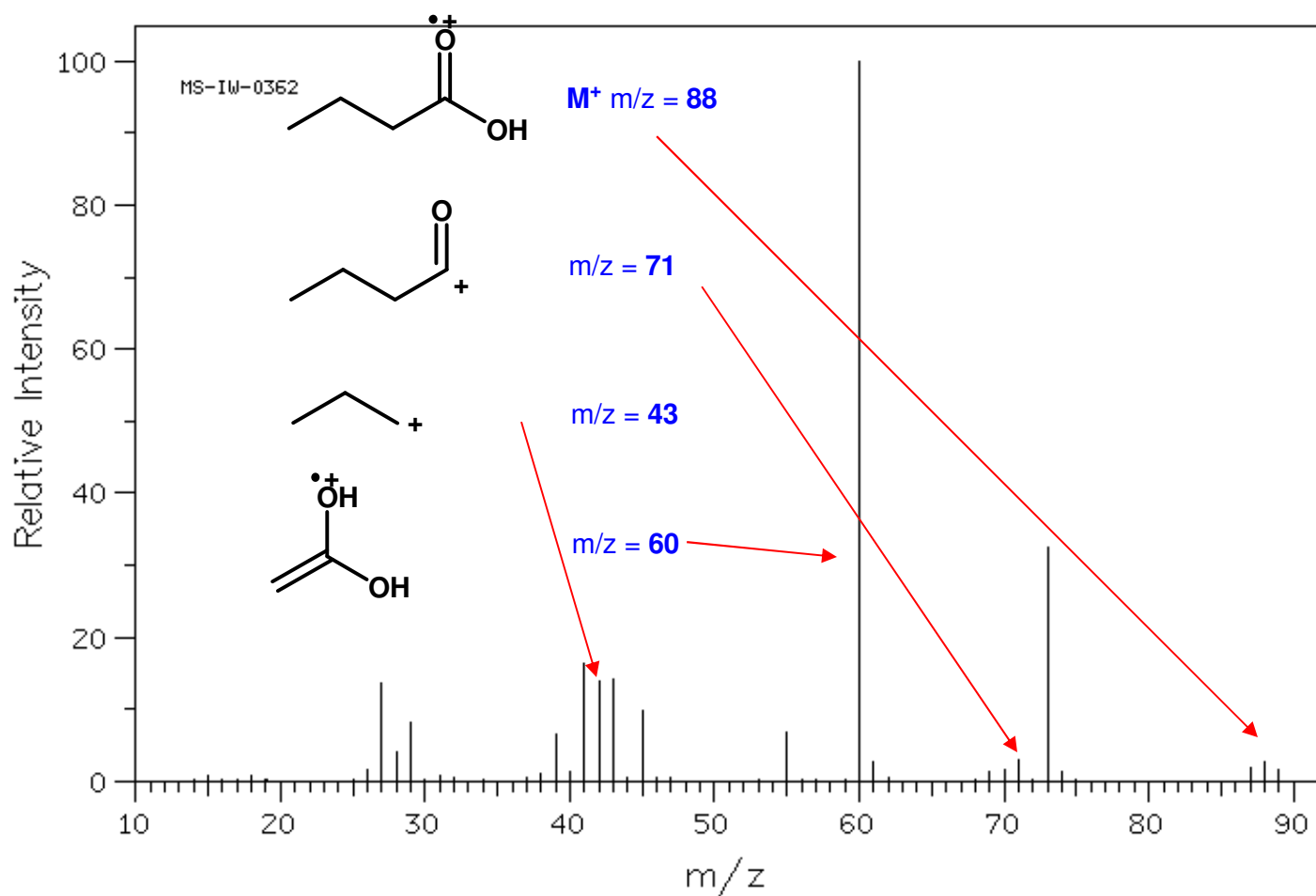
7. Aromatic Aldehydes ...

... are similar to aromatic ketones. M^+ is strong, and $M-1$ (α -cleavage to carbonyl) is also strong to give the $ArCO^+$ ion (m/z 105 for $Ar = Ph$). Loss of CO from this ion is common to give m/z 77 phenyl cation.



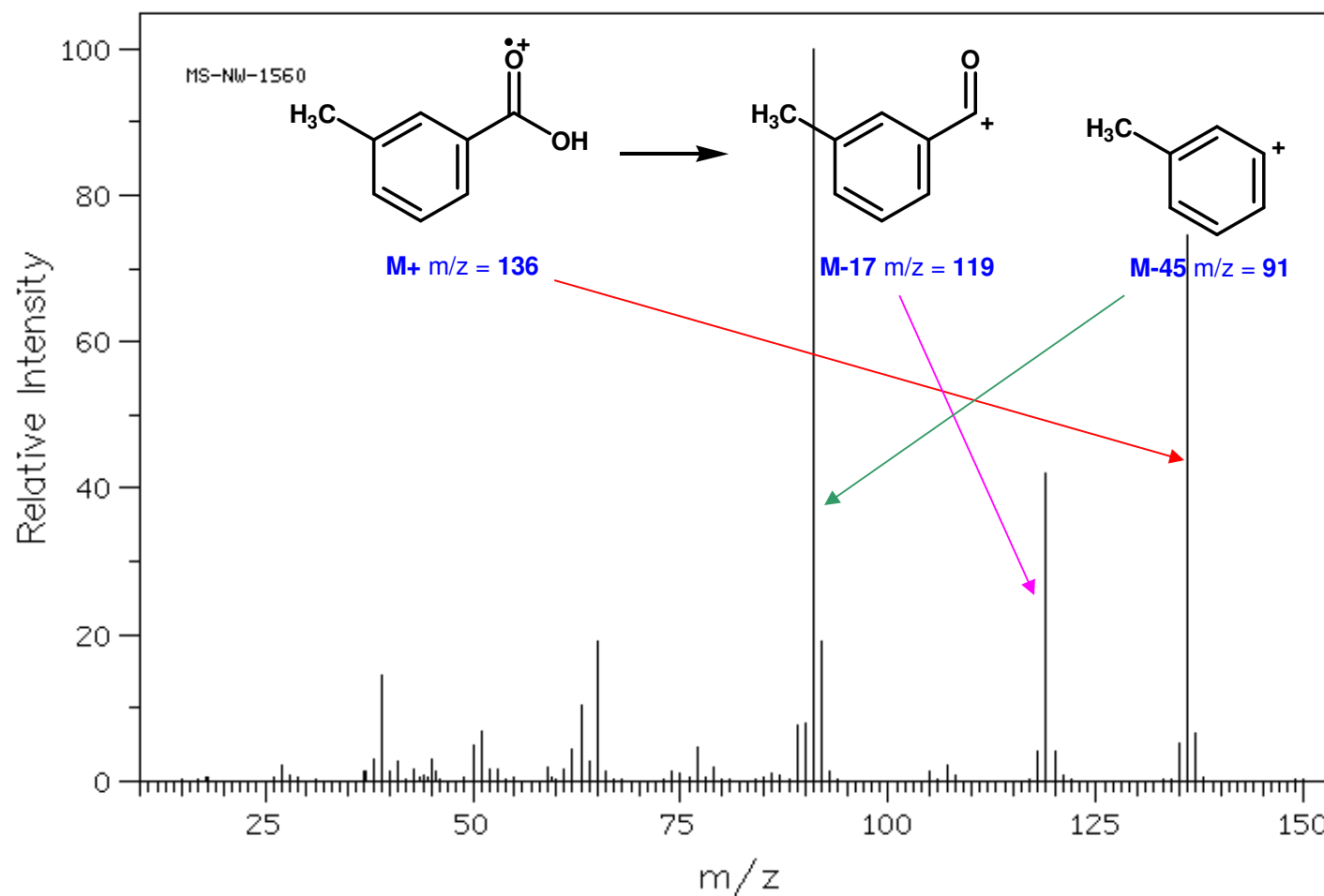
8. Carboxylic Acids (Aliphatic)

M^+ is weak, and not always visible. A characteristic m/z 60 peak is often present due to the McLafferty Rearrangement. Bonds α to carbonyl also frequently break to give $M-OH$ and $M-CO_2H$ peaks.



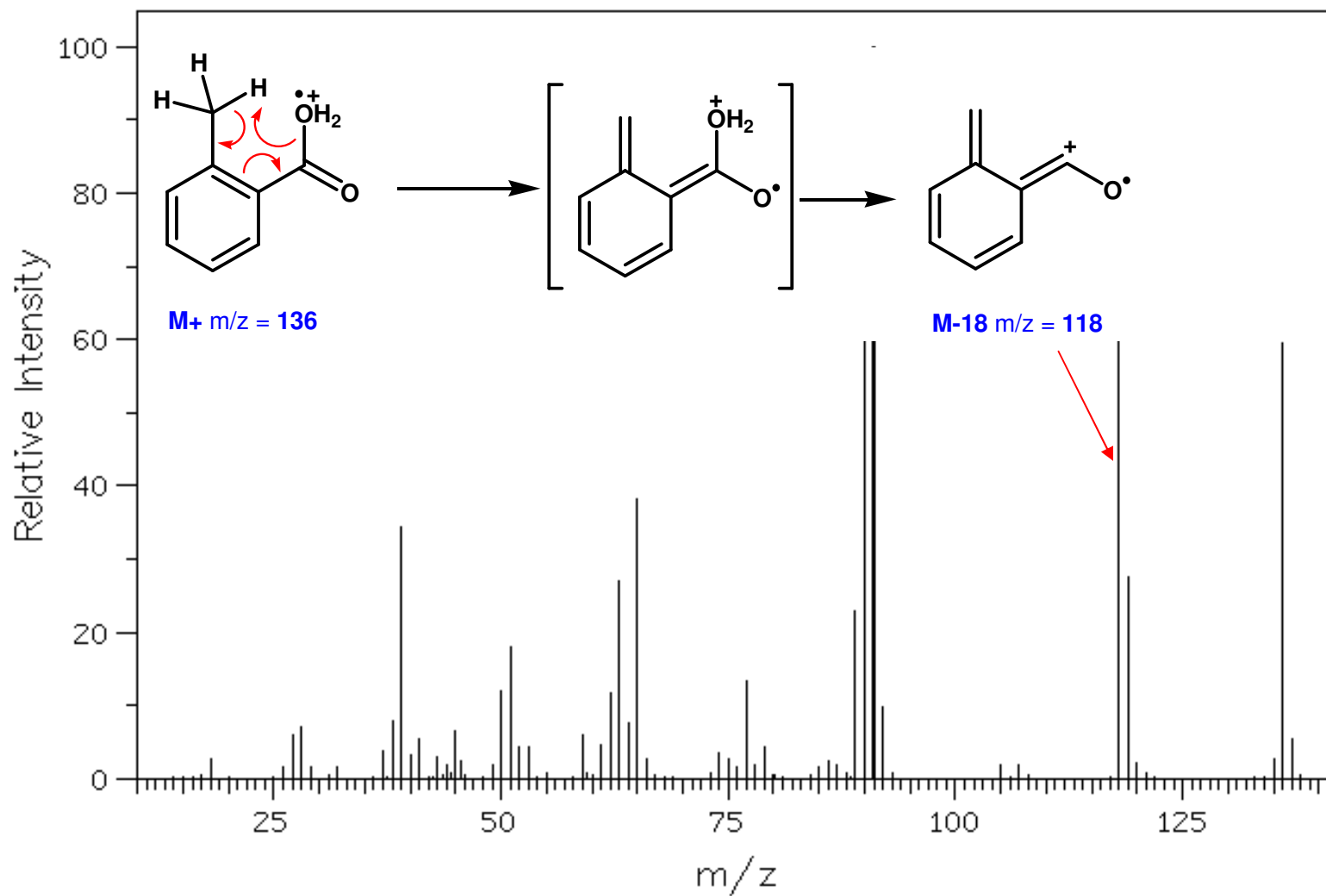
Aromatic Acids

M⁺ is very prominent. Common peaks are loss of OH (M-17) and loss of CO₂H (M-45).



