Journal of Chromatography, 394 (1987) 231–237
Elsevier Science Publishers B.V., Amsterdam — Printed in The Netherlands

CHROM. 19 489

IMPROVEMENTS IN INSTRUMENTATION FOR THERMOSPRAY OPERATION ON A MAGNETIC SECTOR MASS SPECTROMETER

J. R. CHAPMAN* and J. A. E. PRATT
Kratos Analytical Instruments, Barton Dock Road, Urmston, Manchester M31 2LD (U.K.)

SUMMARY

Changes in the design of a thermospray liquid chromatography–mass spectrometry ion source can be made to improve the sensitivity towards solute related ions and therefore extend the practical utility of the complete system. The addition of a discharge ionization facility provides much greater scope for gradient elution analyses and forms the basis of a method which offers increased structural information. All of these changes are illustrated by practical examples.

INTRODUCTION

The thermospray process[1] has become established as an important practical method for interfacing a liquid chromatograph to a mass spectrometer that is suitable for both magnetic sector[2] and quadrupole[3] instruments. It is obviously desirable that a mass spectrometer used in this way, just as any other liquid chromatographic (LC) detector, should respond to as wide a range of analytes as possible and should limit the range of eluents that can be used as little as possible since these features are both major advantages of LC as a separation process.

Fig. 1 is a schematic view of a thermospray ion source used with magnetic sector mass spectrometers. For the experiments described in this paper the mass spectrometer was a sector instrument of conventional double focusing geometry (Kratos MS25). Liquid flow from the liquid chromatograph is converted to a directed jet of small droplets by spraying from a narrow bore, resistively heated, stainless-steel capillary housed in a probe (A). As these droplets are further desolvated within the source block sample ions can evaporate from very small droplets which contain an added electrolyte such as ammonium acetate. This is thermospray ionization. Since ionization is an in-solution process, which does not rely on evaporation of the sample to provide a suitable vapour pressure prior to ionization, there is every reason to believe that less volatile compounds should give a similar quantitative response to volatile compounds with a similar chemical structure. In initial tests with polyethylene glycol as an analyte, however, it was found that this desirable state of affairs did not exist so that, until modifications were made to the ion source, the response to higher-molecular-weight components of any polyethylene glycol fraction was somewhat less than to the lower-molecular-weight components.

0021-9673/87/$03.50

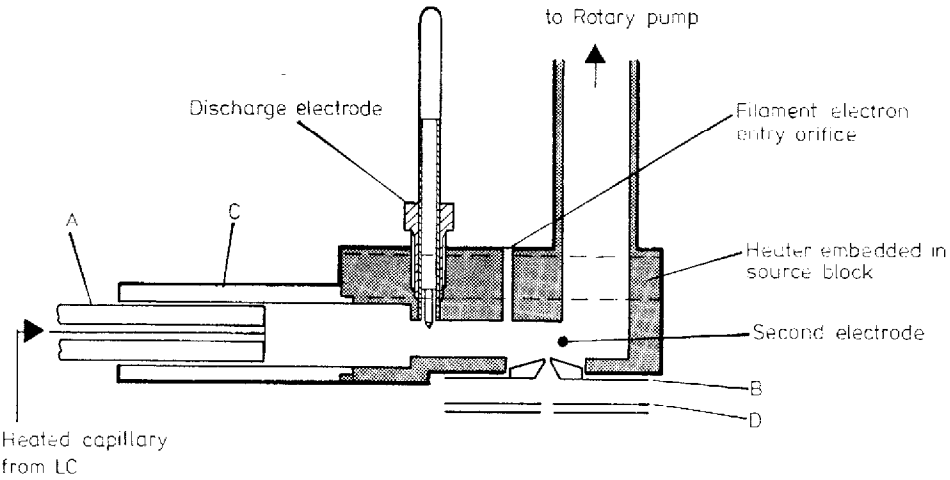

Fig. 1. Schematic of a thermospray ion source.

EXPERIMENTAL

Mass spectra were acquired using a Kratos Analytical LCMS25 mass spectrometer equipped with a thermospray interface and glow discharge accessory. The instrument was operated at a mass resolution of approximately 1500 (10% valley definition). Solvent delivery was made by a Kratos Analytical SF400 LC pump. Solvents used are described in the figure legends. Solvent gradients were produced using a Kratos Analytical SF430 low-pressure gradient former. Solvents used were all HPLC grade. Samples of polyethylene glycol 1000, erythromicin, gramicidin S and caffeine were obtained as GPR standard materials.

