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Synthesis and Post-Polymerization Modification of Poly(*N*-(4-Vinylphenyl)Sulfonamide)s

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Herein, a straightforward synthesis of a novel class of polymers, that is, poly(*N*-(4-vinylphenyl)sulfonamide)s, and their monomers is reported. A set of monomers with varying electron densities, fine-tuned by different substituents on the aromatic sulfonamide moiety, is polymerized by free radical polymerization featuring low molar masses (2300 $\leq M_n \leq$ 3200 g mol^{-1}) and low dispersities (1.15 $\leq Đ \leq$ 1.47). Further, the post-polymerization modification of the obtained polymers via aza-Michael addition with electron-deficient alkenes is demonstrated using organic superbases as catalysts, paving the way toward the facile synthesis of novel polymeric protected β-amino acid derivatives.

1. Introduction

Up to now, an almost unthinkable number of different macromolecules has been synthesized, and reported with regards to their chemical and physical properties. Macromolecules containing sulfur—nitrogen bonds are currently emerging and represent one class of rather unexplored functionalities in the field of polymer chemistry,[1] although the unique chemical properties of sulfur—nitrogen bonds could result in new materials with unprecedented properties compared to more commonly employed polymeric materials.[2] Indeed, polymers featuring sulfur—nitrogen bond motifs outclass their conventional carbon-analogues in many disciplines, that is, in their role as flame retardants,[3] their degradation,[4,5] or high solubility in polar solvents,[6] making them a highly interesting class of materials not only in scientific research, but also in industrial applications. On the contrary, polystyrene is a commonly used polymer with different applications ranging from packaging,[6] domestic appliances,[7] medical items,[7] and as construction goods such as insulation.[8,9] Polystyrene is obtained by polymerization of styrene as widely available, nonpolar monomer. While neat polymerized styrene features a high glass transition temperature (T_g) resulting in a hard and brittle solid at ambient conditions, diverse functionalities (chlorine, bromine, alcohol, carboxylic acid, ether, etc.) could be introduced allowing for the synthesis of new monomer and polymer classes.

The field of post-polymerization modification (PPM) represents a highly versatile and efficient toolbox for the polymer functionalization leading to a great variety of different polymeric structural motifs.[10] PPM dates back to the 1840s, when natural rubbers were treated with sulfur[11] and nitrocellulose was prepared from cellulose as natural polymer.[12] Different kinds of chemistries have been successfully applied to functionalize polymers bearing functional groups that are on the one hand inert to the polymerization process, but are reactive toward different reaction conditions, resulting in a change of the polymer's structure. Important examples for these chemistries are thiol-ene reactions[13] as well as transformations of active esters.[14–16] The latter have been carefully explored and reported on different polymeric systems inter alia by our group, allowing for the preparation of macromolecules that cannot be obtained by direct polymerization of the respective monomer units.[17] PPM also allows for the preparation of single-chain nanoparticles (SCNPs)[18] by folding of the functional, individual polymer chains. The folding can be induced using different kinds of triggers, resulting in interesting properties and thus various potential applications.[19]

Within the present study, 4-vinylaniline, a styrene derivative with a primary amine functionality tethered to the aromatic phenyl motif, was used as take-off point for the preparation of a new class of monomers, that is, *N*-(4-vinylphenyl)sulfonamides, and their respective polymers based on a sulfur—nitrogen bond. In a simple one-step reaction, *N*-(4-vinylphenyl)sulfonamides could be prepared in good yields from commercially available compounds, facilitating the access to the herein reported new class of polymers, that is, aromatic poly(*N*-(4-vinylphenyl)sulfonamide)s.