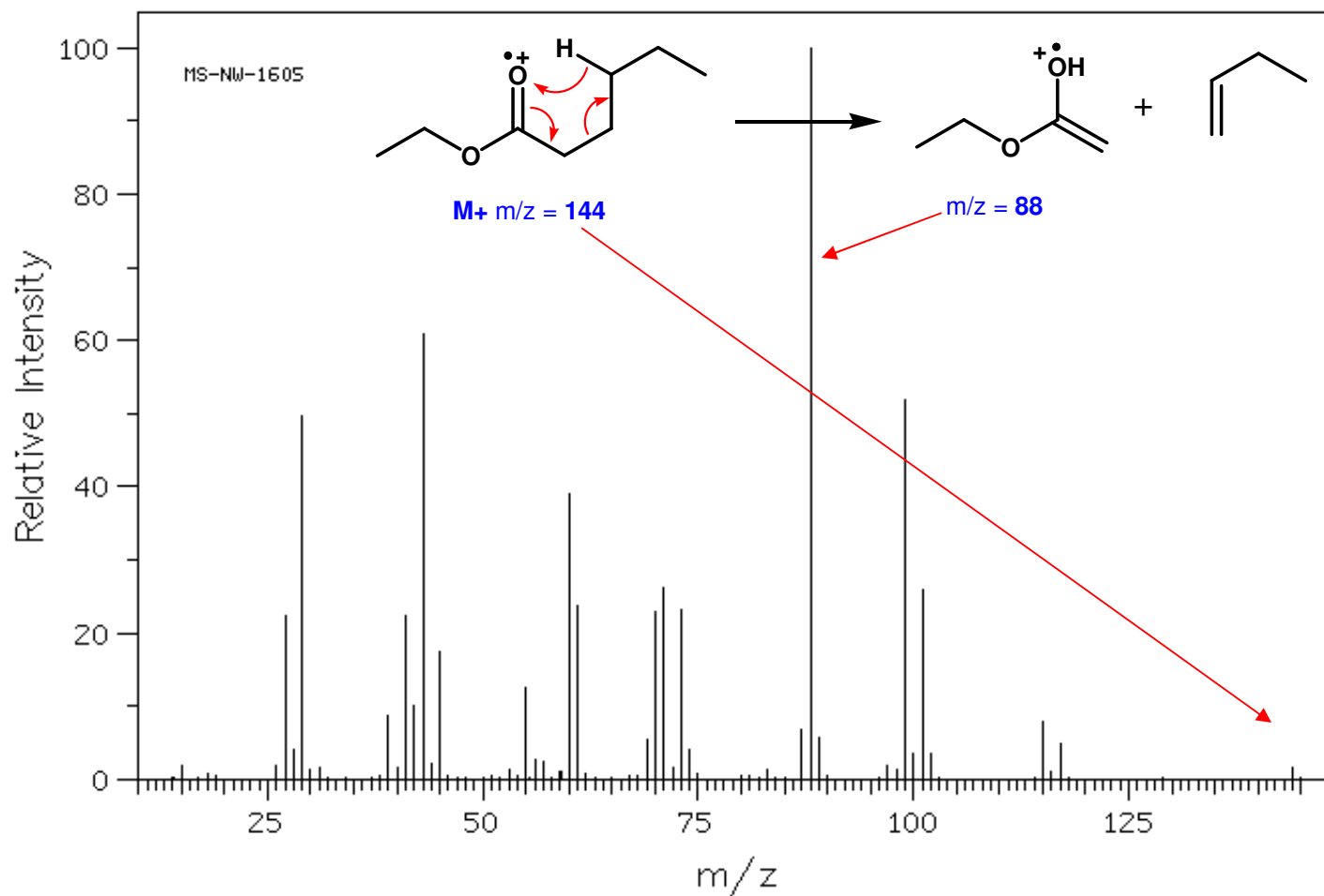
Aromatic Acids

If an *ortho* hydrogen-bearing group is present, loss of water (M-18) is visible as well.



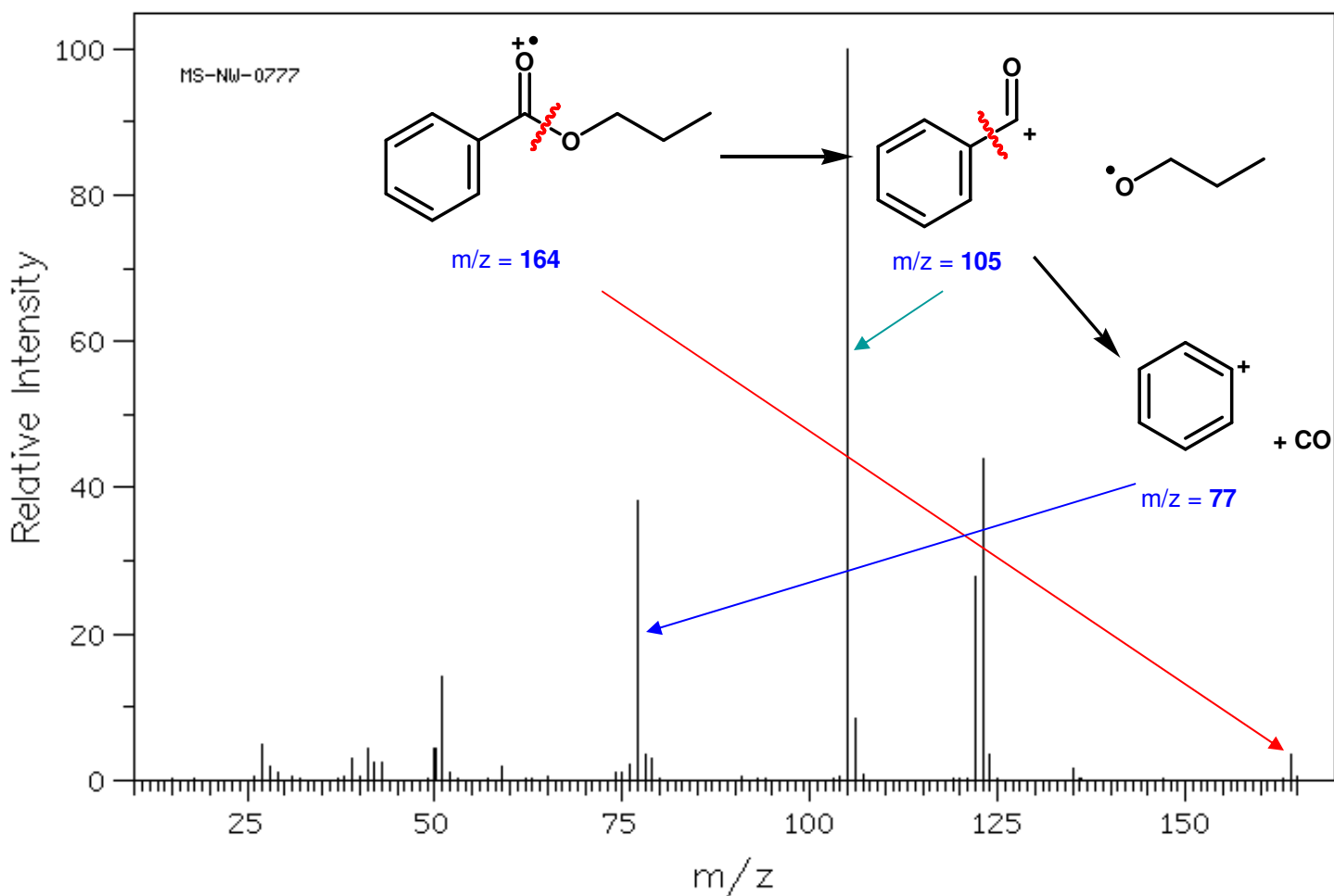
9. Aliphatic Esters

M⁺ is usually distinct. The most characteristic peak is due to the McLafferty rearrangement.



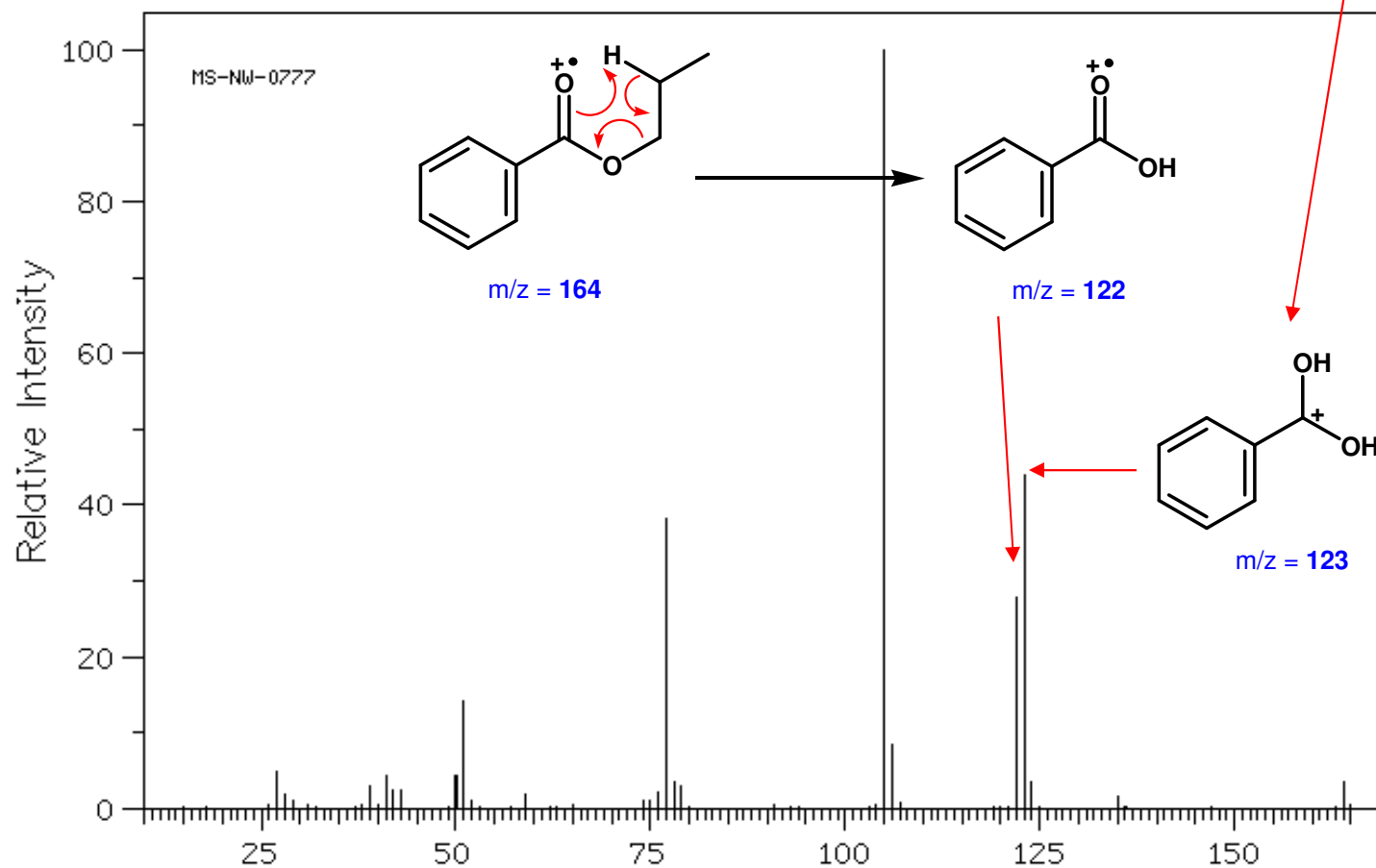
Aromatic Esters

M⁺ is usually prominent, unless RO chain is long. The base peak is loss of RO•.



