Pencil Lead as a Matrix for MALDI-ToF Mass Spectrometry of Sensitive Functional Polymers

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ABSTRACT: With the increase in complexity of functional polymers in recent years, MALDI-ToF has become an important tool for gaining precise information on polymer functionality, end groups, and, in special cases, molecular weights. Here we describe how pencil lead, deposited by simply drawing with a regular pencil onto conventional MALDI-ToF targets, can be used as a very attractive matrix for MALDI-ToF mass spectrometry of synthetic polymers. Highly sensitive polymers such as silyl hydride functional poly(styrene), poly(butadiene), and poly(isoprene) have been investigated using conventional MALDI-ToF matrices as well as pencil lead. In all cases, the use of pencil lead prevented oxidation of the highly sensitive silyl hydride end groups. It is shown that pencil lead represents an interesting alternative to the commonly used matrices in the range between 400 and 6000 g/mol due to the convenient way of deposition, its low cost, nontoxicity, and chemical inertness under sample preparation conditions.

Introduction

In view of the increasing complexity of polymer architectures targeted today, matrix-assisted laser desorption ionization mass spectrometry (MALDI-MS) has become a crucial tool for the detailed characterization of polymer structures. MALDI-ToF mass spectrometry yields information on the masses of individual polymer chains of a molecular weight distribution. Therefore, this technique permits identification of end groups as well as species present in minor amounts in a polymer sample that can often not be detected by other methods. Precise determination of the end-group structure of macromolecules often has important consequences for subsequent reactions of the polymer as well as for the elucidation of mechanistic details. For industrial polymers, information on the structure of capping agents and additives often represents a central issue.[1]

It has been well-established that the choice of matrix is critical for successful MALDI-ToF MS, and to date, no universal matrix has been found that could be employed for all analytes. Many matrices, however, have been developed for use with a wide range of analytes, each of which can perform well for a specific group of polymers. In general, a successful matrix must absorb the incident radiation, promote the chemistry leading to ionization, and assist in the desorption of intact, i.e., unfragmented, analyte ions. Matrices that are frequently used in the analysis of polymers are dithranol, HABA (2-(4-hydroxyphenylazo)-benzoic acid), DHB (2,5-dihydroxybenzoic acid), or IAA (3,β-indoleacrylic acid).[2]

Recently, Black and co-workers[3] presented an impressive study, showing the usefulness of simple pencil lead as a MALDI matrix, in particular for the analysis of actinide metal oxides. In their publication, also one poly(ethylene oxide) sample was successfully characterized using pencil lead. The authors studied different commercially available types of pencil lead and found that the 6B grade (using the HB standard nomenclature) gave the best results for each of the samples tested. Reproducible signals which were due to the matrix (carbon clusters) could also be used for the calibration of the instrument and are ideal for analysis of samples in this mass range.

Pencil lead usually consists of graphite mixed with other components such as clay, wax, and different salts. Graphite has already been used for MALDI-ToF analysis in several studies. Sunner et al.[4] and Dale et al.[5] used graphite mixed with glycerol or a liquid matrix, employing graphite as laser energy transfer medium for desorption and the liquid matrix as a protonating agent and to increase the sample lifetime at a particular desorption spot. Graphite as matrix was also used for the analysis of tetracycline,[6] polymeric materials, such as triterpenoid resins and varnishes,[7−9] and low molecular weight poly(methylsilsesquioxane)s.[10] The use of solid graphite targets has also been described previously.[11−15]

These interesting fundamental studies prompted us to carry out the current investigation, using various end-functional, narrow polydispersity polymers prepared by anionic polymerization. In addition to the obvious simplicity of matrix deposition by merely drawing with a pencil onto the sample holder, the solvent-free nature of matrix deposition avoids all potential immiscibility problems between polymer and matrix solutions. Solvent-free methods in MALDI-MS sample preparation have proven valuable for the characterization of different materials.[16,17]

As we show in this study, pencil lead represents a very mild technique for samples that are sensitive to the routinely used matrix preparations. Naturally, the analyte must “survive” the sample preparation procedure in order to be analyzed, and this is a critical point for many classes of compounds. Silyl hydride-functionalized polystyrenes are known to be sensitive to the common methods of sample preparation. Using dithranol as a matrix and AgTFA as additive (which is a common sample preparation strategy for polystyrene-derivatized polymers), the silane moiety is oxidized, as pointed out in a recent paper by Quirk et al.[18] This study shows the use of pencil lead as a general MALDI matrix for polymers and in particular for the analysis of terminal silyl hydride-functionalized polymers.

