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RESEARCH ARTICLE

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Clickable 2,2-bis(hydroxymethyl)propionic acid-derived AB_2 monomers: Hyperbranched polyesters through the CuAAC cycloaddition (click) reaction

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Abstract

We present the synthesis and characterization of two aliphatic AB_2 monomers derived from the readily available 2,2-bis(hydroxymethyl)propionic acid and containing one alkyne group and two azide functionalities. The distance between the polymerizable groups differs in the two monomers by the insertion of an additional carbon atom in the aliphatic structure that addresses the steric demand during polymerization. The synthetic procedure for the monomers is relatively simple and scalable, and the monomers are able to polymerize through the Copper(I)-catalyzed Azide-Alkyne Cycloaddition (CuAAC reaction). The polymerization affords hyperbranched polymers in good yields and molecular weights and moderate degrees of branching. Copyright © 2021 John Wiley & Sons, Ltd.

KEYWORDS

AB_2 monomers, click reactions, CuAAC polymerizations, hyperbranched polymers

1 | INTRODUCTION

Highly branched, soluble, polymeric structures are receiving increasing scientific attention because of their potential in several technologies. The globular architecture gives unique properties: abundant functional groups decorating the exterior part of the macromolecule and interior cavities with potential for encapsulation of small molecules. They have become an increasingly important class of soft nanomaterials, and found applications in catalysis, biomaterials, microelectronics, and nanomedicines.[1] Furthermore, they are soluble and processable, and they have a low relative viscosity when compared to linear macromolecular analogs of comparable molecular weights, essentially as a consequence of reduced intermolecular friction.

Low viscosity can be very useful in applications such as paints and varnishes.[2] The polymeric base constitutes the essential and indispensable component of the coating system; it forms a continuous film adhering to the substrate and it must be capable of incorporating and binding together the other components of the formulation. On the other hand, the macromolecular system has to be diluted with organic solvents in order to reduce viscosity and to allow easy handling and application to the surface. The use of globular polymers with low viscosity, instead of linear polymers, would give the distinct advantage of reducing the amount of volatile organic compounds (VOC) in the product for commercialization.

Globular, highly branched polymers may be prepared by two distinct routes: (1) a lengthy and stepwise

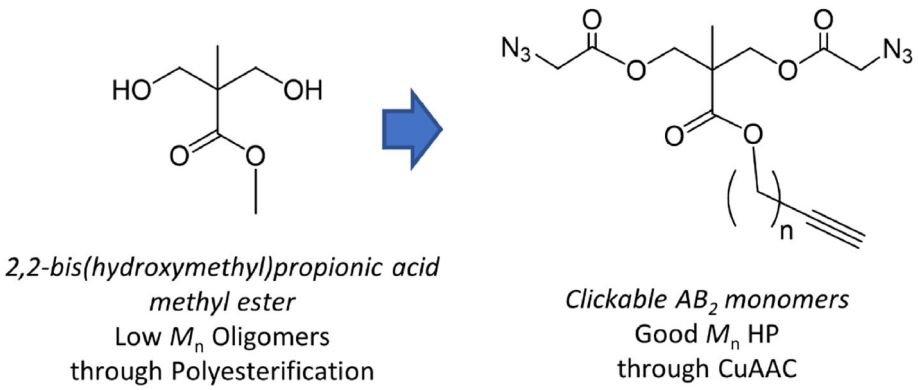


FIGURE 1 Schematic representation of the strategy for the realization of HP polyesters from 2,2-bis (hydroxymethyl)propionic acid

procedure, characteristic of dendrimers, in which the growth process is carried out one generation at a time, and (2) a one-step process, characteristic of hyperbranched polymers (HPs), usually starting from an AB_x-type monomer, where A and B are functional groups that are reactive only toward each other. In contrast to dendrimers, whose synthesis is laborious and multi-step and whose purification is carried out by chromatography, hyperbranched polymers can be synthesized in a relatively facile way and purified by a simple precipitation.[3] The degree of branching (DB) helps to describe their structures; they have been applied in different fields, such as optical, microelectronic and magnetic materials, solar cells, biomaterials, and nanomedicine.[1o]

Polyesters are often used in paints and varnishes. HPs obtained by direct polyesterification have been reported, but they suffer from low degrees of polymerization and of branching. The Cu(I)-catalyzed azide-alkyne cycloaddition reaction (CuAAC, known as the click reaction) has been widely applied for bioconjugation, polymer, and dendrimer synthesis.[4] As reported by recent contributions in the literature,[5] it can also be a very efficient tool used for the construction of high molecular weight HPs.

This contribution reports our exploitation of the CuAAC as the polymerization procedure for relatively simple, ester-containing AB_2 monomers derived from the readily available 2,2-bis(hydroxymethyl)propionic acid (**1**), to make hyperbranched polyesters (Figure 1).

2 | RESULTS AND DISCUSSION

Synthesis of monomers. We focused on the use 2,2-bis (hydroxymethyl) propionic acid (**1**) since it is a cheap, readily available, and scalable starting material. 2,2-bis (hydroxymethyl)propionic acid has been used before as the key synthon in the synthesis of aliphatic dendrimers, and, more recently, for HPs.[6] Initial attempts were carried out on 2,2-bis(hydroxymethyl)propionic acid methyl ester (**2**) with the aim of obtaining HPs by transesterification. However, even in the presence of several catalysts which had proven efficient in previously reported, similar systems,[7] the reaction resulted in the synthesis of oligomeric materials of very low molecular weight. These attempts are summarized in Data S1.

