Primary Amine (−NH_2) Quantification in Polymers: Functionality by ^{19}F NMR Spectroscopy

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ABSTRACT: A convenient, reliable, and general method for determining the primary amine functionality of amino polymers is described. It is based on ^{19}F NMR spectroscopy and has many advantages over known methods. The amino polymer is derivatized in situ with a reactive, trifluoromethylated aromatic aldehyde. The resultant, spontaneously formed imine (Schiff base) is then quantified by integration of its unique ^{19}F resonance vs that of an added internal standard. The quantitative reliability of the method was first unequivocally established using a small molecule amine. Functionality determination was then demonstrated for a very broad range of polymer classes, including PS, PMMA, PEG-like, PDMS, PB, and polyamide. In contrast to, e.g., titration, this method can be carried out quickly, with small sample sizes (e.g., ca. 10 mg) and using routine NMR spectroscopic techniques.

Introduction

Functional/reactive polymers containing primary amine groups are very useful (e.g., for applications in compatibilizing polymer blends[1] and as adhesives[2]). In many cases, knowledge of the precise amine content is important for their optimal use. Because of the small number of amine groups often present, it is a challenge to determine the functionality (f_n)[3] with precision, especially for high molecular weight polymers.

Acid titration of a basic amine is commonly used to determine amine functionality for low molecular weight polymers.[4] However, there are a number of limitations. Distinction among primary, secondary, and tertiary amines is usually not possible. When applied to high molecular weight polymers, a large amount of polymer sample is required. Accurate titers cannot be determined in all solvents.[5] For example, relatively nonpolar polymers have poor solubility in typical titration solvents (e.g., AcOH, H_2O, alcohol).

Alternative methods to titration exist. The thin-layer chromatography and flame ionization detection (TLC/FID) technique[6] has been successfully applied to the determination of polymer composition distribution of acrylonitrile−styrene copolymers[7] and poly(styrene-*co*-ethyl methacrylate)[8] and functionality of telechelic polybutadienes.[9] For example, nonfunctional polystyrene (PS), poly(styryl)amine (PS-NH_2), and poly(styryl)-amide (PS-NHCOR) can be separated by TLC,[4g] and Hirao and co-workers showed that TLC/FID could be used to quantify the amount of amine functionality in aminated polystyrenes.[4d] This has also been used, e.g., to quantify the amine content of perdeuterated polystyrene end-functionalized with an aliphatic amine group (dPS-NH_2).[10] However, this method is also limited in scope. It requires that the functional and nonfunctional components in the sample be separable by TLC, which is typically only feasible for nonpolar polymers of relatively low molecular weight and narrow polydispersity. Reactive coupling of two functional polymers has also been used.[11,12] For example, an amine terminal polymer can be coupled with an anhydride terminal polymer to generate block copolymers, which then can be quantified by gel permeation chromatography (GPC) if the components have a sufficiently low polydispersity index (PDI). This method usually will not be suitable for analysis of a polymer with large PDI or for di- or multifunctional polymers.

To circumvent these problems, we have developed and report here a more universal method, based on ^{19}F NMR spectroscopy, for determining the functionality of mono- and multiamino functional polymers.[13] This method is easy to implement and requires relatively small amounts of analyte. It relies upon the clean, highly thermodynamically favorable, textbook condensation reaction between a primary amine and an aryl aldehyde to form an imine (Schiff base). It uses spectroscopic techniques routinely available to chemists working in preparative or characterization laboratories.

Materials

The source of all polymers is summarized in Table 1. PS−$CH(Me)CH_2NH_2$ was prepared by atom transfer radical polymerization (ATRP) of styrene using 2-bromopropionitrile as initiator, followed by lithium aluminum hydride reduction (LAH).[14] PS−$Si(Me)_2(CH_2)_4$−NH_2 was synthesized by anionic polymerization, trapping with $ClSi(Me)_2(CH_2)_4Cl$, and conversion of −Cl to −NH_2.[11] Telechelic diamino polybutadienes (H_2N−PB−NH_2) were made by ring-opening metathesis polymerization (ROMP) of 1,5-cyclooctadiene using 1,8-dicyano-4-octene as a chain transfer agent and LAH reduction.[15] PMMA−anhydride and PS−anhydride were synthesized by ATRP using 4-bromomethylphthalic anhydride as initiator.[16] Nonfunctional PMMA and PS were synthesized by anionic polymerization. PEG-NH_2 samples were purchased from Nektar Therapeutics. PMMA-NH_2 was purchased from Polymer Source Inc. Nonfunctional PEG was purchased from Nektar Therapeutics. Nylon samples were provided by DuPont Co. Amino-terminated PDMS samples were purchased from Gelest Inc. JEFFAMINE samples were provided by Huntsman Petrochemical Co.

Commercial solvents were used as received. 3,5-Bis(trifluoromethyl)benzaldehyde (BTFBA, **4**) and 4-trifluoromethylbenzaldehde (*p*-TFBA, **10**) were obtained from Sigma-Aldrich Corp. and used as received. They were stored at <0 °C, and