Experimental Section

Chemicals and Solvents. All compounds were purchased from Acros and used as received unless otherwise stated. Cyclohexane

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and THF for polymerizations were purified by cryo-transfer from a dark-red living polystyrene (PS) solution just prior to use. Isoprene and styrene were stored over CaH_2 until used. The concentration of the initiator was determined by the Gilman double titration method.[19] Chlorodimethylsilane was dried over CaH_2 and cryo-transferred into an ampule until used. CaH_2 was purchased from Fluka and used as received. Toluene (extra dry, with molecular sieves, water <50 ppm) was used without further purification. Karstedt's catalyst in xylene (2.1 − 2.4% Pt) was purchased from ABCR GmbH & Co. KG and used as received. All degassing and cryo-transfer procedures were carried out using liquid nitrogen as cooling agent, if not otherwise mentioned. Deuterated chloroform was purchased from Deutero GmbH and used as received. AgTFA and LiTFA used for MALDI-ToF MS analysis were purchased from Aldrich, and dithranol was from Sigma. Pencil lead 6B used as matrix was the "Castell 9000 6B" pencil (Faber-Castell Germany). Polystyrene standards and poly(ethylene oxide) standards for the MALDI-ToF analysis were purchased from Polymer Standard Service (Mainz, Germany). A Proteo Mass peptide and Protein MALDI-MS calibration kit from Sigma was used for calibration.

Polymerization Procedures. All polymerizations were conducted in a 1 L glass reactor, containing a 100 mL flask with living polystyrene solution in cyclohexane (closed by a separate Teflon tap), a magnetic glass stirrer, a Teflon septum, and an additional Teflon tap to separate the reactor from the vacuum line. The reactor was connected to a vacuum line (standard oil pump, ca. 10^{-2} mbar) containing a graduated ampule and the flasks with solvents and reagents. It was evacuated, removed from the line, and rinsed with the living polystyrene solution. Using cryo-transfer procedures, the living PS solution was transferred back into the 100 mL flask with any other impurities. The reactor was connected again to the vacuum line and evacuated for another hour. The monomer was cryo-transferred to the ampule (ca. 20 mL) and then transferred to the reactor. Afterward, the solvent was transferred into the reactor (concentration of monomer ∼10 vol %). The frozen solution was degassed by one further freeze−thaw cycle.

For Cyclohexane (Polystyrene). The reaction mixture was allowed to warm up to −5 °C and was then initiated with the appropriate amount of *sec*-BuLi with a gastight syringe (Hamilton). After stirring for 10 min at −5 °C the mixture was heated to 40 °C for another 10 h to complete the reaction.

For THF (1,3-Butadiene, Isoprene). The reaction mixture was cooled to −100 °C (ethanol/liquid N_2) and initiated with the appropriate amount of *n*-BuLi. The reaction was completed after warming to −20 °C (ca. 2 h).

Quenching of the living chains was established by cryo-transfer of chlorodimethylsilane into the reactor until the color of the living anions disappeared completely.

Data for PI-$SiMe_2H$: ^1H NMR (400 MHz, $CDCl_3$): 0.11 (s, $Si(CH_3)_2$), 0.87−2.15 (m, *n*-Bu (initiator), CH,CH_3, CH_2 (backbone)), 3.93 (m, Si−*H*), 4.52−5.51 (m, −C*H*= (1,4-addition), =CH_2 (3,4- and 1,2-addition)), 5.65−5.95 (m, =C*H*− (1,2-addition)). $^{29}Si\{^1H\}$ NMR (79.43 MHz, $CDCl_3$): 14.5 (s, *Si*Me_2H).