We, therefore, switched our attention to click reactions. Our design for the development of hyperbranched polyesters using click chemistry as the polymerization reaction followed two main design guidelines: (1) the use of an efficient CuAAC click-type polymerization approach; (2) the distancing of the reactive units through the insertion of flexible aliphatic carbon chain in order to reduce steric congestion during HP formation, for the obtainment of high degrees of polymerization and high DB.

The synthesis of the key AB_2 monomers is shown in Scheme 1 and it followed three steps. The first step (Scheme 1) involved the esterification of the carboxylic acid functionality, to afford either 2,2-bis(hydroxymethyl) propionic acid methyl ester **2**, obtained following literature conditions[8] on a multigram scale with a simple liquid–liquid extraction as the purification procedure, or compounds **5**[9] and **6**, which were synthesized by alkylation with the corresponding alkyl bromide containing the terminal alkyne functionality.

No column chromatography was required for these steps, but simple washings to obtain the pure products in good yields. The second step involved the reaction of the esters **2**, **5** or **6** with bromoacetyl bromide in the presence of Et_3N as the acid scavenger and in dry solvent conditions.[10] The corresponding diacetylbromo esters (**3**, **7**, **8**) were obtained in good yields. In the case of **3**, the replacement of the dibromo groups with $-N_3$ groups was carried out with sodium azide and a mixture of acetone/H_2O 3:2 as the solvent, to obtain the corresponding diacetylazido ester (**4**) with a yield of 40%, after liquid–liquid extraction.[11] In the case of **7** and **8**, optimization made it possible to develop a higher yielding procedure, which was modified from a literature protocol[12]: the sodium azide was added to a solution of compound **7** or **8** in dry DMF,

SCHEME 1 Synthesis of key AB_2 monomers

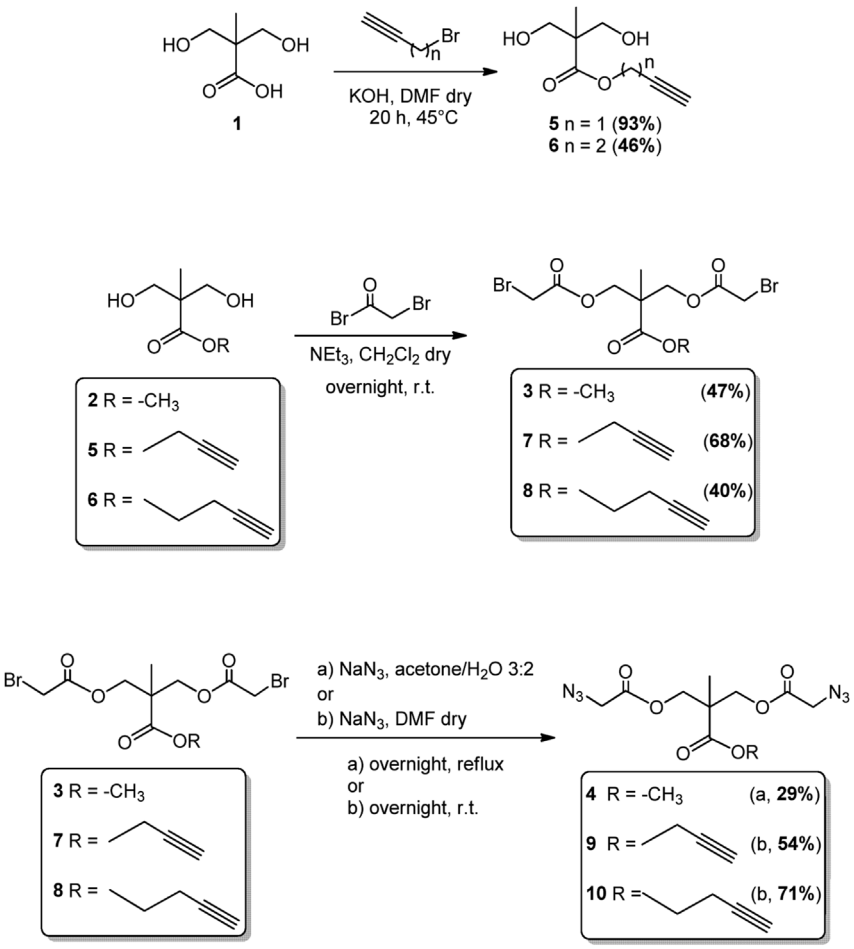


TABLE 1 Experimental conditions and molecular weight distributions for the synthesis of hyperbranched polymers derived from AB_2 monomers **9** and **10**

Entry	Monomer[a]	Monomer/cu salt/ascorbic acid (eq)	T (°C)	Polymer	Yield(%)[b]	M_n	M_w	*DP*[c]	*DB*[d]
1	9	90/1/5	45	**HP11a**	33	8100	11,500	24	0.1
2	9	90/10/50	45	**HP11b**	43	6500	9600	19	0.1
3	9	90/10/50	80	**HP11c**	92	4800	7500	14	0.1
4	9	90/5/25	45	**HP11d**	50	8000	10,500	24	0.1
5	10	90/1/5	45	**HP12a**	80	12,300	20,070	35	0.2
6	10	90/10/50	45	**HP12b**	52	6200	8700	18	0.2

[a]Reaction time: 96 h. $[AB_2]_0 = 0.5$ M.
[b]After precipitation by purification in hexane.
[c]Degree of polymerization. Obtained dividing Mn by the mass of the starting monomer.
[d]Degree of branching. See text for details.

obtaining the AB_2 monomers **9** and **10**, after chromatographic purification, in good yields. Unexpected small changes (<0.05 ppm) in the resonances of the $COC\underline{H}_2X$ units were recorded upon the transformation of the terminal bromide into azide, but further confirmation of the complete transformation to azide came from the IR spectrum, which showed the distinctive peak at 2110 cm^{-1}, corresponding to the stretching of the —N_3 group. The aliphatic AB_2 monomers **9** and **10**, differing for a carbon atom, were submitted to the CuAAC polymerization.

