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Hyphenated Techniques in Gas Chromatography

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1. Introduction

Hyphenated gas chromatography (GC) (Chaturvedi & Nanda, 2010; Coleman III & Gordon, 2006) mainly refers to the coupling of the high-performance separation technique of gas chromatography with 1) information-rich and sophisticated GC detectors which otherwise can be mostly operated as a stand-alone instrument for chemical analysis, and 2) automated online sample preparation systems. The term "hyphenation" was first adapted by Hirschfeld in 1980 to describe a possible combination of two or more instrumental analytical methods in a single run (Hirschfeld, 1980). It is of course not the case that you can couple GC to any detection systems, although many GC hyphenations have been investigated and / or implemented as to be discussed in this chapter. The aim of this coupling is obviously to obtain an information-rich detection for both identification and quantification compared to that with a simple detector (such as thermal-conductivity detection (TCD), flame-ionization detection (FID) and electron-capture detector (ECD), etc.) for a GC system.

According to the detection mechanism, information-rich detectors can be mainly classified as 1) detection based on molecular mass spectrometry, 2) detection based on molecular spectroscopy such as Fourier-Transform infrared (FTIR) and nuclear magnetic resonance (NMR) spectroscopy, and 3) detection based on atomic spectroscopy (elemental analysis) by coupling with such as inductively-coupled plasma (ICP)-MS, atomic absorption spectroscopy (AAS) and atomic emission spectroscopy (AES), respectively. In addition to these hyphenations mentioned above and which are mounted after a gas chromatograph, it can also include automated online sample preparation systems before a GC system such as static headspace (HS), dynamic headspace, large volume injection (LVI) and solid-phase microextraction (SPME). One of the recent developments is the hyphenation of GC with human beings – so called GC-Olfactometry (GC-O) or GC-Sniffer (Friedrich & Acree, 1998). Hyphenated gas chromatography also include coupling of gas chromatographs orthogonally - multidimensional gas chromatography (MDGC or GC×GC).

2. Hyphenated techniques in gas chromatography

This chapter provides a general overview of the current hyphenated GC techniques with focus on commonly applied GC-MS, GC-FTIR (GC-NMR) for detection of molecular

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analytes as well as GC-AAS and GC-AES coupling for elemental analysis. Emphasis will be given to cover various GC-MS techniques including ionization methods, MS analysers, tandem MS detection and data interpretation. For more comprehensive overview on their applications, readers are directed to other chapters in this book or other dedicated volumes (Grob & Barry, 2004; Message, 1984; Jaeger, 1987; Niessen, 2001).

2.1 Gas Chromatography-Mass Spectrometry (GC-MS)

In 1957, Holmes and Morrell (Holmes & Morrell, 1957) demonstrated the first coupling of gas chromatography with mass spectrometry shortly after the development of gas-liquid chromatography (James & Martin, 1952) and organic mass spectrometry (Gohlke & McLafferty, 1993). Years later, improved GC-MS instruments were commercialized with the development of computer-controlled quadrupole mass spectrometer for fast acquisition to accommodate the separation in gas chromatograph. Since then, its applications in various areas of sciences has made it a routine method of choice for (bio)organic analysis (Kuhara, 2005).

As its name suggested, a GC-MS instrument is composed of at least the following two major building blocks: a gas chromatograph and a mass spectrometer. GC-MS separates chemical mixtures into individual components (using a gas chromatograph) and identifies / quantifies the components at a molecular level (using a MS detector). It is one of the most accurate and efficient tools for analyzing volatile organic samples.

The separation occurs in the gas chromatographic column (such as capillary) when vaporized analytes are carried through by the inert heated mobile phase (so-called carrier gas such as helium). The driven force for the separation is the distinguishable interactions of analytes with the stationary phase (liquid thin layer coating on the inner wall of the column or solid sorbent packed in the column) and the mobile phase respectively. For gas-liquid chromatography, it depends on the column's dimensions (length, diameter, film thickness), type of carrier gas, column temperature (gradient) as well as the properties of the stationary phase (e.g. alkylpolysiloxane). The differences in the boiling points and other chemical properties between different molecules in a mixture will separate the components while the sample travels through the length of the column. The analytes spend different time (called retention time) to come out of (elute from) the GC column due to their different adsorption on the stationary phase (of a packed column in gas-solid chromatography) or different partition between the mobile phase (carrier gas) and the stationary phase (of a capillary column in gas-liquid chromatography) respectively.

As the separated substances emerge from the column opening, they flow further into the MS through an interface. This is followed by ionization, mass-analysis and detection of mass-to-charge ratios of ions generated from each analyte by the mass spectrometer. Dependent on the ionization modes, the ionization interface for GC-MS can not only ionize the analytes but also break them into ionized fragments, and also detect these fragments together with the molecular ions such as, in positive mode, radical cations using electron impact ionization (EI) or (de-)protonated molecules using chemical ionization (CI). All ions from an analyte together (molecular ions or fragment ions) form a fingerprint mass spectrum, which is unique for this analyte. A “library” of known mass spectra acquired under a standard condition (for instance, 70-eV EI), covering several hundreds of thousand compounds, is

stored on a computer. Mostly a database search can identify an unknown component rapidly in GC-MS. Mass spectrometry is a powerful tool in instrumental analytical chemistry because it provides more information about the composition and structure of a substance from less sample than any other analytical technique, and is considered as the only definitive analytical detector among all available GC detection techniques.

The combination of the two essential components, gas chromatograph and mass spectrometer in a GC-MS, allows a much accurate chemical identification than either technique used separately. It is not easy to make an accurate identification of a particular molecule by gas chromatography or mass spectrometry alone, since they may require a very pure sample or standard. Sometimes two different analytes can also have a similar pattern of ionized fragments in their standard mass spectra. Combining the two processes reduces the possibility of identification error. It is possible that the two different analytes will be separated from each other by their characteristic retention times in GC and two co-eluting compounds then have different molecular or fragment masses in MS. In both cases, a combined GC-MS can detect them separately.

2.1.1 Ionization techniques and interfaces

The carrier gas that comes out of a GC column is primarily a pressurized gas with a flow about mL/min for capillary columns and up to 150 mL/min for packed columns. In contrast, ionization, ion transmission, separation and detection in mass spectrometer are all carried out under high vacuum system at approximately 10^{-4} Pa (10^{-6} Torr). For this reason, sufficient pumping power is always required at the interface region of a GC-MS in order to provide a compatible condition for the coupling. When the analytes travel through the length of the column, pass through the transfer line and enter the mass spectrometer they can be ionized by several methods. Fragmentation can occur alongside ionization too. After ion separation by mass analyser, they will be detected, usually by an electron multiplier diode, which essentially turns the ionized analytes/fragments into an electrical signal.

The two well-accepted standard types of the ionization techniques in GC-MS are the prevalent electron impact ionization (EI) and the alternative chemical ionization (CI) in either positive or negative modes.

