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Determination of acid and hydroxyl end-groups in end-functionalized polystyrenes using ^{19}F NMR

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Abstract: Carboxyl-terminated polystyrene was esterified with 2,2,2-trifluoroethanol using a carbodiimide-mediated room temperature reaction, and hydroxyl-terminated polystyrene was fluoro-derivatized with trifluoroacetic anhydride. The so-formed fluorine-containing esters were then quantitatively determined with ^{19}F NMR, using α,α,α-trifluorotoluene as secondary standard. This provides a technique for the reliable determination of carboxylic acid and hydroxyl groups in small samples of polymers.

Introduction

Polymers containing minute amounts of functional groups are of great interest for biological applications such as drug delivery, electronic applications such as patterning, and for the synthesis of new macromolecular structures for materials science. For example, coupling of end-functionalized polymers with other end-functionalized polymers, multifunctional core molecules and functionalized surfaces can lead to block copolymers, star polymers and polymer brushes, respectively. Such end-functionalized polymers are prepared by living radical polymerizations starting from functionalized initiators [1-3] or by functionalization of polymeric organolithium compounds made by anionic mechanism [4]. Though MALDI-TOF (matrix-assisted laser desorption ionization - time of flight) mass spectroscopy has proven to be a useful method for the qualitative determination of such functionalization, quantitative determination of such minute functionality in polymers is most often based on flash column chromatography and titration [5], with the following associated problems: large sample size requirement, toxic solvents, difficult determination of end-point, etc.

NMR based techniques can provide an alternative with small sample requirement and small amounts of solvents. However, use of ^{1}H NMR to directly detect minute amounts of functionality (such as hydroxyl end-groups) has been rather limited due to the small and broad peaks. Ho [6] described a technique where hydroxyl end-groups were converted into a ^{19}F NMR detectable adduct with hexafluoroacetone (HFA). However, HFA is very toxic and gaseous (b. p. -29°C) at room temperature. Kenwright *et al.* [7] studied the kinetics of esterification of hydroxyl end-groups of poly(ethylene terephthalate) (PET) with trifluoroacetic acid, and they found the reaction to take several days to complete. We recently described a ^{19}F NMR based

technique for acid end-group determination in PET, using hexafluoroisopropanol (HFIP) both as a solvent and as a derivatizing alcohol [8]. Here, we describe an adaptation of these fluoroderivatization techniques to quantitatively determine the acid and hydroxyl groups in end-functionalized polystyrenes.

Experimental part

Materials

Styrene (99%, Aldrich) was passed through a column of activated basic alumina to remove inhibitor, stored over CaH_2, and then distilled in vacuum before use. CuBr (99.999%, Aldrich) was purified according to the procedure reported in ref. [9]. 4,4'-n-Nonyl-2,2'-bipyridine (dNbpy, 97%, Aldrich) was recrystallized from ethanol. 2-Hydroxyethyl 2-bromo-2-methylpropanoate (HEBMP) was synthesized according to a previously reported procedure [10].

α,ω-Dicarboxy-terminated polystyrene (DCPS, M_n = 9400, M_w/M_n = 1.07) was obtained from Polymer Source, Inc., Canada. They synthesized it by anionic polymerization of styrene, and reacting the living end with highly purified CO_2 gas to generate carboxyl end-groups [11]. Diphenyl ether (> 98%, Merck), 4-pyrrolidinopyridine (98%, Aldrich), trifluoroacetic anhydride (TFAA, 99+%, Aldrich), α,α,α-trifluorotoluene (TFT, 99+%, Aldrich), 2,2,2-trifluoroethanol (TFE, > 99%, Fluka), *N*,*N*-dicyclohexylcarbodiimide (DCC, >99%, Merck), chloroform-d_1 ($CDCl_3$, 99.8%, Merck) and tetrahydrofuran (THF, stabilized, Biosolve) were used as received.

