Synthesis, characterization and chemical degradation of poly(ester-triazole)s derived from D-galactose

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Electronic supplementary information

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Monomer synthesis

Methyl 6-azido-6-deoxy-2,3:4,5-di-*O*-isopropylidene-D-galactonate (3). Sodium azide (0.487 g, 7.49 mmol) was added to a solution of compound **2** (1.507 g, 4.267 mmol) in DMF (4 mL). The mixture was stirred at 80 °C overnight and then filtered through Celite to remove excess of NaN_3. After concentration and purification by column chromatography (10:1 hexane-EtOAC) was isolated compound **3** (1.250 g, 93%) as a colourless syrup; $[\alpha]_D^{25}$ = +29.7 (c = 1.1, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$, δ): 4.54 (d, 1H, $J_{2,3}$ 5.2 Hz; H-2), 4.33 (dd, 1H, $J_{2,3}$ 5.2, $J_{3.4}$ 7.6 Hz; H-3), 4.17-4.14 (m, 1H; H-5), 3.93 (t, 1H, $J_{3.4} = J_{4,5}$ 7.5 Hz; H-4), 3.79 (s, 3H; CH_3O), 3.63 (dd, 1H, $J_{5,\ 6a}$ 3.22 Hz, $J_{6a,6b}$ 13.2 Hz; H-6a), 3.31 (dd, 1H, $J_{5,6b}$ 5.0 Hz; H-6b), 1.45, 1.44, 1.40, 1.39 (4s, 12H, 2 × $C(CH_3)_2$); ^{13}C NMR (125.5 MHz, $CDCl_3$, δ): 171.3 (C-1), 112.5, 110.7 (2 × $C(CH_3)_2$), 79.9 (C-3), 79.0 (C-5), 78.0 (C-4), 77.6 (C-2), 52.7 (CH_3O), 52.1 (C-6), 27.4, 27.1, 27.0, 26.2 (2 × $C(CH_3)_2$). HRMS (ESI/Q-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{13}H_{21}N_3O_6Na$ 338.1323; found: 338.1321.

Figure S1. ^{1}H NMR spectrum (500 MHz, $CDCl_3$) of compound **3**

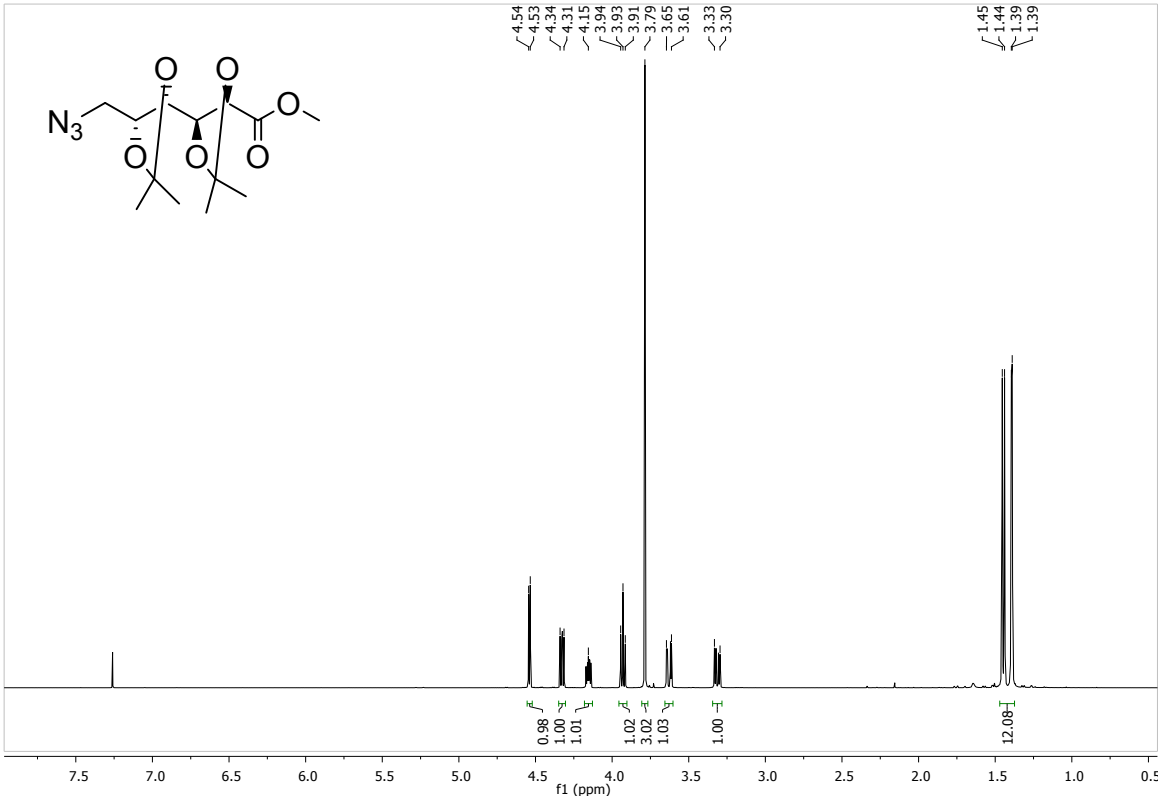
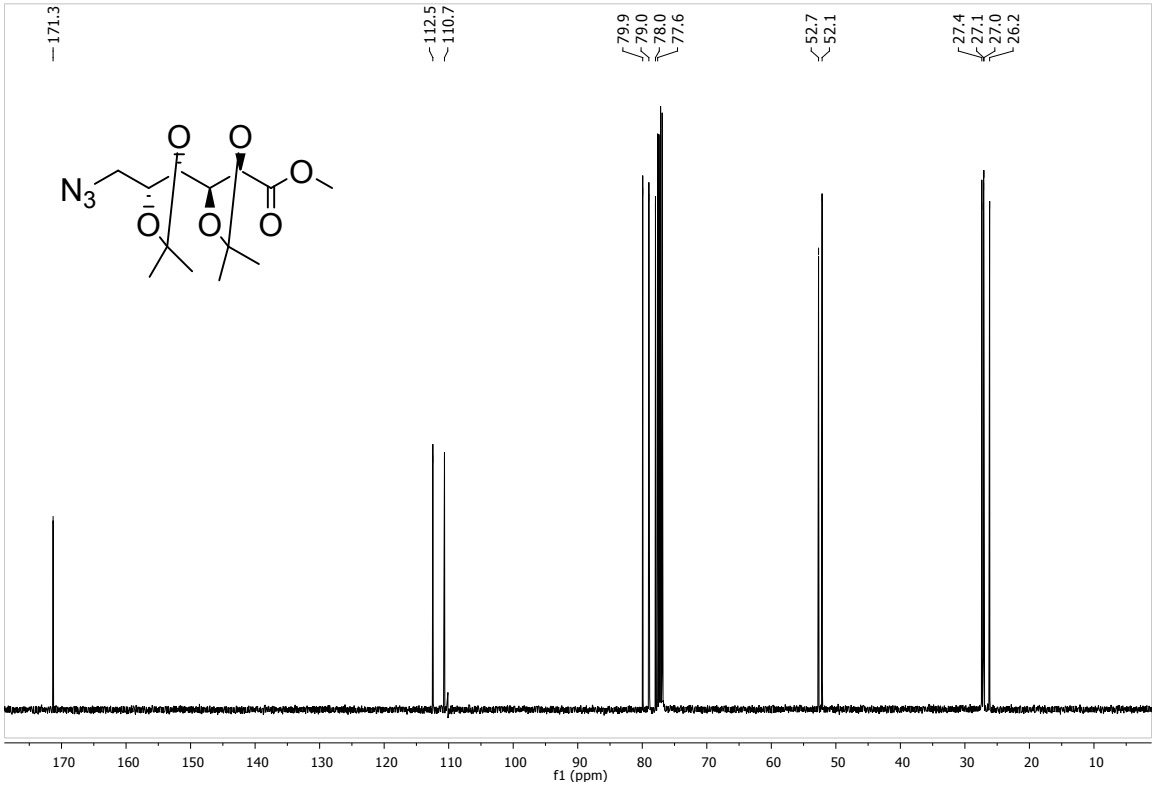


Figure S2. ^{13}C NMR spectrum (125 MHz, $CDCl_3$) of compound **3**



6-Azido-6-deoxy-2,3:4,5-di-*O*-isopropylidene-D-galactonic acid (4). To a solution of compound **3** (3.01 g, 9.54 mmol) in MeOH:H_2O 3:1 (13 mL), KOH (1.3 g) was added. The solution was stirred a room temperature for 3 h. After concentration under reduced pressure, water (20 mL) was added and the aqueous mixture was extracted with EtOAc (3 × 15 mL). The aqueous phase was acidified to pH 2 with 1 M aqueous HCl and extracted with EtOAc (3 × 15 mL). The combined organic extracts were dried over anh $MgSO_4$ and concentrated to give compound **6** (2.67 g, 93%) as a white solid. mp 68 °C; $[\alpha]_D^{25}$ = +35.8 (c = 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$, δ): 4.61 (d, 1H, $J_{2,3}$ 5.5 Hz; H-2), 4.31 (dd, 1H, $J_{2,3}$ 5.5, $J_{3,4}$ 7.3 Hz; H-3), 4.19 (m, 1H; H-5), 3.99 (t, 1H, $J_{3,4} = J_{4,5}$ 7.5 Hz; H-4), 3.65 (dd, 1H, $J_{5,6a}$ 3.2 Hz, $J_{6a,6b}$ 13.2 Hz; H-6a), 3.33 (dd, 1H, $J_{5,6b}$ 4.8 Hz; H-6b), 1.48, 1.47, 1.43, 1.42 (4s, 12H, 2 × $C(CH_3)_2$); ^{13}C NMR (125.5 MHz, $CDCl_3$, δ): 174.2 (C-1), 112.9, 111.0 (2 × $C(CH_3)_2$), 79.6 (C-3), 78.9 (C-5), 78.0 (C-4), 77.2 (C-2), 51.9 (C-6), 27.3, 27.1, 27.0, 26.1 (2 × $C(CH_3)_2$). HRMS (ESI/Q-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{12}H_{19}N_3O_6Na$ 324.1172; found: 324.1165.

