Metal Salts for Molecular Ion Yield Enhancement in Organic Secondary Ion Mass Spectrometry: A Critical Assessment

A. Delcorte* and P. Bertrand

Unité de Physico-Chimie et de Physique des Matériaux, Université catholique de Louvain, 1 Croix du Sud, B-1348, Louvain-la-Neuve, Belgium

In a search for molecular ion signal enhancement in organic SIMS, the efficiency of a series of organic and inorganic salts for molecular cationization has been tested using a panel of nonvolatile molecules with very different chemical characteristics (leucine enkephalin, lrganox 1010, tetraphenylnapthalene, poly styrene). The compounds used for cationization include alkali bromide and group Ib metal salts (XBr with X = Li, Na, K; CF3CO2Ag; AgNO3; [CH3COCH=O(CH2)Cu]. Alkali ions, very good for polar molecule cationization, prove to be of limited interest for nonpolar molecules such as poly styrene Silver trifluoroacetate displays excellent results for all the considered molecules, except for leucine enkephalin (which might be due to the use of different solvents for the analyte and the salt). Instead, silver nitrate mixed with leucine enkephalin in an ethanol solution provides intense molecular signals. The influence of the respective concentrations of analyte and salt in solution, of the silver trifluoroacetate solution stability, and of the sample microstructure on the secondary ion intensities are also investigated. The results of other combinations of analyte and salts are reported. Finally, the use of salts is critically compared to other sample preparation procedures previously proposed for SIMS analysis of large organic molecules.

Limited sensitivity constitutes an issue in several application fields of organic secondary ion mass spectrometry (SIMS). Parentlike ions and large molecular fragments are often detected with a signal/noise ratio that is unsatisfactory, for instance, when characterizing 1000–10 000 Da molecules or performing high-resolution SIMS imaging. In the past decade, new types of projectiles, mostly polyatomic, have been used to compensate the limited desorption and ionization yields of molecular and polymeric samples. The measured molecular ion yields are oftentimes orders of magnitude larger. There are strong indications from theoretical and experimental studies that these polyatomic primary ions create a “splash” effect at the surface (collective motion in a liquidlike region), thereby ejecting large chunks of material in the vacuum. Their effect on the ionization yield of molecular species has been also discussed. Beside the properties of the incident projectiles, the performance of the SIMS analysis of organic samples is largely dependent on the specific routes used for sample preparation. In our previous articles on this topic, the effect of evaporating a small quantity of a noble metal (Ag, Au) on the sample surface has been thoroughly tested and yield increases of several orders of magnitudes have been reported. The results were compared to the traditional cationization method, using a very dilute analyte solution cast on a Ag (Cu, Au) foil.

Another sample preparation procedure consists of adding salts with the analyte in order to provide a source of cationizing agents for the departing molecules. The salts can either be mixed with the analyte in a single solution or deposited independently from a separate solution—which should be more convenient for applications involving bulk samples. Salts are routinely used for synthetic polymer characterization in matrix-assisted laser desorption-ionization (MALDI) but rarely in SIMS. Nevertheless, the first few reports on the subject are found in the SIMS literature before their application to MALDI. In parallel with the enthusiasm for the MALDI analysis, they have reappeared in

MATERIALS AND METHODS

Samples. Four organic molecules, leucine enkephalin (LE), Irganox 1010 (IRGA), tetrphenylanthelene (TPN), and low molecular weight polystyrene (PS), have been selected for this study (Figure 1). The various sample preparation procedures are summarized in Table 1. Samples, salts, matrix, and solvents were mixed in various concentrations and cast on silicon supports or in other cases, they were cast (C) or spin-coated (SC) separately from different solutions. The order of deposition is the order reported in the literature for the deposition of the molecular layers. In addition to the nature of the salts, we investigate the influence of the analyte and salt concentrations, the presence of an organic matrix, and the aging of the solutions in the case of silver trifluoroacetate. Even though the effects of the salts generally depend on the nature of the analyte molecules and solvents used, our results indicate that silver might constitute a more universal cationizing agent than other group Ib and alkali metals.

