Journal of Chromatography, 203 (1981) 139–152
Elsevier Scientific Publishing Company, Amsterdam — Printed in The Netherlands

CHROM. 13,141

ON-LINE LIQUID CHROMATOGRAPHY–MASS SPECTROMETRY OF ION PAIRS

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SUMMARY

An on-line continuous extraction interface between a high-performance liquid chromatograph and a mass spectrometer permits the operation of the chromatograph in the reversed-phase mode without compromising the performance of the spectrometer. Solutes are extracted into a volatile organic solvent which is then transported to the spectrometer by a moving-belt interface. A greatly simplified version of the original extraction interface is shown. In its new design the extractor operates on the principle of solvent rather than air segmentation, and much of the expensive peripheral equipment has been eliminated. Flow-rates of up to 1.0 ml/min each of aqueous (mobile) and organic (extracting) phases are easily accommodated in this on-line operation. We have examined the compatibility of ion-pair chromatography with the high-performance liquid chromatography–extraction–mass spectrometry combination, particularly in terms of the quality of solute spectra obtained and the volatility of the counter ions. The results presented here show that ion pairing and subsequent extraction are compatible with the on-line operation under both chemical ionization and electron impact conditions. Spectra are produced from the ion pairs which consist of the solute spectrum superimposed on but easily discerned through the spectrum of the counter ion. A rationale to explain the mass spectrometric observations is presented. The implication of these results for the analysis of ionic compounds by this technique is discussed.

INTRODUCTION

Although still in its infancy, the on-line use of combined liquid chromatography and mass spectrometry (LC–MS) has already been shown to be a useful technique for organic analysis. Many workers are actively pursuing various approaches to reconcile the incompatibilities between LC and MS, and the applications cited in a recent review of the status of LC–MS[1] reveal the many successes already achieved.

One of the obstacles to the full development of LC–MS has been the inability

0021-9673/81/0000–0000/$02.50

of the combined instruments to accommodate the highly polar mobile phases and inorganic modifiers commonly used with reversed-phase LC. Often, the operation of the chromatograph, or the spectrometer, or both has been compromised. For example, with direct liquid introduction systems, non-volatile salts of all types must be avoided, and with the moving-belt interface only low flow-rates of polar solvents may be used.

The feasibility of using a continuous extraction interface between the chromatograph and the spectrometer as a means of overcoming such problems has been demonstrated by this laboratory in the ion suppression mode[2]. Organic acids were chromatographed in an acidic buffer, extracted into an immiscible, volatile organic phase and admitted to the mass spectrometer by a moving-belt inlet. Inorganic modifiers, as well as polar mobile phase components, were effectively eliminated.

In addition to allowing the facile combination of reversed-phase LC and MS, the use of the above interfacing concept provides added flexibility to the overall system. For example, one has the option of selecting an organic phase independent of LC separation conditions and based only on compatibility with MS operating requirements and the nature of the solutes to be extracted. Also, by proper adjustment of the aqueous/organic phase ratio, one has the ability to preconcentrate solutes in the extracting liquid prior to MS analysis. This preconcentration step also offers a means of flow-rate reduction without loss of solute mass.

The extension of the continuous extraction interface to a more general approach of the LC–MS analysis of ionic compounds, *viz.* ion pairing, is the subject of this report. The extraction interface has been extensively modified from the original design[2] such that its operation is now considerably simplified, and through the elimination of much of the previously required peripheral equipment, its cost is significantly reduced. This new interface will also be discussed.

There were several reasons for considering on-line LC–MS in the ion-pairing mode using the continuous extraction interface. First, the technique of ion-pair extraction is a classical means of separating ionic compounds[3], and ion-pair chromatography is now used routinely in high-performance liquid chromatography. Second, the feasibility of performing post-column extraction of ion pairs has been established[4]. Finally, we[5] and others[6] have shown that it is possible to obtain useful mass spectra of organic compounds from ion pairs. Moreover, we have demonstrated that, in certain instances, ion pairing can be used to convert compounds to a volatile form amenable to MS analysis[5]. Thus, the combined use of LC in the ion pairing mode with MS detection can provide a powerful method for the separation and analysis of a wide variety of ionic compounds.

EXPERIMENTAL

LC system

The liquid chromatograph consisted of either a Waters 6000A solvent delivery system (Waters Assoc., Milford, MA, U.S.A.) or an Altex 110A pump (Altex Scientific, Berkeley, CA, U.S.A.) and a Valco CV6-UHPa-N60 injection valve (Valco Instruments, Houston, TX, U.S.A.) equipped with a 10-μl loop. The UV detector was an LDC Model 1205 operated at 254 nm (Laboratory Data Control, Riviera Beach, FL, U.S.A.) Chromatographic columns were 100 × 4.6 mm I.D. packed in our laboratory with 6.5-μm particle diameter Zorbax-CN (DuPont, Wilmington, DE, U.S.A.) and

were operated at 1.0 ml/min. The mobile phase typically used was 0.1 *M* NaH_2PO_4, pH 2.50, containing 35% (v/v) methanol and 10 m*M* $C_{10}H_{21}SO_4Na$.