Figure S3. ^{1}H NMR spectrum (500 MHz, $CDCl_3$) of compound **4**

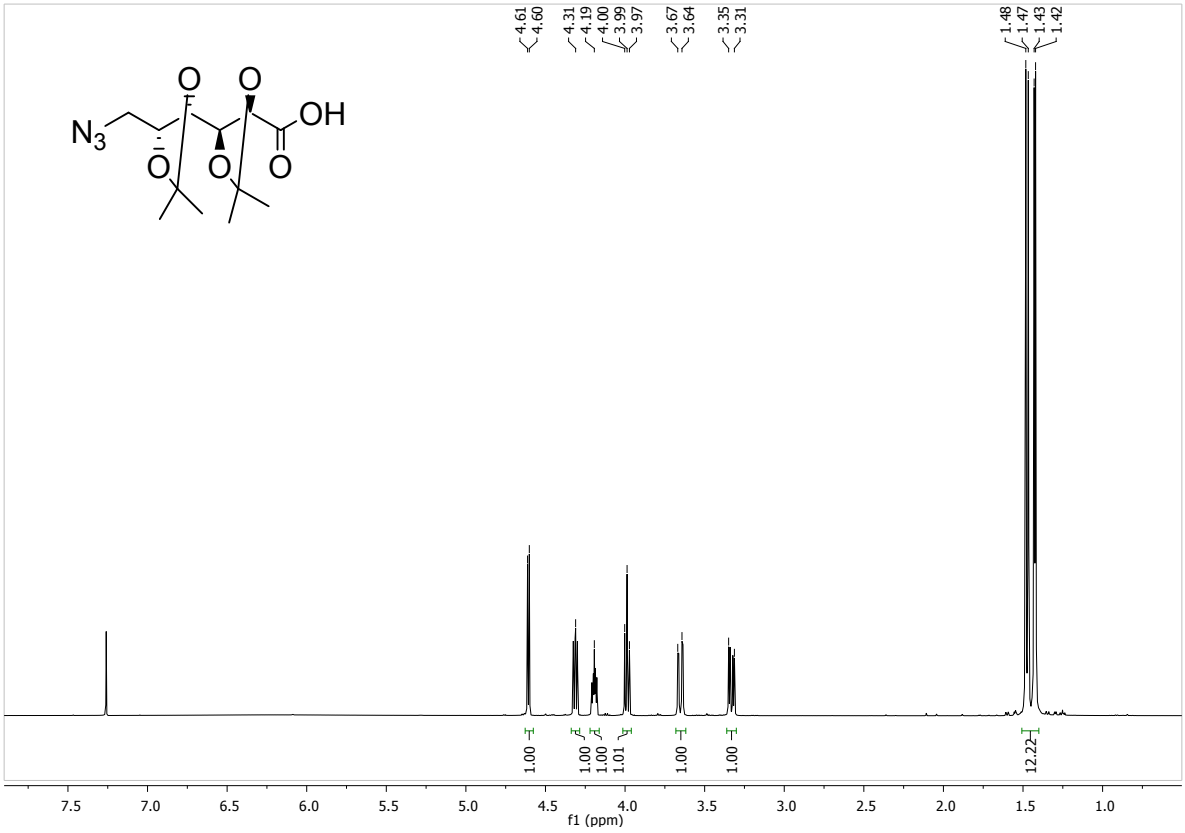
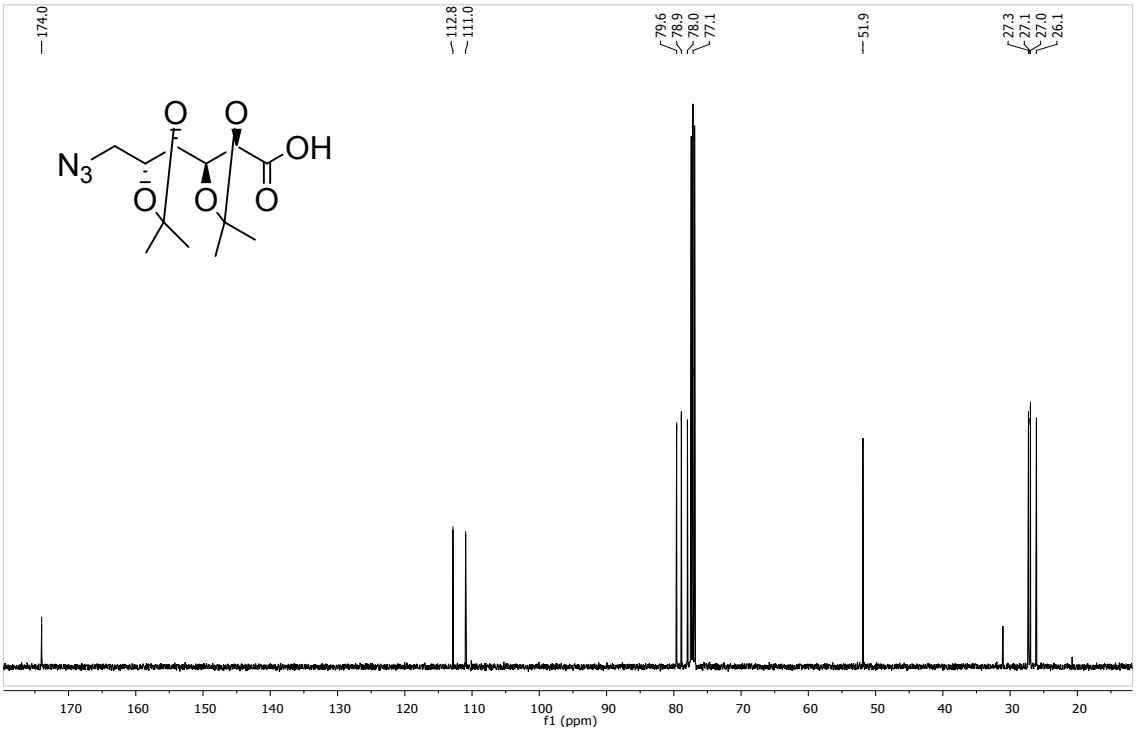


Figure S4. ^{13}C NMR spectrum (125 MHz, $CDCl_3$) of compound **4**



Propargyl 6-azido-6-deoxy-2,3:4,5-di-*O*-isopropylidene-D-galactonate (5). To a solution of compound **4** (384.2 mg, 1.27 mmol) in CH_2Cl_2 (4 mL) were added 1-hydroxybenzotriazole (HOBt, 0.305 g, 2.26 mmol), *N,N*-diisopropylethylamine (DIPEA, 0.071 mL, 0.74 mmol) and *N*-(3-dimethylaminopropyl)-*N′*-ethylcarbodiimide hydrochloride (EDCI, 0.387 g, 2.02 mmol). The solution was stirred under N_2 atm, on an ice bath, for 30 min. Then propargyl alcohol (0.127 mL, 2.20 mmol) was added and the mixture was stirred overnight, under N_2. After a second addition of EDCI (0.136 g, 0.71 mmol) and propargyl alcohol (0.070 ml, 1.21 mmol) the stirring was continued at rt for 5 h. The mixture was concentrated and the residue subjected to column chromatography (9:1 hexane-EtOAC) to afford compound **5** (0.395 g, 91%) as a white solid. mp 61°C; $[\alpha]_D^{25}$ = +26.9 (c = 1.0, $CHCl_3$); IR (ATR ν, cm^{-1}): 3243 (m, *H*C≡C), 2089 (s, N_3), 1758 (s, C=O); ^{1}H NMR (500 MHz, $CDCl_3$, δ): 4.81 (dd, 1H, $J_{1′a,3′}$ 2.5 Hz, $J_{1′a,1′b}$ 15.5 Hz; H-1′a), 4.76 (dd, 1H, $J_{1′b,3′}$ 2.5 Hz; H-1′b), 4.59 (d, 1H, $J_{2,3}$ 5.2 Hz; H-2), 4.34 (dd, 1H, $J_{2,3}$ 5.2, $J_{3.4}$ 7.7 Hz; H-3), 4.17 (m, 1H, $J_{4,5}$ 7.6, $J_{5,6a}$, 3.2, $J_{5,6b}$ 5.1Hz; H-5), 3.94 (t, 1H, $J_{3.4} = J_{4,5}$ 7.6 Hz; H-4), 3.64 (dd, 1H, $J_{5,6b}$ 3.2 Hz, $J_{6a,6b}$ 13.2 Hz; H-6a), 3.32 (dd, 1H, $J_{5,6a}$ 5.1 Hz; H-6b), 2.49 (t, 1H; H-3′), 1.47, 1.45, 1.42, 1.41 (4s, 12H; 2 × $C(CH_3)_2$); ^{13}C NMR (125.5 MHz, $CDCl_3$, δ): 170.2 (C-1), 112.8, 110.8 (2 × $C(CH_3)_2$), 80.0 (C-3), 79.1 (C-5), 77.9 (C-4), 77.5 (C-2), 77.0 (C-2′), 75.6 (C-3′), 53.0 (C-1′), 52.1 (C-6), 27.4, 27.1, 27.1, 26.2 (2 × C(CH_3)$_2$). HRMS (ESI/Q-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{15}H_{21}N_3O_6Na$ 362.1328; found: 362.1338.

Figure S5. ^{1}H NMR spectrum (500 MHz, $CDCl_3$) of compound **5**.

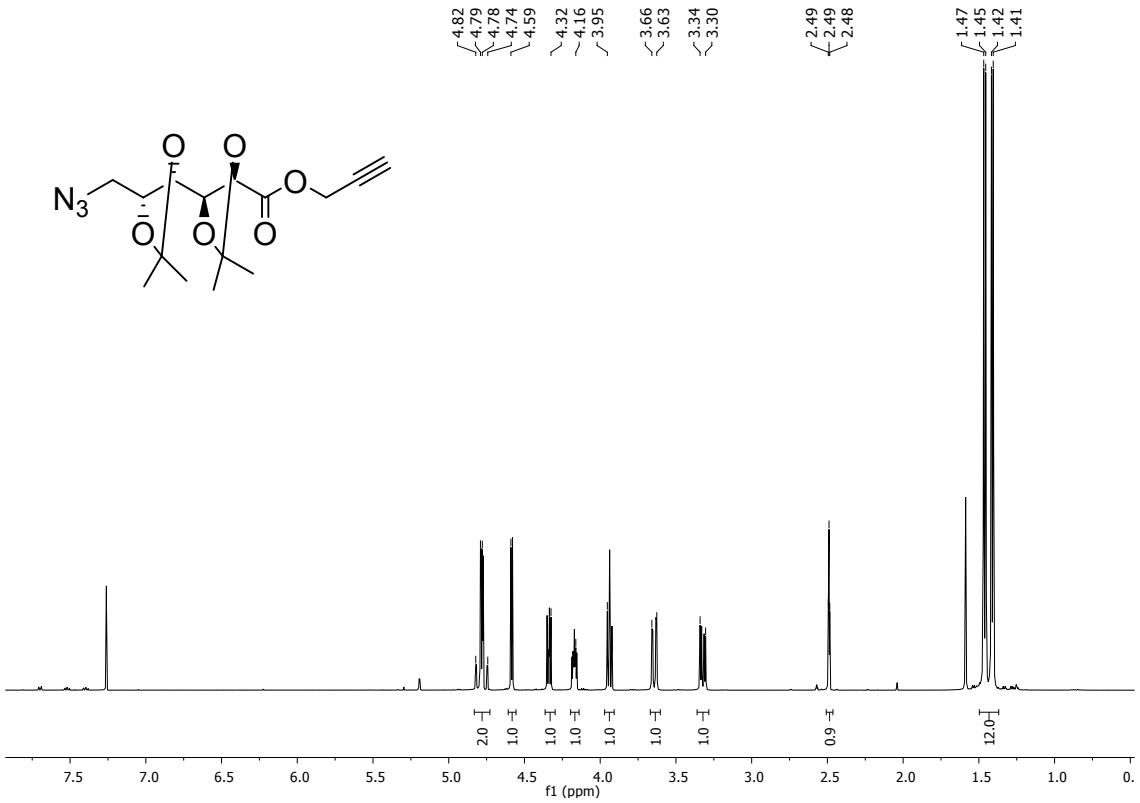
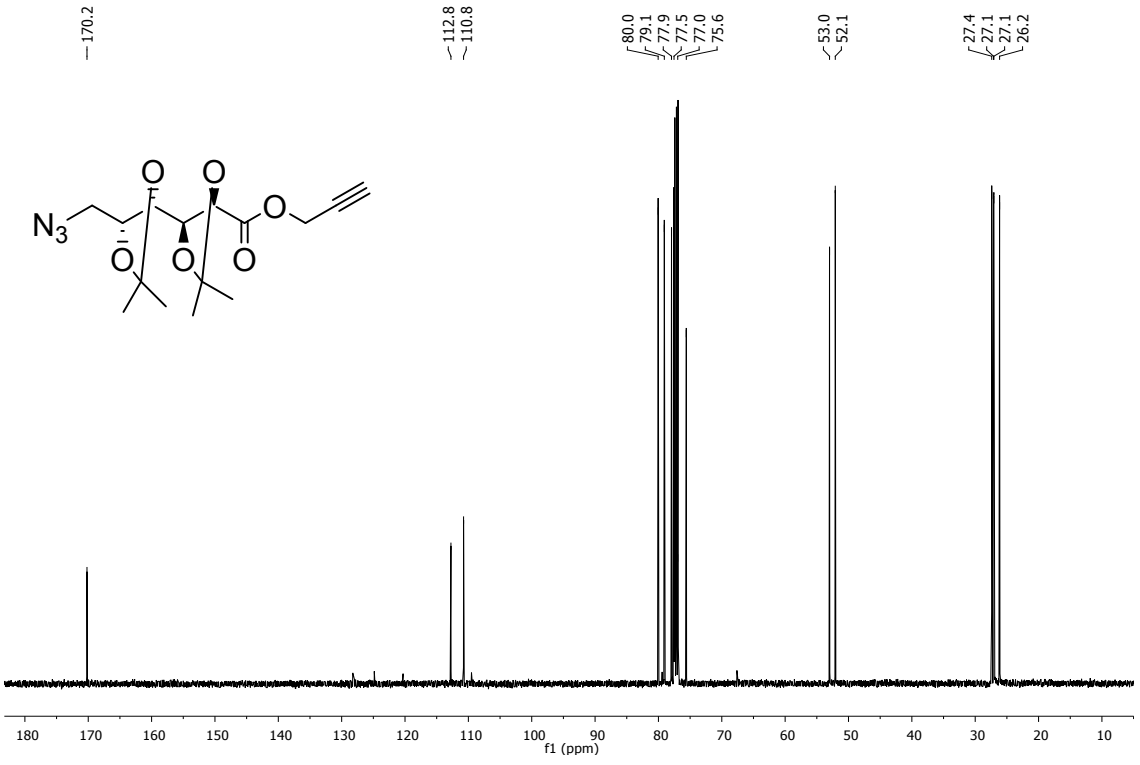