Measurements

^{19}F NMR spectra were recorded on a Varian Mercury Vx400 spectrometer at 400 MHz, scaling with TFT at δ = -62.9 ppm. Acquisition time of 1.2 s and relaxation delay of 4 s were used. Signal to noise ratio was improved by taking an average of 32 repeated scans for each sample.

Molecular weight distributions were measured by gel permeation chromatography (GPC) using a Waters GPC equipped with Waters 510 pump, Waters 410 differential refractometer (40°C), Waters 712 autoinjector (50 µL injection volume), PLgel (5 µm particles) 50 × 7.5 mm guard column and two PLgel mixed-C (5 µm particles) 300 × 7.5 mm columns (40°C). Data acquisition and processing were performed using Waters Millennium 32 (v3.2) software. THF was used as the eluent, at a flow rate of 1.0 mL/min. Calibration was done using polystyrene standards (Polymer Laboratories, 580 to $7.1 \cdot 10^6$ g/mol). The polystyrene samples were prepared for injection by dissolving the polystyrenes in THF at a concentration of 0.1 mg/mL.

Preparation of monohydroxy-polystyrene (MHPS)

A 100 mL three-necked round-bottom flask was charged with styrene (5.2 g, 0.05 mol), CuBr (0.0717g, 0.5 mmol), dNbpy (0.4087 g, 0.001mol), and purged with Ar for 30 min, with vigorous stirring. In another flask, HEBMP (0.0527 g, 0.25 mmol) and diphenyl ether (2.5 g) were added and purged with Ar for 30 min. The mixture was then added dropwise to the homogeneous monomer solution under Ar atmosphere using a degassed syringe. The resulting mixture was placed in a thermostatically controlled oil bath at 110°C. At desired times, samples were withdrawn from the

flask, dissolved in THF, and passed through a basic alumina column to remove the catalyst. From each of these samples, MHPS was precipitated from the eluting solution using heptane, and then dried in vacuum.

Fluoroderivatization of MHPS with TFAA

TFAA (0.03 g, 0.142mmol) was added to a solution of MHPS (0.02 g) in $CDCl_3$ (1 mL). After waiting for 30 min, the excess TFAA was removed by evaporation to dryness by blowing argon and then by applying vacuum. The resulting polymer was redissolved in $CDCl_3$ (1 g). Part (0.1 g) of a solution of TFT (0.0556 g, 0.38 mmol) in $CDCl_3$ (3.7825 g) was added to the reaction mixture to give the sample for NMR analysis.

Characterization of the trifluoroacetate of MHPS (**1**): ^{19}F NMR: δ = -75.13 ppm (s, 3F).

Caution: TFAA may cause burns to skin or eyes, inhalation or ingestion may be fatal!

Fluoroderivatization of HEBMP with TFAA

TFAA (0.3003 g, 1.45mmol) was added to initiator (0.0306 g, 0.145 mmol). A solution of TFT (0.0026 g, 0.0178 mmol) dissolved $CDCl_3$ (1.002 g) was made and a part (0.2 g) of this solution was added to the reaction mixture to give the sample for NMR analysis.

Characterization of the trifluoroacetate of HEBMP: ^{19}F NMR: δ = -75.12 ppm (s, 3F).

Esterification of DCPS with TFE

DCPS (0.0306 g, 0.0032 mmol) was dissolved in $CDCl_3$ (1.6746 g). First, part (0.1413 g) of a solution of 4-pyrrolidinopyridine (0.0018 g, 0.012 mmol) in $CDCl_3$ (1.0046 g) was added. Subsequently, part (0.210 g) of a solution of TFE (0.0241 g, 0.17 mmol) in $CDCl_3$ (1.3614 g) was added, and then part (0.107 g) of a solution of DCC (0.0131 g, 0.053 mmol) in $CDCl_3$ (1.2017 g) was added. After waiting for 10 min, part (0.1238 g) of a solution of TFT (0.0384 g, 0.26 mmol) in $CDCl_3$ (3.3922 g) was added to the reaction mixture to give the sample for NMR analysis.