CuAAC polymerization. The polymerization of the aliphatic AB_2 monomers (**9**, **10**) was conducted with the monomer, $CuSO_4{\cdot}5H_2O$ and dry DMF at the temperatures and using relative stoichiometries indicated in

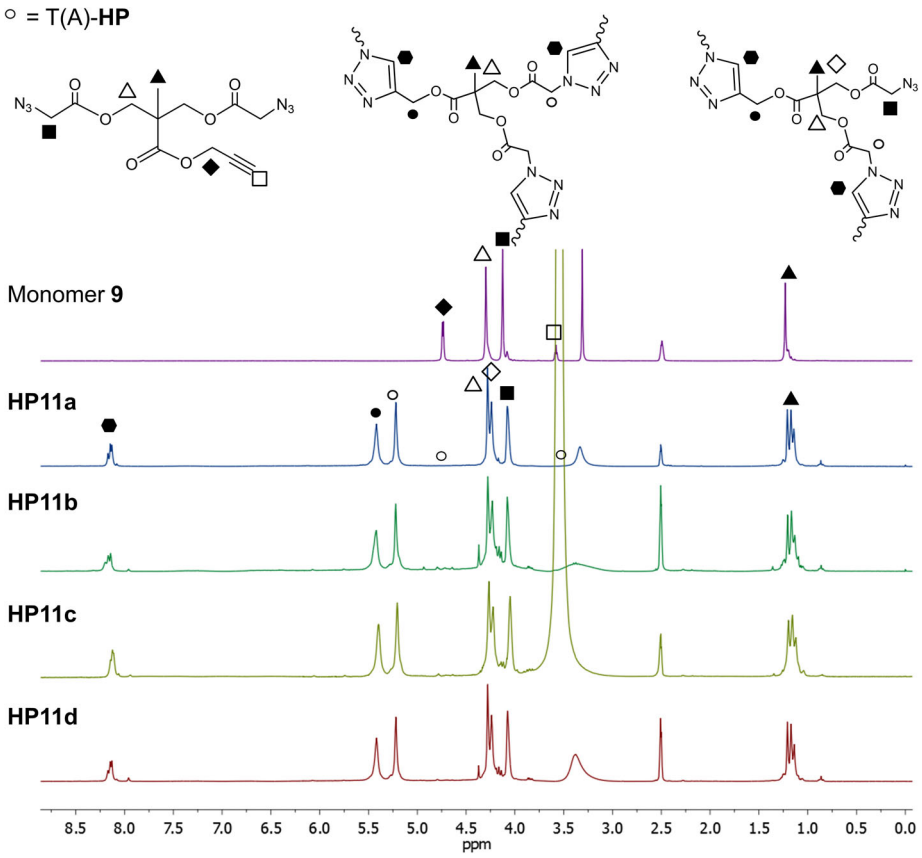


FIGURE 2 ^{1}H-NMR spectra (300 MHz, 298 K, DMSO-d_6) of monomer **9** and **HP11a-d**. for simplicity, some proton groups are unmarked because equivalent by symmetry to other groups marked with dots

Table 1. The crude products were purified by precipitation from THF in hexane as the nonsolvent (THF:hexane, 1:30, v:v). Different conditions, reported in Table 1, were tried and the hyperbranched polymers were obtained with different yields and molecular weights, calculated by GPC (gel permeation chromatography) in THF. At different reaction temperatures (entries 2 and 3), different results in terms of yields and degree of polymerizations were obtained. The HPs were free from unreacted monomer, as shown in the ^{1}H NMR spectra in Figures 2 and 3.

The hyperbranched structures **11** can in principle be composed of a mixture of dendritic, linear and terminal units represented in Scheme 2.

The comparison between the ^{1}H-NMR spectra in DMSO-d_6 among the AB_2 monomer **9** and the hyperbranched polymers **HP11a-d** is shown in Figure 2.

The ^{1}H-NMR spectra of the hyperbranched polymers testified the successful occurrence of the polymerization reaction, since the diagnostic signals of the —CH_2 groups at 4.8 ppm (dark blue dots) and of the terminal alkyne proton signal at ca. 3.5 ppm (pink) have completely disappeared. This has been highlighted with empty dots in the spectra of **HP11a**, and it has been verified also in all the other spectra for **HP11** in Figure 2. The concurrent appearance of the diagnostic triazole proton resonance signal at ca. 8.0 ppm (gray) testified for the successful CuAAC reaction. The newly generated triazole units cause a downfield shift of their neighboring CH_2 protons, which appear between 5–5.5 ppm. All the remaining signals as expected do not shift significantly, but they become broader due to their incorporation in a macromolecular structure in which all repeating units are slightly different from each other. The presence of both linear (L) and dendritic (D) units is evident also when considering the ^{13}C-NMR spectra, in which the diagnostic signal at ca. 50 ppm, related to the CO$\underline{C}H_2N_3$ carbon resonance, is present in all **HP11** spectra (see Data S1). The IR spectra of the hyperbranched polymers confirmed the presence of the distinctive peak of the -N_3 terminal groups at 2110 cm^{-1}, reduced in intensity when compared with the FTIR spectra of the corresponding monomer (Figure S2), and the disappearance of the corresponding peak related to the stretching of the alkyne group at 3300 cm^{-1}.