Electron impact (EI) ionization:

The EI source is an approximately one cubic centimetre device, which is located in the ion source housing as shown in Figure 1. The ion source is open to allow for the maximum conductance of gas from the ion source into the source housing and then into the high-vacuum pumping system. The EI source is fitted with a pair of permanent magnets that cause the electron beam to move in a three-dimensional helical path, which increases the probability of the interaction between an electron and an analyte molecule. Even under this condition, only about 0.01~0.001% of the analyte molecules are actually ionized (Watson, 1997). During the EI ionization, the vaporized molecules enter into the MS ion source where they are bombarded with free electrons emitted from a heated filament (such as rhenium). The kinetically activated electrons (70-eV) collide with the molecules, causing the molecule to be ionized and fragmented in a characteristic and reproducible way.

Due to the very light weight of the electrons (1/1837 that of the mass of a proton or neutron), one collision between an electron and a molecule would bring insufficient internal

energy to the molecule to become ionized. The molecule's internal energy is increased by the interaction of the electron cloud after a collision cascade. The energized molecule, wanting to descend to a lower energy state, will then expel one of its electrons. The result is an odd-electron species called a radical cation, which is the molecular ion and has the same integer mass as the analyte molecule. Some of the molecular ions will remain intact and pass through the *m/z* analyser and be detected. The molecular weight of the analyte is represented by the molecular ion peak in the mass spectrum if there are any. The single-charge molecular ion has the same nominal mass of the molecule, but the accurate mass is differed by that of an electron. Most molecular ions will undergo unimolecular decomposition to produce fragment ions.

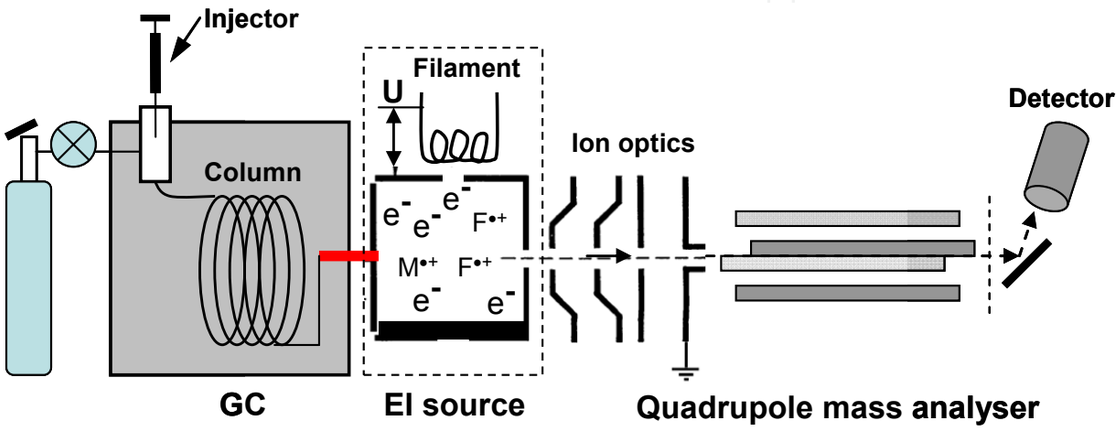


Fig. 1. Schematic drawing of a GC-MS with EI ionization and quadrupole mass analyser.

The reason to apply the 70 eV as the standard ionization energy of electrons is to build a spectrum library with the standard mass spectra and subsequently to perform the MS database searching for unknown identification. The molecular fragmentation pattern is dependant upon the electron energy applied to the system. The excessive energy of electrons will induce fragmentation of molecular ions and results in an informative fingerprint mass spectrum of an analyte (Watson, 1997). The use of the standard ionization energy facilitates comparison of generated spectra with library spectra using manufacturer-supplied software or software developed by the National Institute of Standards (NIST-USA). The two main commercial mass spectra libraries for general purpose are the NIST Library and the Wiley Library. In addition, several small libraries containing a specific class of compounds have also been developed by individual manufacturers or research institutions. This includes libraries for pesticides, drugs, flavour and fragrance, metabolites, forensic toxicological compounds and volatile organic compounds (VOC), just to name a few. Spectral library searches employ matching algorithms such as probability based matching (McLafferty et al., 1974) and dot-product (Stein & Scott, 1994) matching that are used with methods of analysis written by many method standardization agencies. EI is such an energetic process, in some cases, there is often no molecular ion peak left in the resulting mass spectrum. Since the molecular ion can be a very useful structure information for identification, this is sometimes a drawback compared to other soft ionization such as chemical ionization, field ionization (FI), or field desorption ionization (FDI), where the desired (pseudo) molecular ion will be generated and detected. After ionization, the stable

ions (which remain without dissociation during its flight from the ion source to the detector) will be pushed out of the EI source by an electrode plate with the same charge polarity, called the repeller. As the ions exit the source, they are accelerated / transmitted into the mass analyser of the mass spectrometer.

Chemical ionization (CI):

CI is a less energetic process than EI. In the latter case, the ionizing electrons accelerated to have some kinetic energy collide directly with gas-phase analyte molecules to result in ionization accompanied by simultaneous fragmentation. However, CI is a low energetic ionization technique generating pseudo molecular ions such as $[M+H]^+$ rather than the conventional $M^{\bullet+}$, and inducing less fragmentation. This low energy usually leads to a simpler mass spectrum showing easily identifiable molecular weight information. In CI a reagent gas such as methane, ammonia or isobutane is introduced into the relatively closed ion source of a mass spectrometer at a pressure of about 1 Torr. Inside the ion source, the reagent gases (and the subsequent reagent ions) are present in large excess compared to the analyte. Depending on the technique (positive CI or negative CI) chosen, the pre-existing reagent gas in the ion source will interact with the electrons preferentially first to ionize the reagent gas to produce some reagent ions such as CH_5^+ and NH_4^+ in the positive mode and OH^- in the negative mode through self-CI of the reagent gas. The resultant collisions and ion/molecule reactions with other reagent gas molecules will create an ionization plasma. When analytes are eluted (from GC) or evaporated (direct inlet), positive and negative ions of the analyte are formed by chemical reactions such as proton-transfer, proton-subtraction, adduct formation and charge transfer reactions (de Hoffmann & Stroobant, 2003), where the proton transfer to produce $[M+H]^+$ ions is predominate during the ionization. The energetics of the proton transfer is controlled by using different reagent gases. Methane is the strongest proton donor commonly used with a proton affinity (PA) of 5.7 eV, followed by isobutane (PA 8.5 eV) and ammonia (PA 9.0 eV) for 'softer' ionization. As mentioned above, in this soft ionization, the main benefit is that the (pseudo) molecular ions closely corresponding to the molecular weight of the analyte of interest are produced. This not only makes the follow-up identification of the molecular ions easier but also allows ionization of some thermal labile analytes.