All solvents were "distilled in glass" quality (Burdick and Jackson, Muskegon, MI, U.S.A.). Alkyl sodium sulfate and sulfonate salts were purchased from either Eastman-Kodak (Rochester, NY, U.S.A.) or Helix Assoc. (Newark, DE, U.S.A.) and were used as received. Solutes and buffer components were of analytical quality from various commercial sources and were used without further purification.

Continuous extraction interface

Fig. 1 is a schematic diagram of the LC–MS system containing the continuous extraction interface. The LC apparatus section has been described above. The organic (extracting) phase, dichloromethane, was supplied to the mixing T at 1 ml/min with a gas displacement system which consisted of a standard gas cylinder of nitrogen, a Brooks 8601B pressure regulator adjustable from 0 to 30 p.s.i.g. (Brooks Instrument Division, Emerson Electric Co., Hatfield, PA, U.S.A.), a container for the organic phase, a Nupro SS-1SG-TFE fine metering valve (Nupro Company, Willoughby, OH, U.S.A.), and a Brooks Sho-Rate 150 flow meter. These components were assembled as shown in Fig. 1. Air segmentation was not used in these experiments; solvent segmentation alone served to minimize band broadening through the system as has been discussed elsewhere[7].

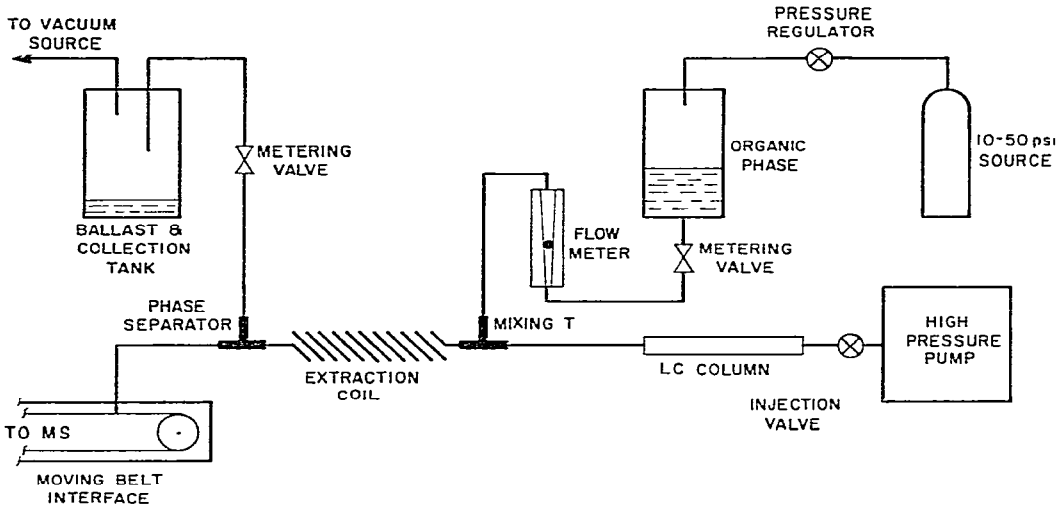


Fig. 1. Schematic diagram of the LC–MS system utilizing the continuous extraction interface. Details are contained in the Experimental Section.

The mixing T was constructed according to the design of Karlberg *et al.*[8] using an A10 T connector (Technicon, Tarrytown, NY, U.S.A.). The extraction coil, 18 mm O.D., was constructed from 0.8 mm I.D. PTFE tubing and had a volume of 0.5 ml. Details of the phase separator have been given elsewhere[2]. The flow-rate of organic phase to the moving-belt interface, typically 0.65–0.75 ml/min, was regulated by

varying the vacuum at the phase separator with the metering valve (Nupro SS-1SG-TFE). Any source capable of producing a vacuum of 10–20 in.Hg is adequate for operating the interface. A water aspirator was used here.

The modified interface shown in Fig. 1 offers significant advantages over the previous design[2]:

(1) The elimination of the need of a peristaltic pump and a mechanical solvent delivery system reduces the cost of the interface.

(2) The elimination of air segmentation and the use of vacuum pumping of the phase separator, in addition to reducing the cost and complexity of the interface, also reduces flow pulsations in the system. This is especially important for smooth operation of the phase separator and also for uniform delivery of solvent to the moving belt.

(3) The use of lighter-than-water extracting solvents can be more easily accommodated, since separate debubbling and phase separating T's are not required.

Mass spectrometry

A Finnigan 4000 quadrupole mass spectrometer (Finnigan Instruments, Sunnyvale, CA, U.S.A.) interfaced to a Finnigan/Incos 2300 data system and equipped with a moving-belt interface (Kapton) was used for the on-line LC–MS experiments. Chemical ionization (CI) (isobutane or ammonia) direct probe spectra were obtained with the Finnigan mass spectrometer. Electron impact (EI) (70 eV) probe spectra were obtained with either the Finnigan apparatus or a Nuclide 12-90-G magnetic mass spectrometer (Nuclide Corp., State College, PA, U.S.A.). The probe temperature was programmed from room temperature to 220°C at *ca.* 10°C/min.