Secondary Ion Mass Spectrometry. The secondary ion mass analyses were performed in a PHI-EVANS time-of-flight SIMS (TRIFT 1) using a 15-keV Ga\(^+\) beam (FEI 83-2 liquid metal ion source; ~550-pA dc current; 22-ns pulse width bunched down to ~1 ns; 5-kHz repetition rate for the mass range 0–5 kDa).\(^{17}\) The experimental setup has been described in detail elsewhere.\(^{22}\) The TOF-SIMS analyses were obtained by collecting the secondary ion signal in the mass range 0–5 kDa. The last column indicates whether cationized molecules have been observed, or not, in the corresponding SIMS spectra.

RESULTS AND DISCUSSION

This article compares the ability of various salts at cationizing the series of molecules depicted in Figure 1. For clarity, the use and limitations of alkali salts will be discussed first (Alkali Salts as Cationizing Agents). Then, the study focuses on group Ib metal salts, especially silver trifluoroacetate. Efficiency and concentration effects (Silver Trifluoroacetate (AgTFA) as Cationizing Agent),

Table 1. Nature and Preparation Procedure of the Analyzed Samples

<table>
<thead>
<tr>
<th>Sample</th>
<th>Salt/matrix</th>
<th>Solvent(s)</th>
<th>Preparation</th>
<th>Cations</th>
</tr>
</thead>
<tbody>
<tr>
<td>LE</td>
<td>NaBr (10)</td>
<td>H$_2$O (10)</td>
<td>Mixed (C)</td>
<td>yes</td>
</tr>
<tr>
<td>LE</td>
<td>AgTFA (10)</td>
<td>THF (5)</td>
<td>AgTFA (C)</td>
<td>no</td>
</tr>
<tr>
<td>LE</td>
<td>AgNO$_3$ (10)</td>
<td>Eth (10)</td>
<td>mixed (C)</td>
<td>yes</td>
</tr>
<tr>
<td>LE</td>
<td>AuCl$_3$ (10)</td>
<td>Eth (10)</td>
<td>mixed (C)</td>
<td>yes</td>
</tr>
<tr>
<td>LE</td>
<td>CuACAC (10)</td>
<td>THF (5)</td>
<td>CuACAC (C)</td>
<td>no</td>
</tr>
<tr>
<td>TPN</td>
<td>LiBr (10)</td>
<td>THF (5)</td>
<td>LiBr (SC)</td>
<td>yes</td>
</tr>
<tr>
<td>PS</td>
<td>NaBr (10)</td>
<td>THF/H$_2$O (53)</td>
<td>mixed (C)</td>
<td>yes</td>
</tr>
<tr>
<td>PS</td>
<td>KBr (10)</td>
<td>H$_2$O (5)</td>
<td>KBr (SC)</td>
<td>(no)</td>
</tr>
<tr>
<td>PS</td>
<td>AgTFA (10)</td>
<td>THF (10)</td>
<td>AgTFA (C)</td>
<td>yes</td>
</tr>
<tr>
<td>PS</td>
<td>CuACAC (10)</td>
<td>THF (5+10)</td>
<td>PS (C)</td>
<td>no</td>
</tr>
<tr>
<td>IRGA</td>
<td>AgTFA (100)</td>
<td>THF (10)</td>
<td>mixed (C)</td>
<td>yes</td>
</tr>
<tr>
<td>IRGA</td>
<td>AgTFA (20)</td>
<td>THF (2)</td>
<td>mixed (C)</td>
<td>yes</td>
</tr>
<tr>
<td>IRGA</td>
<td>AgTFA (10)</td>
<td>THF (5)</td>
<td>mixed (C)</td>
<td>yes</td>
</tr>
<tr>
<td>IRGA</td>
<td>AuCl$_3$ (5)</td>
<td>Eth (5)</td>
<td>mixed (C)</td>
<td>yes</td>
</tr>
<tr>
<td>IRGA</td>
<td>CuACAC (5)</td>
<td>THF (6)</td>
<td>CuACAC (C)</td>
<td>yes</td>
</tr>
</tbody>
</table>


Analytical Chemistry, Vol. 77, No. 7, April 1, 2005

Figure 1. Formulas and origin of the molecules investigated.

