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Quantitative measurement of the polydispersity in the extent of functionalization of glass-forming calix[4]resorcinarenes

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The polydispersity in the degree of functionalization for two calix[4]resorcinarenes was determined by measuring quantitatively their molecular mass distribution with matrix-assisted laser desorption/ionization time-of-flight mass spectrometry. A mathematical method for polydisperse materials is described that creates a calibration curve to correct the ion signal intensities in the mass spectrum to give a more reliable molecular mass distribution. Correction is required due to various sample preparation and instrumental effects that may produce a systematic mass bias in the number of oligomers measured. This method employs gravimetric mixtures of analytes with different degrees of functionalization. One calix[4]resorcinarene was found to give accurate molecular mass distributions with little correction, while another, having a very similar molecular structure, was found to exhibit strong over-counting of the oligomers having a high degree of functionalization. Copyright © 2009 John Wiley & Sons, Ltd.

Photolithography remains the driving technology in the semiconductor industry to fabricate integrated circuits with ever decreasing feature sizes.[1] Current fabrication facilities use chemically amplified photoresists – optimized formulations of a polymer film loaded with photoacid generators and other additives. The photoacid, activated by light exposure, catalyzes a deprotection reaction with the acid-sensitive functionalized polymer to alter film solubility in an aqueous hydroxide developer solution. Next-generation sources use extreme-ultraviolet (EUV) radiation at a wavelength of 13.5 nm in order to provide improved spatial resolution over current generation deep-ultraviolet lithography at a wavelength of 193 nm. However, current materials may be reaching their fundamental limits as the desired feature dimensions (<22 nm) approach the macromolecular size of photoresist polymers.[2] While the resolution limits involve numerous materials and process properties (such as photoacid diffusion length, dissolution behavior, and critical base quenchers), alternative chain-architecture serves as a test for various hypotheses associated with imaging size.[3–6] Calix[*n*]resorcinarenes offer lower molecular mass, hence smaller molecular size, with glass transition temperatures and etch selectivities comparable with those of typical phenol-based photoresist polymers, such as poly(hydroxystyrene).[7,8] These discrete-sized macrocycles may also eliminate properties specific to polymers, such as chain length distribution, chain entanglement, and chain-end effects.

Typically, photoresist polymers, prepared by free radical methods, have statistical molecular mass distributions (MMD). Since calix[*n*]resorcinarenes have multiple sites for functionalization a similar (but narrower) polydispersity in molecular mass may result. In the particular case studied here the phenol -OH groups are protected with acid-sensitive *tert*–butoxycarbonyl (tBOC), typically to less than completion, for the purpose of optimizing spin coating, substrate adhesion, and exposure dose sensitivity. Therefore, rather than a distribution in chain length, the molecule will be characterized by a molecular mass distribution reflecting the degree of functionalization distribution. The correct measurement of this distribution is critical to understanding the physical and chemical behavior of these materials.

In this work the distribution of the extent of functionalization, also called the polydispersity of the extent of functionalization or just simply polydispersity, is measured quantitatively for the two calix[4]resorcinarenes shown in Fig. 1. The analytes are designated C-TBB-4-R and C-HPB-4-R as indicated in the figure where R = OH for unprotected materials and R = tBOC for protected materials. Matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS) was used to obtain the

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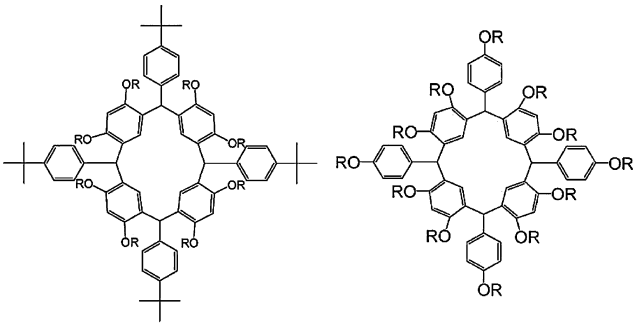

Figure 1. Calix[4]resorcinarene molecular structures. R = OH before functionalization; R = OH or R = tBOC after functionalization which was always found to be incomplete.