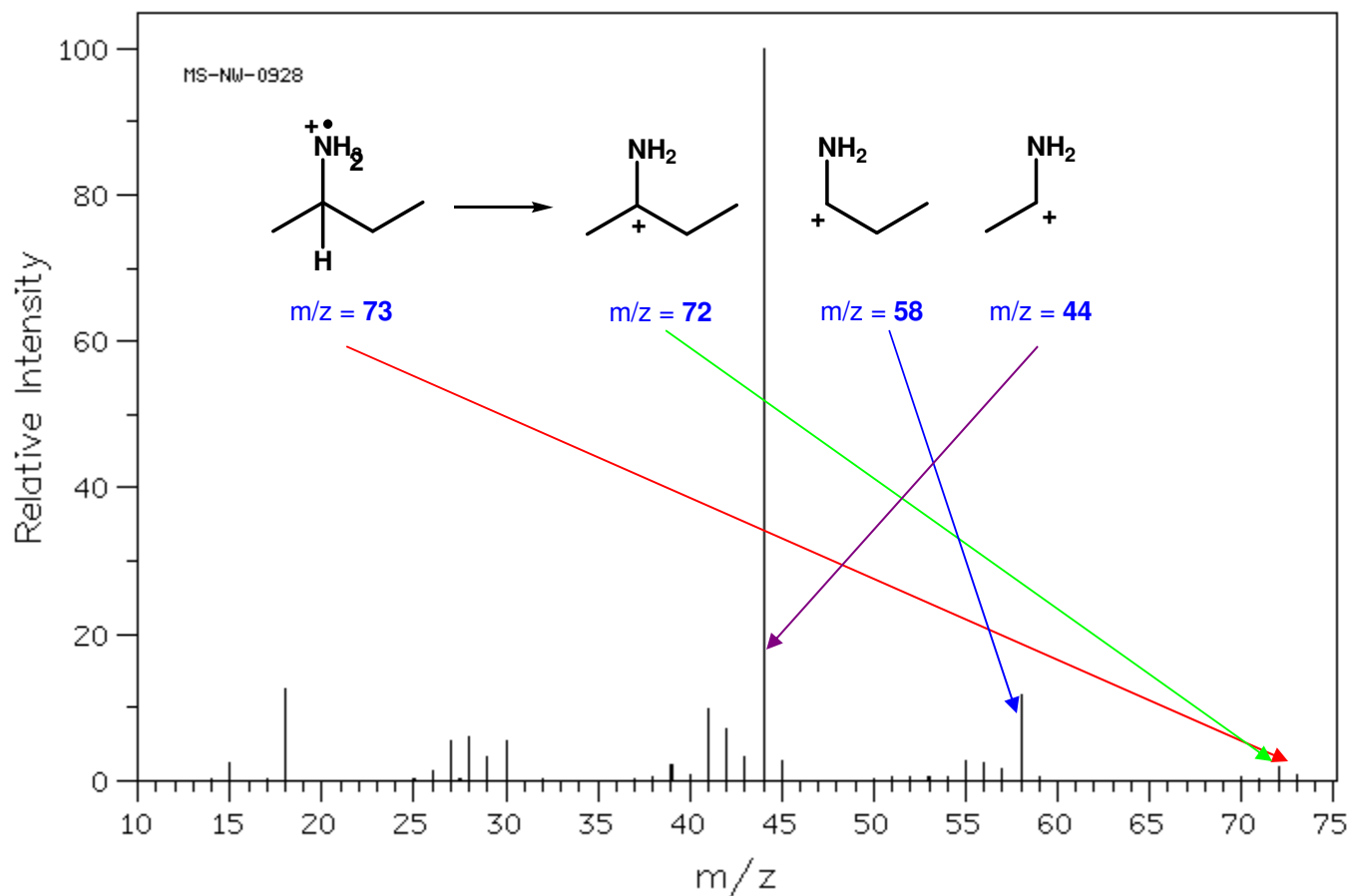
Aromatic Esters

The McLafferty rearrangement give the corresponding acid. A more complicated rearrangement often gives a prominent acid+1 peak.



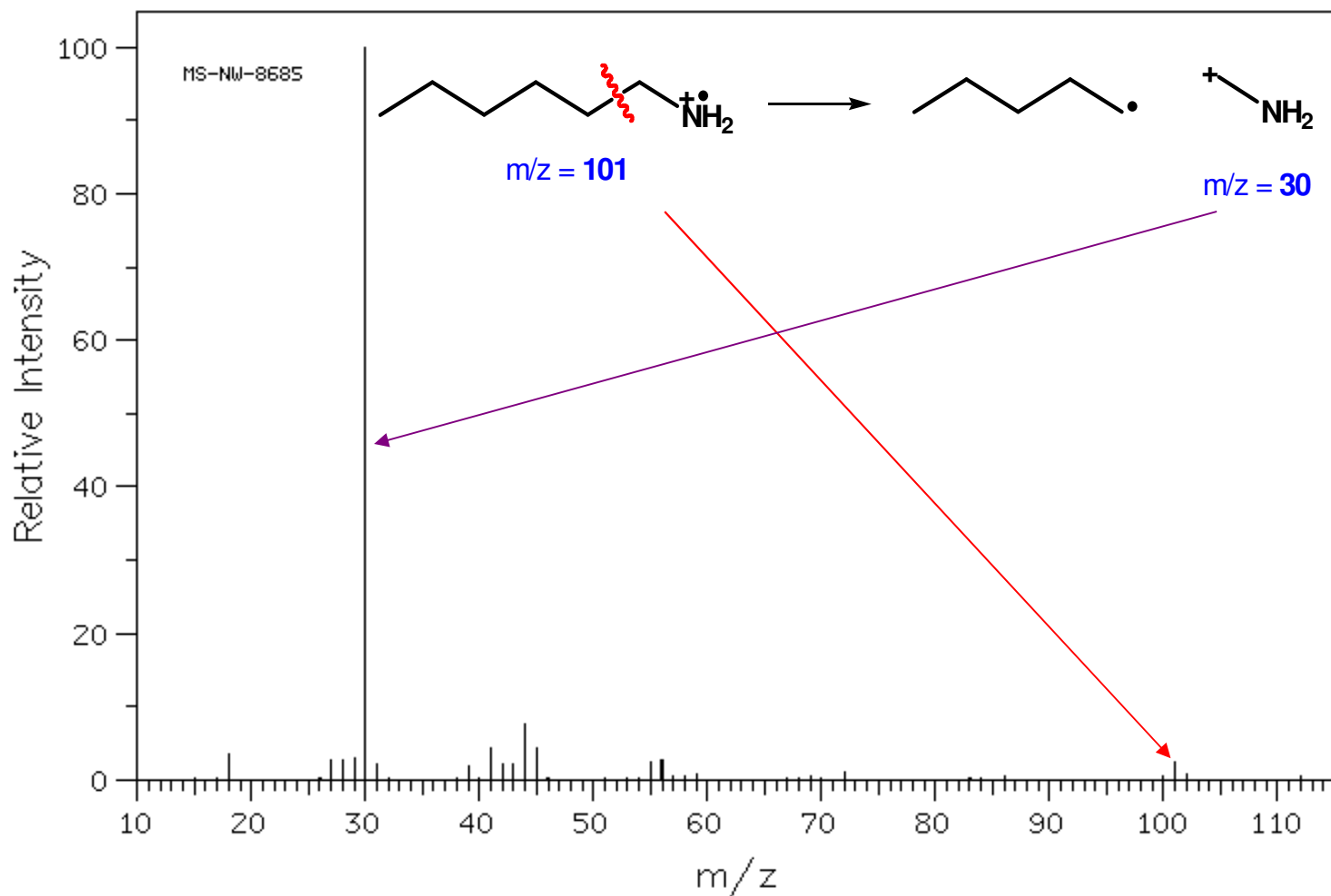
10. Amines

Aliphatic monoamines have odd numbered and weak M^+ peaks. Most important cleavage is usually breakage of the C-C bond next to the C-N bond.



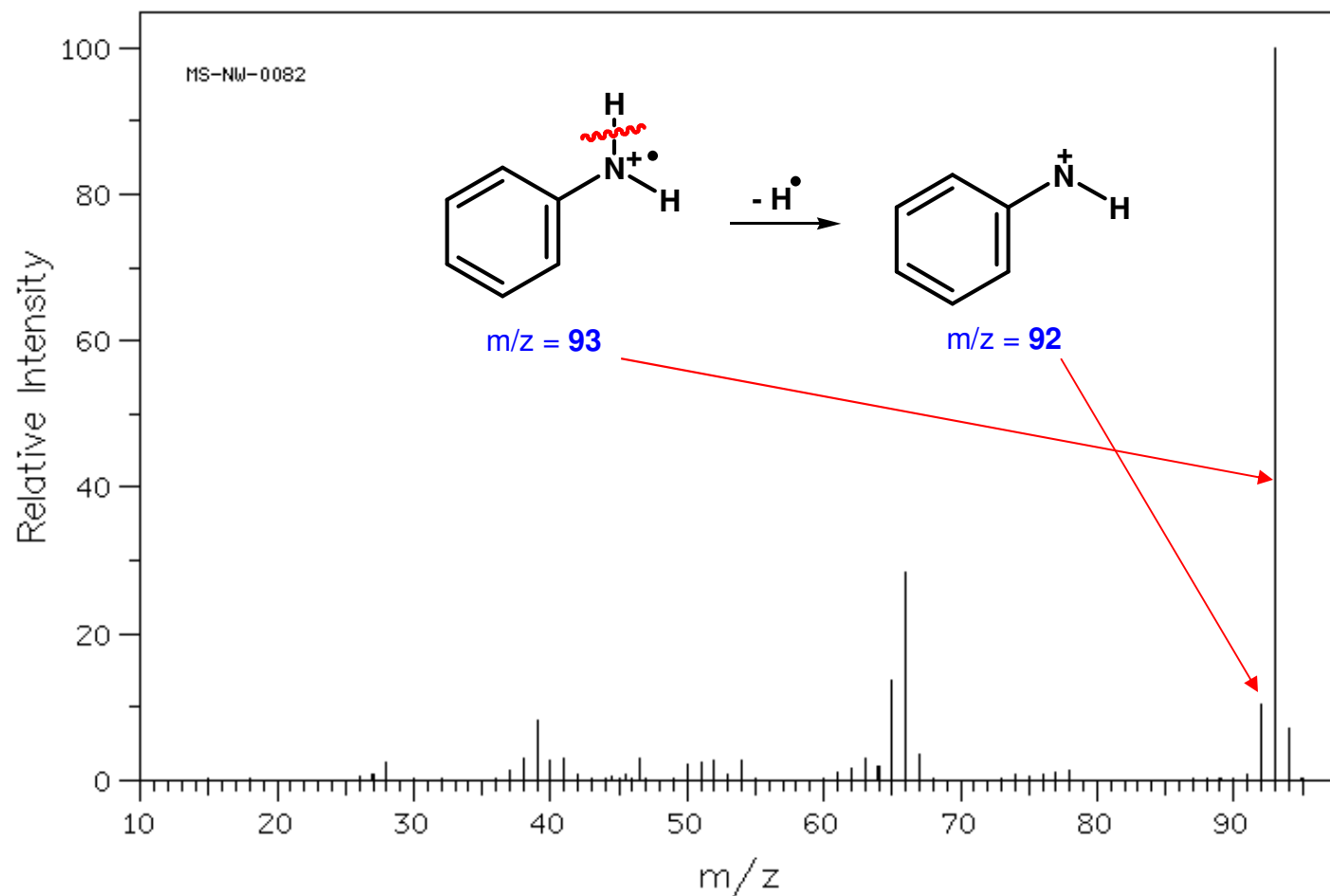
10. Amines

The base peak in nearly all primary amines comes at 30 m/z.