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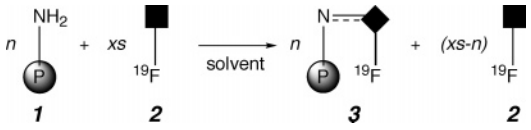
Table 1. Source and Molecular Weight of Each Polymer Sample

polymer	M_n[e] (K)	source[i]
PS−CH(Me)CH_2NH_2	10.6	synthetic (ATRP)
PS−CH(Me)CH_2NH_2	17.7	synthetic (ATRP)
PS−Si(Me)$_2$(CH$_2$)$_4$−NH_2	8.0	synthetic (anionic)
PS−Si(Me)$_2$(CH$_2$)$_4$−NH_2	100	synthetic (anionic)
PS−Si(Me)$_2$(CH$_2$)$_4$−NH_2	55.3	synthetic (anionic)
PS−anhydride	11.8	synthetic (ATRP)
PS	19.8	synthetic (anionic)
PMMA	6.0	synthetic (anionic)
PMMA−NH_2	37.0	Polymer Source
PMMA−anhydride	43.0	synthetic (ATRP)
HO−PEG-OH	2.0[f]	Nektar
MeO−PEG−NH_2	5.0[f]	Nektar
MeO−PEG−NH_2	5.2[f]	Nektar
DMS-A21[a]	5[g]	Gelest
DMS-A31[a]	25[g]	Gelest
NH_2−PB−NH_2	26	synthetic (ROMP)
NH_2−PB−NH_2	38	synthetic (ROMP)
JEFFAMINE D-2000[b]	*h*	Huntsman
JEFFAMINE XTJ-510[b]	*h*	Huntsman
JEFFAMINE XTJ-504	*h*	Huntsman
JEFFAMINE BA-509[b]	*h*	Huntsman
JEFFAMINE T-5000[b]	*h*	Huntsman
Zytel 330[c]	*h*	DuPont
Selar PA3426[c]	*h*	DuPont
Zytel 101[d]	*h*	DuPont

[a] $NH_2(CH_2)_3(CH_3)_2Si$−PDMS−$Si(CH_3)_2(CH_2)_3NH_2$. [b] Amine terminal polyethers (e.g., PPO/PEO). [c] An amorphous nylon. [d] A crystalline nylon. [e] Determined by GPC in THF at ambient temperature using PS standards unless otherwise indicated. [f] From the Certificate of Analysis provided by the company. [g] From the company catalog. [h] Not available. [i] Polymers listed as "synthetic" were prepared and analyzed in our laboratories.

Scheme 1

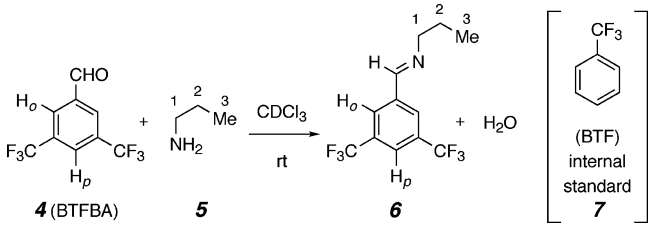


the storage bottles were flushed with nitrogen gas after each use and prior to being closed.[17]

Results and Discussion

Our initial goal was to develop an easy and reliable method for assessing the number of primary amino groups in rather large polymers [P-NH_2 (**1**), Scheme 1]. Specifically, telechelic diamino functional polybutadienes (H_2N−PB−NH_2) with M_ns up to several hundred kg mol^{-1} were of interest.[15] To satisfy this need, we envisioned an assay in which every amino group (−NH_2) would reliably undergo a chemical reaction, whereby there would be an easily observed change in the NMR spectroscopic features of the derivatizing reagent **2** vs the product **3** of the reaction between **1** and **2**. The method should have the following features: (i) it should involve a clean and highly favorable (i.e., strongly thermodynamically favored) reaction between a functional group in **2** (black square) and the primary amino group(s) in **1** to ensure complete conversion of all primary amines in the sample to a single type of new functional group (black diamond); (ii) it should be selective for primary amino groups in the presence of secondary and tertiary amines, free alcohol (OH) functionality, and low levels of water; (iii) it should not require workup or separation of the derivatized sample so that in-situ analysis of the reaction solution is feasible; (iv) it should be quantitatively reliable even for small sample sizes (e.g., ca. 10 mg); (v) it should allow the use of a variety of different solvents so that a wide array of polymer classes can be analyzed; (vi) the NMR chemical shift change accompanying the derivatization reaction should be quantifiable and its trend reproducible from one type of polymer sample to another.

Scheme 2



Compared to the large polymer backbone, the low concentration of amine groups gives rise to a relatively weak (or, even, unobservable) signal in the ^{1}H NMR spectrum that makes the amine content difficult to quantify. Since the NMR sensitivity of the ^{19}F nucleus is also high, we hypothesized that derivatization of amine groups with a fluorinated reagent could offer a good solution. In addition, only rarely would there be interfering fluorine atoms indigenous to the analyte polymers. Such a strategy should allow quantification of amine content by ^{19}F NMR spectroscopy even for large MW polymer. That is, a method based on direct derivatization of the polymeric amine **1** with a small excess of a reactive, fluorinated derivatizing agent **2** to give, exclusively, derivative **3** would be ideal (Scheme 1), as long as the ^{19}F resonances in **2** and **3** are distinct.

The first derivatization reaction examined was the trifluoroacetylation of a primary amine with trifluoroacetic anhydride (TFAA) to form a trifluoroacetamide ($RNH_2 + (CF_3CO)_2O \rightarrow RNHCOCF_3$). It proved unsatisfactory both because of competitive formation of a 2:1 imide adduct [$RN(COCF_3)_2$] and because of interference from the broad resonance of trifluoroacetate salt(s) in the ^{19}F NMR spectrum. We then examined urea formation between the primary amine analyte and the fluorinated aryl isocyanate, 4-CF_3PhN=C=O. While promising, this method was compromised by its intolerance of water (competing urea formation) in the reaction medium. We then turned to the well-known condensation reaction between primary amines and aldehydes to form stable imines (or Schiff bases). This proved successful.