Data for PB-$SiMe_2H$: ^1H NMR (400 MHz, $CDCl_3$): 0.11 (s, $Si(CH_3)_2$), 0.89 (t, CH_2 (initiator)), 1.15−1.36 (m, CH_2 (backbone)), 1.85−2.14 (m, C*H* (backbone)), 3.87 (m, Si−*H*), 4.87−4.96 (m, =CH_2 (1,2-addition)), 5.33−5.56 (m, =C*H*− (1,2-addition), =C*H*− (1,4-addition)). $^{29}Si\{^1H\}$ NMR (79.43 MHz, $CDCl_3$): 14.1 (s, *Si*Me_2H).

Data for PS-$SiMe_2H$: ^1H NMR (300 MHz, $CDCl_3$): 0.1 (s, $Si(CH_3)_2$), 0.65−2.29 (m, *sec*-Bu (initiator), $CHCH_2$(Ph)), 3,87 (m, Si−*H*), 6.5−7.2 (m, $CHCH_2$(*Ph*)). $^{29}Si\{^1H\}$ NMR (79.43 MHz, $CDCl_3$): −7.5 (s, *Si*Me_2H).

Model Reaction: PS-$SiMe_2H$ with 1,4-Hexadiene. 1 g of PS-$SiMe_2H$ was dissolved in dry toluene, and a 2-fold excess of 1,4-hexadiene was added with a syringe. The hydrosilylation reaction was initiated by adding one drop of Karstedt's catalyst to the solution at room temperature. The reaction was complete after 12 h stirring at room temperature. ^1H NMR (300 MHz, $CDCl_3$): −0.17 (m, SiMe_2, 6H), 0.34 (br, SiCH_2, 2H), 0.69 (t, br, CH_3, 6H (initiator)), 1.2−2.3 (br, CH_2C*H*(Ph)), 5.4 (m, C*H*=C*H*, 2H), 6.4−7.2 (br, CH_2CH(*Ph*)). $^{29}Si\{^1H\}$ NMR (79.43 MHz, $CDCl_3$): 4.3 (s, *Si*Me_2).

Instrumentation. ^1H and ^{13}C nuclear magnetic resonance spectra were recorded at a frequency of 300 MHz on a Bruker AC 300 NMR spectrometer or on a Bruker AMX 400, working at 400 MHz, using benzene-d_6 as solvent.

Size exclusion chromatography in THF was performed on an instrument consisting of a Waters 717 plus autosampler, a TSP Spectra series P 100 pump, and a set of three PSS-SDV 5 μm columns with 100, 1000, and 10 000 Å porosity. THF was used as an eluent at 25 °C and a flow rate of 1 mL min^{-1}. The specific refractive index increment (d*n*/d*c*) was measured at 30 °C on an Optilab DSP interferometric refractometer (also RI detector) and determined with the Wyatt ASTRA IV software (Version 4.90.08). Calibration was carried out using poly(styrene) standards provided by Polymer Standards Service and performing a third-order polynomial fit.

Static light scattering measurements were performed on a multiangle laser light scattering detector (MALLS) DAWN EOS laser photometer (Wyatt Technology Co.) equipped with a GaAs laser emitting at a wavelength of 685 nm. Molar masses were calculated during SEC measurements using the Wyatt ASTRA IV software (Version 4.90.08) and ASTRA V (Version 5.1.8.0). Masses were calculated in 0.25 s intervals using the Zimm equation:

$$\frac{Kc}{R_\theta} = \frac{1}{M_w} + 2A_2c \qquad K = \frac{4\pi^2 n_0^{\,2}\left(\frac{dn}{dc}\right)^2}{\lambda_0^{\,4} N_A} \tag{1}$$

n_0 is the refractive index of toluene, N_A is Avogadro's constant, λ is the laser wavelength, M_w is the apparent weight-average molecular weight, A_2 is the second virial coefficient, and R_θ is the Rayleigh ratio of the polymer solution at a given angle. In SEC-MALLS the second virial coefficient is small enough to be neglected at the low concentrations used in chromatographic separation. As the value is unknown, we arbitrarily set it to zero, as the resulting error is very small.