Spectra of polyethylene glycol 1000, erythromicin and gramicidin were obtained by loop injection of unseparated samples into the solvent flow. Electrode induced fragmentation experiments were carried out using a continuous flow of caffeine solution. The liquid chromatographic–mass spectrometric (LC–MS) analysis of polyethylene glycol 1000 used a 15 cm × 4.6 mm I.D. column packed with 5-μm Spherisorb C_{18} particles (Phase Separations).

The thermospray source block temperature was maintained at 250–300°C whilst the probe tip (spraying) temperature was optimised on background ions prior to each analysis (typical temperature 175°C for the analyses shown).

RESULTS AND DISCUSSION

The most effective modifications leading to a uniform response throughout the whole mass range were a re-design of the ion exit plate (B, Fig. 1) and an increase in the length of the copper adaptor (C) to ensure that the ion source was gas tight other than the inevitable leakage via the ion exit orifice. An increase in the length of the copper adaptor also allowed the probe to be optimally positioned further back from the ion exit orifice where it could more easily be maintained at an optimum spraying temperature whilst increasing the source temperature sufficiently to provide

effective desolvation within the source block. The provision of a gas tight source and an elevated source temperature led to spectra which showed the correct molecular weight distribution for polyethylene glycol (Fig. 2).

An increase in source gas tightness provides further benefits since a direct result of increased gas tightness is a reduction in source housing pressure with a consequent reduction in the loss of sample ions by ion–molecule collisions in this area. With a similar aim, a change to the ion extraction optics of the thermospray source allows ions to drift out of the source up to plate D by which stage the very high pressure encountered just after the ion exit orifice has been mostly dissipated. Full acceleration of the ions then occurs only from plate D so that the incidence of energetic ion-molecule collisions which may result in fragmentation is considerably reduced.

The reduced source housing pressure and changes in ion extraction optics lead to an improvement in sensitivity throughout the mass range. A further improvement in source design which leads only to a reduction in fragmentation is also possible. This improvement involves a change in the profile of the conical ion exit plate (B) so that the ion exit orifice is now moved away from its original position on the axis of the thermospray probe. It is believed that this modification leads to a reduced possibility of condensation and re-evaporation of sample from the surface of the cone which in turn minimises the incidence of thermally induced fragmentation. As a result of the ion source modifications detailed above, spectra which show good molecular

