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Synthesis of Side-Chain Functional Polyesters via Baylis−Hillman Polymerization

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Supporting Information

ABSTRACT: Strategies that allow access to side-chain functional polyesters are valuable as they would enable to engineer the properties of these hydrolytically degradable materials. This contribution explores the feasibility of a novel approach toward side-chain functional polyesters that is based on the Baylis−Hillman reaction, which involves the base-catalyzed condensation of an aldehyde and an acrylate building block to produce an α-methylene-β-hydroxycarbonyl compound. Using 1,3-butanediol acrylate and 2,6-pyridinecarboxaldehyde as monomers and DABCO as catalyst, polymers with a degree of polymerization of up to 25 could be prepared. These polymers are attractive as they contain chemically orthogonal side-chain hydroxyl and vinyl groups that can be further modified. In the first experiments, it was demonstrated that the side-chain hydroxyl and vinyl groups can be quantitatively postmodified with phenyl isocyanate and methyl-3-mercaptopropionate, respectively. As the Baylis−Hillman polymerization does not require the use of side-chain protected monomers, this route may represent an interesting alternative strategy for the preparation of side-chain functional polyesters.

INTRODUCTION

Aliphatic polyesters such as polyglycolide, polylactide, polycaprolactone, and their copolymers are attractive materials, which have received widespread interest for applications that require hydrolytically degradable materials. To tune the properties of these materials, e.g., their degradation behavior and to add further functionality, there is significant interest in synthetic strategies than can be used to prepare side-chain functionalized polyesters.[1]

The side-chain functionalized polyesters that have been prepared until now have either been obtained by ring-opening polymerization of functionalized lactones[2−5] or via step polymerization of appropriate side-chain protected diacid or diol building blocks.[6−8] Although these strategies have been successfully used, both of them rely on monomers that are only accessible via multistep synthesis and also require a final reaction step to deprotect the side-chain functional groups, which bears the possible risks of main chain degradation and incomplete deprotection.

In this contribution, we report an alternative approach for the synthesis of side-chain functional polyesters, which is based on the Baylis−Hillman polymerization of bifunctional acrylates and bifunctional dialdehydes (Scheme 1). The Baylis−Hillman reaction involves the base catalyzed reaction of α,β-unsaturated carbonyl compounds with aldehydes to form α-methylene-β-hydroxycarbonyl compounds.[9−11] This reaction has attracted interest in organic synthesis as it is an atom-economical carbon−carbon bond forming reaction that can be carried out with control over stereochemistry and generates a polyfunctional scaffold that can be converted in a variety of other products.

Scheme 1

For polymer synthesis, in contrast, the Baylis−Hillman reaction is largely unexplored. Apart from a preprint by Venkitasubramanian et al., who described the polymerization of 5-hydroxymethylfurfural acrylate,[12,13] no systematic and in-depth studies have been reported to the best of our knowledge that investigate the feasibility of this reaction for the synthesis of functional polyesters.

The Baylis−Hillman reaction, however, has a number of characteristics that make it an interesting candidate for the synthesis of side-chain functional polyesters (Scheme 1): (i) since the side-chain functional groups are generated during the C−C bond forming process, Baylis−Hillman polymerization does not necessitate the use of side-chain protected monomers; (ii) the Baylis−Hillman reaction produces two chemically orthogonal side-chain functional groups, viz. a vinyl group and a hydroxyl group, which can be further modified via appropriate postpolymerization modification.[14] This contribution investigates the feasibility of the Baylis−Hillman polymerization of diacrylates and dialdehydes to prepare side-chain functional polyesters and

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Table 1. Overview of Reaction Conditions Evaluated for the Baylis−Hillman Polymerization of 1 and 2 as Well as GPC Number-Average and Weight-Average Molecular Weights and Number-Average Degrees of Polymerization (DP_n) of the Resulting Polymers (Monomer Concentration: 5 mol/L)

procedure	catalyst	reaction time (h)	M_n[a] (g/mol)	M_w[a] (g/mol)	M_w/M_n[a]	DP_n[a]
1	DABCO	3	1900	3100	1.6	11
1	DABCO	6	3100	5600	1.8	19
1	DABCO	24	4200	9050	2.1	25
1	DABCO	48	3800	8000	2.0	23
1	DABCO	72	3900	8100	2.1	23
2	3-HQD	3	2700	5100	1.9	16
2	3-HQD	6	3000	5900	1.9	18
2	3-HQD	24	2500	5200	2	15
2	3-HQD	48	2100	3700	1.8	6
2	3-HQD	72	1800	3600	2	11
3	DBU	24	630	800	1.3	4
4	DMAP	24	1400	2700	1.9	8
5	PPh_3	24	1300	2300	1.8	4
6	DABCO/$La(OTf)_3$	24	1800	3000	1.6	11
7	DABCO	24	1500	2000	1.3	9

[a] Number-average (M_n) and weight-average (M_w) molecular weight, polydispersity (M_w/M_n), and number-average degree of polymerization (DP_n) determined from GPC (THF, conventional calibration, polystyrene standards).

explores the subsequent postpolymerization modification of these polymers to further enhance their functionality. The present study consists of three parts, which subsequently focus on identifying the most optimal polymerization conditions and the characterization of the synthesized polymers as well as their postpolymerization modification to generate multifunctional side-chain polyesters.

EXPERIMENTAL SECTION

Materials. All reagents and solvents were of commercial grade and used as received. 2,6-Pyridinedimethanol was obtained from Acros. All other chemicals and reagents were acquired from Sigma-Aldrich (Buchs, Switzerland). Deuterated solvents for NMR spectroscopy were acquired from Armar Chemicals (Döttigen, Switzerland).