The sensitivity and selectivity of a mass spectrometer in a hyphenated GC largely depend on the interfacing technique: the ion source and the ionization mode. The sensitivity is related to the ionization efficiency and the selectivity is primarily to the ionization mode. Both sensitivity and selectivity can differ for different classes of compounds. A proper choice of an ionization technique is a key step for a successful GC-MS method development. In most case of EI ionization, the positive mode is much preferred due to its capability efficiently to ionize most analytes and to induce sufficient fragmentation to build up a database with positive mass spectra. The sensitivity in the negative EI mode will be much lower. However, the fragmentation processes in EI can be so extensive that the molecular ion is absent in the mass spectrum of some compounds. As a result, the useful molecular weight information is lost, which is indeed a disadvantage of this ionization technique (Karasek & Clement, 1988; Ong & Hites, 1994). In this aspect, chemical ionization is a reasonable alternative and supplemental to EI as a soft ionization method. Due to the moderate energy transmission to the analytes, the pseudo molecular ions are formed in CI and these even-electron ions are more stable than the odd-electron ions produced with EI

(Harrison, 1992). Unlike EI, both positive chemical ionization (PCI) and negative chemical ionization (NCI) are equally used according to their specific features. The positive mode is best suitable for hydroxyl group-containing alcohols and sugars as well as basic amino compounds. The sensitivity of PCI-MS is comparable with low-resolution EI-MS for most compounds. On the other hand, the negative mode is widely used in environmental analysis because it is highly selective and sensitive to, for instance, organochlorine (halogen-containing) and acidic group-containing compounds (Karasek & Clement, 1988). For this, the sensitivity of the NCI is significantly better compared with that of the PCI. As a result, the NCI has also been equally developed in the sense of the choices of the reagent gases and their combination (Chernetsova et al., 2002). Furthermore, the application of an alternating or simultaneous EI and CI in GC-EI/CI-MS has also been reported (Arsenault et al., 1971 & Hunt et al., 1976). Although it has not been popularly implemented in the commercial GC-MS systems, the advantages of obtaining informative mass spectra in trace analysis of samples with limited quantities are very promising. In addition to the above-mentioned EI and CI ionization interfaces, where the ionization occurs in the vacuum of a mass spectrometer, a recent development has also demonstrated an interfacing technique at the atmosphere. That is the coupling of a GC with a mass spectrometer with the so-called Direct Analysis in Real Time (DART) (Cody et al., 2005 & Cody 2008), where the absence of vacuum interface, electron filament and CI reagent gases offers a robust interfacing technique for rapid analysis.

2.1.2 Molecular weight, molecular ion, exact mass and isotope distribution

For a singly charged analyte, the mass-to-charge ratio of its molecular ion indicates the molecular weight (*a.m.u.*) of the analyte. The molecular ion can be a radical cation $[M]^{\bullet+}$ (positive mode) or a radical anion $[M]^{\bullet-}$ (negative mode), derived from the neutral molecule by kicking off / attaching one electron. According to the IUPAC definition (McNaught & Wilkinson, 1997), the molecular mass (*Mr*) is the ratio of the mass of one molecule of that analyte to the unified atomic mass unit *u* (equal to 1/12 the mass of one atom of ^{12}C). It is also called molecular weight (*MW*) or relative molar mass (*Mr*). Knowing the fact that each isotope ion (rather than their average) of an analyte is detected separately in MS mass analyser, one should pay attention to the different definitions of molecular masses in mass spectrometry and GC-MS.

The nominal mass of an ion is calculated using the integer mass by ignoring the mass defect of the most abundant isotope of each element (Yergey et al., 1983). This is equivalent as summing the numbers of protons and neutrons in all constituent atoms. For example, for atoms H = 1, C = 12, O = 16, etc. Nominal mass is also called mass number. To assign elemental composition of an ion in low resolution MS, the nominal mass is often used, which enable to count the numbers of each constituent elements. However, if the sum of the masses of the atoms in a molecule using the most abundant isotope (instead of the isotopic average mass) for each element is calculated (Goraczko, 2005), the monoisotopic mass is obtained (McNaught & Wilkinson, 1997). Monoisotopic mass is also expressed in unified atomic mass units (a.m.u.) or Daltons (Da). For typical small molecule organic compounds with elements C, H, O, N etc., this is the mass that one can measure with a mass spectrometer and it often refers to the lightest isotope in the isotopic distribution. However, for a molecule containing special elements such as B, Fe and Ar, etc., the most abundant

isotope is not the lightest one any more. Another important and useful term is the exact mass, which is obtained by summing the exact masses of the individual isotopes of the molecule (Sparkman, 2006). According to this definition, several exact masses can be calculated for one chemical formula depending on the constituent isotopes. However, in practical mass spectrometry, exact mass refers to that corresponding to the monoisotopic mass, which is the sum of the exact masses of the most abundant isotopes for all atoms of the molecule. This is the peak one can measure with high resolution mass spectrometry. This results in measured accurate mass (Sparkman, 2006), which is an experimentally determined mass that allows the elemental composition to be determined either using the accurate mass mode of a high resolution mass spectrometer (Grange et al., 2005). For molecules with mass below 200 u, a 5 ppm accuracy is sufficient to uniquely determine the elemental composition. And at *m/z* 750, an error of 0.018 ppm would be required to eliminate all extraneous possibilities (Gross, 1994). When the exact mass for all constituent isotopes (atoms or molecules) are known, the average mass of a molecule can be calculated. That is the sum of the average atomic masses of the constituent elements. However, one can never measure the average mass of a compound using mass spectrometry directly, but that of its individual isotopes.

Some molecular ions can be obtained using EI ionization. If not, the use of soft-ionization techniques (CI, FI) would help to facilitate identification of the molecular ion. Accurate masses can be determined using high resolution instruments such as magnet/sectors, reflectron TOFs (see Section 2.1.4), Fourier-Transform ion cyclotron resonance (FT-ICR) (Marshall et al., 1998) and Orbitrap (Makarov, 2000) mass spectrometers. Because of isotopes of some elements, molecular ions in mass spectrometry are often shown as a distribution of isotopes. The isotopic distribution can be calculated easily with some programs freely available and allows you to predict or confirm the masses and abundances of the isotopes for a given chemical formula. Isotopic patterns observed are helpful for predicting the appropriate number of special elements (e.g., Cl, Br and S) or even C numbers. When a Library mass spectrum is not available, this will be one of the important means for unknown identification. The elucidation process normally requires not only the combined use of hard and soft ionization techniques but also tandem MS experiments to obtain information of fragments for data interpretation. In some cases, an elemental composition might be proposed for the unknown based on isotope patterns and accurate mass measurements of the molecular and fragment ions (Hernández et al, 2011) (see Section 2.1.4).

2.1.3 Typical mass analyzers and MS detectors in GC-MS

MS instruments with different mass analysers, e.g. magnet/electric sectors, quadrupoles (linear), ion traps (Paul traps & quadrupole linear ion trap), FT-ICR and time-of-flight (TOF) mass analysers have all been implemented for the coupling of GC and MS. Since its conception, linear quadrupoles have been dominating the GC-MS applications.

