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Electrospray Mass Spectrometry using Potassium Iodide in Aprotic Organic Solvents for the Ion Formation by Cation Attachment

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Abstract: A solution of KI in DMF-THF (1:1) was used as aprotic solvent in electrospray ionization mass spectrometry (ESI-MS) of neutral organic compounds. The potassium ions brought about the ionization. The new method was tested with poly(ethylene glycol) and applied to compounds unusual for ESI-MS.

Electrospray ionization mass spectrometry (ESI-MS) has become a popular method for the measurement of molecular weights.[1] The soft-ionization technique can be used to produce ions even from thermally labile, non-volatile, polar compounds. During the electrospray process, which is based on the spraying of suitable solutions in an electric field to give charged droplets and on the behavior of these, singly and multiply charged ions of an analyte can be formed.[2-5] Until today most of the applications relate to proteins, other large biomolecules or ionic compounds that are injected into the electrospray interface as dilute solutions.[6-9] The ions are usually formed by protonation of covalent analytes, or by dissociation of ionic compounds. Typical solvent systems used are MeOH, MeCN, H_2O, acetone, and mixtures of these, which are acidified by the addition of organic acids to give positive ions. Different buffer solutions are also in use.

In the present investigation we describe an alternative way to employ ESI-MS for the investigation of covalent organic compounds. The important feature of the method is the use of KI dissolved in the aprotic solvent DMF-THF (1:1). It is shown that the potassium ions can be used for the ionization of covalent organic compounds during the electrospray process to give positive ions. This method can be important when compounds are sensitive towards the solvent systems usually used for ESI-MS, for example towards protons, or when alternative solvents must be used due to solubility problems of the analyte.

Materials and Methods

The poly(ethylene glycol) (PEG) standards (average M.W. = 1500 and 3400) were from Aldrich Chemical Co. Ltd. (±)-exo,endo-Bis(6-(biphen-4-oxy)hexyl)bicyclo[2.2.1]hept-5-ene-2,3-dicarboxylate (**1**) and the cyclotrimer of 2-(3,4-diethynylphenyl)-4,4,5,5-tetramethyl-4,5-dihydro-1H-imidazolyl-1-oxyl-3-oxide (**2**) were prepared as described elsewhere.[10,11] Mass spectra were recorded using a standard Kratos electrospray ion source that was fitted to a Kratos Profile double focussing magnetic sector instrument. The instrument was operated at 2 kV acceleration voltage. The m/z range recorded was 50 to 2000 Da, the scan speed 10 s/Dec, the resolution 1500 (10% valley definition). The potentials applied were 7.5 kV at the spraying capillary, 2.5 kV at the cylinder, and 2.8 kV at the endplate. The temperature of the electrospray ion source was 125 °C. The countercurrent flow of nitrogen was 100 ml/min. A Harvard Apparatus 22 syringe pump was used to deliver a constant solvent flow of 3µL/min (solution of potassium iodide (50 mg/L) in DMF-THF (1:1)). Solutions of the samples (100 pmol/µL in the solution described above) were injected into the solvent flow *via* a 100 µL sample loop. The signal-to-noise ratio was improved by averaging the scans of 15 min. The m/z values are given for the most intensive peak of any isotope distribution.

Results and Discussion

The solution of potassium iodide (50 mg/L) in DMF-THF (1:1) and the voltages applied were found to give very satisfactory results with respect to the stability and the sensitivity of the electrospray. The system could be operated stably over periods of more than 10 hours without loss of sensitivity. Increasing the concentration of KI led to blocking of the electrospray interface. The sensitivity was very poor when the concentration of KI was decreased below 0.5 mg/L.