Analytical Methods. Gel permeation chromatography (GPC) analysis in THF was performed on a Waters 150CV instrument equipped with RI and variable wavelength UV detection. Two Styragel HR-2 and HR-3 columns connected in series were used for the separation. The interdetector volumes were calibrated with Irganox 1015, an antioxidant from BASF SE with a molecular weight of 1177 g/mol. For each analysis, 0.05 mL of a 5 mg/mL sample solution was injected. Molecular weights were determined using a conventional calibration curve, which was created with narrow polydispersity polystyrene standards. GPC analysis in DMF was carried out on a Waters Alliance GPCV 2000 system equipped with refractive index, differential viscometer, and light scattering detectors. Separation was carried out at 60 °C with TSK-Gel Alpha 2500 + 3000 + 4000 columns, using vacuum-distilled HPLC grade DMF + 0.5 g/L LiCl as eluent and a flow rate of 0.6 mL/min. Molecular weights were determined using a universal calibration curve, which was created with narrow polydispersity poly(methyl methacrylate) (PMMA) standards. Results were calculated with the Empower Pro multidetection GPC software (Ver 5.00). The interdetector volume was adjusted from the peak position of uniform PEG oligomers. The volume of the injected loop was 0.214 mL, and the polymer concentration was calculated to give a viscometric signal less than 0.5% of the baseline level. NMR spectra were recorded on a Bruker ARX-400 spectrometer. $CDCl_3$ was used as the solvent. ^1H NMR chemical shifts are reported in ppm relative to the solvent's residual ^1H signal ($CDCl_3$: 7.25 ppm). ^1H NMR assignments were confirmed by 2D-COSY-45 spectra. Coupling constants J are given in hertz. ^{13}C NMR spectra were recorded at 101 MHz. The ^{13}C signal of the solvent ($CDCl_3$: 77 ppm) was used as internal reference. Coupling constants (J) are given in Hz. MALDI-TOF mass spectrometry was carried out on an Axima CFR-Plus instrument (Shimadzu Biotech) operated in positive reflectron and linear modes. Sample solutions were prepared with either α-cyano-4-hydroxycinnamic acid (CHCA, 20 mg/mL) or 2,5-dihydroxybenzoic acid (DHB, 20 mg/mL) as the matrix in the presence of NaI. 0.5 μL of sample solution was mixed on the target with 0.5 μL of matrix solution and allowed to air-dry. External calibration was carried out with a mixture of seven peptides (CHCA, CHCA dimer, reserpine, angiotensin 2, substance P, Glu fib, ACTH frag 18−39, melittin, chain B Ins). Data processing was performed using the Kompact v2.4.3 software. ESI-MS analysis was performed on a Finnigan SSQ 710C single quadrupole mass spectrometer (Finnigan-MAT, Bremen, Germany) equipped with an electrospray (ES) ionization interface. Data were acquired using the ICIS software running on a Digital Unix workstation.

Procedures. *2,6-Pyridinedicarboxaldehyde (**2**).* In a 500 mL round-bottom flask equipped with a condenser, 2,6-pyridinedimethanol (5 g, 37 mmol) was dissolved in hot $CHCl_3$ (250 mL). The flask was cooled to room temperature, and activated manganese oxide (60 g, 20 equiv) was added as a solid. The mixture was vigorously stirred under reflux for 4 days until most of the starting material was consumed. After cooling to room temperature, the suspension was filtered over Celite. The oxidized products were purified by flash column chromatography on silica gel, eluting with ethyl acetate and dichloromethane (1:1 v/v), which afforded **2** as a white, pure solid (2.1 g, yield 42%). ^1H NMR (400 MHz, $CDCl_3$): 10.16 (s, 2H), 8.16 (d, J = 7.8 Hz, 2H), 8.07 (t, J = 7.8 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): 192.34, 152.98, 138.37, 125.32. MS (ESI): 136.96 $(M + H)^+$. ^1H NMR, ^{13}C NMR, and ESI-MS spectra are included in the Supporting Information (Figures S1−S3).

*Butyl-1,3-di(2-(hydroxypyridin-2-ylmethyl) Acrylate) (**4**).* To a stirred mixture of 2-pyridinecarboxaldehyde (285 μL, 3.0 mmol) and 1,3-butanediol diacrylate (177.12 μL, 1.0 mmol) were added 1,4-diazabicyclo[2.2.2]octane (DABCO) (112 mg, 1.0 mmol) and methanol (60 μL, 1.5 mmol). DMF

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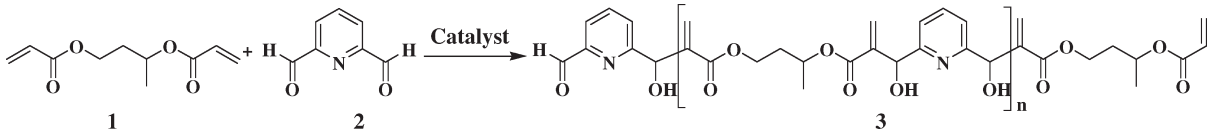
Scheme 2



(0.2 mL) was added to help dissolve the reactants. The light yellow homogeneous reaction mixture was stirred at ambient temperature for 3 h, and the progress of the reaction was monitored by TLC. After stirring for 3 h, the reaction mixture was purified by flash column chromatography on silica gel, eluting with ethyl acetate and dichloromethane (1:1 to 1:0 v/v) to give **4** as a light yellow oil (342 mg, yield 83%). ^{1}H NMR (400 MHz, $CDCl_3$): 8.52 (s, 2H), 7.66 (m, 2H), 7.38 (m, 2H), 7.18 (m, 2H), 6.32 (d, J = 3.6 Hz, 2H), 5.91 (d, J = 3.8 Hz, 2H), 5.57 (t, J = 5.4 Hz, 1H), 4.98 (t, 1H), 4.84 (t, 2H, −OH), 4.05 (t, 2H), 1.8 (m, 2H), 1.19 (d, J = 6.2 Hz, 3H, $-CH_3$). ^{13}C NMR (101 MHz, $CDCl_3$): 165.58, 165.21, 159.64, 159.48, 148, 141.77, 141.53, 136.66, 126.85, 126.66, 122.40, 121.05, 72.22, 72.04, 68.20, 60.78, 34.34, 19.64. MS (ESI): 413.2 $(M + H)^+$. ^{1}H NMR, ^{13}C NMR, and ESI-MS spectra are included in the Supporting Information (Figures S4−S6).