Quadrupole mass analyser:

A single-stage linear quadrupole mass analyser can be considered as a mass filter and it consists of four hyperbolic metal rods placed parallel in a radial array. A pair of the opposite rods have a potential of (U+Vcos(ωt)) and the other pair have a potential of -(U+Vcos(ωt)). An appropriate combination of direct current (DC) and radio frequency (RF, ~ 1 MHz)

electric field applied to the four rods induces an oscillatory motion of ions guided axially into the assembly by means of a low accelerating potential. The oscillating trajectories are mass dependent and ions with one particular mass-to-charge (*m/z*) ratio can be transmitted toward the detector when a stable trajectory through the rods is obtained. At static DC and RF values, this device is a mass filter to allow the ions at this *m/z* pass through and all others will be deflected. Ions of different *m/z* can be consecutively transmitted by the quadrupole mass filter toward the detector when the DC and RF potentials are swept at a constant ratio and oscillation frequencies (de Hoffmann & Stroobant, 2003; Santos & Galceran, 2003).

A single quadrupole mass analyser can be operated in either the full-spectrum scan mode or the selected ion monitoring (SIM) mode. In the scan mode, the ions of a certain *m/z* range will pass through the quadrupole sequentially while scanning the DC and RF potentials to the detector. The advantage is that this allows to record a full mass spectrum containing the information from molecular ion to fragments, which further enables a library searching to compare with the standard mass spectra for unknown identification. It is common to require a scanning of the analyser from about 50 a.m.u. to exclude the background ions from residue air, carrier gases, and CI reagent gases. However, especially in the earlier years, the slow scan speed (250-500 a.m.u. per second) for a quadrupole analyser was an important limiting factor and it is in contrary with the high resolution (narrow peaks about a few seconds wide) of a capillary GC separation. Apparently, a longer dwell time is essentially required to obtain a more sensitive detection. Therefore, the SIM mode is preferred for a selective and sensitive detection in quantification of known analytes, where the DC and RF are set to pre-defined values according to the *m/z* of the analyte (molecular ion or specific fragments) for up to hundred milliseconds. Linear quadrupoles are the most widely used mass analysers in GC–MS, mainly because they make it possible to obtain high sensitivity, good qualitative information and adequate quantitative results with relatively low maintenance. Generally, these instruments are characterised by a bench-top configuration with unit mass resolution and both electron impact and chemical ionisation techniques. The relatively low cost, compactness, moderate vacuum requirements and the simplicity of operation make quadrupole mass spectrometers the most popular mass analyser for GC-MS. The continuous and significant improvements in scanning speed (to allow tandem MS detection), sensitivity and detection limits has also been observed in the past decade. New developments have been implemented in GC–MS instrumentations based on quadrupole technology with regard to the stability of mass calibration, the fast scan-speed with a higher sensitivity. It is now also possible to work simultaneously with full-scan and selected ion monitoring (SIM) modes in a single GC-MS run.

Ion trap (IT) mass analyser:

An ion trap mass spectrometer uses a combination of electric or magnetic fields to capture and store ions in a vacuum chamber. According to its principles of operation, it can be specified as quadrupole ion traps (Paul trap) (Paul & Steinwedel, 1953), quadrupole linear ion traps (Schwartz et al., 2002), FTICR-MS (Penning trap) (Marshall et al., 1998) and Orbitraps (Kington traps) (Kington, 1923; Makarov, 2000), respectively. However, the coupling to GC has been dominated by quadrupole mass analysers and quadrupole ion traps. Due to the applicability and other limitations, only very recently, there have been reports on implementing FTICR-MS (Szulejko & Solouki, 2002) and Orbitrap-MS (Peterson et al., 2010) as detectors in GC-MS.

The three-dimensional Paul ion trap (IT) is composed of a central hyperbolic ring electrode located between two symmetrical hyperbolic end-cap electrodes. The geometry of the device is described by the relationship $r_0^2 = 2 \times z_0^2$, where r_0 is defined as the radius of the ring electrode and $2z_0$ is the distance between the end-cap electrodes. The value r_0 is used to specify a trap, which ranges about 1-25 mm. During the ion trapping, an auxiliary oscillating potential of low amplitude is applied across the end-cap electrodes while a RF potential of ~ 1 MHz is applied to the ring electrode. As the amplitude of the RF potential is increased, the ions become more kinetically energetic and they develop unstable trajectories (excited for dissociation or ejected to detector). One of the significant advantages of ion traps compared to the above-mentioned linear quadrupole mass analysers is their high sensitivity in full scan mode. Based on this, many qualitative and quantitative applications have been reported (Allchin et al., 1999 & Sarrion et al., 2000). Beside the conventional full scan mode of operation, an important advancement by application of ion trap in GC-MS has been the capability of an ion trap mass analyser to perform tandem mass spectrometric investigations of ions of interest in collision-induced dissociation (CID) for ion structure elucidation (Plomley et al., 2000) (see the text below for tandem mass spectrometers).

For both linear quadrupole and 3-D mass spectrometers, after mass-resolved ions passing the mass analyser, they continue to travel to the ion detector. It is essential in GC-MS to have fast responding detector with a broad range of magnification. The most popular detector employed is the electron multiplier composed of a series of dynodes. The ions collide with the first one to generate primary electrons. Due to the increasing high voltage (kV) between the dynodes, the electrons further collide with the next dynode and generate more electrons, and so on. Therefore, a small ion current can be finally amplified into a huge signal. Another commonly used detector is the photomultiplier. The ions collide with a phosphor-coated target and are converted into photons that are subsequently magnified and detected. Typically, these detectors are operated at lower voltages (400-700 V) and, therefore, have a longer lifetime than the electron multipliers (using high kV voltages) (Grob, 1995).

Time-of-flight (TOF) mass analyser:

Time-of-flight mass spectrometry (TOF-MS) is based on a simple mass separation principle in which the *m/z* of an ion is determined by a measurement of its flight time over a known distance (Cotter, 1994; Stephens, 1946). Pulsed ions are initially accelerated by means of a constant homogeneous electrostatic field of known strength to have the same kinetic energy (given they have the same charge). Therefore, the square of the velocity of an ion is reversely proportional to its *m/z*, $E_k = (1/2)mv^2$ and the time of arrival *t* at a detector directly indicates its mass (Equation 1).

$$t = \mathrm{d} \times (m/\mathrm{q})^{1/2} \times (2\mathrm{U})^{-1/2} \quad (1)$$

where d is the length of the flight tube, *m* is the mass of the ion, q is the charge, U is the electric potential difference used for the acceleration. The arrival time *t* can be measured using a transient digitizer or time to digital converter, and is about milliseconds. A TOF mass analyser has theoretically no mass limit for detection and a high sensitivity. However, the spread of kinetic energies of the accelerated ions can lead to different arrival time for the ions with the same *m/z* and result in low mass resolution. This can be overcomed by applying a reflectron flight path (Mamyrin et al., 1973) rather than a linear one to refocus the ions with the same *m/z* value to arrive at the detector simultaneously.