A. Model Study with *n*-Propylamine. We surmised that 3,5-bis(trifluoromethyl)benzaldehyde (BTFBA, **4**) would be sufficiently reactive with P-NH_2 (**1**) to meet criterion i. *n*-Propylamine (**5**) was first studied as a small molecule analogue of amino polymers **1** (Scheme 2). When mixed at ambient temperature in $CDCl_3$ and at 0.3 M, a spontaneous reaction between **4** and **5** produced *N*-(3,5-bis(trifluoromethyl)benzylidene)-1-propanamine (**6**). Imine formation was complete in 2 h even when **4** and **5** were used in a 1:1 molar ratio (i.e., without an excess of the derivatizing agent **4** to drive the reaction). This process could be monitored directly by either ^{1}H NMR (Figure 1a,b) or ^{19}F NMR (Figure 1c) spectroscopy. In the former case, the aliphatic propyl group resonances in **5** (Figure 1b) and the aromatic resonances in **4** (Figure 1a) showing ca. 60% conversion at $t = 40$ min (bottom spectra) are fully converted into those of **6** (top spectra) after 120 min. Likewise, in the ^{19}F NMR spectra (Figure 1c), the CF_3 group resonance

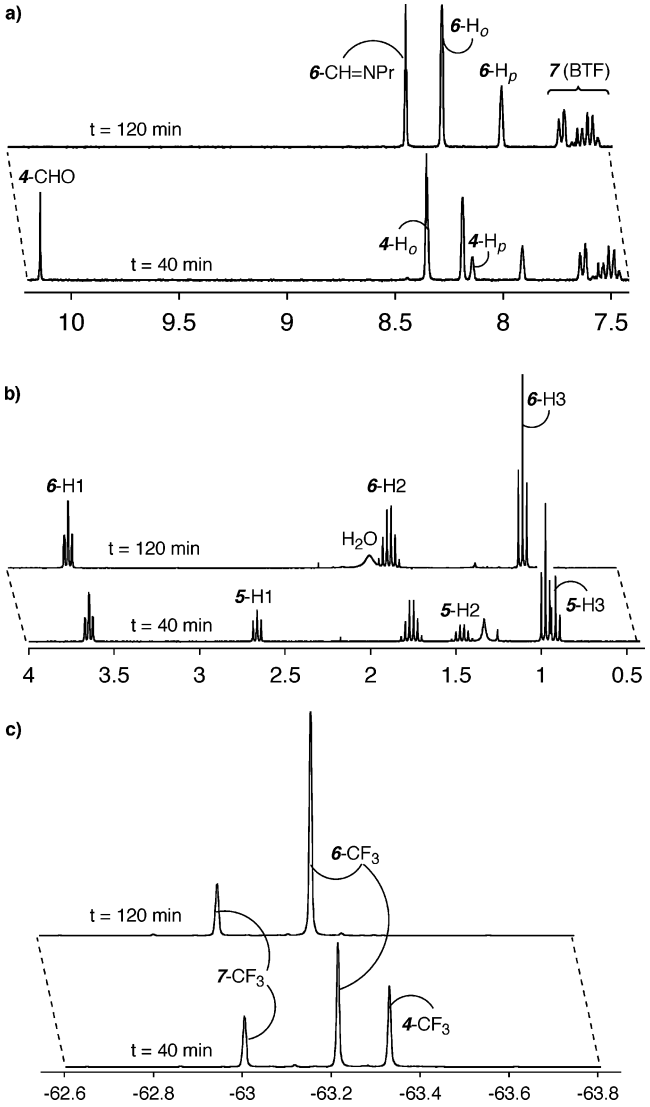


Figure 1. NMR spectra for reaction between *n*-propylamine (**5**) and BTFBA (**4**) containing $PhCF_3$ (BTF, **7**) as an internal standard. Lower spectrum in each panel is at $t = 40$ min; upper at $t = 120$ min. Panel a: aromatic region of ^{1}H NMR spectra. Panel b: aliphatic region of ^{1}H NMR spectra. Panel c: ^{19}F NMR spectra.

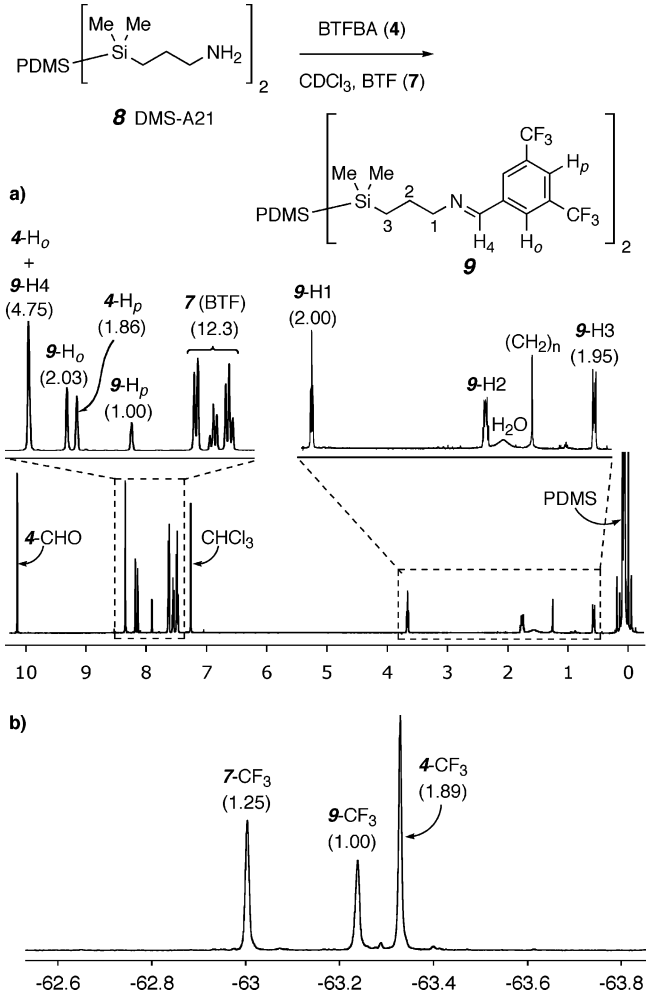


Figure 2. NMR spectra for reaction at $t = 2$ h (full conversion) in $CDCl_3$ between α,ω-bis(aminopropyl)poly(dimethylsiloxane) (DMS-A21, **8**) and BTFBA (**4**) containing $PhCF_3$ (BTF, **7**) as an internal standard. Panel a: ^{1}H NMR spectrum (500 MHz). Panel b: ^{19}F NMR spectrum (282 MHz).