polydispersity of the extent of functionalization of various C-TBB-4-R and C-HPB-4-R samples. While MS can easily resolve the oligomers-to-oligomer mass differences encountered with these samples, quantitatively determining the amount of each mass present is more difficult. This is because the desorption and/or ionization probabilities for each species may not be equal due to the presence of different numbers of functional groups.[9,10] To overcome this challenge we use a signal intensity calibration technique for polydisperse materials first used by Zhu, Yalcin and Li on mixtures of polystyrenes.[11] From the qualitative method of Zhu *et al.*, a rigorous quantitative method was derived by Guttman *et al.*[12] The quantitative method uses a Taylor's expansion approach to develop a calibration curve to correct the ion intensities in the mass spectrum leading to a more reliable measure of the polydispersity of the extent of functionalization. Only the results of this mathematical derivation will be used here; full details can be found elsewhere.[12,13]

EXPERIMENTAL

Materials

The calix[4]resorcinarene derivatives were synthesized using the method of Tunstad *et al.*[14] and are the same materials as used in a previous nuclear magnetic resonance (NMR) study.[15] MALDI-TOF mass spectra in negative ion mode were taken using *trans*,*trans*-1,4-diphenyl-1,3-butadiene (DPB; CAS No. 886-65-7), as a matrix. Acetone was used as the solvent for the MALDI target preparation.

Instrumentation

The mass spectrometry was performed on a REFLEX time-of-flight instrument (Bruker Daltonics, Billerica, MA, USA) with delayed extraction.[a] Reflectron mode ion separation was used to identify species because of its higher mass resolution; however, linear mode is preferred for quantitation because of the chance that oligomers with different numbers of functional groups may undergo metastable fragmentation at different rates. This would lead to inaccurate peak areas

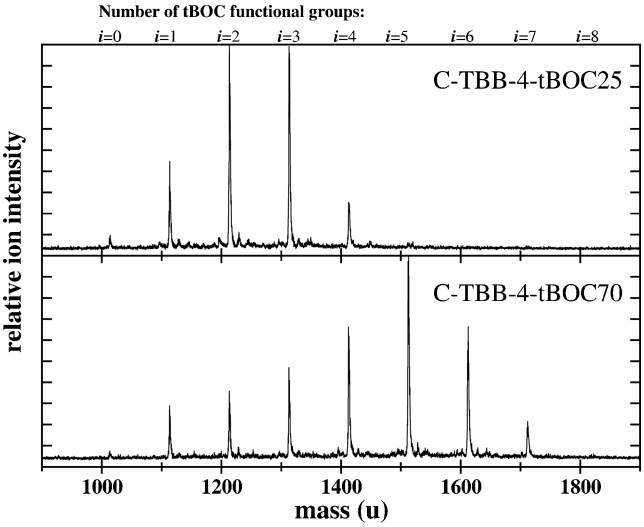

Figure 2. MALDI-TOF mass spectra of the calix[4]resorcinarene C-TBB-4-R. All ions observed in this study were singly charged (z = 1); thus, the abscissa is labeled as mass for all spectra presented.

and cannot be accounted for without measuring the metastable decay rates of the different oligomers. All the spectra shown here were taken in linear mode. Ions were generated with a 337-nm wavelength nitrogen laser with a nominal pulse duration on the order of 3 ns and an average energy of approximately 5 μJ per pulse spread over a spot size of 100 μm in diameter. A delay of 250 ns was used before ions were extracted from the laser plume. Mass calibration was performed daily with neat CsI which forms abundant negative ion clusters. Data analysis was performed using the *Polymerix* computer code (Sierra Analytics, Modesto, CA, USA). All data shown was taken in negative ion mode[b] with each oligomer being of the form $[M-H]^-$. For all experiments a solution of 40 mg/mL DPB was mixed with a 5 mg/mL solution of the analyte in a volume ratio of 2:1. The solutions were hand-spotted onto the stainless steel MALDI target and allowed to air dry. Previous work has shown that the estimated standard uncertainty of the peak position from calibration and repeatability is 0.2 u at 3000 u and the estimated standard uncertainty in the overall signal intensity from repeatability studies is 15%.[16]