The flash vaporizer and clean-up heaters of the moving-belt interface were operated at *ca.* 250°C. The infrared heater which assists in solvent vaporization was operated at an intensity which produced minimum solvent background in the mass spectrometer, while at the same time not causing excessive spattering on the belt. However, the presence of ion peaks due to residual solvent made it impractical to scan below 90 atomic mass units. This limitation is not particularly severe, since LC–MS is used primarily for materials of high molecular weight not readily amenable to gas chromatographic–MS analysis. In such cases, peaks of structural significance in the mass spectrum usually occur above 90 atomic mass units.

Ion-pair samples for direct probe experiments were prepared by extraction with dichloromethane from an acidic buffer (0.1 *M* NaH_2PO_4, pH 2.50, 20% (v/v) methanol) containing 5 m*M* solute and a 2–4 fold excess of counter ion.

RESULTS AND DISCUSSION

Off-line mass spectrometry

Our first investigation consisted of a study of the mass spectral properties of a series of common counter-ion salts (sodium *n*-alkyl sulfates and sulfonates) and then the properties of the ion pairs* formed from these anions and various amine solutes. The objectives of these evaluations were to determine whether the components of the

* We will use the term "ion pair" in this report to stress the concept of ion pairing although the term "organic salt" might also be appropriate in some cases.

ion pair would be compatible with MS volatility requirements and also whether solute spectra produced from ion pairs would be comparable to those produced from the parent compound.

EI- and CI-MS of counter-ion salts. In a preliminary account of this work[5], we reported that characteristic EI and CI spectra were readily produced from sodium *n*-alkyl sulfate salts by direct probe with moderate ($\leqslant$200°C) heating. Each spectrum exhibited $[M-NaHSO_4]^{\ddagger}$(EI) or $[M+H-NaHSO_4]^+$ (CI) as the highest mass ion, and each contained a characteristic hydrocarbon fragment envelope similar to that observed with the corresponding 1-alkene. Fig. 2A shows a typical EI spectrum for decyl sodium sulfate. Note the peak at *m/z* 140 corresponding to $[M-NaHSO_4]^{\ddagger}$ and the peaks at *m/z* 41, 55, 70, 83, 97, and 112 defining the hydrocarbon fragment envelope. Analogous results were obtained for C_6–C_{14} sodium sulfate homologs.

It is important to note that sodium sulfonate salts were not volatile even at probe temperatures of 300°C and hence produced no spectra.

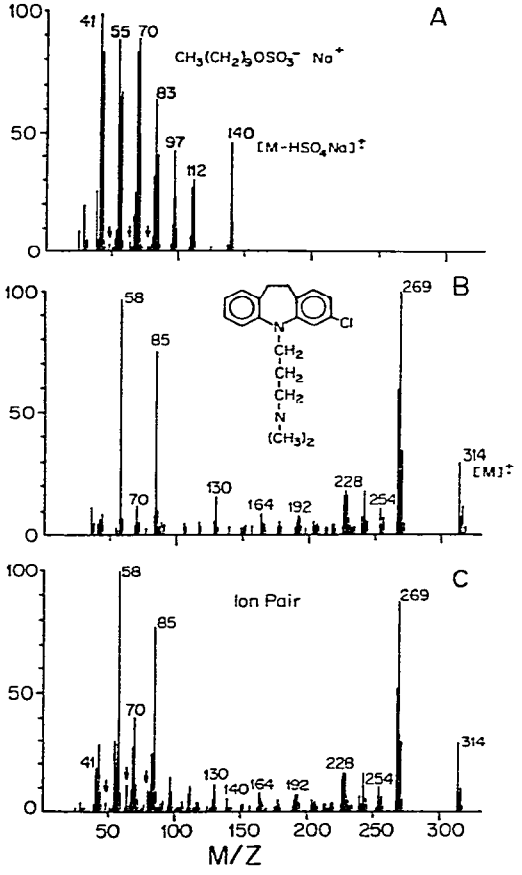


Fig. 2. Direct probe EI (70 eV) spectra obtained with the Nuclide magnetic mass spectrometer. (A) Decyl sodium sulfate; (B) clomipramine; (C) spectrum resulting from the introduction of the ion pair. SO^+, SO_2^+, and SO_3^+ (*m/z* 48, 64, and 80) are indicated (arrows) in (A) and (C).

EI-MS of ion pairs. We next examined the EI spectra produced when ion pairs formed between various amine solutes and either sulfate or sulfonate counter ions were admitted to the mass spectrometer. The spectrum of clomipramine, a typical solute used in these studies, is shown in Fig. 2B. It was found that introduction of ion pairs with sulfate counter ions at temperatures $\leqslant$200°C resulted in spectra which contained all the ions associated with both components of the ion pair, and these ions were present in approximately the same relative intensities as were observed with the unpaired materials. Fig. 2C is the mass spectrum obtained from the clomipramine–$C_{10}H_{21}SO_4$ ion pair. Note the nearly exact correspondence of the relative intensities of solute peaks to those in Fig. 2B (*e.g.*, *m/z* 58, 85, 130, 269, 314, etc.). Comparison of counter ion peaks between Fig. 2A and C shows a similar very close correspondence. The peaks at *m/z* 48, 64, and 80 corresponding to SO^+, SO_2^+ and SO_3^+ (as verified by high-resolution MS measurements) are significantly more intense relative to the hydrocarbon fragments in the ion-pair spectrum (Fig. 2C) than in the counter-ion salt spectrum (Fig. 2A). This observation will be discussed below.