at −63.3 ppm in BTFBA (**4**) was completely converted (ca. 60% at $t = 40$ min and fully after 120 min) into the new singlet at −63.2 ppm for the CF_3 group in **6**. These ^{19}F spectra also contain a resonance at −63.0 ppm due to added trifluorotoluene [or benzotrifluoride (BTF, **7**)]. This was chosen as an added, internal standard against which reliable quantitative measurements could be made (see below). The structure of an isolated sample of imine **6** was confirmed by ^{1}H NMR, ^{19}F NMR, and ^{13}C NMR spectroscopy and high-resolution mass spectrometry. Importantly, this experiment conclusively established that the selected imine derivatization reaction spontaneously proceeded to completion and in time and concentration regimes that would be applicable to polymer samples.

B. Study of First Polymer Derivatization: α,ω-Bis(aminopropyl)poly(dimethylsiloxane). Encouraged by having identified a clean reaction that gave rise to separate resonances (especially in the ^{19}F NMR spectrum), we turned to the analysis of an initial amino-terminated polymer. α,ω-Bis(aminopropyl)-terminated PDMS with M_n ca. 5 kg mol^{-1} (DMS-A21) was chosen because this derivatization could also be examined by both ^{1}H and ^{19}F NMR spectroscopy, since the protons of the −[Si(Me$_2$)O]− repeat unit in the polymer backbone appear as a singlet ($\delta = 0.07$ ppm) in the proton spectrum. DMS-A21 and ca. 6 mol equiv (3 per amine) of a precisely measured amount of BTFBA (**4**) were dissolved in $CDCl_3$, and the reaction progress was monitored as with *n*-PrNH_2. The methylene proton resonance adjacent to the amino groups (−CH_2NH_2) in DMS-A21 appears at $\delta = 2.6$ ppm. Upon derivatization the methylene (−CH_2N=) peak shifted downfield to 3.6 ppm. The absence of a detectable amount of methylene resonance at 2.6 ppm proved the full conversion of the amine group in DMS-A21 (Figure 2a). Integration ratios of product vs starting material resonances within both the proton and the fluorine spectra (relative values in parentheses above resonances sufficiently well separated from nearby resonances to ensure good integration) demonstrate the quantitative reliability of the data (and method). For the example shown in Figure 2, the final ratio of excess BTFBA (**4**) to product imine **9** was measured to be 1.86−1.88 to 1.00 in the proton and 1.89 to 1.00 in the fluorine spectrum. Moreover, the molar ratio of the internal standard BTF (**7**) to product imine **9** measured by both the ^{1}H and ^{19}F NMR spectra were nearly the same. Namely, the ratio of aromatic protons for **7** vs **9** was 2.46 (i.e., 12.3/5) to 1.00 (Figure 2a) and

Table 2. Functionality Determination Relevant to Blended Polymer Samples

entry	polymer	functionality f_n[3] (FGs chain^{-1})	functionality (mmol g^{-1})
1	PS	0.00[a]	
2	PS + benzylamine	1.00[a]	
3	PS−CH(Me)CH_2NH_2[b]	0.99	0.093
4	PS−CH(Me)CH_2NH_2[c]	0.97[a]	0.091
5	PS−CH(Me)CH_2NH_2 + PS (1:1)	0.99	0.093
6	PS−CH(Me)CH_2NH_2 + PS (1:10)	0.99	0.093
7	PS−CH(Me)CH_2NH_2 + PEG (1:1)	0.97	0.092
8	PS−CH(Me)CH_2NH_2 + PMMA (1:1)	0.98	0.093

[a] Single measurement. [b] $f_n = 0.94$ by reactive coupling with PMMA−anhydride. [c] Same sample as in entry 3 but analysis performed in nondeuterated chloroform ($CHCl_3$).

for the CF_3 resonances for **7** vs **9** was 2.50 (i.e., 1.25 × 2) to 1.0 (Figure 2b). Thus, there is excellent consistency between quantitative conclusions reached from analysis of the proton vis-à-vis the fluorine NMR data, when comparing either unreacted excess aldehyde **4** to product imine **9** or internal standard (BTF) to product imine **9**. This demonstrates that integration of the ^{19}F signals has the same reliability as that of the ^1H resonances. Because other classes of polymers and polymers of higher molecular weight would be more challenging systems to handle with proton NMR spectroscopy, the remainder of the data and results to be presented are based on analyses of the fluorine NMR spectra.

Control experiments were performed to assess the potential interference of secondary amines or primary alcohols on the analysis. [Recognize that a full equivalent of water is formed in the derivatizing condensation reaction (cf. broad singlet at 2.0 and 1.6 ppm in Figures 1a and 2a), so it is clear that moist samples or trace levels of water in the reaction mixture do not present a problem.] When either diethylamine or 1-propanol was treated with BTFBA (**4**) in $CDCl_3$, no new resonances from adduct formation were detectable in either the ^1H or ^{19}F NMR spectrum. Subsequent addition of DMS-A21 (**8**) led to conversion to imine **9** in entirely analogous fashion as in the absence of the additive. Therefore, it appears that secondary amines and primary alcohols do not appreciably affect the derivatization reaction.