RESULTS

Figure 2 shows MALDI-TOF mass spectra of C-TBB-4-R with two levels of functionalization, one corresponding to a nominal average of 25% of all reactive sites in the bulk sample being converted from hydroxyl into tBOC groups (C-TBB-4-tBOC25), and one where nominally 70% of the groups have been converted (C-TBB-4-tBOC70). The mass of the unfunctionalized core is 1016 u. Each functional group, *i*, adds 101 u to the mass of the oligomers; thus, each oligomer is easily identified by mass. C-TBB-4-tBOC25 shows

[a]Certain equipment, instruments, or materials are identified in this article to adequately specify the experimental details. Such identification does not imply recommendation by the National Institute of Standards and Technology nor does it imply that the materials are necessarily the best available for the purpose.

[b]Positive ion spectra were not used because they could not be obtained without oligomers charged with both Na^+ and K^+ cations. This added complexity of multiple molecular adduct ions for each oligomer makes quantitative analysis particularly difficult.

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oligomers with zero through five functional groups; while C-TBB-4-tBOC70 shows oligomers with zero through seven functional groups. Eight functional groups per molecule, while hypothetically possible, was never experimentally observed. Varying the laser energy around typical analysis energies did not change the molecular mass distribution, indicating that the ablation process is not removing the tBOC functional groups in measurable quantities. (Extremely high laser energies did, however, remove tBOC groups. These energy levels were well beyond the low levels used for analysis.) Using *Polymerix* these peaks can be integrated to find the relative ion intensity for each oligomer and a molecular mass distribution with corresponding molecular moments may be calculated. Typically this is what most analyses would report. However, different levels of functionality may lead to under- or over-counting of specific oligomers in the mass spectrum. This may come from different solubilities in the original [analyte + matrix] solution, different rates of precipitation when this solution is deposited on the MALDI target, and different rates of laser desorption and/or ionization. What is the magnitude of the correction that may need to be applied to these relative ion intensities, and how can it be determined?

Mixtures of C-TBB-4-tBOC25 and C-TBB-4-tBOC70 in carefully measured gravimetric ratios (1:3, 1:1, and 3:1) were prepared. By comparing the expected MALDI-TOF mass moments of the molecular mass distribution taken from the measurements of the pure analytes with the experimentally measured mass moments a correction factor for each oligomer was calculated. When applied, the correction factor produces a final, more accurate distribution. Full details of the Taylor's expansion method can be found in previous publications;[12,13] here only the pertinent results of that mathematical derivation will be presented.

In general, if the experiments are conducted in the linear range of target concentration versus signal intensity for each oligomer i then:

$$S_i = k_i n_i \tag{1}$$

where k_i converts number of oligomers in the sample n_i into signal intensity S_i in the mass spectrum. k_i is assumed to be a slowly varying function of oligomer mass m_i. Thus, a Taylor's expansion may be made around a mass peak near the center of the MMD, termed M_0. The center is used to assure that the function is changing as little as possible over the entire width of the MMD; however, mathematically the choice is arbitrary. Then:

$$S_i = k_0 n_i + Q(m_i - M_0)n_i + \text{higher order terms in } n_i \text{ and } m_i \tag{2}$$

where k_0 and Q are functions of all the experimental conditions: the instrument parameters, the sample concentrations, and the sample preparation method. From these assumptions, and dropping the higher order terms in Eqn. (2), we can derive[12] the following important relationship:

$$M_w^{\exp} = M_w^0 \left\{ \frac{(1 + (Q/k_0)(M_z^0 - M_0)}{(1 + (Q/k_0)(M_w^0 - M_0)} \right\} \tag{3}$$

where $M_w^{\exp}$ is the MALDI-TOF MS measured mass-average molecular mass for the mixture of analytes. M_w^0 and M_z^0 are calculated values based on MALDI-TOF MS measured mass-average molecular mass for the pure analytes and the gravimetric masses of materials mixed. Rearranging gives an expression for the linear correction term:

$$Q/k_0 = \frac{Z_w}{(M_z^0 - M_w^0) - Z_w(M_w^0 - M_0)} \tag{4}$$

where:

$$Z_n = \frac{M_w^{\exp} - M_w^0}{M_w^0} \tag{5}$$

Dropping the higher order terms and rearranging Eqn. (2) yields:

$$\frac{S_i}{k_0 n_i} = 1 + \frac{Q}{k_0}(m_i - M_0) \tag{6}$$

Equation (6) shows us how to apply the correction factor Q/k_0 to each mass oligomer m_i to arrive at a more reliable measure of the molecular mass distribution.