MALDI-ToF. Mass spectra were acquired by MALDI-ToF (time-of-flight) mass spectrometry using a Shimadzu Axima CFR MALDI-ToF (matrix-assisted laser desorption and ionization time-of-flight) mass spectrometer, equipped with a nitrogen laser delivering 3 ns laser pulses at 337 nm. Samples using dithranol as matrix and AgTFA as additive were prepared by dissolving the polymer in THF at a concentration of 10 g/L. A 10 μL aliquot of this solution was added to 10 μL of a 10 g/L matrix solution, and AgTFA as a MeOH solution (0.1 M) was added as cationization agent. A 1 μL aliquot of the resulting mixture was applied to a multistage target to evaporate the solvent and create a thin matrix/analyte film. In the case of pencil lead, a pencil was used to draw directly onto the target spot, ensuring that the entire surface was covered. Then, 1 μL of the sample solution was added on the top of the matrix using a pipet and left to dry in air. In some cases 1 μL of a LiTFA solution (0.1 M) was added. The samples were analyzed with the operator manually searching for the sample "sweet spot" for data collection. The samples were measured in positive linear or reflectron ion mode.

Results and Discussion

A. Pencil Lead as Matrix for Polystyrene and Poly(ethylene oxide).

In this investigation we used the pencil lead 6B as matrix in analogy to the work of Black et al.[3] In a first series of measurements, polystyrene samples were measured with pencil lead as a matrix with or without AgTFA as additive. As shown in Figure 1, well-resolved spectra in both linear and reflectron positive mode were obtained for three polystyrene samples of differing molecular weight (M_n = 435 g/mol, PDI

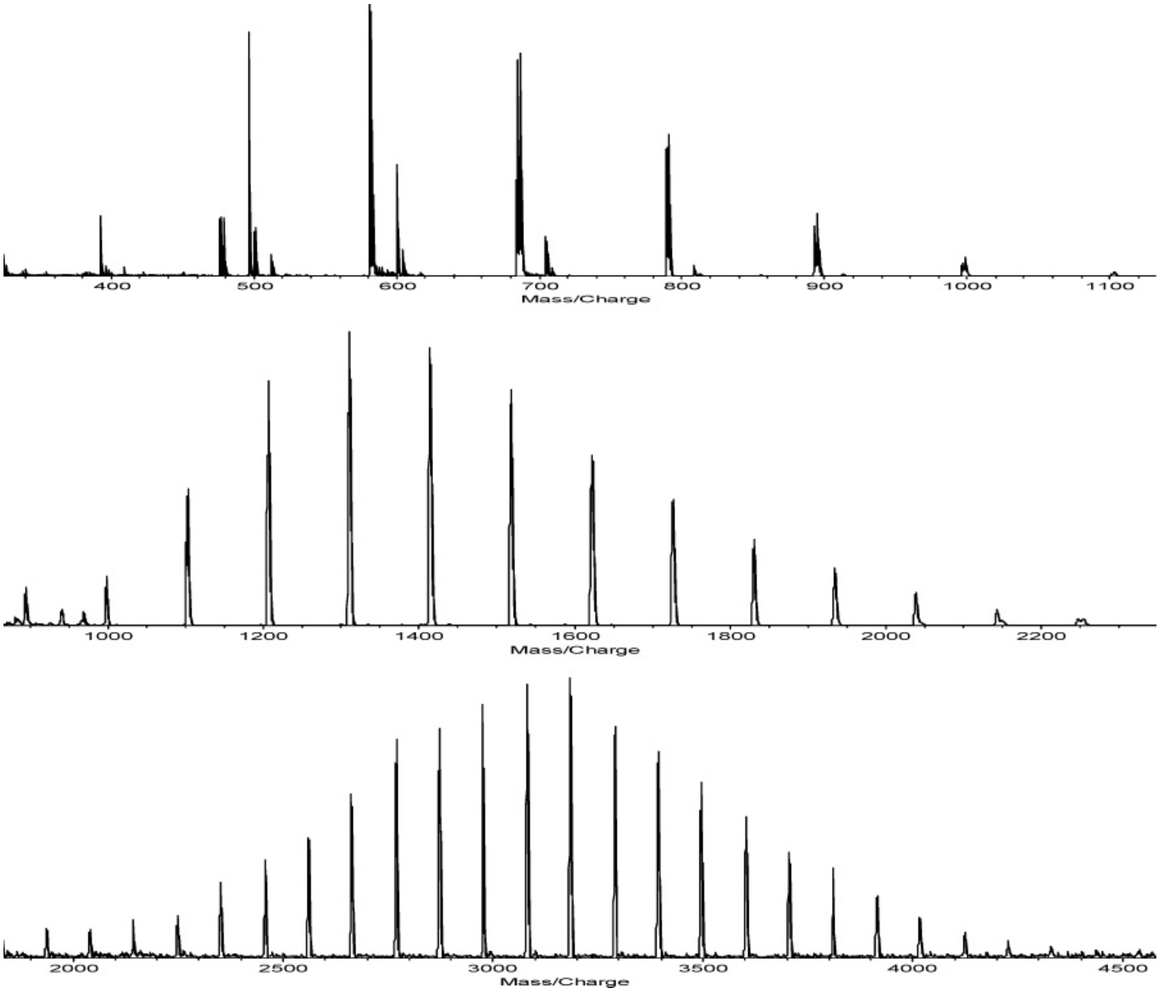
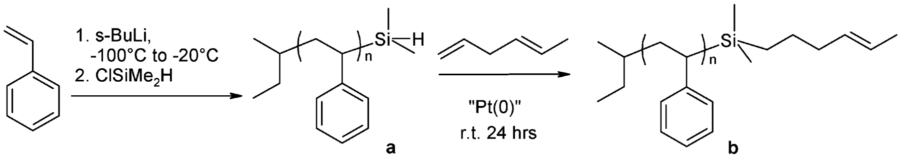