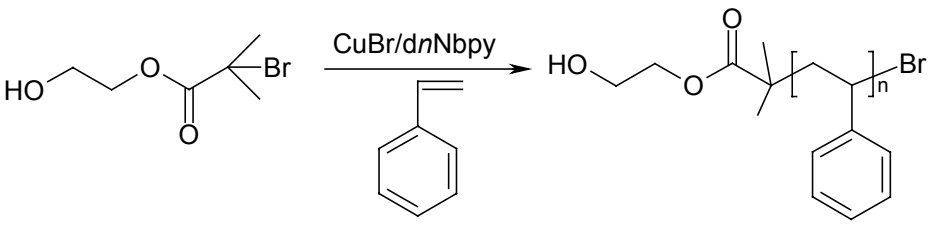
Characterization of the trifluoroethyl ester of DCPS (**2**): ^{19}F NMR: δ = -73.8 ppm (s, 6F).

Results and discussion

Synthesis of MHPS

MHPS was prepared by atom transfer radical polymerization (ATRP) of styrene from the hydroxyl-functionalized initiator HEBMP, using CuBr catalyst and dNbpy ligand (Scheme 1).

Tab. 1 shows the GPC determined M_n and polydispersity (M_w/M_n) of the polymer samples withdrawn during the reaction. The increasing M_n with time of reaction, while maintaining a narrow molecular weight distribution, is an indication of good control during the polymerization [12,13].



HEBMP MHPS

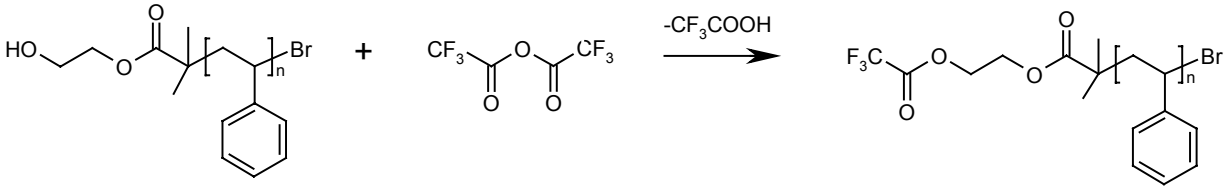
Scheme 1.

Tab. 1. Details of the MHPS samples prepared by ATRP

Sample no.	Time of ATRP in h	M_n	M_w/M_n
1	1	2597	1.09
2	2	4508	1.08
3	3	6299	1.07
4	5	8371	1.07

Determination of the hydroxyl end-groups of MHPS by fluoroderivatization

The hydroxyl end-groups of MHPS were determined by the reaction with TFAA (Scheme 2) leading to the trifluoroacetate of MHPS (**1**):



MHPS TFAA **1**

Scheme 2.

Fig. 1 shows the ^{19}F NMR spectrum of the reaction product. In addition to the sharp peak of TFT (δ = -62.9 ppm), the trifluoroacetate **1** features at δ = -75.13 ppm. This chemical shift of the polymeric trifluoroacetate is comparable to the chemical shift of the trifluoroacetate of the initiator (δ = -75.12 ppm). Quantifying the areas of the signals of the TFT and the trifluoroacetate **1**, the hydroxyl concentrations were calculated for the 4 different samples of MHPS. These results are plotted in Fig. 2 as a function of the GPC determined M_n. Also plotted in Fig. 2 is a continuous line corresponding to 100% (theoretical) end-functionalization in the MHPS samples. The deviation is limited to less than 5%, the accuracy of the NMR peak integrations.

