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CONSTRUCTION OF A SUPERCRITICAL FLUID CHROMATOGRAPH–MASS SPECTROMETER INSTRUMENT SYSTEM USING CAPILLARY COLUMNS, AND A CHEMICAL IONIZATION SOURCE ACCEPTING HIGH FLOW-RATES OF MOBILE PHASE

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SUMMARY

An instrument combining capillary supercritical fluid chromatography (SFC) and mass spectrometry (MS) with chemical ionization is described. Stable experimental SFC–MS conditions were obtained when utilizing a short restrictor at the end of a SFC capillary column, typically a 3 mm × 5 μm I.D. fused-silica capillary tube. The vacuum pumping capacity of the mass spectrometer and the special design of the ion source permitted supercritical fluid flow-rates up to 50 μl/min to be used. Preliminary results obtained with polynuclear aromatic hydrocarbons and various lipids are reported.

INTRODUCTION

Supercritical fluid chromatography (SFC) with capillary columns is progressing rapidly as the method can separate high-molecular-weight and thermally labile molecules with high separation efficiency and short analysis times[1–4]. In addition, the low output flow-rate of mobile phase delivered by capillary columns, typically 2–10 μl/min of liquid mobile phase*, facilitates the coupling of the column to sensitive detectors such as the flame ionization detector or the mass spectrometer[3,4].

While gas chromatography–mass spectrometry (GC–MS) is now a well established technique, some problems are still encountered when coupling liquid chromatography to mass spectrometry (LC–MS), in spite of the development of various types of interfaces[5] such as the direct liquid introduction interface (DLI)[6,7], the moving belt[8] and the thermospray[9]. In SFC, coupling to a given mass spectrometer is easier than in LC–MS because of the much higher volatility of supercritical fluids[4].

Depending on the type of SFC column used, several methods have been de-

* Because of the wide pressure conditions used in SFC, the volumes of mobile phase vary over a wide range. As the fluid is initially pressurized as a liquid in a syringe-type pump, it is convenient to express all fluid volumes in the supercritical state in the capillary column, or in the subcritical state in the mass spectrometer, as the equivalent volume of liquid.

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scribed for interfacing the supercritical fluid chromatograph to the mass spectrometer. With large-bore packed columns, the flow-rate of the mobile phase generally exceeds the tolerance of the mass spectrometer and an enrichment device is required, for instance the jet separator used by Randall and Wahrhaftig[10,11] or the moving belt described by Berry *et al.*[12]. Conversely, microbore packed columns and open-tubular capillary columns can be coupled directly to the ion source. For example, a DLI originally designed for microbore LC–MS was easily adapted for work under supercritical conditions[13]; several possible designs for the direct coupling of capillary columns were described by Smith and co-workers[4,14–18] and application to the analysis and characterization of various non-volatile and thermally labile compounds was demonstrated.

In this laboratory, the direct coupling of capillary supercritical fluid columns to a mass spectrometer with chemical ionization (CI) was investigated because of its apparent simplicity, and in this paper we report the design and construction of a simple interface operating at high flow-rates (*ca.* 30–50 μl/min) in order to minimize dead volume problems in the connections and to avoid plugging of the pressure restrictor.

EXPERIMENTAL

The SFC–MS set-up is shown schematically in Fig. 1 and the construction details are as follows.

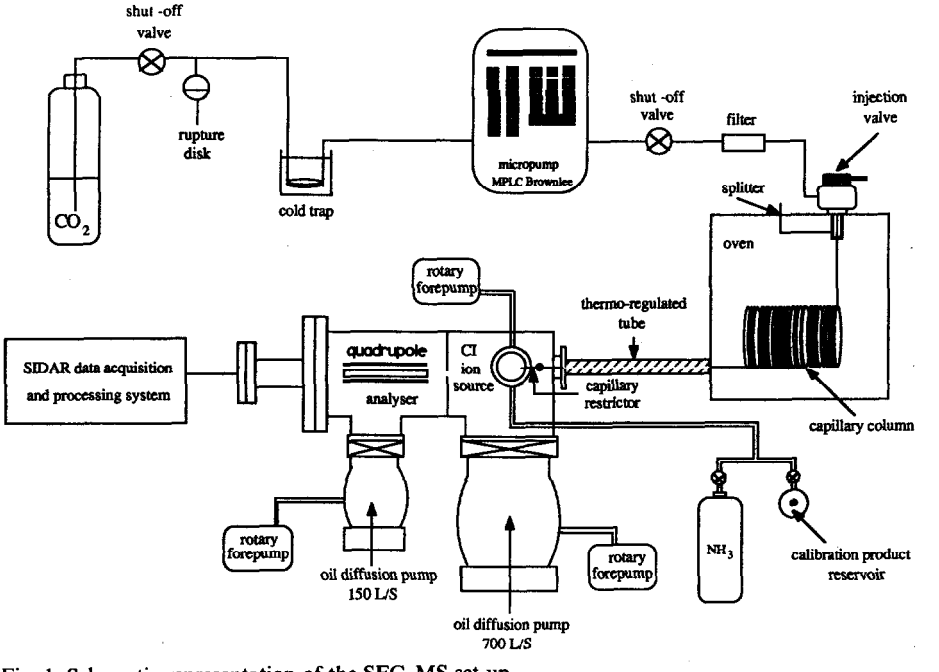


Fig. 1. Schematic representation of the SFC–MS set-up.

SFC instrument

A high-pressure syringe micropump (Brownlee Labs., Santa Clara, CA, U.S.A.) with REV G software delivered low pulse-free flow-rates of mobile phase. Liquid carbon dioxide was supplied from a cylinder with a siphon tube (CO_2, grade N45, Air Liquide, Le Plessis Robinson, France); the bottle was connected directly to the SFC pump, *i.e.*, no pressure regulator was installed at the bottle output. A cold trap kept at −10°C was positioned before the pump and served as a reservoir of liquefied gas; a 100-bar rupture disk was mounted for safety in case of failure of the freezing device, but no rupture has ever been observed since the original installation, *i.e.*, over a period of 1 year. Shut-off valves, an in-line 0.5-μm filter and low-dead-volume unions were obtained from Scientific Systems Inc. (SSI).

The oven into which the fluid temperature is set at or above its supercritical point was built by modifying an old Carlo Erba Model 2150 gas chromatograph equipped with an oven temperature programming unit. A Rheodyne Model 7520 injection valve with a 0.5-μl rotor was mounted on the top panel of the chromatograph. SSI components and the Rheodyne valve were purchased from Touzart et Matignon (Vitry/Seine, France).

The injector was connected to a flow splitter (SGE, Scientific Glass Engineering, Villeneuve St. Georges, France). The splitting ratio was adjusted by installing a length of SGE 10-μm I.D. fused-silica capillary tubing in the exhaust port.