In TOF-MS, ions must be sampled in pulses. This fits well with a laser ionization source. However, when EI or CI are used for GC-MS coupling, a continuous ion beam is produced. Therefore, in most GC-TOF-MS instrumentations, a pulse of an appropriate voltage is applied to deflect and accelerate a bunch of the ions in the orthogonal direction to their initial flight path (so-called oa-TOF-MS). One of the important advantages of TOF-MS as a GC detector is its capability of producing mass spectra within a very short time (a few milliseconds), with high sensitivity. Furthermore, its high mass accuracy (errors in low ppm) has made it an alternative to accurate mass GC-MS using magnet / sector instruments (see Section 2.1.4). In both GC-MS and LC-MS, hybridized TOF-MS instruments with quadrupoles (Q-TOF-MS) (Chernushevich, 2001), ion trap (IT-TOF-MS), and even another TOF (such as TOF/TOF-MS) have all been developed and found more applications than TOF-MS alone (Vestal & Campbell, 2005).

Tandem mass spectrometer as a mass analyser:

Tandem mass spectrometer refers to an arrangement of mass analysers in which ions are subjected to two or more sequential stages of analysis (which may be separated spatially or temporally). The study of ions involving two stages of mass analysis has been termed mass spectrometry/mass spectrometry (MS/MS) (Todd, 1991). For GC applications, it includes mainly triple quadrupole, 3D-ion trap and linear quadrupole ion trap tandem mass spectrometers and only very recently also FTICR (Szulejko & Solouki, 2002 & Solouki et al., 2004) and Orbitrap-MS (Peterson et al., 2010) as detectors in GC-MS.

Triple quadrupole MS/MS involves two quadrupole analysers mounted in a series but operating simultaneously (either as a mass filter or scanner) and with a collision cell between two mass analysers. Since the analysers can be scanned or set to static individually, types of operations include product ion scan, precursor ion scan and neutral loss scan. Product ion scan enables ion structure studies. This is realised by isolation of ions of interest according to their *m/z* using first quadrupole analyser. Then dissociation of the ions after kinetic-energetically activated occurs in the collision cell filled with an inert collision gas. Finally, the product ions will be mass-analysed using the third quadrupole. The fragment information provides further insights into ion structures or functional groups. This can be used to confirm structures of components in question when it is compared with a reference standard or to deduce ion structures for new chemical entities in qualitative identification. Some mass spectra databases include even a library of product ion spectra for some selected compounds to assistant the identification. Furthermore, the precursor ion scan can be utilised to study multiple precursor ions of a certain fragment ion. This is very useful to study a class of compounds producing a common charged fragment during collision-induced dissociation (CID) in the collision cell. For instance, the protonated 1,2-benzenedicarboxylic acid anhydride at *m/z* 149 derived from almost all corresponding phthalate esters can be used as such an ion and, during the precursor scan, all related phthalates will be found. On the other hand, neutral loss scan can be used to study a class of compounds showing a common neutral molecule loss during CID. For instance, the loss of a CO_2 from most deprotonated carboxylic acids or H_2O from protonated alcohols can be applied for this purpose. For dissociation reactions found in either product scan or precursor ion scans, a pair of ions can be selected to detected a specific analyte, which is the so-called selected reaction monitoring (SRM) or multiple reaction monitoring (MRM) when more pairs are chosen in one GC-MS run. SRM and MRM of MS/MS are highly specific and

virtually eliminate matrix background due to the two stages of mass selections. It can be applied to quantify trace levels of target compounds in the presence of sample matrices (Santos & Galceran, 2003). This has further secured its important role in modern discovery researches even in the era of fast liquid chromatography tandem mass spectrometry (LC-MS/MS) (Krone et al., 2010).

In a 3-D ion trap MS, the above-mentioned steps such as ion selection, ion dissociation and scanning of product ions occur in a timed sequence in a single trap in contrast to a triple quadrupole MS, where they are at different spatial locations of the instrument while ions travelling through. For a GC-MS/MS coupling, ion trap instruments offer three significant advantages over triple quadrupoles including low cost, easy to operate and high sensitivity for scanning MS/MS (Larsson & Saraf, 1997). Although in the earlier versions of ion trap instruments, a drawback called low-mass cut-off (which affects or discriminates small fragment ions in lower 1/3 mass range during MS/MS scan) has been observed, this has been solved in the modern instruments nowadays.

Although triple quadrupoles and ion traps have significant superiority in tandem mass spectrometry, their resolving powers are limited. Quadrupoles reach about unit resolution and ion trap a bit higher. With them, accurate mass measurements are generally not possible. This is just opposite to high-resolution TOF mass analysers. Another limitation of a triple quadrupole is that can be used only for one step of MS/MS, while an ion trap can perform multiple steps tandem MS experiments, which is sometimes very useful for structure elucidation.

2.1.4 GC with high resolution mass spectrometry (GC-TOF-MS)

Nowadays, the most investigated and applied coupling of GC with high resolution mass spectrometry is GC-TOF-MS, rather than that with sector instruments (Jeol, 2002). Recent advancements in instrumental optics design, the use of fast recording electronics and improvements in signal processing have led to a booming of the TOF-MS for investigation of organic compounds in complex matrices (Čajka & Hajšlová, 2007). GC-TOF-MS with high resolution of about 7000 is capable of achieving a mass accuracy as good as 5 ppm for small molecules. This allows not only isobaric ions to be easily mass-resolved but also the measurements of accurate masses for elemental composition assignment or mass confirmation, which adds one more powerful means for identification in GC-MS besides mass spectrum database searching and tandem mass spectrometry (Hernández et al, 2011). The moderate acquisition speed (maximum rate 10/s) at high resolution and the high acquisition speed (maximum rate of 500/s) at unit resolution can be achieved readily with a linear range of three to four orders of magnitude. High acquisition speed of GC-TOF-MS at unit resolution is very compatible with very narrow chromatographic peaks eluted from a fast and ultra-fast GC or GC×GC (Čajka & Hajšlová, 2007; Hernández et al, 2011; Pasikanti et al., 2008).

High resolution detection in GC-TOF-MS offers not only the high mass accuracy of molecular and fragment ions but also the accurate isotopic distribution with regard to isotope intensities and isotope-resolved information for element assignments. It is extremely helpful for unknown compounds for which no Library spectrum is available for database searching as reviewed recently (Hernández et al, 2011). With the help of software tools, a

carbon number prediction filter can be applied to reduce the number of possible elemental compositions based on the relative abundance of the isotopic peak corresponding to ^{13}C (relative to the ^{12}C peak, each ^{13}C isotope contributes 1.1% to the ^{13}C peak). The nitrogen rule can also be used to determine whether the ion is an ''even-electron ion'' (for instance, protonated or deprotonated molecule) or an ''odd-electron ion'' (for instance, radical cation or anion) (MaLafferty, 1993). With these considerations, possible elemental compositions can be obtained when it is searched in available databases (e.g., Index Merck, Sigma Aldrich, Chem-Spider, Pubchem, Reaxys) and a chemical structure can be proposed (Hernández et al, 2011; Portolés et al., 2011). Both accurate masses and isotopes of fragment ions should be in agreement with the chemical structure assigned. However, in order to secure this identification, a reference standard will be required in a final step to check the GC retention time and to confirm the presence of fragment ions experimentally by GC-TOF-MS analysis (Hernández et al, 2011).