Figure 1. MALDI-ToF MS spectra of polystyrene (top: $M_n = 435$ g/mol; $M_n = 1500$ g/mol; bottom: $M_n = 3280$ g/mol), measured with pencil lead as matrix and silver trifluoroacetate as additive.

Scheme 1. Synthesis of Silyl Hydride-Functionalized Polystyrene via Anionic Polymerization (Product a); Model Reaction of Silyl Hydride Polystyrene with 1,4-Hexadiene (Product b)



$= 1.06$; $M_n = 1500$ g/mol, PDI $= 1.06$; and $M_n = 3280$ g/mol, PDI $= 1.04$). The samples containing silver salt additives gave more intense spectra (higher signal-to-noise ratio) compared to the ones without silver ions, and the signals corresponding to the polystyrene silver ion adducts were the most intense in the spectra. In the spectra measured without silver ion additives the most intensive signals recorded were those of the sodium adducts. A fourth polystyrene sample of even higher molecular weight was analyzed ($M_n = 10\,000$ g/mol, PDI $= 1.04$) with and without AgTFA addition. Different amounts of the higher molecular weight polystyrene were deposited onto the pencil lead matrix from THF solution, but no meaningful mass spectra could be obtained. In general, one can conclude that pencil lead is a very useful matrix for routine measurements of polystyrene in the mass range between 300 and 4500 g/mol. It is important to mention that, in addition to the obvious advantages of the pencil lead matrix such as low price and ease of preparation, it gave better results for the analysis of polystyrene in the presence of AgTFA than the commonly used dithranol matrix.

For molecular masses below 300 g/mol, the presence of signals due to the pencil lead matrix complicates the spectra. While this is also the case for all commonly used matrices, some of the mass signals originating from the pencil lead matrix are reproducible and can be used as an internal calibrant, as proposed by Black et al.[3]

The laser power intensity also has a strong influence on the quality of the spectra. The presence of carbon clusters at higher molecular weight was observed to increase with increasing laser power. Thus, we can conclude that only for masses exceeding 5000 Da the pencil lead matrix shows some limitations, possibly because of the poor miscibility with the analyte in the solid state.

The molecular weight limitations may be due to the existence of "hot spots" on the sample target.[5] To obtain better results and better homogeneity of the sample in this mass range, the pencil lead might have to be pulverized and mixed in a mortar with the analyte as a solvent-free MALDI-MS preparation.[16] Studies in this direction are currently in progress in our group.