The recent SIMS literature,\(^{19–21}\) but a comprehensive study is not available to our knowledge.

In this article, we study the effects of two types of salts, alkali bromides and group Ib metal salts, on the secondary ion mass spectra of a series of molecules including two hydrocarbons (tetrphenylanthelene and polystyrene), a short peptide (leucine enkephalin), and a common polymer additive (Irganox 1010). In addition to the nature of the salts, we investigate the influence of the analyte and salt concentrations, the presence of an organic matrix, and the aging of the solutions in the case of silver trifluoroacetate. Even though the effects of the salts generally depend on the nature of the analyte molecules and solvents used, our results indicate that silver might constitute a more universal cationizing agent than other group Ib and alkali metals.

The secondary ion mass spectra of a series of molecules including two hydrocarbons (tetrphenylanthelene and polystyrene), a short peptide (leucine enkephalin), and a common polymer additive (Irganox 1010). In addition to the nature of the salts, we investigate the influence of the analyte and salt concentrations, the presence of an organic matrix, and the aging of the solutions in the case of silver trifluoroacetate. Even though the effects of the salts generally depend on the nature of the analyte molecules and solvents used, our results indicate that silver might constitute a more universal cationizing agent than other group Ib and alkali metals.

Secondary Ion Mass Spectrometry. The secondary ion mass analyses were performed in a PHI-EVANS time-of-flight SIMS (TRIFT 1) using a 15-keV Ga\(^+\) beam (FEI 83-2 liquid metal ion source; ~550-pA dc current; 22-ns pulse width bunched down to ~1 ns; 5-kHz repetition rate for the mass range 0–5 kDa). The experimental setup has been described in detail elsewhere.\(^{22}\) The TOF-SIMS analyses were obtained by collecting the secondary ion signal in the mass range 0–5 kDa. The last column indicates whether cationized molecules have been observed, or not, in the corresponding SIMS spectra.

RESULTS AND DISCUSSION

This article compares the ability of various salts at cationizing the series of molecules depicted in Figure 1. For clarity, the use and limitations of alkali salts will be discussed first (Alkali Salts as Cationizing Agents). Then, the study focuses on group Ib metal salts, especially silver trifluoroacetate. Efficiency and concentration effects (Silver Trifluoroacetate (AgTFA) as Cationizing Agent),

Table 2. Origin of the Solvents and Salts

<table>
<thead>
<tr>
<th>solvents origin</th>
<th>salts origin</th>
</tr>
</thead>
<tbody>
<tr>
<td>HNO₃ (65%)</td>
<td>XBr (X = Li, Na, K)</td>
</tr>
<tr>
<td>C₂H₁₄ extra pure</td>
<td>CF₃CO₂Ag (≈AgTFA)</td>
</tr>
<tr>
<td>(CH₂)₂CHOH; p.a grade</td>
<td>AgNO₃</td>
</tr>
<tr>
<td>C₂H₅OH; p.a grade</td>
<td>AuCl₃</td>
</tr>
<tr>
<td>C₆H₁₄O; p.a grade</td>
<td>[CH₂COCH==C(O)-CH₂]Cu(=CuACAC)</td>
</tr>
<tr>
<td>H₂O Millipore system</td>
<td>Sigma-Aldrich</td>
</tr>
</tbody>
</table>

Figure 2. Molecular ion range of the positive secondary ion mass spectrum of leucine enkephalin cationized using a Na salt (sample 1).
one clearly observes the \((M^+ + ^{107}\text{Ag})^+\) and \((M^+ + ^{109}\text{Ag})^+\) at \(m/z = 539; 541\). Weak signals are also detected for molecular dimers, \(M_2^+\) and \((M_2 + \text{Ag})^+\). In comparison with TPN molecules cast on silver, the measured intensities are \(\sim 1\) order of magnitude lower.\(^{25}\)

A series of PS oligomer samples have been prepared with AgTFA as a cationizing agent (samples 11a–11e). These samples differ by the relative fractions of PS molecules and salts, and one of them has been cast from a solution also containing an organic matrix (dithranol), following a sample preparation procedure derived from MALDI experiments.\(^{26}\) A similar PS sample directly cast on a silver foil was used as a reference for this series of analyses.