Figure S6. ^{13}C NMR spectrum (125 MHz, $CDCl_3$) of compound **5**



Polymerization of compound 5

Several polymerization conditions were essayed as indicated in Table 1, the following general procedures were applied.

i) CuAAC Polymerization in solution. To a solution of compound **5** (0.100 g, 0.30 mmol) in the solvent (volume was adjusted to give the concentration indicated), CuOAc was added (0.004 g, 0.030 mmol) under Ar atmosphere. The mixture was stirred in the conditions indicated in the Table. The polymer precipitated out and it was filtered; the solid was dissolved in CH_2Cl_2 (absence of monomer was confirmed by tlc) and extracted with 1 M NH_4OH (3 × 4 mL) and H_2O (2 × 4 mL). The organic layer was dried with $MgSO_4$ and concentrated to give poly(ester-triazole) **6** as a white solid. T_m 194°C; $[\alpha]_D^{25}$ +11.6 (c = 0.95, $CHCl_3$); IR (ATR ν, cm^{-1}): 1741 (s, C=O st); ^{1}H NMR (500 MHz, $CDCl_3$, δ): 7.80 (s, 1H; H-3´), 5.32 (s, 2H; H-1´), 4.71 (dd, 1H, $J_{6a,6b}$ 14.5, $J_{5,6a}$ 2.8 Hz; H-6a), 4.51 (d, 1H, $J_{2,3}$ 5.4 Hz; H-2), 4.50 (dd, 1H, $J_{6a,6b}$ 14.5, $J_{5,6b}$ 6.1 Hz; H-6b), 4.34-4.26 (m, 2H; H-3, H-5), 3.70 (t, 1H, $J_{4,5} = J_{3,4}$ = 7.7 Hz; H-4), 1.47, 1.37, 1.30, 1.28 (4s, 12H; (2 × $C(CH_3)_2$); ^{13}C NMR (125.5 MHz, $CDCl_3$, δ) 170.7 (C-1), 142.1 (C-2´), 125.7 (C-3´), 112.8, 111.0 (2 × $C(CH_3)_2$), 79.8 (C-3), 78.1 (C-5, C-4), 77.7 (C-2), 58.7 (C-1´), 51.8 (C-6), 27.3, 27.1, 26.9, 26.1 (2 × $C(CH_3)_2$). Anal. Calcd. for $C_{15}H_{21}N_3O_6$: C, 53.09; H, 6.24; N,12.38. Found: C, 52.65; H, 6.21; N, 12.11.

Preparative scale. The above polymerization conditions were applied in higher scale (0.350 g of compound **5**) to yield poly(ester-triazole) 6 in 90% yield (Table 1, entry 16).

ii) Cu Free (CuFAAC) click polymerization in solution. A solution of compound **5** (0.100 g, 0.30 mmol) in the solvent (1 mL) was stirred under Ar atmosphere at 70 °C overnight.

The polymer precipitated from the reaction mixture, it was filtered and the solid purified by dissolution in CH_2Cl_2 and precipitation with Et_2O to give poly(ester-triazole) **7** as a white solid. T_m 167 °C; $[\alpha]_D^{25}$ +11.5 (c = 1.0, $CHCl_3$); IR (ν, cm^{-1}): 1741 (C=O); ^1H NMR (500 MHz, $CDCl_3$, δ): 7.80 (s, 1H; H-3´x), 7.70 (s, 1H; H-3´y), 5.32 (s, 4H; H-1´x, H-1´y), 4.81 (dd, 1H, $J_{6a,6b}$ 14.7, $J_{5,6a}$ 2.5 Hz; H-6ay), 4.72 (dd, 1H, $J_{6a,6b}$ 14.3, $J_{5,6a}$ 2.9 Hz; H-6ax), 4.64 (dd, 1H, $J_{6a,6b}$ 14.7, $J_{5,6b}$ 5.8 Hz; H-6by), 4.52 (d, 2H, $J_{2,3}$ 5.3 Hz; H-2x, H-2y), 4.50 (dd, 1H, $J_{6a,6b}$ 14.3, $J_{5,6b}$ 6.2 Hz; H-6bx), 4.34-4.29 (m, 4H; H-3x, H-3y , H-5x, H-5y), 3.71 (2t, 2H; H-4x, H-4y), 1.51-1.25 (8s, 24H; (4 × $C(CH_3)_2$ x,y); ^{13}C NMR (125.5 MHz, $CDCl_3$, δ) 170.7 (C-1x), 170.1 (C-1y), 142.1 (C-2´x), 141.2 (C-2´y), 134.7 (C-3´y), 125.7 (C-3´x), 112.9, 111.0 (2 × $C(CH_3)_2$ x), 113.0, 110.9 (2 × $C(CH_3)_2$y), 79.8 (C-3x, C-3y), 78.1 (C-4x, C-4y, C-5x, C-5y), 77.7 (C-2x, C-2y), 58.7 (C-1´x, C-1´y), 51.8 (C-6x), 49.6 (C-6y), 27.4-26.0 (C(CH_3)$_2$x,y). *Note:* The subscript x refers to the 1.4-triazole fragment and y to the 1.5-triazole segment.

iii) CuAAC Polymerization in bulk. A mixture of compound **5** (0.088 g, 0. 26 mmol) and CuOAc (0.003 g, 0.026 mmol) was subjected to microwave irradiation at 70 °C for 30 min. The solid mixture was dissolved in CH_2Cl_2 (absence of monomer was confirmed by tlc) and extracted with 1 M NH_4OH (3 × 4 mL) and H_2O (2 × 4 mL). The organic extract was dried with $MgSO_4$ and concentrated to give poly(ester-triazole) **6** as a white solid (0.084 g, 95%). T_m 212 °C, $[\alpha]_D^{25}$ +9.5 (c = 1.0, $CHCl_3$). The IR and NMR spectra were the same as those reported in the item *i*).

iv) CuFAAC Polymeryzation in bulk. Compound **5** (0.100 g, 0.29 mmol) was stirred at 70 °C overnight or alternatively for 60 min under MW irradiation. The sample of entry 2, Table 1, was subjected to MW irradiation at increasing temperature (in the range 60-120

°C, stepwise every 10 °C, during 10 min intervals). The resulting solid was purified by dissolution in CH_2Cl_2 and precipitation with Et_2O to give poly(ester-triazole) **7** as a white solid. The IR and NMR spectra were essentially the same as those reported in the item *ii*).

v) CuAAC Reaction to favour the formation of cyclic oligomers. To a solution of compound **5** (0.100 g, 0.30 mmol) in DMF (6 mL), CuOAc was added (0.004 g, 0.030 mmol) under Ar atmosphere. The mixture was stirred at 80 °C for 4 days, when tlc revealed two main products (R_f = 0.52 and 0.44, EtOAC). After concentration, the residue was dissolved in $CHCl_3$ and extracted with 1 M NH_4OH (3 × 4 mL) and H_2O (2 × 4 mL). The organic phase was dried with $MgSO_4$ and concentrated. The residue was subjected to column chromatography (EtOAc). The faster moving fraction (R_f = 0.52) was a mixture of two compounds (**8** and **9**), while the other component (R_f = 0.44) was isolated as a single product, which was identified as the cyclotetramer **10**: mp 212 °C; $[\alpha]_D^{25}$ +20.2 (c = 0.5, acetone); ^{1}H NMR (500 MHz, $CDCl_3$, δ): 7.76 (s, 1H; H-3´), 5.41 (d, 1H, $J_{1'a,1'b}$ 12.8 Hz; H-1´a), 5.27 (d, 1H, $J_{1'a,1'b}$ 12.8 Hz; H-1´b), 4.67 (d, 1H, $J_{2,3}$ 6.8 Hz; H-2), 4.64 (dd, 1H, $J_{5,6a}$ 2.2, $J_{6a,6b}$ 14.2 Hz; H-6a), 4.44 (dd, 1H, $J_{5,6b}$ 2.2 Hz; H-6b), 4.43 (dd, 1H, $J_{3,4}$ 2.1 Hz; H-3), 4.36 (m, 1H, $J_{4,5} = J_{5,6b}$ 8.1 Hz; H-5), 4.06 (dd, 1H; H-4); 1.53, 1.47, 1.38, 1.36 (4s, 12H; 2 × $C(CH_3)_2$); ^{13}C NMR (125.5 MHz, $CDCl_3$; δ): 170.7 (C-1), 141.9 (C-2'), 124.1 (C-3'), 112.2, 111.0 (2 × $C(CH_3)_2$), 78.2 (C-3), 77.6 (C-4), 75.4 (C-5), 74.3 (C-2), 58.6 (C-1'), 52.3 (C-6), 27.3, 26.8, 25.7, 23.2 (2 × $C(CH_3)_2$). HRMS (ESI/Q-TOF) *m/z*: $[M + H]^+$ calcd for $C_{60}H_{85}N_{12}O_{24}$ 1357.5721; found: 1357.5703; $[M + Na]^+$ calcd for $C_{60}H_{84}N_{12}O_{24}Na$ 1379.5619; found: 1379.5000.

