Detectors: Mass Spectrometry

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Introduction

The mass spectrometer provides the most powerful detector available for gas chromatography. It is sensitive, selective and offers vastly superior qualitative information over conventional detectors such as the flame ionization detector (FID) or electron-capture detector (ECD). Modern instruments for gas chromatography–mass spectrometry (GC-MS) are small, reliable and much less expensive than formerly. In many laboratories small 'bench-top' GC-MS instruments have virtually replaced 'stand-alone' gas chromatographs for even routine applications. In this short paper we shall attempt to describe some of the basic principles of mass spectrometry and how they are applied in GC-MS. In order to illustrate some of the techniques available the determination of nitrated polycyclic aromatic hydrocarbons in diesel particulates will be utilized as a case study.

Ion Formation

Mass spectrometers are used to analyse ionized sample molecules. There are essentially four methods in which a neutral sample molecule (M) can be converted into an ionic species:

$$M + e^- \rightarrow M^{+\bullet} + 2e^- \text{ (removal of an electron)}$$

$$M + e^- \rightarrow M^{-\bullet} \text{ (addition of an electron)}$$

$$M + X^+ \rightarrow (M + H)^+ \text{ (addition of a positively charged species, usually a proton)}$$

$$M - X^+ \rightarrow (M - H)^- \text{ (removal of a positively charged species, usually a proton)}$$

The *ion sources* used in GC-MS make use of each of these four processes in order to form positive or negative ions as appropriate.

Electron Ionization (EI)

The most important method for the production of ions in GC-MS instruments uses the electron ionization (EI) ion source. A schematic of a typical EI ion source is shown in **Figure 1**.

The filament, usually a simple coil of tungsten wire, is heated. On heating it produces electrons, which are then accelerated into the ion source chamber by applying a potential difference between the filament and the chamber. This potential difference is usually in the range 50–70 V, giving the electrons a kinetic energy (*the electron energy*) of 50–70 eV (where $1\text{ eV} = 1.602 \times 10^{-19}\text{ J}$). Interaction of neutral sample molecules with the electrons causes ionization by removal of one electron:

$$M + e^- \rightarrow M^{+\bullet} + 2e^-$$

This process creates the positively charged *molecular ion* of the sample molecule, i.e. a radical cation. However, the first ionization energy of most organic compounds is only of the order of 10 eV. Hence molecular ions formed in an EI ion source have excess internal energy and further fragmentation occurs in order to dissipate this energy. Fragmentation occurs via a variety of processes and leads to mass spectra containing a fingerprint of the molecule. The processes of fragmentation are shown below:

$$M^{+\bullet} \rightarrow F_1^+ + R^\bullet$$

and/or:

$$M^{+\bullet} \rightarrow F_2^{+\bullet} + N$$

(where F_1^+ represents an even electron fragment ion, $R^\bullet$ a neutral radical, $F_2^{+\bullet}$ an odd electron fragment ion, often called a radical ion, and N a neutral species).

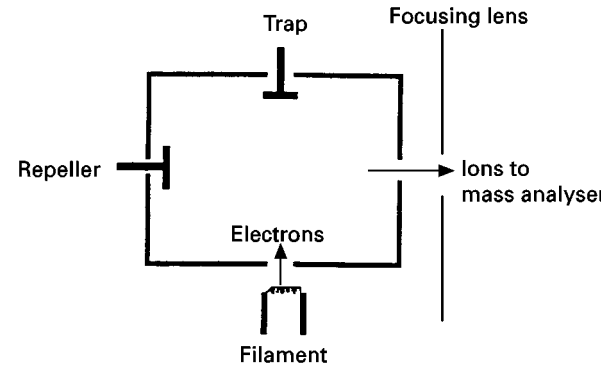

Figure 1 Schematic of an electron ionization (EI) ion source. Ions formed by interaction of the sample molecules with electrons emitted from the filament are extracted and focused into the mass analyser by the action of the repelller and the focusing lens.

Both types of initial *fragment ions* may also further fragment:

$$F_1^+ \rightarrow F_3^+ + N$$

and/or:

$$F_2^{+\bullet} \rightarrow F_4^+ + R^\bullet$$

Fragmentation will continue until the excess internal energy is dissipated. The appearance of EI mass spectra is a function of the compound under investigation, the electron energy used and the ion source temperature. For this reason it is usual to record EI mass spectra at an electron energy of 70 eV which gives good sensitivity, interpretable fragmentation and allows comparison to be made between spectra recorded on different instruments and with standard spectra stored in computerized libraries.

An EI mass spectrum of 2-nitrofluorene, a nitrated polycyclic aromatic hydrocarbon, is shown in **Figure 2**A. This mass spectrum illustrates some of the key features of EI spectra. A small molecular ion can be seen at m/z 211 along with fragment ions corresponding to the loss of $^\bullet OH$ and NO_2 groups. The pattern of fragment ions, i.e. their intensity and distribution is characteristic of 2-nitrofluorene and library search, used where possible in combination with GC retention time (obtained from a standard sample), allows the sample to be easily identified.