*2-Hydroxy-[6-(1-hydroxy-2-methoxycarbonylallyl)pyridin-2-yl]-methylacrylic Acid, 1-Methyl Ester (**5**).* To a stirred mixture of 2,6-pyridinedicarboxaldehyde (139 mg, 1.03 mmol) and methyl acrylate (270 μL, 3.0 mmol) were added DABCO (112 mg, 1.0 mmol) and methanol (60 μL, 1.5 mmol). DMF (0.2 mL) was added to help dissolve the reactants. The light yellow homogeneous reaction mixture was stirred at ambient temperature for 3 h, and the progress of the reaction was monitored by TLC. After stirring for 3 h, the reaction mixture was purified by flash column chromatography on silica gel, eluting with ethyl acetate and hexane (1:1 v/v) to give **5** as a transparent oil (267 mg, yield 87%). ^{1}H NMR (400 MHz, $CDCl_3$): 7.68 (t, J = 7.7 Hz, 1H), 7.37 (d, J = 7.8 Hz, 2H), 6.33 (s, 2H), 5.88 (s, 2H), 5.58 (d, J = 6.9 Hz, 1H), 3.72 (s, 6H), 4.37 (d, J = 7.2 Hz, 2H, OH). ^{13}C NMR (101 MHz, $CDCl_3$): 166.61, 158.49, 141.41, 137.77, 126.99, 120.08, 72.57, 51.91. MS (ESI): 308.2 $(M + H)^+$. ^{1}H NMR, ^{13}C NMR, and ESI-MS spectra are included in the Supporting Information (Figures S7−S9).

*Poly((1,3-butanediol diacrylate)-alt-(2,6-pyridinedicarboxaldehyde)) (**3**). Procedure 1.* To a stirred mixture of 2,6-pyridinedicarboxaldehyde (**2**) (135 mg, 1.0 mmol) and 1,3-butanediol diacrylate (**1**) (192 μL, 1.0 mmol) were added DABCO (112 mg, 1.0 mmol) and methanol (60 μL, 1.5 mmol). 0.2 mL of DMF was added to help dissolve the reactants, and the homogeneous reaction mixture was stirred at ambient temperature. The course of the reaction was followed by ^{1}H NMR spectroscopy and GPC. Samples for ^{1}H NMR and GPC analysis were isolated by taking 50 μL aliquots from the reaction mixture at determined time intervals, which were subsequently diluted with chloroform (50 mL). The chloroform solution was washed with a saturated solution of aqueous $NaHCO_3$ and brine, then separated and dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure to give **3** as a light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): 7.61 (pyridine-H, 1H), 7.26 (pyridine-H, 2H), 6.27 (=CH_2, 2H), 5.84 (=CH_2, 2H), 5.54 (−C*H*−OH, 2H), 4.91 (−C*H*−CH_3, 1H), 4.73 (−OH, 2H), 3.93 (−O−CH_2−CH_2−, 2H), 1.77 (−O−CH_2−CH_2−, 2H), 1.12 (−CH−CH_3, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): 165.72, 158.91, 142.12, 137.40, 126.24, 119.73, 71.87, 68.15, 60.79, 34.37, 19.67. A ^{13}C NMR spectrum is included in the Supporting Information (Figure S10).

Procedure 2. To a stirred mixture of 2,6-pyridinedicarboxaldehyde (**2**) (109.8 mg, 0.81 mmol) and 1,3-butanediol diacrylate (**1**) (154 μL, 0.80 mmol) were added 3-HQD (112 mg, 0.87 mmol) and methanol (60 μL, 1.5 mmol). 0.15 mL of DMF was added to help dissolve the reactants, and the homogeneous reaction mixture was stirred at ambient temperature. The course of the reaction was followed by ^{1}H NMR spectroscopy and GPC. Samples for ^{1}H NMR and GPC analysis were isolated as described under Procedure 1.

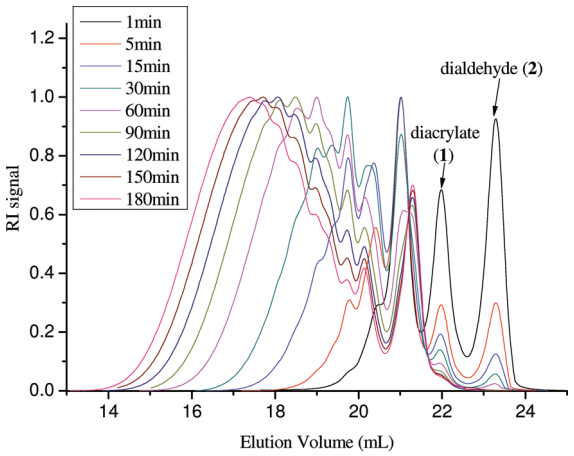


Figure 1. GPC elugrams of samples taken at regular time intervals during the Baylis−Hillman polymerization of **1** and **2** (procedure 1).

Procedure 3. To a stirred mixture of 2,6-pyridinedicarboxaldehyde (**2**) (124.5 mg, 0.92 mmol) and 1,3-butanediol diacrylate (**1**) (177 μL, 0.92 mmol) were added DBU (137 μL, 0.92 mmol) and 0.1 mL of DMF. The homogeneous reaction mixture was stirred at ambient temperature. The course of the reaction was followed by ^{1}H NMR spectroscopy and GPC. Samples for ^{1}H NMR and GPC analysis were isolated as described under Procedure 1.

Procedure 4. To a stirred mixture of 2,6-pyridinedicarboxaldehyde (**2**) (124.2 mg, 0.92 mmol) and 1,3-butanediol diacrylate (**1**) (177 μL, 0.92 mmol) were added DMAP (113 mg, 0.92 mmol) and 0.1 mL of THF. The homogeneous reaction mixture was stirred at ambient temperature. The course of the reaction was followed by ^{1}H NMR spectroscopy and GPC. Samples for ^{1}H NMR and GPC analysis were isolated as described under Procedure 1.

Procedure 5. To a stirred mixture of 2,6-pyridinedicarboxaldehyde (**2**) (138.3 mg, 1.02 mmol) and 1,3-butanediol diacrylate (**1**) (197 μL, 1.02 mmol) under nitrogen were added triphenylphosphine (60 mg, 0.3 mmol) and methanol (60 μL, 1.5 mmol). 0.2 mL of THF was added to help dissolve the reactants, and the homogeneous reaction mixture was stirred at ambient temperature. The course of the reaction was followed by ^{1}H NMR spectroscopy and GPC. For ^{1}H NMR and GPC analysis, 50 μL aliquots were taken from the reaction media at determined time intervals. Samples were isolated by precipitation by addition of 50 mL of cold diethyl ether and subsequent centrifugation, which afforded **3** as light yellow oil.

