Post-Synthetic Functionalization of a Polysulfone Scaffold with Hydrazone-Linked Functionality

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The synthesis, characterization, and post-synthetic functionalization of a readily functionalized step-growth linear polymer derived from divinyl sulfone (DVS) and tert-butylcarbazate (TBC) is presented. Construction of this atom-economic polymer under thermal conditions proceeds in high yield (>94%) at 75°C, achieving a number average molecular weight of 17.0 kDa, a weight-average molecular weight of 26.2 kDa, and a polydispersity of 1.54, corresponding to a number-average degree of polymerization >60, despite the step growth nature of the reaction. Removal of the Boc-groups yields a polymeric scaffold with hydrazine moieties that are readily reacted with aldehydes to yield the corresponding functional polyhydrazone materials. A variety of hydrazone-linked functionalities are readily added under mild conditions, including cationic, anionic, electron-rich/poor, and hetereoatom-containing aromatics. Owing to its rapid functionalization and simple and scalable synthesis, this material is an accomodating and generalized polymer scaffold that is rapidly tailored to a variety of applications with easily introduced functionality.

Introduction

The polymerization of functionalized monomers is the most direct route toward a polymer with desired side-chain functionality.[1,2] However, incompatibility of the ultimate side-chain functionality — ranging from insolubility of the side-chain functionality in the polymerization solvent to cross-reactivity of the side-chain functionality with monomer end-groups and/or polymerization catalysts — often renders the direct route untenable.[3] Though recent advances in controlled radical polymerization[4–7] have greatly facilitated the terminal incorporation of a wide variety of functional groups while enabling exquisite control over polymer molecular weight, composition, and architecture, incompatibilities still exist between potential side-functionality and these state-of-the-art polymerization techniques. For this reason, there is a need to expand the toolbox of novel post-synthetic approaches, in which a monomer with a chemically orthogonal handle (or suitably protected functionality) is polymerized, and in a separate step, the side-chain functionality is installed via conjugation to the chemical handle.[1,3] This approach demands exceptionally high-yielding reactions for the initial polymerization and for post-synthetic modification in order to saturate all potential functionalization sites.[8]

Click chemistry approaches are popular for decorating pre-formed polymer backbones,[9] and cycloaddition reactions are often utilized, including the three common types of azide-alkyne couplings (Cu-catalysed, thermal, or strain-promoted),[8] as well as normal and inverse electron-demand Diels-Alder reactions.[11,12] Though these are atom-economic and largely orthogonal chemical transformations, challenges to all of these approaches exist. The Cu-catalysed azide/alkyne coupling benefits from the large number of easily prepared and commercially available alkyne and azide derivatives; however, the polymer and side chain functionality must be compatible with Cu-catalysis, the Cu-catalyst must typically be removed in a separate step after the reaction, and this approach eliminates the inclusion of potential chelating functionality. In normal and inverse Diels-Alder reactions, only a limited number of appropriate diene/dieneophile partners are readily prepared or available. This problem is even more pronounced for strain-promoted post-synthetic modifications.[13]

Several non-pericyclic reactions have also been used to post-synthetically modify polymers with varying degrees of success, including thiol-ene/yne reactions[14,7,15] or ester modifications.[16] Thiol-ene/yne reactions are frequently complicated by oxidative inactivation of the thiol component, while post-synthetic ester modifications often suffer from low yields, which results in polymer heterogeneity arising from incomplete saturation of the functional sites.

In contrast to these chemistries, stable imine formation — for example, oxime or hydrazone formation, arising from the reaction of alkoxyamines or hydrazines, respectively, with aldehydes/ketones — proceeds without catalysts and benefits from a wide breadth of compatible and available functionalities.[17–20] Moreover, polymers with alkoxyamine or

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aldehyde side- or end-chain functionalities are readily available. For instance, pthalimides, which act as masked alkoxyamines, are compatible with RAFT polymerization,[21] while ATRP polymerization with an alkoxyamine-functionalized initiator efficiently yields alkoxyamine-terminated polymers.[22] Subsequent coupling between the polymer alkoxyamine/hydrazine and the functionalized aldehyde is performed at room temperature, even in aqueous environments.

