Supporting information for:

Polyglyoxylates: A versatile class of triggerable self-immolative polymers from readily accessible monomers

Bo Fan[$], John F. Trant[$], Andrew D. Wong[#], and Elizabeth R. Gillies[$,#*]

[$]Department of Chemistry, [#]Department of Chemical and Biochemical Engineering, The University of Western Ontario, 1151 Richmond St., London, Ontario, Canada, N6A 5B7.

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I. General experimental details

Ethyl glyoxylate in toluene solution (50% w/w), phenyl isocyanate, dibutyltin dilaurate (DBTL), benzyl chloroformate, 4-dimethylaminopyridine (DMAP), 4-bromomethyl-3-nitrobenzoic acid, methanesulfonyl chloride and benzyl bromide were obtained from Alfa Aesar (Canada). Fumaric acid and maleic acid were purchased from Acros Organics (USA). 6-Nitroveratryl chloroformate (NVOC-Cl) was obtained from Chem-Impex International, Inc. (USA). Propargyl amine was purchased from AK Scientific, Inc. (USA). Dimethyl sulfide, sodium azide (NaN_3), phosgene solution (15 wt. % in toluene) and poly(ethylene glycol) methyl ether (2000 Da) were purchased from Sigma-Aldrich (USA). 1-Ethyl-3-(3-dimethylaminopropyl) carbodiimide hydrochloride (EDC·HCl) was purchased from Creo Salus (USA). Triethylamine (Et_3N), pyridine, and dichloromethane were distilled from calcium hydride before use. Anhydrous tetrahydrofuran (THF) and *N*,*N*-dimethylformamide (DMF) were obtained from a solvent purification system using aluminum oxide columns. All the other chemicals were of reagent grade and used without further purification. ^1H NMR spectra were obtained in $CDCl_3$ at 400 MHz or 600 MHz on Varian Inova instruments. NMR chemical shifts (δ) are reported in ppm and are calibrated against residual solvent signals of $CDCl_3$ (δ 7.27), CD_3CN (δ 1.94), $(CD_3)_2SO$ (δ 2.50) or D_2O (δ 4.75). Fourier transform infrared spectra (FT-IR) were obtained using a Bruker tensor 27 instrument with films drop cast from CH_2Cl_2 on KBr plates. Size exclusion chromatography (SEC) was performed using a Viscotek GPC Max VE2001 solvent module equipped with a Viscotek VE3580 RI detector operating at 30 °C, an Agilent Polypore guard column (50x7.5mm) and two Agilent Polypore (300x7.5mm) columns connected in series. Molecular weight calibration was carried out using polystyrene standards. Differential scanning calorimetry (DSC) and thermogravimetric analysis (TGA) were performed on a Mettler Toledo DSC 822e. For TGA the heating rate was 10 ºC/min between 50-400 ºC under nitrogen. For DSC, the heating/cooling rate was 10 ºC/min from -100 to +170 ºC. Glass transition temperatures were obtained from the second heating cycle.

II. Synthesis of monomers

Synthesis of dimethyl maleate (**5**)

Maleic acid (25.0 g, 216 mmol) was dissolved in methanol (250 mL). Concentrated sulfuric acid (2.5 mL) was then added dropwise. After refluxing at 75 ºC for 16 hours, the methanol was removed by rotary evaporator. Ethyl acetate (100 mL) was then added to the residue, and the solution was washed twice with saturated sodium bicarbonate (20 mL), and then with deionized water (20 mL). The organic layer was then dried over $MgSO_4$, filtered and concentrated under reduced pressure to provide a clear, colorless, oily liquid (30.0 g, 97%) after distillation of the oil at 140 ºC (190 mbar). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.26 (s, 2H), 3.79 (s, 6H). Spectral data are consistent with published values.[1]

Synthesis of dibutyl fumarate (**6**)

Fumaric acid (20.0 g, 172 mmol) was dissolved in *n*-butanol (250 mL). Concentrated sulfuric acid (2.5 mL) was then added dropwise. After stirring at 120 ºC for 16 hours, the residual *n*-butanol was removed *in vacuo*. Ethyl acetate (100 mL) was then added to the residue, and the solution was washed with saturated sodium bicarbonate (20 mL) solution twice, and deionized water (20 mL) once. The organic layer was then dried over $MgSO_4$, filtered and concentrated under reduced pressure to provide a clear, colorless, oily liquid (36.8 g, 94%) after distillation at 100 ºC (40 mbar). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.85 (s, 2H), 4.20 (t, J = 6.6 Hz, 4H), 1.63-1.70 (m, 4H), 1.36-1.46 (m, 4H), 0.95 (t, J = 7.4 Hz, 6H). Spectral data are consistent with published values.[2]

Synthesis of dibenzyl fumarate (**7**)

Fumaric acid (10.0 g, 86 mmol, 1.0 equiv.) was dissolved in anhydrous DMF (200 mL), and then triethylamine (24.0 mL, 172 mmol, 2.0 equiv.) was added dropwise to the stirring solution. Benzyl bromide (19.5 mL, 164 mmol, 1.9 equiv.) was then injected into the reaction mixture. After stirring at 100 ºC for 16 hours, the solution was precipitated into deionized water (800 mL) to provide a pale yellow solid (18.8 g, 78%) after filtration and drying. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31-7.41 (m, 10H), 6.94 (s, 2H), 5.24 (s, 4H). Spectral data are consistent with published values.[3]

Synthesis of methyl glyoxylate (**8**)

Diester **5** (20.0 g, 139 mmol, 1.0 equiv.) was dissolved in dichloromethane (200 mL), and the solution was cooled to -78 ºC in a dry ice/acetone bath. Ozone was bubbled into the solution under stirring until the solution turned blue. The solution was then purged with oxygen. Dimethyl sulfide (12.2 mL, 167 mmol, 1.2 equiv.) was added dropwise to quench the system. After stirring for 5 hours, and warming to room temperature, the solvent and residual dimethyl sulfide were removed by distillation at 70 ºC under argon. A pale yellow liquid (18.3 g, 75%) was obtained via distillation at 100 ºC under a slightly reduced pressure. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.33 (s, 1H), 3.86 (s, 3H). Spectral data are consistent with published values.[4]

Synthesis of benzyl glyoxylate (**10**)

Diester **7** (10.0 g, 34 mmol, 1.0 equiv.) and Sudan Red III (20.0 mg) were dissolved in dichloromethane (100 mL), and the solution was cooled to -78 ºC by dry ice/acetone bath. Ozone was then bubbled into the stirred solution until the red solution turned clear and colorless, and then the solution was immediately purged with oxygen. Dimethyl sulfide (3.0 mL, 41 mmol, 1.2 equiv.) was then added dropwise into the solution to quench the ozonide. The mixture was stirred for an additional 5 hours, and allowed to warm to ambient temperature. The solvent and the residual dimethyl sulfide were then removed by distillation at 70 ºC under argon to provide a pale yellow liquid (6.0 g, 55%) following distillation at 150 ºC (40 mbar) from P_2O_5. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.43 (s, 1H), 7.21-7.51 (m, 5H), 5.35 (s, 2H). Spectral data are consistent with published values.[5]

III. Synthesis of polymers

Due to the highly reactive nature of these monomers, even trace water can lead to oligomerization or polymerization. Therefore, immediately before polymerization, a second vacuum distillation with P_2O_5 was conducted to crack any oligomers and remove any remaining traces of water.

Polymerization of ethyl glyoxylate without end-capping (polymer **1**)

Ethyl glyoxylate in toluene solution (20 mL) was fractionally distilled under vacuum (55 ºC, 125 mbar) over P_2O_5 to remove toluene and trace water in the first, discarded fraction. The residue was then distilled twice successively over P_2O_5 at atmospheric pressure under argon protection at 130 ºC to obtain the highly pure monomer. This pale yellow liquid (5.0 mL, 50 mmol, 1.0 equiv.) was dissolved in dichloromethane (5.0 mL) and Et_3N (3.5 μL, 25 μmol, 0.0005 equiv.). The solution was stirred for one hour at -20 ºC, and the resulting polymer was purified by precipitation into methanol. After drying *in vacuo* for 48 hours, polymer **1** was obtained (1.8 g, 35%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.48-5.75 (m, 100H), 4.12-4.38 (m, 204H), 1.24-1.44 (m, 298H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 164.7-167.1, 90.6-93.8, 61.7, 13.5. SEC: M_n = 103 kDa, M_w = 266 kDa, $Đ$ = 2.6. T_g = -32 ºC.

Polymerization of ethyl glyoxylate with phenyl isocyanate as end-cap (polymer **2**)

The same distillation and polymerization procedure was conducted to obtain poly(ethyl glyoxylate) as described for polymer **1**; however, prior to precipitation, phenyl isocyanate (100 μL, 920 μmol, 0.018 equiv.) was added to end-cap the polymer along with 3 drops of DBTL. The solution was then stirred for 24 hours at room temperature and a further 16 hours at 40 ºC.

Purification was achieved by precipitation of the crude reaction mixture into methanol. After decanting the excess methanol, the residue was dried *in vacuo* for 48 hours to provide polymer **2** (2.3 g, 45%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.26-7.43 (m, 10H), 5.48-5.73 (m, 79H), 4.10-4.30 (m, 171H), 1.17-1.36 (m, 249H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 164.7-166.9, 90.3-94.8, 61.7, 13.5. FT-IR (KBr, thin film): 2982, 1762, 1447, 1376, 1020 cm^{-1}. SEC: M_n = 27 kDa, M_w = 66 kDa, $Đ$ = 2.5. T_g = -1 ºC.

Polymerization of ethyl glyoxylate with benzyl chloroformate as end-cap (polymer **3**)

Poly(ethyl glyoxylate) was prepared as described for polymer **1**. Following polymerization, but prior to precipitation, benzyl chloroformate (100 μL, 710 μmol, 0.014 equiv.) was added at 0 ºC along with Et_3N (99.0 μL, 710 μmol, 0.014 equiv.). The solution was stirred for 24 hours at room temperature and a further 16 hours at 40 ºC. Purification was achieved by precipitation of the crude reaction mixture into methanol. After the solvent was decanted, the residue was dried *in vacuo* for 48 hours to provide polymer **3** (2.6 g, 50%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.26-7.41 (m, 15H), 5.48-5.82 (m, 750H), 5.20 (s, 4H), 4.05-4.32 (m, 1562H), 1.19-1.49 (m, 2349). ^{13}C NMR (150 MHz, $CDCl_3$): δ 165.0-167.5, 127.2-128.9, 90.6-94.0, 62.0, 13.8. FT-IR (KBr, thin film): 2982, 1762, 1448, 1379, 1020 cm^{-1}. SEC: M_n = 31 kDa, M_w = 59 kDa, $Đ$ = 1.9. T_g = -3 ºC.

Polymerization of methyl glyoxylate with NVOC-Cl as end-cap (polymer **11**)

Freshly distilled methyl glyoxylate (5.0 mL, 63 mmol, 1.0 equiv.) was dissolved in dichloromethane (5.0 mL) and Et_3N (4.4 μL, 32 μmol, 0.0005 equiv.). After the solution had been stirred for one hour at -20 ºC, Et_3N (0.2 mL, 1.5 mmol, 0.023 equiv.) and NVOC-Cl (0.4 g, 1.5 mmol, 0.023 equiv.) were added into the mixture to end-cap the polymer. The solution was then stirred for 24 hours at room temperature and a further 16 hours at 40 ºC. Purification was achieved by precipitation of the crude reaction mixture into methanol. After decanting the excess methanol, the residue was dried *in vacuo* for 48 hours, to provide polymer **11** (3.3 g, 59%). ^1H NMR (400 MHz, $CDCl_3$): δ 7.75 (s, 1.8H), 7.14 (s, 1.2H), 5.55-5.78 (m, 83H), 4.06 (s, 6H), 3.97 (s, 6H), 3.73-3.86 (m, 262H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 164.7-166.5, 153.8, 148.1, 109.2, 107.6, 90.0-93.9, 86.7, 66.8, 56.4, 56.2, 52.6. FT-IR (KBr, thin film): 2960, 1760, 1440, 1019 cm^{-1}. SEC: M_n = 3800 Da, M_w = 4800 Da, $Đ$ = 1.3. T_g = 24 ºC, T_m = 72 ºC.

Polymerization of *n*-butyl glyoxylate with NVOC-Cl as end-cap (polymer **12**)

Freshly distilled *n*-butyl glyoxylate (5.0 mL, 38 mmol, 1.0 equiv.) was dissolved in dichloromethane (5.0 mL) and Et_3N (2.7 µL, 19 µmol, 0.0005 equiv.). After the solution was stirred for one hour at -10 ºC, Et_3N (0.2 mL, 1.5 mmol, 0.038 equiv.) and NVOC-Cl (0.4 g, 1.5 mmol, 0.038 equiv.) were added into the mixture to end-cap the polymer. The solution was then stirred for 24 hours at room temperature and a further 16 hours at 40 ºC. The solvent was removed by high vacuum and the crude polymer was re-dissolved in tetrahydrofuran (5.0 mL) and dialyzed against water for 24 hours (200 mL, 2 solvent changes) using a regenerated cellulose membrane (6000-8000 Da MWCO). The residual content was then lyophilized to afford polymer **12** (2.2 g, 44%).^1H NMR (400 MHz, $CDCl_3$): δ 7.75 (s, 3H), 7.09 (s, 2.9H), 5.46-5.77 (m, 49H), 4.06-4.24 (m, 83H), 4.05 (s, 6H), 3.96 (s, 6H), 1.55-1.73 (m, 88H), 1.25-1.45 (m, 82H), 0.81-1.04 (m, 120H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 164.1-166.4, 153.9, 147.5, 109.2, 107.6, 90.2-94.3, 65.7, 56.6, 56.3, 30.2, 18.8, 13.6. FT-IR (KBr, thin film): 2963, 2936, 2876, 1759, 1464, 1379, 1219, 1016 cm^{-1}. SEC: M_n = 5000 Da, M_w = 9800 Da, *Đ* = 1.9. T_g = -30 ºC.

Polymerization of benzyl glyoxylate with NVOC-Cl as end-cap (polymer **13**)

Freshly distilled benzyl glyoxylate (5.0 mL, 36 mmol, 1.0 equiv.) was dissolved in dichloromethane (5.0 mL) and Et_3N (2.5 µL, 18 µmol, 0.0005 equiv.). After the solution was stirred for one hour at 0 ºC, Et_3N (0.2 mL, 1.5 mmol, 0.042 equiv.) and NVOC-Cl (0.40 g, 1.5 mmol, 0.042 equiv.) were added into the mixture to end-cap the polymer. The solution was then stirred for 24 hours at room temperature and a further 16 hours at 40 ºC. The solvent was removed under high vacuum and the crude polymer was re-dissolved in DMF (5.0 mL) and dialyzed against DMF for 24 hours (200 mL, 2 solvent changes) and water for 24 hours (200 mL, 2 solvent changes) using a regenerated cellulose membrane (6000-8000 Da MWCO). The residual content was then lyophilized to afford polymer **13** (1.9 g, 36%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.69 (s, 1.7H), 6.89-7.36 (m, 106H), 5.46-5.83 (m, 26H), 4.74-5.20 (m, 50H), 3.93 (s, 6H), 3.73 (s, 6H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 164.6-166.6, 153.9, 147.4, 134.8, 128.2, 109.1, 107.7, 91.1-94.2, 67.4, 56.5, 56.3. FT-IR (KBr, thin film): 3034, 2968, 1763, 1583, 1522, 1500, 1456, 1217, 974, 746, 696 cm^{-1}. SEC: M_n = 2100 Da, M_w = 3500 Da, *Đ* = 1.6. T_g = 12 ºC.

Copolymerization of ethyl glyoxylate and methyl glyoxylate with NVOC-Cl as end-cap (polymer **14**)

Freshly distilled methyl glyoxylate (4.0 mL, 50 mmol, 1.0 equiv.) and ethyl glyoxylate (4.0 mL, 40 mmol, 0.8 equiv.) were dissolved in dichloromethane (8.0 mL) and Et_3N (12.6 µL, 90 µmol, 0.001 equiv.). After the solution was stirred for one hour at -20 ºC, Et_3N (0.2 mL, 1.5 mmol, 0.03 equiv.) and NVOC-Cl (0.4 g, 1.5 mmol, 0.03 equiv.) were added into the mixture to end-cap the polymer. The solution was then stirred for 24 hours at room temperature and a further 16 hours at 40 ºC. Purification was achieved by precipitation of the crude reaction mixture into methanol. After decanting the excess methanol, the residue was dried *in vacuo* for 48 hours to provide polymer **14** (4.8 g, 57%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.75 (s, 3H), 7.09 (s, 2), 5.48-5.78 (m, 770H), 4.16-4.32 (m, 840H), 4.05 (s, 6H), 3.97 (s, 6H), 3.73-3.86 (m, 1072H), 1.21-1.39 (m, 1253H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 164.6-166.8, 148.1, 107.9, 90.1-94.4, 66.8, 61.9, 56.2, 52.5, 13.6. FT-IR (KBr, thin film): 2960, 1759, 1445, 1377, 1016 cm^{-1}. SEC: M_n = 40 kDa, M_w = 81 kDa, $Đ$ = 2.0. T_g = 15 ºC.

Copolymerization of ethyl glyoxylate and *n*-butyl glyoxylate with NVOC-Cl as end-cap (polymer **15**)

Freshly distilled *n*-butyl glyoxylate (3.0 mL, 25 mmol, 1.0 equiv.) and ethyl glyoxylate (4.0 mL, 40 mmol, 1.6 equiv.) were dissolved in dichloromethane (7.0 mL) and Et_3N (9.0 µL, 65 µmol, 0.001 equiv.). After the solution was stirred for one hour at -10 ºC, Et_3N (0.2 mL, 1.5 mmol, 0.023 equiv.) and NVOC-Cl (0.40 g, 1.5 mmol, 0.023 equiv.) were added into the mixture to end-cap the polymer. The solution was then stirred for 24 hours at room temperature and a further 16 hours at 40 ºC. After that the solvent was removed by high vacuum and the crude polymer was re-dissolved into DMF (5.0 mL) and dialyzed against DMF for 24 hours (200 mL, 2 solvent changes) and distilled water for 24 hours (200 mL, 2 solvent changes) using a regenerated cellulose membrane (6000-8000 Da MWCO). The residual content was then lyophilized to afford polymer **15** (3.4 g, 45%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.75 (s, 1.7H), 7.16 (s, 0.8H), 5.46-5.75 (m, 108H), 4.09-4.43 (m, 221H), 4.05 (s, 6H), 3.97 (s, 6H), 1.57-1.73 (m, 72H), 1.17-1.46 (m, 294H), 0.84-0.99 (m, 95H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 164.7-166.7, 153.7, 148.2, 141.4, 126.7, 109.9, 107.9, 90.4-94.5, 66.8, 65.7, 61.9, 56.7, 56.3, 30.2, 18.8, 13.8,13.6. FT-IR (KBr, thin film): 2964, 2939, 2876, 1765, 1468, 1381, 1219, 1024 cm^{-1}. SEC: M_n = 11 kDa, M_w = 22 kDa, $Đ$ = 2.0. T_g = -10 ºC.

Polymerization of ethyl glyoxylate with compound **18** as end-cap (polymer **19**)

Poly(ethyl glyoxylate) was prepared as described for polymer **1**. Following polymerization, but prior to precipitation, compound **18** (0.22 g, 730 μmol, 0.014 equiv.) was added at 0 ºC to end-cap the polymer along with Et_3N (100 μL, 730 μmol, 0.014 equiv.). The solution was stirred for 24 hours at room temperature and a further 16 hours at 40 ºC. Purification was achieved by precipitation of the crude reaction mixture into methanol. After decanting the excess methanol, the residue was dried *in vacuo* for 48 hours to provide polymer **19** (2.8 g, 56%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.65 (s, 1.9H), 8.19 (s, 2H), 7.82 (s, 2.8H), 5.46-5.71 (m, 627H), 4.12-4.30 (m, 1303H), 2.29 (s, 4H), 1.12-1.40 (m, 1949H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 169.4, 164.9-166.7, 128.3, 90.9-94.5, 81.7, 62.9, 62.2, 29.9, 13.9. FT-IR (KBr, thin film): 2988, 1759, 1468, 1379, 1021, 1028 cm^{-1}. SEC: M_n = 42 kDa, M_w = 89 kDa, $Đ$ = 2.1.

Coupling of polymer **19** with polymer **20** (polymer **21**)

Polymer **20**[6] (150 mg, 75 µmol, 3 equiv.) and polymer **19** (500 mg, 25 µmol, 1 equiv.) were dissolved into DMF (5 mL). After removing the air and refilling with argon, $CuSO_4$ (4 mg, 25 µmol, 1 equiv.) and sodium ascorbate (5 mg, 25 µmol, 1 equiv.) were added into the solution, and the mixture was stirred at 40 ºC for 16 hours. Then it was transferred into a regenerated cellulose membrane (50 kDa MWCO) and dialyzed against deionized water for 48 hours (300 mL, 6 solvent changes). The dialyzed material was then lyophilized to afford polymer **21** (430 mg, 79%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.47-5.75 (m, 421H), 4.15-4.31 (m, 769H), 3.65 (s, 364H), 3.39 (s, 6H), 1.17-1.40 (m, 1152H). Note - aromatic peaks are not sufficiently differentiated from the noise to perform integration. ^{13}C NMR (150 MHz, $CDCl_3$): δ 164.7-166.3, 127.5, 124.1, 90.8-93.9, 71.8, 70.5, 62.0, 13.7. FT-IR (KBr, thin film): 2985, 2941, 2908, 2876, 1759, 1447, 1377, 1231, 1021 cm^{-1}. SEC: M_n = 40 kDa, M_w = 85 kDa, $Đ$ = 2.1. T_g = -5 ºC.