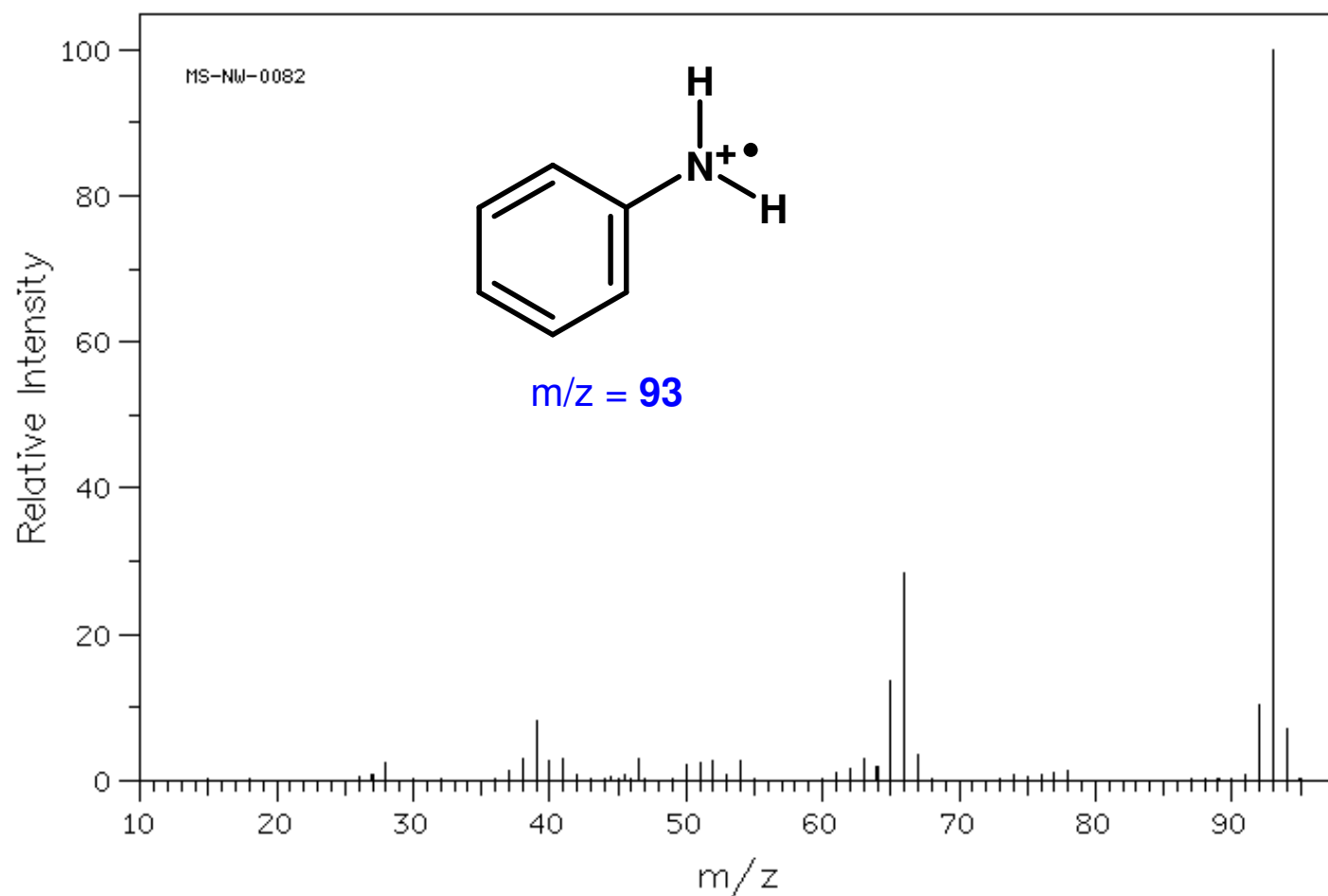
Aromatic Amines

M⁺ is intense (why?). An NH bond can be broken to give a moderately intense M-1 peak.



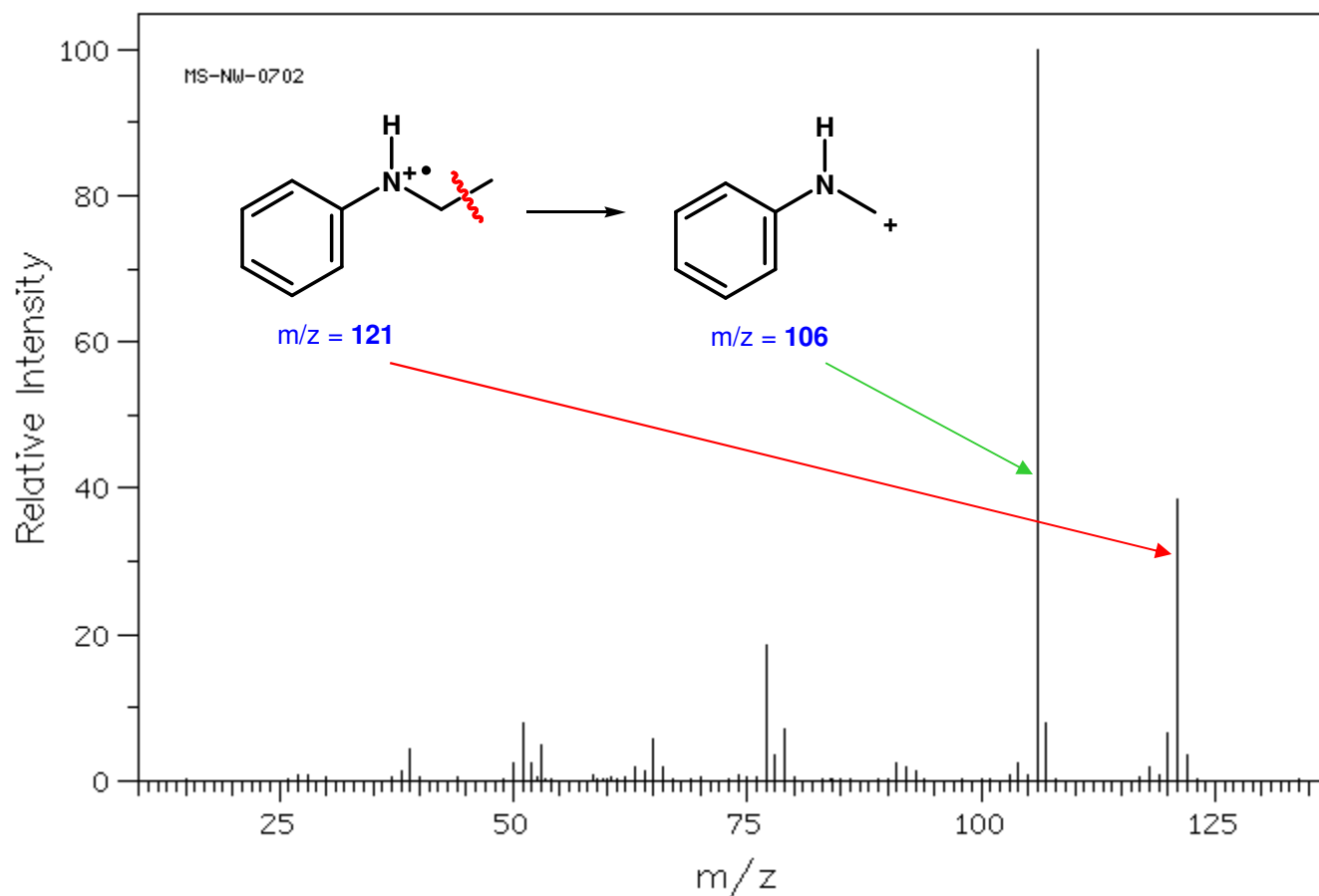
Aromatic Amines

A common fragmentation is loss of HCN and H₂CN to give peaks at 65 and 66 m/z.