Sulfonate ion pairs produced spectra at temperatures $\leqslant$100°C which were identical to those from the sulfates except that SO^+, SO_2^+, and SO_3^+ ions were absent. It should be recalled that no spectra could be obtained from the corresponding sodium sulfonate salts.

During the course of these studies, we examined ion pairs with sulfates and sulfonates having *n*-alkyl chain lengths from C_6 through C_{14}. In all cases, solute portions of the spectra were unaffected by either the alkyl chain length or the type of counter ion, and the counter-ion portions were unaffected by the type of amine solute. That is, from an MS point of view, anions and cations acted independently. Thus, given the spectrum or identity of the counter ion, one can readily discern the spectrum of the solute. The background due to the counter ion is easily recognized and does not present a significant hindrance to the interpretation of the spectrum. The spectrum in Fig. 2C illustrates this point. It is clear that all peaks with $m/z > 140$ are solute related, since $[M-NaHSO_4]^+$ is invariably the highest mass observed with alkyl sulfates. Inspection of the lower mass end of the spectrum shows several peaks (*m/z* 58, 70, 85 and 130) which are clearly outside of the hydrocarbon fragment envelope and are, therefore, also solute related. The approximate relative intensities of overlapping ions can be determined by applying the appropriate spectral subtractions, as was done for picrate ion pairs[6].

CI-MS of ion pairs. The CI spectra of the ion pairs were, as expected, much simpler than the corresponding EI spectra. Spectra obtained from sulfate ion pairs with isobutane as the reagent gas contained characteristic solute peaks (*e.g.*, $[M+H]^+$ and $[M+H-NH_3]^+$) and also characteristic counter ion-related peaks (*e.g.*, $[M+H-NaHSO_4]^+$ and other hydrocarbon fragments). Sulfonate ion pairs, on the other hand, produced the same solute related peaks but only a single counter ion-related peak, which corresponded to the protonated sulfonic acid of the anion. For example, as we have shown[5], the CI spectrum of the ion pair formed between $C_8H_{17}SO_4$ and phenylcyclopropanemethylamine (PCMA, mol.wt. 147) contained solute peaks at *m/z* 148 and 131 and counter-ion peaks at *m/z* 113 and 71. The corresponding sulfonate ion pair produced the same solute peaks, but only a single counter-ion peak at *m/z* 195 corresponding to protonated octyl sulfonic acid ($[C_8H_{17}SO_3H+H]^+$).

In no case, under either EI or CI conditions, were higher mass ions indicative

of an intact ion pair observed, even under gentler ionization conditions using NH_3 as reagent gas.

Rationalization of the mass spectral results

Counter-ion salts. The mass spectral behavior of the counter-ion salts can be rationalized by considering the relative stability of the sulfate and sulfonate structures. It is known from surfactant chemistry that the alkyl sulfonate structure is more resistant to hydrolysis than the corresponding alkyl sulfate structure[9–11]. Based on this fact and on our observations of the MS properties of the two classes, it seems reasonable to assume that the sulfonate system is also thermally more stable than the sulfate system. Thus, in the case of the *n*-alkyl sodium sulfate salts, thermolysis of the C–O bond and transfer of a proton produces an alkene (most likely the 1-alkene) and nonvolatile $NaHSO_4$. As a result, spectra of the sulfate salts show intense hydrocarbon fragment ions but only very weak SO^+, SO_2^+, and SO_3^+ ions (see Fig. 2A). However, since the analogous process of thermolysis is inhibited in the sulfonate system at normal mass spectrometric temperatures ($\leqslant$300°C), no spectra are observed with the *n*-alkyl sodium sulfonate salts.

Ion pairs. As has been discussed above, when ion pairs containing either sulfate or sulfonate counter ions are admitted to the mass spectrometer, spectra result which contain ions originating from both the anion and cation. The probable mechanism with both types of counter ion involves a proton transfer from cation to anion. This reaction, most likely thermally induced and in the condensed phase, results in neutral species, in this case an amine and either an alkyl sulfuric or alkyl sulfonic acid. A similar thermally induced proton transfer was used by Kralj *et al.*[12] to obtain spectra of organic acid salts. Note the increased intensities of SO^+, SO_2^+, and SO_3^+ ions relative to hydrocarbon fragments between Fig. 2A and C as evidence of the increased volatility of the sulfuric acid compared to that of the sodium sulfate salt. (Corresponding S–O ions are not observed in reference spectra of free alkyl or aryl sulfonic acids, and thus are not observed in spectra produced from sulfonate ion pairs.) As we have pointed out[5], the formation of neutral species through proton transfer can be considered a form of derivatization since it imparts increased volatility to certain classes of compounds, in this instance alkyl sulfonate salts.