All the analyzed samples, including the one dissolved in dithranol, exhibit a distribution of Ag-cationized molecular ions in the mass range 1000–3500, roughly corresponding to the sample molecular weight as determined by GPC analysis (Figure 5). In comparison with the same PS sample cast on a silver foil, the absolute intensities are again \(\sim 1\) order of magnitude lower. There are also relative intensity differences between the samples, as exemplified by the spectra of samples 11a and 11d.

which differ by the concentration of salts and PS molecules in solution (10 times larger in sample 11d). The maximum of the distribution is shifted toward lower masses for sample 11d, and the relative amount of cationized chains below m/z = 1500 is larger. Sample 11c, with the same amount of PS as sample 11a, but 10 times more salts, has an intermediate shift (not shown). Finally, the “dithranol” sample (d), which contains the same fraction of PS and AgTFA in solution as sample 11a, but with an additional quantity of organic matrix, also exhibits a distribution shifted toward low masses. This observation is at odds with the report of Hanton and co-workers, who did not measure any signal of cationized PS oligomers using a similar sample preparation procedure. In general, we note that an increase of the organic molecule or salt concentration induces a shift of the Ag-cationized oligomer distribution toward lower masses.

The shift of the distribution toward low masses, with increasing analyte concentration, might be explained by the entanglement of the longer chains, favored for thick layers. In this respect, preliminary studies conducted in our laboratory showed that PS oligomers larger than 3–4 kDa could not be detected using a similar sample preparation procedure. This effect, however, does not explain why an independent increase of the AgTFA concentration also leads to a shift. Another possibility is that shorter oligomers naturally segregate at the surface of the sample for thick layers, masking some of the longer chains. As a third possibility, one cannot exclude a variation of desorption or ionization probability related to the nature and the thickness of the considered layers.

One should also keep in mind that, for these specific PS oligomers with a butyl and an hydrogen chain end, the low-mass range of the distribution is constituted in part by fragments of longer chains having lost the H-chain end plus a few repeat units (see discussion in ref 27). As indicated by the intermediate peaks intertwined within the main distribution, fragmentation is the most pronounced for samples 11c and 11d. This larger fragmentation probability, whether it is due to increased entanglement or to other desorption/ionization factors, can also explain the observed shift.

Silver trifluoroacetate salts also provide good results with polymer additives such as antioxidants. These molecules tend to segregate at the surface of polymers, and enhancing their detection by the use of selected cationizing agents would be appreciated. Figure 6 shows the positive mass spectrum of Irganox 1010, a common polymer antioxidant cast from a solution containing AgTFA salts (sample 14a). The low-mass range exhibits the characteristic fragments of Irganox (m/z = 57; 219), along with silver cations (m/z = 107; 109). In the molecular ion region, one detects the Ag-cationized molecule (m/z = 1284). The use of silver salts enhances the molecular ion signal by more than 3 orders of magnitude. Interestingly, the inset shows that other metal–molecule adducts are present at higher masses, corresponding to the formula (M + Ag)\(^+\) with 1 ≤ n ≤ 4. These additional adduct ions, not observed in the case of TPN, are probably stabilized by the interaction with the four phenyl rings, but also with the carboxyl groups, and by the greater flexibility of the molecule that allows it to rearrange around the metal atoms. To gain insights into the most stable molecular configurations of these ions, electronic structure calculations would be necessary. It should be noted that Ag\(^+\) clusters are also observed as such, for instance, Ag\(^+\) at m/z = 321–327 (second frame). The presence of these clusters in the mass spectrum demonstrates that there are metal aggregates on the sample surface.

Finally, the case of leucine enkephalin is important to mention. It has been shown in Figure 2 that LE is cationized by silver when deposited as a submonolayer on a Ag foil. However, when codeposited with AgTFA salts (sample 2), LE does not provide any cationized molecular ion, even when the silver signal is intense in the mass spectrum. The explanation might be somehow related to the fact that LE and AgTFA have markedly different chemical properties (polarity, solubility) and, therefore, must be cast from two separate solvents.