Procedure 6. To a stirred mixture of 2,6-pyridinedicarboxaldehyde (**2**) (134.9 mg, 0.99 mmol) and 1,3-butanediol diacrylate (**1**) (191 μL, 0.99 mmol) were added DABCO (111.4 mg, 0.99 mmol), lanthanum triflate (30 mg, 0.05 mmol), and triethanolamine (66 μL, 0.5 mmol). 0.2 mL of DMF was added to help dissolve the reactants, and the homogeneous reaction mixture was stirred at ambient temperature. The course of the reaction was followed by ^{1}H NMR spectroscopy and GPC.

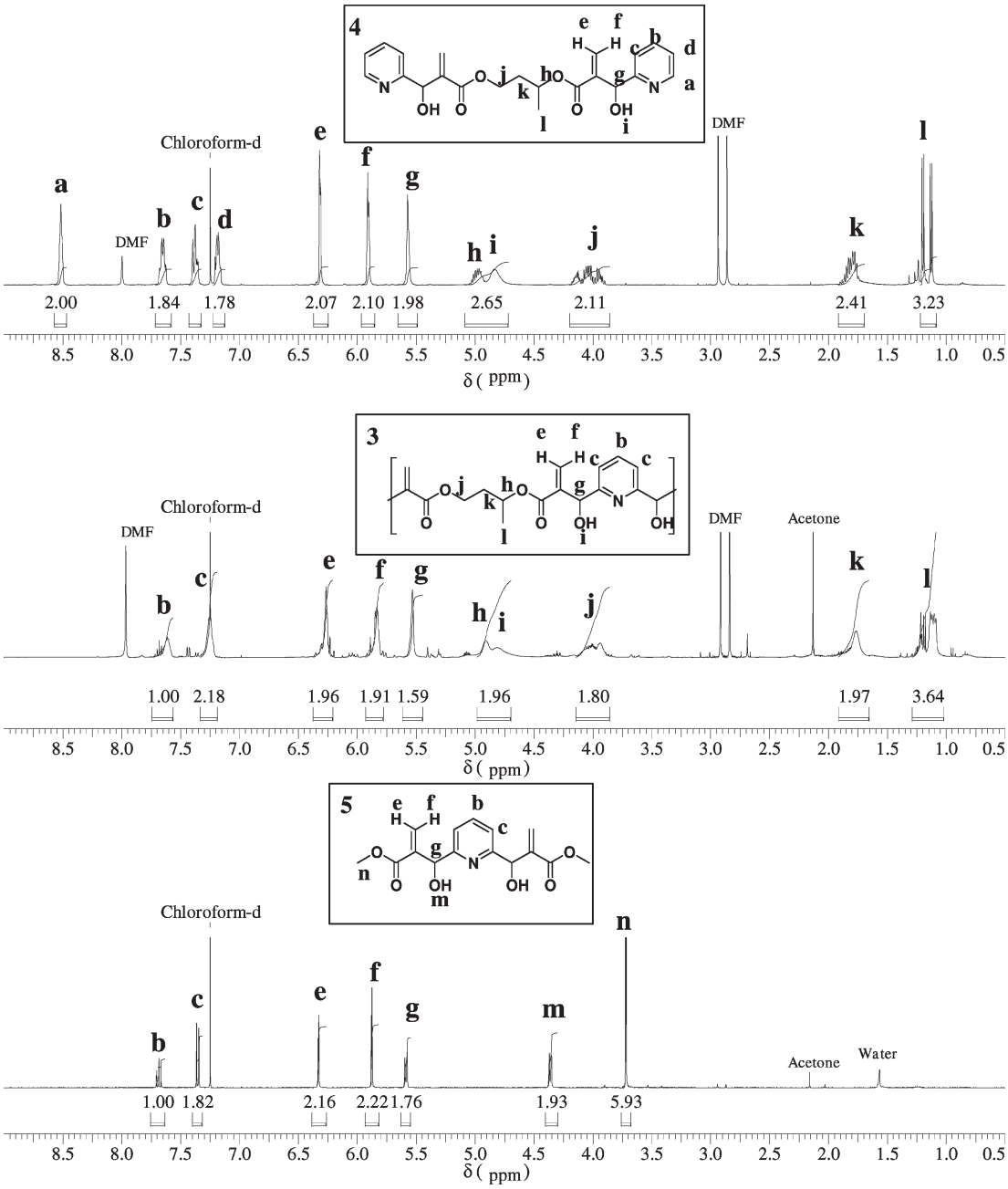


Figure 2. ^{1}H NMR spectra (400 MHz, $CDCl_3$) of (A) model compound **4**, (B) polymer **3** (procedure 1, after a polymerization time of 24 h), and (C) model compound **5**.

Samples for ^{1}H NMR and GPC analysis were isolated as described under Procedure 1.

Procedure 7. The polymerization was carried out in a CEM Discover monomode microwave reactor (5 W) at 50 °C using DMF (0.2 mL) as solvent. To a stirred mixture of 2,6-pyridinedicarboxaldehyde (**2**) (129.7 mg, 0.96 mmol) and 1,3-butanediol diacrylate (**1**) (184 μL, 0.96 mmol) were added DABCO (108 mg, 0.96 mmol), 1-butyl-2,3-dimethylimidazolium tetrafluoroborate (125.5 mg, 0.5 mmol), and methanol (60 μL, 1.5 mmol). The course of the reaction was followed by ^{1}H NMR spectroscopy and GPC. Samples for ^{1}H NMR and GPC analysis were isolated as described under Procedure 1.

*Postpolymerization Modification of **3** with Phenyl Isocyanate (**6**).* To polymer **3** (148 mg, 0.88 mmol of hydroxyl groups; Table 1, procedure 1 after 6 h) dissolved in dichloromethane (1.2 mL), phenyl isocyanate (400 μL, 3.55 mmol) was added and the solution stirred for 6 h at ambient temperature. The postmodified product was precipitated by addition of cold diethyl ether (50 mL) and isolated by centrifugation. Polymer **6** was obtained as a transparent oil (103.3 mg, yield: 41%). M_n = 9200; M_w/M_n = 1.4. ^{1}H NMR spectroscopy indicated quantitative conversion of the hydroxyl groups. ^{1}H NMR (400 MHz, $CDCl_3$): 7.57 (pyridine-H, 1H), 7.35 (Ar, 8H), 7.25 (pyridine-H, 2H), 6.99 (p-Ar, 2H), 6.64 (=CH_2, 2H), 6.34 (=CH_2, 2H), 5.71 (−C*H*−OH, 2H), 4.95 (−C*H*−CH_3, 1H), 4.00 (−O−CH_2−CH_2−, 2H), 1.67 (−O−CH_2−CH_2−, 2H), 1.06 (−CH−CH_3, 3H).