The comparison between the ^{1}H-NMR spectra in DMSO-d_6 and the AB_2 monomer **10** and the hyperbranched polymers **HP12a-b** is shown in Figure 3. A similar analysis can be applied to monomer **10** in relation to the corresponding **HP12a-b**, with the: (1) appearance of the diagnostic triazole proton resonance signal at ca. 8.0 ppm (gray); (2) a downfield shift of their neighboring CH_2 protons, which appear between 5 and 5.5 ppm; disappearance of the unique resonances associated with

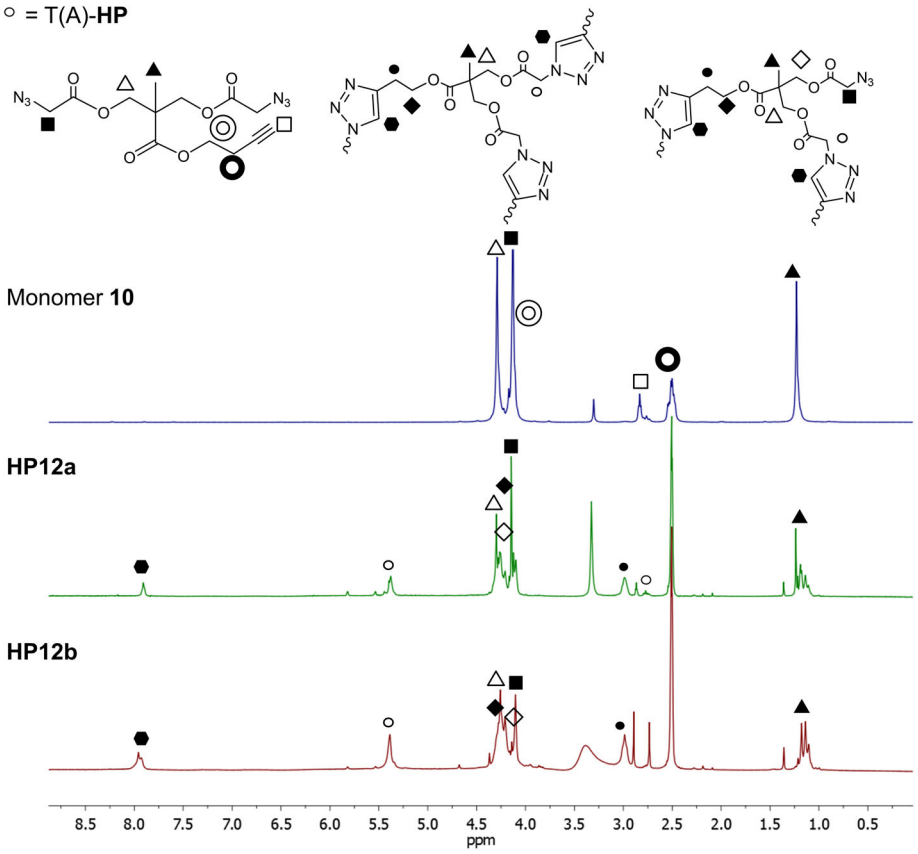
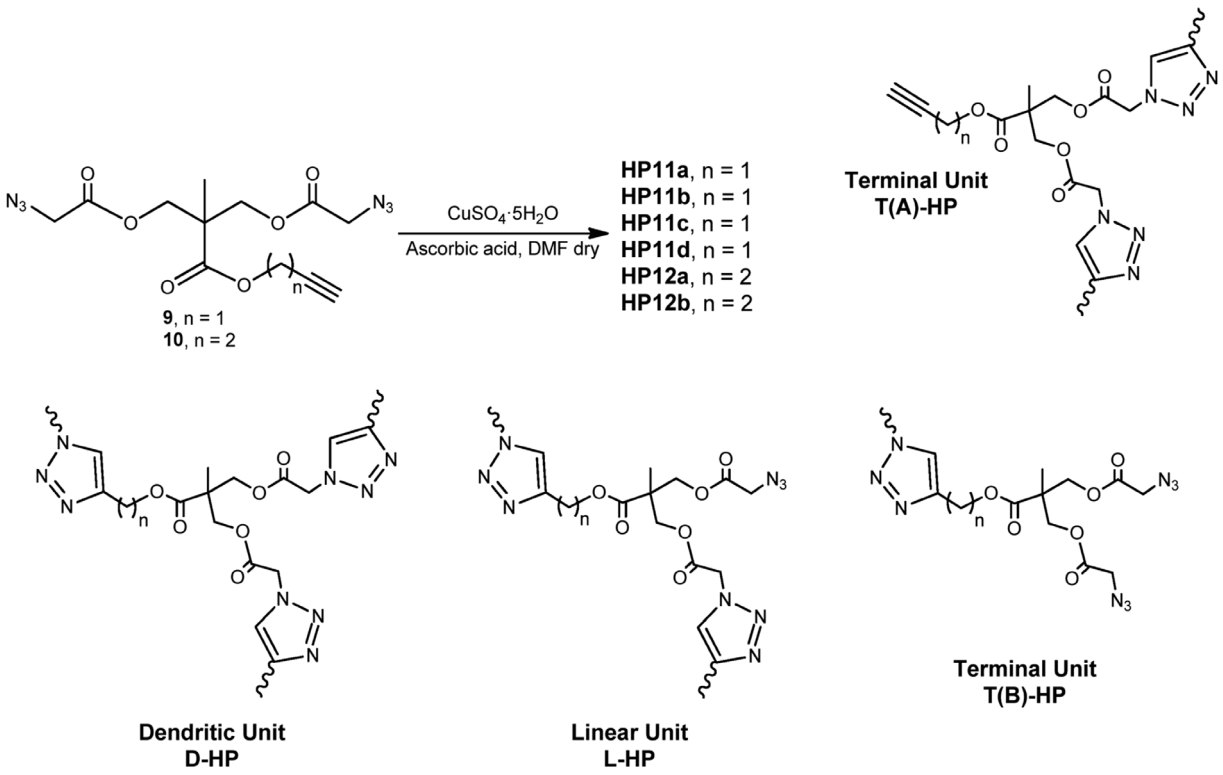