**Figure 6.** Positive secondary ion mass spectrum of Irganox 1010 cast on silicon from a THF solution containing silver trifluoroacetate salts (sample 14a). Inset: High-mass range of the same mass spectrum with intensities in a Log scale showing the various adduct ions, (M + Ag\(^n\))\(^+\).


Analytical Chemistry, Vol. 77, No. 7, April 1, 2005 2111
Figure 7. Effect of silver trifluoroacetate solution aging time on the secondary ion intensities measured after casting onto silicon wafers. (a) Ag-cationized polystyrene oligomers. Open diamonds: cast from a mixed solution (sample 11a); full diamonds: cast from separate solutions for the analyte and the salt (sample 11b). (b) Irganox 1010 sample (sample 14a). Full circles: fragment at \( m/z = 219 \); open diamonds: Ag-cationized molecules.

oligomer intensity with solution aging time for samples 11a and 11b (signal integrated between \( m/z = 1500 \) and 2500). Several extracts have been cast on silicon from solutions of analyte and salt with increasing aging time. The open symbols are for sample 11a (PS and AgTFA mixed in the same solution) and the full symbols for sample 11b (PS and AgTFA in different solutions, AgTFA cast first). For both samples, the extracts cast during the first couple of hours after the preparation of the solutions provide the best molecular signals in SIMS. One also notices that the results are quite comparable even after the sputtering process is still under way.\(^{27,31}\) In the specific scenario illustrated here for Irganox, the emission of Ag-molecule aggregates would be partly due to a direct process (preformed complex\(^{32,33})\), without the need of a recombination step.

Microstructure of the Cast Samples. To assess the microstructure of the deposited samples, we recorded a series of SIMS images for the same group of PS samples cast from solutions with various amounts of analyte, salts, or organic matrix (samples 11a and 11b in Table 1). Under the optical microscope, samples 11a and 11d present a similar aspect, made of a distribution of globules on a flat surface. This aspect is reflected in the SIMS images of Figure 8a–c, obtained from sample 11d. The difference between sample 11a, not shown, and sample 11d lies in the fact that the globules (dark regions in Figure 8a) are significantly smaller for sample 11a. For sample 11d, the contrast of the images of Ag\(^+\), C\(_{15}\)H\(_{23}\)O\(_{5}\)\(^+\), and cationized PS oligomers (PSAg\(^+\)) is quite similar. In all of the images, the globules appear darker, and their aspect observed under the microscope suggests that they actually are PS droplets, quite thick and therefore, inducing little secondary ion emission. Nevertheless, the line scan drawn across one of the droplets (OP in Figure 8a) shows that, even though the signal is depleted, silver cations are also sputtered with a significant intensity from their surface (Frame a1).

The second set of images (Figure 8d–f) was obtained from a sample where the weight fraction of salt in solution was 10 times larger than that of the PS analyte (sample 11c). The optical microscope shows that this sample is covered by pin- and filament-like structures of tens or hundreds of micrometers long. Figure 8d and the corresponding line scan, frame d1, reveal that intense Ag\(^+\) signals correspond to these filaments. The PS fragment image mirrors the Ag\(^+\) image with a lesser intensity, except for some specific regions where a large Ag\(^+\) signal corresponds to a somewhat depleted C\(_{15}\)H\(_{23}\)O\(_{5}\)\(^+\) intensity (arrow). Despite the much lower fraction of PS, the cumulated intensity of cationized PS oligomers (Figure 8f) is similar to that of sample 11d (Figure 8c).

The last series of images (Figure 8g–i) corresponds to sample 11e, the only sample for which an organic matrix (dithranol) was used in addition to the cationizing agent. This sample preparation procedure is similar to the one used in MALDI analysis of synthetic polymers.\(^{11,20}\) Sample 11e is covered by a dendrite network attributed to the dithranol matrix. Inside this treelike structure, the silver and PS-related signals are low. In addition, the optical microscope indicates that the dendrites form a pronounced relief in an otherwise very flat sample surface microstructure. The observed thickness, together with the dilution of the analyte and salt in the matrix, might again explain the low