IV. NMR spectra

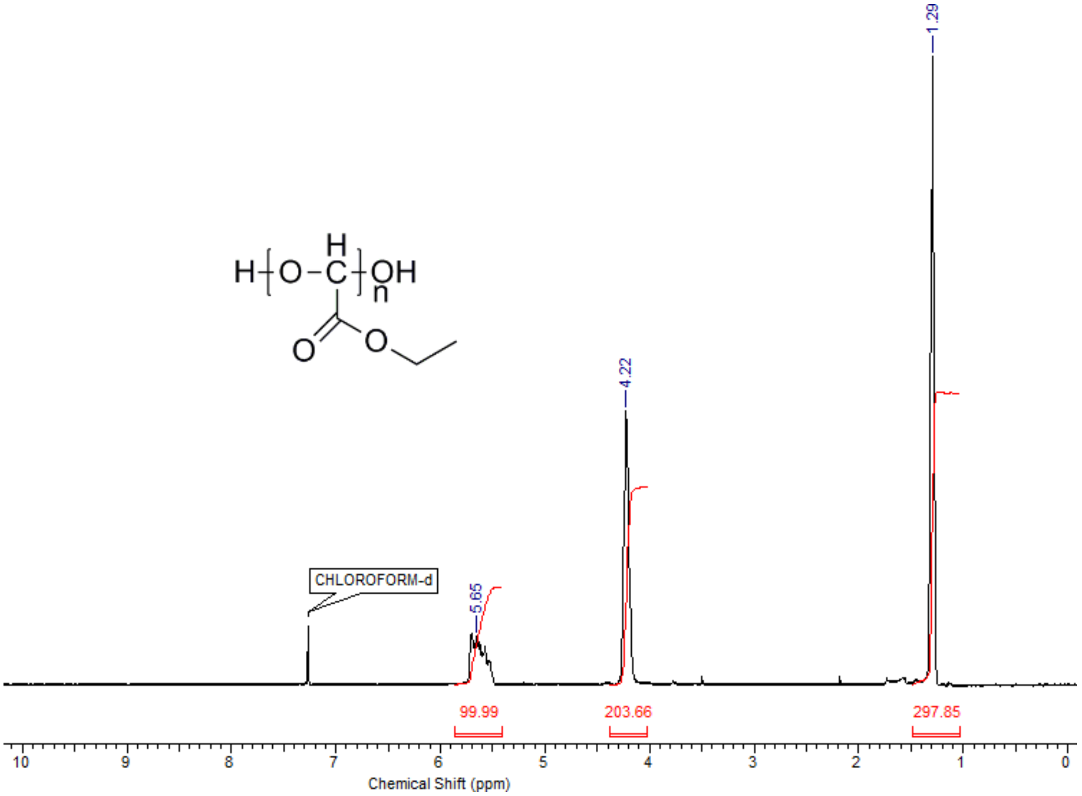

Figure S1. ^{1}H NMR spectrum of poly(ethyl glyoxylate) without end cap (Polymer **1**) ($CDCl_3$, 400 MHz).

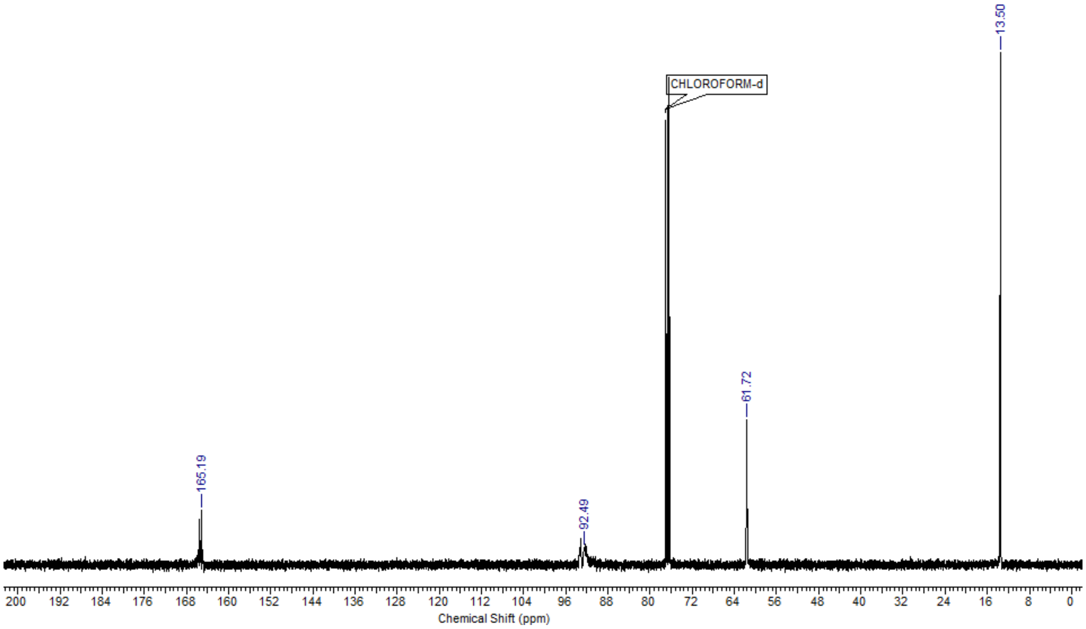

Figure S2. ^{13}C NMR spectrum of poly(ethyl glyoxylate) without end cap (Polymer **1**) ($CDCl_3$, 150 MHz).

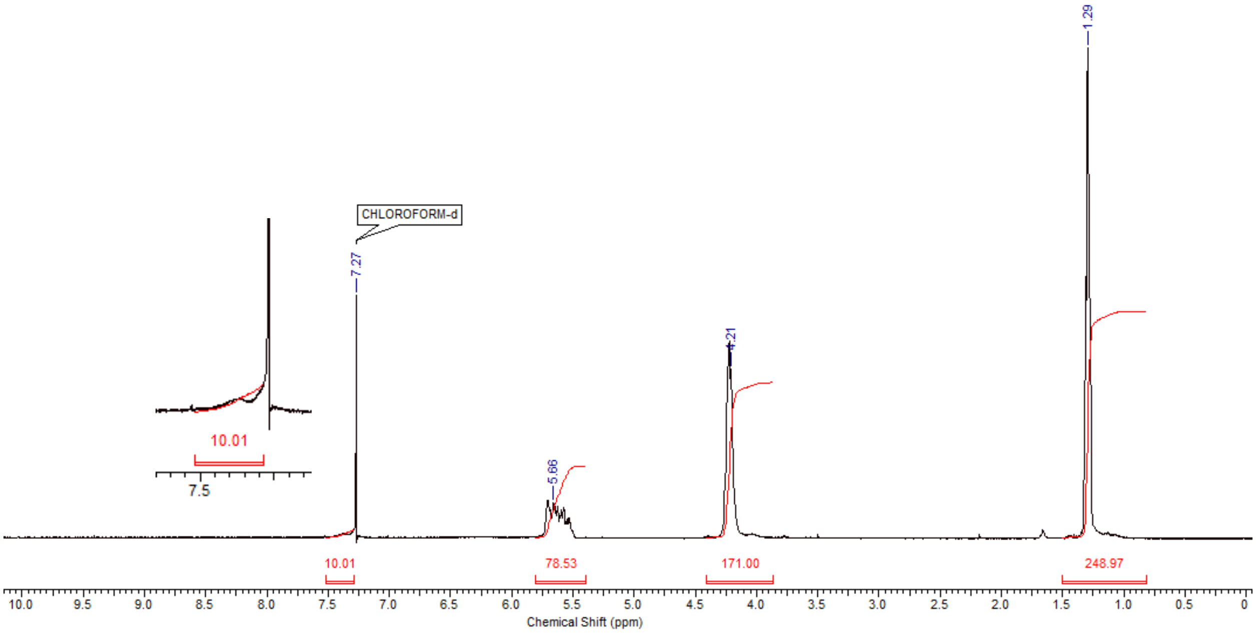

Figure S3. ^{1}H NMR spectrum of poly(ethyl glyoxylate) end capped by phenyl isocyanate (Polymer **2**) ($CDCl_3$, 400 MHz). Integration of the end cap peak from 7.2-7.5 ppm is inaccurate due to overlap with the $CHCl_3$ peak.

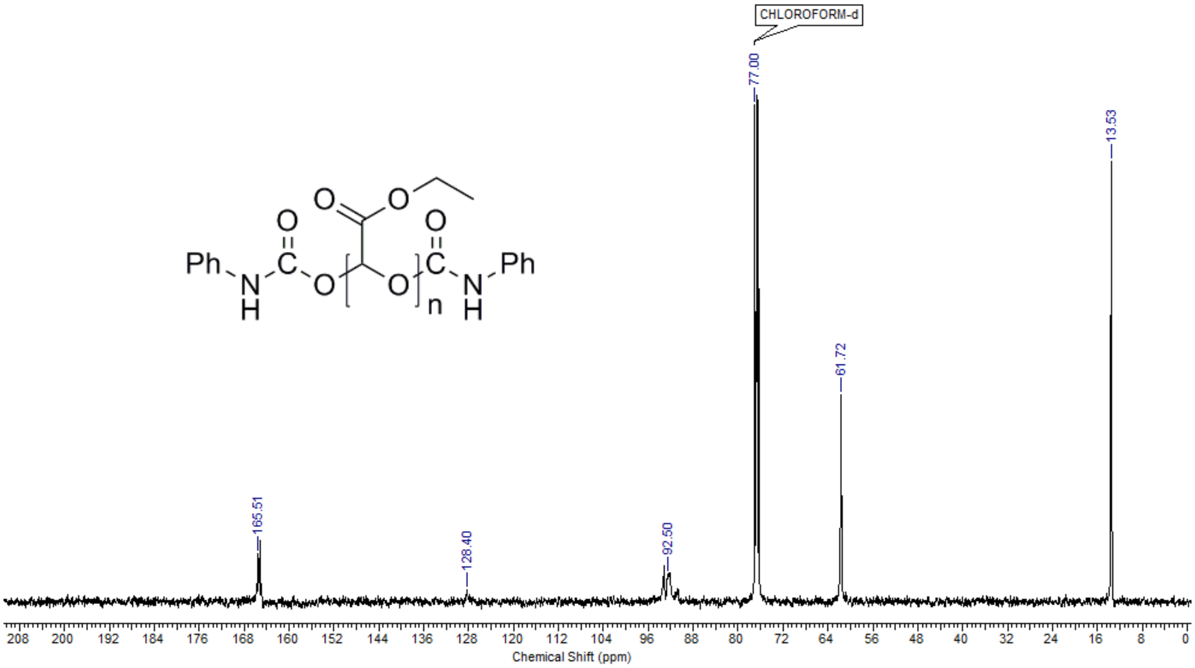

Figure S4. ^{13}C NMR spectrum of poly(ethyl glyoxylate) end capped by phenyl isocyanate (Polymer **2**) ($CDCl_3$, 150 MHz).

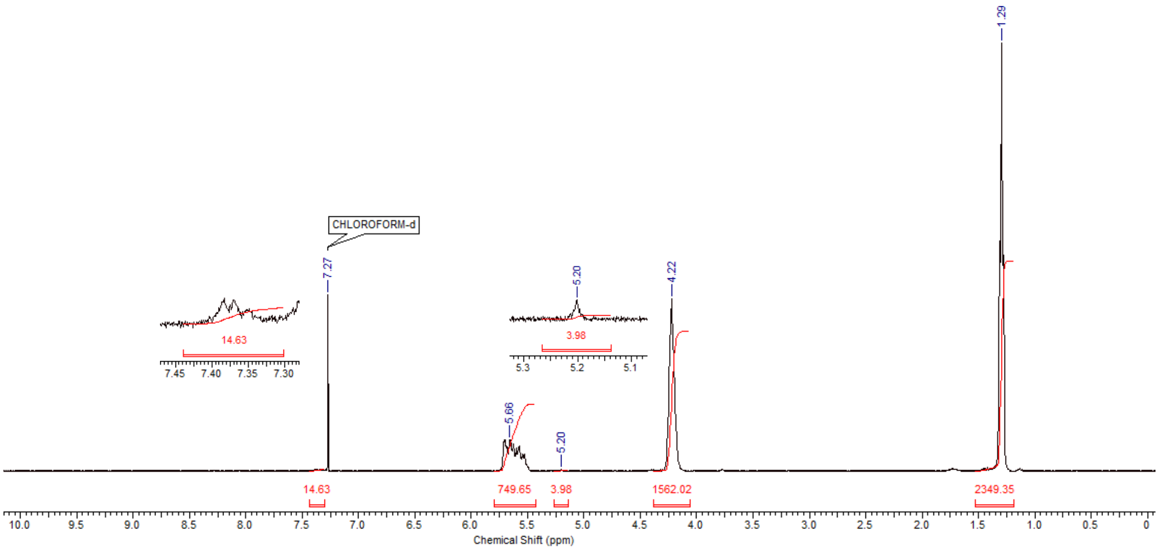

Figure S5. ^{1}H NMR spectrum of poly(ethyl glyoxylate) end capped by benzyl chloroformate (Polymer **3**) ($CDCl_3$, 400 MHz).

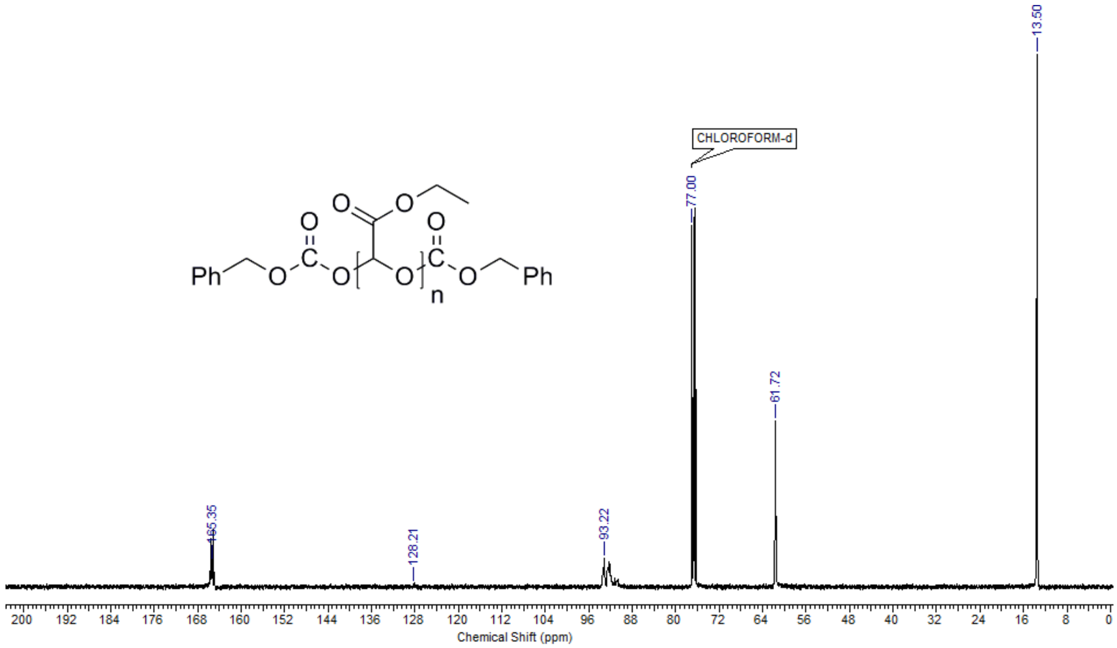

Figure S6. ^{13}C NMR spectrum of poly(ethyl glyoxylate) end capped by benzyl chloroformate (Polymer **3**) ($CDCl_3$, 150 MHz).

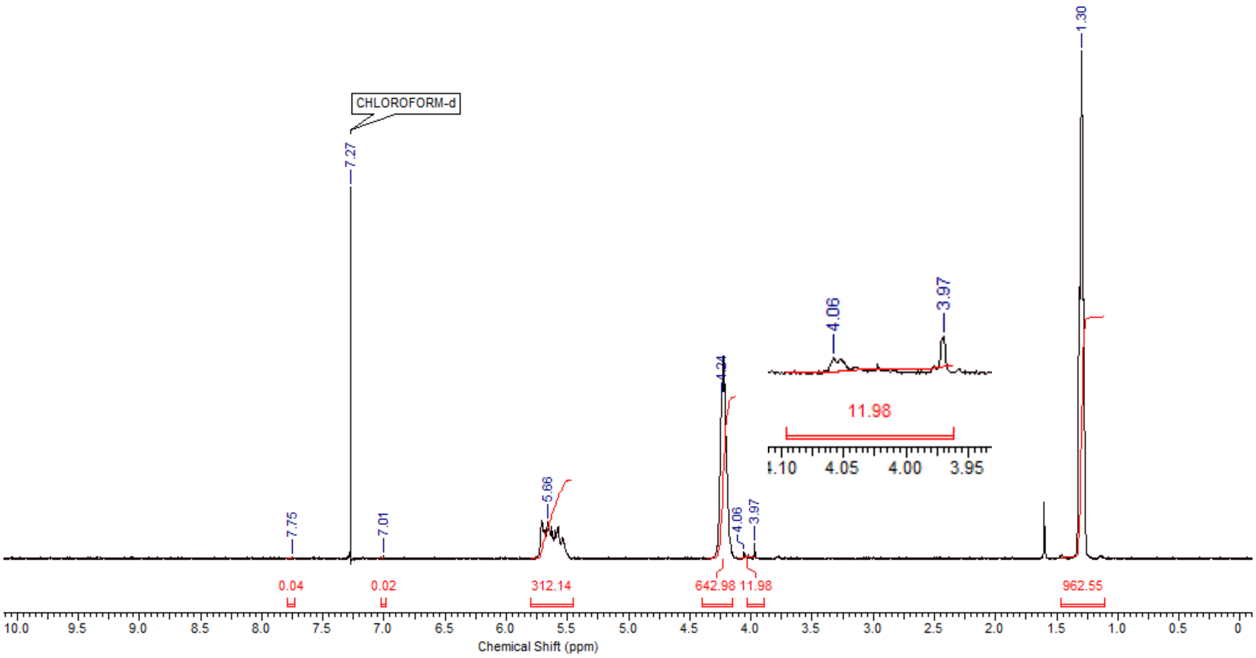

Figure S7. ^{1}H NMR spectrum of poly(ethyl glyoxylate) end capped by NVOC-Cl (Polymer **4**) ($CDCl_3$, 400 MHz).

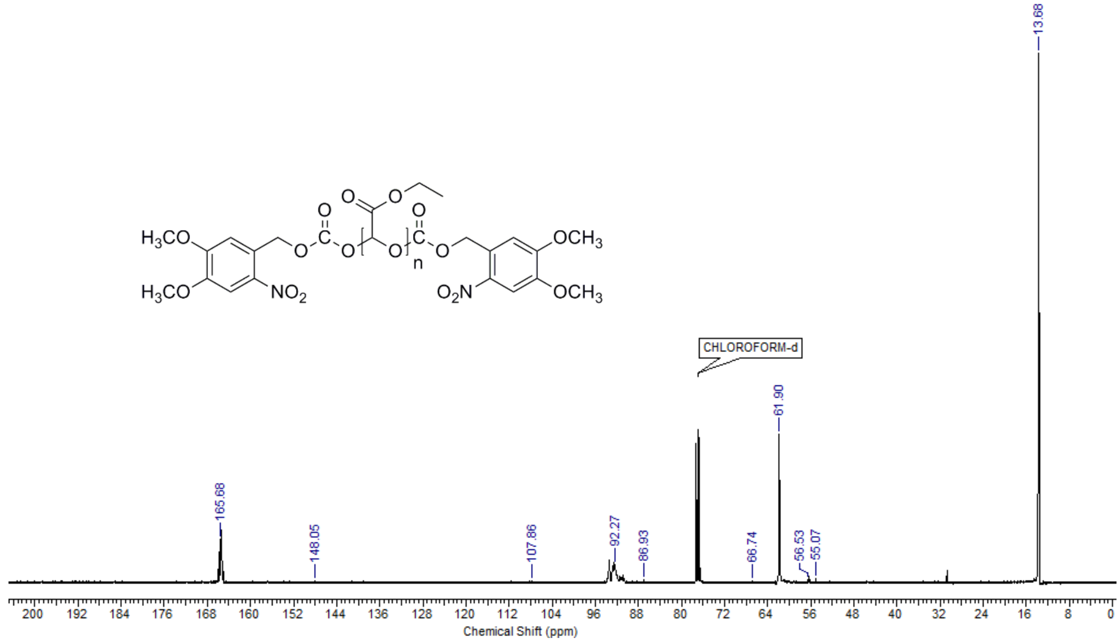

Figure S8. ^{13}C NMR spectrum of poly(ethyl glyoxylate) end capped by NVOC-Cl (Polymer **4**) ($CDCl_3$, 150 MHz).