The combined effects due to the difference in stability between the sulfate and sulfonate structures and the production of neutral species through proton transfer are seen in Fig. 3A and B. Fig. 3A shows the evolution profiles of various ions from the PCMA–$C_8H_{17}SO_4$ ion pair obtained by direct probe. The probe temperature is increasing with increasing scan number. Based on this data, it appears that thermolysis of the C–O bond to release the alkene precedes proton transfer to the anion. Thus, as a function of temperature, evolution of alkene related ions precedes that of sulfate and solute related ions which evolve simultaneously. Note in Fig. 3A that solute related ions ($[M+H]^+$ and $[M+H-NH_3]^+$) reach peak evolution after the alkyl portion of the counter ion ($[C_8H_{16}+H]^+$). Fig. 3B shows the situation with the PCMA–$C_8H_{17}SO_3$ ion pair. In this instance, since no thermal decomposition occurs within the sulfonate structure, the neutral species evolve simultaneously when proton transfer occurs. Thus, all species ($[M+H]^+$, $[M+H-NH_3]^+$ and $[C_8H_{17}SO_3H_2]^+$) reach peak evolution together.

The data in Fig. 3A and B were obtained under CI (isobutane) conditions. The

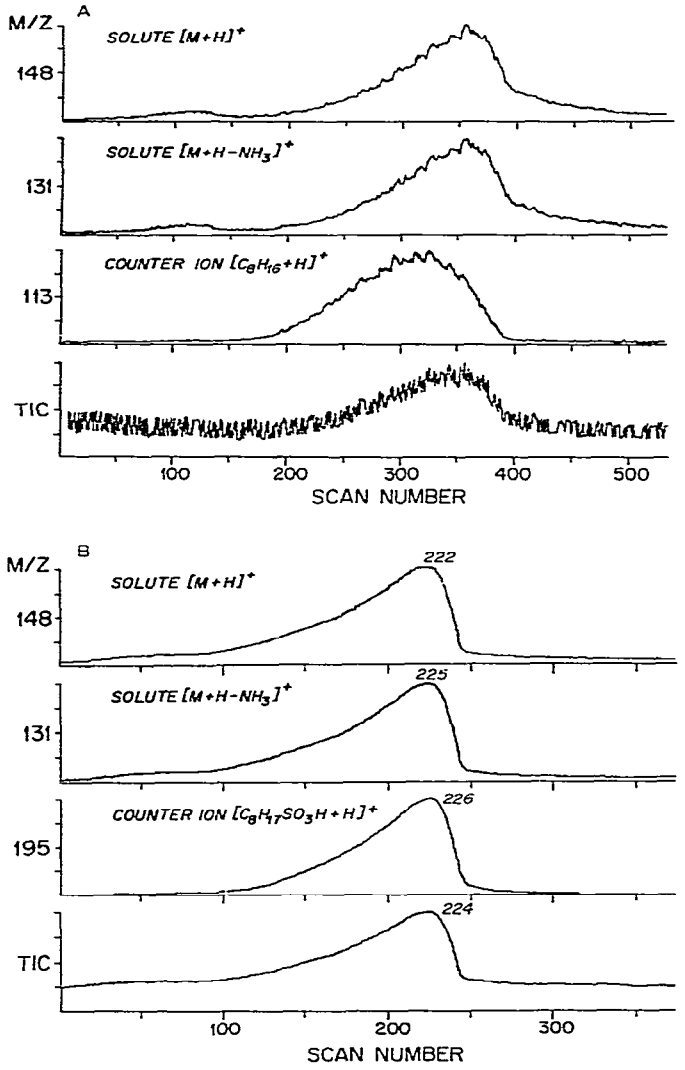
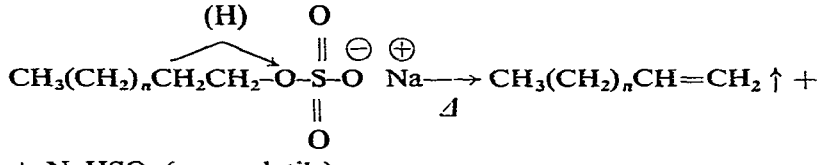


Fig. 3. Mass ion currents and total ion current obtained by direct probe introduction under CI (isobutane) conditions using the Finnigan 4000 mass spectrometer. (A) PCMA–$C_8H_{17}SO_4$ ion pair, and (B) PCMA–$C_8H_{17}SO_3$ ion pair. Probe temperature was programmed from room temperature to 220°C at *ca.* 10°C/min. As a point of reference, scan No. 200 corresponds to *ca.* 100°C.

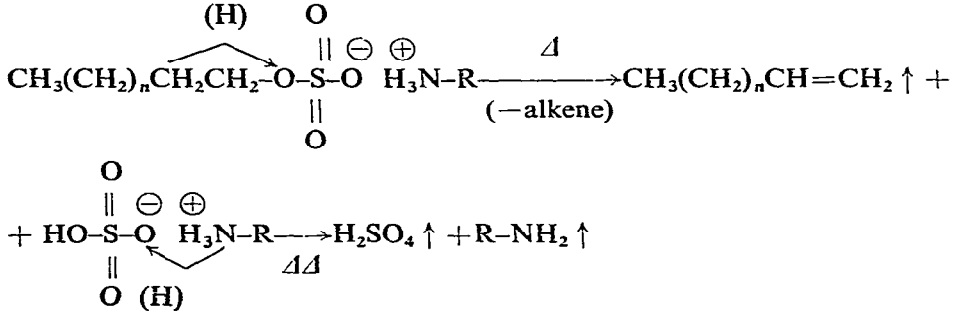
same effects were observed under CI (NH_3) and EI conditions with alkyl chain lengths from C_6 through C_{14} and with a wide variety of solutes.