PS and Ag signals in these dendrite regions. The line scan drawn across one of the dendrites (frame g1) shows that there is some Ag\textsuperscript{+} intensity inside the dendrite; i.e., the cationizing agent is not totally excluded from the dithranol crystals. The same is true for the PS characteristic ions. Except for the contrast related to the dendrites, the comparison between Figure 8g and h shows that there exists areas with a very intense Ag\textsuperscript{+} ion signal and a very low PS signal (top left corner of the images and region indicated by an arrow). The sample is thus strongly nonuniform and the three components (matrix, analyte, cationizing agent) are not well mixed after solvent evaporation, even though they were cast together from a single solution. In particular, the crystallization of the matrix into separated dendrites, together with the observation that Ag-cationized PS molecules are detected as well without the use of a matrix, leads us to question its usefulness for SIMS analysis.

In summary, SIMS imaging and optical microscopy concur to show that samples cast from solutions and subsequently air-dried are all nonuniform. They also confirm that the average analyte ion intensity is almost independent of the analyte concentration in solution (comparable signal for 1 and 10 mg/mL; see also Figure 5). Finally, the segregation of the dithranol matrix into a separate dendrite structure helps explain why the presence of a matrix has little effect on the Ag-cationized PS ion intensity. The nonuniformity of the samples certainly constitutes a problem for reproducibility, and as proposed by other authors for MALDI analysis, sample deposition via electrospray could elegantly solve this issue, at least for samples where the analyte is in solution with the cationizing agent.

Other Analyte--Metal Salt Combinations. Three other salts, namely, AgNO\textsubscript{3}, AuCl\textsubscript{3}, copper acetylacetonate ([CH\textsubscript{3}COCH=\textsubscript{C}(O)-(CH\textsubscript{2})\textsubscript{3}]\textsubscript{2}Cu or CuACAC) have been tested in combination with the four sample molecules depicted in Figure 1. The mass spectrum obtained after casting of a mixed solution of polystyrene and CuACAC on a silicon substrate is displayed in Figure 9a. It is obvious that this preparation procedure gives rise to Cu-cationized molecular ions of PS. Nevertheless, the distribution peaks around 1500 Da, which is much lower than the expected value, and the average intensity of these large ions is more than 1 order of magnitude weaker than that measured for the blend of PS and AgTFA. A similar intensity reduction is observed for Irganox 1010 (Figure 9b). In comparison, AuCl\textsubscript{3} salts do not lead to a significant
signal of Au-cationized PS molecules, and their efficiency for the cationization of Irganox is similar to that of CuACAC (Figure 9c).

As mentioned before, leucine enkephalin, our model peptide, could not be successfully cationized with AgTFA salts, when cast from separate solutions (different solvents). Further attempts using AuCl3 and CuACAC did not give better results. Finally, an ethanol solution containing leucine enkephalin and AgNO3 salts in the usual proportions (see Table 1, sample 3) was prepared and cast on a silicon substrate. This time, the molecular ion range of the obtained positive mass spectrum, Figure 10, shows the peaks of the Ag-cationized molecule. The mass spectrum is qualitatively similar to that of leucine enkephalin cast on silver foils from a solution containing Na salts (Figure 2). The average peak intensity, however, is more than 1 order of magnitude lower, demonstrating again the high efficiency of silver substrates at enhancing secondary ion emission. The residual Na-cationized molecular signals probably arise from a contamination of the leucine enkephalin solution by sodium, a common effect when analyzing peptides. The observation of (M – H + 2Na)+ and (M – H + Na + Ag)+ ions in the mass spectrum, as was the case in Figure 2, suggests that an H residue of the peptide is replaced by Na in a fraction of the analyzed molecular extract. Even though silver foils provide a larger molecular signal (Figure 2), there might be situations in which a preparation procedure using AgNO3 salts should be preferred, for example, when characterizing a layer of peptides adsorbed on a different substrate.

**Comparison with Other Sample Preparation Procedures.**
For PS and Irganox 1010, the results obtained with AgTFA salts as cationizing agents can be compared with data recently collected using the same molecular samples and the same TOF-SIMS instrument. Some of these data have been reported in two published articles.6,7 First, the Ag-cationized ion yields measured using AgTFA salts are, roughly, 1 order of magnitude lower than those measured from molecular submonolayers cast on silver foils, as illustrated in Figure 5 for polystyrene (see Figure 2 in ref 7 for Irganox).