Figure S7. ^{1}H NMR spectrum (500 MHz, $CDCl_3$) of poly(ester-triazole) **6**

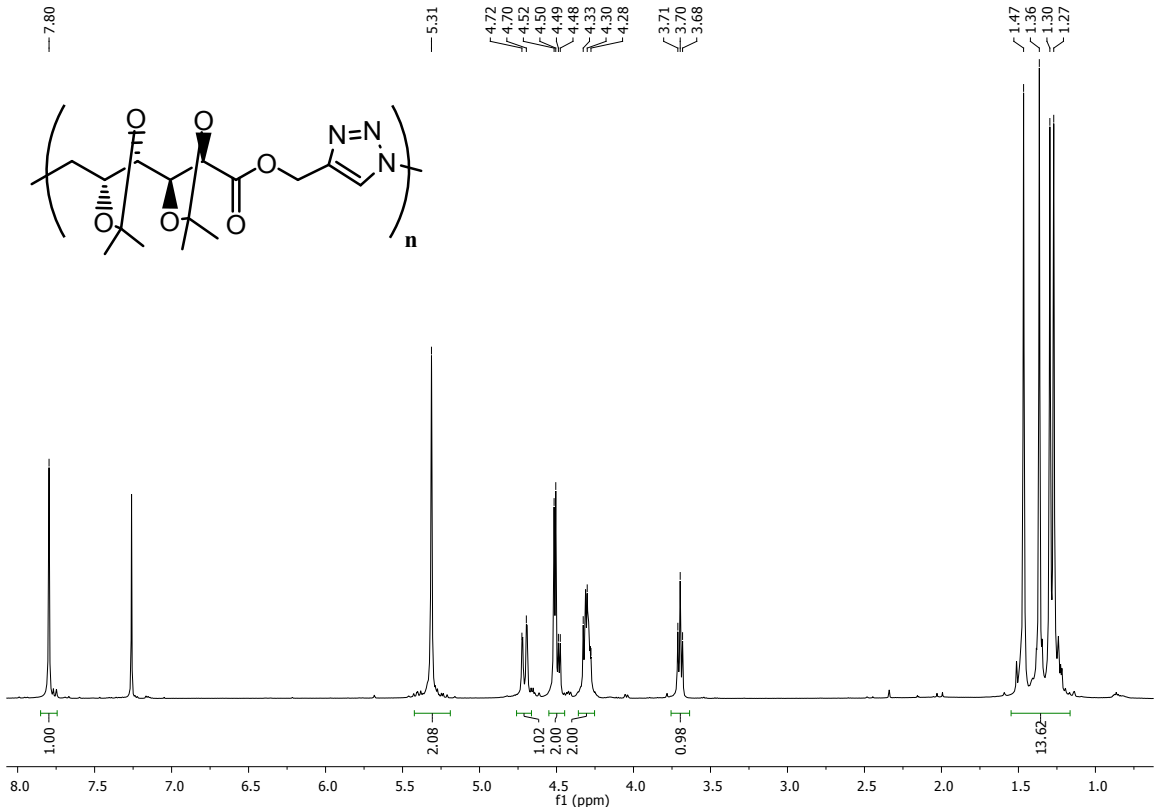


Figure S8. ^{13}C NMR spectrum (125 MHz, $CDCl_3$) of poly(ester-triazole) **6**

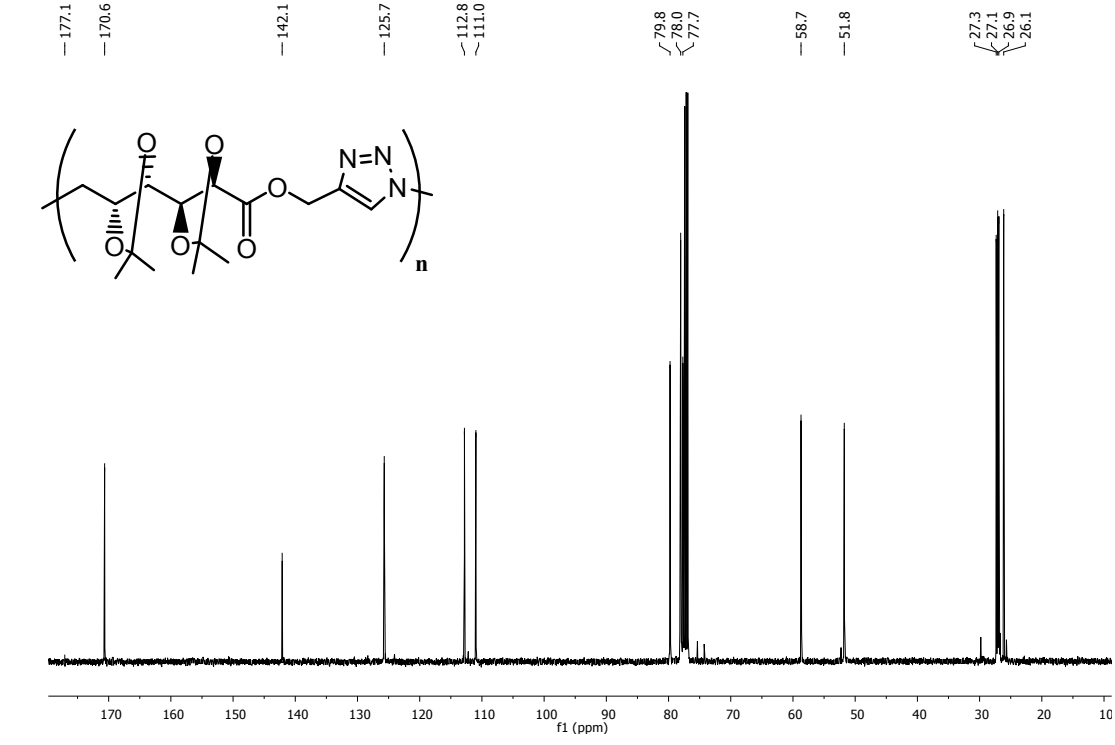


Figure S9. ^{1}H NMR spectrum (500 MHz, $CDCl_3$) of poly(ester-triazole) **7.**

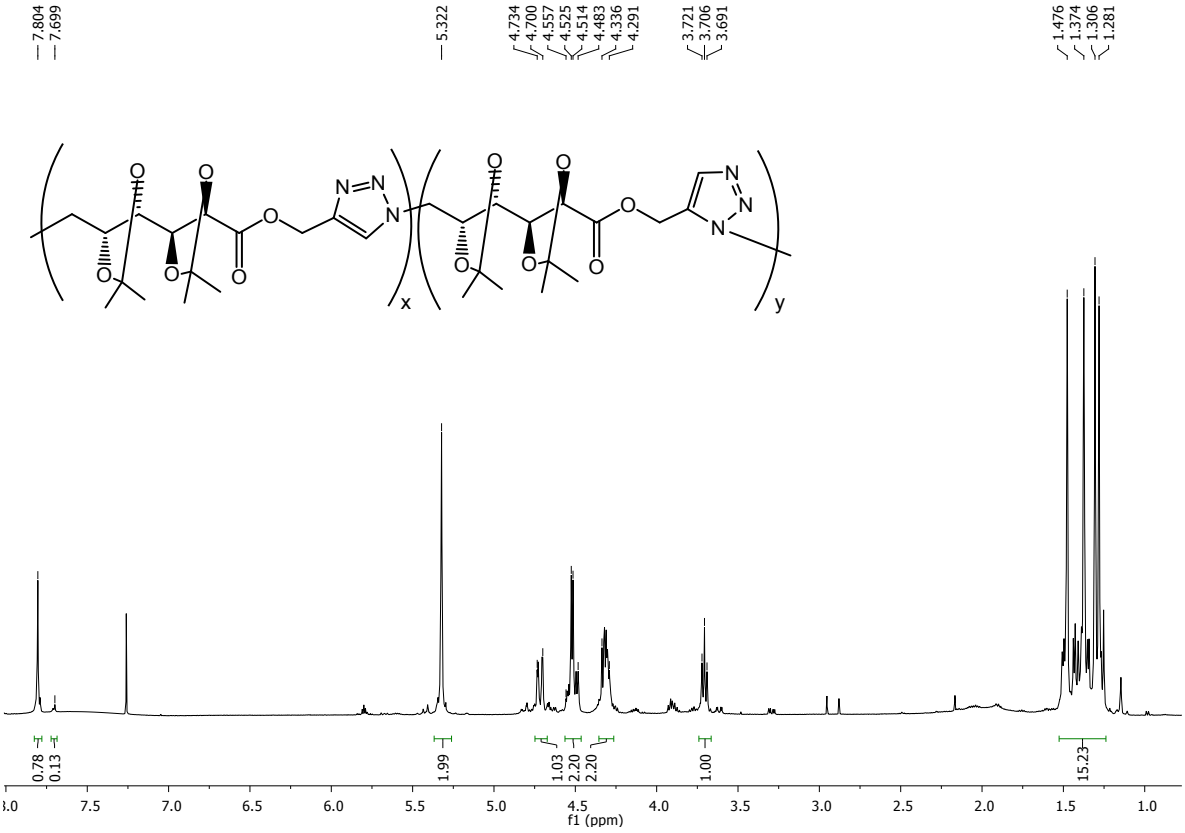


Figure S10. ^{13}C NMR spectrum (125 MHz, $CDCl_3$) of poly(ester-triazole) **7**

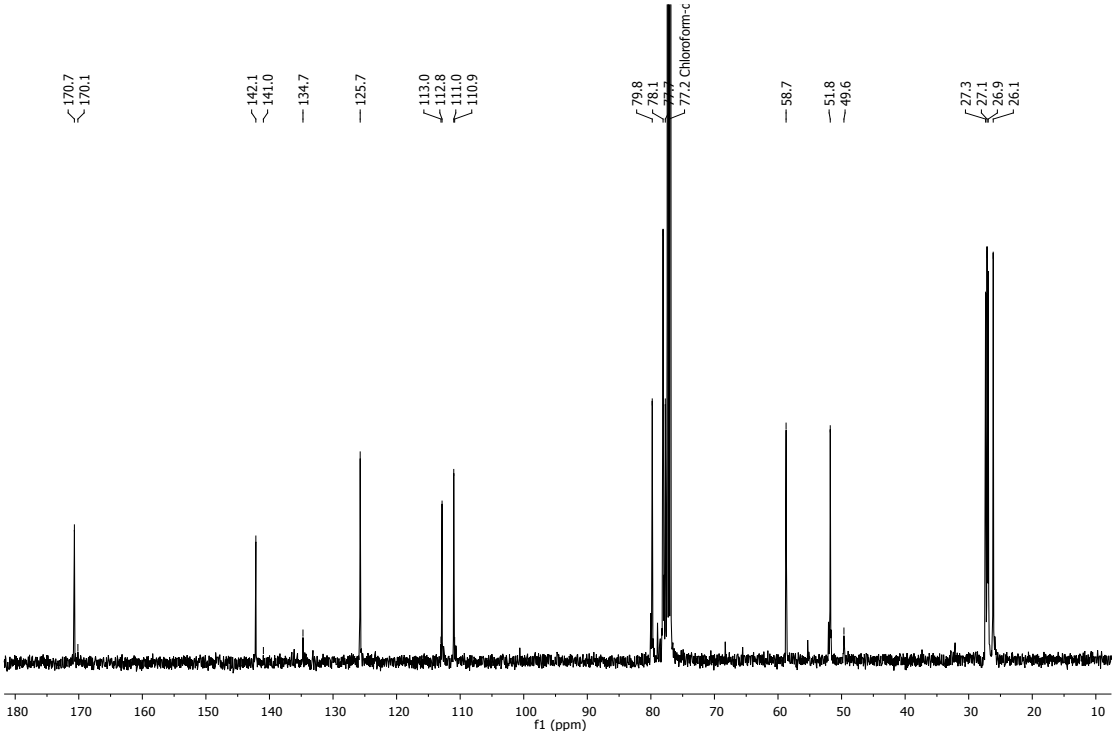


Figure S11. ^{1}H NMR spectrum (500 MHz, $CDCl_3$) of cyclic oligo(ester-triazole)s **8** and **9.**