In polymer chemistry, oximes are typically preferred over hydrazone-linked functionality, owing to their higher hydrolytic stability.[21,23] Hydrazones, depending on their functionality, have reported half-lives in aqueous environments on the order of minutes to days, while oximes are stable for almost a month at room temperature at pH 7.[24] However, this feature opens up the intriguing possibility of using the dynamic nature of the hydrazone bond to evolve a polymer that can bind a target template. Fulton and co-workers used precisely this strategy to show that a RAFT co-polymer with displayed aldehyde functionalities acts as a polymer scaffold for exchanging acylhydrazines.[25] This material self-assembles into polymers that bind either bovine serum albumin or poly(sodium-4-styrene sulfonate). Ghadiri and co-workers used a polypeptide scaffold with thioester groups linking the four native nucleobases and showed that a distinct DNA sequence could direct the assembly of a complementary sequence of the synthetic thioester system.[29]

Here, we introduce a new polymer that merges a polysulfone scaffold with the rapid post-synthetic functionalization afforded by hydrazone chemistry. As a result, a single polymer backbone is rapidly elaborated into a set of diverse polymers, including chromophoric, water-soluble, or heterocycle-containing, depending on the subsequently introduced functionality. Two inexpensive commercially available materials — divinyl sulfone and tert-butylcarbazate — react efficiently to create a step-growth polymer with alternating Boc-protected hydrazine and sulfone groups. Subsequent removal of the Boc groups unveils the reactive hydrazines, which are readily elaborated with a variety of aryl aldehydes to yield polyhydrazone materials in good to excellent yields. This approach is a rare example of a polymer amenable to post-synthetic processing in which the main-chain functionality is also involved in coupling the side-chain functionality.

Experimental

Materials

Unless otherwise noted, all chemicals and solvents were of analytical grade and used as received from commercial sources. Divinyl sulfone (97%, 0.05% hydroquinone) and *tert*-butylcarbazate (98%) were used as received. Water (dd-H_2O) used in biological procedures or as a reaction solvent was deionized using Milli-Q Advantage A-10 water purification system (MilliPore, USA). Centrifugations were carried out in an X-22R benchtop centrifuge (Beckman Coulter, USA). Divinyl sulfone (DVS) was acquired from Matrix Scientific (Columbia, SC). Gel permeation chromatography was carried out with a TOSOH ECO SEC HLC-8320GPC equipped with two polystyrene columns and UV and refractive index detectors operating at 50 °C with DMSO as the eluent. Molecular weight data were calibrated using poly(methyl methacrylate) standards.

Synthesis

Polymer (1) (10 mmol scale): A 20 mL scintillation vial was charged with a stirbar, DVS (1.00 mL, 10 mmol), DMSO (2.7 mL), and TBC (1.32 g, 10 mmol) and heated at 75 °C for 120 h with stirring. The resulting viscous solution was added dropwise to a 50 mL conical tube containing H_2O (40 mL) to precipitate the polymer as a white solid. Centrifugation for 10 minutes at room temperature provided a white pellet. The aqueous phase was removed, and the resulting pellet was washed with H_2O (2 × 20 mL), with centrifugation after each washing. The polymer was lyophilized, which delivered **1** as a bench-stable, free-flowing, white solid (2.36 g, 94%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.19 (s, 1H), 3.28 (t, *J* = 7.0 Hz, 4H), 3.15 (t, *J* = 7.2 Hz, 4H), 1.40 (s, 9H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 155.46, 79.40, 50.84, 49.99, 28.58. M_n: 17000; D: 1.54. IR(KBr) ν_{max} cm^{-1} 3180 (NH), 1710 (CO), 1500 (*trans* NH), 1460 (*cis* NH), 1290 and 1150 (SO_2), 1250 (CN, carbamate).

Polymer (1) (85 mmol scale): A flask was charged with a stirbar, DVS (10.00 g, 85 mmol), DMSO (23 mL), and TBC (11.2 g, 85 mmol) and heated at 75 °C for 120 h with stirring. The resulting viscous solution was added dropwise to a flask containing 2 L of H_2O, and the precipitate was filtered off. The precipitate was washed with H_2O (2 × 100 mL), acetone (2 × 100 mL), and hexanes (1 × 100 mL) and dried under vacuum to yield **1** as a bench-stable, free-flowing, white solid (18.6 g, 88%; M_n: 15,400; D: 1.49.)