With respect to the noble metal deposition procedure reported in the above-mentioned articles (see introduction and refs 6 and 7), the molecular ion yields measured using AgTFA salts appear equivalent or even larger. For PS samples, the yields measured with the two methods are comparable. For Irganox, AgTFA salts lead to higher intensities than those measured upon sample metallization with Ag; they differ by a factor of 4.

Therefore, from the strict viewpoint of efficiency, AgTFA salts are equivalent or even better than evaporated metal atoms. The preparation protocol using salts, however, has one important drawback, in the case of samples that should be analyzed as received. Because the salts must be cast from a liquid solution, the procedure can induce a redissolution of the molecular sample surface, if they are soluble in the same solvent or, at the least, layer nonuniformity, diffusion, (de)wetting, or contamination problems (even when sample and salt are not soluble in the same solvent). In comparison, metal evaporation is a dry technique, and per se, it circumvents most of these issues. In particular, SIMS imaging of samples covered with metal salts cast from solution would not appear as reliable. This important issue is also encountered in MALDI.11 Nevertheless, in comparison with sample metallization, the use of salts does not require any expensive equipment (no evaporator, only beakers), which makes it quite attractive for an analytical chemistry laboratory.

Leucine enkephalin is efficiently ionized by alkali salts, in particular, Na salts, which confirms previous reports from the
MALDI\textsuperscript{11} and SIMS\textsuperscript{19} communities concerning the ionization of peptides. It can be cationized by silver, though, in the form of a molecular submonolayer on metal, but also when cast from a AgNO\textsubscript{3}-containing solution on an “inert” substrate (Figure 10). It should be noted that cationized peptides such as leucine enkephalin could not be successfully observed from thick layers metallized with Ag and Au\textsuperscript{6,7} or from samples containing AgTFA salts. Therefore, the use of AgNO\textsubscript{3} salts appears to be an interesting alternative.

CONCLUSION

In this article, the specific ability of a series of alkali (Li, Na, K) and group Ib (Cu, Ag, Au) metal salts to induce cationization of various organic analytes has been empirically determined. Overall, the results are in broad agreement with the concepts of Lewis bases and acids: weak bases such as aromatic molecules are better cationized by weak acids (group Ib metal cations), and hard bases such as peptides are more efficiently ionized by hard acids (alkali cations). It should be emphasized, however, that complex molecules such as Irganox 1010 and leucine enkephalin, bearing various residues, are efficiently cationized by both types of salts. In addition to the chemical nature of the salt and analyte compounds, our results show that the concentration of analyte and salts, the nature of the solvents, whether a common solvent is used for the salt and the analyte or not, the sequence of deposition, the aging of the solution, and the microstructure of the sample after casting are important parameters that should be well controlled if one wishes to obtain reproducible SIMS spectra using this sample preparation procedure. In comparison with other preparation routes, the use of salts has specific advantages—large intensity of cationized analytes even for “thick” samples, no costly equipment required—and drawbacks—problems of reproducibility, analyte and salt migration on the surface—which make it a very useful alternative, but not a universal method. Concerning the combined use of a low molecular weight organic matrix together with metal salts, our preliminary results are not conclusive. This topic should be investigated in detail in future works. Finally, the present study only considered sample desorption induced by monatomic Ga\textsuperscript{+} projectiles. We believe that the combination of this sample preparation procedure with the use of polyatomic primary ions such as fullerenes, outstanding for the characterization of thick organic samples,\textsuperscript{3} should lead to very exciting new results.

ACKNOWLEDGMENT

A.D. thanks the Fonds National de la Recherche Scientifique (FNRS) for financial support. This work is partly funded by the Interuniversity Attraction Pole program on “Quantum sized effects in nanostructured materials” of the Belgian Federal State. The ToF-SIMS equipment was acquired with the support of the Région Wallonne and FRFC-Loterie Nationale of Belgium.

Received for review September 1, 2004. Accepted December 10, 2004.

AC040158S