C. Quantification Studies of Amine Content with Aminopolystyrene. As is the case with any method for determination of f_n,[3] the accuracy of the results can be no better than one's confidence/knowledge in the molecular weight characteristics of the polymer. There is inherent error in every value of M_n, and it is often significantly large. Therefore, we began our quantification studies using a nonfunctional sample of PS doped with a small molecule amine, benzylamine, as a mimic of amino functional PS. With this system we could most reliably know the true number of primary amino groups in the sample and most rigorously test the accuracy of our method. First, a negative control, a nonfunctional polystyrene (PS, 19.8K) was mixed with BTFBA (**4**), and of course, no detectable amount of imine terminal polymer was observed by ^{19}F NMR spectroscopy (Table 2, entry 1). Next, a mixture of benzylamine and the nonfunctional PS (mass ratio = 1:91, which is similar to the ratio of residues that would be present in a ca. 10K monofunctional PS) were added to BTFBA (**4**). A known amount of BTF (**7**) (ca. 2 equiv) was also added, and the measured amount of imine corresponded to 99.5% conversion of benzylamine to *N*-(3,5-bis(trifluoromethyl)benzylidene)-1-benzylamine (entry 2). Several other solvents (DMSO, CF_3CH_2OH, CF_3CH_2OH/$CDCl_3$ cosolvent) were used for this analysis of benzylamine, which suggests that the method would likely be applicable to an array of polymer classes. THF is one solvent that was not viable; its use was complicated by partial overlap of two of the key CF_3 resonances. If this solvent choice (or any other that users might need) was an absolute requirement for a given polymer, selection of a different reference standard than BTF (**7**) should readily resolve the overlap issue.

To establish the reliability of the method for the determination of polymer functionality, we elected to study an amine-terminated polystyrene (PS−CH(Me)-CH_2NH_2, 10.6K), prepared by ATRP (Table 1, entry 1, MeCHBrCN initiation[14] and $LiAlH_4$ reduction). Functionality was determined by analyzing integration in the ^{19}F NMR spectrum of the derivatized polymer. The intensity of the resonance from the BTF internal standard was measured against that of the product imine (PSCH(Me)CH_2N=CHAr). Data were collected with long acquisition times to ensure reliable integral values (see Experimental Section for additional details about data collection and analysis). The functionality determined by the ^{19}F NMR method was 0.99 (Table 2, entry 3). For comparison, we also measured the f_n by reactive coupling of the PS−CH(Me)CH_2NH_2 with 1.5-fold excess of anhydride-terminated poly(methyl methacrylate) (PMMA−anhydride). The result ($f_n = 0.94$) was in reasonably good agreement. When the analysis was carried out using nondeuterated chloroform as the solvent for reaction and spectroscopic analysis,[18] the ^{19}F NMR data were essentially the same as with $CDCl_3$ (entry 4).

Since the presence of the nonfunctional PS did not affect the reactivity of the small molecule, it should also not affect reactions of amino functional PSs. We then blended PS−CH(Me)CH_2NH_2 (10.6K) with nonfunctional polystyrene (19.8K) in a mass ratio of 1:1 and 1:10 (entries 5 and 6, Table 2). Even when 10 times the mass of nonfunctional PS was used, the functionality (0.99) obtained from the ^{19}F NMR method was the same as the number for the PS−CH(Me)CH_2NH_2 alone (entry 3, Table 2). This suggests that the method can be expected to be applicable to polymers with molecular weight of ca. 100K and likely considerably higher. Individually, poly(ethylene glycol) (PEG) and poly(methyl methacrylate) (PMMA) were also mixed with PS−CH(Me)CH_2NH_2 in a 1:1 mass ratio. These blended mixtures of amino-PS and different homopolymers also gave the same f_n values (entries 7 and 8), indicating that amino polyethers and amino polyacrylates should also be compatible with the method. Finally, nearly all of the measurements reported in Table 2 were measured in triplicate; for any one sample, results were reproducible to within 2%.

D. Amine Content of Other Monoamino PSs, PMMA, and PEGs. The method was then used to assay several additional monoamino polymers (Table 3). The amine content of most was also available from an alternative source or measurement (see "f_n by Other Means" in Table 3). The functionalities of the seven samples—four amino PSs, one amino PMMA, and two amino PEGs—were determined by the ^{19}F NMR method. Again, there is good agreement with the f_n values from each of the alternative assays.

Table 3. Functionality Determination of Monoamino-Terminated Polymers

		functionality		
entry	monoamino polymer	f_n[a] by ^{19}F NMR method	f_n[a] by other means	(mmol g^{-1}) by ^{19}F NMR method
1	PS−Si(Me)$_2$(CH$_2$)$_4$−NH$_2$ (8.0 K)	0.94	0.95[b]	0.12
2	PS−Si(Me)$_2$(CH$_2$)$_4$−NH$_2$ (55.0 K)	0.66	0.60[b]	0.012
3	PS−Si(Me)$_2$(CH$_2$)$_4$−NH$_2$ (100 K)	0.51	na	0.0051
4	PS−CH(Me)CH$_2$NH$_2$ (17.7 K)	0.94	1.00[b]	0.053
5	PMMA-NH$_2$ (31.0 K)	0.28	0.27[b]	0.0090
6	PEG-NH$_2$ (5.0 K)	0.92	0.94[c]	0.18
7	PEG-NH$_2$ (5.2 K)	0.93	0.96[c]	0.18

[a] f_n = number of functional groups per polymer chain. [b] Reactive coupling followed by GPC analysis (our measurements). [c] HPLC (Certificate of Analysis).

E. Amine Content of Di- and Triamino Polymers. Quantifying the functionality of amino polymers containing more than one functional amine group is more challenging. The difficulty of separation of multifunctional polymers makes reactive coupling/GPC analysis and the TLC/FID method less feasible. While titration methods give total amine content, they generally do not distinguish primary from secondary and tertiary amines. The ^{19}F NMR method described above does not rely on separation and only detects primary amino groups, so we were interested to examine its applicability for quantifying primary amine sites in di- and triamino polymers.