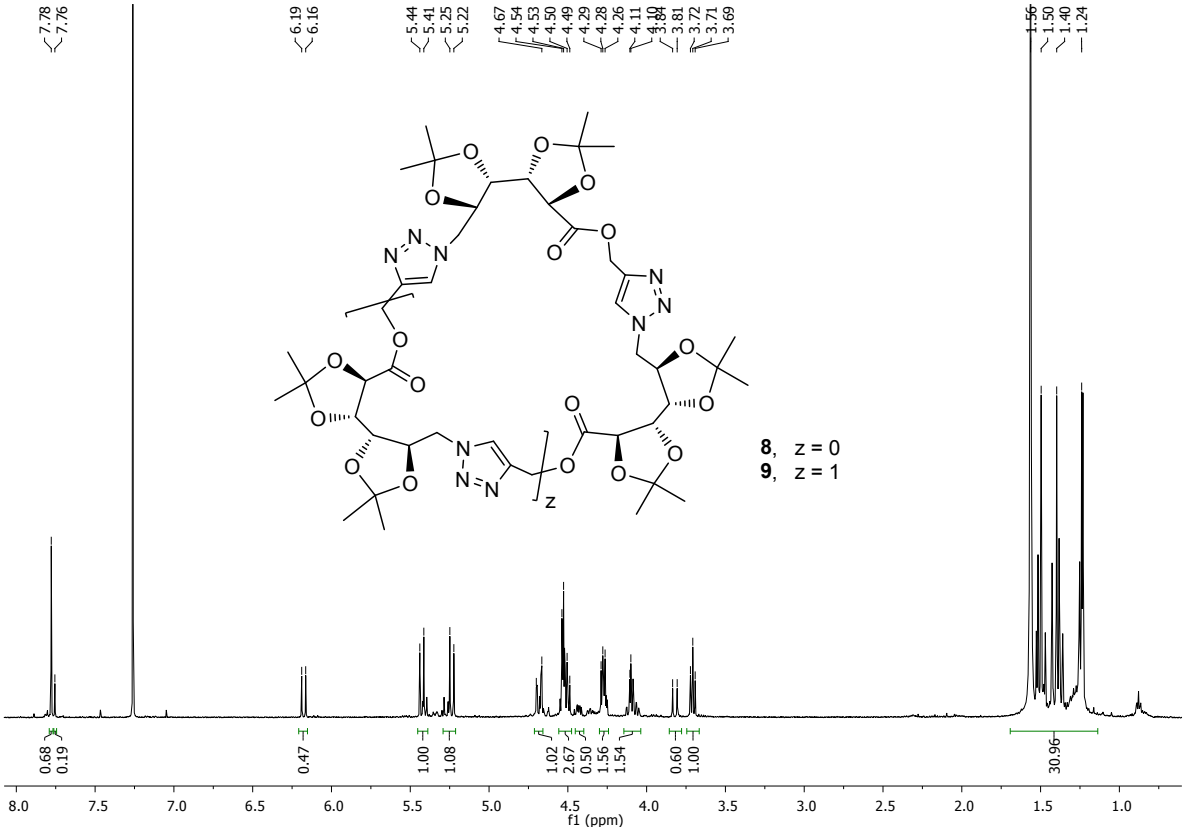


Figure S12. ^{13}C NMR spectrum (125 MHz, $CDCl_3$) of cyclic oligo(ester-triazole)s **8** and **9.**

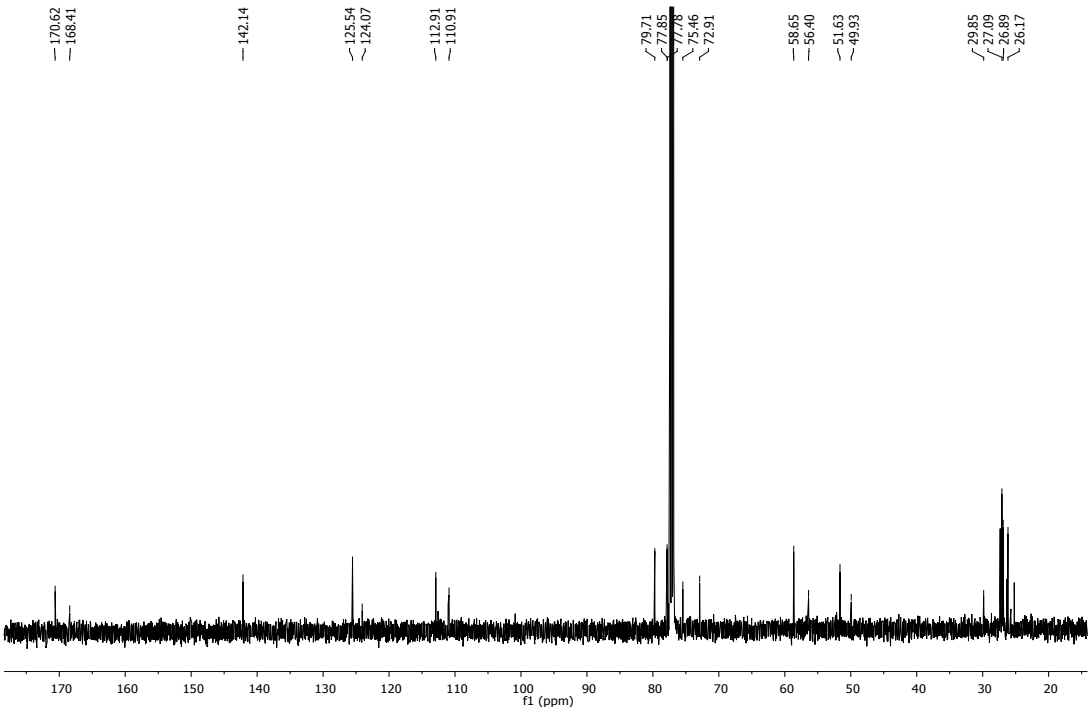


Figure S13. ^{1}H NMR spectrum (500 MHz, $CDCl_3$) of cyclic oligo(ester-triazole) **10**

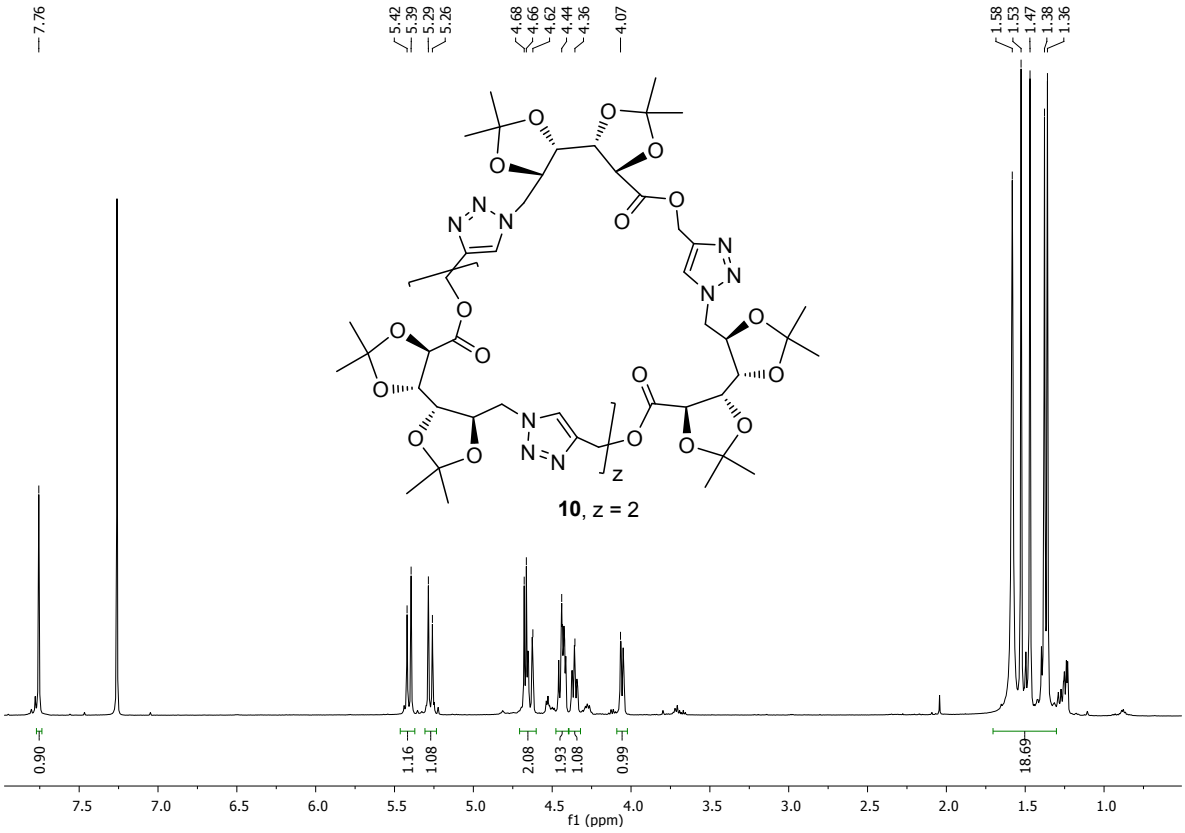


Figure S12. ^{13}C NMR spectrum (125 MHz, $CDCl_3$) of cyclic oligo(ester-triazole)s **10**

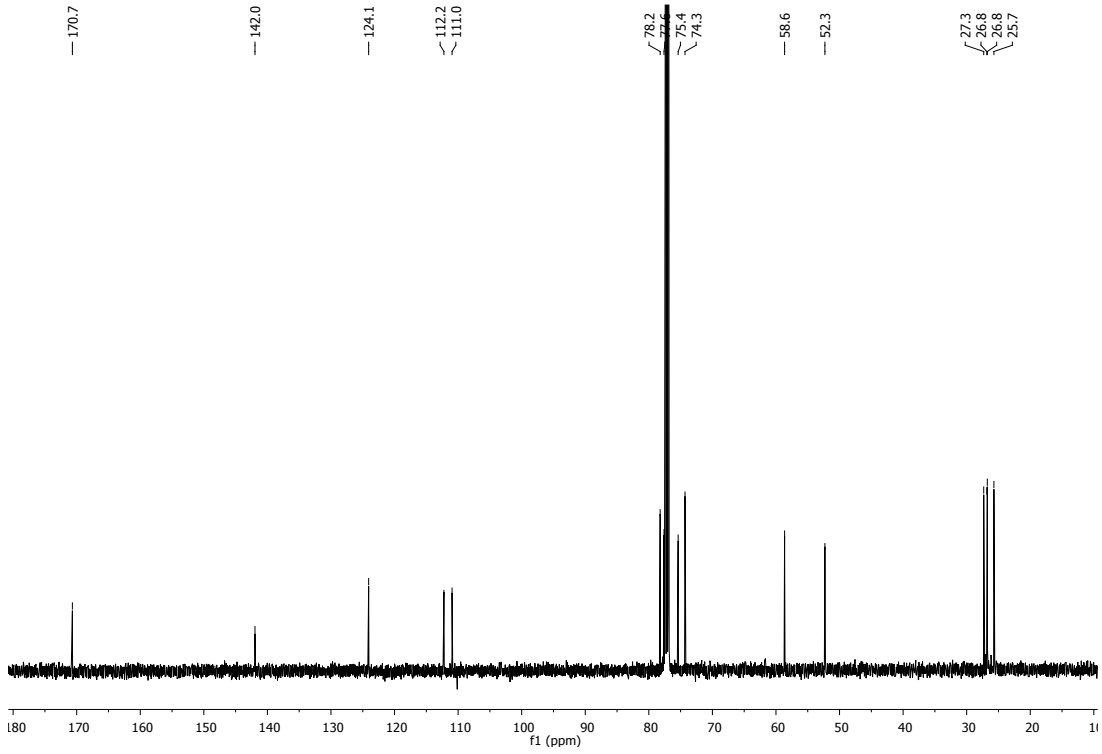


Figure S13. ^{1}H NMR spectrum (500 MHz, $CDCl_3$) of the material isolated according to Table 1, entry 4