2. Results and Discussion

Aromatic sulfonyl chlorides with different electron densities were employed for the syntheses of three monomers M1, M2,

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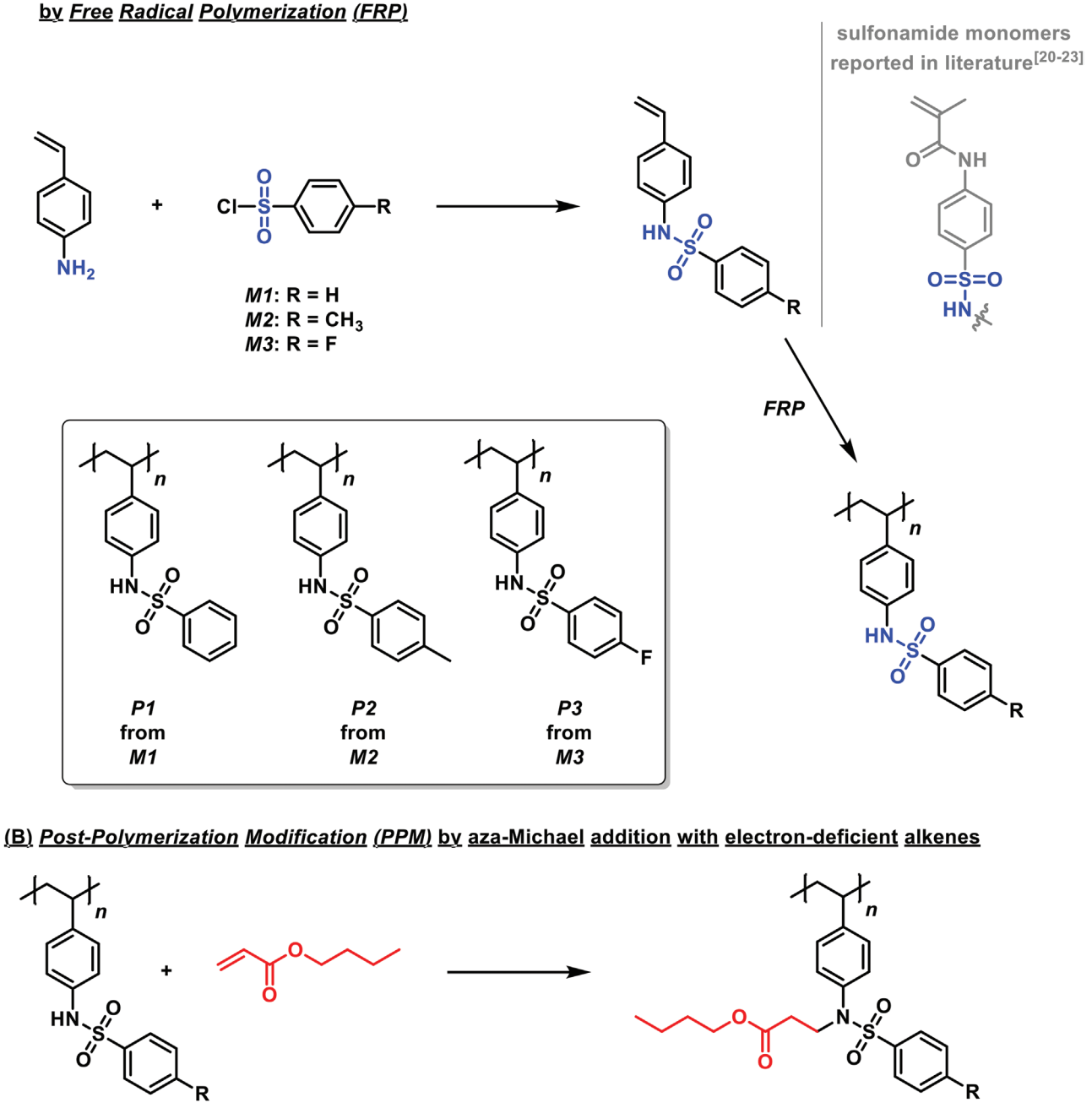

Scheme 1. A) One-step synthesis of styrene-derived, aromatic sulfonamide monomers M1, M2, and M3 from commercially available 4-vinylaniline in the presence of different aromatic sulfonyl chloride derivatives. Important: The direction of the NH-SO_2 functionality is inverted in comparison to reported sulfonamide monomers. The straightforward synthesis of monomers M1–M3 enabled the preparation of a novel class of sulfonamide-based polymers, that is, P1, P2, and P3, by FRP, resulting in polymers with varying electron densities and an inherent secondary amine functionality. B) The latter allows for PPM of the sulfonamide-based polymers via aza-Michael addition with butyl acrylate serving as exemplary electron-deficient alkene, leading to the formation of polymeric protected β-amino acid derivatives.