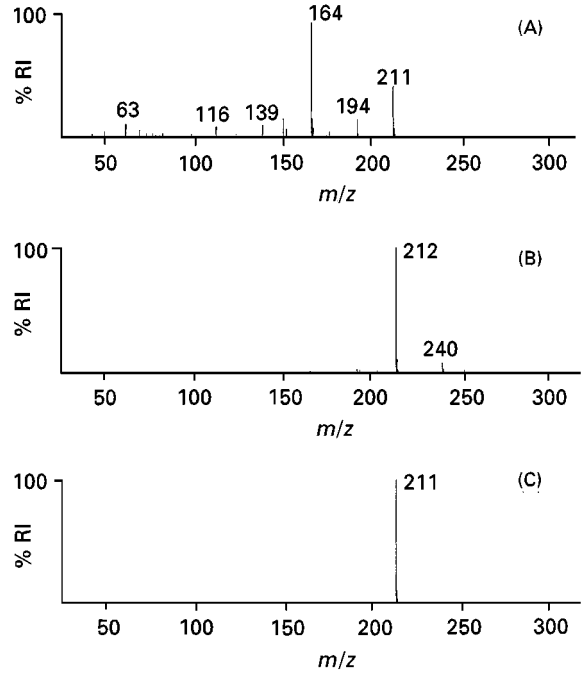

Figure 2 Comparison of (A) electron ionization, (B) positive chemical ionization and (C) negative chemical ionization mass spectra of 2-nitrofluorene. Note the higher degree of fragmentation in the EI mass spectrum.

Electron ionization is the most widely used ionization technique for GC-MS. However, it has a number of limitations. The most important of these is caused by the excess internal energy of the initially formed molecular ions. For certain classes of compounds, they all fragment in the ion source and hence a molecular ion is not observed in the recorded mass spectrum. This removes one of the key pieces of information from the mass spectrum, i.e. the relative molecular mass of the compound under investigation. In order to overcome this, other ionization techniques are available to the mass spectroscopist, the most important of these being chemical ionization (CI).

Chemical Ionization (CI)

Positive ion chemical ionization In positive ion CI an ion source slightly modified from that shown in Figure 1 (by reduction of the size of the ion exit aperture) is filled with a *reagent* gas (e.g. methane, isobutane or ammonia) to a pressure of about 0.1–1.0 mbar. At this pressure ion–molecule reactions can occur between ions of the gas (created by EI processes) and neutral gas molecules. Taking as an example some of the processes that occur when methane is used as a reagent gas:

$$n\mathrm{CH_4} + n\mathrm{e^-} \rightarrow n\mathrm{CH_4^{+\bullet}} + n\mathrm{CH_3^+} + n\mathrm{CH_2^+} + n\mathrm{CH^+}$$

$$n\mathrm{CH_4} + n\mathrm{CH_4^{+\bullet}} \rightarrow n\mathrm{CH_5^+} + n\mathrm{CH_3^\bullet}$$

$$n\mathrm{CH_4} + n\mathrm{CH_3^+} \rightarrow n\mathrm{C_2H_5^+} + n\mathrm{H_2}$$

In a similar way when sample molecules are introduced into the ion source, ion molecule reactions between reagent gas ions and gaseous sample molecules can occur, to produce sample ions, i.e.

$$n\mathrm{M} + n\mathrm{CH_5^+} \rightarrow n(\mathrm{M}+\mathrm{H})^+ + n\mathrm{CH_4}$$
proton transfer

$$n\mathrm{M} + n\mathrm{C_2H_5^+} \rightarrow n(\mathrm{M}+\mathrm{H})^+ + n\mathrm{C_2H_4}$$
proton transfer

$$n\mathrm{M} + n\mathrm{C_2H_5^+} \rightarrow n(\mathrm{M}+\mathrm{C_2H_5})^+$$
electrophilic addition

The formation of sample ions via these reactions is much less energetic than molecular ion formation via electron ionization. Hence the mass spectra obtained show less fragmentation than the corresponding EI mass spectra. When methane or isobutane are used as the reagent gas, proton transfer is the dominant reaction. Hence the relative molecular mass of the compound of interest can now be derived from the

$n(M + H)^+$ *protonated molecular species* with additional confirmation of the assignment being given by the presence of the $(M + C_2H_5)^+$ *adduct ion*. Where ammonia is used as the reagent gas electrophilic addition is often as important or the dominant process and in this case the $(M + NH_4)^+$ adduct ion may be used.