Figure 1 shows the mass spectrum obtained for PEG 1500. The spectrum can be interpreted with two major series of ions. Series *A* consists of ions in the m/z range 849.4 to 1950.1 Da, the m/z differences between the ions are 44 Da. The most abundant ion was at 1201.7 Da and was found to be singly charged by the isotope peaks. This ion is $[HO(CH_2CH_2O)_{26}H \cdot K]^+$ (theoretical m/z = 1201.7 Da). The other ions of the series are $[HO(CH_2CH_2O)_nH \cdot K]^+$ with n = 18 to 43. Series *B* (m/z range 554.3 to 1082.6 Da; m/z difference between the ions 22 Da; z = 2) is $[HO(CH_2CH_2O)_nH \cdot 2K]^{2+}$ with n = 23 to 47. The most abundant ion of this series was found at 774.4 Da and is $[HO(CH_2CH_2O)_{33}H \cdot 2K]^{2+}$ (theoretical m/z = 774.4 Da).

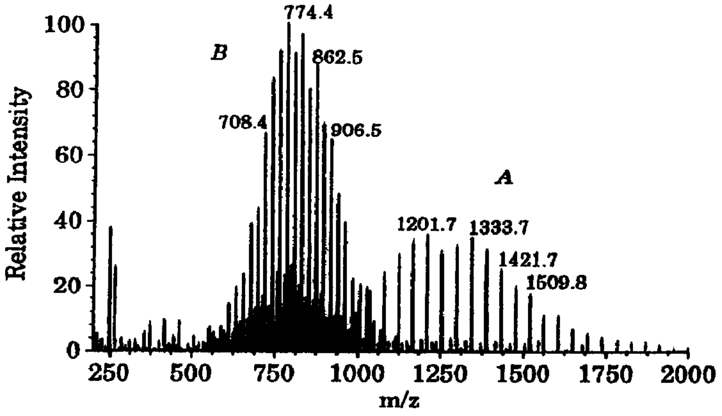


Figure 1: ESI-MS spectrum of PEG 1500 in DMF-THF (1:1) / KI (50 mg/L); *A*: z = 1; *B*: z = 2.

It is worth noting that for PEG 1500 both the polymerization degree n of the oligomeric ion with the highest abundance and the range of different values of n are higher for series *B* than for series *A*. Thus the addition of more than one potassium ion can only be stabilized with increasing values of the polymerization degree n. The mass spectrum obtained for PEG 3400 stands in good agreement with this observation (Figure 2). The spectrum shows two series of ions that can be interpreted as $[HO(CH_2CH_2O)_nH \cdot 3K]^{3+}$ (n = 61 to 86) and $[HO(CH_2CH_2O)_nH \cdot 4K]^{4+}$ (n = 63 to 89), respectively. These results are very similar to mass spectra of PEG that were obtained from solutions in MeOH-H_2O with KCl or NaCl.[8] This proves that the solvent mixture DMF-THF (1:1) can be used for ESI-MS investigations. In addition to the series discussed, series of $[HO(CH_2CH_2O)_nH\cdot mK\cdot THF]^{m+}$ can be found. At low temperatures of the electrospray ion source these series are preferred in comparison to those without THF.

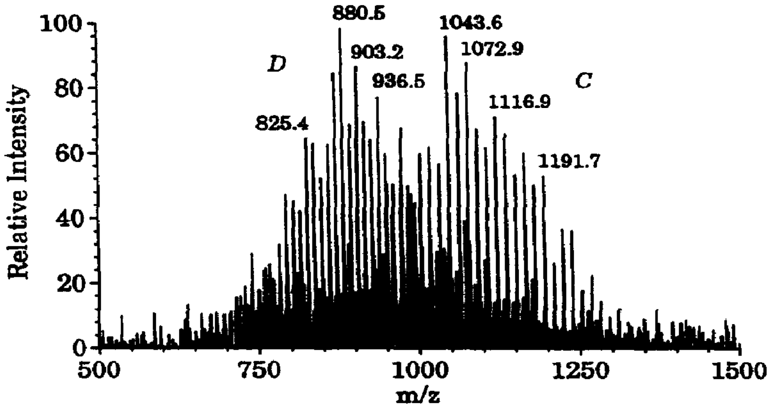
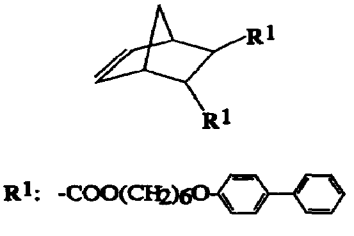


Figure 2: ESI-MS spectrum of PEG 3400 in DMF-THF (1:1) / KI (50 mg/L); *C*: z = 3; *D*: z = 4.