*Postpolymerization Modification of **3** with Methyl 3-Mercaptopropionate (**7**).* Polymer **3** (256 mg, 1.54 mmol double bonds; Table 1, procedure 1 after 6 h) was dissolved in dry THF (0.2 mL), and pyridine (0.9 mL) was added to the mixture. Then, a large excess of methyl

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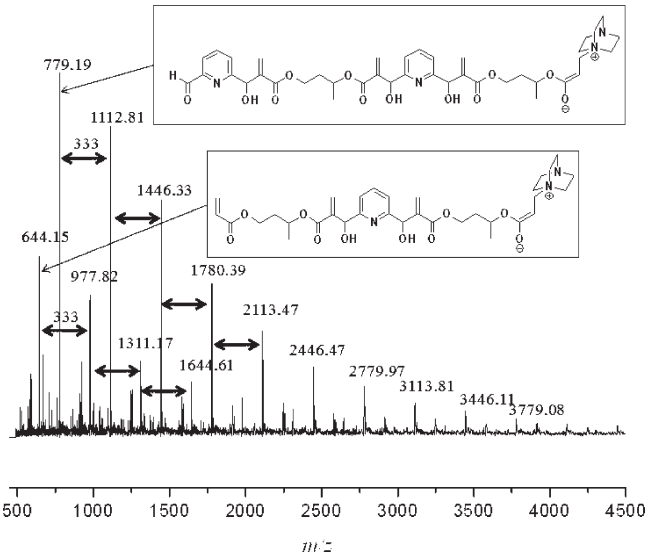

Figure 3. MALDI-TOF mass spectrum of polymer **3** prepared according to procedure 1 (polymerization time 24 h).

3-mercaptopropionate (1.7 mL, 15 mmol) was added. The solution was stirred overnight at ambient temperature. The postmodified polymer was precipitated by addition of cold diethyl ether (100 mL) and isolated by centrifugation to afford **7** as obtained a transparent oil (122.8 mg, yield: 27.8%). M_n = 2100; M_w/M_n = 1.5. ^{1}H NMR spectroscopy indicated quantitative conversion of the double bonds. ^{1}H NMR (400 MHz, $CDCl_3$): 7.31−7.88 (pyridine-H, 3H), 4.98 (−C*H*−CH_3, 1H), 4.88 (−C*H*−OH, 2H), 4.09 (−O−CH_2−CH_2−, 2H), 3.70 (−OCH_3, 6H), 3.15 (−C*H*−CH_2−S−), 2.78 (−CH_2−S−CH_2−CH_2, 4H), 2.65 (−S−CH_2−CH_2−, 4H), 2.48 (−S−CH_2−CH_2−, 4H), 1.83 (−O−CH_2−CH_2−, 2H), 1.25 (−CH−CH_3, 3H).

*Sequential Postpolymerization Modification (**8**). Via Polymer **6**.* Polymer **6** (90 mg, 0.31 mmol double bonds) was dissolved in dry THF (0.1 mL), and pyridine (0.2 mL) was added to the mixture. Then, a large excess of methyl 3-mercaptopropionate (0.35 mL, 3.15 mmol) was added. The solution was stirred overnight at ambient temperature. The postmodified polymer was precipitated by addition of cold diethyl ether (50 mL) and isolated by centrifugation to afford **8** as a transparent oil (31 mg, yield: 24.4%). M_n = 5500; M_w/M_n = 1.8. ^{1}H NMR spectroscopy indicated quantitative conversion of the double bonds.

*Via Polymer **7**.* To polymer **7** (105 mg, 0.36 mmol hydroxyl groups) dissolved in dichlromethane (0.8 mL), phenyl isocyanate (163 μL, 1.5 mmol) was added, and the solution stirred for 6 h at ambient temperature. The postmodified product was precipitated by addition of cold diethyl ether (50 mL) and isolated by centrifugation, which afforded **8** as a transparent oil (59 mg, yield: 39%). M_n = 3200; M_w/M_n = 1.4. ^{1}H NMR spectroscopy indicated 42% conversion of the hydroxyl groups. ^{1}H NMR (400 MHz, $CDCl_3$): 7−8 (Ar, 11H), 4.98 (−C*H*−CH_3, 1H), 4.88 (−C*H*−OH, 2H), 4.13 (−O−CH_2−CH_2−, 2H), 3.63 (−OCH_3, 6H), 3.11 (−C*H*−CH_2−S−), 2.74 (−CH_2−S−CH_2−CH_2, 4H), 2.63 (−S−CH_2−CH_2−, 4H), 2.54 (−S−CH_2−CH_2−, 4H), 1.79 (−O−CH_2−CH_2−, 2H), 1.16 (−CH−CH_3, 3H).

RESULTS AND DISCUSSION

Polymerization. Although the Baylis−Hillman reaction has been reported to suffer from a limited substrate scope and long reaction times, many advances have been made over the past decade, and numerous examples have been reported of reaction conditions that are applicable to a broad range of substrates and which allow near to quantitative conversion within a few hours.[9] These advances provide a firm basis to explore the feasibility of the Baylis−Hillman reaction for the synthesis of side-chain functional polyesters. In this study, for a first series of experiments, the polymerization of 1,3-butanediol diacrylate **1** and 2,6-pyridinedicarboxaldehyde **2** was investigated (Scheme 2). These monomers were selected since the Baylis−Hillman reaction of 2-pyridinedicarboxaldehyde and methyl acrylate has been reported to proceed with 93−100% yield.[15,16] Since the polymerization outlined in Scheme 2 is a step polymerization, high yielding Baylis−Hillman coupling steps are a prerequisite to obtain high molecular weight polymers. For the polymerization of **1** and **2** a variety of reaction conditions was evaluated, and the resulting polymers were analyzed by GPC. The results of these experiments are summarized in Table 1. All polymerizations listed in Table 1 were carried out in DMF, which is a good solvent for both monomers and the polymer and allowed to carry out the reaction under homogeneous conditions.