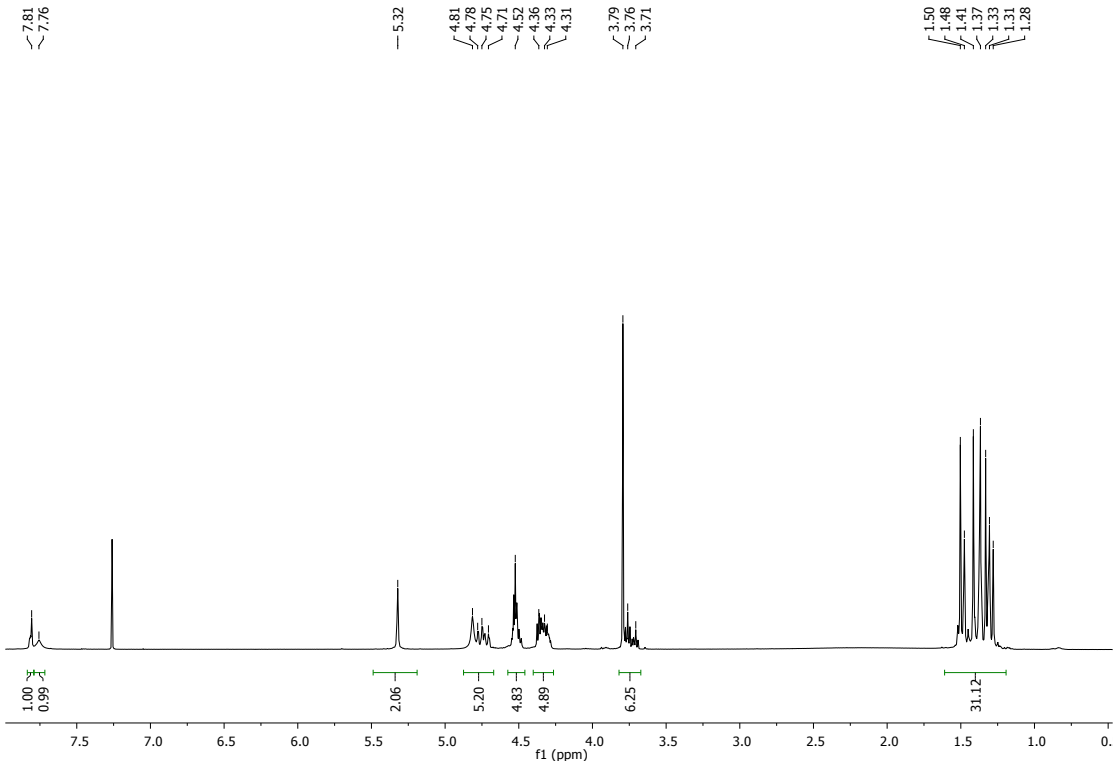
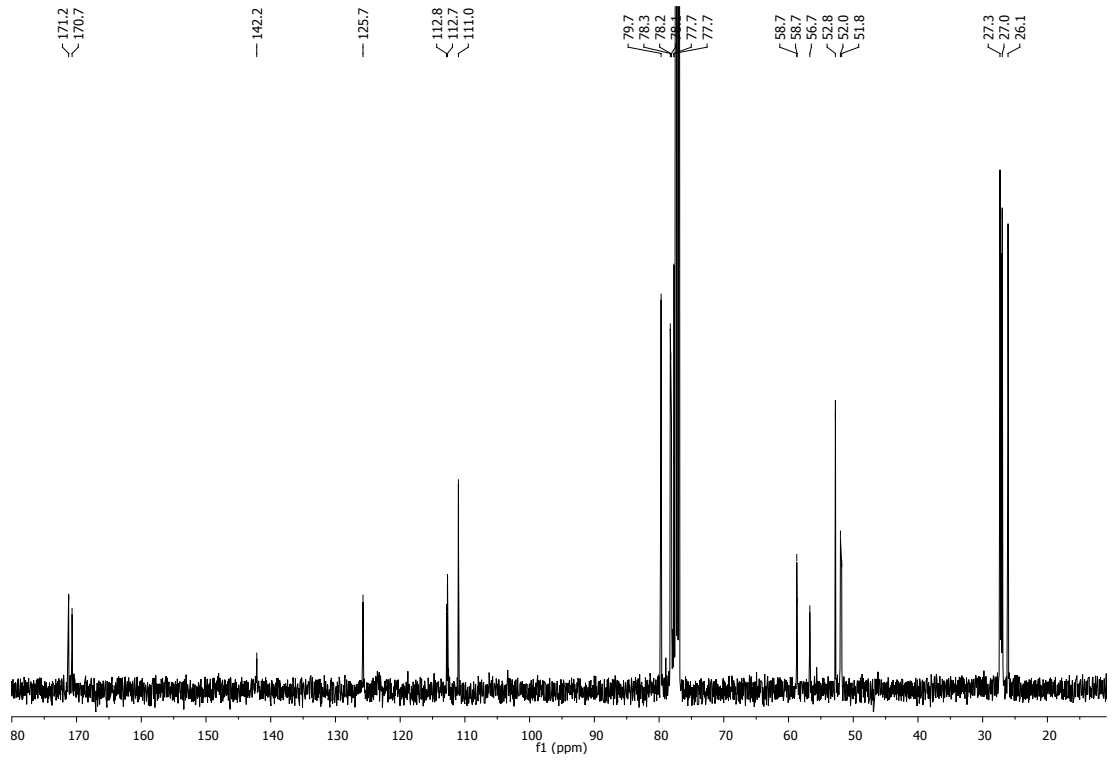


Figure S14. ^{13}C NMR spectrum (125 MHz, $CDCl_3$) of the material isolated according to Table 1, entry 4



Hydrolysis of poly(ester-triazole) 6

Hydrolysis experiments were carried out on poly(ester-triazole) **6**. In a typical procedure, polymer **6** (30 mg) was suspended in a buffer solution (3 mL) at pH 2 (0.1 M H_3PO_4/NaCl) and stirred mat room temperature. Aliquots of 1 mL of the supernatant were taken every 2 weeks. The reactor volume was adjusted to 3 mL with buffer. The aliquot was filtered and concentrated. The residue was dissolved in D_2O was examined by NMR. No degradation products were detected up to 6 months. The polymer that remained insoluble after 6 months was dissolved in $CDCl_3$ and analyzed by NMR spectroscopy. The spectra showed no changes compared with that of the original sample.

In a similar manner, no degradation was detected when the hydrolysis was conducted in aqueous buffers at pH 2 (0.1 M H_3PO_4/NaCl) or pH 7.4 (0.1 M Na_2HPO_4/KH_2PO_4) at 80 ºC for 4 days.

The same procedure was applied to polymer **6** using a buffer solution at pH 10 (0.1 M glycine/NaCl) heated at 80 ºC. Aliquots were taken every 15 h, and NMR monitoring showed the increasing formation of a degradation product, while the solid polymer was gradually dissolving. After 90 h (about 4 days) the dissolution was complete and the solution showed by NMR (D_2O) a single degradation product, which was identified as **6-deoxy-6-(4'-(hydroxymethyl)-1'H-1',2',3'-triazol-1'-yl)-2,3:4,5-di-*O*-isopropylidene-D-galactonic acid (13)**: ^{1}H NMR (500 MHz, D_2O, δ): 8.05 (s, 1H; H-3´), 5.43 (dd, 1H, $J_{5,6a}$ 3.6, $J_{6a,6b}$ 14.8 Hz; H-6a), 5.36 (dd, 1H, $J_{5,6b}$ 6.4, $J_{6a,6b}$ 14.8 Hz; H-6b), 5.35 (s, 1H, H-1‘), 5.22 (m, 1H, $J_{4,5}$ 7.8, $J_{5,6a}$ 3.6, $J_{5,6b}$ 6.4 Hz; H-5), 5.06 (dd, 1H, $J_{2,3}$ 6.3, $J_{3,4}$ 4.8 Hz; H-3), 4.97 (d, 1H, $J_{2,3}$ 6.3; H-2), 4.76 (dd, 1H, $J_{3,4}$ 4.7, $J_{4,5}$ 7.8 Hz; H-4), 1.48, 1.43, 1.42, 1.34 (4s, 12H; 2 × $C(CH_3)_2$); ^{13}C NMR (125.5 MHz, D_2O; δ): 176.8 (C-1), 146.6 (C-2’), 124.6

(C-3'), 110.8, 110.7 (2 × *C*(CH_3)$_2$), 77.8 (C-3), 77.1 (C-4), 76.8 (C-2), 75.7 (C-5), 54.2 (C-1'), 51.2 (C-6), 25.5, 25.5, 25.4, 24.4 (2 × C(*C*H_3)$_2$).

Alternatively, the hydrolysis was conducted using 0.5 M TFA (3 mL) solution and the mixture was stirred at 65 °C. After 16 h complete dissolution of the polymer was observed. The solution was concentrated and the residue analyzed by NMR spectroscopy (in DMSO-d_6), which revealed the structure of the degradation product, **6-Deoxy-6-(4'-(hydroxymethyl)-1'H-1',2',3'-triazol-1'-yl)-D-galactonic acid (14)**: ^{1}H NMR (500 MHz, DMSO-d_6, δ): 7.95 (s, 1H; H-3´), 4.51(s, 1H; H-1'), 4.38 (dd, 1H, $J_{5,6a}$ 4.75, $J_{6a,6b}$ 13.7 Hz; H-6a), 4.31 (dd, 1H, $J_{5,6b}$ 8.6, $J_{6a,6b}$ 13.7 Hz; H-6b), 4.28 (s, 1H, H-2), 4.07 (m, 1H; H-5), 3.82 (d, 1H, $J_{3,4}$ 9.5 Hz; H-3), 3.37 (m, 1H; H-4); ^{13}C NMR (125.5 MHz, DMSO-d_6; δ): 175.4 (C-1), 147.5 (C-2'), 123.4 (C-3'), 71.4 (C-3), 69.9 (C-2), 69.6 (C-4), 68.8 (C-5), 55.1 (C-1'), 53.3 (C-6).

Figure S15. ^{1}H NMR spectrum (500 MHz, D_2O) of the degradation product obtained by hydrolysis of poly(ester-triazole) **6** at pH 10.

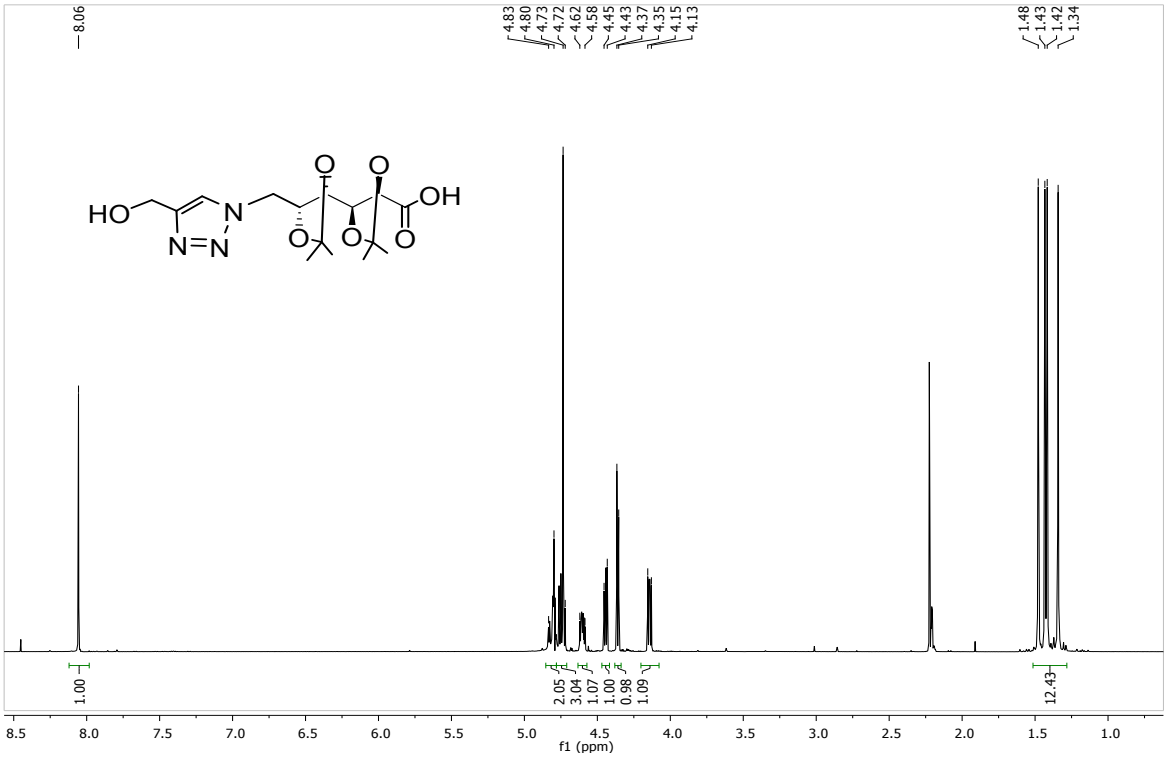


Figure S16. ^{13}C NMR spectrum (125 MHz, D_2O) of the degradation product obtained by hydrolysis of poly(ester-triazole) **6** at pH 10.