As described above, the ^{19}F NMR method was reliable for diaminopolysiloxane, DMS-A21 (**8**). The integrations of both ^{1}H NMR and ^{19}F NMR spectra were self-consistent. The functionality we determined for **8** (entry 1) by the ^{19}F NMR method was 0.46 mmol/g; its reported value[19a] was 0.38−0.44 mmol/g. A second diamino-PDMS was reported to have 0.069−0.075 mmol/g and a molecular weight of 25 kg/mol.[19b] Our NMR analysis showed it to have a substantially higher functionality of 0.13 mmol/g (entry 2). We then analyzed the molecular weight by examining the ^{1}H NMR spectrum. Specifically, comparison of the intensity of the resonance of the methylene protons adjacent to the terminal amines (−C*H*$_2$NH$_2$ at 2.66 ppm) with that of the methyl resonances in the silicone backbone indicated that the proper molecular weight of this sample was ca. 14 kg/mol. Applying this correction leads to a revised "functionality by other means" value of 0.12−0.13 (entry 2), again in good agreement with the ^{19}F NMR method. Thus, in this instance our initial measurement led us to reanalyze the sample, which revealed that the initial M_n value was incorrect.

Two synthetic diamino-PBs prepared in our laboratory[15] were also analyzed using the ^{19}F NMR method. Each of these polymers had a broad distribution (PDI ~1.8), so the accuracy of the M_n values is necessarily compromised. The f_ns for each sample were independently measured by reactive coupling with anhydride-terminated polystyrene (PS-anhydride) followed by GPC analysis (Table 4, entries 3 and 4). These two pairs of determinations are consistent, especially in light of the inherent error in M_n determination by GPC of samples having broad distribution.

Three diamino polyethers (JEFFAMINED-2000, XTJ-504, and XTJ-510) and two triamino polymers (JEFFAMINE BA-509 and T-5000) were also determined by our ^{19}F NMR method, and the results are summarized in Table 4 (entries 5−9). With the exception of the D-2000 sample (entry 5), the values for these JEFFAMINE samples obtained by our ^{19}F NMR method are in excellent agreement with those provided by the manufacturer. The determinations for the triamino polymers

Table 4. Functionality Determination of Di- and Triamino Functional Polymers

entry	multiamino polymers	functionality[a] by ^{19}F NMR method	functionality[a] by other means
1	DMS-A21 (**8**) [H$_2$N−PDMS−NH$_2$ (5 K[b])]	0.46	0.38−0.44[19] (0.60−0.70)[c]
2	DMS-A31 [H$_2$N−PDMS−NH$_2$ (25 K[b])]	0.13	0.069−0.075[19] (0.11−0.12)[c]
3	H$_2$N−PB−NH$_2$ (26 K)	0.080 (2.1)[d]	(1.8)[e]
4	H$_2$N−PB−NH$_2$ (38 K)	0.048 (1.8)[d]	(1.7)[e]
5	JEFFAMINE D-2000	1.1	1.01[f]
6	JEFFAMINE XTJ-510	0.49	0.48[f]
7	JEFFAMINE XTJ-504	13	13.3[f]
8	JEFFAMINE BA-509	0.95	0.95[f]
9	JEFFAMINE T-5000	0.53	0.53[f]

[a] In mmol/g. [b] "Molecular weight" of the commercial sample from the manufacturer's catalog. [c] "Weight percent of (NH$_2$)" of the commercial sample from the manufacturer's catalog. [d] f_n = number of functional groups per polymer chain, value obtained by eq 1 or simply by multiplying M_n × the functionality in mmol g^{-1}. [e] f_n = number of functional groups per polymer chain, from GPC analysis (UV detection of conjugate with PS-anhydride and using Gaussian multipeak fitting,[11] assuming all PBs bear one or two amino groups). [f] From manufacturer's Certificate of Analysis.

BA-509 and T-5000 indicate that the method is also suitable for quantifying multifunctional polymers.

F. Polyamide Amine Functionality Determination. Polyamide (e.g., nylon) amine content determination is made challenging because of the poor solubility of polyamides in most common solvents. DMSO is a good solvent for amorphous nylon; mixtures of trifluoroethanol (TFE) and chloroform have been used as a solvent for crystalline nylon. In particular, NMR studies have been carried out in TFE/CDCl$_3$.[20]

DMSO was used to test the viability of our method for amorphous nylon **11**. Benzylamine was chosen as a model compound. BTFBA (**4**) and benzylamine (ca. 2:1) were mixed in DMSO-d_6. The reaction went smoothly to completion (no detectable amount of PhCH$_2$NH$_2$ resonances by ^{1}H NMR spectroscopy). However, in the ^{19}F NMR spectrum the resonances of the newly formed imine, PhCH$_2$N=CHPh(3,5-(CF$_3$)$_2$), and BTFBA (**4**) overlapped. One solution to this problem was found when the nature of the derivatizing aldehyde itself was changed. Namely, 4-trifluoromethylbenzaldehyde (*p*-TFBA, **10**) was used instead of BTFBA (**4**). In this case the resonance of the imine PhCH$_2$N=CHPh(4-CF$_3$) did not overlap with that of *p*-TFBA (**10**). That this was a quantitatively reliable approach was demonstrated by measuring benzylamine to have a functionality of 0.993.

Functionalities of amorphous nylons (Zytel 330 and Selar PA 3426) were also determined under the same conditions. The ^{19}F NMR spectrum for each showed

Table 5. Functionality Determination of Amorphous and Crystalline Nylons

polyamide	functionality[a] with *p*-TFBA (**10**) (mmol/g)	functionality[b] with BTFBA (**4**) (mmol/g)	functionality[c] by titration (mmol/g)
Zytel 330	0.025	0.024	0.025
Selar PA 3426	0.032	0.031	0.031
Zytel 101	na	0.048	0.045

[a] In DMSO-d_6. [b] In 4:1 TFE/$CDCl_3$. [c] In *m*-cresol.