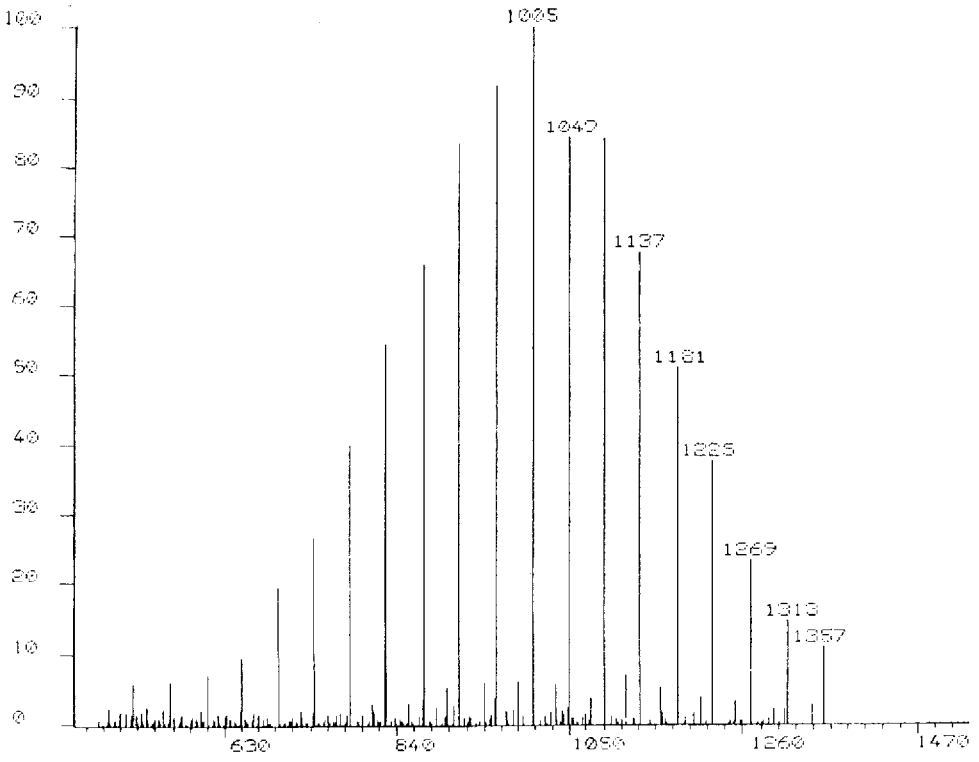

Fig. 2. Thermospray ionization mass spectrum of polyethylene glycol (average mol. wt. 1000). Loop injection into methanol (30%) and 0.1 *M* aqueous ammonium acetate (70%).

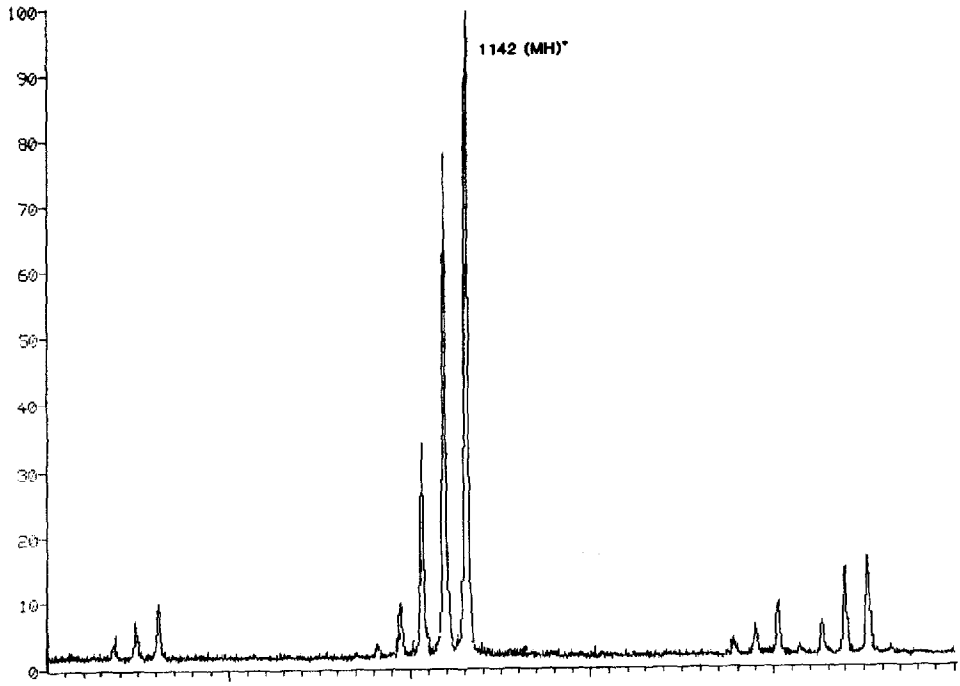

Fig. 3. Thermospray ionization mass spectrum of gramicidin S (mol. wt. 1141). Average of five scans. Mass range displayed 1120–1160. Loop injection into methanol (30%) and 0.1 *M* aqueous ammonium acetate (70%).