FIGURE 3 ^{1}H-NMR spectra (300 MHz, DMSO-d_6) of monomer **10** and **HP12a-b**. for simplicity, some proton groups are unmarked because equivalent by symmetry to other groups marked with dots



SCHEME 2 Synthesis of **HP11** and **HP12** and possible units to be found in the polymeric structures

the monomer. The presence of both linear and fully branched units is, also in this case, evident.

The corresponding Degree of Branching (DB) was calculated by using the Equation DB = 2D/(2D + L).[13] The percentages of D and L units was obtained by integrations of selected regions of the ^{1}H NMR spectra. An expansion with integration for the NMR spectra of **HP11** and **HP12** are reported in Figures S3 and S4, respectively. The calculated DB is between 0.1 and 0.2 in all cases (Table 1), and it is significantly lower than the theoretical value of DB ~ 0.5 which can be calculated when all the same B groups share the same reactivity.[14] The degree of branching seem to increase when monomer **10**, bearing an additional carbon atom as a spacer between the reactive units of the CuAAC reaction, was used. As a consequence of the low degree of branching, the percentage of linear units is high (ca. 90% for **HP11**), and therefore of N_3 units available for further functionalization, showing the potential of such polymeric structures to further postmodification through the use of the same CuAAC reaction.

3 | CONCLUSIONS

We have demonstrated the possibility of constructing new and interesting AB_2 monomers suitable for polymerization through click chemistry. Both AB_2 monomers (**9**, **10**) are able to polymerize yielding structures (**HP11**, **HP12**) with significant degrees of polymerization. The calculation of the degree of branching highlights a reactivity of the two B groups which is far from statistical, presumably because of the steric hindrance of the reactive functionalities. Future work will focus on increasing sustainability and scalability of the syntheses of these and related systems, and an improved design in order to obtain higher DBs, useful for industrial applications.

4 | EXPERIMENTAL SECTION

General methods. All commercially available compounds and the reaction solvents were purchased from Sigma Aldrich, Alfa Aesar and Fluorochem, and used as received. If required, dry dichloromethane was obtained through distillation of the solvent in presence of calcium hydride. Analytical thin-layer chromatography was performed on silica gel, chromophore loaded, commercially available plates. Column chromatography was carried out using silica gel (pore size 60 Å, 230–400 mesh). ^{1}H and ^{13}C-NMR spectra were recorded on Bruker AX200 or AMX300 instruments and calibrated with the solvent residual proton signal or tetramethylsilane. Mass spectra were obtained with a ion trap mass spectrometer equipped with an ESI ion source. Infrared spectra were recorded on a FTIR spectrophotometer equipped with a diffuse reflectance accessory using KBr powder as the inert support. *Gel Permeation Chromatography*. Hyperbranched polymers, obtained after the purification procedures and dissolved in tetrahydrofuran (THF), were prefiltered using 0.45-μm polytetrafluoroethylene filters and then directly injected. Size exclusion chromatography was carried out on a Waters system equipped with a DRI detector. Low polydispersity polystyrene standards (12) were used for the calibration curve, and the mobile phase was THF stabilized with BHT (2,6-di-*t*-butyl-4-methylphenol) (1 ml/min, 40°C). A set of two universal columns (Styragel 4E and 5E) in series was used.

4.1 | Compound 2

$SOCl_2$ (24.3 ml, 335 mmol) was added, dropwise at 0°C, to a solution of 2,2-bis(hydroxymethyl) propionic acid (**1**) (30 g, 224 mmol) in MeOH (350 ml) and the reaction mixture was refluxed for 15 h. The solvent was removed, a saturated solution of $NaHCO_3$ (60 ml) was added and the residue was extracted with EtOAc (4 x 100 ml). The organic phase was dried over Na_2SO_4, filtered, and concentrated under reduced pressure to afford a colorless oil corresponding to pure compound **2** (24.82 g, 75%). ^{1}H-NMR ($CDCl_3$, 200 MHz): δ (ppm) = 3.94–3.89 (d, 2H, —C$\underline{H_2}$OH), 3.77 (s, 3H, —OC$\underline{H_3}$), 3.75–3.69 (d, 2H, —C$\underline{H_2}$OH), 2.68 (broad, 2H, —O$\underline{H}$), 1.07 (s, 3H, —C$\underline{H_3}$).