Polymer (2): A 20 mL scintillation vial was charged with a stirbar, **1** (200 mg), CH_2Cl_2 (2 mL), and TFA (2 mL), and the reaction was stirred at room temperature for 90 minutes. The volatiles were removed under rotary evaporation, and the residue was evaporated with hexanes (2 mL). This process was repeated twice more to yield a **2** as a flaky, off-white solid after drying under vacuum overnight (193 mg, 92%). The material was used within 24 of deprotection. ^{13}C NMR (101 MHz, DMSO-d_6) δ 159.36 (q, *J* = 34.9 Hz), 116.55 (q, *J* = 293.5 Hz), 49.83, 48.62. IR($CDCl_3$) ν_{max} cm^{-1} 3450 (NH_3^+), 1770 (CO of TFA acid), 1670 and 1430 (CO of TFA salt), 1300 and 1170 (SO_2).

Polymer (3). A 1.5 mL Eppendorf tube was charged with **2** (26.4 mg), DMSO (0.5 mL), and benzaldehyde (20 μL, 0.2 mmol, 2 eq. / monomer), and the reaction was allowed to proceed at room temperature for 24 h, at which point the polymer was precipitated with the addition of water (0.5 mL). The resulting pellet was resuspended in ethanol (1 mL), sonicated for 30 s, and centrifuged to remove excess aldehyde. This process was repeated twice more, and the pellet was dried overnight under vacuum to yield **3** as a flaky white solid (20.5 mg, 86%). ^{1}H NMR

(400 MHz, DMSO-d_6) δ 7.54 – 7.47 (m, 2H), 7.43 (s, 1H), 7.28 (t, *J* = 7.8 Hz, 2H), 7.25 – 7.18 (m, 1H), 3.74 (t, *J* = 6.7 Hz, 4H), 3.52 (d, *J* = 6.6 Hz, 4H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 136.52, 134.12, 128.86, 128.11, 126.11, 49.96, 46.47. M_n: 16850; D: 1.40

Polymer (4). A 1.5 mL Eppendorf tube was charged with **2** (26.8 mg), DMSO (0.5 mL), and 4-chlorobenzaldehyde (29 mg, 0.2 mmol, 2 eq. / monomer), and the reaction was allowed to proceed at room temperature for 24 h, at which point the polymer was precipitated with the addition of water (0.5 mL). The resulting pellet was resuspended in ethanol (1 mL), sonicated for 30 s, and centrifuged to remove excess aldehyde. This process was repeated twice more. The pellet was dried overnight under vacuum to furnish **4** as a flaky white solid (21.2 mg, 77%).^{1}H NMR (400 MHz, DMSO-d_6) δ 7.51 – 7.45 (m, 2H), 7.39 (s, 1H), 7.30 (d, *J* = 8.6 Hz, 2H), 3.75 (t, *J* = 6.9 Hz, 4H), 3.58 – 3.48 (m, 4H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 142.02, 130.18, 127.87, 126.63, 125.73, 49.97, 46.49. M_n: 19650; D: 1.44.

Polymer (5). A 1.5 mL Eppendorf tube was charged with **2** (26.4 mg), DMSO (0.5 mL), and N,N-dimethylaminobenzaldehyde (29.8 mg, 0.2 mmol, 2 eq. / monomer), and the reaction was allowed to proceed at room temperature for 24 h. The reaction turned a wine red color. The reaction mixture was lyophilized overnight, and the resulting red pellet was washed with ethanol (5 × 0.5 mL) to remove excess aldehyde. Drying *in vacuo* provided **5** as a dark red solid (23.9 mg, 85%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.45 (s, 1H), 7.37 (d, *J* = 8.6 Hz, 2H), 6.67 (d, *J* = 8.2 Hz, 2H), 3.71 – 3.54 (m, 4H), 3.49 – 3.39 (m, 4H), 2.89 (s, 6H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 137.81, 129.36, 128.67, 127.64, 125.78, 50.04, 46.87, 21.52. M_n: 14300; D: 1.59