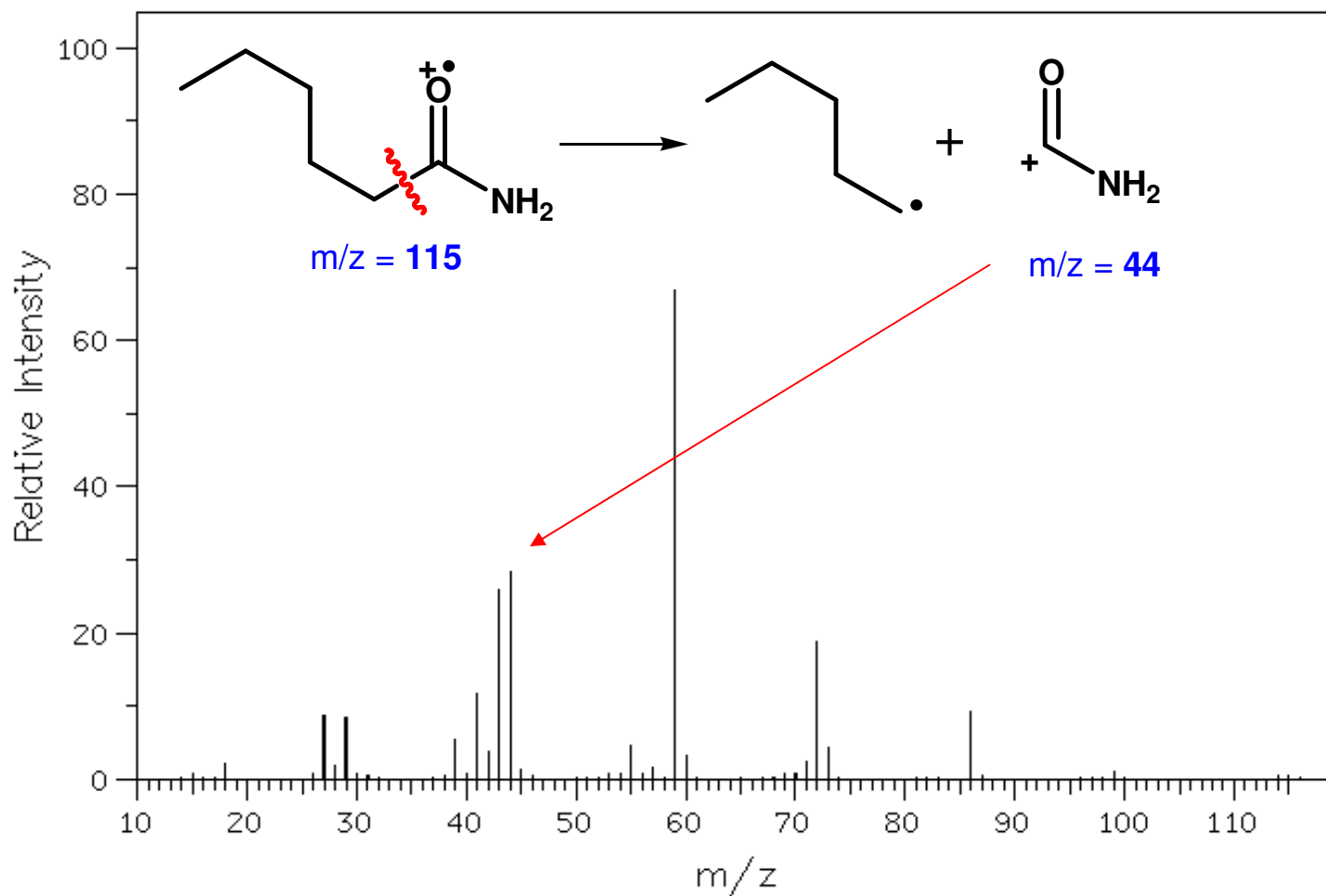
Aromatic Amines

Alkyl substituted aromatic amines typically show breakage of the C-C bond next to the C-N to give a strong peak at 106 when Ar = Ph.



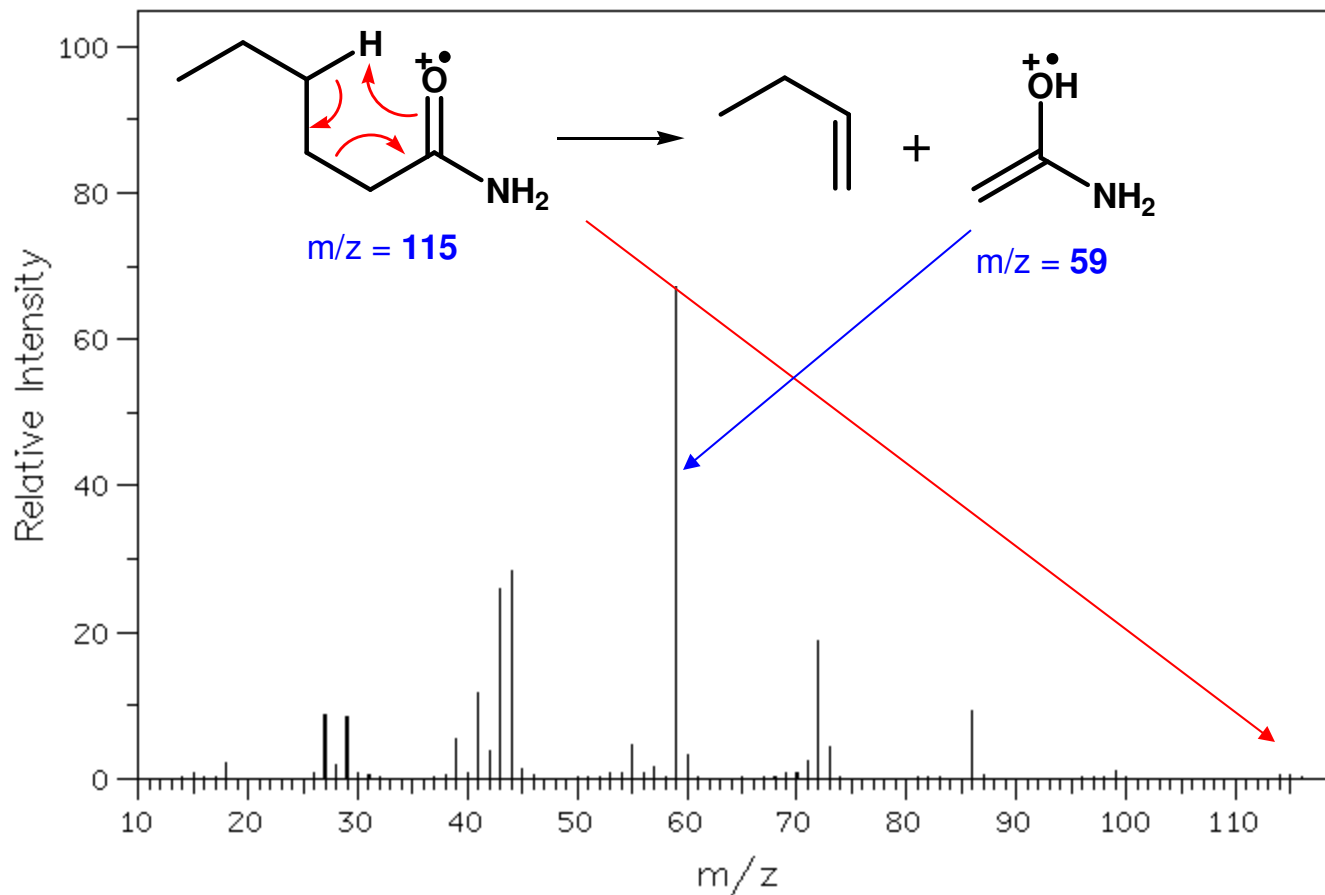
11. Amides

Primary amides give a strong peak at m/z 44 due to breakage of the R-CONH_2 bond.



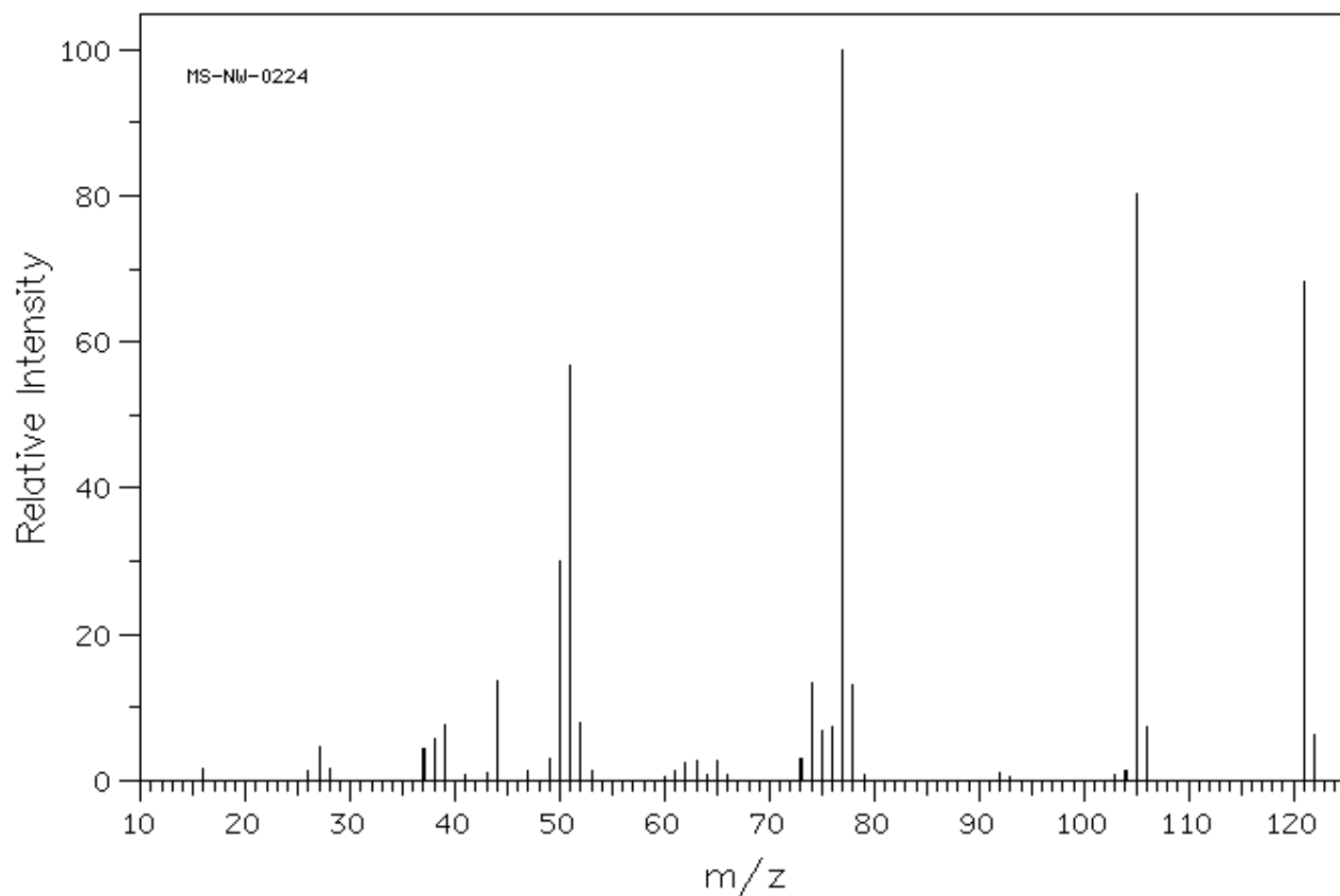
11. Amides

Aliphatic amides – M^+ is weak but discernible. For straight-chain amides more than 3 carbons, McLafferty gives the base peak at m/z 59.