Figure 2B shows the positive ion chemical ionization mass spectrum of 2-nitrofluorene obtained using methane as reagent gas. Note the large $(M + H)^+$ peak at m/z 212 and the reduced fragmentation compared to the corresponding EI spectrum. Also visible is the adduct ion at m/z 240 corresponding to the $(M + C_2H_5)^+$ ion formed by the electrophilic addition process discussed earlier.

Negative ion chemical ionization (NCI) Chemical ionization is also a useful way of producing negatively charged species for mass spectrometry. There are two important mechanisms for ion formation in NCI. The first, which is analogous to the processes already described for positive CI, is proton transfer:

$$M + B^- \rightarrow (M - H)^- + BH$$

This type of reaction will occur when the relative proton affinity of the reagent gas anion (B^-) is high. It is a relatively low energy process and leads to mass spectra containing intense $(M - H)^-$ ions and little fragmentation.

However, a more important mechanism of ion formation in NCI, and one that has been widely utilized in GC-MS, is via an electron capture process. If a compound containing one or more suitable electronegative groups is introduced into the ion source in the presence of a high pressure ($\sim$1 mbar) of a *buffer gas* (e.g. methane) the following reaction can occur:

$$M + e^{-th} + CH_4 \rightarrow (CH_4.M^{-\bullet})^* \rightarrow M^{-\bullet} + CH_4$$

In the above equation the thermal electrons (e^{-th}) are produced from the electron ionization of the methane. The neutral methane molecules also act to collisionally stabilize the excited radical anion formed by associative resonance electron capture. This leads to the observation of a radical anion ($M^{-\bullet}$) in mass spectra recorded using this ionization method.

Electron capture is a very low energy process and the recorded mass spectra contain little or no fragmentation. The NCI mass spectrum of 2-nitrofluorene is shown in Figure 2C. This compound contains an electronegative nitro group, and is ionized via the electron capture process. An intense $M^{-\bullet}$ ion can be seen at m/z 211 with no evidence of fragmentation.

In a similar manner to the use of the electron-capture detector for gas chromatography, the use of electron capture NCI GC-MS can introduce sensitivity and specificity into an analysis. Whereas approximately 100 pg of sample are required to record a mass spectrum in EI mode, NCI spectra have been recorded from a little as 500 fg (for appropriate electron capturing compounds). This will be further illustrated below.

The Separation of Ions and Recording of Mass Spectra

There are many methods available for the separation of ions and recording of mass spectra. The ionization methods described above have been incorporated into all of the current commercial types of mass spectrometer. In this section only brief descriptions of these are offered. For a more complete discussion see either Chapman (1993) or Johnstone and Rose (1996).

The key parameters to take into account in the selection of a particular type of mass spectrometer for a GC-MS experiment are the masses of the compounds under consideration and the selectivity and sensitivity required for the analysis. Where the largest compounds to be encountered are likely to have a relative molecular mass of less than 1000 any of the types of mass spectrometer described below is useful.

The Quadrupole Mass Filter

The quadrupole mass filter is the most widely employed type of mass analyser in current use. It comprises four metal rods accurately aligned around a central axis. RF and DC voltages on the rods create a complex electrostatic field within the area bound by them. Ions entering this region are acted on by the electrostatic field and their motion through the rods can be likened to two superimposed sine waves. Under these conditions the forces acting on most ions cause the amplitude of the oscillations to increase and accelerate them into the quadrupole rods. However, some ions are not accelerated into the rods and undergo trajectories that traverse the full length of the rods. The parameters that govern the equations of motion of ions in a quadrupole mass filter are the mass to charge ratio of the ions, the spacing between the rods, the frequency of the RF voltage and the magnitude of the RF and DC voltages. Hence the RF and DC voltages may be selected such that ions of only one m/z value have 'stable' trajectories. By varying the RF and DC voltages but keeping the ratio between them the same a range of m/z values can be made to undergo stable trajectories, be brought to focus on the detector and a mass spectrum recorded.

The Ion Trap

The ion trap operates in a similar manner to a quadrupole mass filter. It comprises a doughnut-shaped ring electrode to which the RF voltage is applied and two end caps either earthed or with supplementary AC or DC voltages. Ions formed either in the trap, or externally to the trap and transported into it, are initially stored within the trap. Mass separation is then achieved by increasing the RF voltage such that ions are ejected from the trap in ascending m/z order.

The Double Focusing Magnetic Sector Mass Spectrometer

The double focusing magnetic sector mass spectrometer differs from those discussed so far in that the mass analyser comprises two distinct components, an electromagnet and an electrostatic analyser. The magnet acts as a momentum analyser and affects mass separation, while the addition of an electrostatic analyser corrects for some variations in the kinetic energy of ions of the same m/z value and allows them to be brought to focus on the detector at the same time. Hence the use of a double focusing arrangement as a mass analyser allows very high *resolution* to be achieved. In mass spectrometry resolution is defined as the ability of the mass spectrometer to separate ions of very similar m/z value.