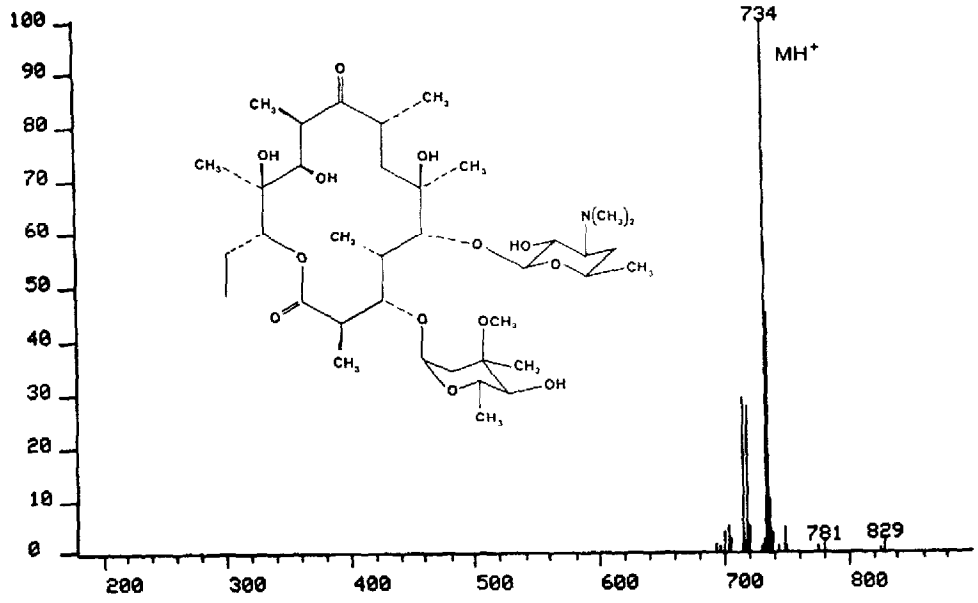

Fig. 4. Thermospray ionization mass spectrum of erythromicin (mol. wt. 733). Loop injection into methanol (30%) and 0.1 *M* aqueous ammonium acetate (70%).

ion sensitivity (Fig. 3) and minimum thermally induced fragmentation (Fig. 4) have become available from a wide range of relatively high-molecular-weight labile materials.

If we now turn our attention from analytes to eluents, an obvious requirement for the mass spectrometer as an LC detector is that it should be compatible with the use of gradient elution techniques. At a constant flow-rate, the optimum probe temperature for the spraying of small droplets is a function of solvent composition so that changes in spraying temperature are needed to provide the maximum ion current throughout a gradient elution experiment using thermospray ionization. In the absence of an automatic method of providing this temperature gradient, setting a constant temperature which is optimal for a solvent mixture of intermediate composition often provides an effective compromise, particularly with less extreme variations in solvent composition. If, however, ionization does not depend on the presence of an added electrolyte, such as ammonium acetate, but is effected by an external means such as a discharge electrode or a filament, then the dependence on solvent composition is much reduced.

The source illustrated in Fig. 1 has provision for the use of a discharge electrode or a filament which each have different optimum positions within the desolvation region. The discharge electrode has proved to be a particularly valuable accessory. With a voltage of *ca.* 1000 V between the central cathode and the source block, a discharge current of approximately 100 μA and a very stable ion beam, which is not dependent on the presence of any electrolyte, are observed. Under these conditions, a full gradient from a completely aqueous to a completely organic phase may be run without any requirement for a change in spraying temperature and with no obvious variation in response (Fig. 5).

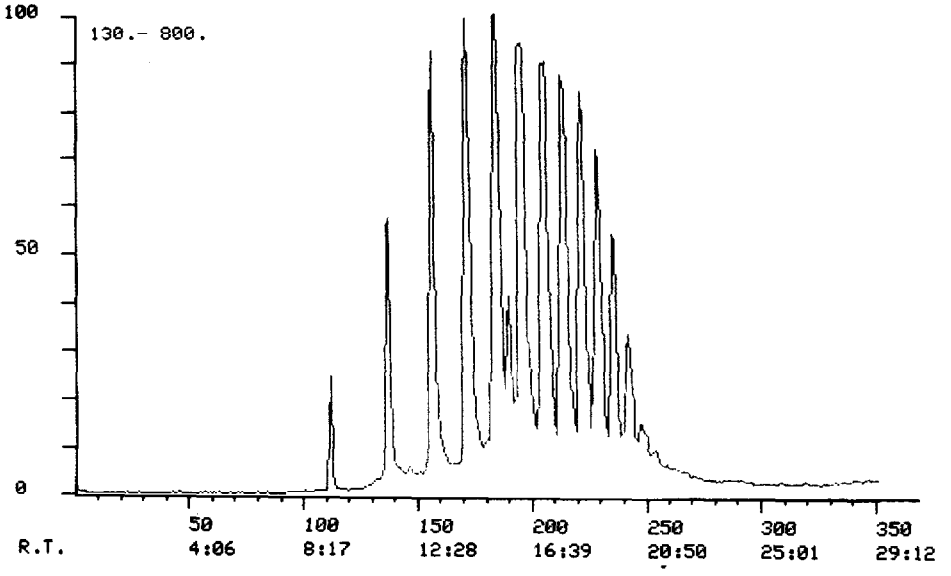

Fig. 5. LC–MS analysis of polyethylene glycol 400. Solvent gradient 0–100% methanol in water over 30 min. Discharge ionization. Summed ion intensity (m/z 130–800) is plotted against scan number and retention time.