SFC–MS interface

The right-hand panel of the chromatograph was drilled and a 1-cm heating tube (Model P503-1m-NW6, Heraeus, Orsay, France), monitored with a Heraeus Model TFE 5020 temperature controller, was installed between the chromatograph and the SFC–MS interface. This zone was generally kept cold, at *ca.* 60°C, in order to maintain supercritical conditions as near the ion source inlet as possible, even

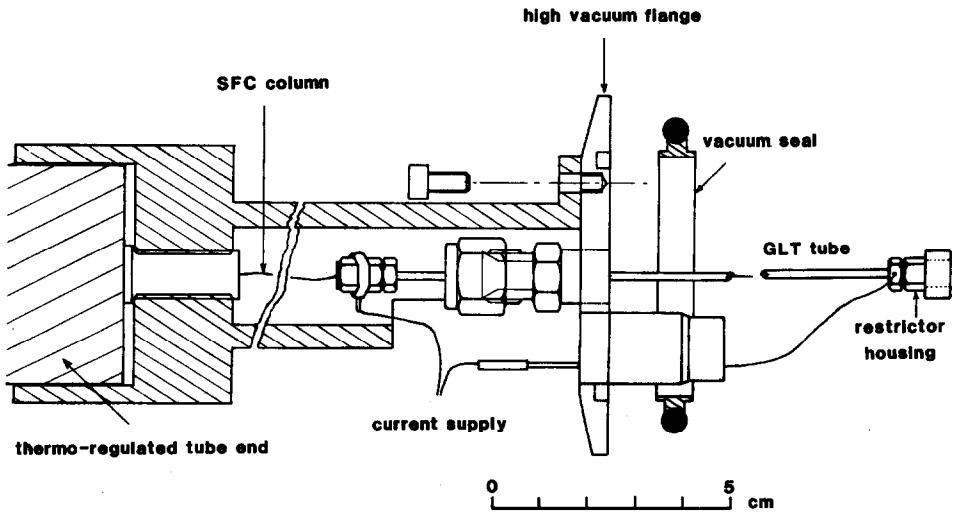


Fig. 2. Details of the SFC–MS interface showing the high-vacuum flange attached to the mass spectrometer.

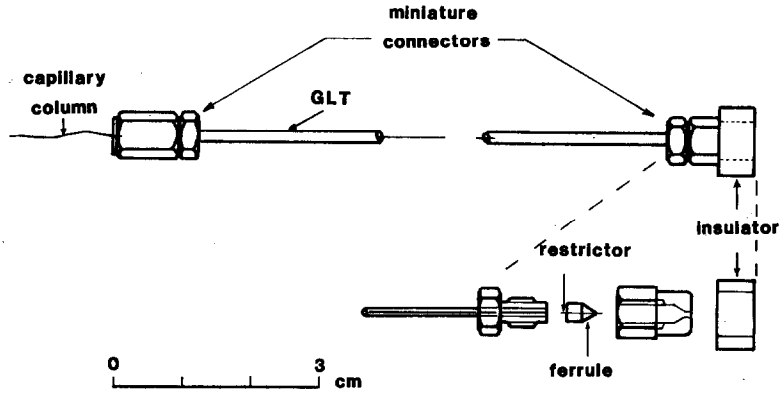


Fig. 3. Capillary column and restrictor positions with respect to the interface.

when the capillary column in the chromatograph oven was held at temperatures above 100°C.

The capillary column was inserted into the Rheodyne valve at one end; the other end was routed through the heating tube, then inside the interface so that the column end was abutted against the nebulizing restriction.

The interface (Figs. 2 and 3) consisted of an SGE 8 cm × 1.6 mm O.D. × 0.5 mm I.D. glass-lined metal tube (GLT), held through the vacuum flange by an insulating 1/4-in. Vespel ferrule drilled to 1.6 mm; thus the tube could be heated directly by supplying an electrical current of 3–4 A across both ends; about two thirds of the tube length and the final restriction were under vacuum and could be heated to 300°C. Both ends of the GLT tube were fitted with low dead volume SGE fittings. The pressure restrictor consisted of a 3 mm × 5 μm fused-silica tube and was installed in the 1/16-in. Vespel ferrule of the SGE fitting as described under Results and discussion.

A Vespel ring was attached to the interface end to make a tight seal to an expansion chamber (Fig. 4). The purpose of the chamber was to reduce the gas pressure of the expanding CO_2 jet before it entered the ion source. It was heated by electrical cartridges in order to compensate for the cooling by the expanding gas jet and was held at a constant temperature by means of an iron–constantan thermocouple and a PID controller.

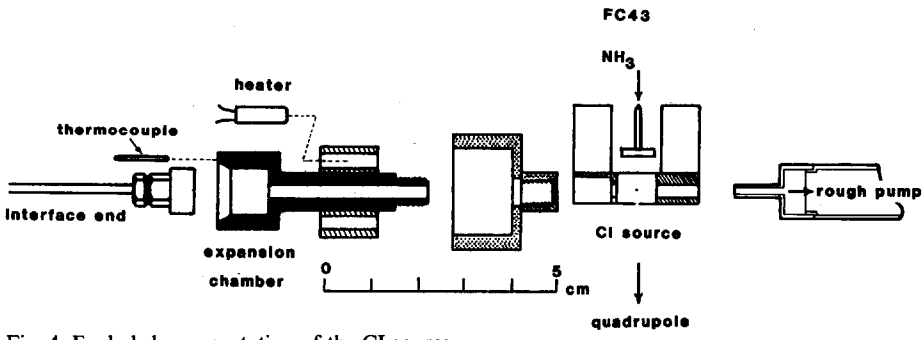


Fig. 4. Exploded representation of the CI source.

Mass spectrometer and ion source block

The mass spectrometer, a Nermag Model SQ 156 quadrupole filter equipped with a standard CI ion source (Nermag, Rueil Malmaison, France), was originally assembled in this laboratory for LC–MS work, and has been described elsewhere[6,19–21]. The vacuum equipment consisted of two separate conventional pumping lines for the analyser and source housing, of 150 and 700 l/s, respectively. An additional 12 m^3/h mechanical vacuum pump was connected directly to the CI source block. It fitted into the opening normally used for introduction of calibration standards, opposite the entrance of the sample solution.

The repeller block at the rear of the ion source (Fig. 4) was modified and connected to a reservoir of heptacosafluorotributylamine for calibration of the data system, and to a bottle of ammonia for CI work. Data were acquired with a PDP-8 computer and a Nermag Model SIDAR data system.