Resolution is important in mass spectrometry since it may be used to introduce specificity into an experiment. An important application of high resolution arises in the determination of polychlorinated dibenzodioxins (PCDDs) and polychlorinated dibenzofurans (PCDFs) by GC-MS. These compounds are found ubiquitously in the environment and their determination is important owing to concern about their toxicity, mutagenicity and carcinogenicity. The only method that has been found to offer the appropriate degree of sensitivity and specificity for this analysis is GC followed by high resolution MS detection. High resolution is required since matrices which accumulate PCDDs and PCDFs are also likely to accumulate other polychlorinated aromatic hydrocarbons, e.g. polychlorinated biphenyls. These compounds, which may co-elute with the PCDDs and PCDFs of interest, contain fragment ions in their EI mass spectra which have the same integer m/z value as the molecular ions of PCDDs and PCDFs. However, by monitoring the accurate mass value of the PCDD and PCDF molecular ions (i.e. the exact mass value of their elemental composition), at an adequate resolution to separate them from likely interfering ions, specificity is introduced. GC-MS is used extensively in environmental analysis for a range of applications including dioxin analysis. For further details the interested reader is referred to Bruner (1993).

Interfacing Mass Spectrometers with Gas Chromatographs

There are several methods available for interfacing gas chromatographs with mass spectrometers. These include the use of jet separators for packed columns and a variety of ways of interfacing capillary columns. For packed columns the jet separator, a form of momentum separator, is required to remove the majority of the carrier gas. A 'solvent dump valve' is also incorporated into these devices in order that the injection solvent can be vented to waste rather than it passing into the mass spectrometer.

Although a number of interfaces for packed column GC-MS have been described in the past, capillary columns are currently almost exclusively used for GC-MS. The most widely used interface, in this case, is the direct interface, where the column is passed through a simple heated transfer line directly into an EI or CI ion source. The low (1 mL min^{-1}) carrier gas flow commonly used with capillary columns can readily be accommodated by the MS pumping system in order to maintain a good vacuum. **Figure 3** shows a complete instrument based around the use of a capillary column, a simple direct interface and a quadrupole mass spectrometer. For a more complete discussion of the full range of GC-MS interfaces see either Chapman (1993) or Johnstone and Rose (1996).

GC-MS Experiments

Full or Normal Scan

The standard GC-MS mode of operation is the full or normal scan mode. On injection of the sample into the GC, the mass spectrometer is set to repetitively scan over a preset mass range. Typically this would involve the mass spectrometer recording a mass spectrum over the scan range 35–500 Da once a second.

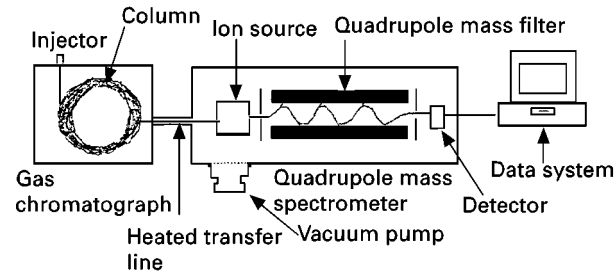

Figure 3 A quadrupole based GC-MS instrument employing a direct interface for connection between the GC and the MS.

The requirement for relatively fast acquisition rates is due to the fact that open tubular GC columns typically produce peaks of only about 10–15 s wide. Hence, in order to acquire a representative number of mass spectra from each peak, fast scan rates are required. A second consequence of these fast acquisition rates is the requirement for a data system on all GC-MS instruments. Each mass spectrum can then be stored in the data system for subsequent examination/data processing.

Full scan data are used by the data system to generate a total ion chromatogram (TIC). This is achieved by summing the intensity of the ions in each mass spectrum to create a value for the total ion intensity, as a number of ions or total number of analogue to digital converter bits. This number is then plotted against time/scan number to create a chromatogram. One of the great strengths of GC-MS using EI ionization is that the TIC generated by this method is then directly comparable with a chromatogram produced from the same sample using flame ionization detection.

Selected Ion Monitoring (SIM)

Selected ion monitoring (SIM) is a technique widely used for trace analysis. In this technique, rather than the mass spectrometer being set to scan over a predefined mass range and record full mass spectra it is set to monitor the intensity of specific m/z values. SIM is used to introduce selectivity into an analysis and improve sensitivity. Sensitivity is enhanced over the full scan mode experiment since in the full scan experiment a large proportion of the scan time is spent recording areas of the spectrum where no ions of interest occur. Ions are still being produced in the ion source but are lost in the mass analyser as it brings others into focus on the detector. In SIM, in a 1 s duty cycle, only a few, i.e. 1–10, ions are selected. Hence, the mass analyser transmits these ions for a longer percentage of the time in which they are being produced and therefore more of the ions of the particular m/z values of interest are recorded.