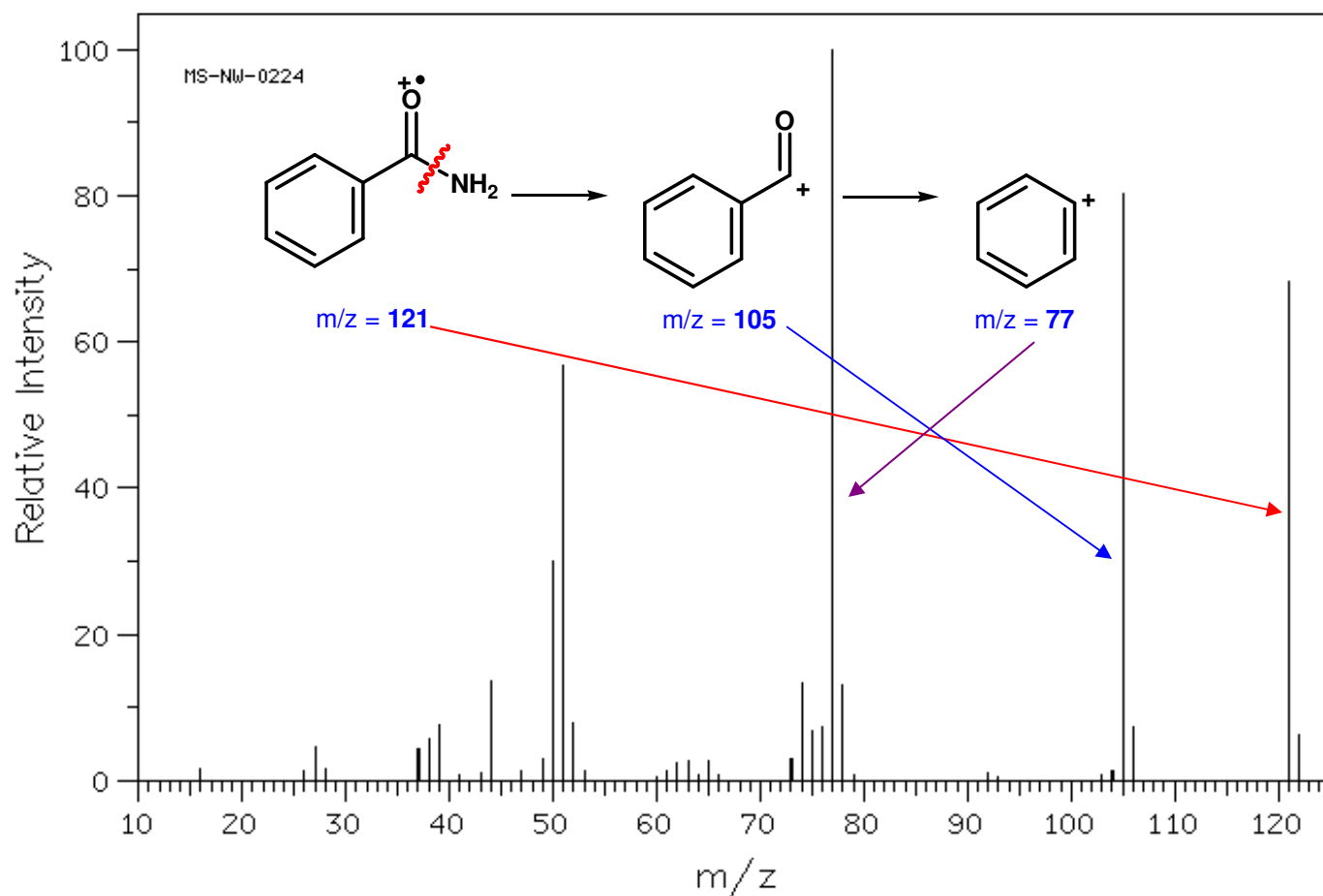
Aromatic Amides

Any familiar features?



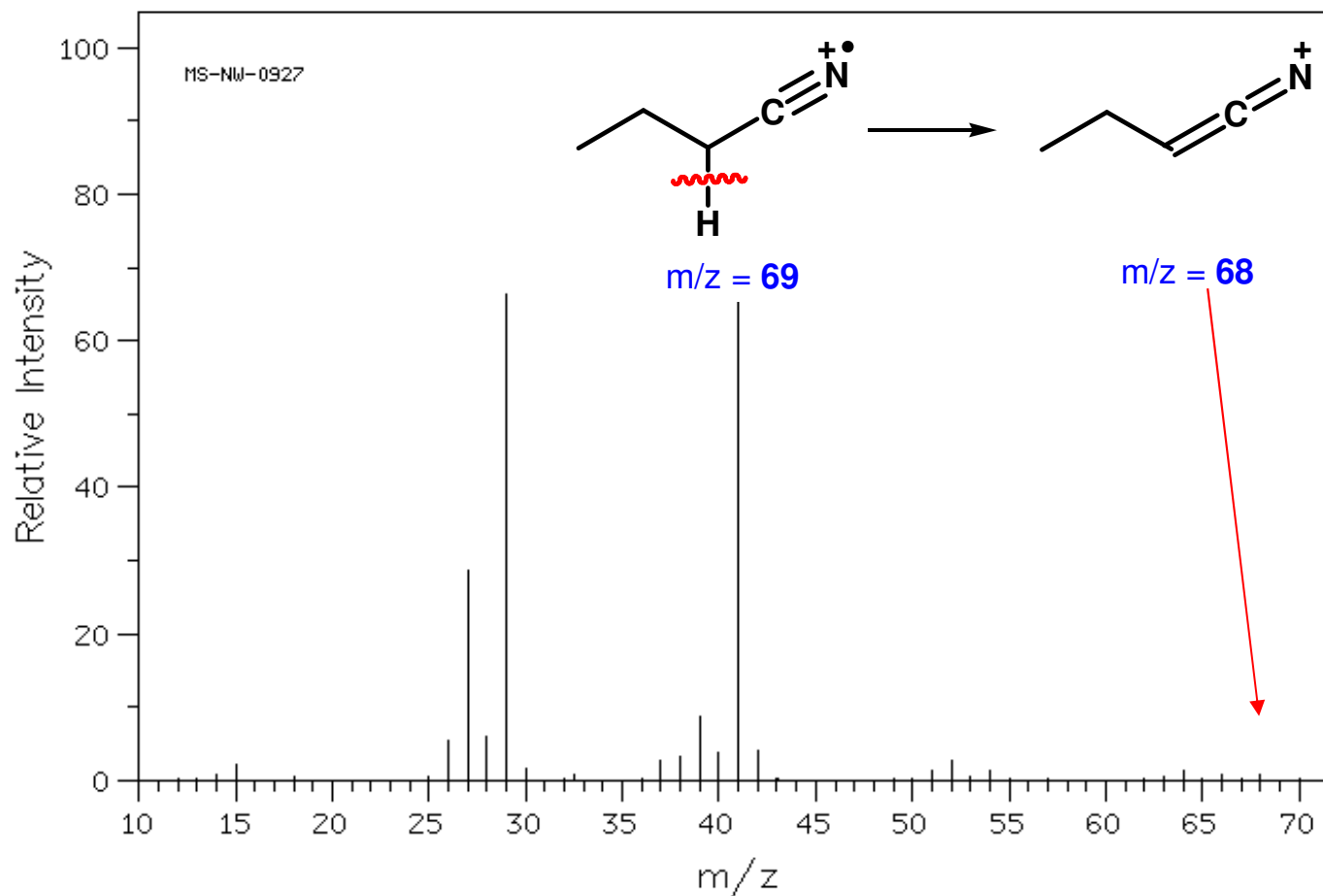
Aromatic Amides

M⁺ is strong. Loss of NH₂ to make PhCO⁺ (105) followed by loss of CO to make the phenyl cation (77).



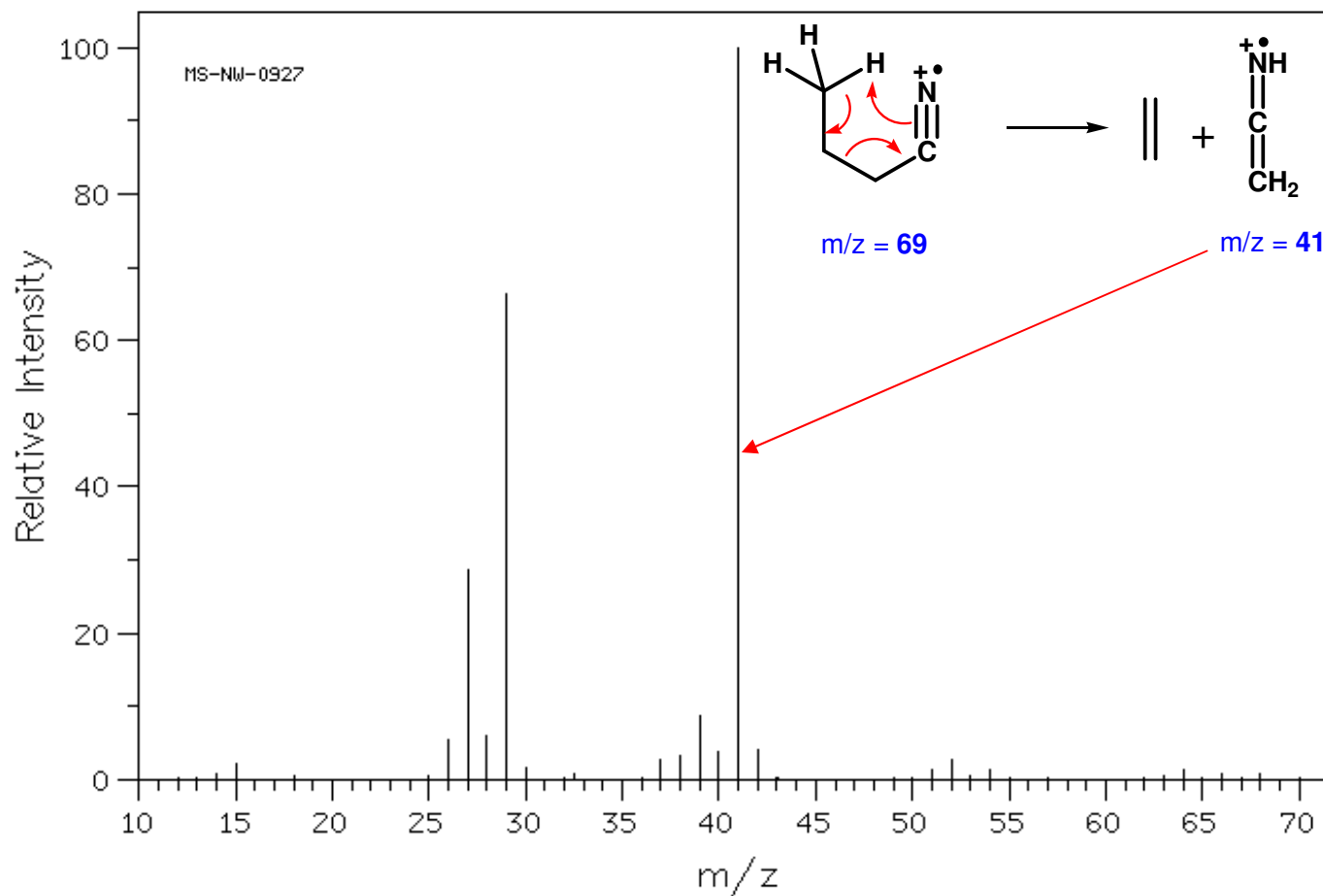
12. Nitriles

M⁺ are weak or absent for aliphatic nitriles. Loss of the α -hydrogen can give a weak M-1 peak.