In order to investigate the scope and limitations of the pencil lead matrix method, a series of poly(ethylene oxide) samples were analyzed (PEO 2000, M_n = 1840 g/mol, PDI = 1.09; PEO 3000, M_n = 2800 g/mol, PDI = 1.09; PEO 6000, M_n = 5610 g/mol, PDI = 1.16; PEO 10 000, M_n = 10 600 g/mol, PDI = 1.15). Well-resolved mass spectra were obtained for PEOs up to 6000 g/mol, while the spectrum obtained for PEO 10 000 could not be interpreted in a meaningful way. All measurements were carried out in the absence of salt additives, yet metal ion adducts (Na^+, K^+) were observed in agreement with the results reported by Black et al. for PEO 2000.[3]

We would like to stress that while the sample preparation employed here does not allow for an intimate mixing between the insoluble matrix and the analyte, we were able to obtain well-resolved MALDI mass spectra. In our case, interaction of the analyte with the matrix surface appears to be sufficient for successful characterization. This observation is interesting for further investigation related to matrix−analyte interactions in MALDI-MS.

B. Pencil Lead as Matrix for Sensitive Silyl Hydride-Functionalized Polymers. Silyl hydride-functionalized polymers are an important class of polymers because they can react with a variety of readily available substituted alkenes to give chain-end-functionalized polymers. This is typically achieved via an efficient, regioselective transition-metal-catalyzed hydrosilylation reaction.[18,20−23]

MALDI-ToF mass spectrometry is a very useful analytical technique to analyze such end-group-modified polymers. Especially in the mass range below 20 kDa it is often possible to obtain well-resolved spectra and therefore information on the constitution of individual polymer chains. This permits determination of the nature of the end groups of polymers and has largely contributed to the popularity of the MALDI-MS method.

Often, both sample preparation and MALDI-MS measurement have to be carried out under inert conditions to preserve the integrity of the sample and especially that of the end group. In the case of silyl hydride-functionalized polystyrenes it was observed that the sample preparation using the common dithranol matrix in the presence of Ag^+ led to considerable side reactions challenging the results.[18] Additional studies showed that the use of dithranol and Ag^+ causes oxidation of the silyl hydride functionality.

Using pencil lead as matrix and LiTFA as additive, we could obtain the spectra of the unaltered silyl hydride-functionalized polystyrene, polyisoprene, and polybutadiene in a convenient manner. These silyl hydride-functionalized polymers were synthesized following Scheme 1, exemplified for polystyrene.

In order to evaluate our new pencil lead matrix, a MALDI-MS spectrum of Si−H-functionalized polystyrene (M_n = 3000 g/mol, PDI = 1.06 from GPC) was first recorded with the classical dithranol matrix and AgTFA as additive. The mass spectrum was recorded in reflectron positive mode and gave an isotopically well-resolved spectrum with a bimodal mass distribution (Figure 2). The same sample was then studied using a pencil lead matrix and LiTFA as additive in linear positive mode (Figure 3). (The spectrum recorded in reflectron positive mode was of inferior quality.) While it was not possible to achieve isotopic resolution with the pencil lead matrix, a monomodal distribution was obtained. A closer look at the spectrum recorded with dithranol/Ag^+ (Figure 2, expanded region) revealed that the signal at *m*/*z* 2530.8 corresponds to $C_4H_9-(C_8H_8)_{22}-Si(CH_3)_2OH{\cdot}Ag^+$ (calculated most abundant mass: 2530.4 g/mol) and the signal at *m*/*z* 2560.8 to $C_4H_9-(C_8H_8)_{23}-H{\cdot}Ag^+$ (calculated most abundant mass: 2560.4 g/mol). The formation of the silanol chain end can be explained by oxidation of the silyl hydride functionality; the presence of unfunctionalized polystyrene arises from a further side reaction, in which the silanol probably acts as a leaving group. A mass distribution for the expected product structure could not be observed under these sample preparation conditions.