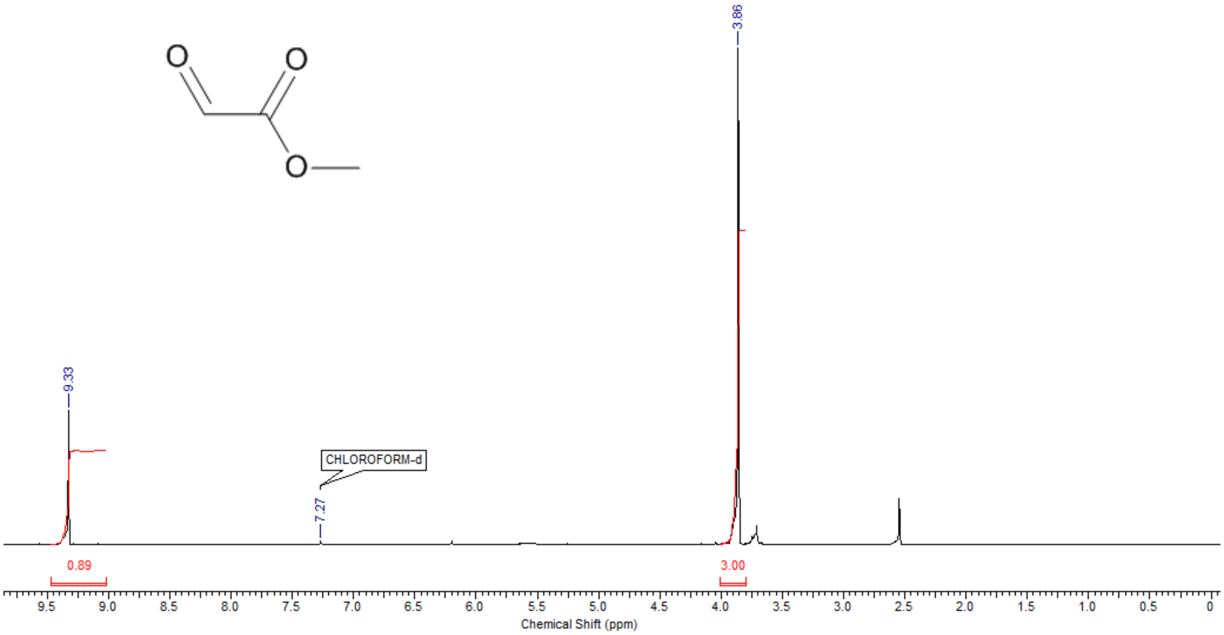

Figure S9. ^{1}H NMR spectrum of methyl glyoxylate compound **8** ($CDCl_3$, 400 MHz).

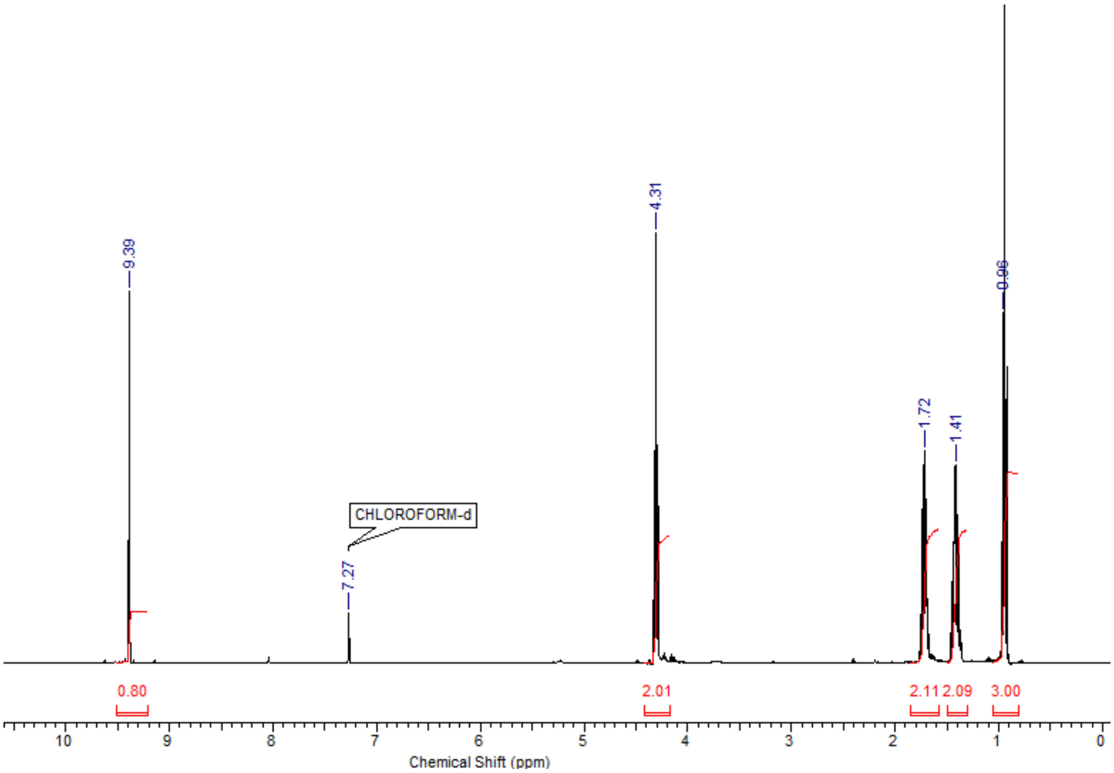

Figure S10. ^{1}H NMR spectrum of *n*-butyl glyoxylate compound **9** ($CDCl_3$, 400 MHz).

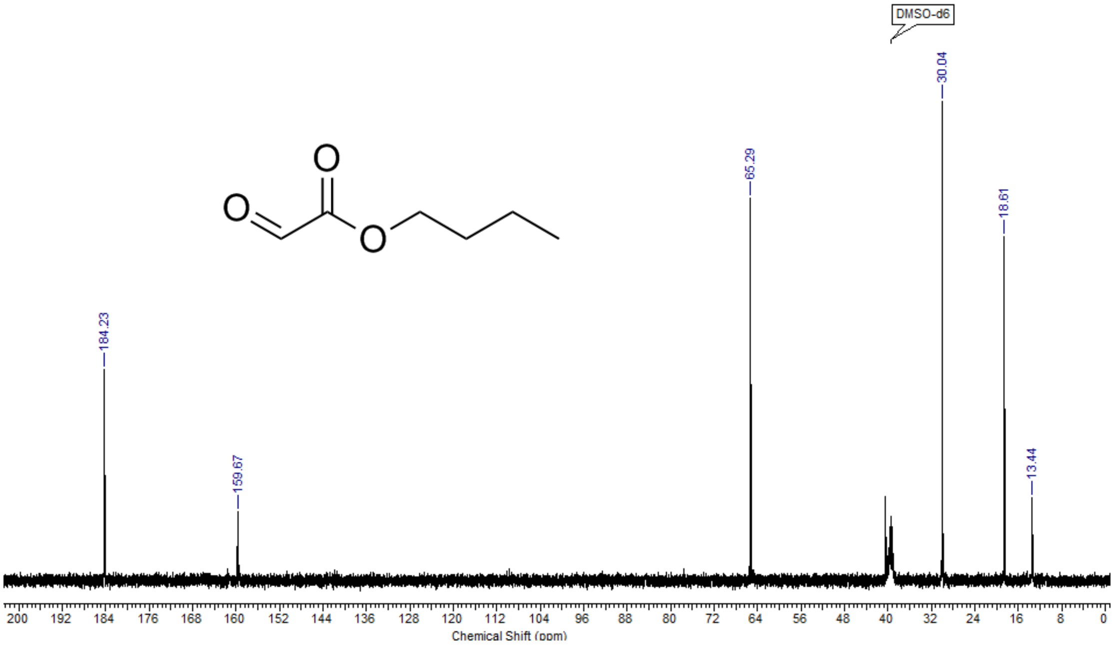

Figure S11. ${}^{13}C$ NMR spectrum of *n*-butyl glyoxylate compound **9** ($CDCl_3$, 150 MHz).

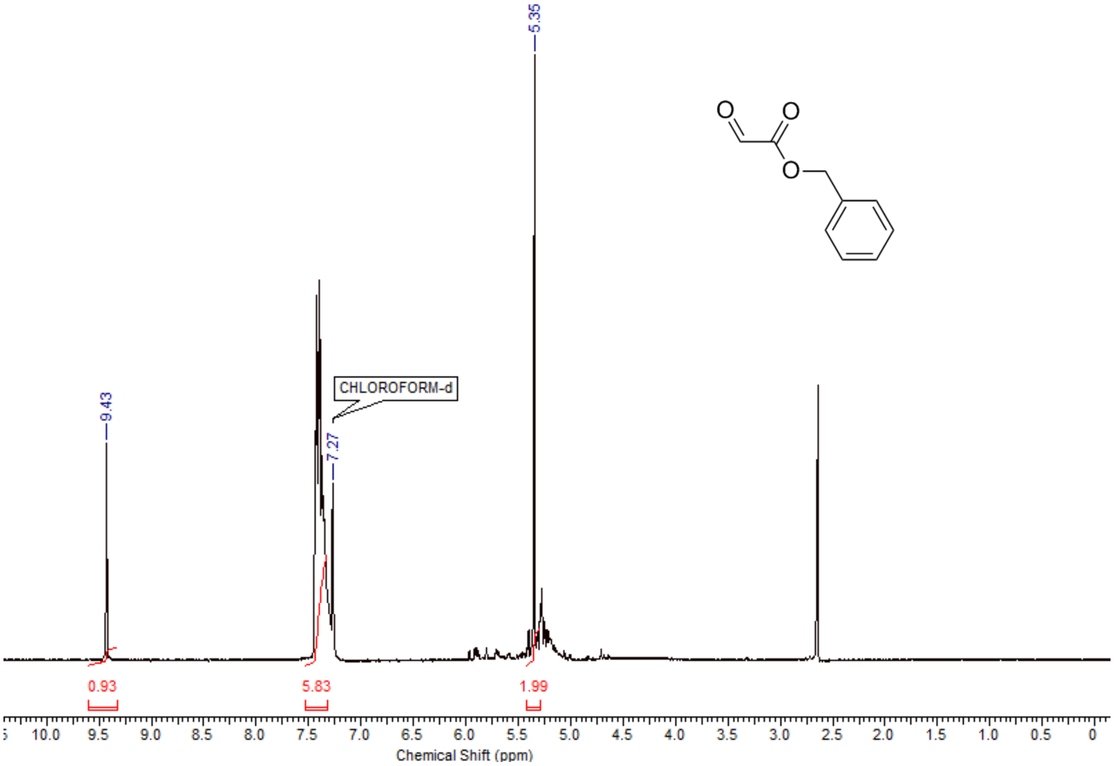

Figure S12. ${}^{1}H$ NMR spectrum of benzyl glyoxylate compound **10** ($CDCl_3$, 400 MHz).

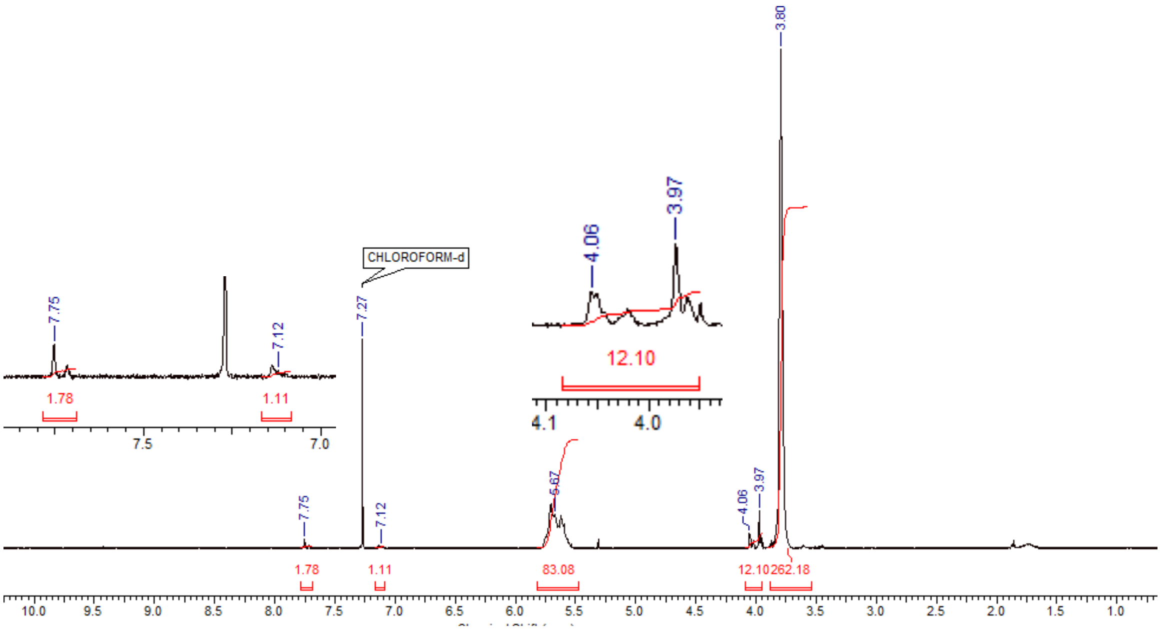

Figure S13. ^{1}H NMR spectrum of poly(methyl glyoxylate) end capped by NVOC-Cl (Polymer **11**) ($CDCl_3$, 400 MHz).

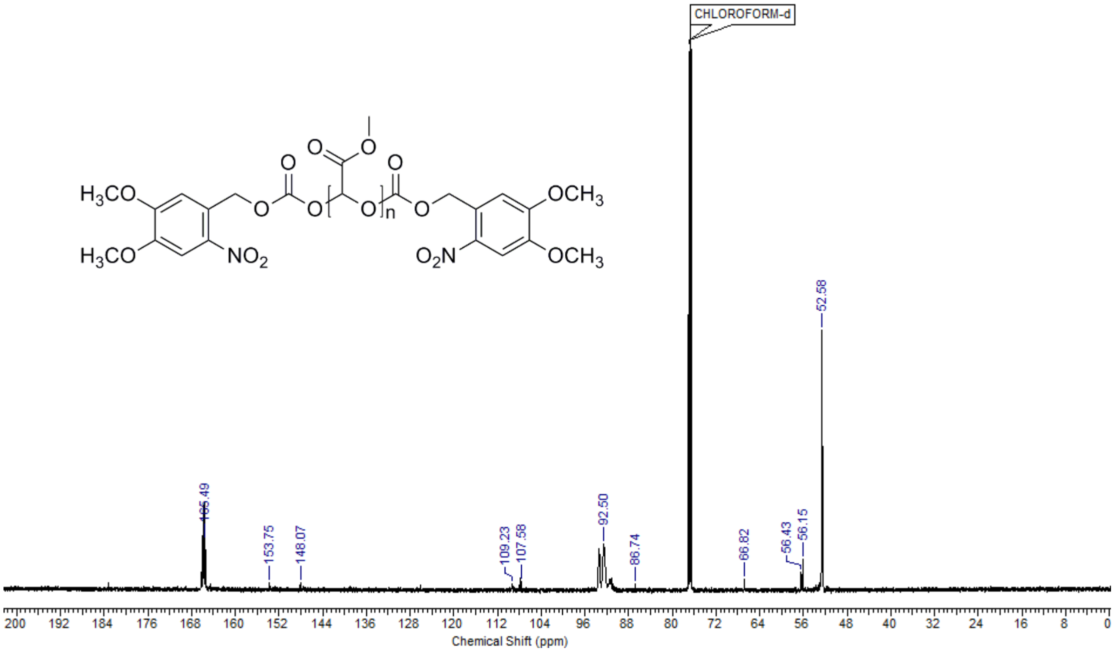

Figure S14. ^{13}C NMR spectrum of poly(methyl glyoxylate) end capped by NVOC-Cl (Polymer **11**) ($CDCl_3$, 150 MHz).

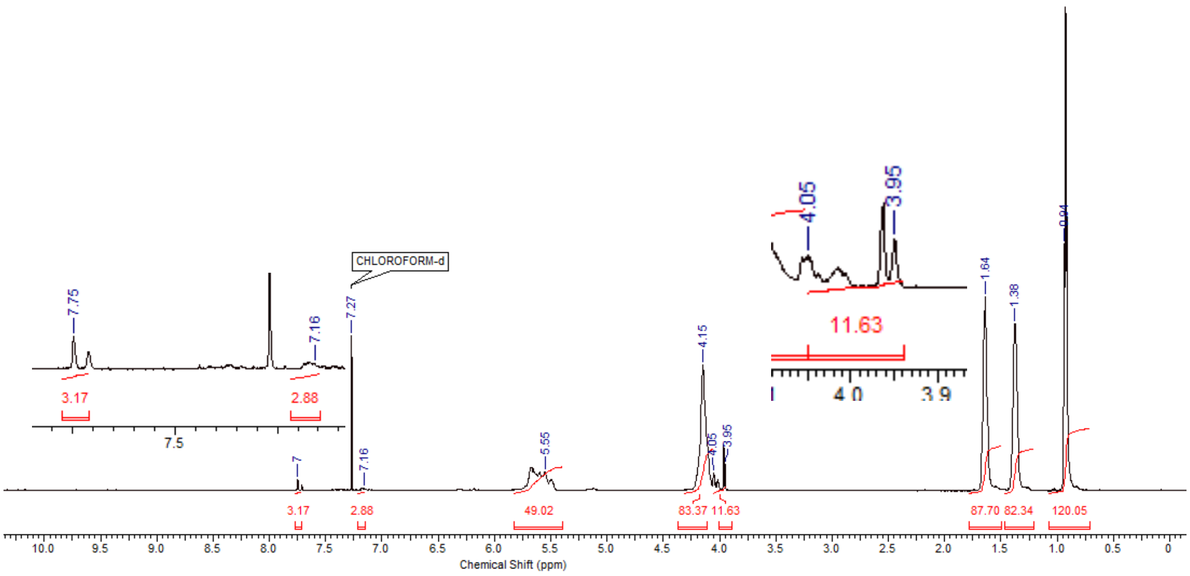

Figure S15. ^{1}H NMR spectrum of poly(butyl glyoxylate) end capped by NVOC-Cl (Polymer **12**) ($CDCl_3$, 400 MHz).

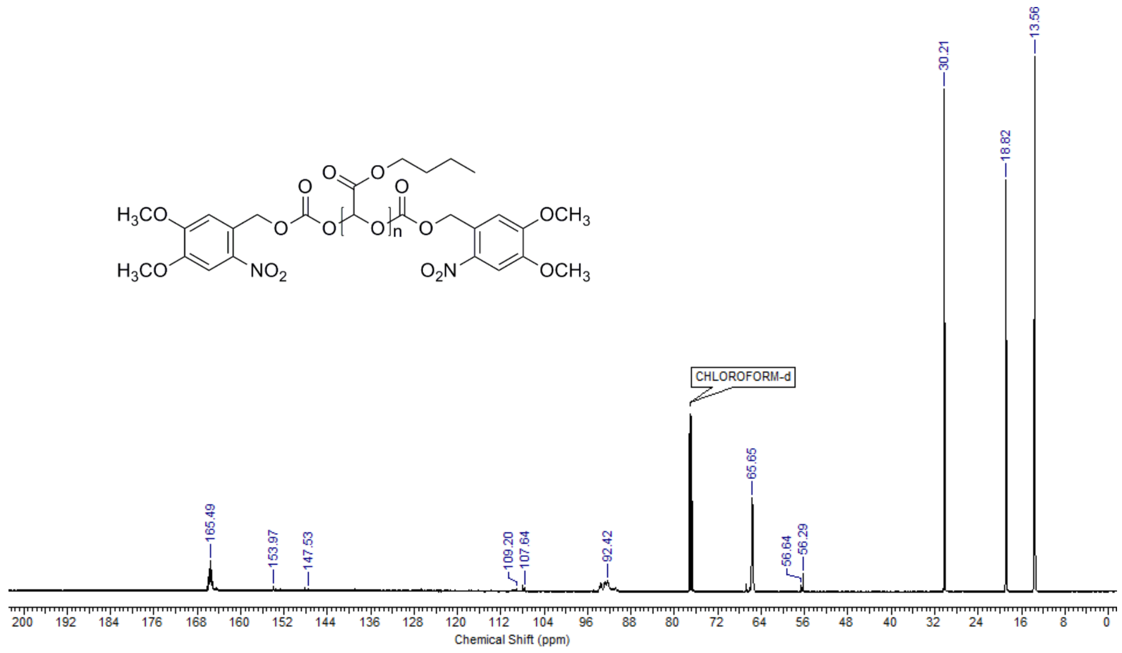

Figure S16. ^{13}C NMR spectrum of poly(butyl glyoxylate) end capped by NVOC-Cl (Polymer **12**) ($CDCl_3$, 150 MHz).

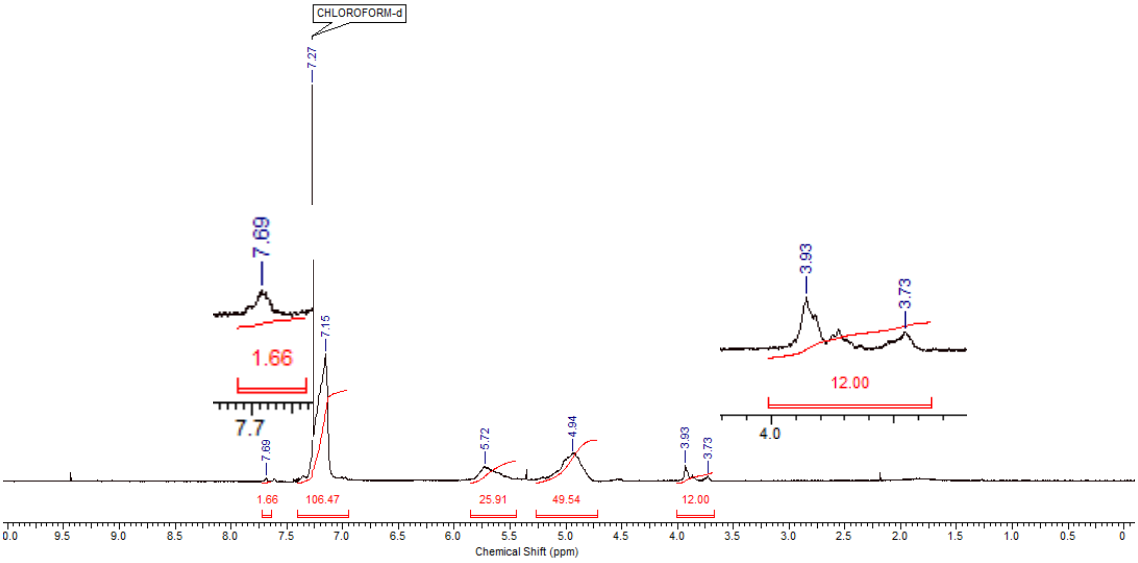

Figure S17. ${}^{1}H$ NMR spectrum of poly(benzyl glyoxylate) end capped by NVOC-Cl (Polymer **13**) ($CDCl_3$, 400 MHz).