After the first applications of high resolution GC-TOF-MS such as on extracts of well water (Grange, Genicola & Sovocool, 2002), this approach has been well accepted and has triggered the rapid instrumentation and software developments. GC-TOF-MS has been proven very useful for target screening of organic pollutants in water, pesticide residues in food, anabolic steroids in human urine and xenoestrogens in human-breast tissues as well as non-target screening (Hernández et al, 2011). It has also been successfully applied in metabolomics. As an example, GC-TOF-MS coupled to an APCI source was applied to human cerebrospinal fluid for metabolic profiling (Carrasco-Pancorbo et al., 2009). Moreover, the use of GC×GC coupled to TOF-MS for the metabolic profiling of biological fluids has been discussed in a recent review (Pasikanti et al., 2008). Although it is a very helpful tool, studies have also indicated that the elucidation of unknowns cannot be achieved by following a standardized procedure, as both expertise and creativity are essential in the process (Portolés et al., 2011).

Despite its excellent mass accuracy and sensitivity for qualitative studies, GC-TOF-MS is not as robust as other MS detectors such as triple quadrupoles for quantitation due to its limited dynamic range.

2.1.5 GC coupled with tandem mass spectrometry

The use of capillary gas chromatography coupled with tandem mass spectrometry (GC-MS/MS) can in principle result in a superlative technique in terms of both sensitivity and specificity, as necessary for ultra trace analysis.

For qualitative identification with MS/MS, product ion scan, precursor ion scan and neutral loss with a triple quadrupole or product scan with an ion trap can be used. However, the high-resolution performance of a capillary GC also requires a MS/MS with high scanning speed. Its applications had been limited for a period until the recent decade when the scan speed of a quadrupole has been dramatically improved with an enhanced sensitivity instead of loss. This has greatly extended its applicability for trace unknown identification. For quantification with SRM or MRM, a short dwell time in order to reach sufficient data points for a narrow peak is also required. Improvements on this aspect has been from hundreds milliseconds reduced to a few millisecond for a triple quadrupole instrument. Typical applications are mainly found in contaminations in environment and foods such pesticides

and PCBs in foods and biological samples (Krumwiede & Huebschmann, 2008). A large number of applications of tandem mass spectrometry in GC-ITMS for trace analysis can be found in the literature, for example, in environmental analysis (Santos & Galceran, 2003), microorganism characterisation (Larsson & Saraf, 1997) and forensic analysis (Chiarotti & Costamagna, 2000).

2.1.6 Two-dimensional GC coupled with mass spectrometry (GC×GC-MS)

Nowadays a one-dimensional GC offers a peak capacity in the range of 500-1000 (Mondello et al., 2008). Mass spectrometry already adds another dimension (resolving *m/z* of ions) to enhance GC-MS selectivity. However, it is not surprising that samples (e.g., extracts of natural products or metabolites) containing several hundreds or even thousands of volatile constituents are of common occurrence. With the increasing demands and improvements on sensitivity, many trace components have also to be investigated. The fact is that, in a one-dimensional GC separation, analytes are generally not equally distributed along the whole retention time scale but frequently co-elute. As a result, it is required that the system should have much higher peak capacity than the number of sample constituents in order to accommodate all sample components (Davis & Giddings, 1993; Mondello et al., 2008). It is obvious that comprehensive two-dimensional gas chromatography (GC×GC) can significantly enhance the resolving power of a separation (Liu & Phillips, 1991). Its developments and applications have been reviewed recently (Mondello et al., 2008). With thousands of compounds eluting at any time in both dimensions, MS detector has a superior power over any others with regard to sensitivity and specificity. Since the first application of GC×GC-MS (Frysinger & Gaines, 1999), its potential has been gradually exploited for analysis of petroleum, PCBs and food samples and complex extracts of natural products or metabolites (Dallüge et al., 2002; Pasikanti et al., 2008). The advantages of comprehensive two-dimensional gas chromatography in combination with mass spectrometry include unprecedented selectivity (three separation dimensions with regard to volatility, polarity, and mass), high sensitivity (through band compression), enhanced separation power, and increased speed (comparable to ultra-fast GC experiments, if the number of peaks resolved per unit of time is considered) (Mondello et al., 2008). With the development of interfacing techniques, fast MS scanning and data interpretation/presentation methods, it will become an important tool to uncover the wealth of undiscovered information with respect to the complex composition of samples.

2.2 Gas Chromatography-Fourier Transform Infrared Spectroscopy (GC-FTIR)

For novel structures or new chemical entities, it is possible that no matched reference spectra can be found in MS databases. Manual interpretation of mass spectra requires sound knowledge on organic mass spectrometry and dedicated experience and often not possible to suggest any candidate structures. With the help of the molecular spectroscopy FT-IR, information on functional groups or structure moieties with specific infrared absorptions is complementary to MS and can be very valuable for structure elucidation, as already being used as stand-alone.

After the inspiration of the first reported IR spectrum of a trapped GC peak in 1967 (Low & Freeman, 1967) and the first commercial instrument introduced in 1971 by Digilab, there has been a rapid development of hyphenated GC-FTIR techniques. Commonly for on-line GC-

FTIR coupling, the effluent from the GC flows through a heated transfer-line into the light-pipe. A schematic drawing of a typical GC-FTIR is shown in Figure 2. The interferograms are scanned continuously to record either 'on-the-fly' gas-phase vapour IR spectra or trapped component spectra (Jackson et al., 1993). This makes it possible to reconstruct a chromatogram in real time by a vector technique called the Gram-Schmidt method (Malissa, 1983). After the acquisition is finished, the spectra of each GC peak can be normalized and searched by comparison with an IR spectra library (Hanna et al., 1979; Seelemann, 1982). In the earlier days of this technique, there were many discussions and studies about its sensitivity followed by the possible overloading of the columns when a capillary GC is used. Nowadays a GC-FTIR system having *ng* sensitivity of absolute substance amount has been introduced (Bruker Optics, 2009). GC-FTIR has been applied for analysis of polychlrorinated dibenzo-p-dioxins, dibenzofurans (Sommer et al., 1997), aromatic polymers (Oguchi et al., 1991), petroleum (Scharma et al., 2009), etc., respectively. The combination of a gas chromatograph with both FT-IR and MS detectors on one instrument allows the simultaneous measurement of one peak by two supplementary detections. In fact, at each retention time, two different chromatograms were obtained. The sample passes the IR detector without destruction and is registered by the subsequent MS detector (Sommer et al., 1997).