A first series of polymerization experiments (procedure 1, Table 1) was performed at room temperature using 1,4-diazabicyclo[2.2.2]-octane (DABCO) as catalyst and methanol as additive. Methanol was added since it was identified in previous studies to accelerate the Baylis−Hillman reaction.[16] Polymerization of **1** and **2** in DMF with DABCO and methanol as additive afforded a polymer with a molecular weight of 4200 g/mol after 24 h. Increasing the reaction time up to 72 h did not result in a further increase in molecular weight but instead afforded slightly lower molecular weight materials, which could indicate a depolymerization at prolonged reaction times. Also, further variation of the monomer concentration (Table S1), polymerization temperature (Table S2), or the solvent (Table S3) did not result in polymers with increased molecular weights. The molecular weights, degrees of polymerization, and polydispersities listed in Table 1 were obtained using a conventional calibration curve that was created with polystyrene standards. For a number of samples prepared via procedure 1 additional GPC experiments were carried out, which were evaluated using a conventional calibration curve. These analyses, which are included in the Supporting Information (Table S4), afforded slightly higher molecular weights and degrees of polymerization (e.g., a degree of polymerization of 29 instead of 25 after a polymerization time of 24 h).

To obtain further insight into the kinetics of the polymerization under these conditions, GPC was used to monitor monomer consumption and the evolution of molecular weight during the first 3 h (Figure 1). The chromatograms in Figure 1 show a broad polymer peak, which gradually shifts to lower elution volumes with increasing reaction time and reflects the increasing molecular weight of the polymer. In addition, monitoring the intensity of the monomer peaks in Figure 1 indicates that **1** and **2** are quantitatively consumed after 180 min. These results are in good agreement with literature data, which reported quantitative coupling of 2,6-pyridinedicarboxaldehyde with methyl acrylate in 2.5 h.[15]

As already mentioned above, the Baylis−Hillman reaction has traditionally been hampered by slow reaction rates and conversions, and lots of efforts have been devoted to develop reaction conditions that allow to overcome these problems. In a next series of experiments, a variety of alternative protocols for the polymerization of **1** and **2** was evaluated and compared with regards to the molecular weight of the resulting polymers (Table 1). First, 3-hydroxyquinuclidine (3-HQD) and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) were evaluated as

Scheme 3

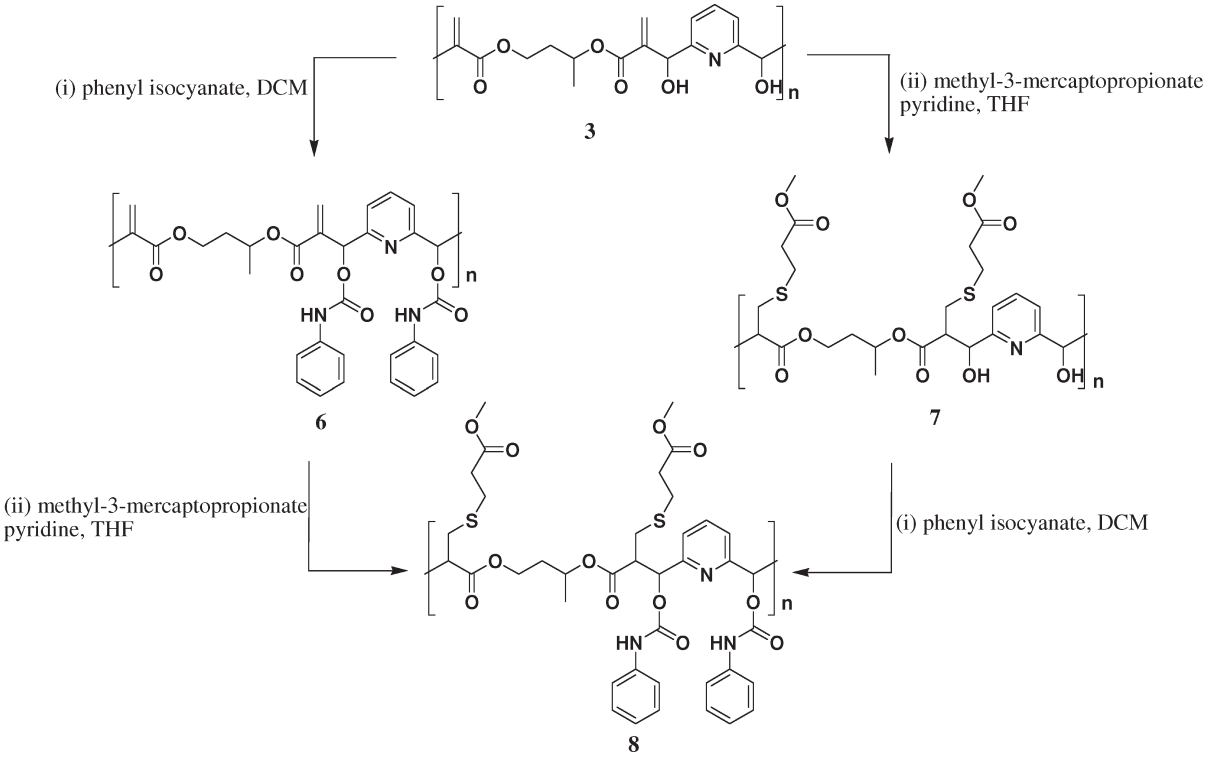

Table 2. Results of the Postpolymerization Modification of 3

polymer	comments	M_n[a] (g/mol)	M_w[a] (g/mol)	M_w/M_n[a]	conversion[b] (%)
3		3100	5600	1.8	
6		9200	12700	1.4	100
8	via **6**	5500	9800	1.8	100
7		2100	2900	1.4	100
8	via **7**	3200	4400	1.4	42

[a] Number-average (M_n) and weight-average (M_w) molecular weight, polydispersity (M_w/M_n), and number-average degree of polymerization (DP_n) determined from GPC (THF, conventional calibration, polystyrene standards). [b] Side-chain functional group conversion as determined by ^{1}H NMR.