Calibration and tuning of the ionization mode

Calibration of the mass spectrometer was possible under SFC–MS conditions, *i.e.*, in the presence of up to 50 µl/min of liquid CO_2 introduced in the source. The charge-exchange mass spectrum of perfluorotributylamine when ionized by $CO_2^+\cdot$ was identical with its low-pressure electron-impact (EI) spectrum with one exception, the presence of an additional peak at $m/z = 88$ due to the cluster $(CO_2)CO_2^+\cdot$; this value was conveniently included in the calibration table for tuning the data acquisition system.

The amount of ammonia necessary for shifting from $CO_2^+\cdot$ charge-exchange conditions, which produce odd-electron molecular ions and EI-type mass spectra, to chemical ionization with NH_4^+ as primary reagent ions, was determined experimentally by introducing an increasing amount of ammonia until the ion current for the $m/z = 44$ ion vanished to *ca.* 5% of the ion current for $m/z = 18$, as checked in real time on an oscilloscope. Mixed charge-exchange/chemical-ionization spectra were produced by creating an ion source plasma with equal abundances of NH_4^+ and $CO_2^+\cdot$ ions.

Sample solutions and testing conditions

An SGE 5 m × 100 µm I.D. fused-silica capillary column bonded with a polymethylsiloxane stationary phase was connected at one end to the Rheodyne valve, and to the SFC–MS interface at the other end. Solutions of samples of 1 µg/µl concentration were generally prepared in dichloromethane. Solution volumes of 0.5 µl were injected using the valve. When the injection splitter was in use, the splitting ratio was held at approximately 1:3.

At CO_2 pressure and temperature of 250 bar and *ca.* 60°C, respectively, samples were not retained by the column, so the retention time was equal to t_0, i.e., solute mass spectra were recorded 3–4 min after injection.

Rapid separations of polynuclear aromatic hydrocarbons (PAHs) and fatty acid methyl esters were achieved by rapid pressure programming from 100 to 250 bar in 7 min. Separations were optimized by varying the column temperature; for the solutes studied, an increase in the column temperature resulted in a longer retention time.

RESULTS AND DISCUSSION

Vacuum requirements inside the mass spectrometer

The vacuum pumping of a conventional chemical ionization (CI) mass spectrometer can accept 2–10 μl/min of organic liquids[19], or higher for a specially modified mass spectrometer. The freezing point of CO_2 being at −56.6°C, a cryopump chilled at a lower temperature could be introduced around the ion source, as was done in early DLI experiments[19], but it is more convenient to increase the vacuum pumping by attaching a rough pump to the ion source block[6,9].

The requirements for the performance of the vacuum pumping equipment in LC–MS and SFC–MS are the same. The important difference is that the heat energy coupled to the fluid for its vaporization is considerably reduced in SFC–MS. In LC–MS, both the latent heat of vaporization and compensation for the expansion of the gas jet must be provided. Heat transfer under a vacuum is very inefficient, and becomes impossible when liquid flow-rates around 1 ml/min are introduced into an ion source, so the heat must be supplied before expansion of the jet, as done in a thermospray experiment[9]. In SFC–MS, the fluid expands naturally and only the cooling resulting from the expansion of the jet must be compensated for. For a CO_2 flow-rate of 50 μl/min, supplying *ca.* 10 W of electrical power to the heaters of the expansion volume was sufficient to keep the temperature at 260°C. The CI source block temperature was kept at a lower temperature than that of the expansion chamber, generally 220°C.

With our quadrupole MS system, the upper tolerable CO_2 flow-rate was limited by two factors: the sensitivity, which was reduced when the CO_2 flow-rate was increased, and more important, the mass range. When the gas pressure in the MS source housing increases, loss of sensitivity affects heavy mass ions preferentially. The solute ion beam from the source is scattered by collisions with residual CO_2 molecules, but as ions exit from the ion source with nearly constant kinetic energies, high-mass ions travel slower and remain a longer time in the drift space between the ion source and the quadrupole entrance, so they have more chance of undergoing a scattering collision with a molecule of residual CO_2.

At a CO_2 flow-rate of 50 μl/min, the ion transmission was not affected for ions of $m/z \leqslant 600$ u, the normal usable mass range of our old machine. At a CO_2 flow-rate of 100 μl/min, although the mass spectrometer could be turned on, ions of $m/z \geqslant 300$ u were not detected; we expect that by optimizing the potentials applied to the ion optics, ion transmission at flow-rates up to 200 μl/min could be increased significantly.

The pressure restrictor

Several recent studies have emphasized the importance of the geometry of the restrictor placed at the end of the capillary column and which provides the necessary pressure drop between the high pressure into the capillary column and the vacuum into the MS ion source. The minimum pressure drop is of 70 bar with CO_2. The capability of transmitting non-volatile substances into the vacuum side depends strongly on the abruptness of the pressure drop; the relative merits of diaphragms[14], straight and narrow capillaries[22], pinched or drawn capillaries[14,23] and metal frits[24] have been discussed and ingenious devices for making reproducible restrictions have

been described[23,25]. In general, the choice of a given type is a compromise between several factors: ease of construction, cost, facility of replacement, lifetime before partial or total plugging and ability to transmit non-volatile solutes.

Short and narrow fused-silica capillaries of 5 μm I.D. were selected as they are cheap and readily available. However, straight and uniform tubes are not entirely satisfactory as the pressure drop occurs along a relatively long distance, so a procedure for making more suitable restrictors was conceived, as follows.

A *ca.* 3 mm long piece of 5 μm I.D. tubing was cut and inserted into a 1/16-in. graphitized Vespel ferrule drilled to 0.5 mm. The ferrule was inserted into the SGE compression fitting at the interface outlet. This fitting differs from other commercially available miniature connectors in that the ferrule is in a reverse position. To begin, the fitting was tightened so that the capillary tube was immobilized, then a constant flow-rate of 50 μl/min of CO_2 was pumped through the restriction. Next, the fitting was further tightened until a pressure drop of 250 bar was developed as monitored on the pressure gauge of the Brownlee pump, recalling that the pressure drop across a 5 m × 100 μm I.D. tube is negligible compared with that across the restrictor. Fused-silica tubing is malleable, and tightening the fitting squeezes the graphitized Vespel ferrule, which in turn pinches the fused-silica tube. As the conical ferrule is in a reverse position, squeezing takes place at the restrictor end facing the vacuum side.

Installation and calibration of a new restriction could be effected in a few minutes, and the procedure was considered to be easy and reproducible. It was used at column pressures up to 280 bar; the upper pressure limit that would destroy or expel the restrictor from the ferrule was not determined.

Total plugging of the restriction during experiments described below was never observed, but changes in permeability due to sudden partial plugging occurred occasionally. This means that under common SFC conditions, *i.e.*, at a regulated head pressure of CO_2, the fluid flow-rate and the CI source pressure may vary, thus affecting the reproducibility of chromatographic retention times and ion abundances. Although the restrictor dimensions and the operating flow-rates were chosen in order to minimize these drawbacks, they were not entirely eliminated. Nevertheless, the possibility of sampling to the MS ion source at up to 50 μl/min covers all practical SFC conditions when utilizing capillary columns with internal diameters $\leqslant 100$ μm, and is an important advantage as also recently emphasized by Smith and Udseth[4].