Polymer (6). A 1.5 mL Eppendorf tube was charged with **2** (26.4 mg), DMSO (0.5 mL), and 4-carboxybenzaldehyde (29.8 mg, 0.2 mmol, 2 eq. / monomer), and the reaction was allowed to proceed at room temperature for 24 h. The reaction mixture was lyophilized overnight, and the resulting pellet was sonicated with MeCN:EtOH (1:1, 1 mL) to remove excess aldehyde and centrifuged. This process was repeated another four times. Drying *in vacuo* gave **6** as a white solid (28.0 mg, 99%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.86 (s, 1H), 7.85 (d, *J* = 8.3 Hz, 1H), 7.57 (d, *J* = 8.2 Hz, 1H), 7.43 (s, 1H), 3.87 – 3.77 (m, 4H), 3.56 (t, *J* = 6.7 Hz, 4H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 167.58, 140.81, 131.86, 130.02, 129.57, 125.76, 49.98, 46.46. M_n: 16890; D: 1.45

Polymer (7). A 1.5 mL Eppendorf tube was charged with **2** (26.3 mg), DMSO (0.5 mL), and methyl 4-formylbenzoate (31 mg, 0.19 mmol), and the reaction was allowed to proceed at room temperature for 24 h, at which point the polymer was precipitated by water. The resulting pellet was resuspended in ethanol (1 mL), sonicated for 30 s, and centrifuged. This process was repeated four more times to furnish **7** as a white solid (18.8 mg, 67%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.80 (d, *J* = 8.4 Hz, 2H), 7.54 (d, *J* = 8.4 Hz, 2H), 7.40 (s, 1H), 3.81 (s, 7H), 3.54 (t, *J* = 7.0 Hz, 4H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 166.41, 141.14, 131.59, 129.79, 128.26, 125.78, 52.42, 50.01, 46.51. M_n: 20220; D: 1.48

Polymer (8). A 1.5 mL Eppendorf tube was charged with **2** (24.2 mg), DMSO (0.5 mL), and 4-hydroxybenzaldehyde (29.8 mg, 0.2 mmol, 2 eq. / monomer), and the reaction was allowed to proceed at room temperature for 24 h. The reaction mixture was lyophilized overnight, and the resulting pellet was sonicated with MeCN:EtOH (1:1, 1 mL) and centrifuged. This process was repeated another four times. Drying *in vacuo* gave **8** as a white solid (12.8 mg, 55%)**.** ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.57 (s, 1H), 7.40 (s, 1H), 7.35 (d, *J* = 8.0 Hz, 2H), 6.71 d, *J* = 8.0 Hz, 2H), 3.64 (m, 4H), 3.46 (m, 4H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 158.02, 136.17, 127.78, 127.61, 115.77, 49.96, 46.57. M_n: 18920; D: 2.37

Polymer (9). A 1.5 mL Eppendorf tube was charged with **2** (26.9 mg), DMSO (0.5 mL), and 4-nitrobenzaldehyde (31 mg, 0.2 mmol, 2 eq. / monomer), and the reaction was allowed to proceed at room temperature for 24 h. The reaction turned a bright lemon yellow. The reaction was lyophilized overnight, and CH_2Cl_2 (0.5 mL) was added to the yellow pellet. After sonicating for 5 minutes, the sample was briefly centrifuged, and the CH_2Cl_2 was removed. This process was repeated four more times to yield **9** (21.2 mg, 75%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.06 (d, *J* = 8.6 Hz, 2H), 7.62 (t, *J* = 8.3 Hz, 2H), 7.41 (s, 1H), 3.86 (t, *J* = 6.9 Hz, 4H), 3.57 (t, *J* = 6.7 Hz, 4H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 146.04, 143.24, 129.88, 126.15, 124.23, 50.06, 46.66. M_n: 18550; D: 1.32

Polymer (10). A 1.5 mL Eppendorf tube was charged with **2** (26.6 mg), DMSO (0.5 mL), and 2,4-dinitrobenzaldehyde (39.4, 0.20 mmol, 2 eq. / monomer), and the reaction was allowed to proceed at room temperature for 24 h. The reaction was then lyophilized overnight to remove the DMSO, and the resulting pellet was sonicated with acetone, centrifuged, and the supernatant was removed. This process was repeated four more times. Drying *in vacuo* provided **10** as an off-white solid (21.4 mg, 68%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.53 (d, *J* = 3.2 Hz, 2H), 8.22 (dd, *J* = 8 Hz, 2.2 Hz, 1H), 8.07 (d, *J* = 4 Hz, 1H), 3.97 (s, 4H), 3.58 (s, 4H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 145.47, 144.99, 136.32, 128.09, 127.05, 123.92, 120.95, 49.89, 47.01. M_n: 16,500; D: 1.46