For a gravimetric mixture A (say with a ratio of 1:1 or 1:3), M_{nA}^0 is calculated from the values for the individual components M_{n1}^0 and M_{n2}^0 using a simple weighted average:

$$M_{nA}^0 = \frac{G_1 + G_2}{\frac{G_1}{M_{w1}^0} + \frac{G_2}{M_{w2}^0}} \tag{7}$$

where G_1 is the gravimetric mass of species one in the mix, etc. By summing the second moment of the distribution we obtain the same result but expressed in a different form:

$$M_{wA}^0 = \frac{G_1}{G_1 + G_2} M_{w1}^0 + \frac{G_2}{G_1 + G_2} M_{w2}^0 \tag{8}$$

M_0 can be chosen at any point; however, choosing the center of the distribution will give a symmetric correction.

Figure 3 shows example mass spectra of gravimetric mixtures of C-TBB-4-tBOC25 and C-TBB-4-tBOC70 in the mass ratios 1:3, 1:1, and 3:1. From the average of three repeats of each mixture the moments of the molecular mass distribution were calculated and substituted in Eqn. (4) to find Q/k_0. In each case the M_0 used was the calculated gravimetric M_0 from the 1:1 mixture. The three mixtures each produced somewhat different values of Q/k_0; therefore, the

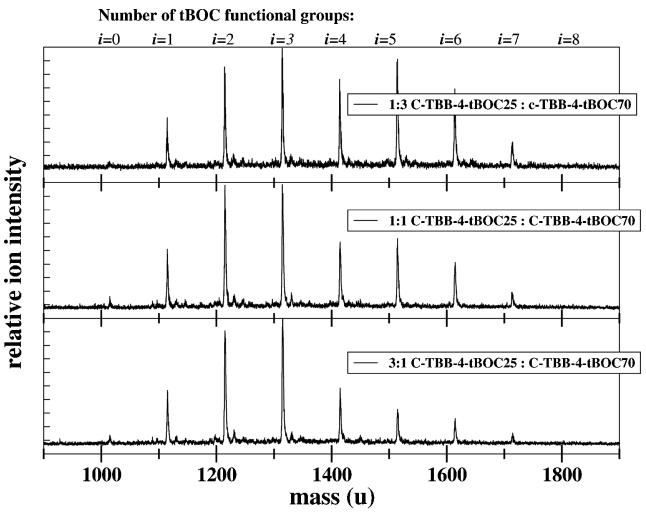

Figure 3. MALDI-TOF mass spectra of gravimetric mixtures of C-TBB-4-R with different degrees of functionalization.

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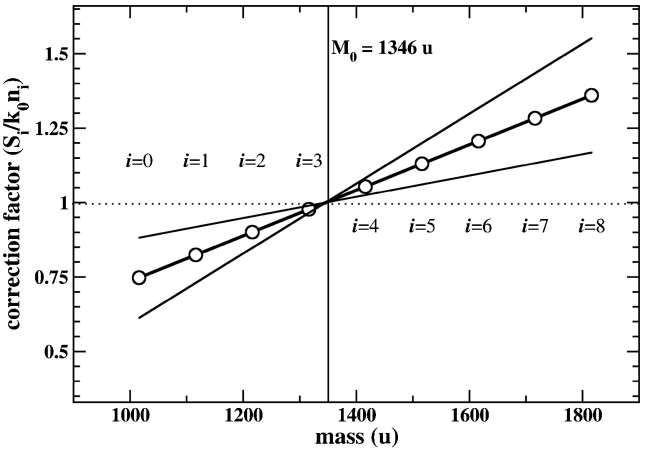

Figure 4. Calibration curve (S_i/k_0n_i vs. mass) for C-TBB-4-R.