Direct injection of non-retained solutes

The interface capability for transferring non-volatile solutes to the CI source was evaluated by injecting model substances under supercritical conditions producing no column retention (Figs. 5–9).

The direct injection at 250 bar and 60°C of 500 ng of coronene (boiling point 565°C under atmospheric pressure), in solution in dichloromethane, produced sharp ion current profiles (total ion current and selective ion current for m/z 300 u) with no tailing rear edges (Fig. 5). Mass spectra were scanned in 3 s, so the sample was eluted after 3 min and the baseline peak widths in Fig. 5 correspond to *ca.* 10 s. The charge-exchange $CO_2^{+}\cdot$ mass spectrum showed molecular species corresponding to the odd-electron ion $M^{+}\cdot$.

The possibility of rapid switching from charge-exchange $CO_2^{+}\cdot$ to NH_4^{+} CI

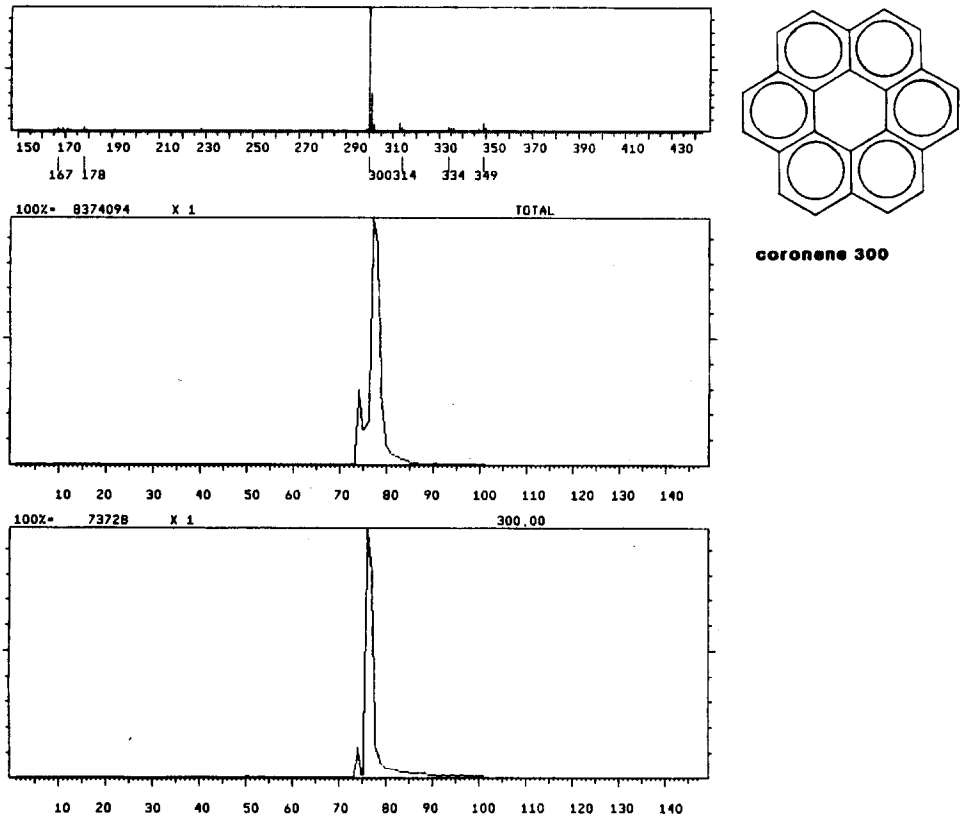


Fig. 5. $CO_2^{+\cdot}$ charge-exchange mass spectrum and ion current profiles from the injection of 500 ng of coronene in 0.5 μl of dichloromethane at a CO_2 pressure and temperature of 250 bar and 60°C. MS scan time and SFC retention time, 3 s and *ca.* 3 min, respectively.

was evidenced during the analysis of a mixture of two triglycerides (Fig. 6). Injection at 270 bar and 70°C coeluted the samples after 2 min, using a more permeable restriction than in the previous analysis. Peak widths at the baseline were 6 s, with no significant tailing rear edges.

The pure charge-exchange $CO_2^{+\cdot}$ mass spectrum (Fig. 7) of the non-separated mixture only shows ions corresponding to the loss of one acyl unit from the non-visible $M^{+\cdot}$ ion: a typical fragmentation under conventional EI conditions. Conversely, abundant MNH_4^+ adducts, giving molecular weight information, were formed when ammonia was added to the CI source (Fig. 7).

A mixture of polyethylene glycol oligomers, of average molecular weight 400, was injected under the same conditions as the triglycerides and eluted as a single peak. Ion current profiles for all molecular ion species, up to m/z 520 u, again were without tailing rear edges. The ammonia CI spectrum (Fig. 8) shows abundant $(MH)^+$ and $(MNH_4)^+$ ions for the different oligomers, with peak abundances compatible with the estimated distribution pattern of the oligomer mixture of average molecular weight 400.

Repeated injection of 500 ng of phenanthrene (Fig. 9) revealed some small variations. These are assumed to arise from a poor injection technique, as also revealed during the separation of simple mixtures (see below). The total current trace mostly consists of ion currents from ionization of dichloromethane, the solvent for the phenanthrene solution injected on to the capillary column and which elutes at the same time as the solute. Peak shape similarity for the total ion trace and the m/z 178 ion trace indicates that the variation in absolute peak areas is due to non-reproducible injection volumes. This is probably because no splitting or a low splitting ratio was selected for preliminary experiments, and the problem needs to be further investigated.