Schemes of the various mechanisms which have been discussed are summarized below. Note that position in the alkyl chain from which protons are abstracted and identity of the alkene isomers produced are those thought most likely to occur. There is not, however, data to prove these specified mechanisms, and they are included only for illustration.

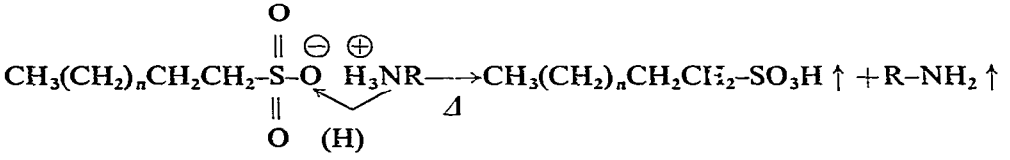
Scheme I: Sodium *n*-alkyl sulfate salts



Scheme II: *n*-Alkyl sulfate–amine ion pairs



Scheme III: 5-Alkyl sulfonate–amine ion pairs



The results in Fig. 2A–C reveal that the initial requirements for compatibility of on-line LC–MS with the model ion-pairing system are met. The presence in the mass spectra of recognizable ions originating from both the cation and the anion confirms the volatility of the ion-pair components. Also, spectra of compounds introduced as ion pairs are essentially the same as those obtained from the unpaired materials, both anions and cations. Thus, given the spectrum or identity of one component, one can readily discern the spectrum of the other either manually or with the aid of a data system. The extension of these results to other ion-pairing systems composed of various anionic (carboxylic acids, phosphates, acidic phenols) and cationic (alkyl amines, quaternary ammonium) solutes and counter ions is currently under study.

On-line LC–MS

In the final part of this study, we evaluated the overall performance of the on-line LC–MS system. These evaluations were made with a mixture of thermally sensitive, basic materials which included procainamide, N-acetyl procainamide, N-propionyl procainamide and lidocaine. The structures of these compounds are shown in Fig. 6A–D along with their mass spectra, which will be discussed later. The chroma-

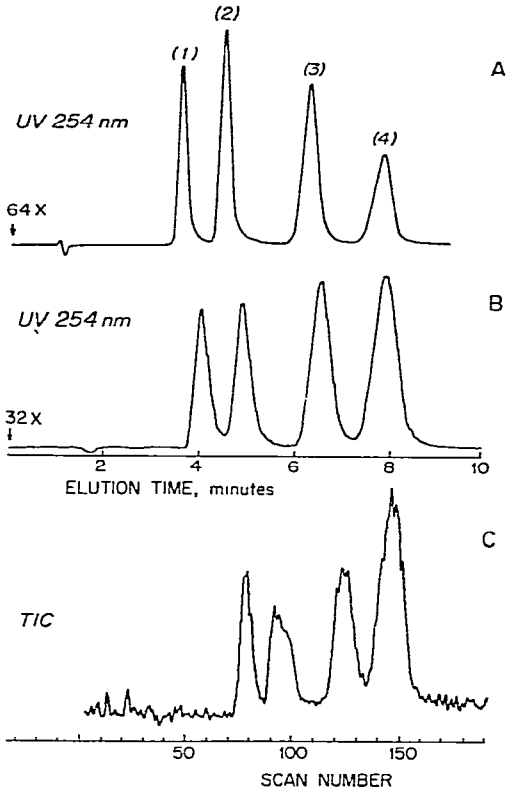


Fig. 4. Chromatograms resulting from the injection of 10 μg each of (1) procainamide, (2) N-acetyl procainamide, (3) N-propionyl procainamide and (4) lidocaine. (A) Chromatogram of mixture using the LC–UV combination. (B) Chromatogram of mixture using the LC–extraction interface–UV combination. (C) Reconstructed ion chromatogram of the mixture using the LC–extraction interface–MS combination. Chromatographic conditions: column, 100 × 4.6 mm I.D. Zorbax CN (6.5 μm); mobile phase, 0.1 *M* NaH_2PO_4, 35% (v/v) methanol, pH 2.50, 10 m*M* decyl sodium sulfate; flow-rate, 1 ml/min. Extraction conditions: dichloromethane, flow-rate 1 ml/min (*ca.* 75% to moving belt). CI (isobutane) MS using the Finnigan 4000 and moving-belt inlet.

tograms in Fig. 4 show the results for this mixture chromatographed with a mobile phase consisting of 0.1 *M* NaH_2PO_4, 35% (v/v) methanol, pH 2.50 and 10 m*M* $C_{10}H_{21}SO_4Na$. In other on-line experiments not shown here, mobile phases containing up to 55% (v/v) methanol and 20 m*M* counter ion were used successfully. Other relevant information is included in the figure caption. The upper chromatogram (A) was made by monitoring the aqueous phase (UV, 254 nm) immediately after the column. The center chromatogram (B) is the result of monitoring the organic phase (UV, 254 nm) at the outlet of the phase separator of the extraction interface. Note the change in attenuation between (A) and (B). The lower trace (C) is the total ion chromatogram obtained for the mixture with the on-line LC–MS system under CI (isobutane) conditions. Extraction efficiencies here, estimated by comparing peak heights before and after extraction, ranged from 33% for procainamide to 100% for lidocaine. In the absence of a counter ion, extraction efficiencies were less than 5%.