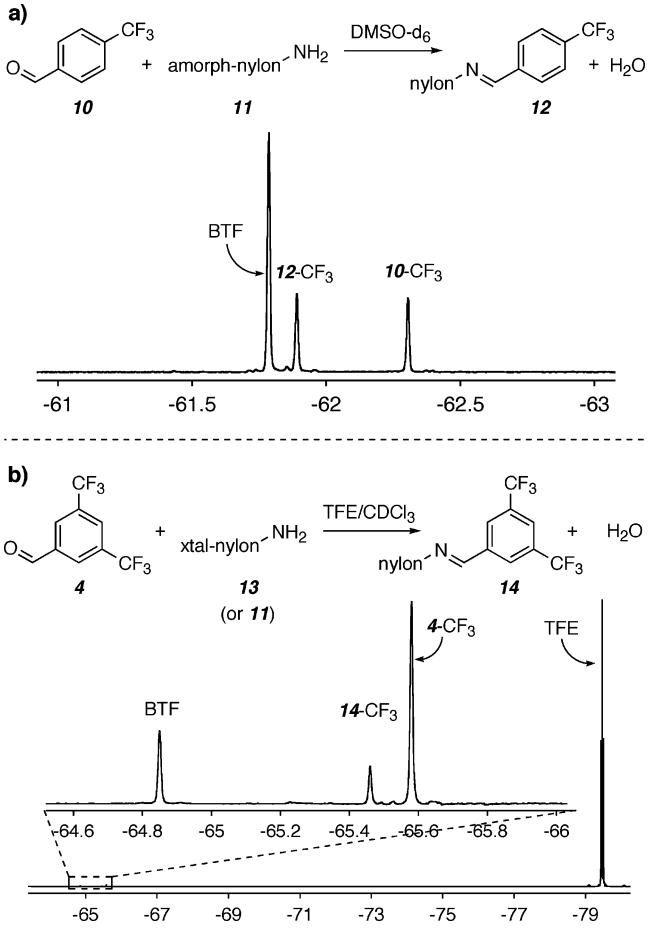


Figure 3. ^{19}F NMR spectra of reaction between amorphous (**11**) or crystalline (**13**) nylons and *p*-TFBA (**10**)//DMSO-d_6 or BTFBA (**4**)//TFE/$CDCl_3$, respectively.

complete separation of nylon-imine (**12**) from BTF (**7**) and *p*-TFBA (**10**), which gave reliable integration and could be used to determine nylon primary amine content (Figure 3a). By comparing with the added internal standard BTF (**7**), we deduced the amount of primary amine in nylons (Table 5, entries 1 and 2). The amine contents of Zytel 330 and Selar PA 3426 were also determined by titration[21] and were found to be in good agreement with the values from our ^{19}F NMR method (Table 5).

A cosolvent consisting of TFE/$CDCl_3$ (4:1) was then explored as a solvent for determination of the amine content of crystalline nylon **13**. That this can be a quantitatively reliable approach, even though the intensity of the ^{19}F resonance from the TFE solvent (at −79.3 ppm) was ca. 800 times larger than that of the BTF reference, was demonstrated by measuring benzylamine to have a functionality of 1.04. The resonance of the newly formed imine, $PhCH_2N{=}CHPh(3,5\text{-}(CF_3)_2)$, is well separated from those of BTFBA (**4**), BTF (**7**), and TFE.

The same conditions were then applied to a sample of the crystalline nylon, Zytel 101. Initially, only a trace of imine formation was observed by ^{19}F NMR spectroscopy. We hypothesized that the terminal amine groups might be largely protonated as ammonium salts. Accordingly, the soluble tertiary amine base, 1,4-diazabicyclo[2.2.2]octane (DABCO) or triethylamine (TEA), was added. Formation of imine **14** (e.g., Figure 3b) ensued. The amount of amine in Zytel 101 was determined to be 0.048 mmol/g (Table 5, entry 3). The amine content of Zytel 101 was determined by titration[21] and, again, was found to be in good agreement with the number from our ^{19}F NMR method (Table 5). Finally, for comparison, we remeasured the amorphous nylon samples in TFE/$CDCl_3$ (Table 5) solvent, and the results matched well with those earlier determined in DMSO-d_6 and by titration. Thus, we are confident recommending the use of this method even for the challenging class of nylon polyamides.

Conclusions

A new ^{19}F NMR spectroscopy-based assay for determining the primary amine functionalities of polymers has been developed. We have demonstrated that the functionality of primary amines can be determined for a broad range of polymers (including PS, PMMA, PEG, PDMS, polyethers, PB, and polyamides) and that the method is applicable to mono-, di-, and triamino polymers as well as those with broad distribution (e.g., PDI approaching 2). This new method has several advantages over known assays (e.g., classical, wet chemical titration; reactive coupling/GPC; and TLC/FID). It can be carried out quickly and requires only small amounts of sample (ca. 10 mg). It is convenient, reliable, and general.