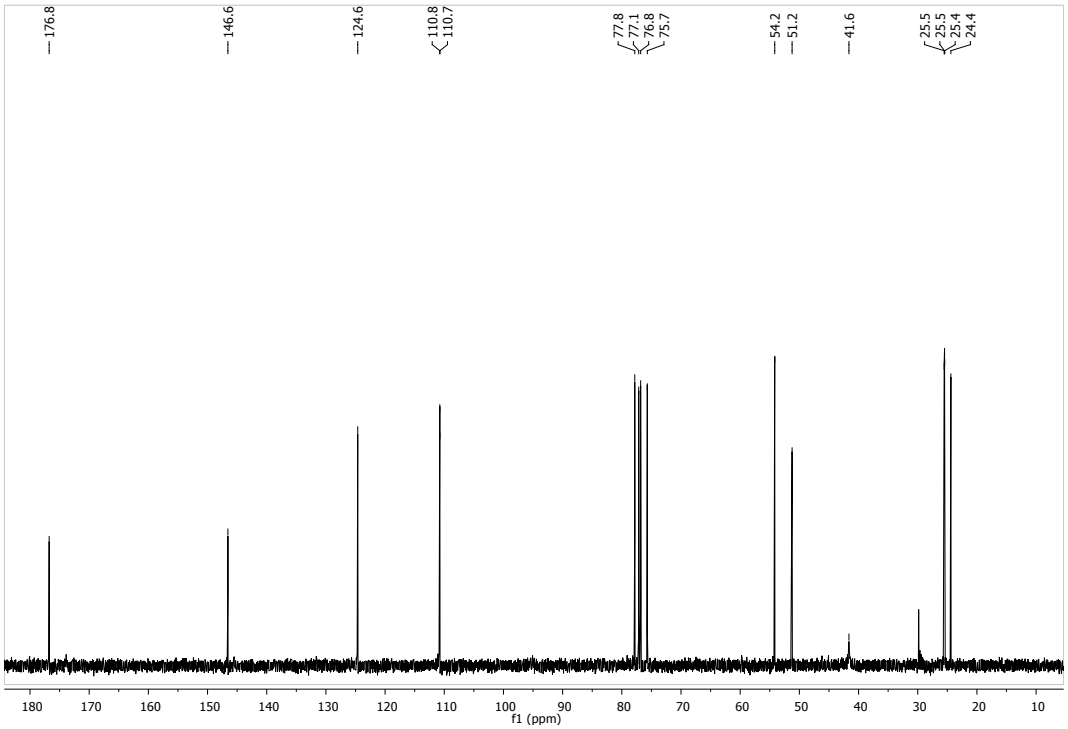


Figure S17. ^{1}H NMR spectrum (500 MHz, D_2O) of the degradation product obtained by hydrolysis of poly(ester-triazole) **6** in 0.5 M TFA

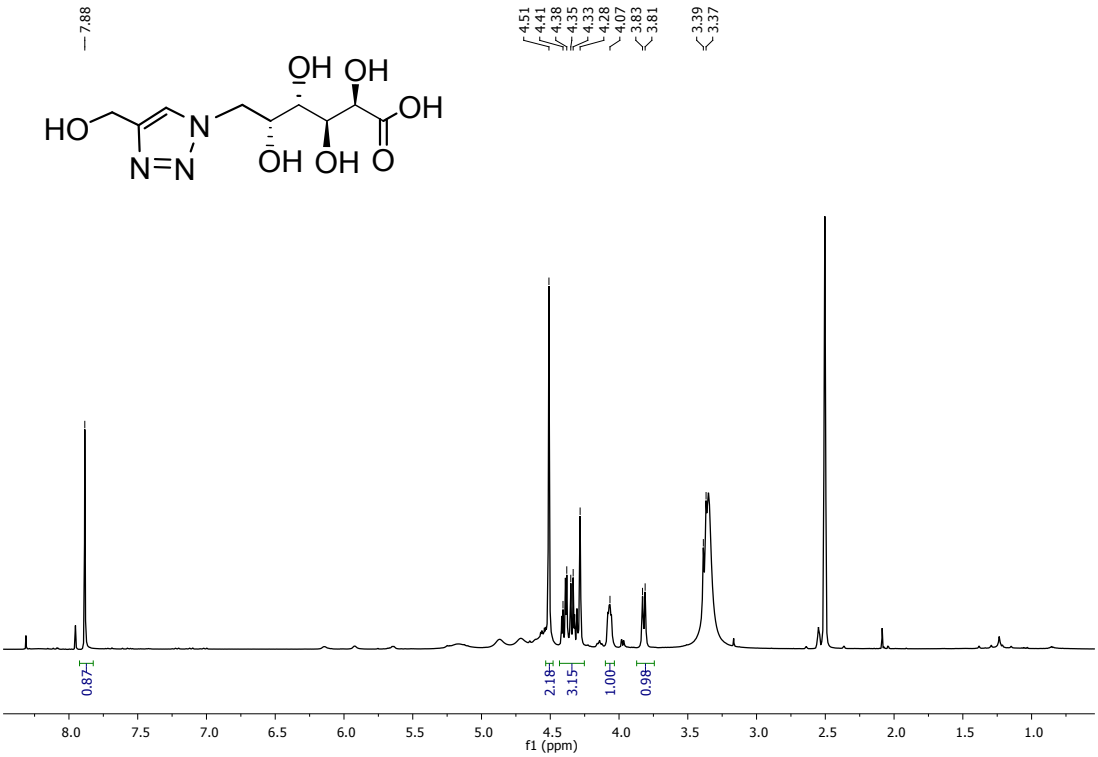
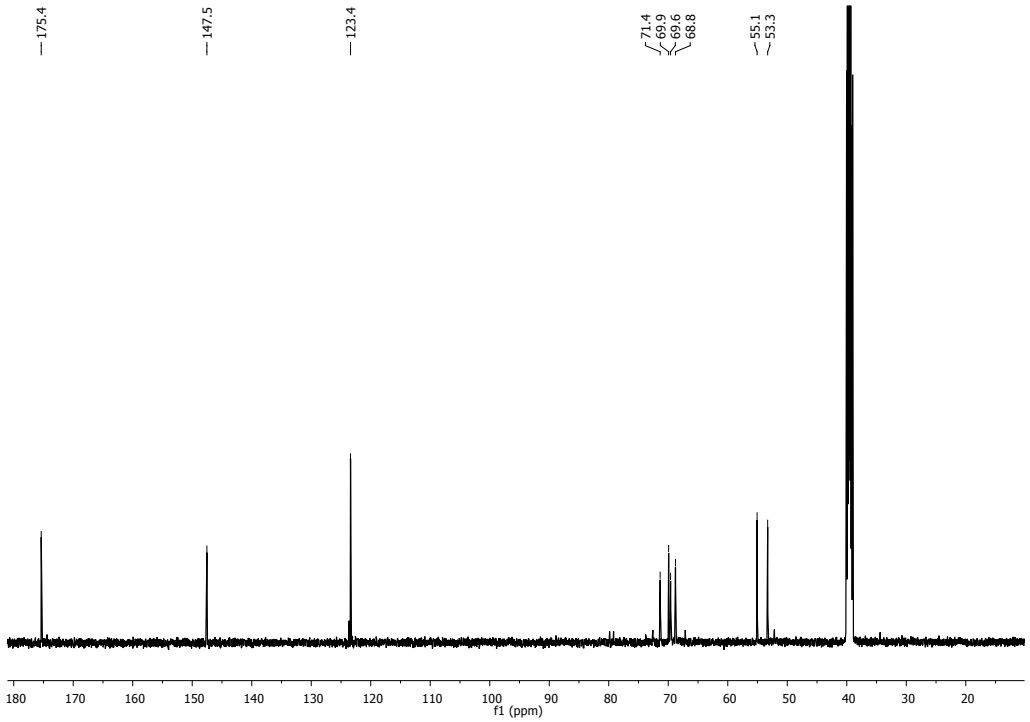


Figure S18. ^{13}C NMR spectrum (125 MHz, D_2O) of the degradation product obtained by hydrolysis of poly(ester-triazole) **6** in 0.5 M TFA



MALDI-TOF Experimental conditions. External calibration was performed with commercial peptide calibration from Sigma Aldrich containing bradykinin (1-7) ([M+H]+ 757.399), angiotensin II ([M+H]+ 1046.542), angiotensin I ([M+H]+ 1296.685); while 2,5-dihydroxybenzoic acid (DHB), nor-harmane (nHo), nor-harmane hydrochloride, and dithranol were used as matrices. AgNO3, NaCl, CuOAc were employed as additives. Matrices solutions were prepared as saturated solutions in acetonitrile-H2O (nHo and nor-harmane hydrochloride), water (DHB) or THF (dithranol). Analyte solutions (1 □g/mL) were freshly prepared in CHCl3. Sample solutions were spotted on a MTP 384 target plate polished steel from Bruker Daltonics (Leipzig, Germany). For MALDI-MS experiments, sandwich method was used according to Nonami et al.19 loading successively matrix solution (0.5 μl), analyte solution (0.5 μl) and matrix solution (0.5 μl × 2) after drying each layer at open atmosphere and room temperature. The matrix to analyte ratio was 3:1 (v/v) and the matrix and analyte solution loading sequence was: i) matrix, ii) analyte, iii) matrix, iv) matrix. Experiments were performed using firstly the full range setting for laser firing position in order to select the optimal position for data collection, and secondly fixing the laser firing position in the sample sweet spots. The laser power was adjusted to obtain high signal-to-noise ratio (S/N) while ensuring minimal fragmentation of the parent ions and each mass spectrum was generated by averaging 100 lasers pulses per spot. Spectra were obtained and analyzed with the programs FlexControl and FlexAnalysis, respectively. Experiments were conducted on two spots (duplicate) prepared with each individual sample. In order to check reproducibility of data, sample preparation and measurements were conducted independently, for each sample, at least on two different days.

SEM Experimental conditions. The surface morphology of the poly(ester-triazole)s was analyzed using SEM with a Zeiss NTS Supra 40 FEG instrument with an in-lens secondary detector. Samples were attached to the holder by using a conductive adhesive carbon tape, and before examination they were coated with a thin layer of gold.

Figure S19. MALDI mass spectra of the poly(ester-triazole) obtained according to Table 1, entry 13. Matrices (M), dopants (D) and ionic mode of detection are indicated in each spectrum as: M+D(+) positive ion mode and M+S(-) negative ion mode.