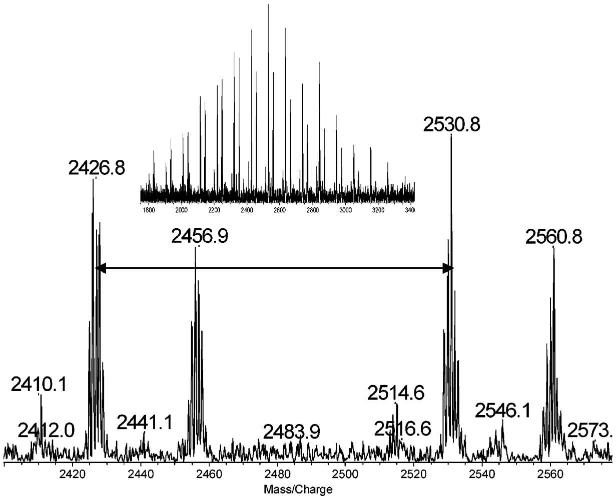


Figure 2. MALDI-ToF MS spectrum of silyl hydride-functionalized polystyrene measured with dithranol as matrix and silver trifluoroacetate as a cationizing agent.

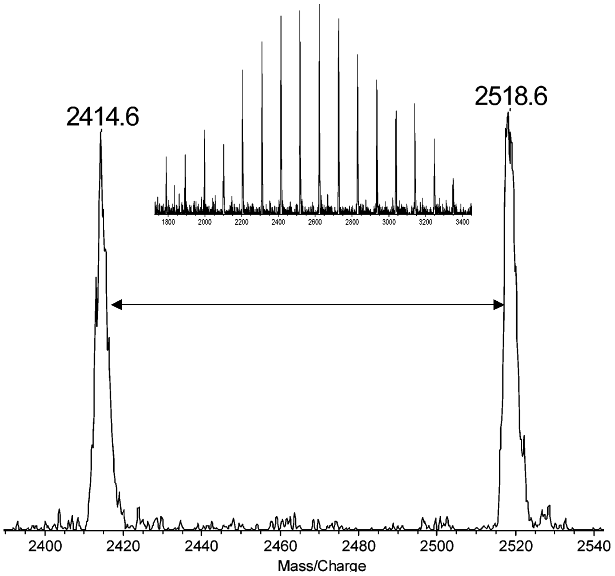


Figure 3. MALDI-ToF MS spectrum of silyl hydride-functionalized polystyrene measured with pencil lead as matrix and lithium trifluoroacetate as a cationizing agent.

In contrast, using pencil lead as a matrix and LiTFA as additive, we obtained a monomodal distribution and the signals correspond precisely to the expected structure. The expanded region in Figure 3 shows a signal at *m*/*z* 2414.6 corresponding to $C_4H_9-(C_8H_8)_{22}-Si(CH_3)_2H{\cdot}Li^+$ (calculated most abundant mass 2414.5 g/mol), as expected. The presence of the −Si−H moiety was further confirmed by NMR and IR spectroscopy. To further support the presence of the $-Si(CH_3)_2-H$ group, the silyl hydride-functionalized polystyrene was derivatized with 1,4-hexadiene (Scheme 1). The resulting end-group-modified polymer was analyzed both by ^1H NMR and MALDI-ToF MS,