Polymer (11): A 1.5 mL Eppendorf tube was charged with **2** (26.8 mg), DMSO (0.5 mL), and 2-thiophenecarboxaldehyde (19 μL, 0.2 mmol, 2 eq. / monomer), and the reaction was allowed to proceed at room temperature for 24 h. Water (0.5 mL) was added to the solution to precipitate the polymer. After centrifugation, the resulting pellet was resuspended in ethanol (1 mL), sonicated for 30 s, and centrifuged to remove excess aldehyde. This process was repeated twice more, and the pellet was dried overnight under vacuum to provide **11** as a light yellow solid (19.0 mg, 77%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.67 (s, 1H), 7.34 (dd, *J* = 5.2, 1.3 Hz, 1H), 7.08 (dd, *J* = 3.7, 1.2 Hz, 1H), 7.00 (dd, *J* = 5.1, 3.5 Hz, 1H), 3.70 (d, *J* = 7.6 Hz, 4H), 3.51 – 3.44 (m, 4H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 142.02, 130.18, 127.87, 126.63, 125.73, 49.97, 46.49. M_n: 10940; D: 1.51.

Polymer (12): A 1.5 mL Eppendorf tube was charged with **2** (28.0 mg), DMSO (0.5 mL), and 4-pyridinecarboxaldehyde (20.0 μL, 0.21 mmol, 2 eq. / monomer), and the reaction was allowed to proceed at room temperature for 24 h. The reaction was then lyophilized overnight to remove the DMSO, and the resulting pellet was sonicated with toluene (0.5 mL), centrifuged, and the supernatant was removed. This process was repeated four more times. Drying *in vacuo* provided **12** as an off-white solid (23.1 mg, 91%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.51 – 8.37 (m, 2H), 7.46 – 7.35 (m, 2H), 7.30 (s, 1H), 3.83 (t, J = 6.6 Hz, 4H), 3.56 (t, J = 6.9 Hz, 4H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 150.16, 143.68, 129.63, 120.07, 49.94, 46.50. M_n: 21700; D: 1.90.

Results and discussion

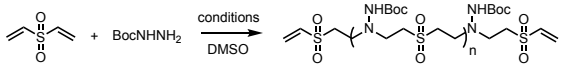
Polymerization optimization

Initial results revealed that polymerization between divinyl sulfone (DVS) and *tert*-butylcarbazate (TBC) in DMSO was slow at room temperature, taking more than a month to deliver a polymer with more than 15 repeat units, even at 2.0 M DVS and TBC. When the temperature was fixed at 65 °C and the concentration of monomers was screened at 0.25 M, 0.5 M, and 1.0 M for 24 h, the reactions at 0.25 M and 0.5 M did not provide isolable polymers after aqueous precipitation, while the reaction at 1.0 M showed the major product had a number average molecular weight (M_n) of 3.8 kDa, a weight-average molecular weight (M_w) of 6.0 kDa, and an associated dispersity (D) of 1.58 after precipitating the polymer and drying.

A survey of catalysts revealed that neither phosphines nor bases increased the polymerization kinetics while preserving polymer quality over that of a pure thermal process. In a series of reactions with a constant monomer concentration (1.0 M), temperature (65 °C), and time (24 h), a bicyclic amine base ((1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) gave dark brown reaction mixtures in 60 minutes and no observable polymer after 24 h. Even at low catalyst loading (1 mol% DBU), the additive inhibited the polymerization rather than promoting it. Triethylamine-catalysed polymerizations provided polymeric material (M_n = 2 kDa, M_w = 2.8 kDa, D = 1.40), albeit at a lower M_n than in an identical reaction in the absence of TEA (M_n = 3.8 kDa, M_w = 6.0 kDa, D = 1.58). Attempts to catalyze the reaction with either 10 mol% or 1 mol% triphenylphosphine did not improve the polymerization performance above that achieved under the control conditions. Finally, a catalyst with a pendant base (4-dimethylaminopyridine (DMAP)), which could potentially combine nucleophilic catalysis via its pyridine group while also acting as a base via its dimethylamino group, neither improved the degree of polymerization nor the polymerization kinetics.