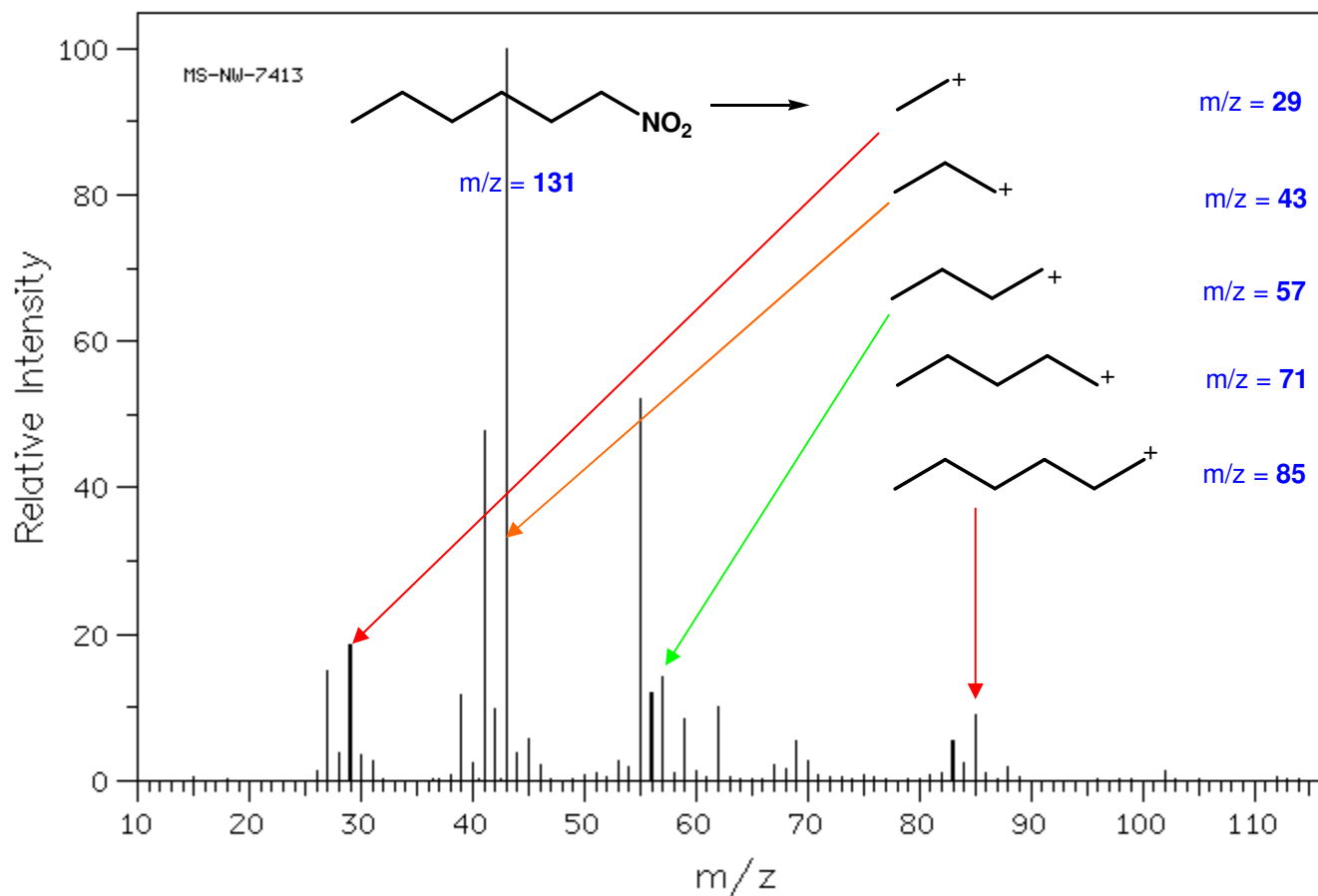
Nitriles

Base peak is usually 41 due to a rearrangement like the McLafferty. This has limited diagnostic value since $(C_3H_5^+)$ has the same mass.



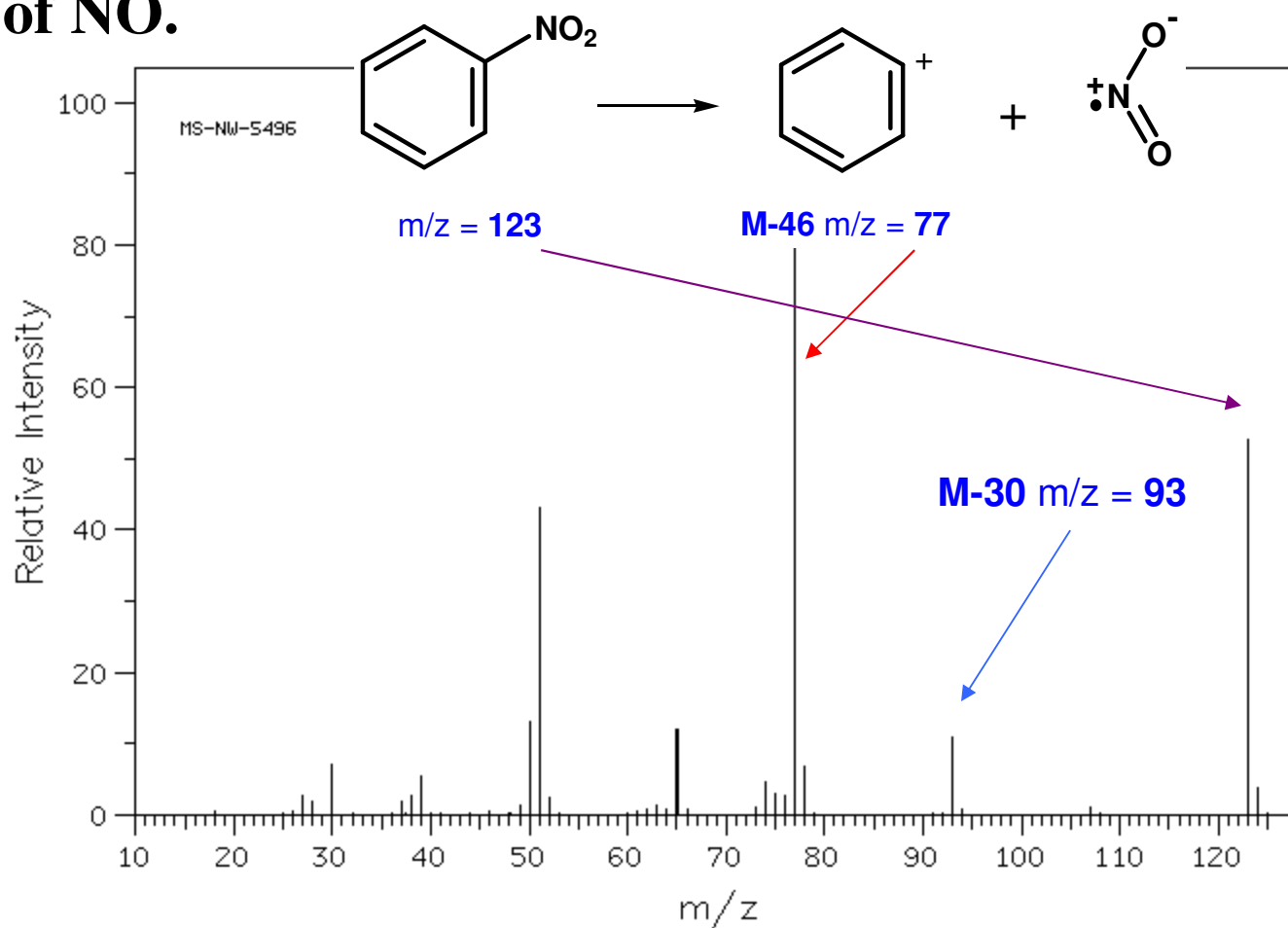
13. Nitro compounds

Aliphatic nitro compounds have weak odd M^+ . The main peaks are hydrocarbon fragments up to $M-NO_2$.