Rapid separation of simple mixtures

A synthetic mixture of equal amounts (125 ng) of four PAHs with 3–5 aromatic rings, including phenanthrene, chrysene, benzacridine and dibenzacridine, was analysed at 100°C and 100 bar for 3 min, then under a programmed CO_2 pressure from

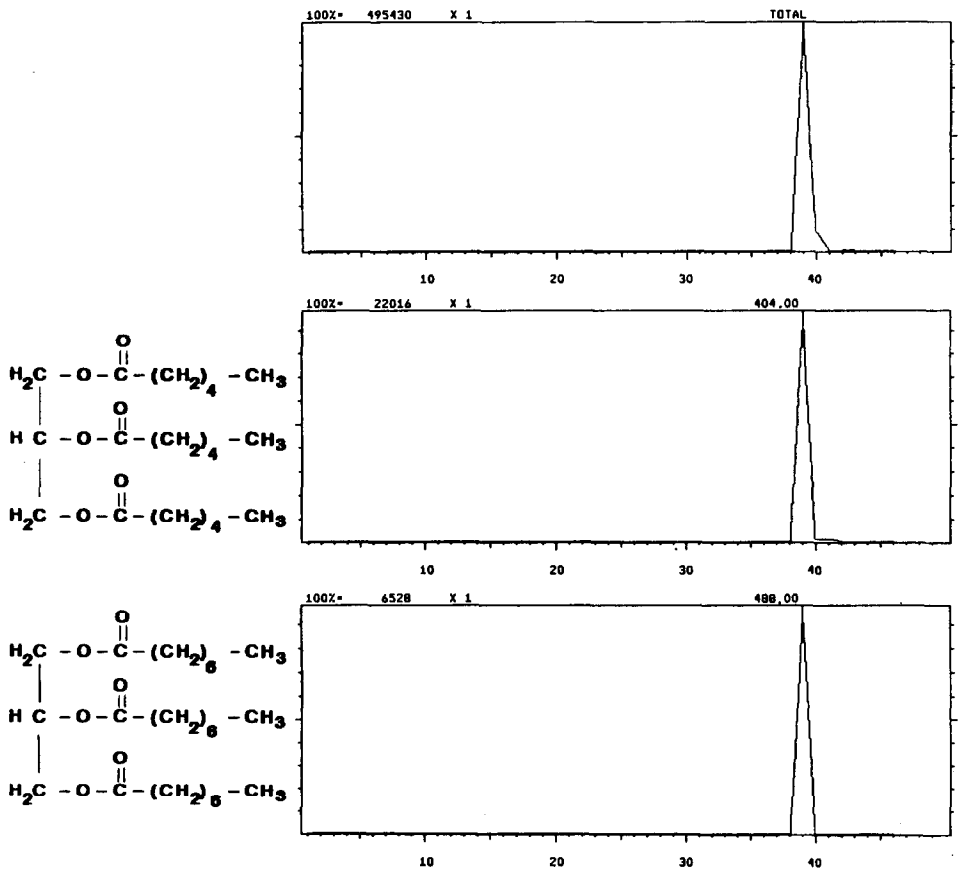


Fig. 6. Ion current profiles showing rapid elution of a non-separated mixture of glyceryl trihexanoate (250 ng, M = 386) and trioctanoate (250 ng, M = 470) when injected at 270 bar and 70°C.

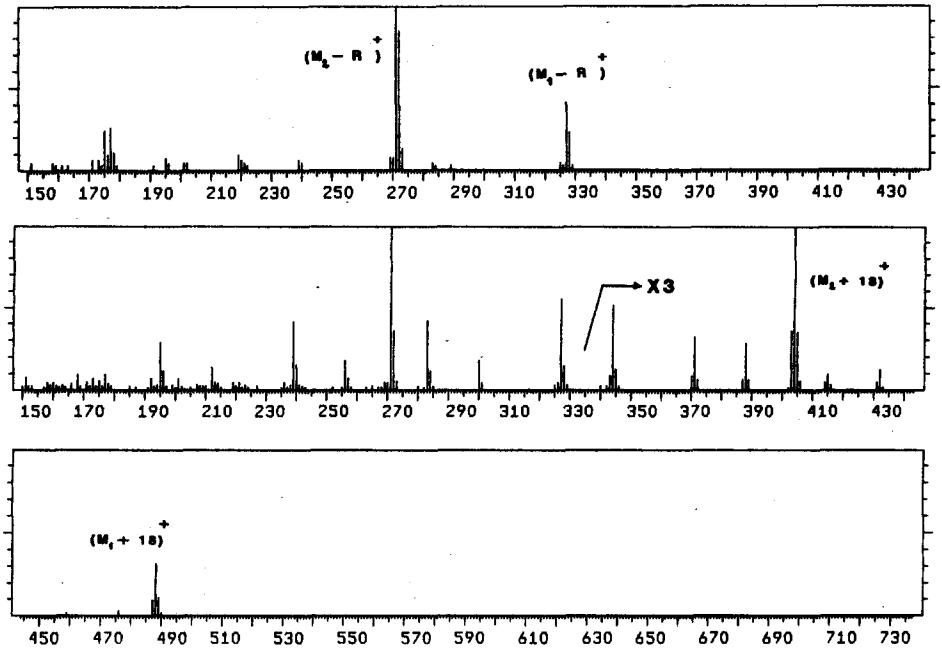


Fig. 7. Pure $CO_2^+\cdot$ charge-exchange (top) and mixed ammonia CI/$CO_2^+\cdot$ charge-exchange (bottom) mass spectra recorded during elution of the triglyceride mixture, depending on the gas composition entering the CI source.

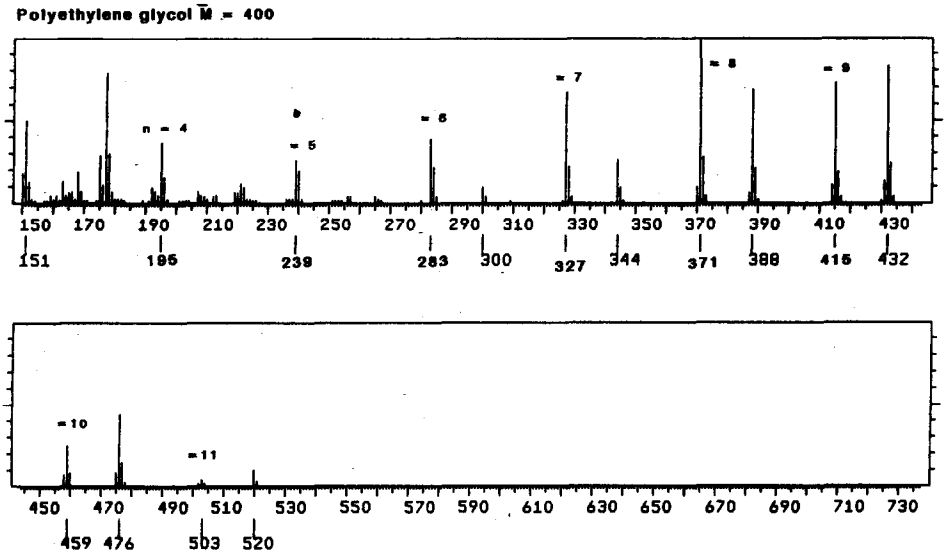


Fig. 8. Ammonia CI mass spectrum recorded during the rapid elution of a PEG 400 sample. SFC conditions as in Fig. 6. The number on top of peaks at m/z = 195 + n44 is the MH^+ for the oligomer with n ethylene glycol units. Series at m/z = 300 + n44 are the ammonia clusters MNH_4^+.