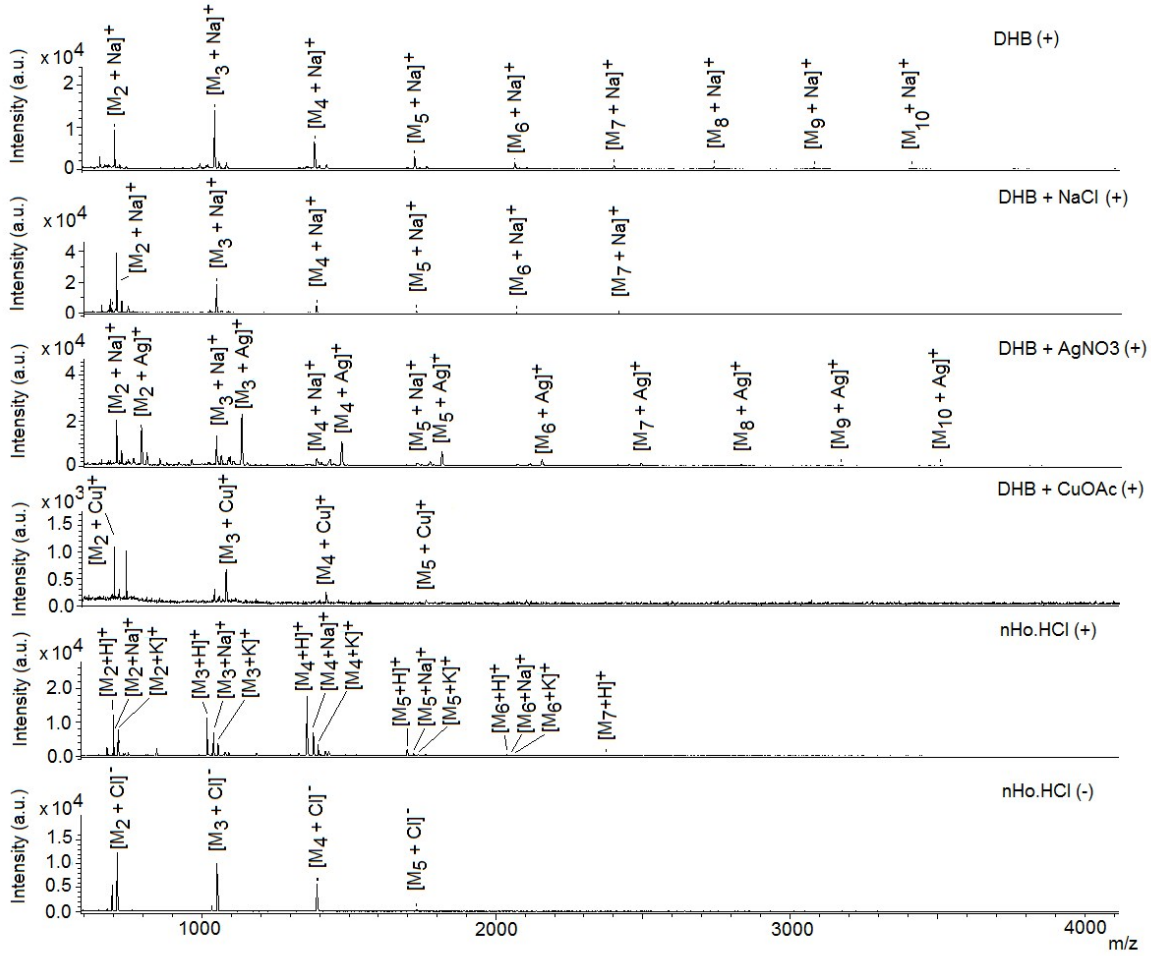


Figure S20. UV-MALDI-TOF spectra of poly(ester-triazole) obtained according to Table 1, entry 4. Matrix (DHB) and dopants (D) are indicated as DHB + D, in each spectrum. Positive ion mode.

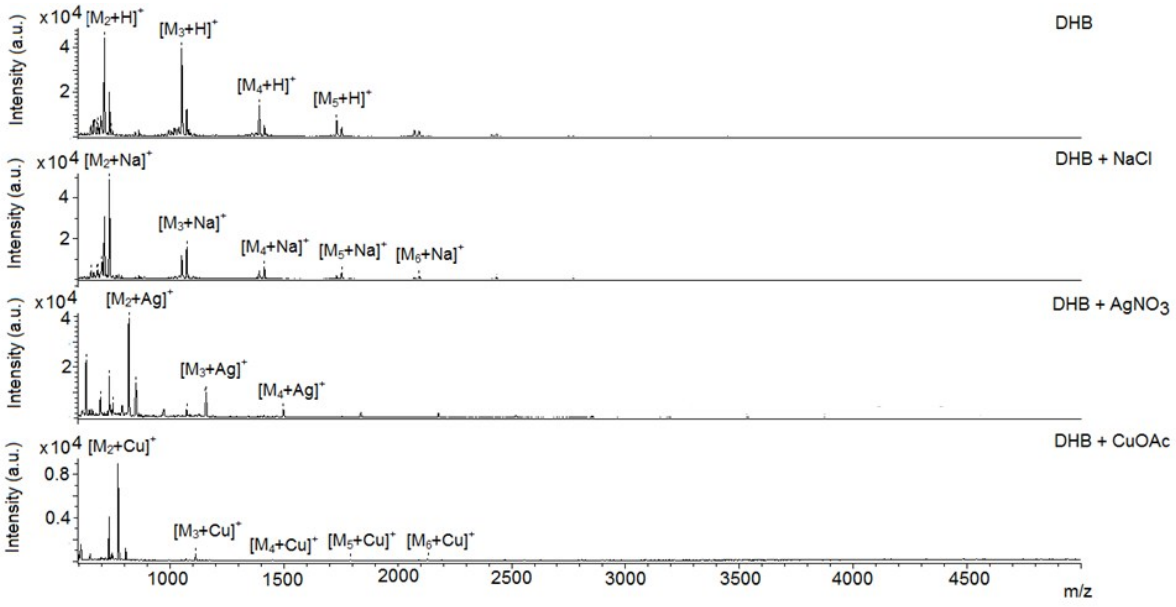


Figure S21. UV-MALDI-TOF spectra of poly(ester-triazole) obtained according to Table 1, entry 4. Matrix (M) and ionic mode of detection are indicated in each spectrum as: M(+) positive ion mode and M(-) negative ion mode. Matrix: nHo.HCl.

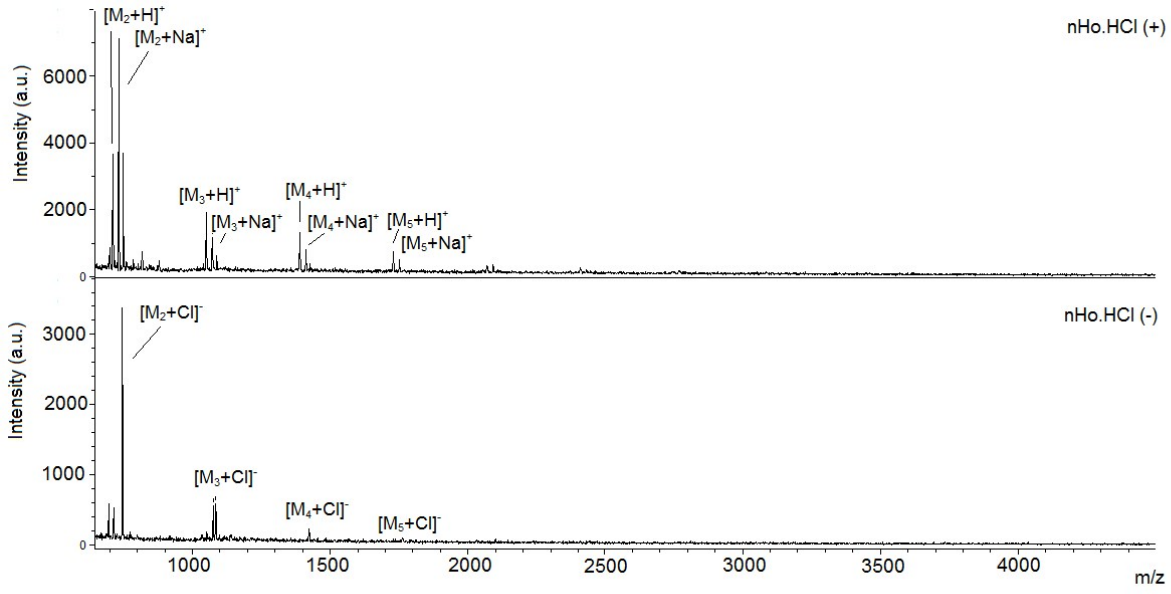


Figure S22. UV-MALDI-TOF spectrum of poly(ester-triazole) obtained according to Table 1, entry 11. Matrix: DHB. Positive ion mode.

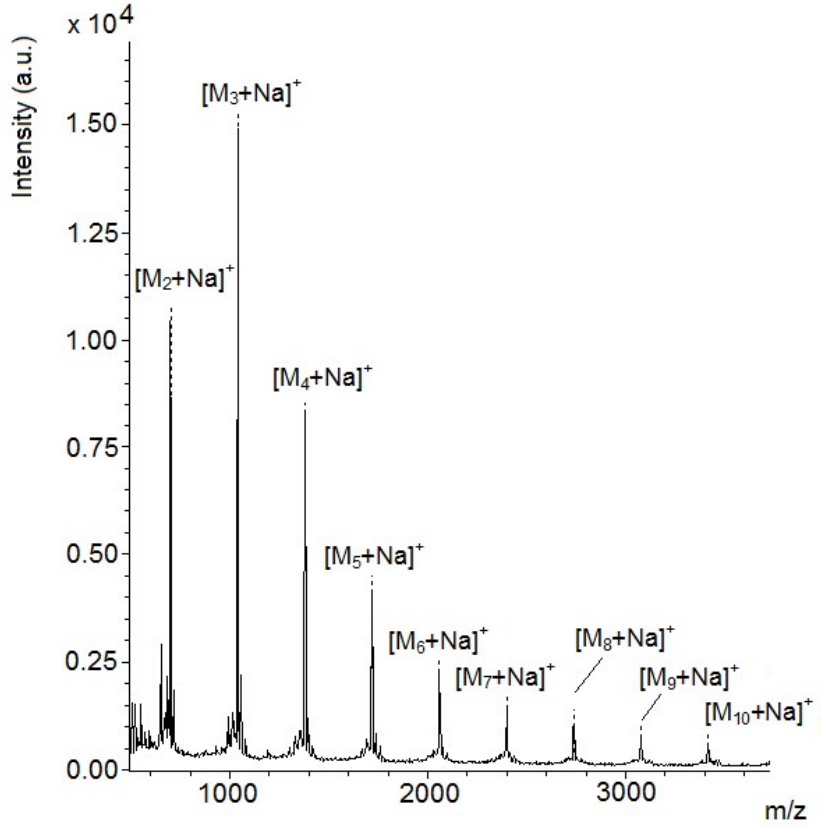


Table S1. MALDI-TOF mass spectrum, main mass peaks of the poly(ester-triazole) obtained according to Table 1, entry 4.

M_n	Chemical formula	$[M+H]^+$		$[M+Na]^+$		$[M+Ag]^+$		$[M+Cu]^+$		$[M+Cl]^-$	
		Calcd	Exp	Calcd	Exp	Calcd	Exp	Calcd	Exp	Calcd	Exp
2	$C_{31}H_{46}N_6O_{13}$	711.32	712.30	733.30	734.27	817.22	818.07	773.24	773.24	745.28	746.38
3	$C_{46}H_{67}N_9O_{19}$	1050.46	1051.72	1072.44	1073.84	1156.36	1157.52	1112.38	1112.38	1084.42	1085.11
4	$C_{61}H_{88}N_{12}O_{25}$	1389.60	1391.37	1411.58	1413.32	1495.50	1496.90	1451.52	n.d.[a]	1423.56	1423.65
5	$C_{76}H_{109}N_{15}O_{31}$	1728.74	1730.92	1750.72	1752.66	1834.64	n.d.	1790.66	1790.77	1762.70	1762.02

[a]Not detected

Table S2. MALDI-TOF mass spectrum: Main mass peaks of poly(ester-triazole) obtained according to Table 1, entry 11

M_n	Chemical formula	$[M+Na]^+$	
		Calculated	Experimental
2	$C_{30}H_{43}N_6O_{12}$	702.29	701.924
3	$C_{45}H_{64}N_9O_{18}$	1041.43	1041.31
4	$C_{60}H_{85}N_{12}O_{24}$	1380.57	1380.68
5	$C_{75}H_{106}N_{15}O_{30}$	1719.71	1720.03
6	$C_{90}H_{127}N_{18}O_{36}$	2058.86	2059.34
7	$C_{105}H_{148}N_{21}O_{42}$	2398.00	2399.04
8	$C_{120}H_{169}N_{24}O_{48}$	2737.14	2738.42
9	$C_{135}H_{190}N_{27}O_{54}$	3076.28	3077.82
10	$C_{150}H_{211}N_{30}O_{60}$	3415.42	3416.00