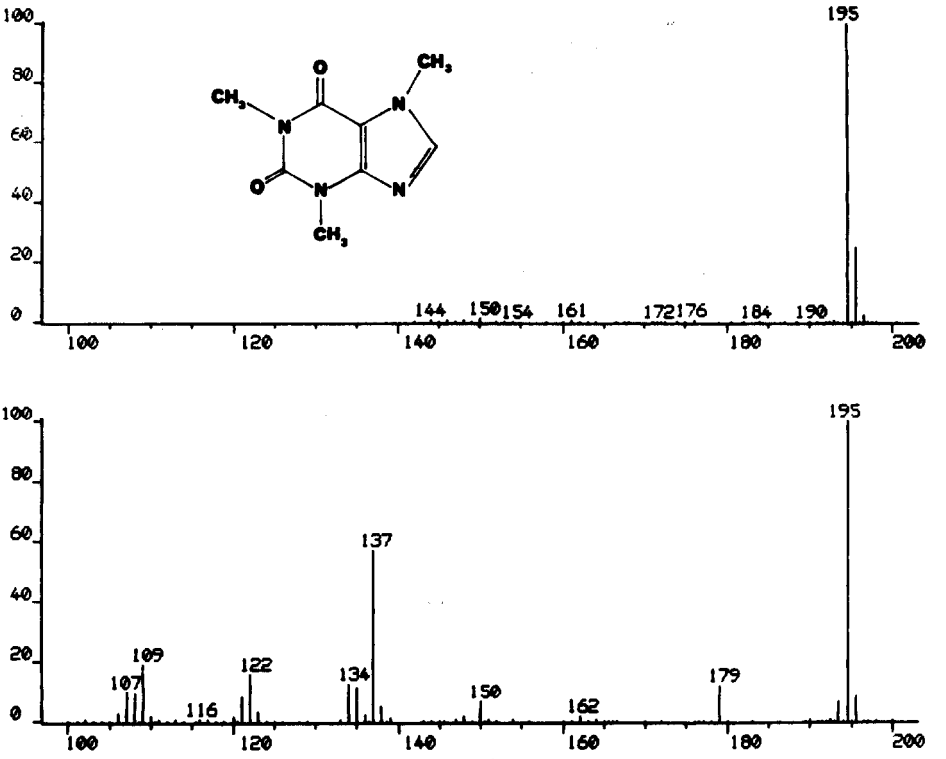

Fig. 6. Discharge ionization mass spectra of caffeine. Above, fragmentation electrode 0 V; below, fragmentation electrode 160 V. Solvent methanol.

The use of a discharge electrode provides a further advantage since it now becomes possible to induce fragmentation in a controlled manner to provide structural information by the use of a second electrode (Fig. 1) which carries a small positive voltage (100–200 V) relative to the source block[3] (Fig. 6). It is not certain at this stage whether this electrode induced fragmentation, which is only observed with discharge ionization, is in fact a collision process[4] or whether it is related to the very large secondary electron current observed in the source with this electrode configuration. The use of a second electrode in this way provides fragment ion data in a very simple manner but, unlike MS–MS experiments which are also accessible on a double focusing instrument such as the one used here, fragment ions cannot be linked to a specific parent ion and operation is limited to discharge ionization. Further investigation of this technique is, however, certainly warranted.

CONCLUSIONS

Changes to the design of a thermospray LC–MS ion source have improved the analytical potential with a wide range of higher-molecular-weight analytes. Spectra obtained with this source now show good molecular ion sensitivity and minimal thermal decomposition. Controlled fragmentation, whether electrode induced or ob-

tained by more conventional collision induced techniques, especially when used in conjunction with elemental compositions from accurate mass measurement data, can then provide a considerable amount of the information needed for structural elucidation.

REFERENCES

1 C. R. Blakley and M. L. Vestal, *Anal. Chem.*, 55 (1983) 750.
2 J. R. Chapman, *J. Chromatogr.*, 323 (1985) 153.
3 W. H. McFadden and S. A. Lammert, *J. Chromatogr.*, 385 (1987) 201.
4 H. Kambara and I. Kanomata, *Anal. Chem.*, 49 (1977) 270.