and M3 (**Scheme 1**A, see Supporting Information for details on the syntheses of the monomers), allowing for the manipulation of the monomers' electronic properties and their polymers, respectively. These monomers are based on a sulfonamide functionality, but in contrast to reported monomers bearing this bond motif,[20–23] the sulfonamide groups of the moieties reported herein are inverted. In other words, instead of a SO_2—NH group, the novel monomers are based on a NH—SO_2 functionality, in the order of bonds from a backbone perspective. This bond sequence allows for the preparation of a broad variety of different amine-based polymers, in other words, the aromatic sulfonamide group can, on the one hand, be removed

by deprotection right after polymerization, resulting in polystyrene featuring amine functionalities in the *para* position, which can be further functionalized. On the other hand, a deprotection upon aza-Michael addition would result in the formation of another secondary amine moiety, representing an additional handle for PPM. Additionally, most reported sulfonamide monomers are based on methacrylamide, while this report is dealing with styrene-derived sulfonamide monomers. Nevertheless, only one report exists on sulfonamide polymers based on a styrene repeating unit, which was synthesized by PPM of poly(pentafluorophenyl-4-vinylbenzenesulfonate) derivatives.[24] Accordingly, the synthesized monomers M1, M2, and M3 were polymerized by free radical polymerization (FRP) (Scheme 1A), since it is the most facile and straightforward radical polymerization technique, and explicitly enhances the industrial applicability of this class of sulfonamide-based polymers. Nonetheless, polymers featuring low dispersities ($1.15 \leq Đ \leq 1.47$, according to size-exclusion chromatography (SEC) using THF as eluent. Dispersity values obtained by SEC analysis using *N,N*-dimethylacetamide as solvent matched the character of FRP, being in the order of $Đ \approx 1.6$, see Figure S15, Supporting Information) could be obtained (**Figure 1**). Low molar masses ($2300 \leq M_n \leq 3200$ g mol^{-1}) were targeted to mimic the chemistry of small organic molecules and enable characterization. 2,2′-Azobis(2-methylpropionitrile) (AIBN) was used as commonly known thermal radical initiator in *N,N*-dimethylformamide (DMF) as solvent. The polymerizations were each conducted at $T = 80$ °C for different polymerization times. The different electron densities appeared to influence the reactivity of the monomers toward radical polymerization, depending on the respective monomer structure, and were adjusted accordingly (see Supporting Information for polymerization procedures). After polymerization, the polymers P1, P2, and P3 were purified by precipitation in cold diethyl ether yielding in colorless solids in all cases. The polymerizations were followed by ^{1}H NMR spectroscopy, showing the decrease of the respective vinyl protons (e.g., $\delta = 5.70$ ppm and $\delta = 5.15$ ppm) and arising signals, ascribed to the polymer, in the course of the polymerization. The sulfonamide functionalities were not affected by the polymerization itself and remained intact throughout the polymerizations (see Figures S16, S22, and S28, Supporting Information, respectively). Thermogravimetric analysis (TGA)

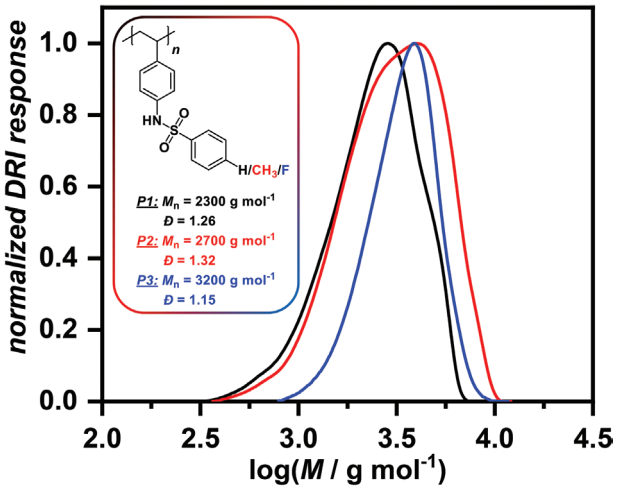

Figure 1. Comparison of SEC results (eluent: THF) for the prepared sulfonamide-based polymers P1, P2, and P3 with different electron densities, featuring low molar masses ($2300 \leq M_n \leq 3200$ g mol^{-1}) and low dispersity values ($1.15 \leq Đ \leq 1.47$).

exhibited a high thermal stability of the prepared polymers up to almost 400 °C (see Figures S20, S26, and S33, Supporting Information, respectively).