Scanning a range of temperatures (25, 50, 75, and 100 °C) revealed that 75 °C was an ideal temperature that optimized the yield and maximized the molecular weight (Figure 1). Clean molecular weight evolution over five days occurred in all of these conditions, with the reaction at 100 °C as the exception (SI Figure 1). Though initially promising, the reaction at 100 °C led to material decomposition with extended heating. Heating a prepared sample of polymer at 100 °C confirmed this result and showed non-specific degradation by ^{1}H NMR (SI Figure 2). Thus, a purely thermal process (75°C for 5 d at 2.0 M monomer concentration in DMSO) provided the best polymerization conditions, and this procedure was used to synthesize the material on 10 mmol and 85 mmol scales in 94% and 88% yields, respectively. The polymer can be isolated by aqueous precipitation; washing with acetone and hexanes removes low molecular-weight impurities, making production and isolation of the polymer an operationally simple and inexpensive process (SI Figure 3). GPC revealed an M_n of 17.0 kDa corresponding to number average degree of polymerization (DP_n) > 60, a M_w of 26.2 kDa, and D of 1.54 on the 10 mmol scale. For a step growth polymerization of difunctional monomers, this number average molecular weight corresponds to a functional group conversion of greater than 98%, assuming ideal stoichiometry and molecular weight evolution.

Table 1. Optimization of synthetic conditions.



Entry[a]	Conc / [M]	Catalyst[b]	Temp / ˚C	M_n (g mol^{-1})[c] (D)[d]
1	0.25	-	65	No polymer
2	0.50	-	65	No polymer
3	1.0	-	65	3,800 (1.58)
4	1.0	mTBD (10%)	65	No polymer
5	1.0	DBU (10%)	65	No polymer
6	1.0	TEA (25%)	65	2,000 (1.40)
7	1.0	TEA (10%)	65	1,800 (1.35)
8	1.0	PPh_3 (10%)	65	No polymer
9	1.0	PPh_3 (1%)	65	2,800 (1.29)
10	1.0	DMAP (1%)	65	910 (1.2)
11	1.0	DMAP (10%)	65	460 (1.1)
12	2.0	-	25[e]	870 (1.39)
13	2.0	-	50[e]	5,000 (1.39)
14	**2.0**	**-**	**75[e]**	**17,000 (1.54)**

[a] Reactions were carried out in DMSO-d_6 (500 μL) for 24 h at the indicated concentration. [b] Catalysts loaded by mol %. [c] Number average molecular weight was determined by GPC after precipitating the polymer in water and drying. [d] Dispersity (D) was determined by GPC against a PMMA standard. [e] Reactions were carried out for 5 days.

Polymerization mechanism

The polymerization behaviour is consistent with a step-growth mechanism. As the conversion increases, the polymer peak shifts to higher molecular weights (Figure 1A; SI Figures 4, 5). Moreover, lower monomer concentrations decrease the overall polymer molecular weight and contribute to increased intramolecular cyclization, which not only terminates the polymerization, but also decreases the reservoir of available monomer. Cyclization products are observed by GPC (SI Figure 6). The molecular species at 18.5 min, 17.5 min, and 17.2 min correlate to cyclized dimers, 6-mers, and 8-mers, respectively. Performing the polymerization at reduced concentrations at 75