4.2 | Compound 3

The methyl ester (**2**) (1 g, 6.75 mmol) was dissolved in dry CH_2Cl_2 (40 ml) at 0°C; NEt_3 (2.07 ml, 14.8 mmol) was added followed by a solution of bromoacetyl bromide (2.35 ml, 27 mmol) in dry CH_2Cl_2 (20 ml), dropwise. The mixture was stirred at room temperature, overnight, then washed with a saturated solution of $NaHCO_3$ (3 x 40 ml). The organic phase was dried over Na_2SO_4, filtered and concentrated under reduced pressure, and the residue was purified by column chromatography (silica gel, R_f = 0.42, hexane:EtOAc, 8:2, v:v) to afford product **3** as a colorless oil (1.24 g, 47%). ^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) = 4.44–4.38 (d, 2H, —C$\underline{H_2}$OCOCH$_2$Br), 4.35–4.29 (d, 2H, —C$\underline{H_2}$OCOCH$_2$Br), 3.84 (s, 4H, —CH$_2$OCOC$\underline{H_2}$Br), 3.76 (s, 3H, —OC$\underline{H_3}$), 1.31 (s, 3H, —C$\underline{H_3}$). ^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) = 172.49 (—$\underline{C}$OOCH$_3$), 166.58 (2C, —CH$_2$O$\underline{C}$OCH$_2$Br), 66.43 (2C, —$\underline{C}$H$_2$OCOCH$_2$Br), 52.48 (—O$\underline{C}$H$_3$), 46.21 (CH$_3$$\underline{C}$—), 25.19 (2C, —CH$_2OCO\underline{C}H_2$Br), 17.70 (—$\underline{C}H_3$). ESI-MS: *m/z* 391 $[M + H]^+$, 413 $[M + Na]^+$, 803 $[2M + Na]^+$.

4.3 | Compound 4

NaN_3 (500 mg, 7.69 mmol) was added to a solution of compound **3** (1 g, 2.56 mmol) in a mixture of acetone/H_2O 3:2 (10 ml) and the suspension was refluxed overnight. The reaction mixture was evaporated to remove acetone, water (10 ml) was added and an extraction was performed with CH_2Cl_2 (3 x 20 ml). The organic phase was dried over Na_2SO_4, filtered and the solvent was evaporated under reduced pressure; the residue was purified by column chromatography (silica gel, $R_f = 0.55$, hexane:EtOAc, 7:3, v:v) to afford product **4** as a colorless oil (234 mg, 29%). ^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) = 4.45–4.40 (d, 2H, —C$\underline{H_2}$OCOCH$_2$N$_3$), 4.36–4.31 (d, 2H, —C$\underline{H_2}$OCOCH$_2$N$_3$), 3.89 (s, 4H, —CH$_2$OCOC$\underline{H_2}$N$_3$), 3.75 (s, 3H, —OC$\underline{H_3}$), 1.30 (s, 3H, —C$\underline{H_3}$). ^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) = 172.43 (—$\underline{C}$OOCH$_3$), 167.75 (2C, —CH$_2$O$\underline{C}$OCH$_2$N$_3$), 66.06 (2C, —$\underline{C}$H$_2$OCOCH$_2$N$_3$), 52.55 (—O$\underline{C}$H$_3$), 50.14 (2C, —CH$_2$OCO$\underline{C}$H$_2$N$_3$), 46.12 (CH$_3\underline{C}$—), 17.82 (—$\underline{C}$H$_3$). ESI-MS: *m/z* 337 $[M + Na]^+$. FTIR (cm^{-1}): 1747.5 (C═O str), 2109.7 (N_3 str).

4.4 | Compound 5

KOH (13.8 g, 246 mmol) was added to a solution of 2,2-bis(hydroxymethyl) propionic acid (**1**) (30 g, 224 mmol) in dry DMF (75 ml) and the suspension was stirred for 1 h at 100°C. Propargyl bromide (27.41 ml, 246 mmol) was then added, dropwise, to the solution and the reaction mixture was stirred for 20 h at 45°C. The solvent was removed, water (60 ml) was added and the residue was extracted with EtOAc (3 x 100 ml). The organic phase was dried over Na_2SO_4, filtered and concentrated under reduced pressure to give a pale yellow oil corresponding to product **5** (35.86 g, 93%). ^{1}H-NMR ($CDCl_3$, 200 MHz): δ (ppm) = 4.75–4.74 (d, 2H, —OC$\underline{H_2}$CCH), 3.94–3.88 (d, 2H, —C$\underline{H_2}$OH), 3.75–3.69 (d, 2H, —C$\underline{H_2}$OH), 2.92 (broad, 2H, —O$\underline{H}$), 2.51–2.50-2.49 (t, 1H, —C$\underline{H}$), 1.10 (s, 3H, —C$\underline{H_3}$).