SIM may also used to introduce selectivity into the experiment. This also has the effect of increasing sensitivity by decreasing the amount of 'chemical noise', i.e. real signal, but not from the compound of interest, observed when peaks of interest elute. The increase in selectively may also be achieved by the use of a double focusing mass spectrometer and high resolution and this may be enhanced by, for example, the use of negative chemical ionization.

An example of the increase in selectivity obtained by the use of SIM combined with NCI from our own laboratory can be seen in the determination of nitrated polycyclic aromatic hydrocarbons (nitro-PAH) in vegetation extracts. Nitro-PAH are absorbed on to vegetation from anthropogenic emissions, however their determination is made complex by the large amount of other compounds extracted from the vegetation by the sample preparation procedure. **Figures 4**A and B show a comparison between the chromatogram obtained from an extract of bark from a maple tree in an urban region using an ECD and the individual mass chromatograms obtained from the same extract using GC-MS in NCI-SIM mode. The

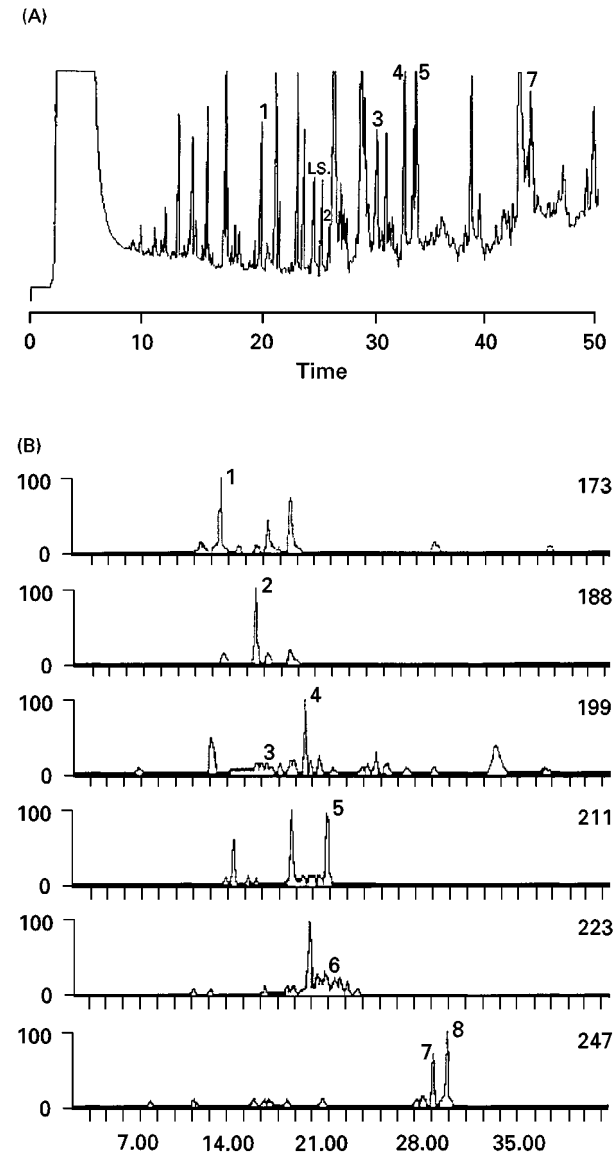

Figure 4 A comparison of the chromatograms obtained from the analysis of a complex extract containing nitrated polycyclic aromatic hydrocarbons by gas chromatography (A) using an electron-capture detector and (B) by GC-MS employing negative chemical ionization and selected ion monitoring. Note the increase in specificity afforded by the use of GC-MS under these conditions.

quadrupole mass spectrometer used in this case was set to monitor the $M^{-\bullet}$. ions obtained from 9 nitro-PAH. The complex chromatogram shown in Figure 4A does not allow simple identification of the peaks of interest and the possibility of interferences/peak overlap leads to difficulties when attempting quantification. This can be observed for peak 5 ($t_r = 34.1$ min) in Figure 4A. This peak arises from the presence of 2-nitrofluorene in the bark extract. As can be seen, accurate and precise integration of this peak is made difficult by the presence of peaks with very similar retention time. In contrast the peaks from the nitro-PAH monitored by NCI-SIM can be seen clearly in Figure 4B. Each chromatographic trace in this figure represents the ion current observed from monitoring the m/z value of the $M^{-\bullet}$ ion of a series of nitro-PAH. Peaks are readily integrated for quantification with the 2-nitrofluorene peak (peak 5) appearing well resolved on the m/z 211 trace.