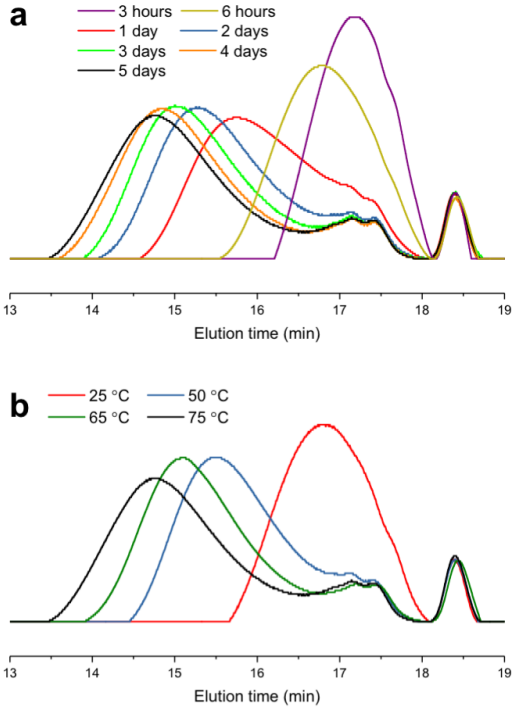


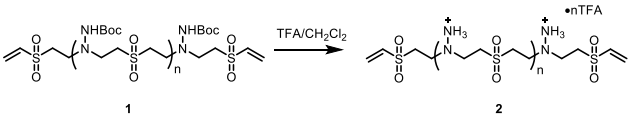
Figure 1. GPC traces of polymer evolution as a function of time and temperature. A) Time-course evolution of polymer **1** at 75 °C arising from the reaction of 2.0 M DVS and 2.0 M TBC in DMSO. B) GPC traces of polymers arising from the reaction of 2.0 M DVS and 2.0 M TBC in DMSO after 5 d at the indicated temperature. ^{1}H NMR end-group analysis provides M_n estimates at 25, 50, 65, and 75°C of 1.1, 5.5, 9.3, and 17.3 kDa, respectively.

°C leads to more cyclized species; only low molecular weight species persist at concentrations ≤ 0.1 M. Although the formation of the cyclized products is expected due to the high effective concentration of the secondary hydrazine/vinyl sulfone intermediates, this side reaction is effectively suppressed at high monomer concentrations. While the exact mechanistic rationale for this observation is unclear, the resistance to cyclization seems to be a consequence of the TBC nucleophile. For instance, attempts to polymerize allyl amine and DVS gave exclusively short oligomeric cycles as indicated by GPC, even with dropwise addition of the allyl amine at low temperature, which should bias the reaction toward polymerization (SI Figure 7).

Because of the ideal step-growth nature of the reaction, the DP_n predicted by the conversion of the vinyl sulfone functionality corresponds well with M_n values calculated from the GPC traces. Additionally, the average number of repeats in the polymer chain is predictably altered by changing the stoichiometry of the reaction. These reaction conditions also suppress cyclization by biasing the reaction toward intermolecular aza-Michael reactions (SI Figure 8). This strategy results in the majority of chains terminated with terminal vinyl sulfones, which provides a useful functionality to elaborate this scaffold to more sophisticated polymers tailored toward precise applications.

Scope of Reaction

Having established a simple, atom-efficient, cost-effective, and scalable approach for producing the poly[sulfone-alt-(Boc-hydrazinyl)] polymer, standard Boc deprotection conditions were used to globally remove the Boc groups and unveil the pendant hydrazine moieties (Scheme 1). ^{1}H NMR analysis

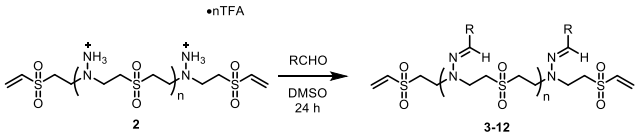


Scheme 1. Conversion to polyhydrazine **2**.

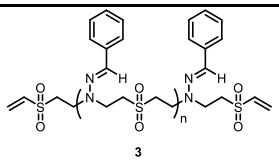
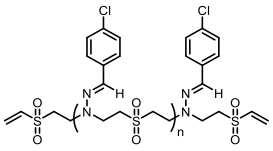
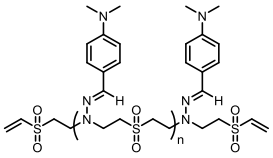
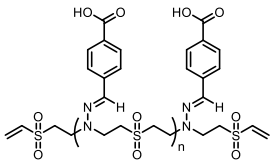
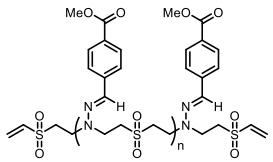
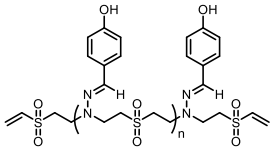
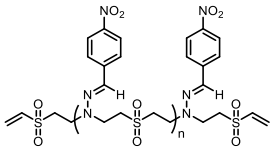
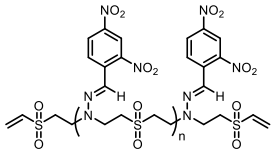
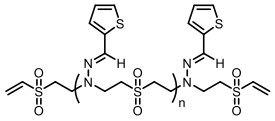
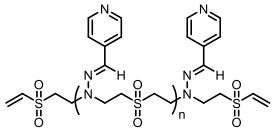
revealed complete removal of the Boc groups, and the resulting poly[sulfone-*alt*-(hydrazine)] polymer (**2**) was isolated as its corresponding trifluoroacetate salt in excellent yield (92%) as a brittle white foam.