three values were averaged and the standard deviation calculated. Figure 4 shows that value of S_i/k_0n_i as a function of molecular mass. Each point represents the factor by which the oligomer (given by i) was under-counted (for values of S_i/k_0n_i less than one) or over-counted (for values greater than one). The thin lines represent one standard deviation of the correction factor based on the three replicate measurements of each of the three different concentration ratios. The raw and corrected molecular mass distributions are shown in Fig. 5. For C-TBB-4-tBOC25 the uncorrected M_w was 1266 u while the correct value was 1259 u giving a change of approximately 0.55% while for C-TBB-4-tBOC70 the respective values are 1463 u, 1448 u and 1%. For C-TBB-4-R the over-counting of high mass oligomers was indeed minimal resulting in only a very minor correction to the molecular mass distribution and its moments. From the corrected molecular mass distributions the average degree of functionalization may be calculated: 30% for C-TBB-4-tBOC25 and 53% for C-TBB-4-tBOC70, slightly above and below the nominal values, respectively.

Although the material designated as C-HPB-4-R is structurally similar to C-TBB-4-R its behavior was significantly different in all respects related to mass spectrometry. Figure 6 shows the mass spectra of C-HPB-4-tBOC25 and C-HPB-4-tBOC70. C-HPB-4-tBOC25 has a molecular mass distribution with a continuously decreasing intensity of peaks very different from the pseudo-Gaussian distribution found for C-TBB-4-tBOC25 (Fig. 2). Some oligomers in C-HPB-4-tBOC25 have up to eleven functional groups, only one short of the maximum number possible. Furthermore, fragmentation-free spectra could not be obtained even at very low laser power. The peaks marked with an asterisk (*) in the C-HPB-4-tBOC25 spectrum are due to fragmentation of the tBOC group itself leading to a loss of the three methyl groups from the *sec*-butyl terminus of the group. Loss of alkyl groups during MALDI-TOF MS of similar calix[4]resorcinarenes has been reported previously.[9] Fragmentation complicates the determination of a quantitative molecular mass distribution. This is because to calculate the C-HPB-4-tBOC25 molecular mass moments properly the intensity of the fragment ions must be assigned to the corresponding precursor ion without regard to whether the charge resides on the main ion or the lost fragment. If it is assumed that the lost methyl fragments are neutral, the procedure will cause no additional error. No negative methyl groups were seen in the mass spectra adding strength to this assumption. Interestingly, the mass spectrum of C–HPB-4-tBOC70 (Fig. 6) shows fragment ions (#) due to the loss of a single methyl group from the *sec*-butyl terminus of the tBOC functional group. The same caveats regarding calculation of the molecular mass moments also apply to these fragments.

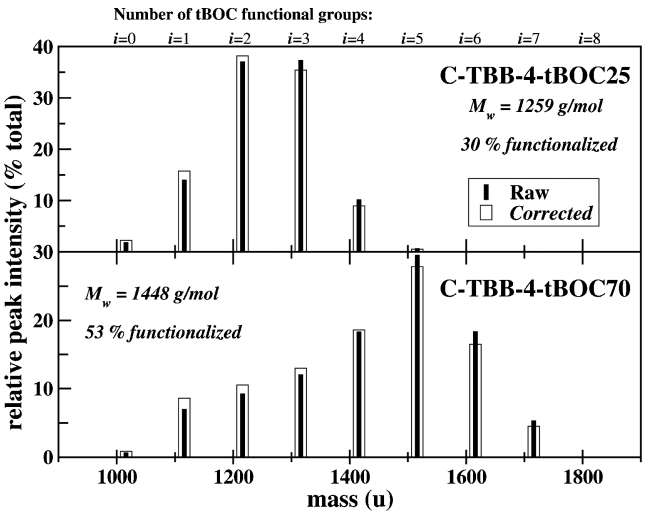

Figure 5. Corrected molecular mass distributions and average degrees of functionalization.