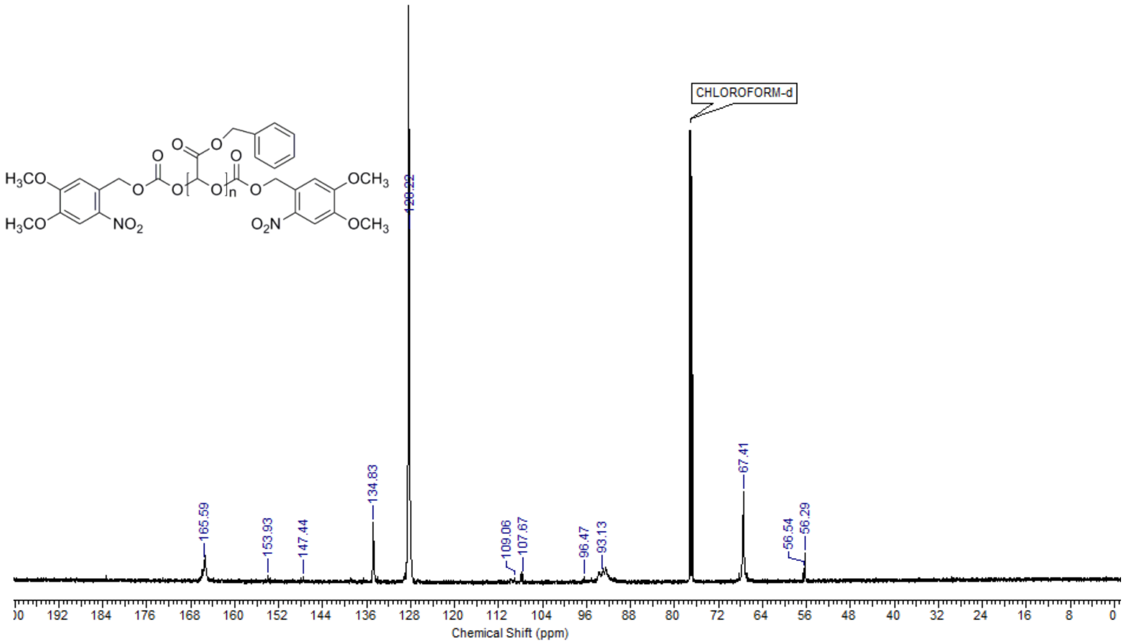

Figure S18. ${}^{13}C$ NMR spectrum of poly(benzyl glyoxylate) end capped by NVOC-Cl (Polymer **13**) ($CDCl_3$, 150 MHz).

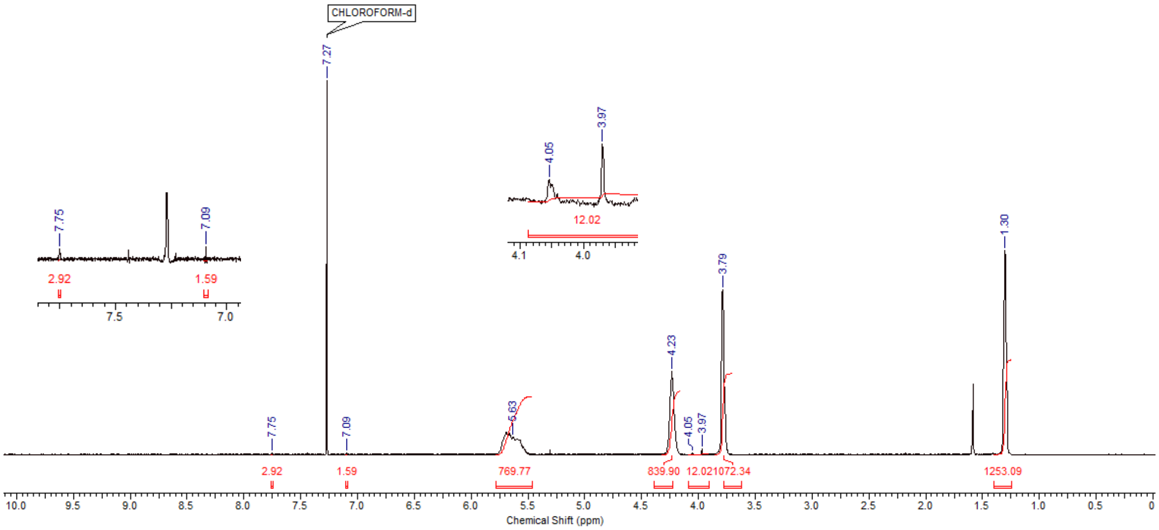

Figure S19. ^{1}H NMR spectrum of poly(ethyl glyoxylate)-*co*-(methyl glyoxylate) end capped by NVOC-Cl (Polymer **14**) (CDCl$_3$, 400 MHz).

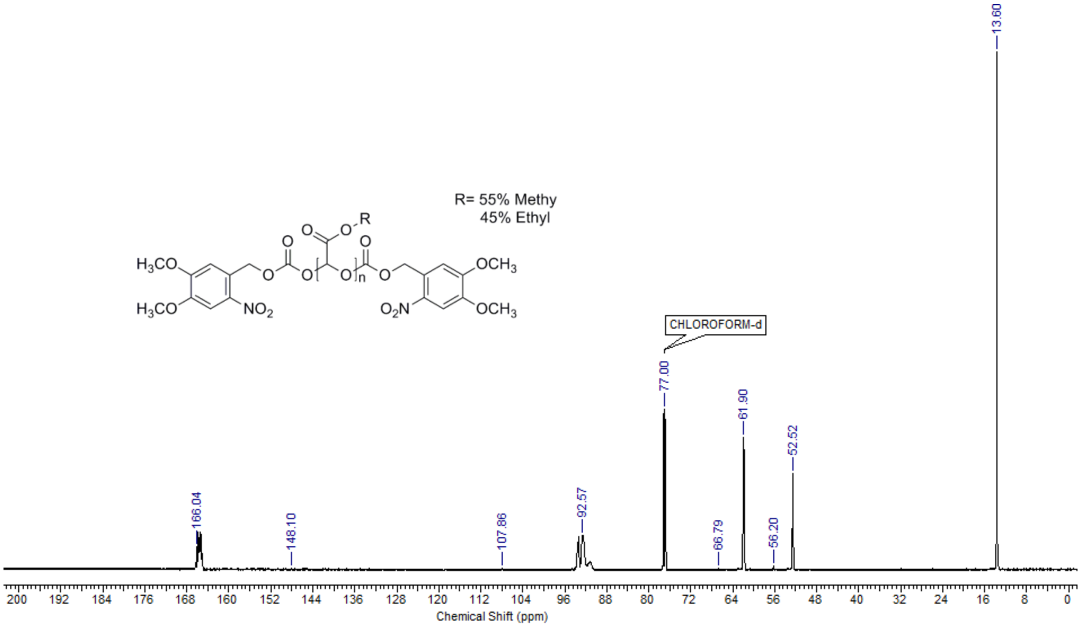

Figure S20. ^{13}C NMR spectrum of poly(ethyl glyoxylate)-*co*-(methyl glyoxylate) end capped by NVOC-Cl (Polymer **14**) (CDCl$_3$, 150 MHz).

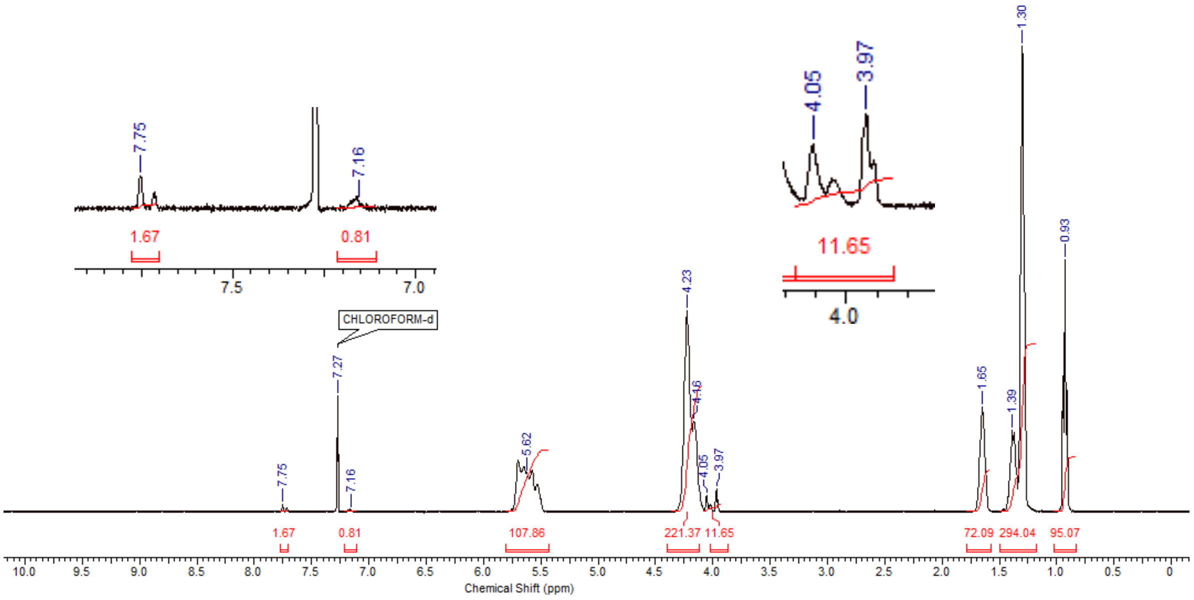

Figure S21. ^{1}H NMR spectrum of poly(ethyl glyoxylate)-*co*-(butyl glyoxylate) end capped by NVOC-Cl (Polymer **15**) ($CDCl_3$, 400 MHz).

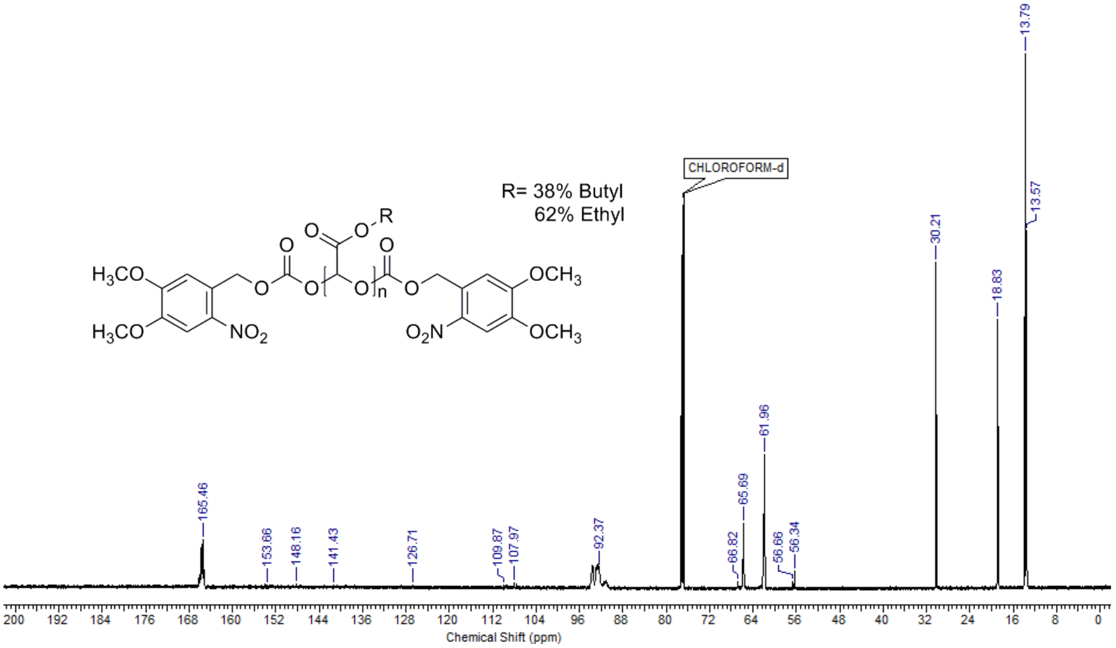

Figure S22. ^{13}C NMR spectrum of poly(ethyl glyoxylate)-*co*-(butyl glyoxylate) end capped by NVOC-Cl (Polymer **15**) ($CDCl_3$, 150 MHz).

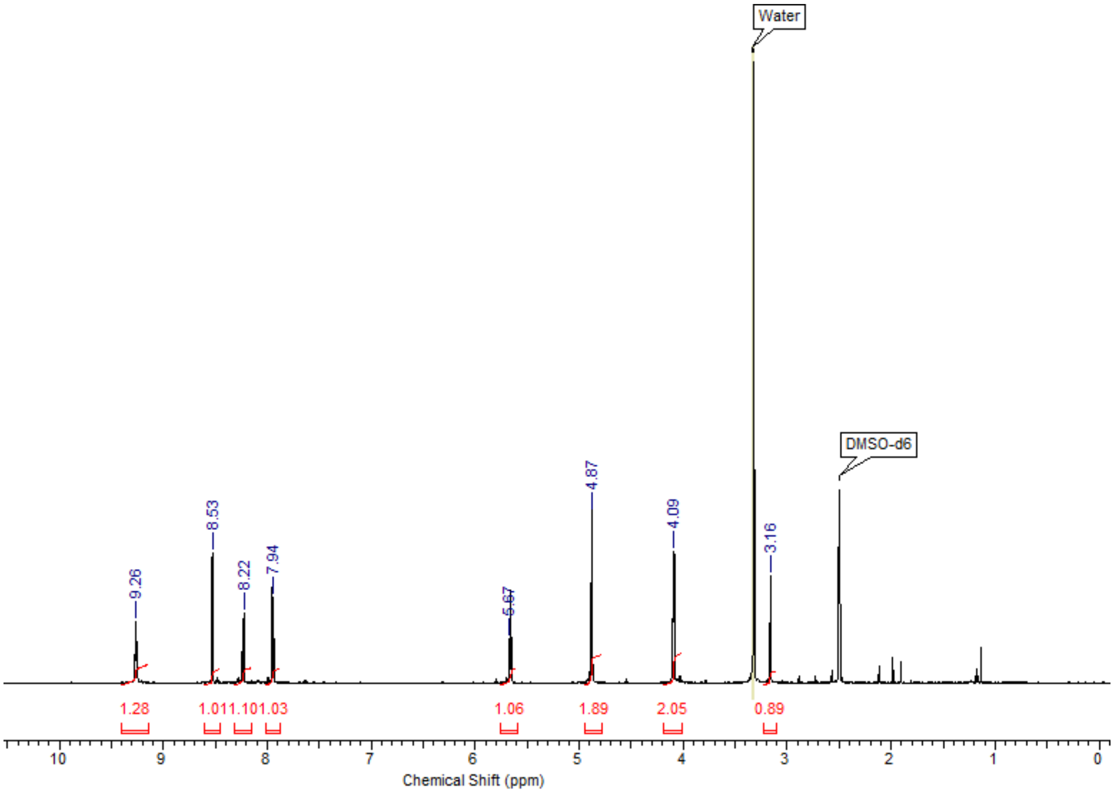

Figure S23. ^{1}H NMR spectrum of compound **17** (DMSO-*d6*, 400 MHz).

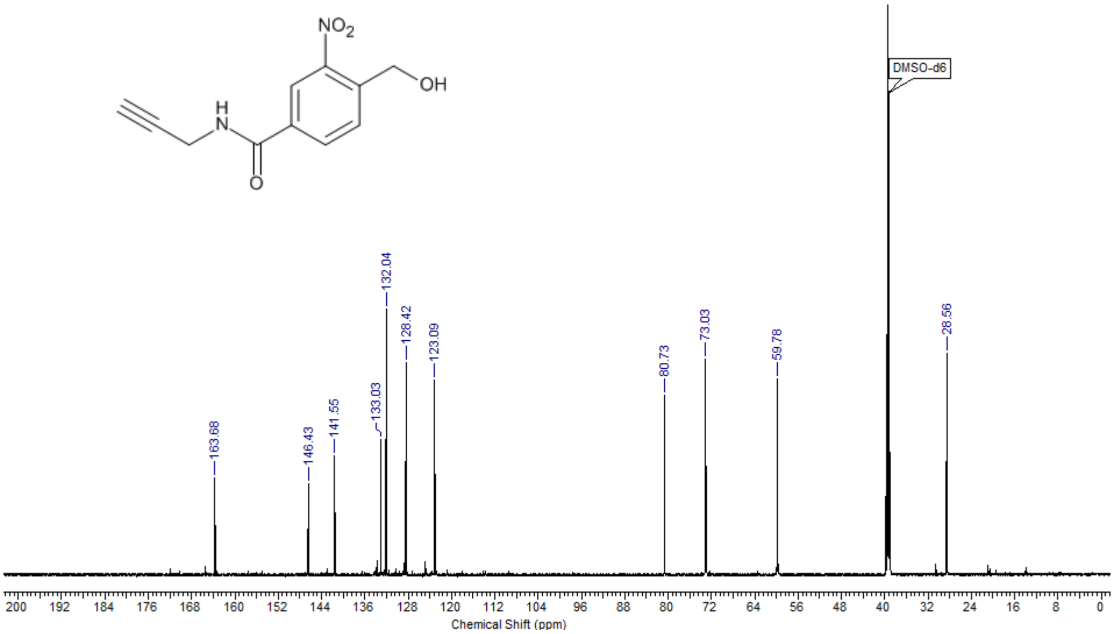

Figure S24. ^{13}C NMR spectrum of compound **17** (DMSO-*d6*, 150 MHz).

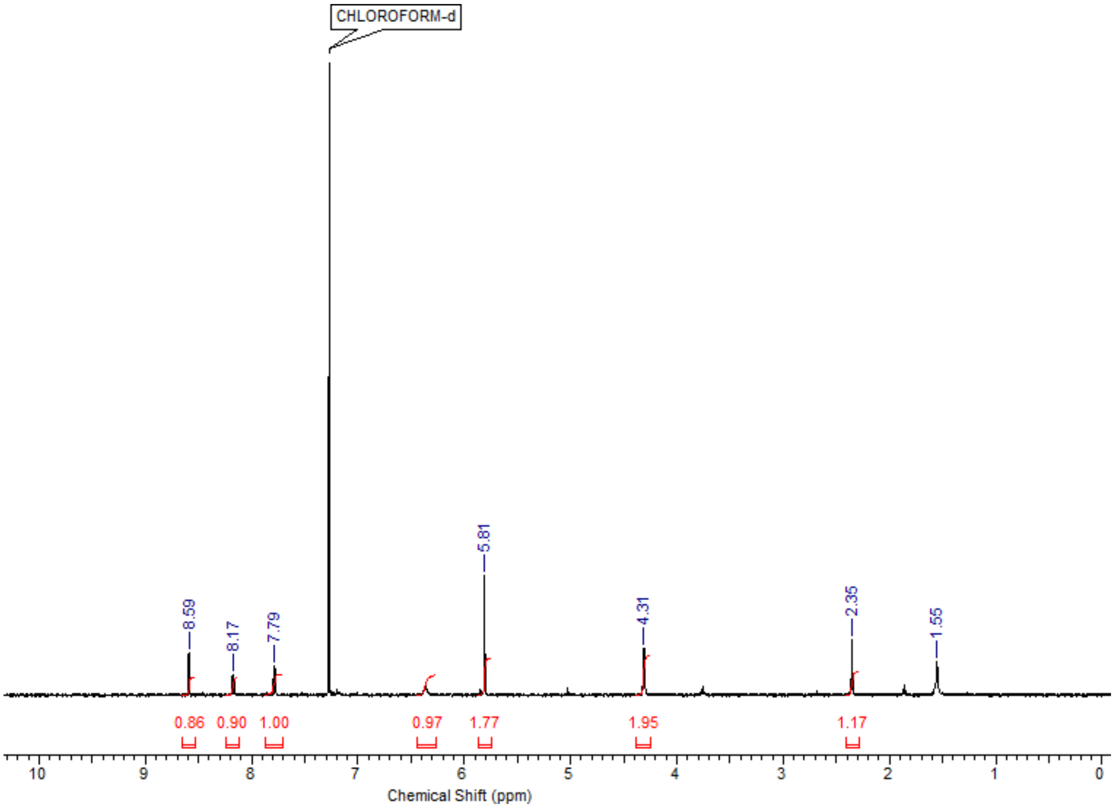

Figure S25. ^{1}H NMR spectrum of compound **18** ($CDCl_3$, 400 MHz).