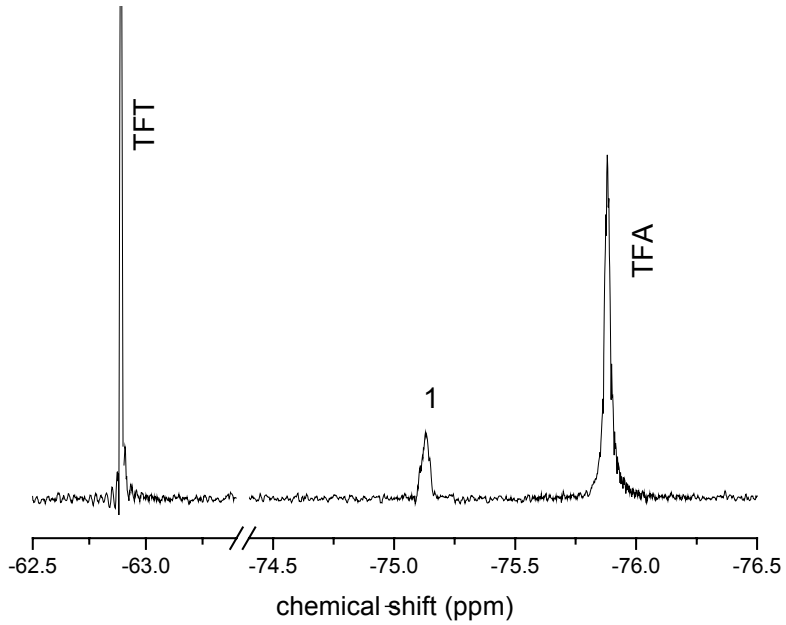


Fig. 1. ^{19}F NMR spectrum of the reaction product of MHPS (M_n = 8371) with TFAA

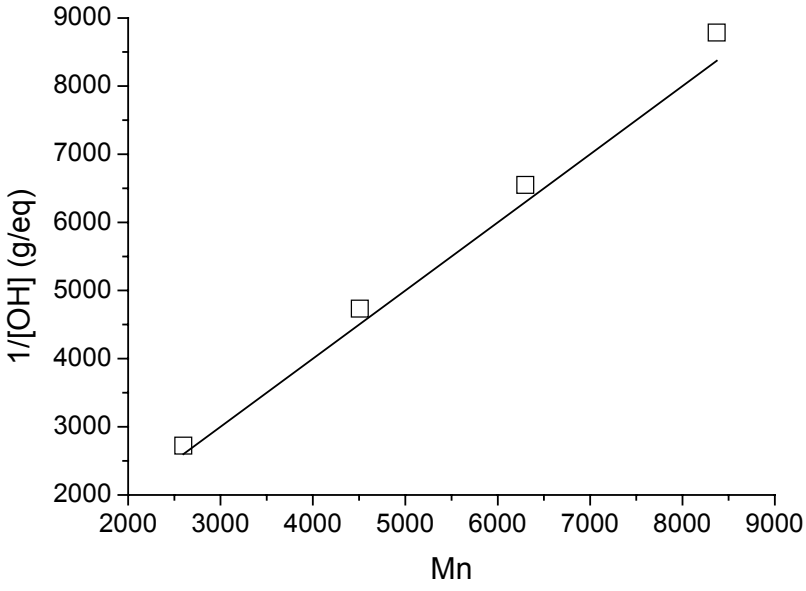
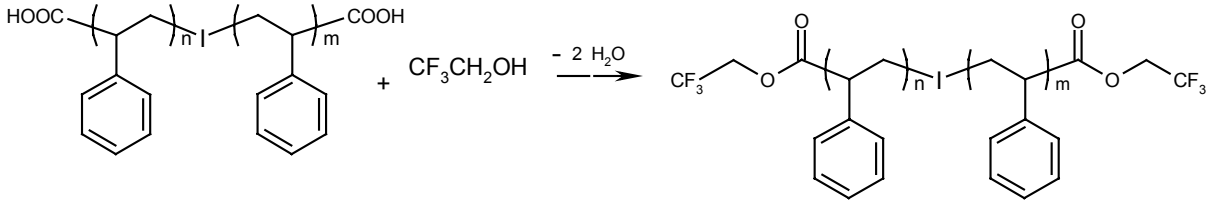