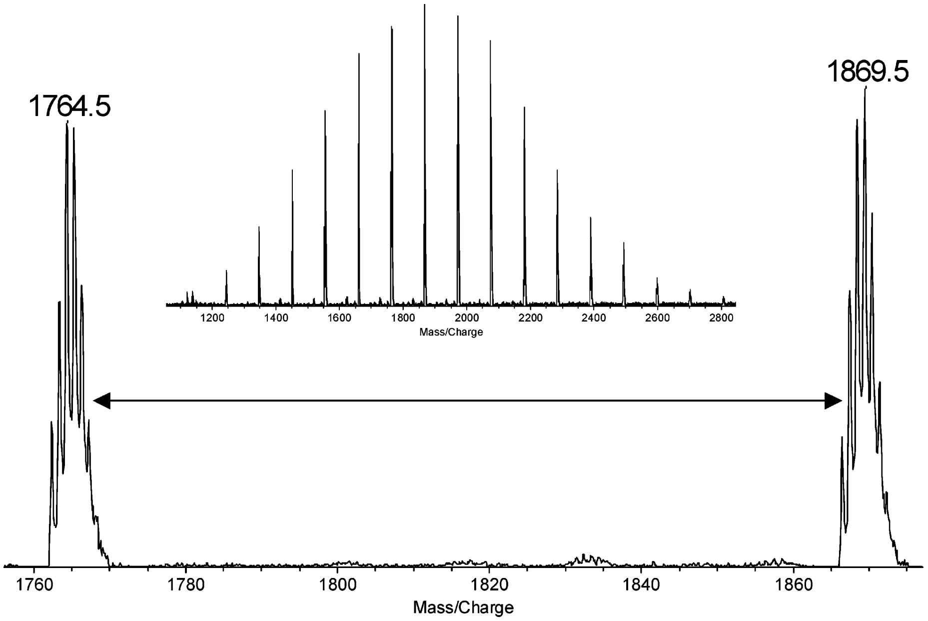


Figure 4. MALDI-ToF MS spectrum of hexadiene-functionalized polystyrene, measured with dithranol as matrix and silver trifluoroacetate as a cationizing agent.

and the spectra show the completely derivatized polymer, which confirms the presence of the initial SiH group (Figure 4). In the expanded region of Figure 4 it is possible to observe a signal at *m*/*z* 1869.5, which corresponds to $C_4H_9-(C_8H_8)_{22}-Si(CH_3)_2C_6H_{11}\cdot Ag^+$ (calculated most abundant mass: 1869.0 g/mol), confirming complete functionalization.

To establish the general applicability of pencil lead as a mild MALDI-ToF matrix, two other nonpolar polymers were investigated. Silyl hydride end-functionalized polyisoprene (M_n = 1050 g/mol, PDI = 1.08 from GPC) and silyl hydride-functionalized polybutadiene (M_n = 1600 g/mol, PDI = 1.10 from GPC) were first of all analyzed by MALDI-ToF MS using the classical dithranol matrix in the presence of silver ion additives (AgTFA). Both spectra were measured in reflectron positive mode (not shown) and were isotopically resolved. Two distributions were observed in both cases.

In the case of functional polyisoprene, the principal signal distribution was assigned to the silver ion adduct of the product structure, while the second signal distribution could be unequivocally assigned to the general molecular formula $C_4H_9-(C_5H_8)_n-SiC_2H_6O_2\cdot Ag^+$. In this case only partial degradation of the sample was observed.

However, employing pencil lead with a LiTFA additive in the sample preparation only the silyl hydride-functionalized polyisoprene was observed as Li^+ adduct and Na^+ adduct (less intense signals). In the mass spectrum of silyl hydride-functionalized polybutadiene recorded using the pencil lead matrix in positive reflectron mode, we observed a monomodal distribution and isotopically resolved signals that correspond to the general molecular formula $C_4H_9-(C_4H_6)_n-Si(CH_3)_2H\cdot Li^{+\cdot}$ The spectrum of the same sample recorded with dithranol as a matrix and AgTFA as additive shows a principal signal distribution that can be assigned to the silyl hydride-functionalized polybutadiene silver adduct and a second signal distribution that was assigned to the general molecular formula $C_4H_9-(C_4H_6)_n-SiC_2H_6O_2\cdot Ag^+$. Also in this case, only partial degradation of the sample was observed as in the case of the functionalized polybutadiene above. We believe that the degree of sample degradation is highly dependent on the time used for the measurement. Further kinetic studies will be required to understand this reaction better.

On the basis of the presented results, it can be concluded that pencil lead is a very useful matrix for the MALDI-ToF MS characterization of silyl hydride derivatized polymers with different backbone structure.

Conclusion

It has been shown that MALDI analysis of structurally different polymers is possible using pencil lead, applied by simply drawing on a target, as a matrix. MALDI-ToF mass spectra of Si−H-functionalized polymers that are sensitive in the usual sample preparation using common matrices and additives can be advantageously recorded using pencil lead as a matrix. Furthermore, pencil lead is inexpensive, safe, and easy to apply as a matrix. Thus, the use of pencil lead provides a quick, convenient, and reproducible analytical method, particularly for polymers with M_n between ca. 300 and 6000 Da, which is the most useful range in the case of end-group analysis because of the improved resolution of the spectra. We believe that the pencil lead matrix has great potential for the analysis of various sensitive polymers that currently suffer from deterioration during sample preparation.

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