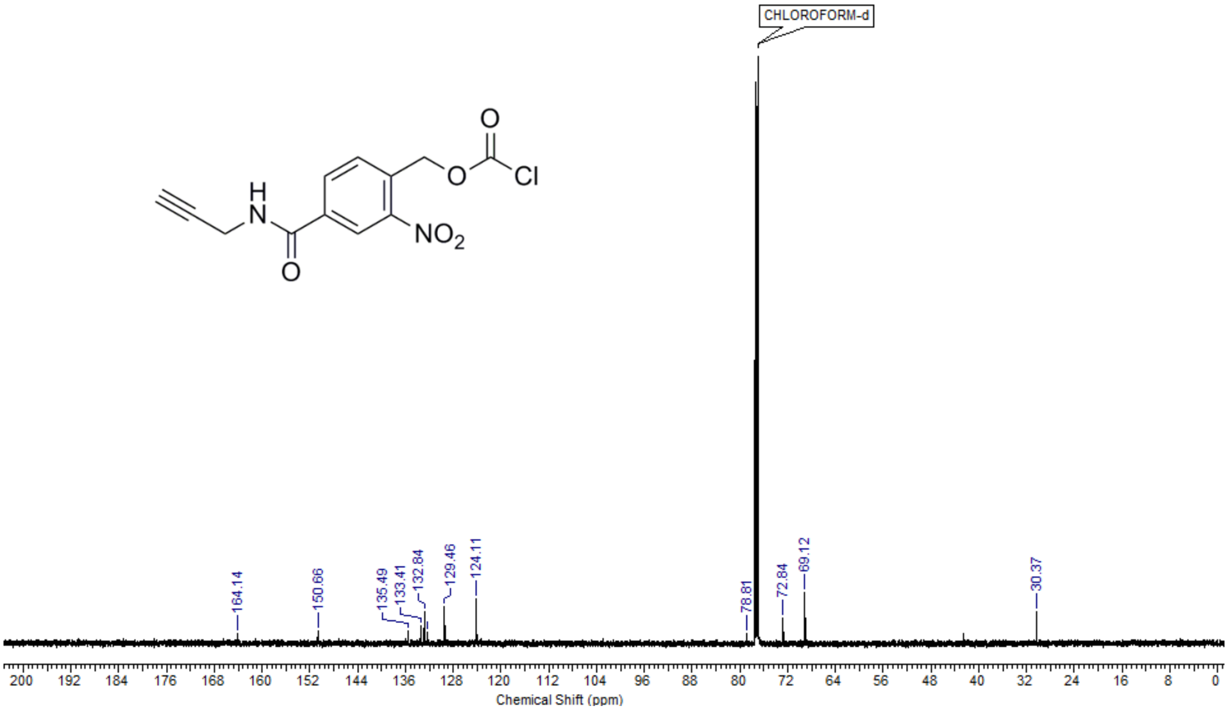

Figure S26. ^{13}C NMR spectrum of compound **18** ($CDCl_3$, 150 MHz).

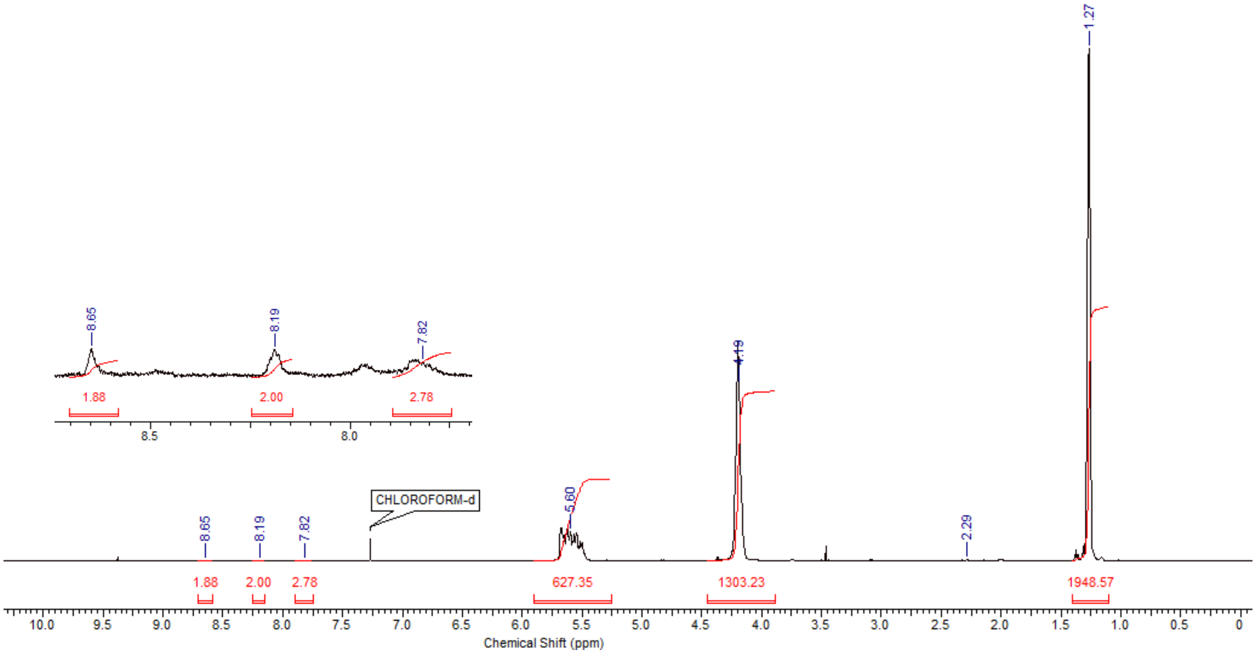

Figure S27. ^{1}H NMR spectrum of poly(ethyl glyoxylate) end capped by compound **18** (Polymer **19**) ($CDCl_3$, 400 MHz).

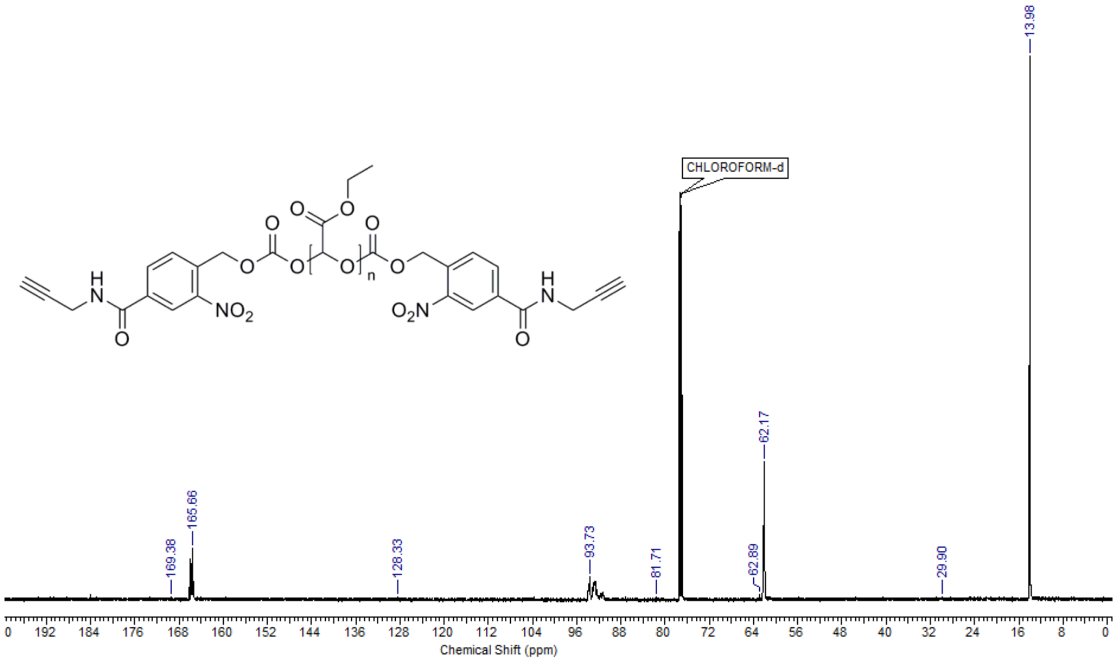

Figure S28. ^{13}C NMR spectrum of poly(ethyl glyoxylate) end capped by compound **18** (Polymer **19**) ($CDCl_3$, 150 MHz).

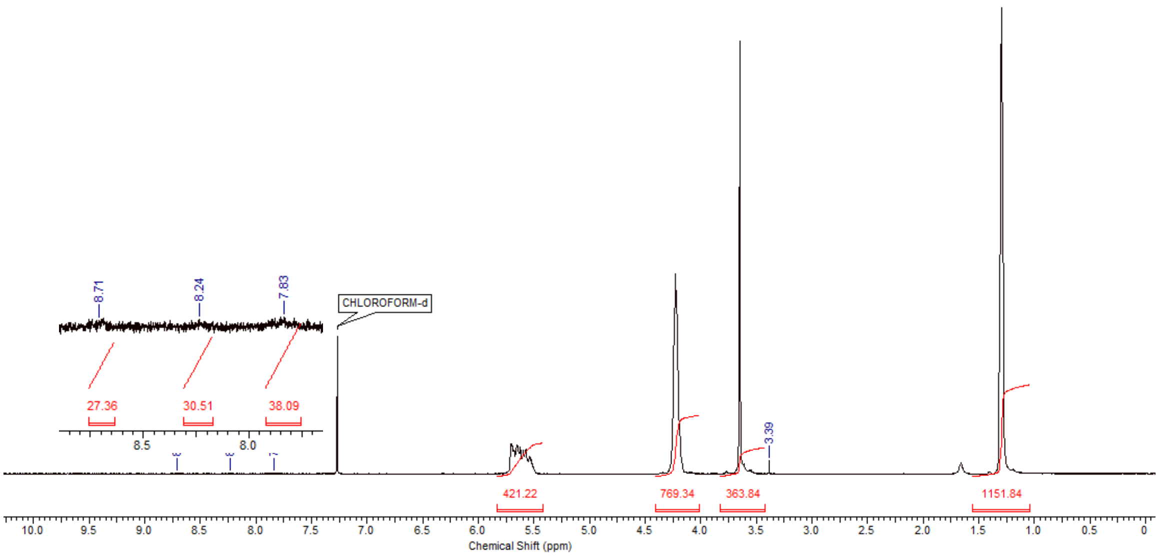

Figure S29. ^{1}H NMR spectrum of block polymer (Polymer **21**) ($CDCl_3$, 400 MHz). As accurate integration of the aromatic peaks is not possible, the PEG "end-cap" peak at 3.65 ppm was integrated corresponding to 2 × 2 kDa chains.

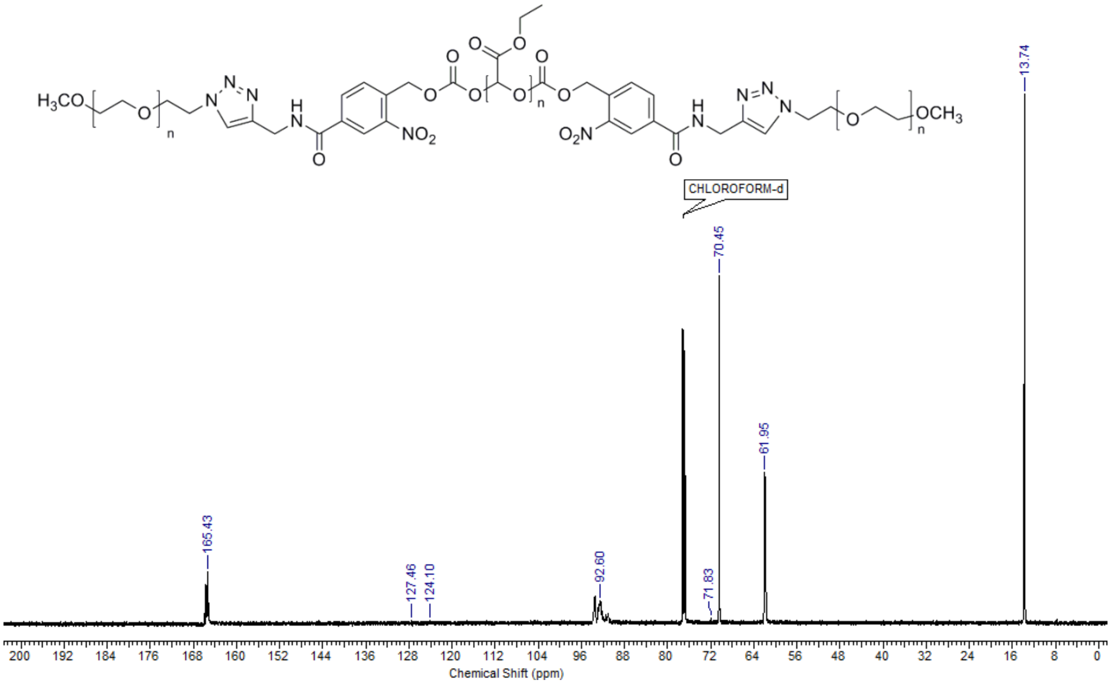

Figure S30. ^{13}C NMR spectrum of block polymer (Polymer **21**) ($CDCl_3$, 150 MHz).

V. Summary of polyglyoxylate M_n results obtained by ^{1}H NMR spectroscopy

Table S1. Summary of M_n calculated based on ^{1}H NMR spectroscopy versus SEC. M_ns based on NMR spectra were calculated according to the following equation: M_n = (degree of polymerization (DP) × monomer molar mass) + (end-cap molar mass × 2). DP was determined as the integration of the peak at 5.6 ppm after setting the integration of the end-cap peak to the appropriate value corresponding to an end-cap at each terminus. It should be noted that the accuracy of NMR integration is limited when the DP is > 200 due to limitations of NMR, so M_n values measured by this technique mainly provide confirmation that high molar mass polymers were obtained. [a]End-cap integration is not possible due to no end-cap. [b]End-cap integration is not possible due to overlap with the residual NMR solvent ($CHCl_3$) peak.

Polymer	M_n (NMR) (kDa)	M_n (SEC) (kDa)
1[a]	**----**	103
2[b]	**----**	27
3	79	31
4	32	53
11	7.3	3.8
12	6.3	5.0
13	4.3	2.1
14	69	40
15	13	11
19	64	42
21	43	40

VI. Representative SEC traces of polymers

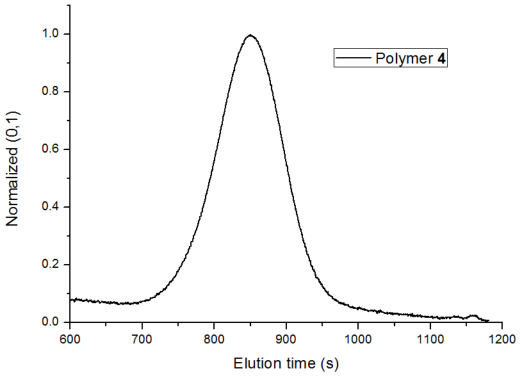

Figure S31. SEC trace for Polymer **4**.

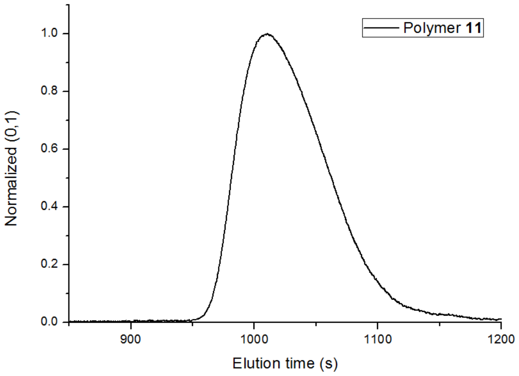

Figure S32. SEC trace for Polymer **11**.

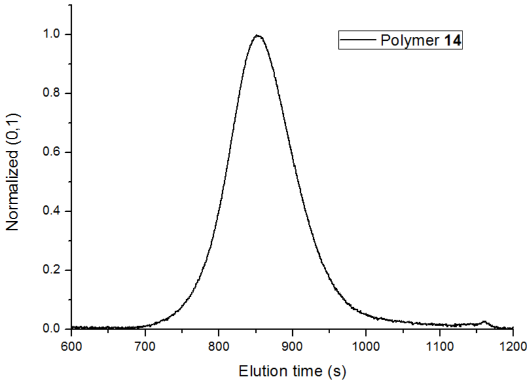

Figure S33. SEC curve of Polymer **14**.

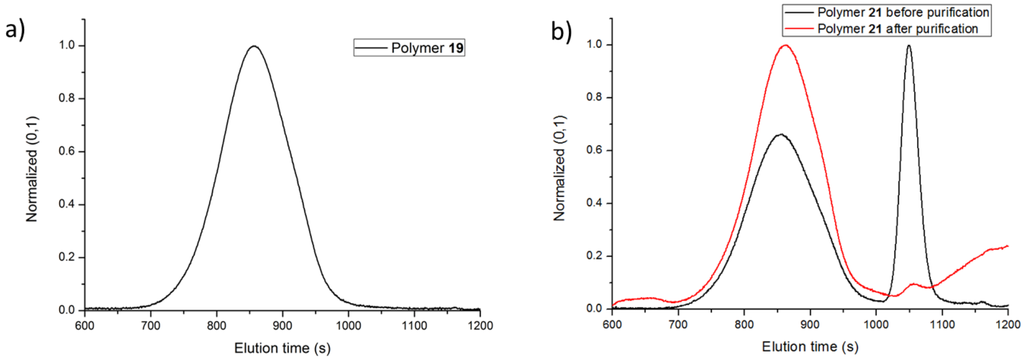

Figure S34. SEC traces for a) polymers **19** and b) polymer **21** both before and after purification, showing effective removal of all but trace levels of uncoupled PEG.

VII. TGA of polyglyoxylates

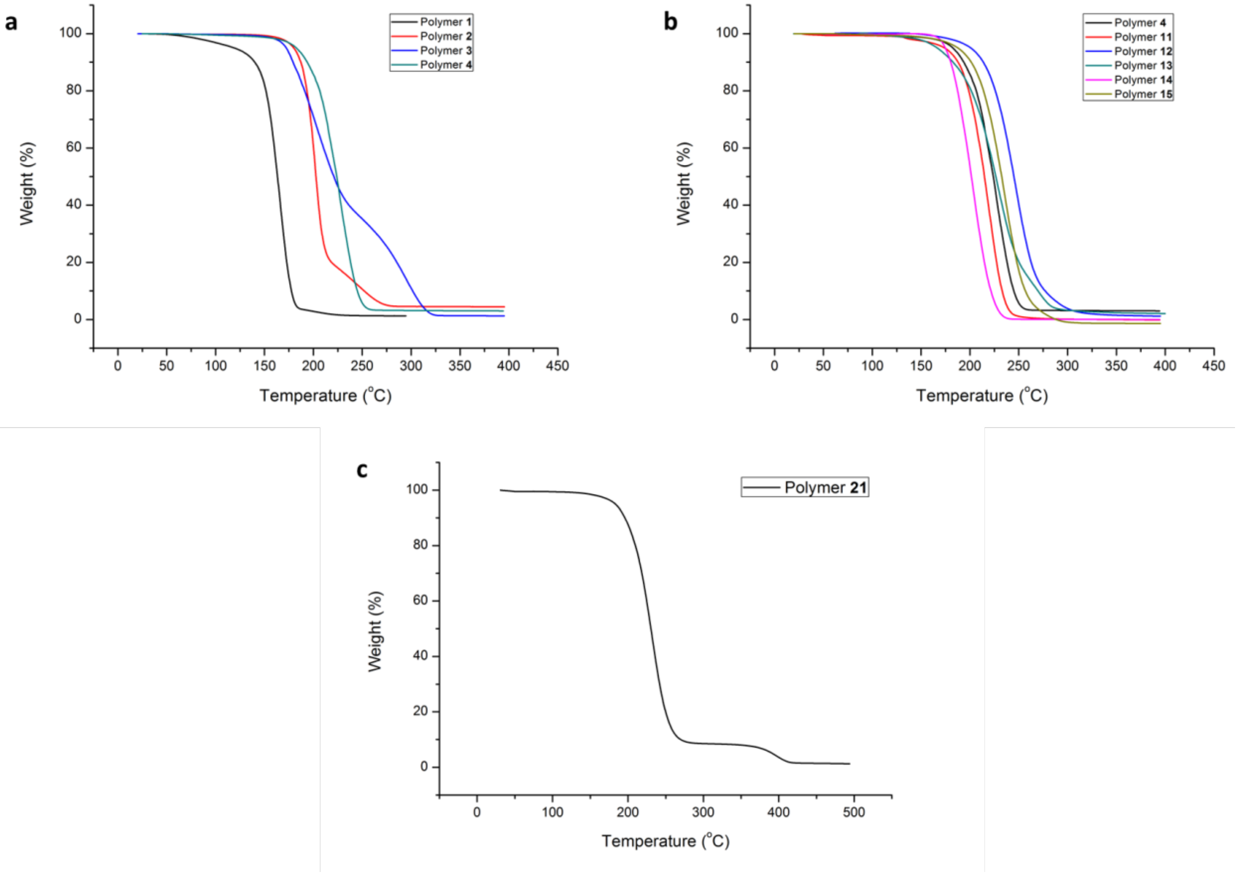

Figure S35. TGA curves for: (a) PEtGs **1 - 4**; (b) polyglyoxylates **11-15** compared with PEtG **4**; (c) triblock copolymer **21**.

Table S2**.** Summary of the thermal stabilities of polyglyoxylates measured by TGA. $T_{98\%}$ = maximum temperature at which 98% of mass is still present; T_o = onset degradation temperature; T_p = peak degradation temperature.

Polymer	$T_{98\%}$ (ºC)	T_o (ºC)	T_p (ºC)
1	84	148	165
2	168	190	202
3	161	173	203
4	164	202	228
11	139	196	220
12	180	218	247
13	147	195	229
14	169	181	203
15	164	208	236
21	160	203 (375)[a]	232 (398)[a]

[a] The values in brackets represent the values for the second stage of a two-stage decomposition.