Experimental Section

***N*-(3,5-Bis(trifluoromethyl)benzylidene)-1-propanamine.** 3,5-Bis(trifluoromethyl)benzaldehyde (**4**, 73.5 mg, 0.303 mmol), propylamine (17.9 mg, 0.303 mmol), and ca. 10 pellets of molecular sieves (3 Å)[22] were added to 1 mL of $CDCl_3$ in a 4 mL vial. After 2 h the solution was transferred and concentrated under vacuum to give 85.8 mg (100%) of *N*-(3,5-bis(trifluoromethyl)benzylidene)-1-propanamine. ^1H NMR (300 MHz, $CDCl_3$): δ 8.36 (t, 1H, J = 1.2 Hz, $-CH{=}N-$), 8.19 (br s, 2H, 2,6-Ar*H*), 7.91 (br s, 1H, 4-Ar*H*), 3.65 (dt, 2H, J = 1.5 Hz, 6.9 Hz, $=NCH_2-$), 1.74 (sextet, 2H, J = 7.2 Hz, $-CH_2CH_2CH_3$), and 0.97 (t, 3H, J = 7.2 Hz, $-CH_3$). ^{13}C NMR (75 MHz, $CDCl_3$): δ 157.8, 138.5, 132.3 (q, J = 33.2 Hz), 128.1 (d, J = 2.9 Hz), 123.9 (pentet, J = 3.7 Hz), 123.4 (q, J = 271.6 Hz), 63.7, 24.1, and 12.0. ^{19}F NMR (282 MHz, $CDCl_3$, BTF (**7**) as reference [−63.0 ppm]): δ −63.2. HR-ESI-MS ($M + H^+$): found (calcd) 284.0885 (284.0874).

Typical Procedure for Amino Functional Polymers. $PS{-}CH(Me)CH_2NH_2$ (M_n = 10.6K, 11.0 mg) was dissolved in 1 mL of $CDCl_3$ in a 4 mL Teflon-capped vial at ambient temperature. A 100 μL portion of a stock solution containing the standard **7** and derivatizing agent **4** [2.5 μL of BTF (**7**) and ca. 4.0 μL of BTFBA (**4**) in 1.0 mL of $CDCl_3$] and several pellets of molecular sieves (3 Å) were added. After standing for 6 h at ambient temperature, 0.2 mL of the reaction mixture (containing ca. 2 mg of polymer) was transferred to 0.5 mL of $CDCl_3$ in a 5 mm NMR tube. The ^{19}F NMR spectrum was

collected (32−64 transients) with an acquisition time of 15 s and a pulse delay of 5 s (T_1 of the fluorines: BTF ca. 2.7 s, BTFBA ca. 2.4 s, imine ca. 1.9 s) to ensure complete relaxation and quantitative fluorine integration. ^{19}F NMR (282 MHz, $CDCl_3$, BTF as reference [−63.0 ppm]): δ −63.2 (imine) and −63.3 (BTFBA).

f_n (in number of functional groups per polymer chain) was determined by eq 1. f_n can be further converted to functionality in mmol/g by dividing by M_n.

$$f_n = \frac{\text{mmol of BTF} \times \left(\frac{\text{integral of } ^{19}\text{F resonance of imine from } \mathbf{4}}{2 \times \text{integral of } ^{19}\text{F resonance of BTF}}\right)}{\left(\frac{\text{mg of polymer}}{M_n \text{ of polymer}}\right)} \quad (1)$$

Amorphous Nylon Analysis. Amorphous nylon (39.1 mg, Zytel 330, DuPont) in 1 mL of DMSO-d_6 was stirred at room temperature. After the nylon was dissolved, 100 μL of a stock solution [5.0 μL of BTF (**7**) and ca. 3.0 μL *p*-TFBA (**10**) in 1.0 mL of DMSO-d_6] and several pellets of 3 Å molecular sieves were added. After standing overnight at ambient temperature, 0.3 mL of the reaction mixture (containing ca. 12 mg of polymer) was transferred to 0.5 mL of DMSO-d_6 in a 5 mm NMR tube. The ^{19}F NMR spectrum was collected (128−256 transients) with an acquisition time of 10 s (T_1 of the fluorines: BTF ca. 2.4 s, *p*-TFBA ca. 1.9 s, imine ca. 1.0 s) and a pulse delay of 5 s to ensure complete relaxation and quantitative fluorine integration. ^{19}F NMR (282 MHz, DMSO-d_6): δ −61.7 (BTF), −61.8 (imine), −62.2 (*p*-TFBA).

Crystalline Nylon Analysis. Crystalline nylon (95.0 mg, Zytel 101, DuPont) and 5 mg of DABCO (or 25 μL TEA) were stirred in 0.8 mL of 2,2,2-trifluoroethanol (TFE) at room temperature. After the nylon was dissolved (ca. 2 h), 100 μL of a stock solution [20.0 μL of BTF (**7**) and ca. 30.0 μL of BTFBA (**4**) in 1.0 mL of $CDCl_3$] was added. An additional 0.1 mL of $CDCl_3$ was added to achieve a final TFE/$CDCl_3$ ratio to ca. 4:1. Several molecular sieves (3 Å) were added to this solution. After standing overnight at ambient temperature, the solution was transferred to a 5 mm NMR tube. The ^{19}F NMR spectra were collected (64−128 transients) with an acquisition time of 15 s and a pulse delay of 5 s to ensure complete relaxation and quantitative fluorine integration. ^{19}F NMR (282 MHz, TFE/$CDCl_3$): δ −64.8 (BTF), −65.4 (imine), −65.5 (BTFBA), and −79.4 (t, TFE).

Nylon functionality (in mmol g^{-1}) was determined by eq 2 or 3 depending on whether aldehyde **10** or **4** was used, respectively.

$$\text{functionality} = \frac{\text{mmol of BTF} \times \left(\frac{\text{integral of } ^{19}\text{F resonance of imine from } \mathbf{10}}{\text{integral of } ^{19}\text{F resonance of BTF}}\right)}{\text{g of nylon}} \quad (2)$$

$$\text{functionality} = \frac{\text{mmol of BTF} \times \left(\frac{\text{integral of } ^{19}\text{F resonance of imine from } \mathbf{4}}{2 \times \text{integral of } ^{19}\text{F resonance of BTF}}\right)}{\text{g of nylon}} \quad (3)$$

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