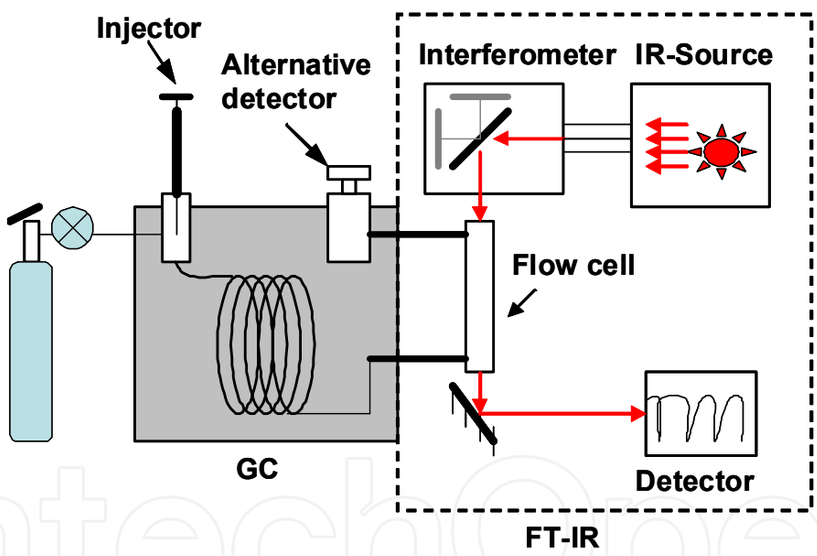


Fig. 2. Schematic drawing of a typical GC-FTIR

2.3 Gas Chromatography-Nuclear Magnetic Resonance spectroscopy (GC-NMR)

Nuclear Magnetic Resonance (NMR) (Rabi, 1938) spectroscopy is considered one of the most powerful analytical techniques for structural elucidation and identification of unknown compounds. It utilizes a physical phenomenon in which magnetic nuclei in a magnetic field absorb and re-emit electromagnetic radiation. Although the most commonly studied nuclei have specific chemical shifts, the abundances of the useful naturally occurring isotopes are generally low. That has significantly limited the sensitivity of NMR. Often mg of pure substance is required in order to obtain a meaningful spectrum. However, organic compounds of synthetic or natural products are often not in the pure form but are found as

mixtures. Normally the analysis of such mixtures is performed in two independent steps: separation of the mixture into individual components and followed by identification. An on-line combination with GC separation can apparently accelerate this study.

The investigation on the coupling of GC and NMR has been very promising development because of the valuable information provided by NMR on molecular structure for each separated component (Buddrus & Herzog, 1981; Herzog & Buddrus, 1984). Unlike liquid or solid samples commonly analysed by NMR, the carrier gas in GC causes experimental difficulties in handling and results in low signal-to-noise ratio of the NMR signals obtained at atmospheric pressure. With the applications of Fourier-transform and averaging techniques, and gases can now be studied at fairly low pressures. However, the recording of the NMR spectra of flowing gases, especially those leaving a gas chromatograph containing only trace amount of analytes, imposes some problems. At short dwell times, the line broadening makes the recording of the spectra nearly impossible. Considerable progress towards overcoming its relative lack of sensitivity has been achieved using microcells for the optimum use of available samples and computers to improve signal-to-noise ratio (Milazzo, Petrakis & Brown, 1968). With the aid of stronger magnets and the newly developed microprobes, the first online GC-NMR spectra was recorded recently (Grynbaum et al., 2007; Kühnle et al., 2008). These experiments revealed the high potential of this technique, but it was also shown that the peaks in the GC separation elute up to 10 min, so that the advantage of the high separation performance of GC was lost in the experiment. The required amount for a GC-NMR run was between 1 and 2 mg for each analyte (Grynbaum et al., 2007). Problems arise in the form of partial condensation in the capillary connections (the transfer capillary and the probe head) for analytes with boiling points above 65 °C. It is suggested that the use of a transfer capillary being heated by a bifilar coil constructed from zero-susceptibility wire in combination with a strong magnetic field may solve overcome this problem (Grynbaum et al., 2007). Using stopped-flow measurements, very low sample amounts (~ 100-300 µg at 400 MHz), the potential applications of the hyphenation of high performance capillary GC to microprobe 1H NMR detection with the help of a spectra database has been demonstrated and an identification of stereoisomers in a complex mixture has been achieved (Kühnle et al., 2008). However, nanograms of volatile small compounds such as cockroach sex pheromones, mosquito attractants as well as a model compound geranyl acetate, which were prepared with an off-line GC, have already been investigated successfully using ^{1}H and COSY NMR (Nojima et al., 2011). Since the hyphenation of enantioselective capillary gas chromatography and mass spectrometry is not always sufficient to distinguish between structural isomers, thus requiring peak identification by NMR spectroscopy. The first online coupling of enantioselective capillary gas chromatography with proton nuclear magnetic resonance spectroscopy has been reported (Künhle et al. 2010). NMR allows constitutional and configurational isomers (diastereomers and enantiomers) to be distinguished. Enantiomers display identical spectra at different retention times, which enable an indirect identification of those unfunctionalized alkanes. Further developments in this field are still highly desirable.

2.4 Hyphenated gas chromatographic techniques for elemental analysis

Hyphenated techniques involving ICP-MS, AAS and AES are among the fastest growing research and application areas in atomic spectroscopy. The preferred chromatographic

separation techniques include GC, HPLC, capillary electrophoresis (CE) and ion chromatography (IC) as well as field flow fractionation (FFF). General procedure for speciation analysis using GC-hyphenation include separation of the analytes from the sample matrix, formation of volatile derivatives, pre-concentration / cleanup and determination using different elemental analysis techniques.

2.4.1 Gas Chromatography - Inductively Coupled Plasma - Mass Spectrometry (GC-ICP-MS)

Stand-alone ICP-MS does not provide information on the chemical structure of the analyte at molecular level since all forms of the analytes are converted to positively charged atomic ions in the plasma. However, as an excellent elemental analyser (ICP) with resolution on masses (MS), ICP-MS can also be used as gas chromatographic detector. Resulting from this hyphenation, target analytes are separated into their constituent chemical forms or oxidation states before elemental analysis. In GC-ICP-MS, where the sample is gaseous, the transfer line should be inactivated and heated to eliminate sample degradation and condensation and will guide the sample directly into the ICP torch. In this way, the sample is maintained at constant high temperature from the end of the chromatographic column in the GC oven to the tip of the ICP injector (Agilent, 2007). It is almost a universal detector (only H, He, Ag, F, Ne cannot be directly measured), fits perfectly with a wide range of GC carrier gases and flows, and is capable of quantification with isotope dilution. A *pg* level of sensitivity can be achieved. The combination of the high performance chromatographic separation and the ICP atomizer also eliminates some interference of co-eluting compounds. For example in organic analysis, it has been used to study trace halogenated solvent residues in edible oils (Gomez-Ariza & Garcia-Barrera, 2006). GC-ICP-MS is very useful technique for speciation analysis such as sulphur speciation (Gomez-Ariza & Garcia-Barrera, 2006) or organometallic speciation (Bouyssiere, 2001; Kresimon et al., 2001).