Hydrazines are especially useful functional groups: they react rapidly in organic solvents, including polar protic (e.g., EtOH) or polar aprotic (e.g., DMSO) or in aqueous conditions with aldehydes and ketones to yield hydrazones, chemical bonds that form an important cornerstone in the field of dynamic covalent chemistry.[30] Polymer **2** was easily elaborated with a variety of side-chain functionality. Reaction of the polymer in its TFA salt form with a variety of aryl aldehydes in DMSO proceeds cleanly to yield a heavily decorated backbone. Owing to the coordinated trifluoroacetic acid, no additional acid catalyst is required when the reaction is carried out in DMSO. A wide range of functional groups are well-tolerated, including aromatic, cationic, halogenated, amino, anionic, ester, phenolic, and nitro functionalities (Table 2, entries 1-8). Heteroatom containing aromatics such as pyridine and thiophene are also readily incorporated (Table 2, entries 9, 10). The polymers are isolated by removing the solvent under reduced pressure and washing the resulting pellet to deliver the functionalized polymer in moderate to excellent yields.

Table 2. Polyhydrazone materials derived from **2**.



2 3-12

Entry[a]	Polymer	Yield	M_n (g mol $^{-1}$) (D)
1	 3	86%	16850 (1.40)
2	 4	77%	19650 (1.44)
3	 5	85%	14300 (1.59)
4	 6	99%	16890 (1.45)
5	 7	67%	20220 (1.48)
6	 8	55%	18920 (2.37)
7	 9	75%	18550 (1.32)
8	 10	68%	16500 (1.46)
9	 11	77%	10940 (1.51)
10	 12	91%	21700 (1.90)

Conclusions

To close, an operationally simple synthesis of a step-growth polymer that is readily elaborated to unique polymer products by virtue of the embedded hydrazine functionality is reported. Two inexpensive commercially available building blocks react in the absence of catalysts or additives to efficiently form a step-growth polymer with more than 60 repeat units, each of which is easily elaborated under mild conditions to include a variety of functionalities. Experiments interrogating the ability to exchange polymer-linked hydrazones revealed that the materials were remarkably recalcitrant to hydrolysis and exchange. A survey of acidic hydrolysis conditions (TFA/$CDCl_3$; $Sc(OTf)_3/CDCl_3$; refluxing 1 N HCl) and analysis by ^1H NMR showed that neither hydrolysis nor hydrazine exchange occurred. This behaviour appears not to be a consequence of the hydrazone linkage to the polymer, but rather, a result of the poor solubility of most of the aryl-linked polyhydrazones in any solvent except DMSO. Current studies are focused on identifying catalysts that enable access to the dynamic nature of the hydrazone, and ultimately, employing this material in templated dynamic assembly systems.

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Conflicts of interest

There are no conflicts to declare.

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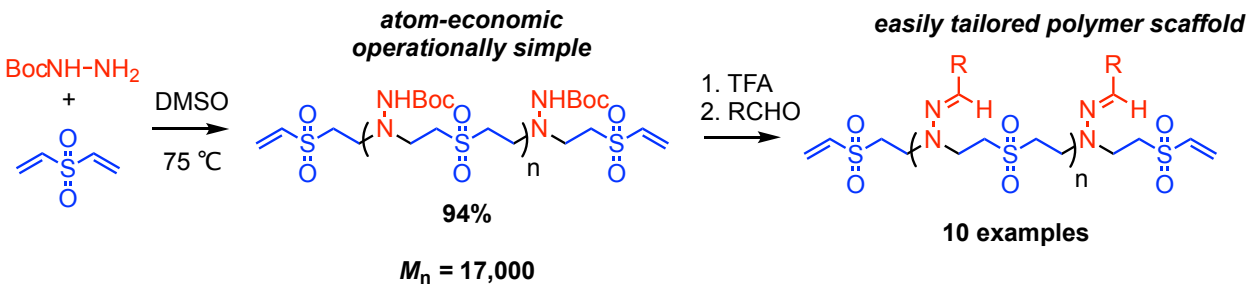

94%

M_n = 17,000

10 examples