One of many areas in which the use of resolution to introduce specificity into SIM experiments is important is the petroleum industry. Dibenzothiophenes (DBT) have been suggested as marker compounds for oil pollution. However, taking as an example dibenzothiophene itself, this has the same nominal molecular mass (184 Da) as the C_4-alkylated naphthalenes which are also present in crude oil. Hence in order to specifically measure dibenzothiophene in crude oil it is necessary to monitor the accurate mass to charge ratio (m/z 184.0347) of its molecular ion at high resolution in a SIM experiment. **Figure 5** compares the GC-MS-SIM analysis of dibenzothiophene in crude oil carried out using low and high resolution. As can be clearly seen the C_4-naphthalenes are not observed in the high resolution data. The power of such analyses can be seen in **Figure 6** which shows a comparison of the GC-HRMS-SIM data obtained from the analysis of methyl and C_2 substituted dibenzothiophenes for three different crude oils obtained from two North Sea oil fields. The different crude oils can be clearly distinguished with such data.

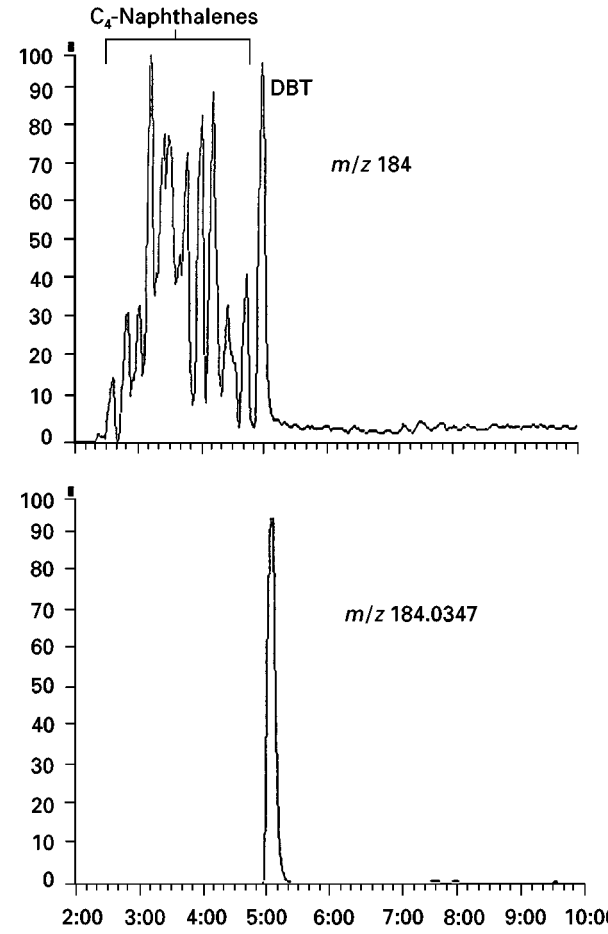

Figure 5 GC-MS analysis of dibenzothiophene (DBT) in a crude oil using low resolution (top) and high resolution (bottom) selected ion monitoring. (Reproduced from Tibbets and Large (1988) by kind permission of John Wiley and Sons.)

Other Techniques

Mass Spectrometry–Mass Spectrometry (MS-MS)

Mass spectrometry–mass spectrometry, also known as tandem mass spectrometry, is the term used to describe mass spectrometric methods employing instruments that contain more than one mass analyser. Such instruments may be used to increase the amount of structural information obtained or to introduce more specificity.

The simplest tandem mass spectrometer to consider is the triple quadrupole mass spectrometer. This comprises two quadrupole mass filters and a multipole collision cell and is shown schematically in **Figure 7**. In principle the operation of such an instrument follows the following sequence: ion selection in the first quadrupole mass filter, ion dissociation in the collision cell and separation of the products of ion dissociation in the second quadrupole mass filter. For illustration, Figure 2C, the NCI mass spectrum of 2-nitrofluorene, only contains the $M^{-\bullet}$ ion at m/z 211. Hence the only information contained in this mass spectrum is the relative molecular mass of the compound. In order to generate structural information a *product ion scan* could be carried out. To do this the first quadrupole mass filter would be set to transmit only m/z 211. This ion would then be subjected to collisions with a gas held in the collision cell (collisonally induced decomposition (CID)) and the resulting *product ions* recorded using the second quadrupole mass filter. The resulting *product ion spectrum* then shows only ions that have arisen