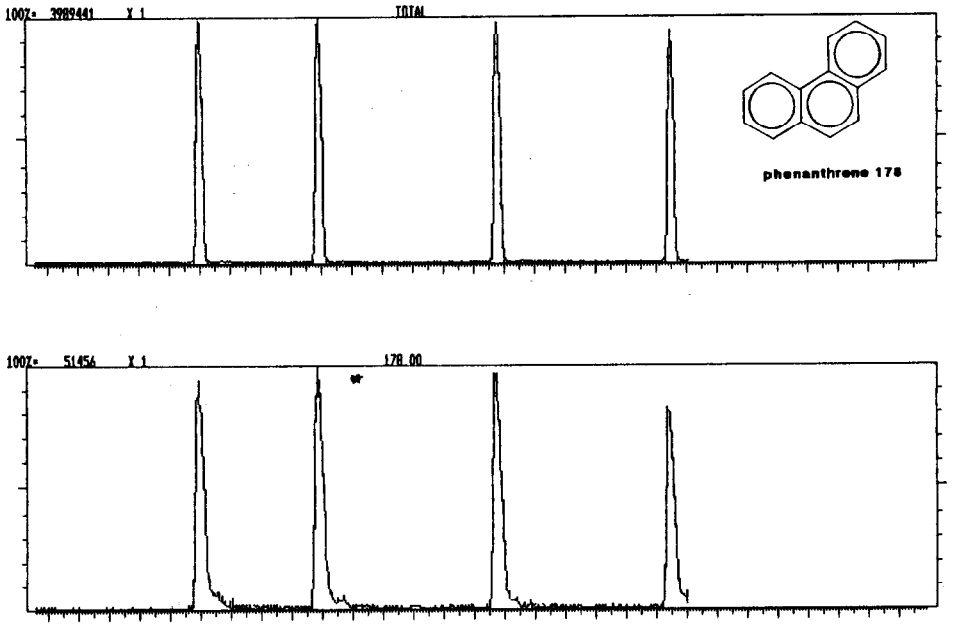


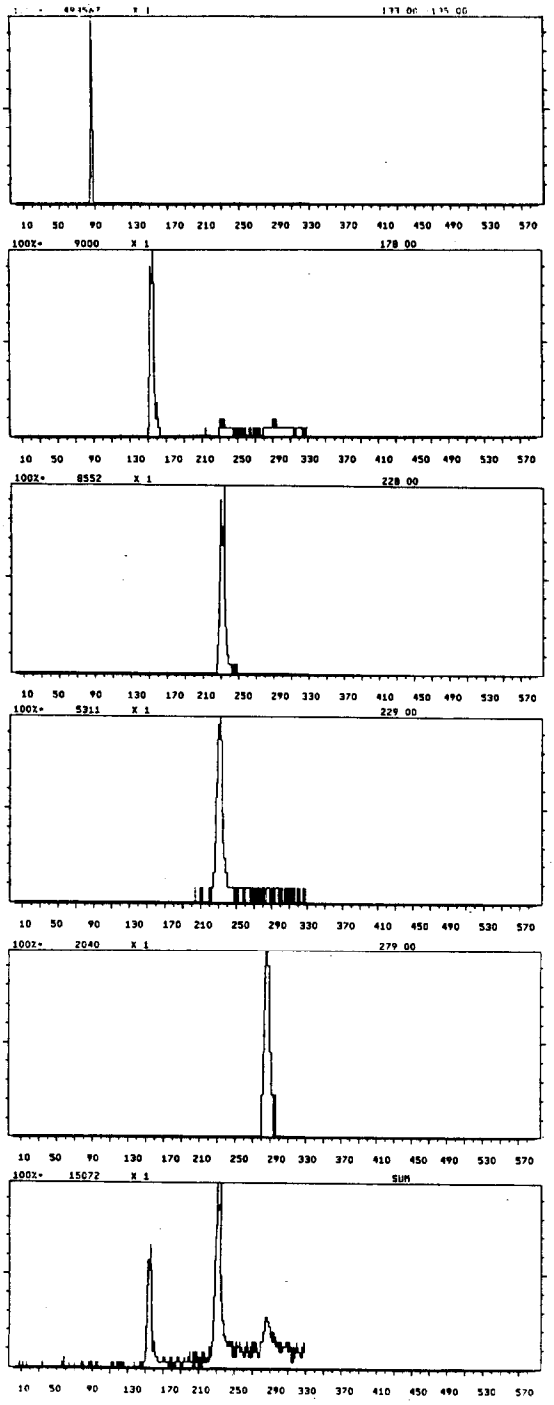
Fig. 9. Signals for total ion current and $M^{+\cdot}$ ion during repeated injections of 500 ng of phenanthrene in 0.5 μl of dichloromethane. SFC conditions as in Fig. 6.

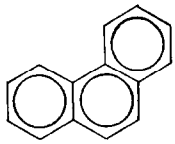
100 to 250 bar in 7 min (Fig. 10). The scan time was 3 s and the total analysis time was 10 min. The peak eluting after 3 min, being the signal for ions in the mass range 133–135 u, is due to unretained dichloromethane from the injected solution and is an indication of t_0. The solvent molecules undergo a series of ion–molecule reactions in the high-pressure MS source ending in the synthesis of $(CH_2Cl_2 \cdot CHCl_2^+)$ cluster ions.

Chrysene and benzacridine, the two four-fused-ring PAHs, were, as normally expected, not separated by the short capillary column. Mass spectra for phenanthrene and dibenzacridine are simple $CO_2^{+\cdot}$ charge-exchange mass spectra (Fig. 11). Assuming identical ionization cross-sections by $CO_2^{+\cdot}$ for the four PAHs, peak areas of the three peaks should be in the ratio 0.63:1:0.4, a result in agreement with the experimental relative peak heights of 0.65:1:0.15, the dibenzacridine peak being broader than the two early eluting peaks.

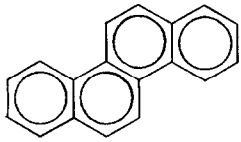
The result compares favourably with similar SFC–MS determinations of polyaromatic substances[14,15] and confirms the high potential of this technique for solving increasingly important analytical problems, in particular for heavy crude oils and environmental analyses.

Under similar SFC conditions, a synthetic mixture of 125 ng of each of three fatty acid methyl esters with 12, 14 and 18 carbon atoms was deposited on top of the capillary column. A constant pressure of ammonia was introduced directly into the MS source to produce CI conditions. On the other hand, the CO_2 flow-rate into the source increased continuously as a result of the pressure programming of the mobile phase. The reconstructed chromatographic information obtained from mass spectral

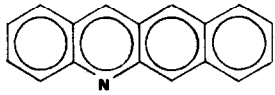




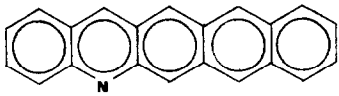
phenanthrene 178



chrysene 228



benzacridine 229



dibenzacridine 279

Fig. 10. Rapid separation of a PAH mixture (125 ng each) at 100°C on an SGE 5 m × 100 μm I.D. fused-silica capillary column bonded with a polymethylsiloxane stationary phase. The CO_2 pressure was constant at 100 bar for 3 min, then programmed to 250 bar in 7 min. MS scan time, 3 s.