The LC–MS system, and particularly the extraction interface, was not optimized for minimum band broadening. However, inspection of the chromatograms in Fig. 4 reveals that baseline separation was maintained for all the compounds. Thus, dispersion through the system was well within the limits necessary to accomplish the primary purpose of this study, which was to demonstrate the feasibility of the concept. It should also be pointed out that the issue of band broadening with MS detection is less of a problem than with UV detection, for example, because of the added advantage provided by the selectivity of the mass spectrometer.

Fig. 5 shows molecular ion chromatograms (A–D) and the total ion chromatogram (E) obtained from the on-column injection of 1 μg of each compound in the test mixture. Except for the sample size, the conditions were the same as in Fig. 4. Note particularly the increase in the signal-to-noise ratio between the total ion and mass ion chromatograms. Fig. 6A–D are CI (isobutane) spectra obtained from the compounds in Fig. 5. These spectra were obtained by summing several scans across the center of each peak and subtracting an approximately equivalent number of background scans.

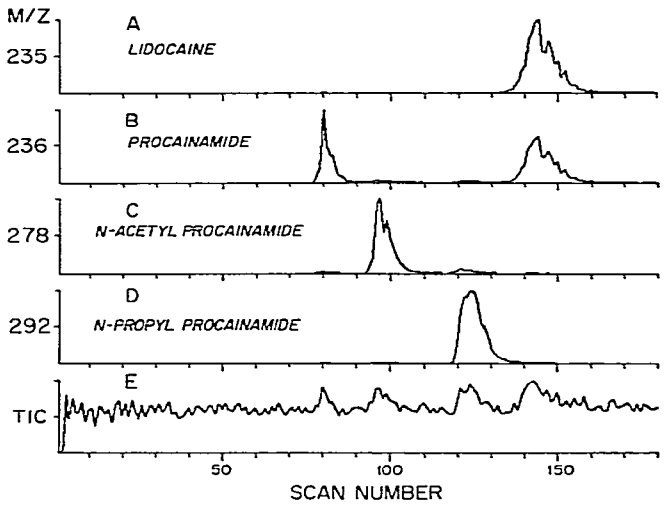


Fig. 5. Molecular ion (A–D) and total ion (E) chromatograms of 1 μg each of the components in Fig. 4. Conditions are the same as in Fig. 4.

The peak at *m/z* 141 is the sole counter-ion interference remaining in these spectra. In every case, solute spectra obtained on-line under either EI or CI conditions were identical to those obtained off-line by direct probe.

It is worth noting here that there are several means by which chromatographic and extraction conditions can be decoupled such that variation of one does not influence the other. One method is the post-column addition of counter ions and other reagents. (The examples discussed in this paper involved only the pre-column addition of reagents such that retention and extraction were affected simultaneously.) This technique has been used recently[13] for the addition of a fluorescent counter ion to weakly basic compounds eluting from a reversed-phase column. The ion pairs were continuously extracted into an organic solvent and detected fluorimetrically. A second

method is to use a polar bonded phase[4], such as diol, cyano, or amide, where it is possible to minimize the influence of the hydrophobic character of the counter ion on retention. Of course, this hydrophobic character will affect the extent of extraction in the interface.

The counter-ion background present in the mass spectrometer in the on-line configuration was higher than anticipated based on off-line examination of extraction blanks. The reason for this is not clear but may be due to the formation of emulsions in the extraction interface. This background, however, was not detrimental to the operation of the system as it was relatively constant and of low signal. Moreover, it allowed counter-ion interferences to be partially or completely removed from solute spectra.