VIII. DSC thermograms for polyglyoxylates

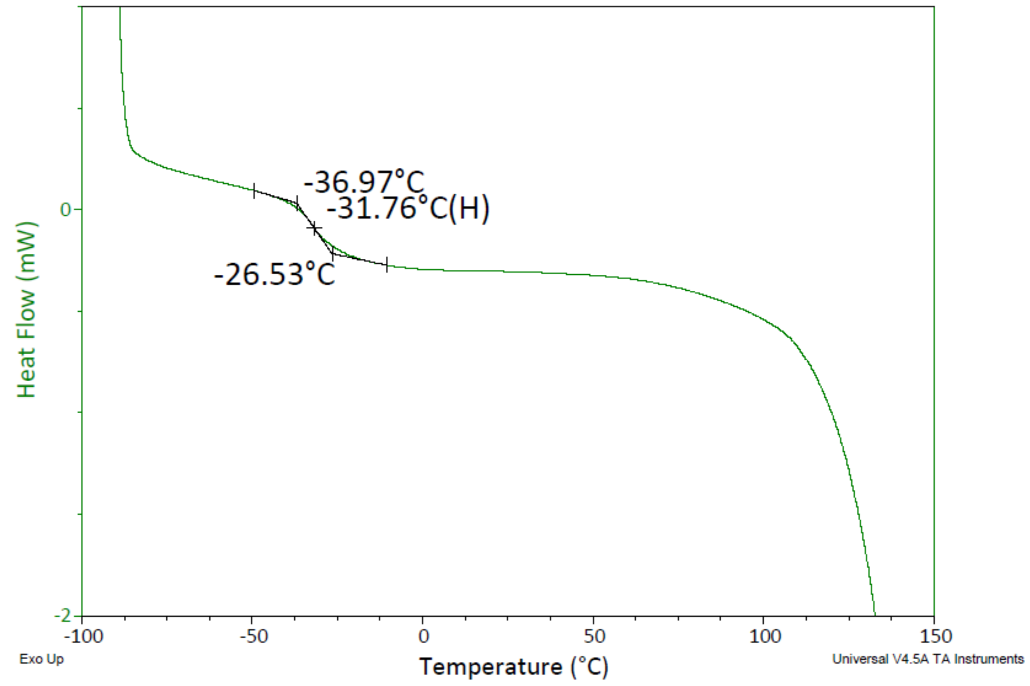

Figure S36. DSC of poly(ethyl glyoxylate) (polymer **1**).

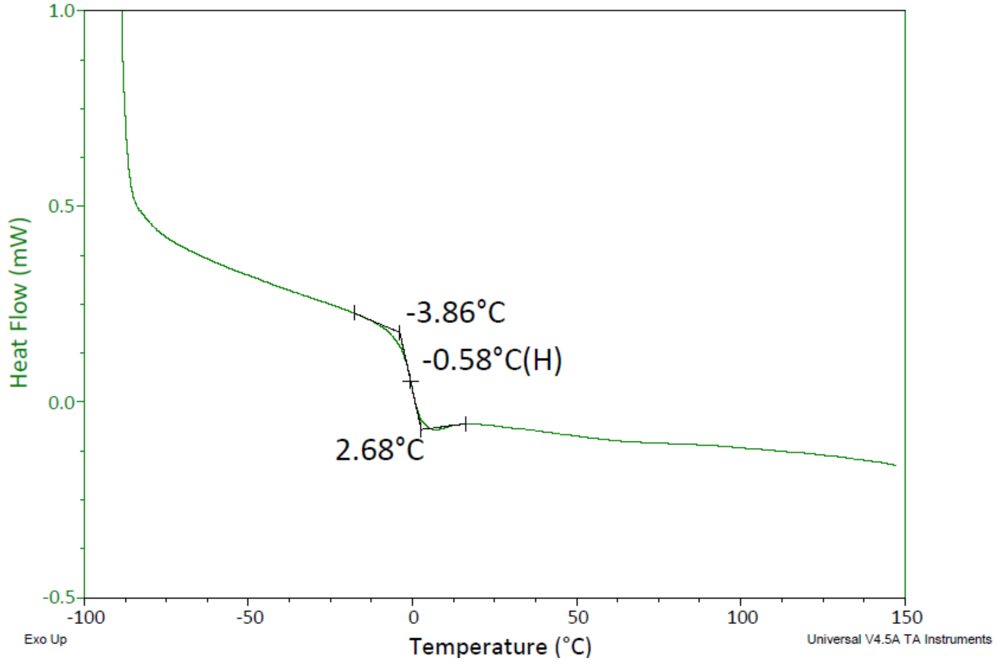

Figure S37. DSC of poly(ethyl glyoxylate) end-capped by phenyl isocyanate (polymer **2**).

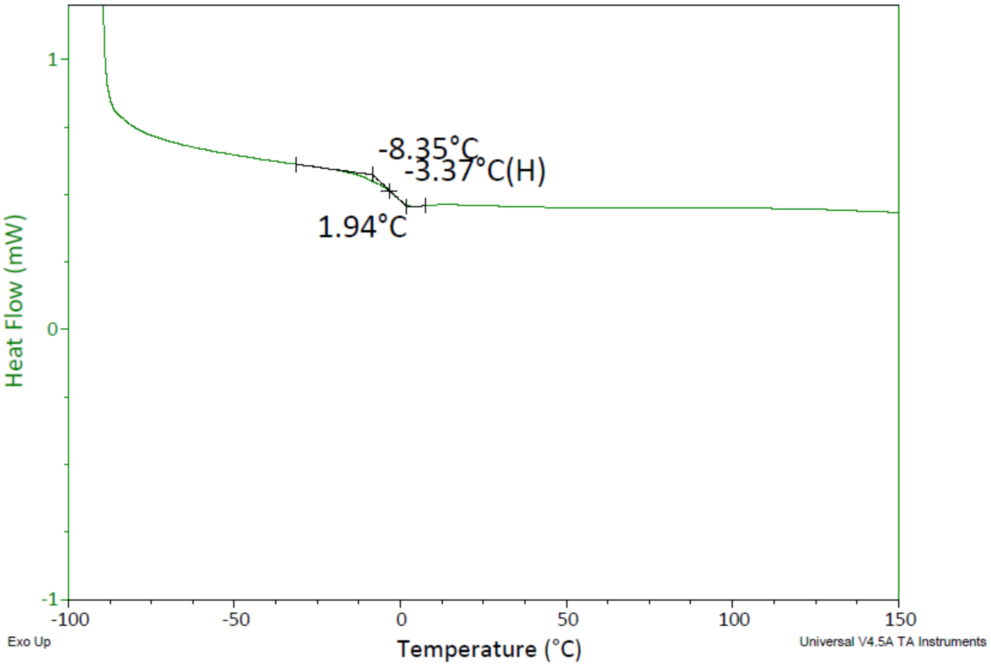

Figure S38. DSC of poly(ethyl glyoxylate) end-capped by benzyl chloroformate (polymer **3**).

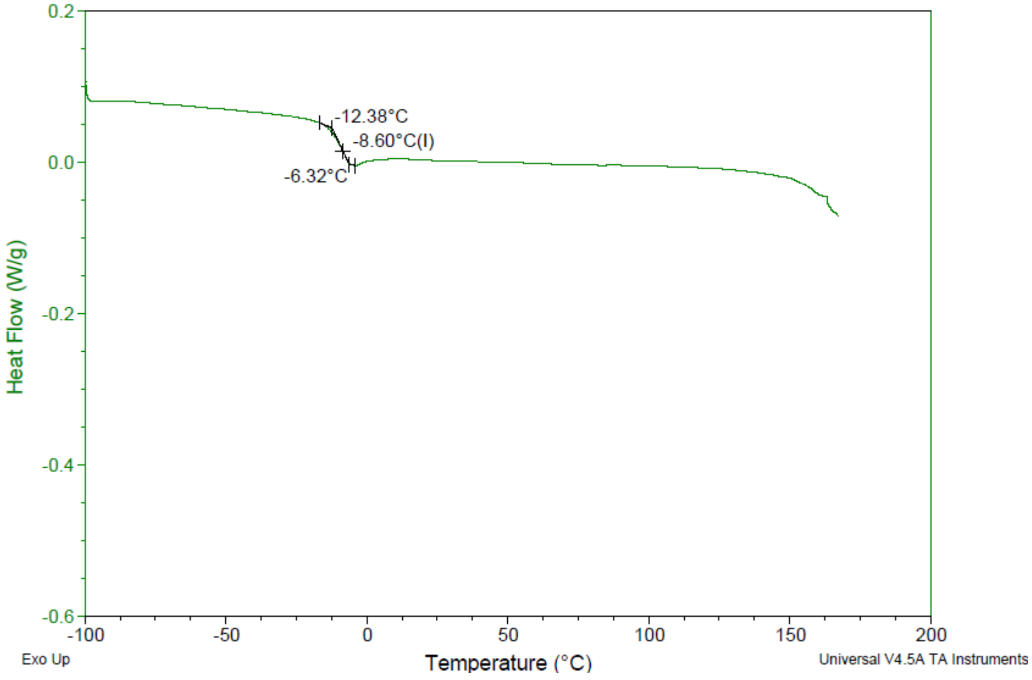

Figure S39. DSC of poly(ethyl glyoxylate) end-capped by NVOC-Cl (polymer **4**).

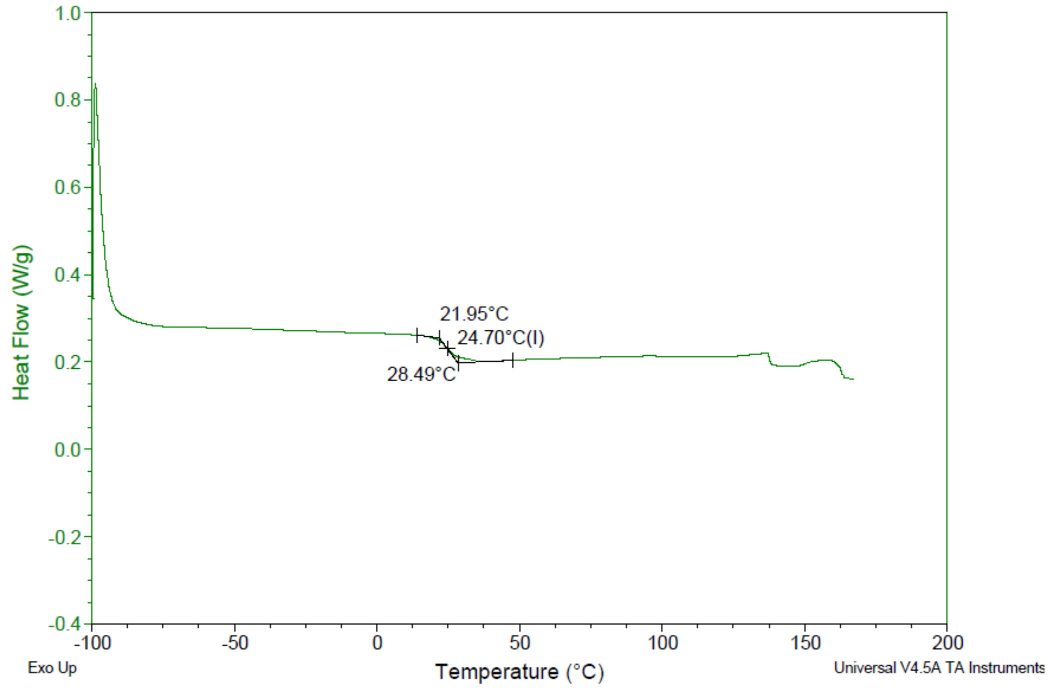

Figure S40. DSC of poly(methyl glyoxylate) end-capped by NVOC-Cl (polymer **11**).

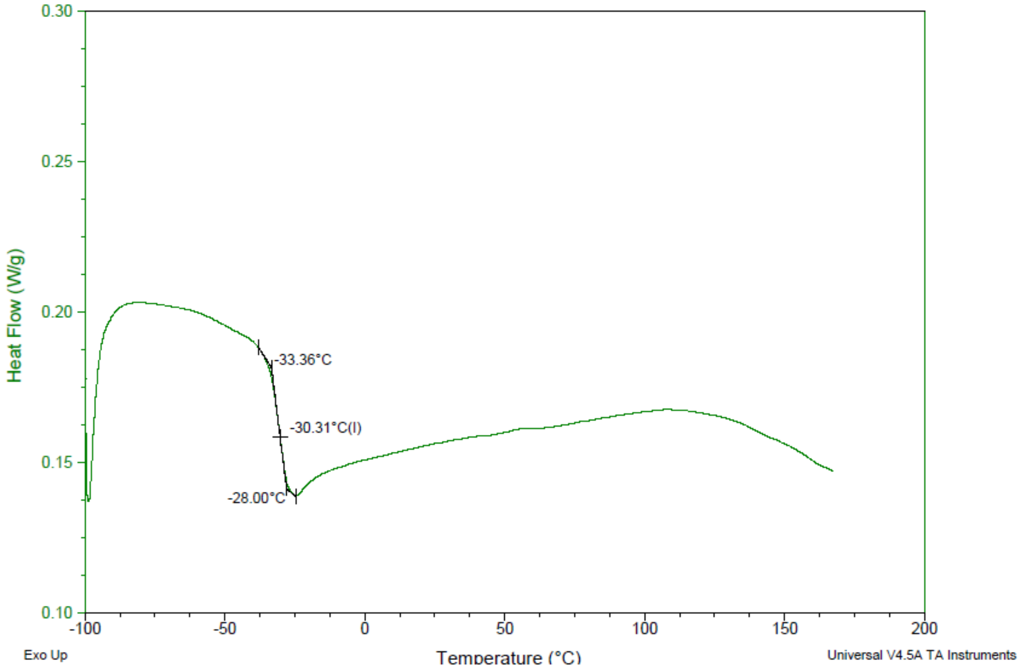

Figure S41. DSC of poly(butyl glyoxylate) end-capped by NVOC-Cl (polymer **12**).

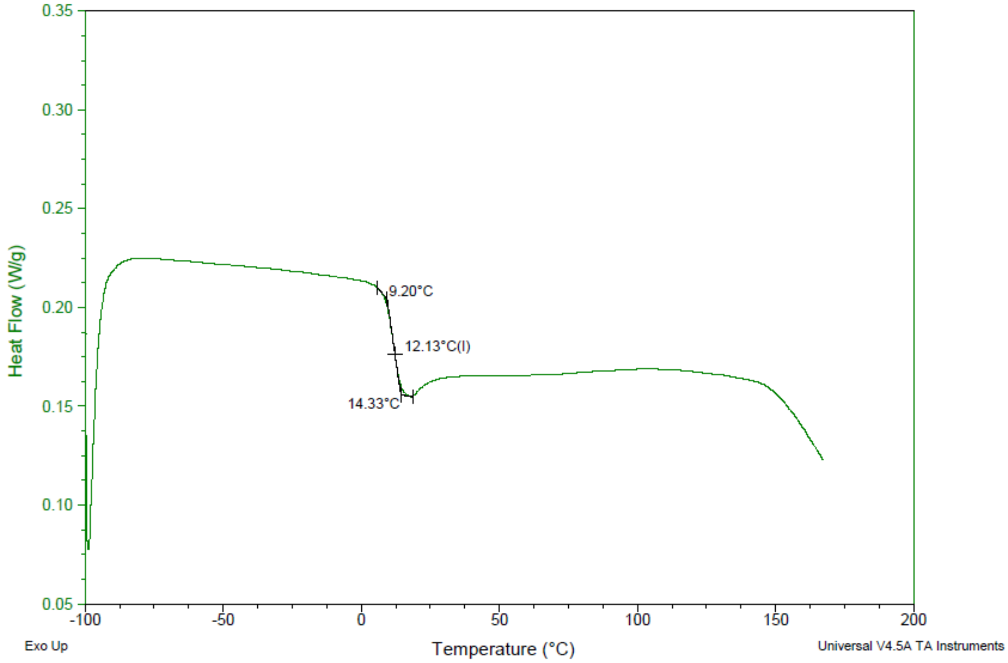

Figure S42. DSC of poly(benzyl glyoxylate) end-capped by NVOC-Cl (polymer **13**).

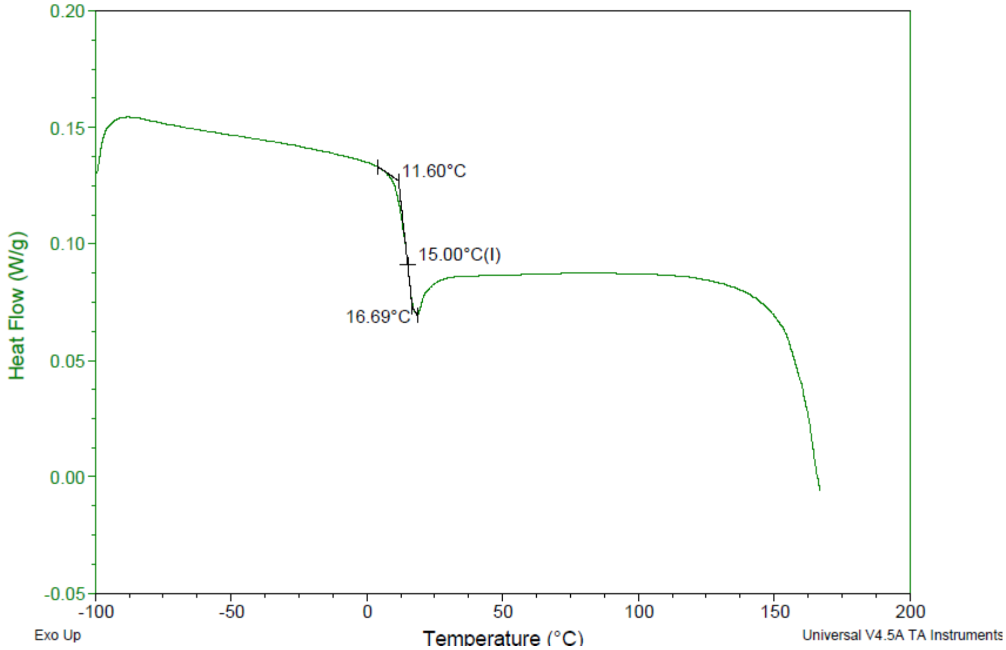

Figure S43. DSC of poly(ethyl glyoxylate)-*co*-(methyl glyoxylate) end-capped by NVOC-Cl (polymer **14**).

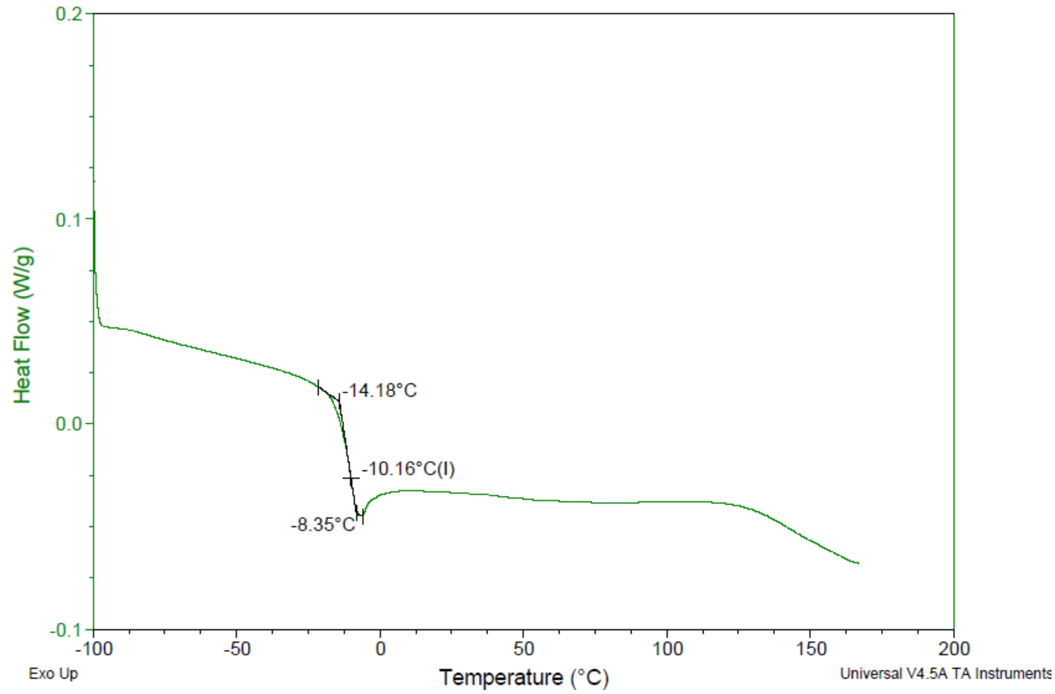

Figure S44. DSC of poly(ethyl glyoxylate)-co-(butyl glyoxylate) end-capped by NVOC-Cl (polymer **15**).

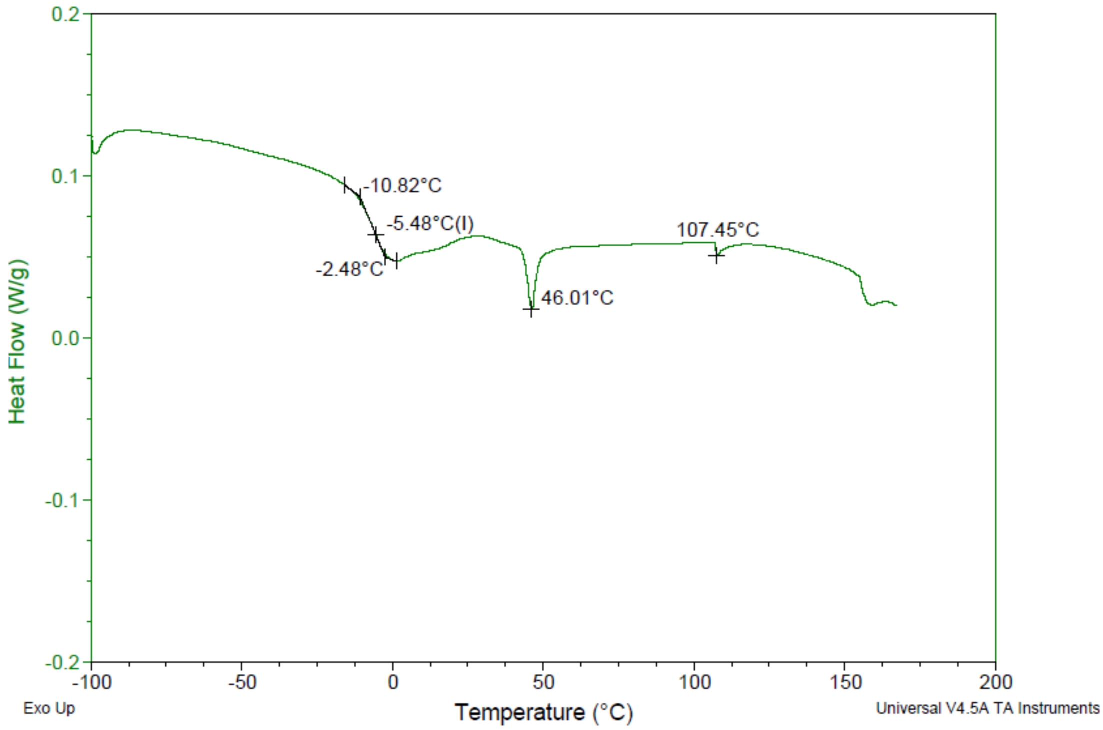

Figure S45. DSC of block polymer (polymer **21**).