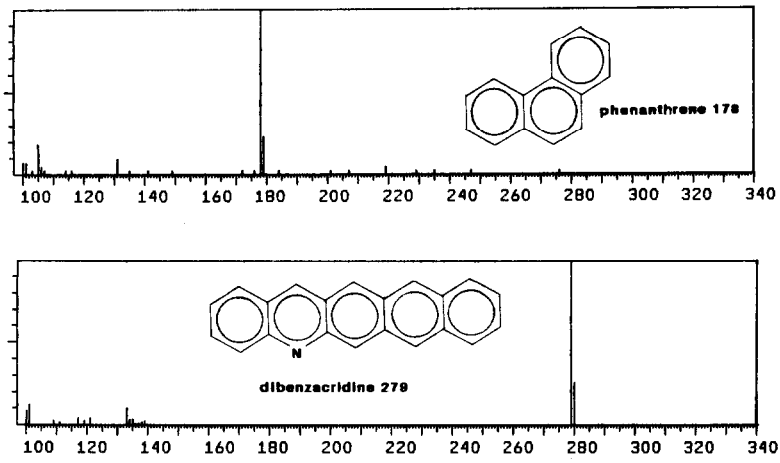


Fig. 11. Pure $CO_2^+\cdot$ charge-exchange mass spectra for the first and the last peak taken during the analysis in Fig. 10.

data (Fig. 12) indicate that the rapid separation on a short column was possible, but double peaks were obtained owing to an incorrect injection with a too low splitting ratio.

Mass spectra (Fig. 13) reveal that they result from two competitive ionization mechanisms: ammonia CI (producing MH^+ and MNH_4^+ ions) and charge-exchange $CO_2^+\cdot$ ionization (forming $M^+\cdot$). The odd-electron molecular ion dissociates to produce typical fatty esters fragments [the $(M-31)^+$ and $(M-43)^+$ ions] as also observed under conventional EI conditions. The relative abundances of the $M^+\cdot$ over MH^+ ions reflect the pressure changes in the MS source: as the partial pressure of CO_2 increases because of the pressure programming, the contribution of the charge-exchange ionization mechanism increases, while the CI conditions remain constant. Note that the initial ammonia pressure could have been set such that at the end of the programme the preponderance of the CI mechanism would be maintained.

An important consequence is that mixed ionization mechanisms, producing both molecular weight information and structure-related fragments, are easily achieved under SFC–MS conditions. The advantages of dual mechanisms in MS had been advocated several years ago by Arsenault[26]: gaseous mixtures combining a charge-exchange reagent (*e.g.*, argon, nitrogen monoxide) and a proton donor (*e.g.*, methane, isobutane or ammonia) had been used successfully, but nevertheless the method did not gain wide acceptance in laboratories. In SFC–MS, switching between ionization mechanisms or setting mixed ionization modes is easily achieved. This may revive new applications of mixed-ionization modes for structure elucidation by MS.

The fatty acid methyl ester analysis also reveals a drawback of pressure programming in SFC–MS: the ion source pressure varies, and consequently the transmission of high mass ions and the overall detection sensitivity during the analysis may be affected, and the ionization mechanisms could change, depending on the CO_2 and NH_3 partial pressures.

It is sometimes said that SFC–MS with CO_2 produces EI mass spectra at will. This is not absolutely true for direct fluid injection SFC–MS. Ionization always re-