2.4.2 Gas Chromatography-Atomic Absorption Spectroscopy (GC-AAS) and -Atomic Emission Spectroscopy (GC-AES)

Atomic absorption spectrometry (AAS) is a well-established detection technique in elemental analysis. In AAS, when the UV light with the right wavelength irradiates on a ground-state free atom, the atom may absorb the light to enter an excited state in a process known as atomic absorption. The wavelength of the light is somehow specific for an element. By measuring the amount of light absorbed, a quantitative determination of the amount of analyte element present can be made. A careful selection of wavelengths allows the specific quantitative determination of individual elements in the presence of others. By supplying enough thermal energy (such as in a flame), analyte compounds dissociate into free atoms. The ease and speed, at which precise and accurate determinations can be achieved, have made AAS one of the most popular methods for the analysis of metals.

Atomic emission spectroscopy (AES), also called optical emission spectroscopy (OES), is another elemental analysis technique in atomic spectroscopy. In this process, analytes are first atomized using either ICP or microwave irradiation (high temperatures), where the atoms are raised to electronically excited states. As they return to lower electronic energy levels, photons are emitted at wavelengths that are characteristic of the particular element. Both the wavelength and intensity of the emitted photons will be recorded. This data may

be used to identify the elements present and quantify them after a calibration. GC-AES determines the elemental composition for each GC peak.

The tailored operation condition of a gas chromatograph fits again nicely with the AAS atomizer since the analytes are already present in the gas phase. The coupling can be done by introducing the GC effluent via a heated nickel transfer line into the quartz atomization furnance (Dirkx et al., 1992). Although the interface is rather simple, in practice, several conditions need to be optimized in order to obtain good sensitivity and selectivity for specific analytical problems. Efforts include exploiting the quartz furnace, heating with flame or a thermostat, or using the graphite furnace as the atomization device (Dirkx et al., 1995). The widespread use of organometallic compounds in agriculture, plastics industry and subsequently the release into the environment has led to an increasing concern about their persistence and toxicity. For instance, organotins unlike inorganic tin, it may occur at toxic levels in aquatic and sedimentary environments. The distribution of organotins as well as its bioavailability and toxicity depend critically on the chemical form in which the species are actually present. This is why total tin determination is not able to provide reliable information on the hazards of this element to human health and environment. Therefore, speciation analysis of these organometallic compounds are of great importance (Dirkx et al., 1995). Since its introduction, GC-AAS has been extensively applied to speciation of organometallic compounds such as Sn, Pb and As. Typical examples include speciation of organolead in environment (Baxter & Frech, 1995; Dirkx et al., 1992; Harrison & Hewitt, 1985) and in biological samples (Baxter & Frech, 1995); speciation of organotin compounds in agriculture and plastics industry (Dirkx et al., 1995) as well as arsenic speciation. The reason for the existence of various forms of organometallic compounds is that Sn, Pd and As all have very rich organic chemistry. Just because of this, several derivatization methods have been reported in order to convert them to volatile species for GC analysis and a sensitivity of picogram level can be achieved together with a highly selective detection as the result of the coupling (Dirkx et al., 1995; Harrison & Hewitt, 1985).

As for GC-AES, it has been much less investigated than GC-AAS. Nevertheless, the available reports have indicated that GC-AES coupled with microwave-induced plasma (MIP) can be used to study organic polymers (Oguchi et al., 1991) and to perform speciation analysis of organotin compounds in human urine. This provides a method suitable for rapid sensitive screening of human urine samples without dilution of the sample (Zachariadis & Rosenberg, 2009a, 2009b).

3. Conclusion and remarks

Apparently, the motivation of the enormous efforts on investigating a variety of hyphenated systems is the increasing demands on the wealth of undiscovered information of trace components in a sample. Many stand-alone instrumental analytical techniques are already well developed and able to provide specific information about analytes in samples, although each of them has its advantages and disadvantages. The complexity of real-world sample matrices often exceeds the analytical capabilities of any conventional chromatographic separations. The development and employment of more comprehensive coupling techniques to enable a deeper insight into the composition of natural and synthetic matrices has become a necessity.

The most powerful separation technique in chromatography is still capillary gas-liquid chromatography (one-dimensional or its extension - comprehensive two-dimensional gas chromatography). On the other hand, mass spectrometry including various high resolution MS and tandem MS provides analyte-specific selectivity. Their combination GC-MS is still the most flexible and powerful analytical technique available today for volatile organic substances with many unchallengeable advantages such as unprecedented selectivity, sensitivity, enhanced separation power and speed of analysis (Mondello et al., 2008).

The coupling with other detection techniques further extends the GC applicability. However, the rule of thumb is that the hyphenation of two techniques would only make sense when the analytical powers (separation and detection) of both instruments are enhanced rather than compromised in order to couple. One of the recent good examples is implementation of the very soft ionization APCI interface for GC-TOF-MS (Carrasco-Pancorbo et al., 2009) to generate abundant molecular ions in order to utilize the high resolution and MS/MS capabilities for structure elucidation. Both CI and EI may be too hard to preserve valuable molecular ions. This feature makes this technique very attractive for such as wide-scope screening of a large number of analytes at trace levels. In the future developments, efforts should be put to make hyphenated GC techniques also user-friendly and robust with regard to automatic data interpretation and reporting software, standardized interfaces and even consumables.

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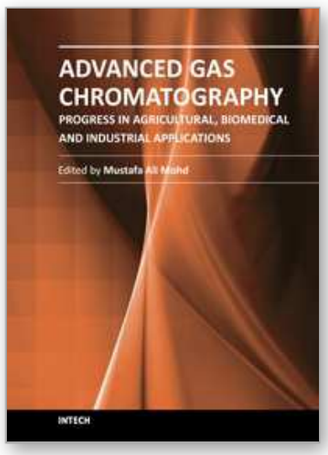
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Progress in agricultural, biomedical and industrial applications' is a compilation of recent advances and developments in gas chromatography and its applications. The chapters cover various aspects of applications ranging from basic biological, biomedical applications to industrial applications. Book chapters analyze new developments in chromatographic columns, microextraction techniques, derivatisation techniques and pyrolysis techniques. The book also includes several aspects of basic chromatography techniques and is suitable for both young and advanced chromatographers. It includes some new developments in chromatography such as multidimensional chromatography, inverse chromatography and some discussions on two-dimensional chromatography. The topics covered include analysis of volatiles, toxicants, indoor air, petroleum hydrocarbons, organometallic compounds and natural products. The chapters were written by experts from various fields and clearly assisted by simple diagrams and tables. This book is highly recommended for chemists as well as non-chemists working in gas chromatography.

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