In the following, the prepared aromatic poly(*N*-(4-vinylphenyl)sulfonamide)s were employed in aza-Michael additions[25–27] with butyl acrylate as well as methyl acrylate and dodecyl acrylate as electron-deficient alkenes, using 1,5,7-triazabicyclo[4.4.0]dec-5-ene (TBD) as organic superbase catalyst[28] (Scheme 1B). We chose acrylate-based moieties for the PPM since the aza-Michael addition of the latter to the polymers would result in polymeric β-amino acid derivatives, which are—to the best of our knowledge—not known up to now, in three steps, counting the one-step synthesis of the respective monomer from commercially available compounds, its polymerization, and eventually the PPM, to deliver the desired polymers. The aza-Michael additions were conducted in DMF at elevated temperature ($T = 80$ °C) for 4 days under an inert argon atmosphere (**Table 1**). The resulting post-modified polymers were precipitated in cold diethyl ether in the case of butyl acrylate and methyl acrylate or cold methanol in case of dodecyl

Table 1. Details for the aza-Michael additions of different Michael acceptors to polymers P1–P3 with the respective SEC and DSC results before and after PPM. TBD was used as catalyst (0.50 eq. per repeating unit) in DMF at elevated temperatures ($T = 80$ °C) for 4 days.

Entry	Polymer used inPPM	Michael acceptor	Before PPM			After PPM		
			M_n[a)] [g mol^{-1}]	$Đ$[a)] (M_w/M_n)	T_g[b)] [°C]	M_n[a)] [g mol^{-1}]	$Đ$[a)] (M_w/M_n)	T_g[b)] [°C]
1	P1	Butyl acrylate	2300	1.26	120	3900	1.39	48
2	P1	Dodecyl acrylate	2300	1.47	120	7700	1.34[c)]	56
3	P2	Butyl acrylate	2700	1.32	125	4300	1.42	72
4	P2	Methyl acrylate	2700	1.32	125	3600	1.40	56
5	P3	Butyl acrylate	3200	1.15	123	6400	2.12[d)]	86 193

[a)]Determined by SEC using THF as eluent; [b)]Determined by DSC; [c)]Decrease of dispersity after functionalization could be explained by altered solubility behavior after reaction, causing problems of purification by precipitation; [d)]The functionalization of P3 led to tailing in the size-exclusion chromatogram, which was not observed for the other samples. The obtained product probably interacted with our SEC system, the only difference between the materials being a fluorine substituent in the case of P3.