alternatives to replace DABCO. 3-HQD[17,18] and DBU[19] were selected since they have been reported to enhance the rate of Baylis−Hillman reactions. The use of these catalysts for the polymerization of **1** and **2**, however, was not found to result in polymers with molecular weights higher than those obtained via the DABCO catalyzed polymerization (see procedures 2 and 3 in Table 1). Similarly, replacing DABCO by 4-(dimethylamino)-pyridine (DMAP)[20] or triphenylphosphine[21,22] also did not to result in polymers with increased molecular weights (Table 1, procedures 4 and 5). For procedures 3−5, Table 1 only lists a single data point. Additional data that illustrate the evolution of polymer molecular weight with reaction time for these experiments are included in the Supporting Information (Table S5). Other strategies that have been proven successful to enhance the rate and conversion of Baylis−Hillman reactions include the use of lanthanum triflate as a cocatalyst,[23] the application of microwave irradiation,[24,25] and the use of ionic liquids[25,26] as the reaction medium. None of these modifications, however, were found to result in an increase in polymer molecular weight as compared to the DABCO-catalyzed polymerization of **1** and **2** (Table 1, procedures 6 and 7, and Table S6).

Characterization. The structure of the polymers prepared via polymerization of **1** and **2** was confirmed by ^{1}H NMR spectroscopy and MALDI-TOF mass spectrometry. As an example, Figure 2 shows the ^{1}H NMR spectrum of polymer **3** prepared following procedure 1 after a polymerization time of 24 h. Peak assignments in the ^{1}H NMR spectrum of polymer **3** were made by comparison with the spectra of two model compounds (**4** and **5**), which are also included in Figure 2. One of the most characteristic signals in the ^{1}H NMR spectrum of **3** is peak *g* at 5.53 ppm, which is due to the C−H resonance of the tertiary carbon atom that is formed during the Baylis−Hillman coupling of **1** and **2**. Furthermore, comparison of the integrals in the ^{1}H NMR spectrum of **3**, and in particular those of signals *e*, *f*, and *g*, confirms that the polymer that has been formed indeed is the result of the Baylis−Hillman coupling of **1** and **2**. The ^{1}H NMR spectrum of **3** reveals a number of smaller signals in close proximity to the main peaks. Since the chemical shifts of several of these peaks match well with those of the model compounds, these less intense resonances are attributed to short oligomers (di-, tri-, and tetramers, for example) that are also formed during the polymerization.

The structure of polymer **3** was further confirmed by MALDI-TOF mass spectrometry. Figure 3 shows the MALDI-TOF mass spectrum of polymer **3** prepared via procedure 1 after a polymerization time of 24 h. The MALDI-TOF mass spectrum reveals two main series of peaks. Within each series, neighboring peaks are separated by 333 Da, which is the molecular weight of a

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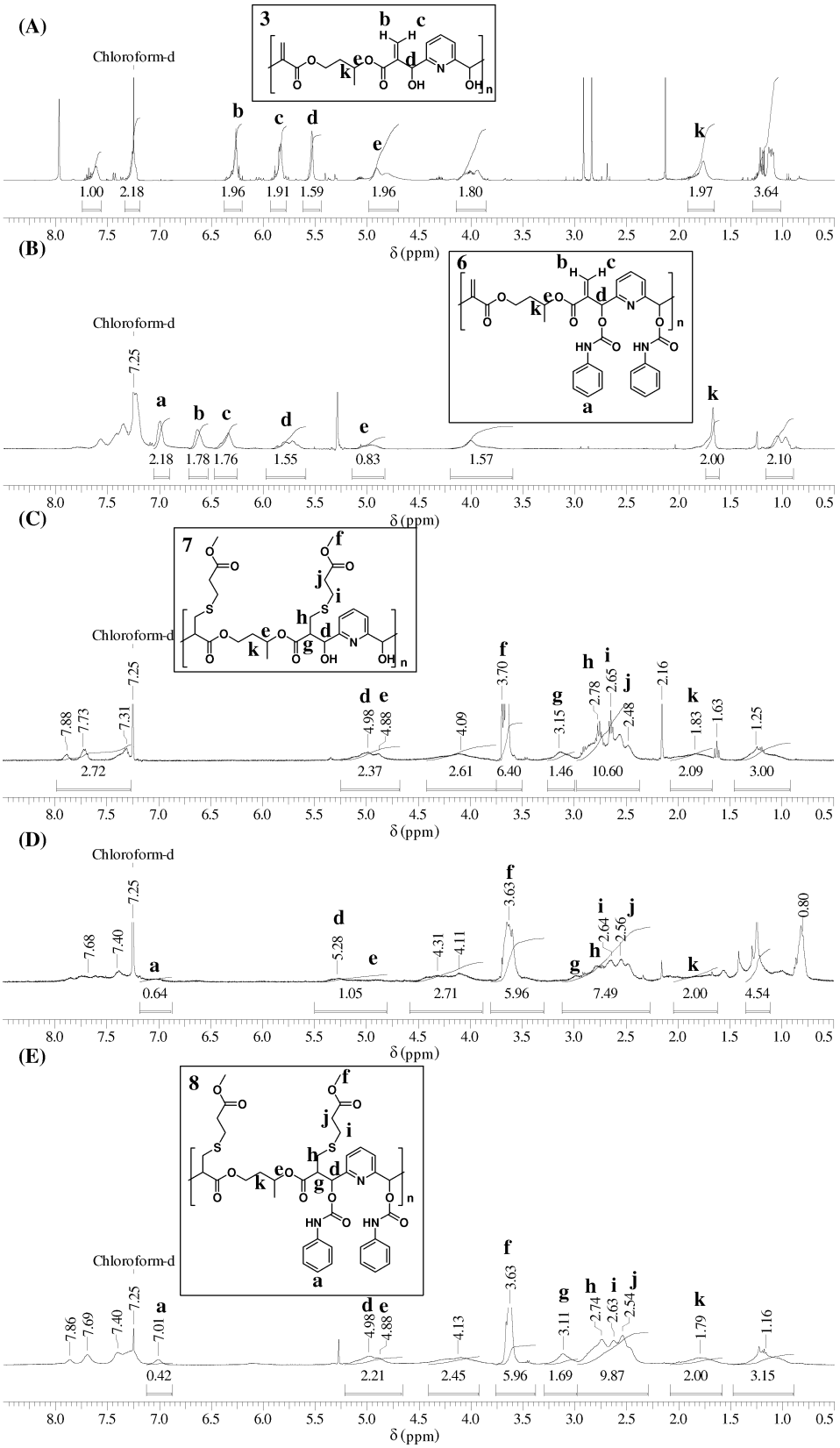

Figure 4. ^{1}H NMR spectra (400 MHz, $CDCl_3$) of (A) polymer **3** (procedure 1, polymerization time 24 h), (B) polymer **6**, (C) polymer **7**, (D) polymer **8** (prepared from polymer **6**), and (E) polymer **8** (prepared from **7**).