IX. UV-vis spectral changes of polymer 4 during UV irradiation

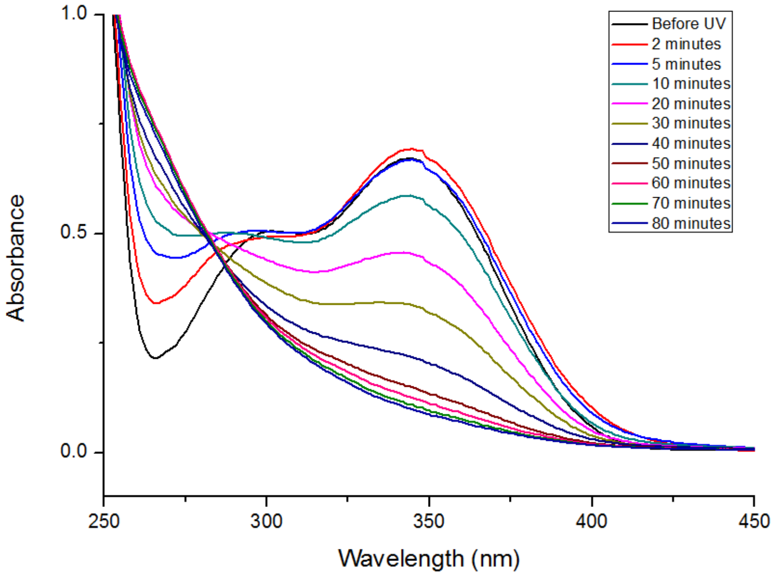

Figure S46. UV-visible spectroscopy of polymer **4** and its end-cap cleavage following different irradiation time with UV light.

X. NMR degradation studies of polyglyoxylates

Degradation studies on polymer **3**.

To demonstrate that UV light was selective for cleaving the end-cap to initiate depolymerization rather than the polymer backbone, polymer **3** was treated as described in the manuscript for the study of PEtG **4** degradation in solution.

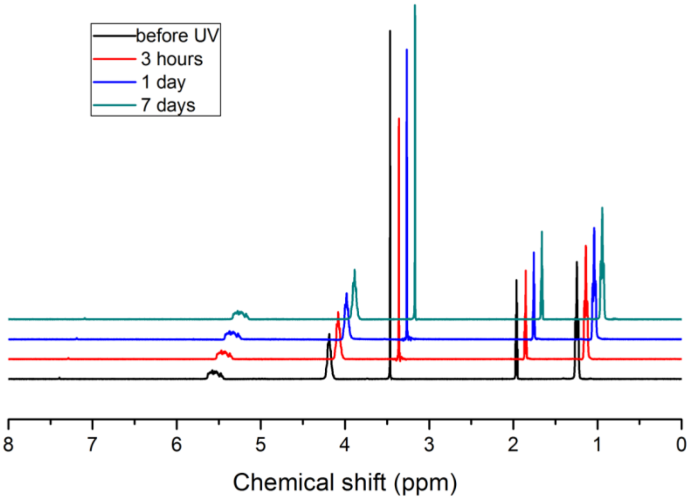

Figure S47. ^{1}H NMR spectrum of polymer **3** after UV irradiation following the same procedure described for the study of polymer **4** (following incubation in 9:1 CD_3CN:D_2O). No changes were observed, indicating that the polymer is stable under these conditions and UV irradiation does not cleave the polymer backbone.

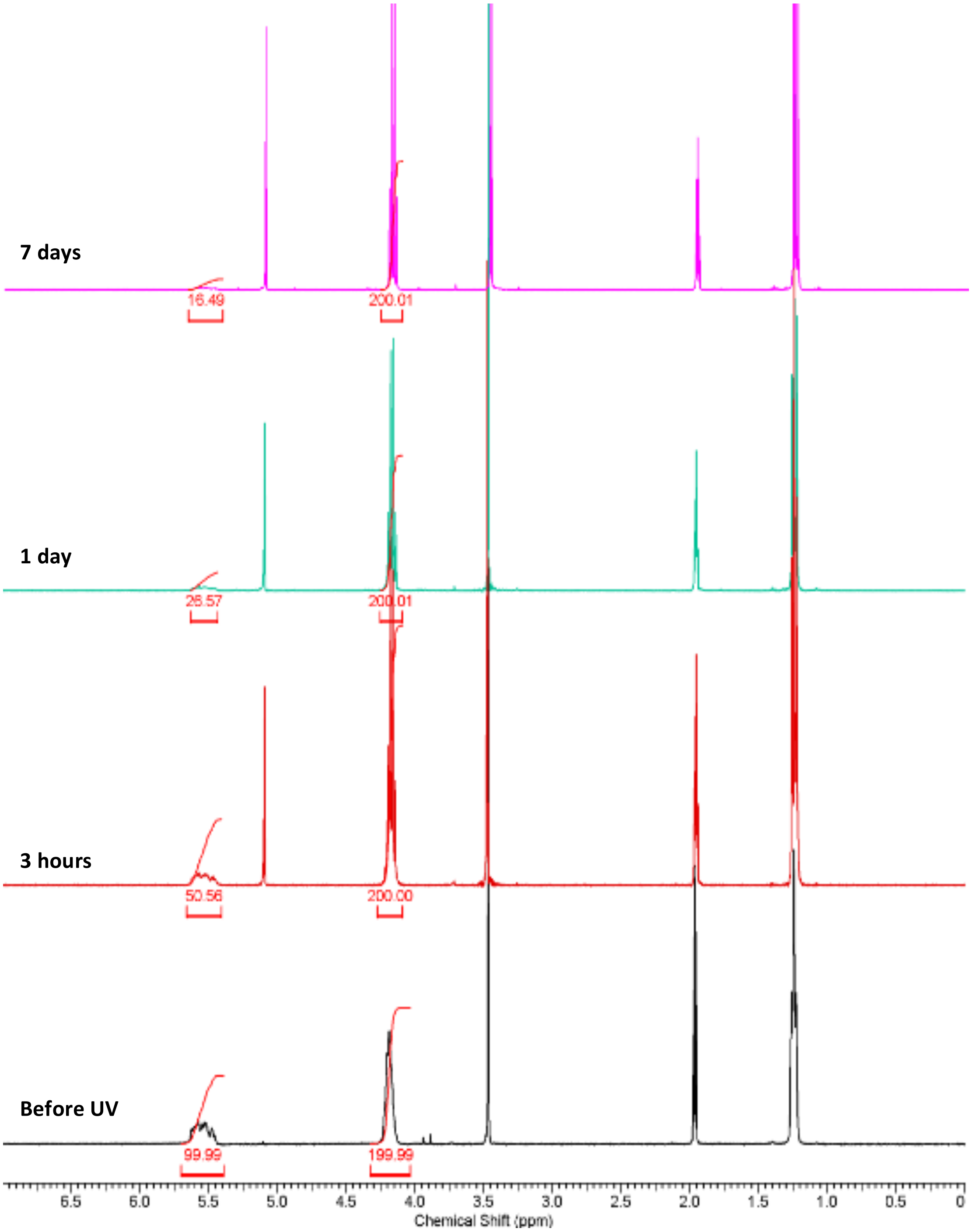

Figure S48. Zoom of ^{1}H NMR spectra corresponding to Figure 1a from the manuscript, showing relative peak integrals that were used to calculate the % polymer remaining for Figure 3 of the manuscript. The initial integral (t = 0) for the peak at 5.6 ppm was set to 100 to indicate 100% polymer and it decreased over time. Integration of the peak at 4.2 ppm remained constant as it corresponds to the $CH_3C\underline{H}_2$-O- in both the polymer and degradation product.

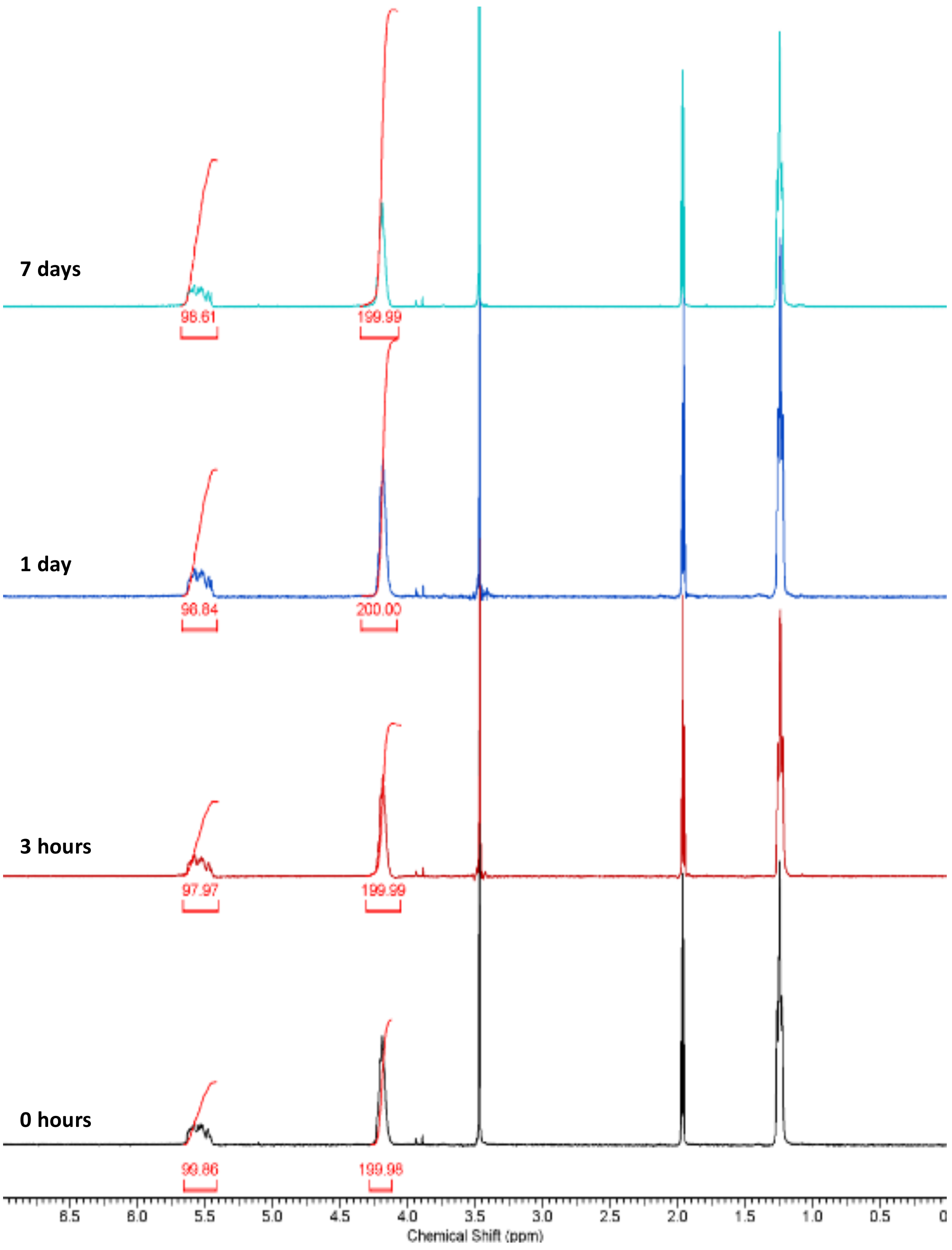

Figure S49. Zoom of ^{1}H NMR spectra corresponding to Figure 1b from the manuscript. The initial integral (t = 0) for the peak at 5.6 ppm was set to 100 to indicate 100% polymer and it decreased over time. Integration of the peak at 4.2 ppm remained constant as it corresponds to the $CH_3C\underline{H}_2$-O- in both the polymer and degradation product. No detectable degradation was observed.

Degradation studies on polymers **11** to **15** and **21**.

As for polymer **4**, before irradiation, the polymers showed broad peaks and several small peaks corresponding to the end cap. However, following irradiation of a 9:1 $CD_3CN:D_2O$ solution of the polymer with UV light and incubation at ambient temperature (21 °C), the broad peak at 5.6 ppm started decreasing, and a new singlet at 5.1 ppm (alkyl glyoxylate hydrate) began increasing (a in Figures S35 - S40). Peaks associated with the alkyl/benzyl chains became sharper. In each case the control group (b in Figures S35 - S40) did not show any signs of significant degradation.

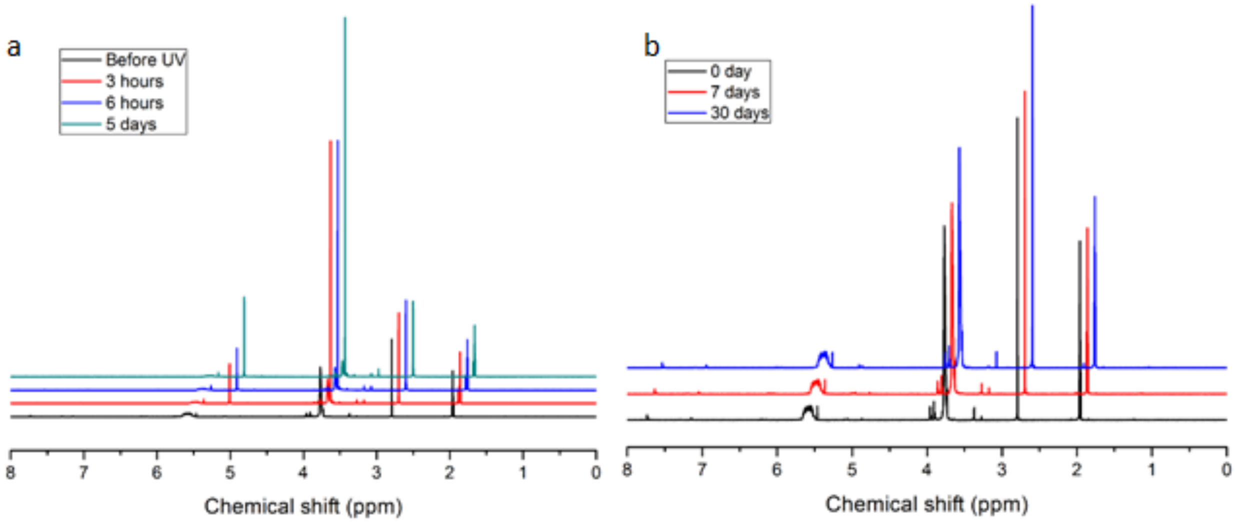

Figure S50. (a) ^{1}H NMR spectra of polymer **11** after irradiation; (b) ^{1}H NMR spectra of polymer **11** without irradiation (following incubation in 9:1 $CD_3CN:D_2O$).

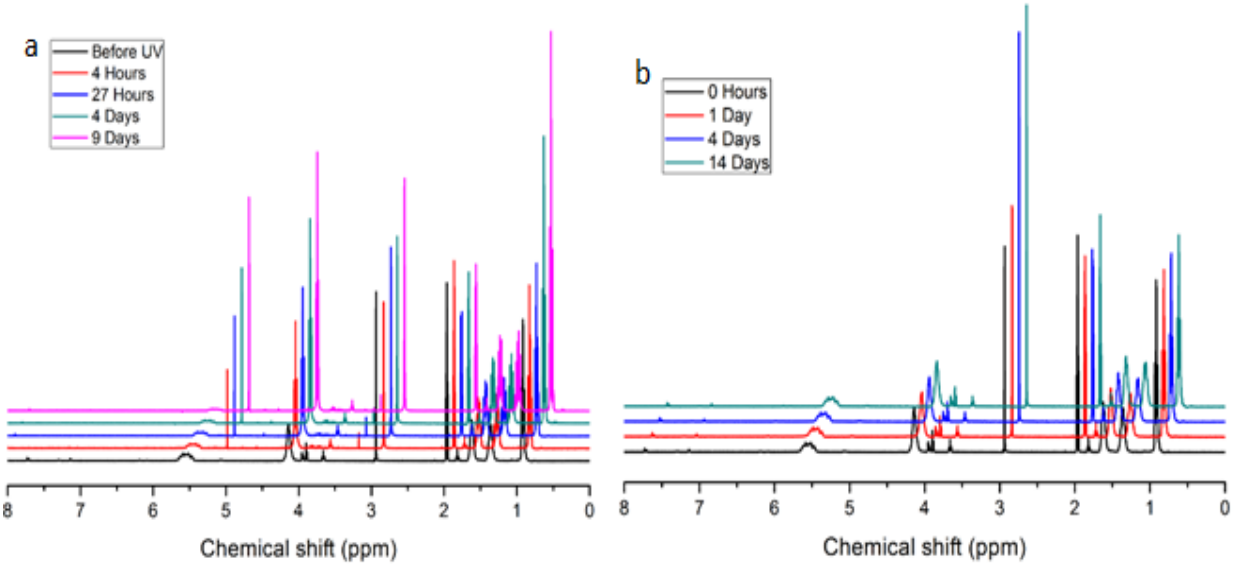

Figure S51. (a) ^{1}H NMR spectra of polymer **12** after irradiation; (b) ^{1}H NMR spectra of polymer **12** without irradiation (following incubation in 9:1 CD_3CN:D_2O).

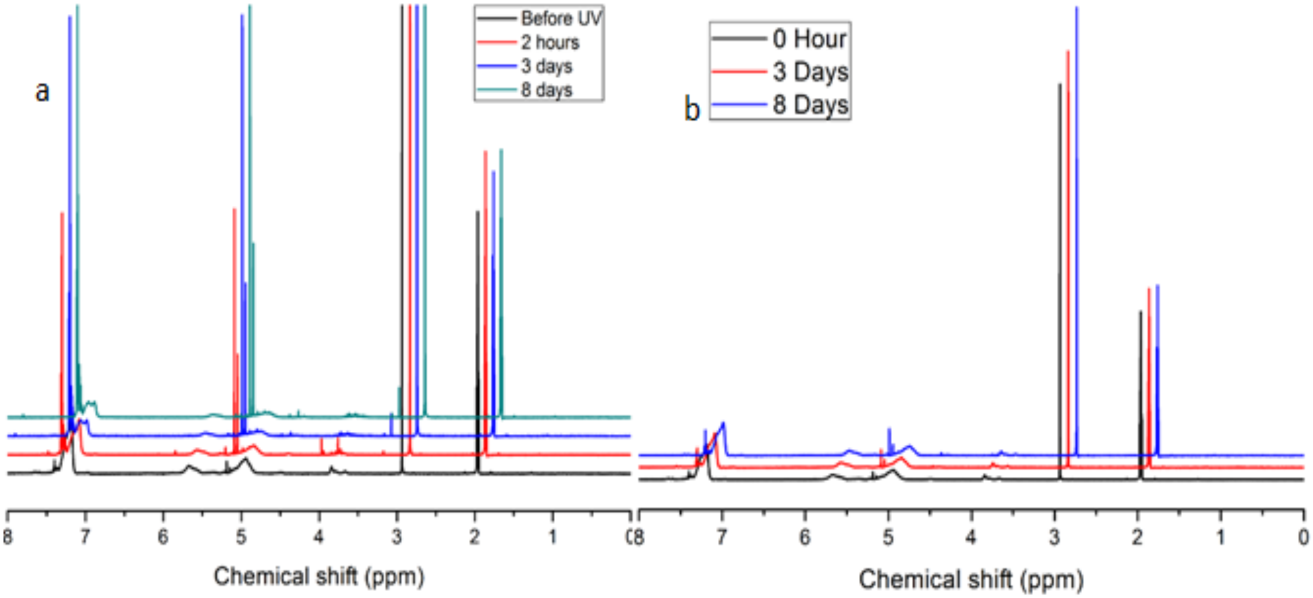

Figure S52. (a) ^{1}H NMR spectra of polymer **13** after irradiation; (b) ^{1}H NMR spectra of polymer **13** without irradiation (following incubation in 9:1 CD_3CN:D_2O).