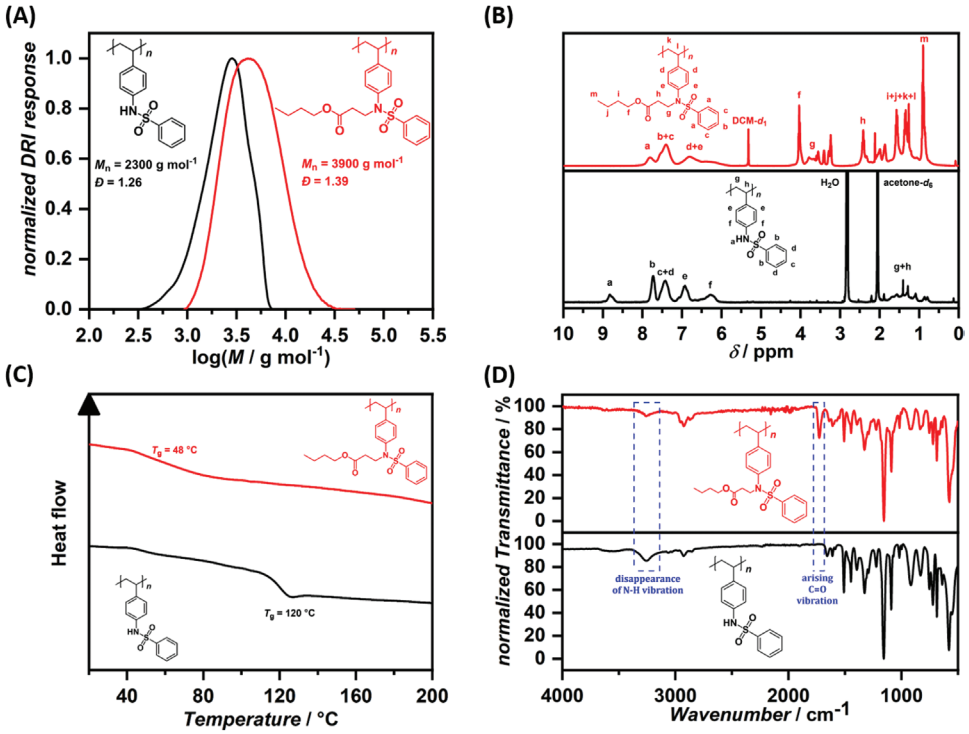

Figure 2. Comparison between poly(*N*-(4-vinylphenyl)benzenesulfonamide) P1 (black line) before PPM via aza-Michael addition using butyl acrylate as electron-deficient alkene with TBD as catalyst and its β-amino acid derivative counterpart poly(butyl 3-(*N*-(4-vinylphenyl)phenylsulfonamido)propanoate) (red line). A) The SEC trace is shifted after PPM toward higher molar masses with a slight increase of dispersity. B) Comparison of ^{1}H NMR spectra exhibits arising signals after PPM attributed to the formation of the aza-Michael adduct. C) Comparison of DSC results showing a drastic decrease of the glass transition temperature, T_g, from T_g = 120 °C before and T_g = 48 °C after PPM. D) IR spectroscopical analysis exhibits the disappearance of the N—H vibration after PPM accompanied by an arising C=O vibration.

acrylate and subjected to aqueous work up steps (see Supporting Information for PPM procedures). The successful PPM was followed by NMR and IR spectroscopy, as well as SEC and differential scanning calorimetry (DSC) measurements, exemplarily depicted for the aza-Michael addition of butyl acrylate to polymer P1 (**Figure 2**). The proton NMR spectrum of modified P1 exhibits the expected signals arising from the formation of a tertiary amine, especially the signals arising from the attached butyl acrylate; in this case the CH_2O motif attached to the carbonyl of the ester (δ = 3.94–4.10 ppm), the CH_2 group next to the nitrogen atom (δ = 3.48–3.90 ppm) as well as the adjacent CH_2 moiety (δ = 2.36–2.48 ppm) are clearly proving that the reaction was successful (Figure 2B). To confirm the chemical shifts of the new signals, a model reaction of a small molecule aza-Michael addition with a similar compound was conducted. Therefore, aniline instead of 4-vinylaniline was used for the synthesis of the respective sulfonamide. The procedure was adapted from the syntheses of monomers M1–M3. Subsequently, conditions analogous to the aza-Michael addition to the polymers P1–P3 were used for the aza-Michael addition on the small molecule level to our model compound *N*-phenylbenzenesulfonamide. The desired product was isolated and analyzed by NMR spectroscopy (see Figure S64, Supporting Information). The observed chemical signals and their shifts are in accordance with the proton NMR signals of the obtained product after aza-Michael addition of the polymers. Also, the comparison of the obtained IR spectra (Figure 2D) showed the appearance of a signal at $\tilde{\nu}$ = 1728 cm^{-1}, which is characteristic for the presence of a carbonyl group as it was the case after a successful reaction. In addition, the signal arising from the secondary amine functionality (N—H vibration at $\tilde{\nu}$ = 3256 cm^{-1}) disappeared almost completely after the reaction, confirming a successful addition of butyl acrylate to the secondary amine, turning the polymer into a protected β-amino acid derivative. Furthermore, the SEC traces were, as expected, clearly shifted toward higher molecular weights (before functionalization: M_n = 2300 g mol^{-1}; after functionalization: M_n = 3900 g mol^{-1}) (Figure 2A), indicating a successful PPM by aza-Michael addition and consequently the formation of a tertiary amine side group in the polymers. Moreover, the comparison of the DSC results (Figure 2C) of polymers before and after PPM revealed a decrease of the glass transition temperature (T_g) due to the formation of a bulkier repeating unit. The glass transition temperature of our polymer before functionalization was around T_g = 120 °C, which was higher than reported $T_g \approx$ 100 °C of polystyrene.[29,30] This is probably due to both intermolecular interactions of the secondary amine functionalities in the repeating units hindering the polymer chains from freely moving in contrast to pure polystyrene, in addition to the π–π stacking of the aromatic sulfonamide protecting groups. On the one hand, the PPM via aza-Michael addition with butyl acrylate drastically reduced the glass transition temperature