Fig. 2. Concentration of the hydroxyl end-groups ([OH], expressed as equivalents of OH groups per g of MHPS, in the MHPS samples of Tab. 1, as determined by ^{19}F NMR after fluoroderivatization with TFAA (Scheme 2). The continuous line represents the theoretical values corresponding to 100% end-functionalization in the MHPS samples

Determination of the acid end-groups of DCPS by fluoroesterification

In an earlier work [8] we had reported the DCC mediated fluoroesterification of the carboxylic end-groups in PET with HFIP, the latter being also used as the solvent for

PET. In a similar vein, we tried to use HFIP also for the esterification of DCPS, but the resulting fluoroester peak in ^{19}F NMR could not be resolved from the peak of the HFIP-DCC adduct [8]. As an alternative, we achieved trifluoroesterification of the carboxylic acid end-groups in DCPS with TFE, also through a DCC mediated reaction, to afford the trifluoroethyl ester of DCPS (**2**) (Scheme 3).



DCPS TFE **2**

Scheme 3.

Fig. 3 shows the ^{19}F NMR spectrum of the product of this reaction. In addition to the sharp peaks of the added secondary standard TFT (δ = -62.9 ppm) and the excess reagent TFE (δ = -77.3), a broad peak features at δ = -73.8 ppm corresponding to the ester **2**. Comparing the ratio (1 : 0.65) between the integrals of signals of the TFT and the ester **2**, the ester group concentration was estimated as 205 meq/kg, which compares well to the expected acid concentration of 213 meq/kg for the difunctional DCPS with M_n = 9400.

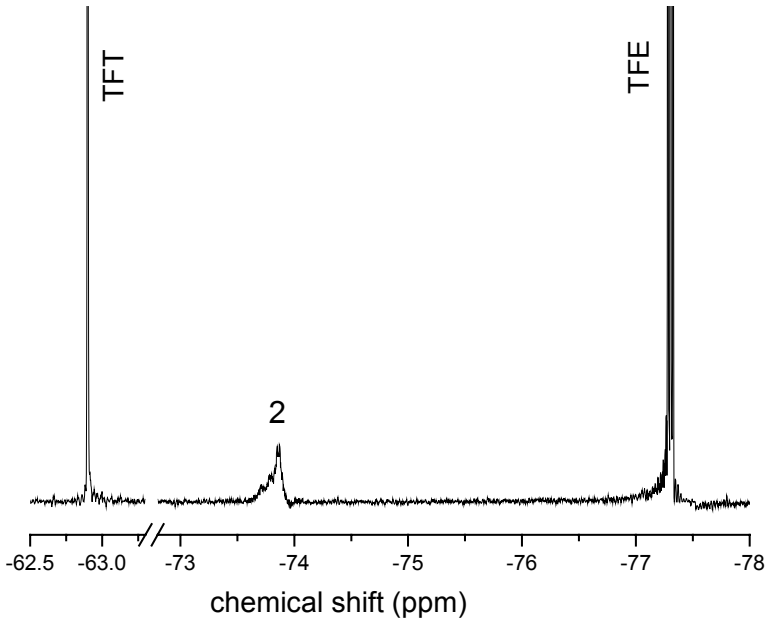


Fig. 3. ^{19}F NMR spectrum of the reaction product of DCPS with TFE

In our earlier work with PET, we had to use HFIP as the derivatizing fluoroalcohol *and* as the solvent, resulting in its presence in the reaction mixture while DCC was added. The DCC added was then partially used up in formation of an adduct with

HFIP, and an excess of DCC was thus required [8]. However, DCPS dissolves easily in chloroform and TFE could be conveniently added subsequent to DCC. Further, TFE does not form any adduct with DCC.

Conclusions

We have presented methods for the determination of the acid and hydroxyl groups in functionalized polystyrenes. These involve fluoroderivatization of the end-functionality in small samples by fast esterification reactions, followed by quantitative ^{19}F NMR with respect to an added secondary standard. Given the limited accuracy of NMR integrations ($\pm$ 5%), we find that these NMR based measurements compare very well with the values based on molecular weights of the end-functionalized polystyrenes.

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