We investigated several organic compounds with the method described. The examples given below were the most interesting as yet, because these compounds are unusual for ESI-MS investigations. Compound **1** was used as monomer for liquid crystalline polymers.[10] Compound **2**, a cyclic triradical, was obtained as a byproduct during the synthesis of the corresponding polydiacetylene.[11] For both compounds no mass spectra have as yet been available.



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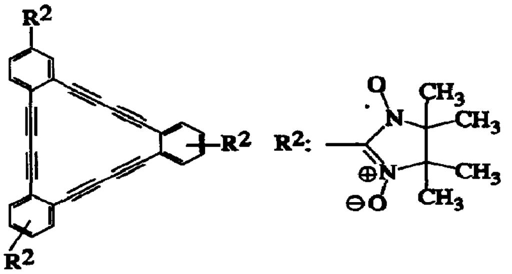

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Figure 3 gives the results obtained for compound 1 ($C_{45}H_{50}O_6$). The spectrum shows a singly charged ion with a molecular mass of 725.3 Da (theoretical mass for $[C_{45}H_{50}O_6\cdot K]^+$ = 725.3 Da). In Figure 4 the results obtained for compound 2 ($C_{51}H_{45}N_6O_6$) are reproduced. The mass of the singly charged ion is 876.3 Da (theoretical mass for $[C_{51}H_{45}N_6O_6\cdot K]^+$ = 876.3 Da). These examples show that the use of KI dissolved in DMF-THF can be a good method to obtain electrospray mass spectra of organic compounds. Investigations of compounds sensitive to protons and air, and compounds that must be multiply charged to be in a reasonable m/z range are in progress and will be published in a following paper.

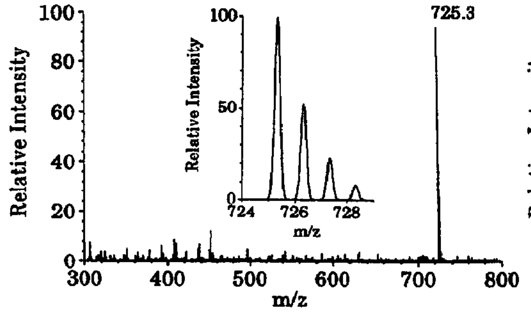

Figure 3: ESI-MS spectrum of compound 1 in DMF-THF (1:1) / KI (50 mg/L). Insert: isotopic mass distribution of peak 725.3

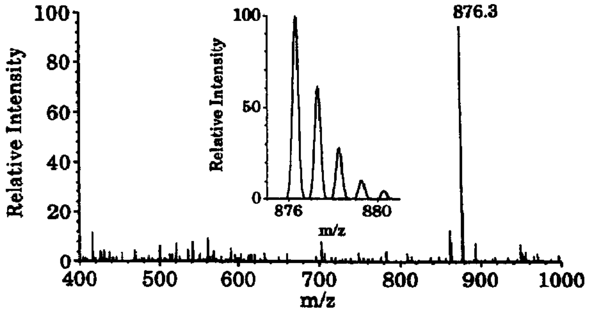

Figure 4: ESI-MS spectrum of compound 2 in DMF-THF (1:1) / KI (50 mg/L). Insert: isotopic mass distribution of peak 876.3

Conclusions

In this work it is shown that potassium ions in aprotic organic solvents such as DMF-THF can be used for the ionization of covalent organic molecules during the electrospray process. The observation is important because of the prospect that structural information about compounds or reaction intermediates that are sensitive towards solvent systems usually used in ESI-MS, especially towards protons, could be obtained. Furthermore it is important to note that the use of solvents as yet untypical for ESI-MS will make this technique a more powerful analytical tool.

Acknowledgment

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