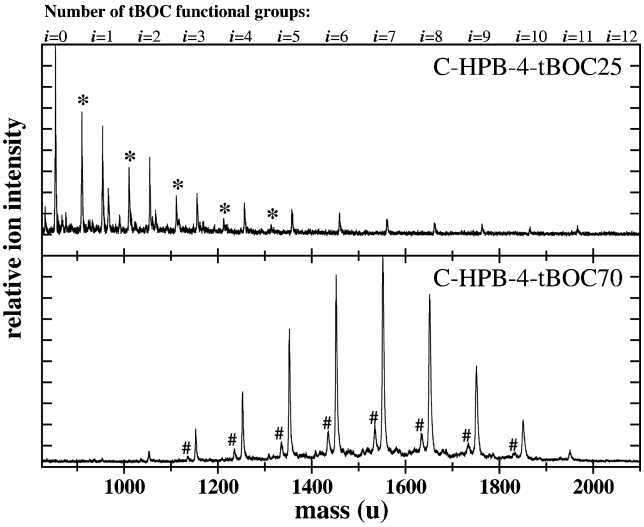

Figure 6. MALDI-TOF mass spectra of the calix[4]resorcinarene C-HPB-4-R. The symbols * and # indicate ion fragmentation (see text).

While the first example of C-TBB-4-R showed a modest over-counting of the high mass oligomers, C-HPB-4-R showed a drastically greater bias toward the high masses, as shown in Fig. 7. Even when the sample was gravimetrically 75% C-HPB-4-tBOC25 the approximate total ion intensity from C-HPB-4-tBOC25 was only 21% including fragment ions. (The value is approximate because there is an overlap between the two distributions due to the long high mass tail for C-HPB-4-tBOC25.) This leads to very large

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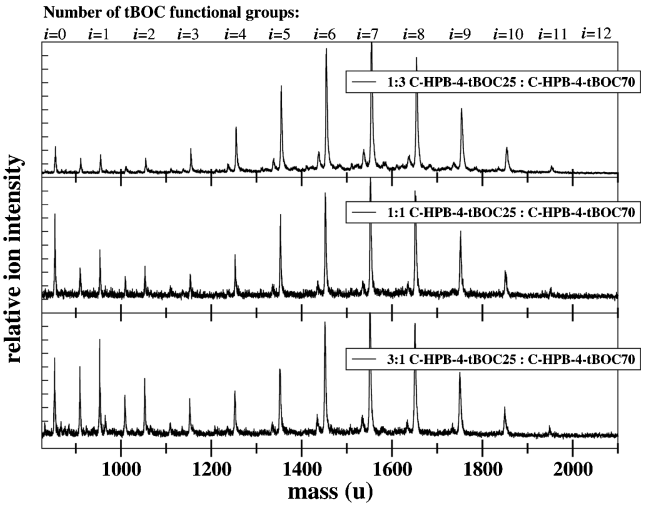

Figure 7. MALDI-TOF mass spectra of gravimetric mixtures of C-HPB-4-R with different degrees of functionalization.

correction factors, as shown in Fig. 8. In fact, the high mass over-counting is so great that the correction factors for the low mass oligomers ($i = 0$ and $i = 1$) are negative which is a physical impossibility. This indicates that k_i is not a slowly varying function of mass and that the linear term is insufficient to capture the mass bias. Higher terms in the Taylor's expansion are required; however, methods to determine the values of these coefficients are still a matter of active research in our laboratory.

DISCUSSION

The qualitative and the quantitative differences in the mass spectrometry of C-TBB-4-R and C-HPB-4-R are both surprising findings. C-TBB-4-R shows pseudo-Gaussian distributions in the distribution of functionalization, virtually no ion fragmentation, and only a very small bias towards high mass molecules in the mass spectra. C-HPB-4-R shows an exponential decay in the molecular mass