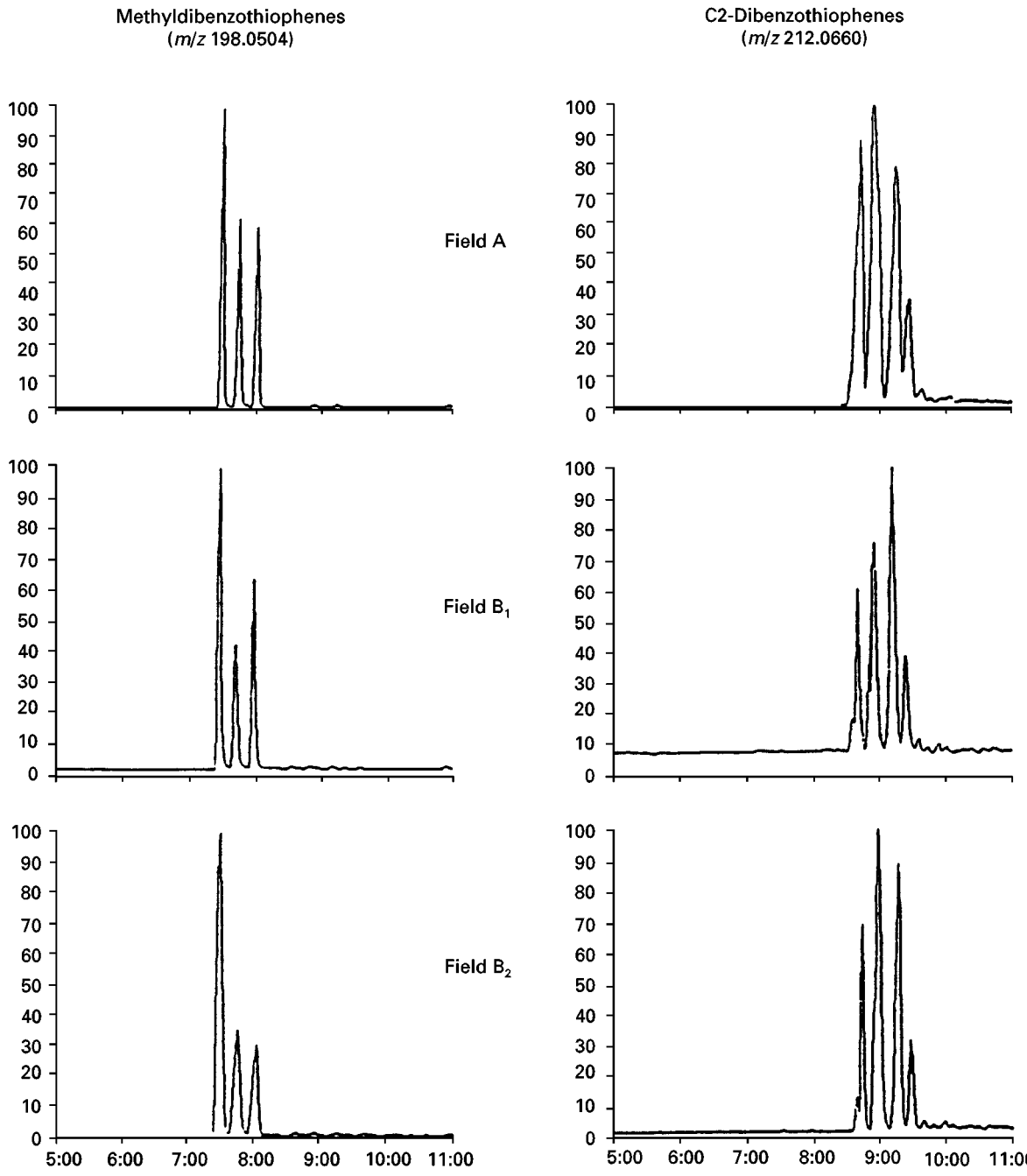

Figure 6 A comparison of the GC-HRMS-SIM fingerprints of methyldibenzothiophenes and C_2-dibenzothiophenes in three crude oils from two North Sea fields. (Reproduced from Tibbets and Large (1988) by kind permission of John Wiley and Sons.)

directly from the fragmentation of *m/z* 211 and contains structural information. It can be seen that this method is also useful for clearing up ambiguities in the interpretation of EI spectra, since it allows *precursor/product ion* relationships to be clearly defined.

A second application of tandem mass spectrometry often used in conjunction with GC-MS utilizes a technique called *multiple reaction monitoring* (*MRM*). This technique, like high resolution SIM, is used to increase the specificity of an analysis. After first recording product ion mass spectra of the analyte(s) of interest, one or more precursor/product ion relationships are chosen. The criteria for this are that the product ions selected are intense and characteristic of the specified analyte. Then in order to carry out the MRM experiment, the first quadrupole mass analyser is set up in SIM mode, to switch between the precursor ions of interest. The collision cell is operated in

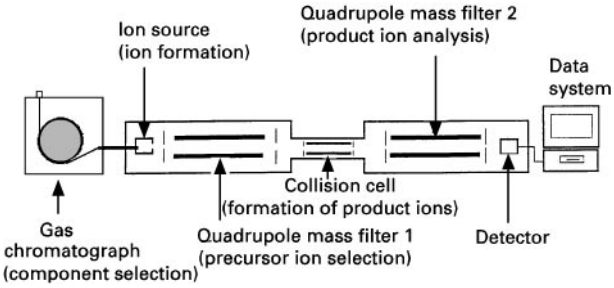

Figure 7 A triple quadrupole mass spectrometer. On leaving the GC column sample components are first ionized, then ions selected by the first quadrupole mass filter are fragmented in the collision cell for analysis by the second quadrupole mass filter. Such instruments may yield greater structural information than single stage instruments and allow further selectivity to be introduced into GC-MS experiments.

the normal way, and the second quadrupole mass filter is set up to switch between the characteristic product ions.