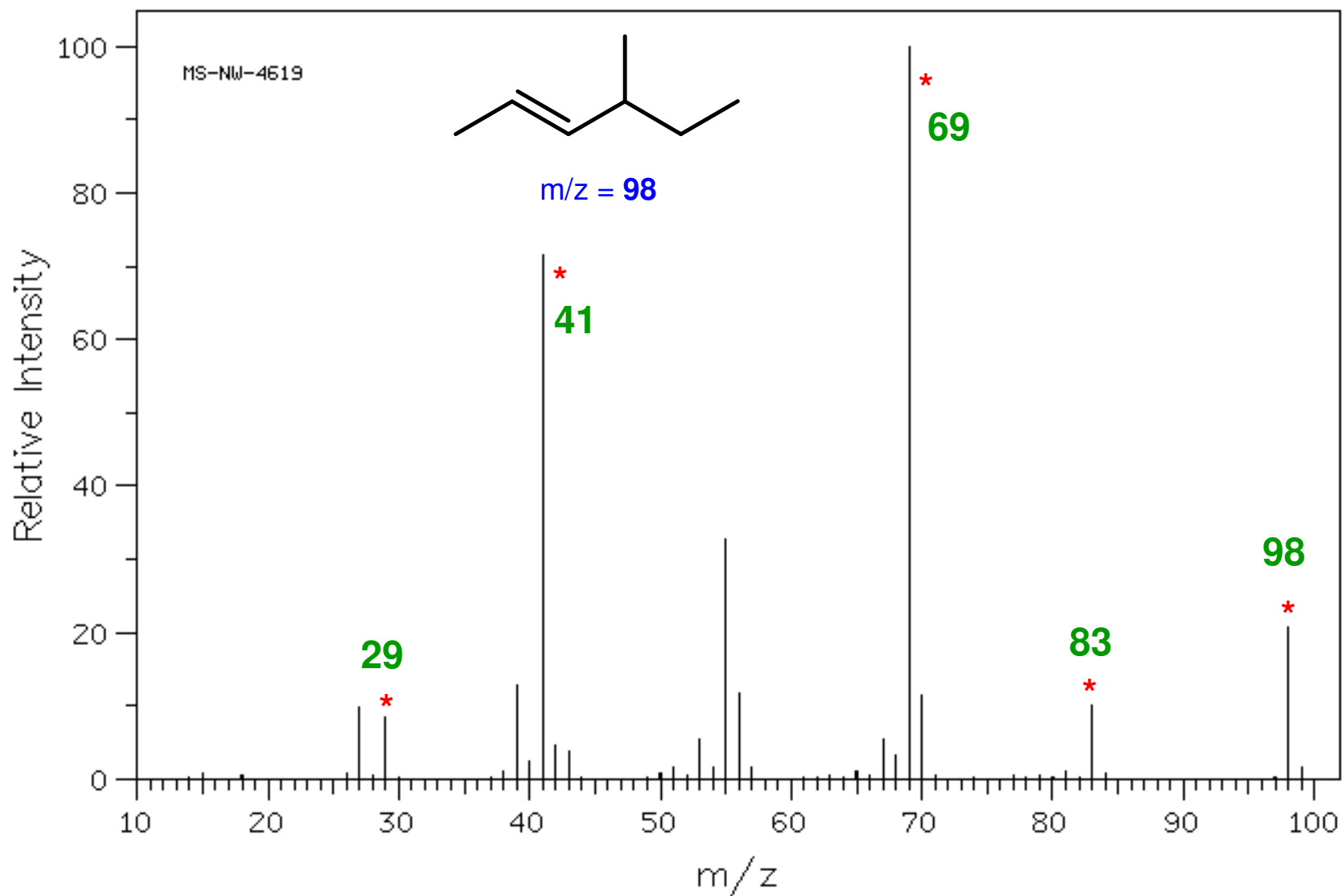


Aromatic Nitro Compounds

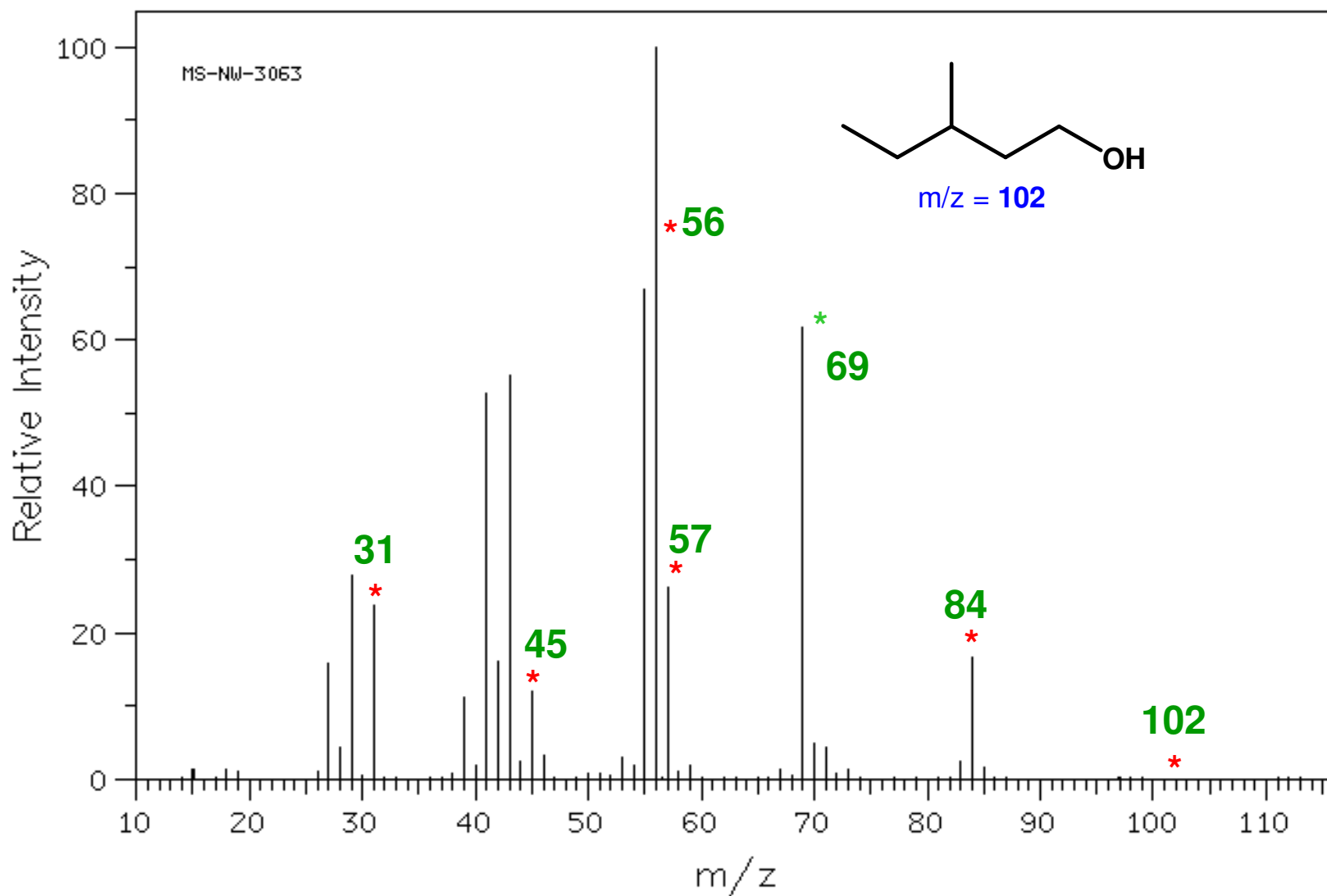
M⁺ is strong. Prominent peaks result from loss of NO₂ radical to give an M-46 peak. Also prominent is M-30 from loss of NO.



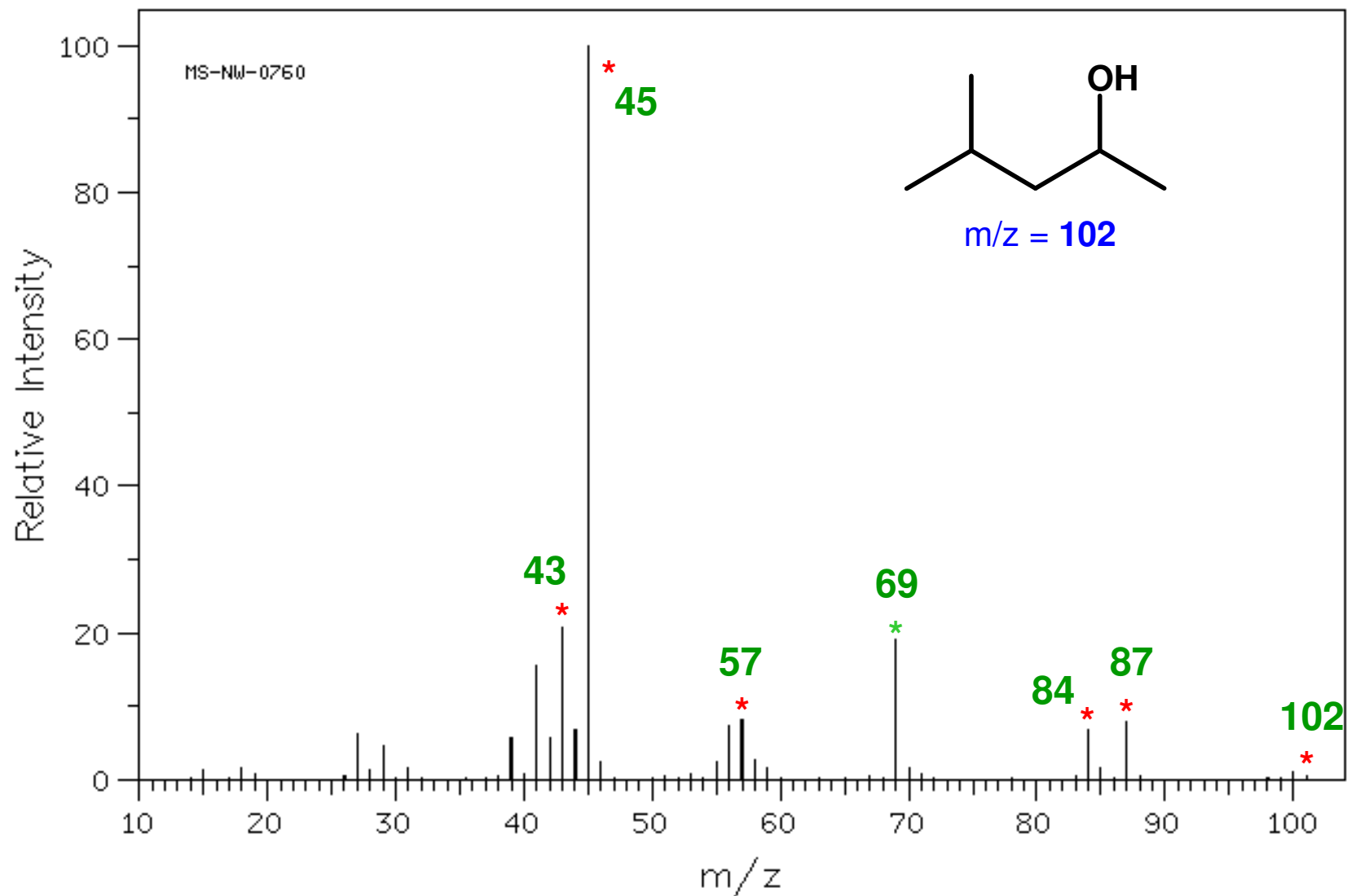
Example: 4-methyl-2-hexene



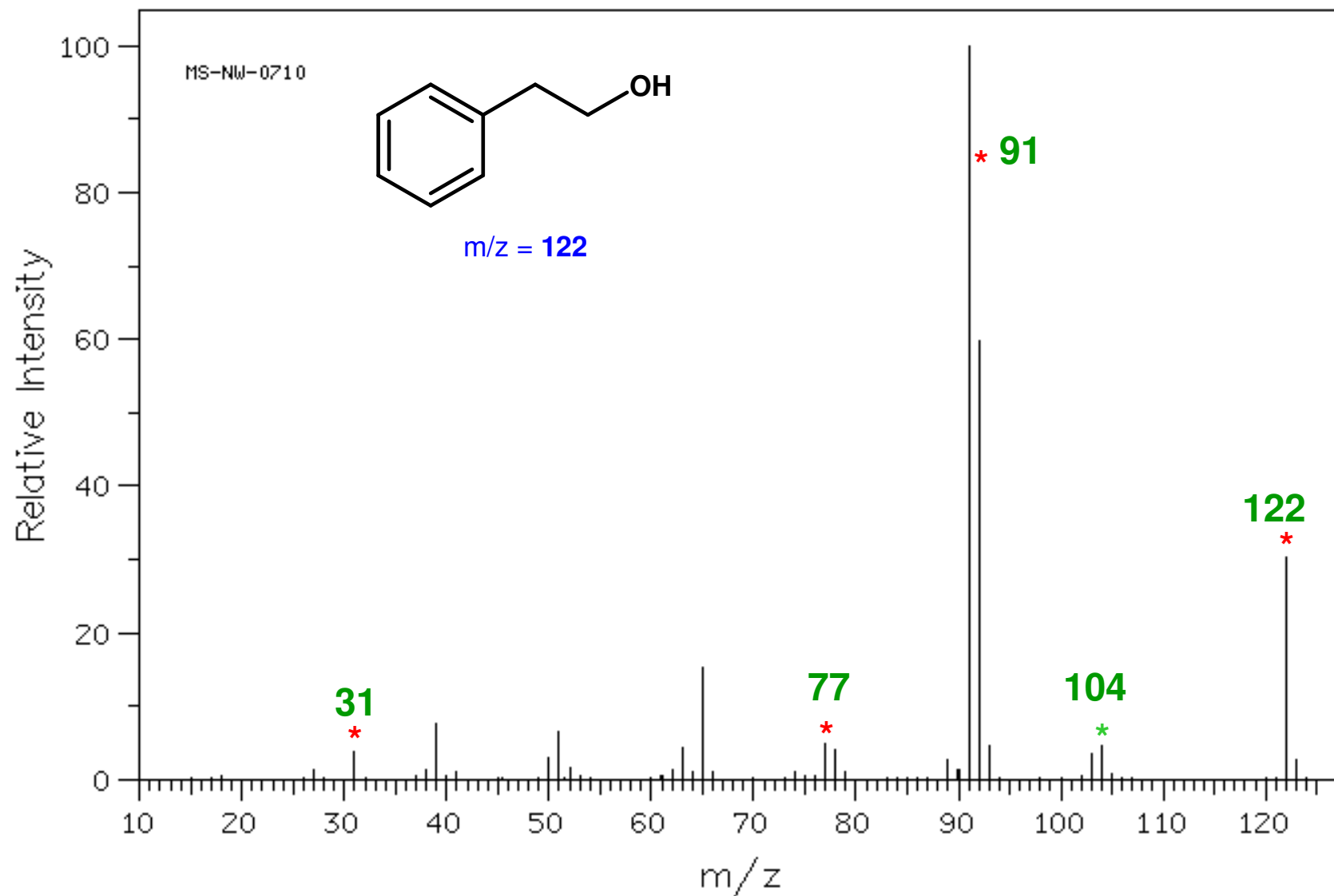
Example: 3-methyl-1-pentanol



Example: 4-methyl-2-pentanol



Example: 2-phenylethanol



Example: 1-phenylethanol