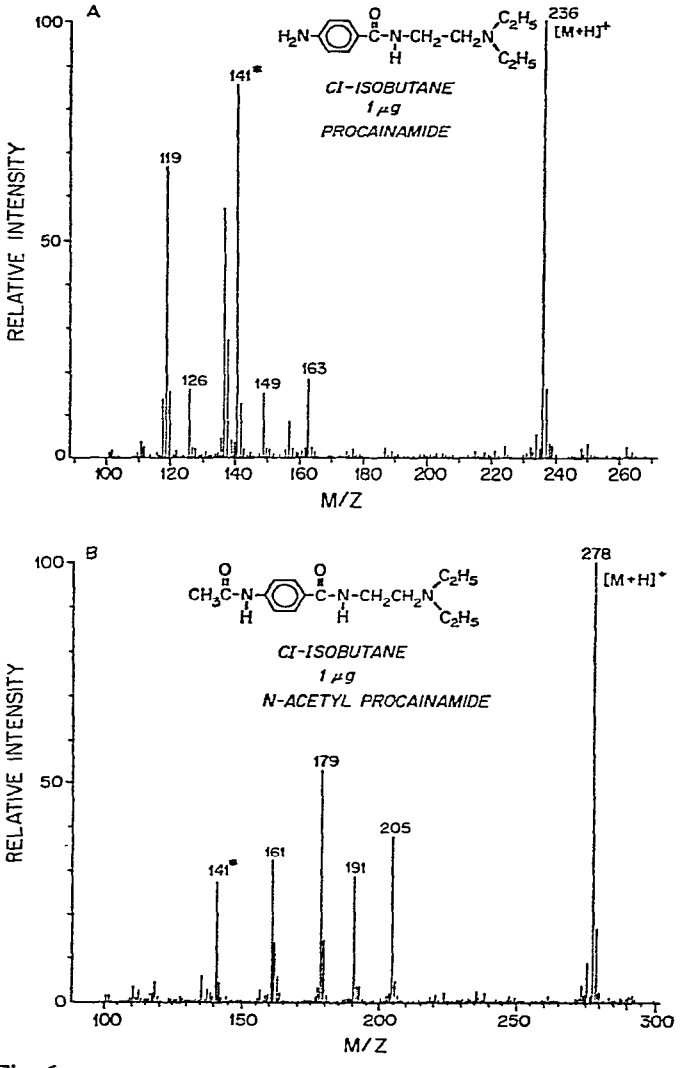


Fig. 6.

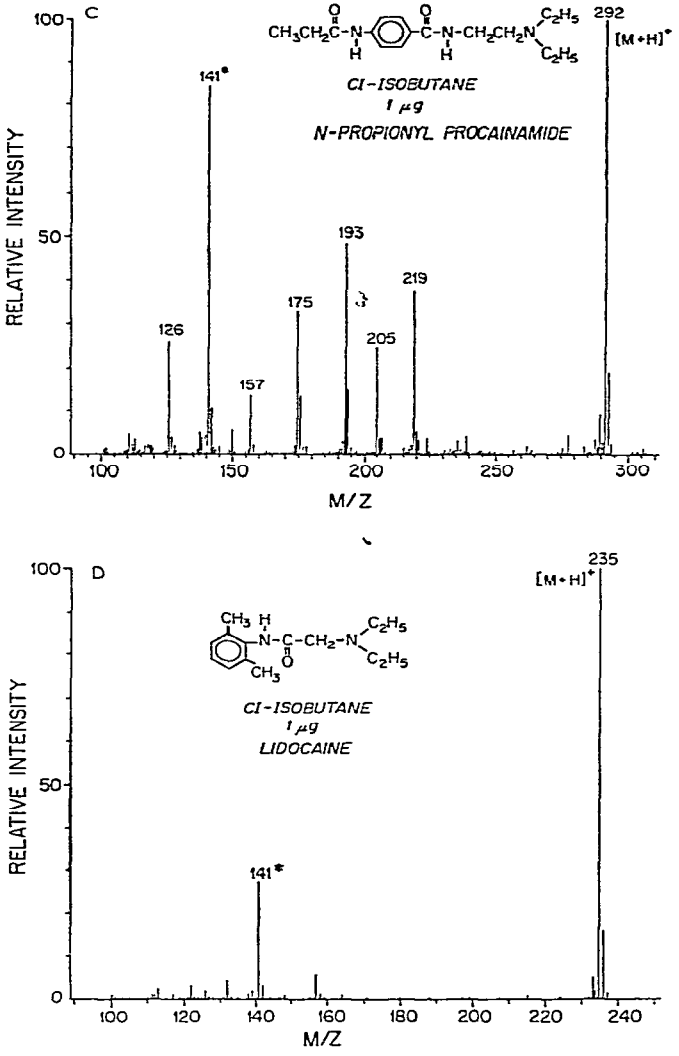


Fig. 6. CI (isobutane) MS of test compounds from injection shown in Fig. 5. Spectra have been partially background corrected. *m/z* 141 (*) is the only counter-ion peak.

Although the combined system was not optimized for sensitivity (for example, by optimizing the vaporization temperature, organic/aqueous phase ratio and MS scanning conditions) excellent CI and EI spectra were obtained with 1-μg injections of a variety of materials. Under single ion monitoring conditions, many compounds could be detected at the 100-ng level and in a few cases at the 10-ng level. Obviously, there are many means available for increasing the sensitivity in this type of system, most of which have not yet been examined.

CONCLUSION

We have demonstrated the feasibility of conducting on-line LC–MS in the ion pairing reversed-phase mode by incorporating a continuous extraction interface in the LC–MS system. Use of a volatile extracting solvent allowed the mass spectrometer to be operated in either the EI or CI mode with polar mobile phase flow-rates of 1 ml/min. Significantly, the mass spectrometer was operated for an extended period of time under these conditions and no adverse affects were noted.

The combined use of MS with LC in the ion-pairing mode can provide a powerful method for the separation and analysis of a wide variety of ionic compounds. The concerns of volatility of the model ion-pair components and usefulness of resultant solute spectra have been examined and found to be compatible with MS analysis. Extension of the methods used here to other ion-pairing systems is under study and will be reported later.

ACKNOWLEDGEMENTS

We thank the IBM Corporation for the support of Daniel P. Kirby through their Resident Study Program. The authors gratefully acknowledge support of this work by the National Institutes of Health under grant number GM 15847 (B.L.K.) and GM 22787 (P.V.). This is contribution number 77 from the Institute of Chemical Analysis.

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