The output from such an experiment is chromatographic, producing one or more plots of signal intensity against time. Peaks are only observed in such chromatograms when an ionized compound yields an ion of the selected precursor ion m/z value, which also subsequently fragments, under CID, to give a product ion of the selected product ion m/z. The two stages of mass selection make this a highly selective technique and it has been proposed as a viable alternative to high resolution SIM for a variety of applications.

Recent advances in ion trap technology have meant that similar modes of operation also available on these compact, relatively low cost instruments. In this case ions other than the precursor ion of interest are selectively ejected from the trap. The selected precursor ion is then subjected to CID in the trap and a product ion mass spectrum may be recorded by ejecting these ions. For a fuller discussion of tandem mass spectrometry see Busch *et al*. (1988).

Conclusions

A developing field in GC-MS is the use of time of flight mass analysers with short capillary columns for very rapid analyses. We have described time of flight mass analysers and the advantages offered by their use for the acquisition of mass spectral data from narrow chromatographic/electrophoretic peaks in the companion paper to this one, on the use of mass spectrometry as a detector for liquid chromatography. The same arguments apply for fast GC-MS analyses and a number of manufacturers have recently launched instruments of this type. Specialist GC-MS instrumentation is also increasingly being use in the clinical field in order to accurately determine isotope ratios, e.g. the presence of *Helicobacter pylori* in the gastric epithelium has been linked with gastritis, peptic ulcers and gastric cancer. The presence of *Helicobacter pylori* can be determined by measuring the $^{13}C/^{12}C$ isotope ratio in exhaled breath following ingestion of isotopically labelled urea. Gerhards *et al*. (1999) have examined the use of GC-MS in clinical analysis and Platzner (1997) provides a full discussion of modern isotope ratio mass spectrometry.

The future of mass spectrometry as the detector of choice for gas chromatography looks secure. In this paper we have illustrated some of the benefits of this happy marriage of techniques. Modern GC-MS instruments are compact, robust, sensitive, selective and give access to a range of information not possible when using conventional detectors, hence their importance in the modern GC laboratory.

See also: **II/Chromatography: Gas:** Detectors: Selective. **Chromatography: Liquid:** Detectors: Mass Spectrometry. **Mass Spectrometry:** Spectrometry - Mass Spectrometry Ion Mobility. **III/Clinical Diagnosis: Chromatography. Geochemical Analysis:** Gas Chromatography.

Further Reading

Bruner F (1993) *Gas Chromatographic Environmental Analysis*. New York: VCH Publishers.

Busch KL, Glish GL and McLuckey SA (1988) *Mass Spectrometry–Mass Spectrometry*. New York: VCH Publishers.

Chapman JR (1993). *Practical Organic Mass Spectrometry*, 2nd edn. Chichester, UK: John Wiley.

Davis R and Frearson M (1987) *Mass Spectrometry*. Analytical Chemistry by Open Learning Series. Chichester, UK: John Wiley.

Evershed R. (1993) In: Baugh PJ (ed.) *Gas Chromatography – A Practical Approach*. Oxford, UK: Oxford University Press.

Gaskell SJ (ed.) (1986) *Mass Spectrometry in Biomedical Research*. Chichester, UK: John Wiley.

Gerhards P, Bons U and Sawazki J (1999) *GC/MS in Clinical Chemistry*. Chichester, UK: John Wiley.

Johnstone RAW and Rose ME (1996) *Mass Spectrometry for Chemists and Biochemists* 2nd edn. Cambridge, UK: Cambridge University Press.

Lee TA (1998) *A Beginners Guide to Mass Spectral Interpretation*. Chichester, UK: John Wiley.

Oehme M (1998) *Practical Introduction to GC-MS Analysis with Quadrupoles*. Heidelberg: Hüthig Verlag.

Platzner I (1997) *Modern Isotope Ratio Mass Spectrometry*. Chichester, UK: John Wiley.

Smith RM and Busch KL (1999) *Understanding Mass Spectra. A Basic Approach*. New York: John Wiley.

Tibbets PJC and Large R (1988) In Crump GB (ed.) *Petroanalysis '87*. Chichester, UK: John Wiley.