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single repeat unit of polymer **3**. One series of peaks in Figure 3 can be assigned to polymers containing two acrylate end groups, whereas the other main series is due to polymers carrying one acrylate and one aldehyde end group. Analysis of the masses for each of the two series of peaks indicates that (one of) the acrylate end group(s) of **3** is a zwitterionic adduct resulting from 1,4-addition of DABCO with (one of) the acrylate end groups.[27−29] The MALDI-TOF mass spectrum in Figure 3 also reveals series of lower intensity signals. A version of the mass spectrum in which two of these series are assigned is included in the Supporting Information (Figure S11).

Postpolymerization Modification. One of the attractive features of polymer **3** is that it contains two chemically orthogonal handles, viz. a vinyl group and a hydroxyl group, which can be further modified with various reagents to generate a broad variety of side-chain functional polyesters. As a first proof-of-concept, the postpolymerization modification of **3** with methyl-3-mercaptopropionate and phenyl isocyanate was investigated (Scheme 3).

Both the single postpolymerization modification of **3** with phenyl isocyanate and methyl-3-mercaptopropionate to afford polyesters **6** and **7**, respectively, as well as the two-step modification of **3** to produce the double functionalized polyester **8** were investigated. The postpolymerization modification reactions were monitored with ^{1}H NMR spectroscopy and GPC, and the results of these experiments are summarized in Table 2 and Figure 4. Comparison of the ^{1}H NMR spectra of the starting polymer **3** with those of **6** and **7** indicates that the single step postpolymerization modification proceeds smoothly with quantitative conversion of the side-chain double bonds and hydroxyl groups in **3**, respectively. Quantitative postpolymerization modification of the side-chain double bonds is evident from the absence of the olefinic protons *b* and *c* in the ^{1}H NMR spectrum of **7** and is also supported by comparison of the integral of signals *f* and *k* in the ^{1}H NMR spectrum of **7**. The modification of the side-chain hydroxyl groups of **3** results in a shift of the proton resonance of *d* as well as additional signals between 7 and 7.5 ppm, which are due to the phenyl carbamate side chain of **6**. Comparison of the signals *k* and *a* in the ^{1}H NMR spectrum of **6** suggests that this postpolymerization modification reaction also proceeds quantitatively. Subsequent postpolymerization modification of **6** with methyl-3-mercaptopropionate proceeded with quantitative conversion of the double bonds as is evidenced by the absence of ^{1}H NMR resonances *b* and *c* in the corresponding ^{1}H NMR spectrum of **8**. The alternative pathway to **8** via postpolymerization modification of **7** turned out to be less efficient. Reaction of **7** with phenyl isocyanate only resulted in 42% conversion of the hydroxyl groups as calculated by comparison of the ^{1}H NMR integrals of peak *a* (6.8−7.2 ppm, from the phenyl ring at the side chain) and peak *k* (1.5−2 ppm, from the backbone). It should be noted here, however, that the resolution of the ^{1}H NMR spectra in Figure 4D and E is not excellent. The integral of signal *a* in the spectrum in Figure 4D is also lower than expected, and as a consequence it seems likely that the actual hydroxyl group conversion in **8** in Figure 4E is higher than 42%, although certainly not quantitative. The GPC chromatograms of the postmodified polymers **6**, **7**, and **8** all revealed monomodal molecular weight distributions, which in several cases were narrower than those of the starting polymer **3** (Supporting Information, Figures S12 and S13). This is most likely due to fractionation that occurred during work-up and isolation of the postmodified polymer, which involved precipitation. Fractionation inherently leads to loss of some of the material, which is also evident from the relatively low isolated yields as reported in the Experimental Section. Table 2 also lists the GPC molecular weights of the polymers **6**−**8**. The anomalous trends in the molecular weights of some of the samples among each other as well as compared to the starting polymer **3** are most likely due to differences in hydrodynamic properties and as a consequence GPC elution behavior.

CONCLUSIONS

This contribution has explored the feasibility of the Baylis−Hillman reaction for the synthesis of side-chain functional polyesters. Using 1,3-butanediol diacrylate and 2,6-pyridinedicarboxaldehyde as monomers and DABCO as the catalyst, polymers with degrees of polymerization of up to 25 could be prepared. These polymers are attractive as they contain chemically orthogonal side-chain hydroxyl and vinyl groups, which can be further modified to generate a diverse range of functional polyesters. In first proof-of-concept experiments, it was demonstrated that the side-chain hydroxyl and vinyl groups can be quantitatively modified with phenyl isocyanate and methyl-3-mercaptopropionate, respectively. Bifunctional polyesters could be obtained via successive postpolymerization modification of the starting polymer with phenyl isocyanate and methyl-3-mercaptopropionate. The results of this study indicate that the Baylis−Hillman polymerization represents an interesting alternative approach to synthesize side-chain functional polymers, which complements e.g. the ring-opening polymerization of functional lactones or the step polymerization of functional diacid or diol building blocks. In contrast to the latter two approaches, the Baylis−Hillman polymerization does not necessitate the use of side-chain protected monomers and generates polymers that contain two chemically orthogonal side-chain functional groups, which can be further modified to generate a vast diversity of functional polyesters. While the relatively low molecular weight polymers reported in this contribution may be of interest, e.g., as dual cure coatings, further work may lead to increased molecular weights and could further expand the possible scope of applications of these materials.

ASSOCIATED CONTENT

Supporting Information. GPC chromatograms, ESI-MS spectra, and NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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