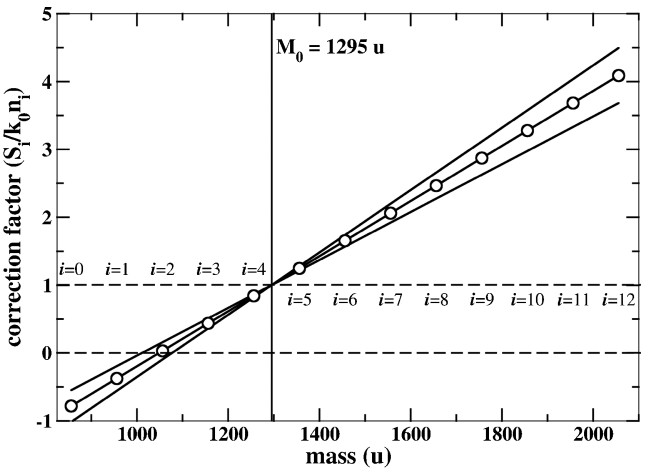

Figure 8. Calibration curve (S_i/k_0n_i vs. mass) for C-TBB-4-R. The negative values for the low mass oligomers $i = 0$ and $i = 1$ indicate that a first-order Taylor's expansion correction is not suitable.

distribution at low levels of functionalization that changes to a pseudo-Gaussian at higher levels, substantial fragmentation especially for the C-HPB-4-tBOC25 sample, and a very great bias toward high mass molecules in the mass spectra. The decay in signal intensity as a function of mass of the fragment ions in C-HPB-4-tBOC25 is faster than the decay in intensity of the main series peaks. This indicates that the fewer the functional groups the more likely they are to fragment. When more groups are added to the core, bearing in mind its calix shape, they may attract one another through hydrogen bonding and thus suppress fragmentation. The level of fragmentation decreases significantly beyond four tBOC groups. This may indicate that the first sites functionalized are those on the aldehyde groups of which there are four. For C-HPB-4-tBOC70 the fragmentation is less pronounced and of a different type. The close packing of the tBOC groups must further suppress fragmentation and the only fragmentation that can occur is the loss of a single methyl group. This close packing of the tBOC groups must also create a stable environment for electron attachment leading to the easy formation of negative ions of C-HPB-4-tBOC70 resulting in its over-counting in the molecular mass distribution. The over-counting is not, however, due to fragmentation.

The spectrum of C-HPB-4-tBOC25 (Fig. 6, top panel) showing the molecular mass distribution with a continuously decreasing intensity of peaks suggests that there may be a type of autocatalytic reaction going on during functionalization. After placing the first one or two tBOC groups on the C-HPB-4-R molecule the energy barrier is lowered for the addition of more groups, leading to a small fraction of the oligomers having a very high degree of functionalization, and thus skewing the average value higher. Unfortunately, due to the over-counting of the high mass oligomers, it was impossible to make a quantitative determination of the polydispersity of this material. However, it is still important to know that there is bias in the mass spectrum even if it cannot be corrected for by the method outlined here. The strong over-counting in MALDI-TOF MS could be due to several factors. First, if there are different concentrations of impurities in the two original samples the gravimetric ratios would be incorrect. However, the mass spectrometry showed no peaks that could not be assigned to the analyte or the MALDI matrix. Second, there may be phase separation on the basis of degree of functionalization as the solvent dries during the deposition step. This may place higher functionalized oligomers in a position to be more advantageously desorbed. Furthermore, the higher functionalized calix[4]resorcinarenes may desorb more easily since they form fewer hydrogen bonds in the solid.[15] On the other hand, higher functionalized materials will be glassy as opposed to crystalline making their desorption more facile. (It has been shown that polyethylene desorbs during the MALDI event far more easily above its melting temperature than below it.[17]) Third, pertaining to ionization, if the added electron resides on the tBOC group then the greater the degree of functionalization the greater the probability of ionization. However, why these factors would affect C-HPB-4-R more than C-TBB-4-R is a question that remains unanswered.

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CONCLUSIONS

MALDI-TOF MS offers a way to measure the polydispersity in the degree of functionalization in calix[4]resorcinarenes. A mathematical method is described which employs gravimetric mixtures of analytes with different degrees of functionalization in order to create a calibration curve. This calibration curve is used to correct the ion intensities in the mass spectrum to give a more reliable molecular mass distribution. One calix[4]resorcinarene was found to give accurate molecular mass distributions with little correction, while another very similar in structure was found to exhibit strong over-counting of oligomers with a high degree of functionalization. Average values for the degree of functionalization determined by NMR do not capture the subtle aspects of the functionalization distribution that may be critical to the performance of these photoresist materials.

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