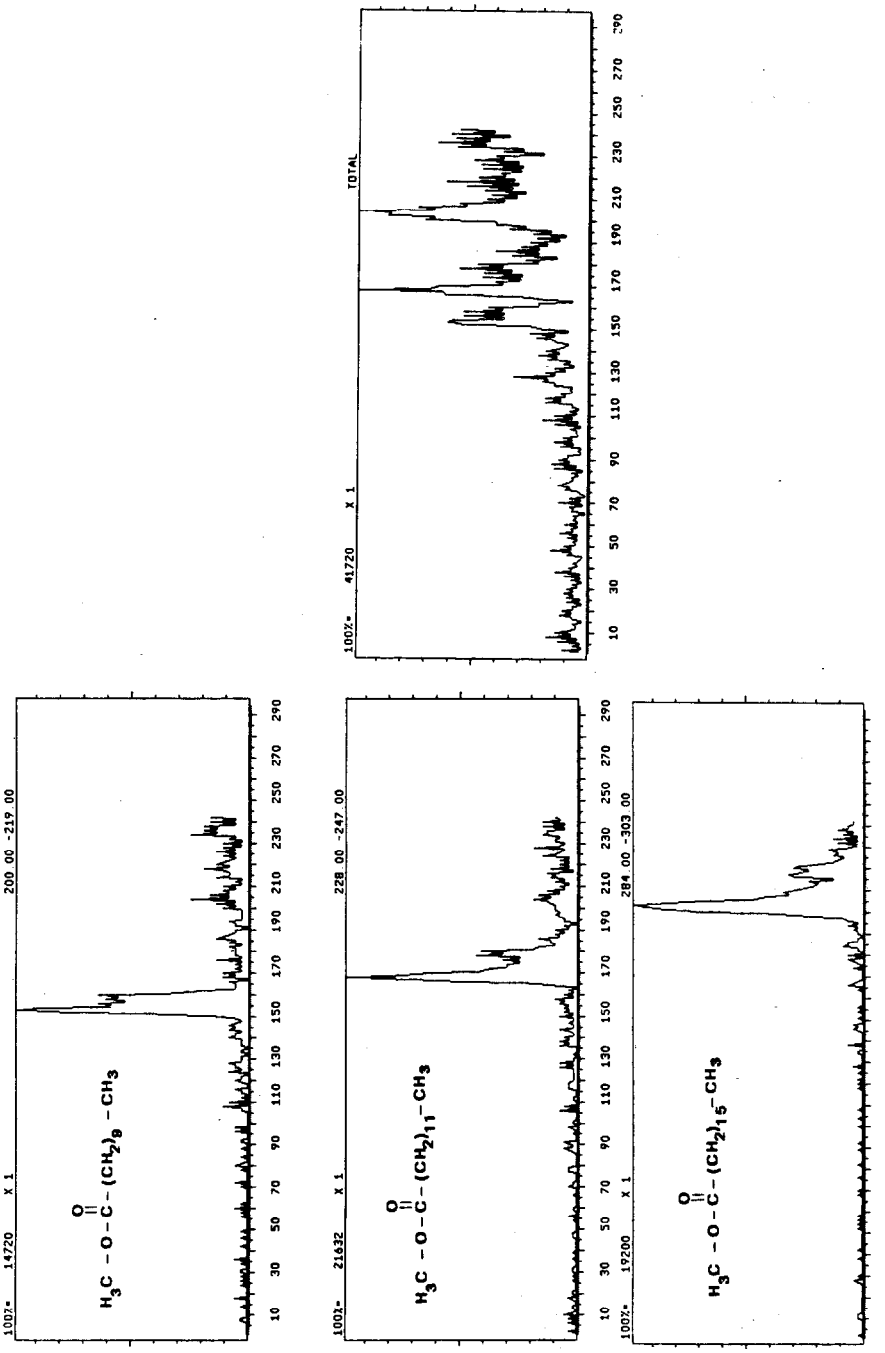


Fig. 12. Rapid separation of a fatty acid methyl ester mixture analysed under same SFC conditions as in Fig. 10.

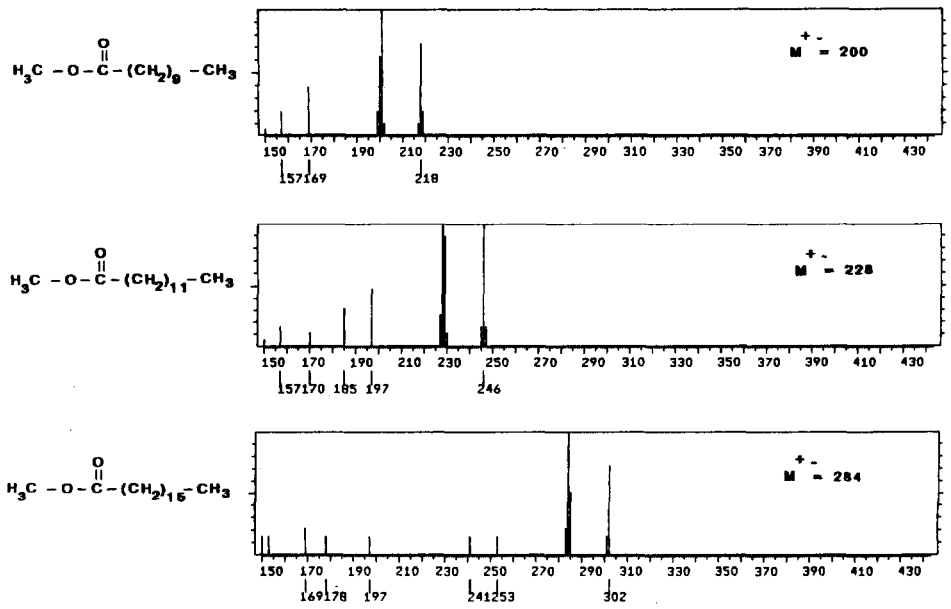


Fig. 13. Mixed ammonia CI/$CO_2^{+\cdot}$ charge-exchange mass spectra recorded during the analysis in Fig. 12. Changes in the ratio of the $M^{+\cdot}/MH^+$ ions, as a function of the peak elution order, reflect the evolution of the gas composition in the CI source during mobile phase pressure programming.

sults from chemical ionization mechanisms, *i.e.*, ion–molecule reactions with second-order or pseudo-first-order kinetics. Although charge-exchange ionization using pure CO_2 produces odd-electron molecular ions, as under EI, molecular ions are presumably formed with lower internal energies and may dissipate a fraction of it by collisions with neutral molecules in the high-pressure ion source. It is verified that charge-exchange CO_2 spectra and true electron-impact spectra show a great similarity, but minor qualitative and quantitative differences are observed as a function of the CO_2 pressure in the source. Mass spectral acquisition parameters are then more or less linked to conditions selected for the supercritical fluid chromatography, although the dependence is not so strong as, for instance, in thermospray LC–MS.

Comparison with other SFC–MS interfaces

With the exception of the moving belt interface used by Games's group[12], direct coupling using capillary columns, as pioneered by Smith and co-workers, is universally investigated: although the moving belt interface accepts the full eluent from a wide-bore SFC column[27–29], it has some limitations for the transmission into the ion source of high-boiling solutes and direct coupling is probably more suitable for their analysis.

The pressure restrictor made from a squeezed short fused-silica capillary tube is an improvement over a pinched capillary metal tube, a laser-drilled diaphragm or a drawn fused-silica or glass capillary tube[14–18]. They were easily installed or replaced with a good performance reproducibility. However, the high mass limitation imposed by our mass spectrometer has prevented the investigation of very involatile sub-

stances and a complete evaluation of the restrictor performance remains to be carried out.

From the beginning of this work, we chose to design a system operating at a high gas throughput across the ion source, in order to encompass the largest interval of possible gas flow-rates delivered by a SFC column, making possible the use of either a wide-bore (*ca.* 100 μm I.D.) capillary column or a 0.5–1 mm I.D. packed column, as they offer a higher peak capacity and pose less difficult injection problems. A higher tolerable gas flow-rate also implies the use of a more permeable flow restrictor that is less prone to plugging. The same approach was recently followed by Smith and Udseth[4], whose results appeared during the preparation of this paper. However, their system differs in that the additional pumping line, which permits the introduction of a higher gas throughput, is located prior to the ion source entrance, whereas our evacuation line is attached after the source, so ionization is produced in our system at a much higher source pressure, which is an apparent disadvantage for an old quadrupole because of the high mass limitation.

Nevertheless, the basic instrumentation used in this laboratory is similar to a LC–MS thermospray set-up working at a high source pressure, and such a design offers the possibility of delivering high-mass ions to the MS analyser on modern instruments. As these systems are already present in several laboratories, this could stimulate the rapid development of SFC–MS. It is probable that employing ionizing electrons of kinetic energy higher than 100 eV or a stable Townsend discharge, as is now currently done in LC–MS, will also increase the overall SFC–MS instrument performance.

CONCLUSION

The conversion of an LC–MS mass spectrometer into an SFC–MS instrument is not particularly difficult, but we are aware of minor imperfections in our machine that will be corrected in the future. The instrumental conditions showed a great similarity with DLI experiments carried out in the past in this laboratory. However, we found SFC–MS easier to run routinely: plugging problems were minimal; preparation of the instrument before or after SFC–MS runs took a much shorter time: rapid pressure oscillations in MS, frequent in DLI, were never observed in SFC–MS. These advantages had been observed by other workers who investigated SFC–MS after LC–MS[4,12–14] and are an important aspect for future developments as more and more examples of superior chromatographic separations using SFC instead of HPLC are published[27–29].

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