4.5 | Compound 6

KOH (920 mg, 16.4 mmol) was added to a solution of 2,2-bis(hydroxymethyl) propionic acid (**1**) (2 g, 14.9 mmol) in dry DMF (20 ml) and the suspension was stirred for 1 h at 100°C. 4-bromo-1-butyne (1.54 ml, 16.4 mmol) was then added, dropwise, to the solution and the reaction mixture was stirred for 20 h at 45°C. The solvent was removed, water (10 ml) was added and the residue was extracted with EtOAc (3 x 15 ml). The organic phase was dried over Na_2SO_4, filtered and concentrated under reduced pressure to give a pale yellow oil corresponding to product **6** (1.28 g, 46%). ^{1}H-NMR ($CDCl_3$, 200 MHz): δ (ppm) = 4.33–4.26 (t, 2H, —OC$\underline{H_2}$CH$_2$CCH), 3.95–3.89 (d, 2H, —C$\underline{H_2}$OH), 3.77–3.71 (d, 2H, —C$\underline{H_2}$OH), 2.63–2.55 (dt, 2H, —OCH$_2$C$\underline{H_2}$CCH), 2.53 (broad, 2H, —O$\underline{H}$), 2.05–2.04-2.03 (t, 1H, —C$\underline{H}$), 1.10 (s, 3H, —C$\underline{H_3}$).

4.6 | Compound 7

The propargyl ester (**5**) (10 g, 58.1 mmol) was dissolved in dry CH_2Cl_2 (140 ml) and NEt_3 (17.81 ml, 128 mmol) at 0°C; a solution of bromoacetyl bromide (20.24 ml, 232 mmol) in dry CH_2Cl_2 (60 ml) was added dropwise. The mixture was stirred at room temperature overnight, then washed with a saturated solution of $NaHCO_3$ (3 x 140 ml). The organic phase was dried over Na_2SO_4, filtered and concentrated under reduced pressure, and the residue was purified by column chromatography (silica gel, $R_f = 0.33$, hexane: EtOAc, 8:2, v:v) to afford product **7** as a colorless oil (16.35 g, 68%). ^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) = 4.76–4.75 (d, 2H, —OC$\underline{H_2}$CCH), 4.44–4.41 (d, 2H, —C$\underline{H_2}$OCOCH$_2$Br), 4.37–4.34 (d, 2H, —C$\underline{H_2}$OCOCH$_2$Br), 3.86 (s, 4H, —CH$_2$OCOC$\underline{H_2}$Br), 2.52–2.51-2.50 (t, 1H, —C$\underline{H}$), 1.34 (s, 3H, —C$\underline{H_3}$). ^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) = 171.26 (—$\underline{C}$OOCH$_2$CCH), 166.52 (2C, —CH$_2$O$\underline{C}$OCH$_2$Br), 77.33 (—OCH$_2\underline{C}$CH), 75.33 (—$\underline{C}$H), 66.30 (2C, —$\underline{C}$H$_2$OCOCH$_2$Br), 52.75 (—O$\underline{C}$H$_2$CCH), 46.34 (CH$_3\underline{C}$—), 25.15 (2C, —CH$_2$OCO$\underline{C}$H$_2$Br), 17.54 (—$\underline{C}$H$_3$). ESI-MS: *m/z* 437 $[M + Na]^+$, 850 $[2M + Na]^+$.

4.7 | Compound 8

The ester **6** (1.17 g, 6.28 mmol) was dissolved in dry CH_2Cl_2 (20 ml) and NEt_3 (1.93 ml, 13.8 mmol) at 0°C; a solution of bromoacetyl bromide (2.19 ml, 25.1 mmol) in dry CH_2Cl_2 (5 ml) was added dropwise. The mixture was stirred at room temperature overnight, then washed with a saturated solution of $NaHCO_3$ (3 x 20 ml). The organic phase was dried over Na_2SO_4, filtered and concentrated under reduced pressure, and the residue was purified by column chromatography (silica gel, $R_f = 0.35$, hexane:EtOAc, 8:2, v:v) to afford product **8** as a colorless oil (1.09 g, 40%). ^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) = 4.44–4.39 (d, 2H, —C$\underline{H_2}$OCOCH$_2$Br), 4.36–4.30 (d, 2H, —C$\underline{H_2}$OCOCH$_2$Br), 4.30–4.27-4.23 (t, 2H, —OC$\underline{H_2}$CH$_2$CCH), 3.85 (s, 4H, —CH$_2$OCOC$\underline{H_2}$Br), 2.60–2.26 (dt, 2H, —OCH$_2$C$\underline{H_2}$CCH), 2.02–2.01-2.00 (t, 1H, —C$\underline{H}$), 1.33 (s, 3H, —C$\underline{H_3}$). ^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) = 171.77 (—$\underline{C}$OOCH$_2$CH$_2$CCH), 166.55 (2C, —CH$_2$O$\underline{C}$OCH$_2$Br), 79.49 (—OCH$_2$CH$_2\underline{C}$CH), 70.01 (—$\underline{C}$H), 66.46 (2C, —$\underline{C}$H$_2$OCOCH$_2$Br), 62.80 (—O$\underline{C}$H$_2$CH$_2$CCH), 46.29 (CH$_3\underline{C}$—), 25.20 (2C,

—$CH_2OCO\underline{C}H_2Br$), 18.78 (—$OCH_2\underline{C}H_2CCH$), 17.68 (—$\underline{C}H_3$). ESI-MS: *m/z* 429 $[M + H]^+$, 451 $[M + Na]^+$, 879 $[2\,M + Na]^+$.