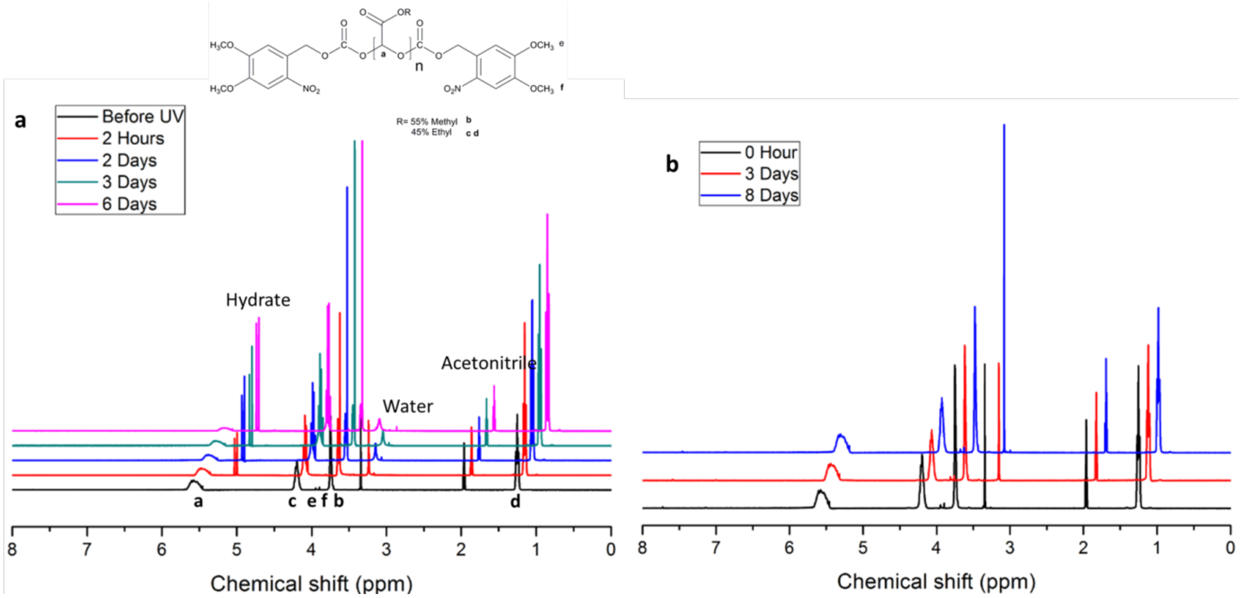

Figure S53. (a) ^{1}H NMR spectra of polymer **14** after irradiation; (b) ^{1}H NMR spectra of polymer **14** without irradiation (following incubation in 9:1 $CD_3CN:D_2O$).

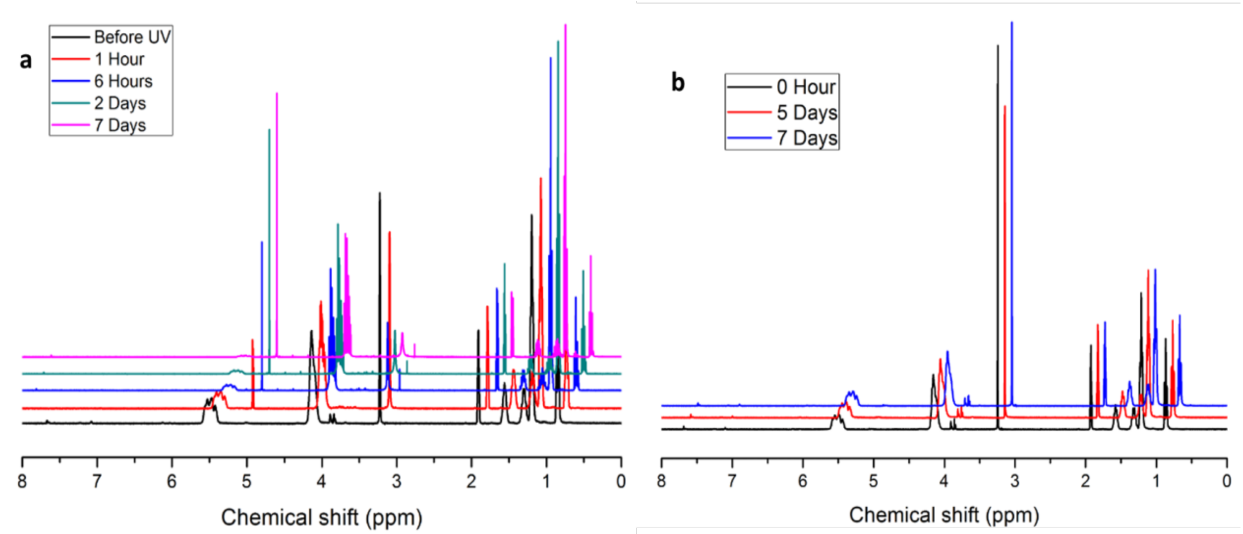

Figure S54. (a) ^{1}H NMR spectra of polymer **15** after irradiation; (b) ^{1}H NMR spectra of polymer **15** without irradiation (following incubation in 9:1 $CD_3CN:D_2O$).

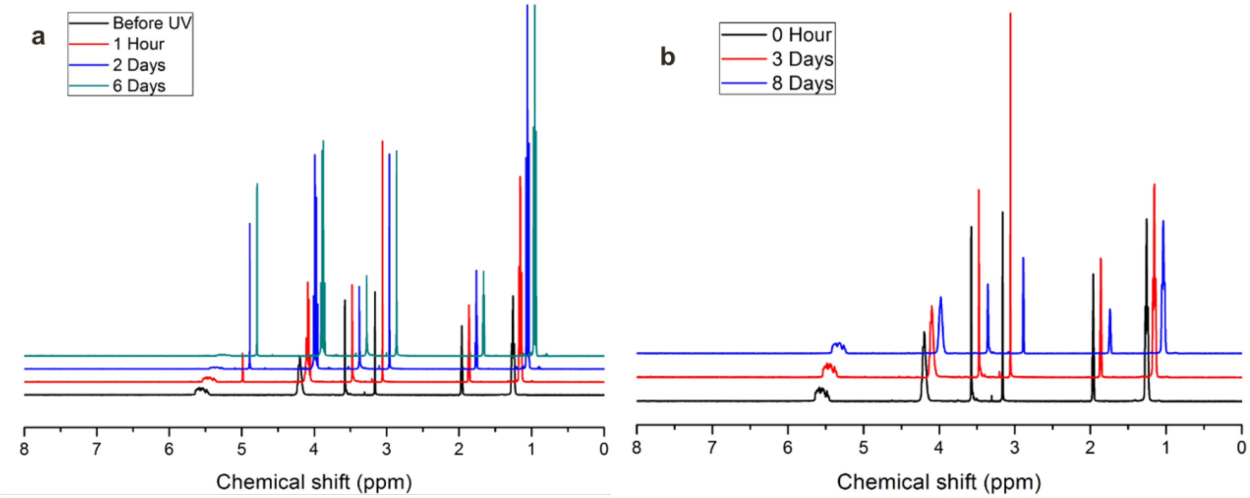

Figure S55. (a) ^{1}H NMR spectra of polymer **21** after irradiation; (b) ^{1}H NMR spectra of polymer **21** without irradiation (following incubation in 9:1 CD_3CN:D_2O).

XI. Depolymerization profiles of individual polyglyoxylates

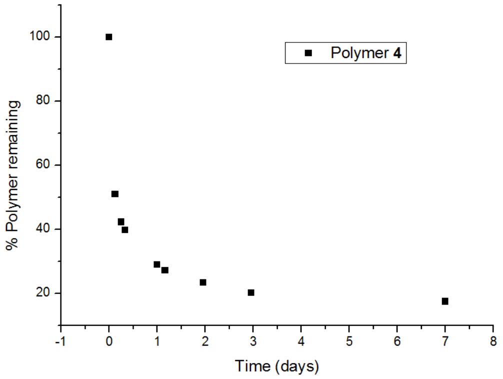

Figure S56. Depolymerization of polymer **4** following cleavage of the NVOC end-caps by UV irradiation in 9:1 $CD_3CN:D_2O$ following by incubation at ambient temperature (21°C).

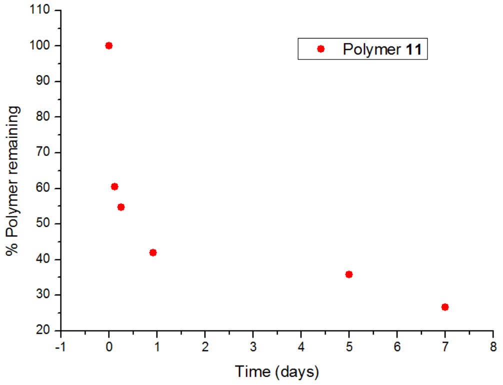

Figure S57. Depolymerization of polymer **11** following cleavage of the NVOC end-caps by UV irradiation in 9:1 $CD_3CN:D_2O$ following by incubation at ambient temperature (21°C).

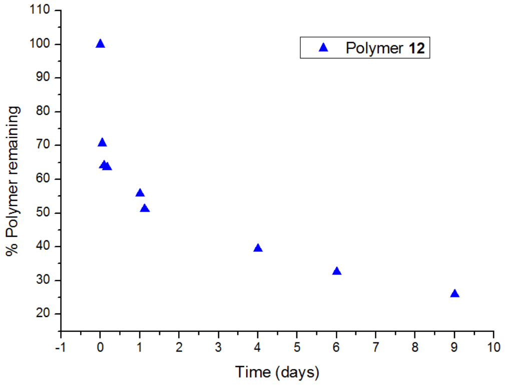

Figure S58. Depolymerization of polymer **12** following cleavage of the NVOC end-caps by UV irradiation in 9:1 $CD_3CN:D_2O$ following by incubation at ambient temperature (21°C).

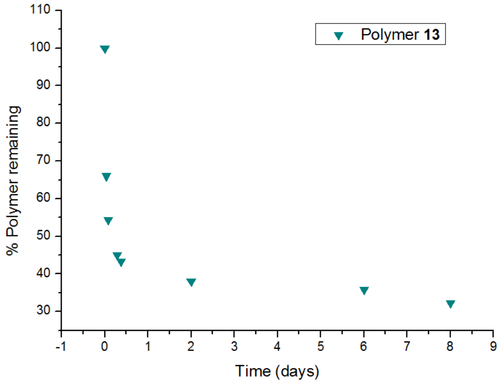

Figure S59. Depolymerization of polymer **13** following cleavage of the NVOC end-caps by UV irradiation in 9:1 $CD_3CN:D_2O$ following by incubation at ambient temperature (21°C).

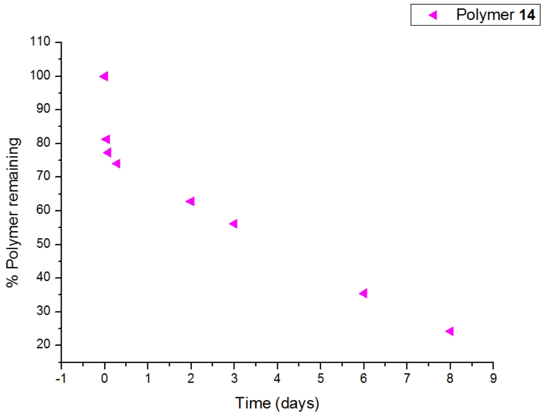

Figure S60. Depolymerization of polymer **14** following cleavage of the NVOC end-caps by UV irradiation in 9:1 CD3CN:D2O following by incubation at ambient temperature (21°C).

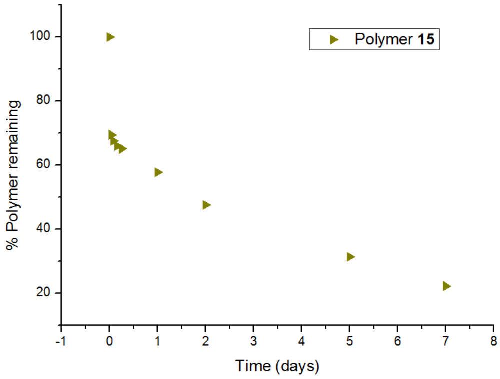

Figure S61. Depolymerization of polymer **15** following cleavage of the NVOC end-caps by UV irradiation in 9:1 CD3CN:D2O following by incubation at ambient temperature (21°C).

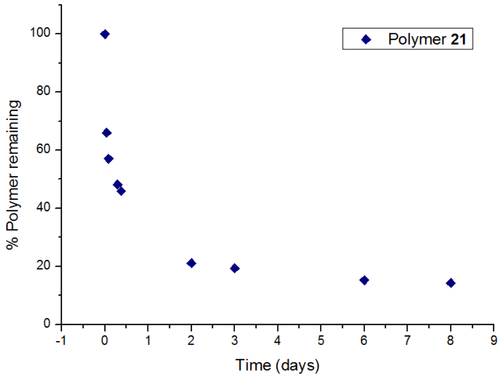

Figure S62. Depolymerization of polymer **21** following cleavage of the NVOC end-caps by UV irradiation in 9:1 CD3CN:D2O following by incubation at ambient temperature (21°C).

XII. Preparation and study of micelles formed from triblock copolymer 21.

Micelle preparation and characterization.

8 mg of polymer **21** was dissolved in 1.0 mL DMSO. The DMSO solution (0.1 mL) was rapidly injected into 0.9 mL of stirring deionized water. After stirring for 0.5 h, the micelle suspension was then transferred into a regenerated cellulose membrane (3 kDa MWCO) and dialyzed against deionized water for 12 h (300 mL, 2 solvent changes) to remove DMSO. The micelle hydrodynamic diameter was measured by dynamic light scattering (Zetasizer Nano Series, Malvern Instruments, UK) at room temperature (25 ºC) in a glass cuvette. TEM imaging was performed using a Phillips CM10 microscope operating at an acceleration voltage of 80 kV. The sample was prepared by depositing 3 μL of micelle suspension (prepared as described above, then diluted to 0.08 mg / mL) onto a copper grid. The resulting sample was air-dried overnight before imaging.

NMR degradation study of micelles

16 mg of polymer **21** was fully dissolved in 0.8 mL of DMSO-d_6. 0.2 mL of the resulting solution was rapidly injected into 1.0 mL stirring 100 mM, pH 7.4 phosphate buffered D_2O. After stirring for 0.5 h, the micelle suspension was then divided and transferred to two NMR tubes. One tube was then irradiated for 10 min in the UV light (wavelength: 300-350 nm, 23 mWcm^{-2}), while the other one was kept in the dark. A ^{1}H NMR spectrum was obtained immediately following irradiation (10 min time point in the graph), then the samples were incubated at 37 ^{o}C and spectra were obtained at regular intervals over 24 h. Complete depolymerization was confirmed for the irradiated sample as the sum of the integration of the methyl peaks corresponding to EtGH and ethanol (1.0-1.2 ppm) plateaud at a very similar (1198) value to that of the methyl peak at 1.17-1.45 ppm in the block copolymer **21** taken in $CDCl_3$ (Figure S29, integration 1152) when setting the PEG peak integral to 364. The % polymer remaining was calculated as 100 - (sum of integration from 1.0-1.2 ppm/1198))*100.

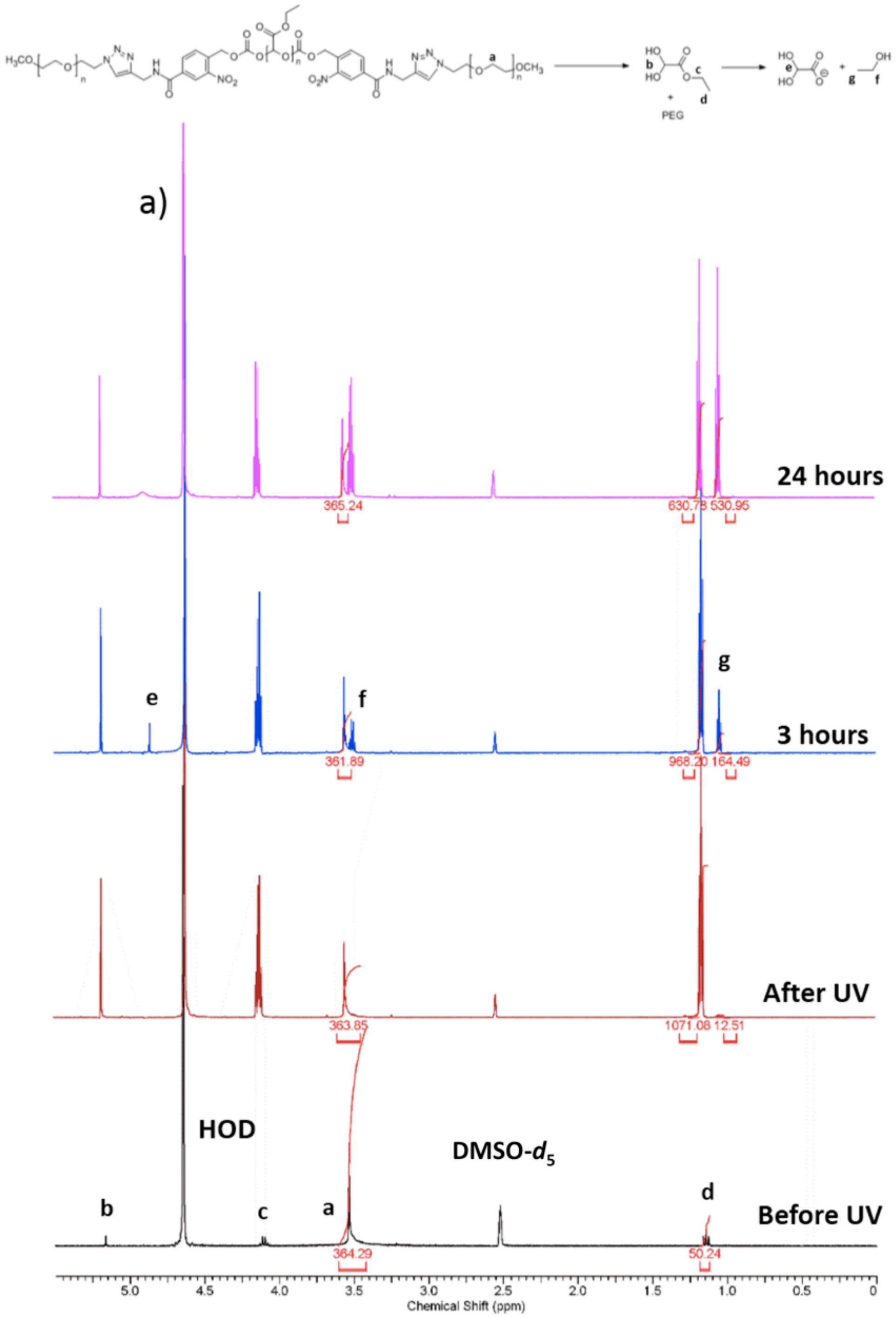

Figure S63. Representative ^{1}H NMR spectra of micelles over time following UV irradiation and incubation at 37 °C in 5:1 pH 7.4 phosphate buffered D_2O:DMSO-d_6.

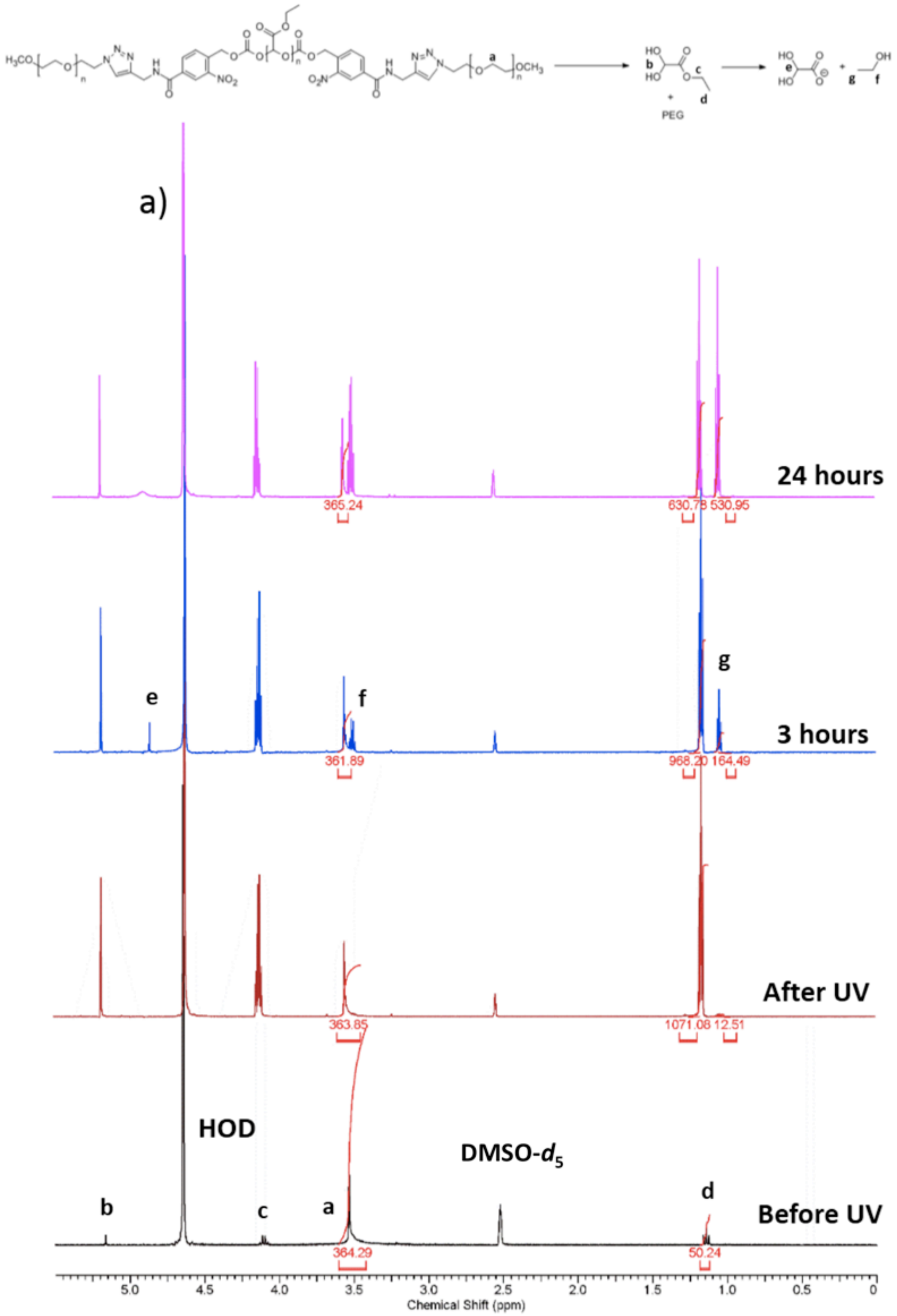

Figure S64. Representative ^{1}H NMR spectra of micelles over time without UV irradiation but with incubation at 37 °C in 5:1 pH 7.4 phosphate buffered D_2O:DMSO-d_6.

XIII. References

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