to a value of T_g = 48 °C. The shift of the glass transition temperature also indicated the successful functionalization and is in accordance to the expectation, presumably the bulky substituent drastically decreasing the amount of π–π stacking between the polymer chains, resulting in a free movement of the polymer chains at lower temperatures. On the other hand, introducing longer alkyl side chains on the polymer resulted in a glass transition temperature of T_g = 56 °C, which is in contradiction to the general rule implying that the T_g of the polymer backbone is decreasing with increasing alkyl chain lengths. In this case, however, the functionalization did not proceed quantitatively (only approximately half of the sulfonamide functionalities reacted with dodecyl acrylate according to ^{1}H NMR spectroscopy, presumably due to the long alkyl chain of the Michael acceptor); a full functionalization might have a more drastic influence on the glass transition temperature. A similar trend was also observed for polymer P2, when modified with methyl and butyl acrylate (compare Table 1, entries 3 and 4). However, besides the length, the shape or bulkiness of the side-group also has a predictable effect on the T_g of the polymers. Indeed, with the performed PPM, the density of pendent chain is increased. Accordingly, a stronger interaction among these bulkier side-groups could take place, which is further restricting the free rotation.

3. Conclusion

In summary, we report a novel class of sulfonamide-based polymers and their monomers in a straightforward fashion. A set of aromatic poly(*N*-(4-vinylphenyl)sulfonamide)s with varying electron densities was prepared by FRP of monomers derived from commercially available 4-vinylaniline and different aromatic sulfonyl chlorides, whereas alternative polymerization techniques such as reversible-deactivation radical polymerization could be potentially used as well. Subsequently, the inherent secondary amine functionalities of the prepared macromolecules were used as handle for PPM via aza-Michael addition with electron-deficient alkenes for the preparation of polymeric β-amino acids. Instead of using a monofunctional electron-deficient alkene, multifunctional ones could be used among others for cross-linking, the synthesis of hydrogels, and the preparation of SCNPs. Moreover, increased electrical conductivity in these polymers could be envisioned due to the conjugation between the nitrogen and sulfur atoms, and also the aromatic rings, thus we believe that this intriguing approach for polymer synthesis has potential for delivering specialty materials that could be used not only in the field of biomedicine but also for energy-related applications. Further, β-amino acids attract growing scientific attention due to their antibacterial and antifungal activities among others[31] and are used in the synthesis of β-peptides, featuring proteolytic stability both in vitro and in vivo.[32] Also, the herein presented sulfonamide-based polymers could potentially be implemented in the field of energy storage; different reports about sulfonamides, both on a small organic molecule level[33,34] and on a polymer level,[35] show interesting characteristics of materials involving sulfonamide moieties useful for battery applications. Moreover, a first qualitative study showed a pH-dependent, switchable water solubility of the prepared polymers in an analogous fashion to reported polymers based on sulfonamide functionalities,[20–23] hinting toward smart materials behavior of our novel class of sulfonamide-based polymers.

Supporting Information

Supporting Information is available from the Wiley Online Library or from the author.

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Conflict of Interest

The authors declare no conflict of interest.

Data Availability Statement

The data that supports the findings of this study are available in the supplementary material of this article.

Keywords

free radical polymerization, post-polymerization modification, sulfonamide-based polymers, β-amino acids

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