4.8 | Compound 9

NaN_3 (598 mg, 9.2 mmol) was added to a solution of compound **7** (1.27 g, 3.07 mmol) in dry DMF (20 ml) and the suspension was stirred at room temperature overnight. An aqueous solution of NH_4Cl 1 M (15 ml) was added to the reaction mixture and the product was extracted with CH_2Cl_2 (3 x 15 ml). The organic phase was washed with an aqueous solution of NH_4Cl 1 M (6 x 50 ml), then dried over Na_2SO_4 and filtered; the solvent was evaporated under reduced pressure. The residue was purified by column chromatography (silica gel, $R_f = 0.55$, hexane:EtOAc, 7:3, v:v) to afford product **9** as a colorless oil (558 mg, 54%). ^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) = 4.76–4.75 (d, 2H, —$OC\underline{H_2}CCH$), 4.47–4.44 (d, 2H, —$C\underline{H_2}OCOCH_2N_3$), 4.40–4.37 (d, 2H, —$C\underline{H_2}OCOCH_2N_3$), 3.92 (s, 4H, —$CH_2OCOC\underline{H_2}N_3$), 2.53–2.52-2.51 (t, 1H, —$C\underline{H}$), 1.35 (s, 3H, —$C\underline{H_3}$). ^{1}H-NMR ($CDCl_3$, 75 MHz): δ (ppm) = 4.74–4.73 (d, 2H, —$OC\underline{H_2}CCH$), 4.30 (s, 4H, —$C\underline{H_2}OCOCH_2N_3$), 4.13 (s, 4H, —$CH_2OCOC\underline{H_2}N_3$), 3.59–3.58-3.57 (t, 1H, —$C\underline{H}$), 1.23 (s, 3H, —$C\underline{H_3}$). ^{13}C-NMR ($CDCl_3$, 300 MHz): δ (ppm) = 171.20 (—$\underline{C}OOCH_2CCH$), 167.71 (2C, —$CH_2O\underline{C}OCH_2N_3$), 77.34 (—$OCH_2\underline{C}CH$), 75.37 (—$\underline{C}H$), 65.94 (2C, —$\underline{C}H_2OCOCH_2N_3$), 52.80 (—$O\underline{C}H_2CCH$), 50.10 (2C, —$CH_2OCO\underline{C}H_2N_3$), 46.23 ($CH_3\underline{C}$—), 17.66 (-$\underline{C}H_3$). ESI-MS: *m/z* 361 $[M + Na]^+$, 699 $[2\,M + Na]^+$. FTIR (cm^{-1}): 1748.1 (C═O str), 2108.4 (N_3 str), 3286.6 (CCH str).

4.9 | Compound 10

NaN_3 (460 mg, 7.08 mmol) was added to a solution of compound **8** (1.01 g, 2.36 mmol) in dry DMF (15 ml) and the suspension was stirred at room temperature overnight. An aqueous solution of NH_4Cl 1 M (15 ml) was added to the reaction mixture and the product was extracted with CH_2Cl_2 (3 x 15 ml). The organic phase was washed with an aqueous solution of NH_4Cl 1 M (6 x 50 ml), then dried over Na_2SO_4 and filtered; the solvent was evaporated under reduced pressure. The residue was purified by column chromatography (silica gel, $R_f = 0.55$, hexane:EtOAc, 7:3, v:v) to afford product **10** as a colorless oil (590 mg, 71%). ^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) = 4.46–4.40 (d, 2H, —$C\underline{H_2}OCOCH_2N_3$), 4.37–4.32 (d, 2H, —$C\underline{H_2}OCOCH_2N_3$), 4.28–4.25-4.22 (t, 2H, —$OC\underline{H_2}CH_2CCH$), 3.90 (s, 4H, —$CH_2OCOC\underline{H_2}N_3$), 2.58–2.51 (dt, 2H, —$OCH_2C\underline{H_2}CCH$), 2.01–2.00-1.99 (t, 1H, —$C\underline{H}$), 1.32 (s, 3H, —$C\underline{H_3}$). ^{1}H-NMR (DMSO-*d6*, 300 MHz): δ (ppm) = 4.29 (s, 4H, —$C\underline{H_2}OCOCH_2N_3$), 4.17–4.15-4.13 (t, 2H, —$OC\underline{H_2}CH_2CCH$), 4.13 (s, 4H, —$CH_2OCOC\underline{H_2}N_3$), 2.84–2.83-2.82 (t, 1H, —$C\underline{H}$), 2.54–2.48 (dt, 2H, —$OCH_2C\underline{H_2}CCH$), 1.23 (s, 3H, —$C\underline{H_3}$). ^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) = 171.71 (—$\underline{C}OOCH_2CH_2CCH$), 167.73 (2C, —$CH_2O\underline{C}OCH_2N_3$), 79.52 (—$OCH_2CH_2\underline{C}CH$), 70.03 (—$\underline{C}H$), 66.09 (2C, —$\underline{C}H_2OCOCH_2N_3$), 62.85 (—$O\underline{C}H_2CH_2CCH$), 50.12 (2C, —$CH_2OCO\underline{C}H_2N_3$), 46.15 ($CH_3\underline{C}$—), 18.74 (—$OCH_2\underline{C}H_2CCH$), 17.80 (—$\underline{C}H_3$). ESI-MS: *m/z* 353 $[M + H]^+$, 375 $[M + Na]^+$. FTIR (cm^{-1}): 1754.5 (C═O str), 2110.2 (N_3 str), 3292.9 (CCH str).

4.10 | Polymers HP11a-d

Monomer **9** (60–150 mg, 0.17–0.44 mmol), $CuSO_4{\cdot}5H_2O$ (0.11 eq) and dry DMF ($[AB_2]_0 = 0.5$ M) were charged in a Schlenk flask, which was capped with rubber septa and bubbled with nitrogen gas for 40 minutes; ascorbic acid (0.55 eq) was added and the flask was immersed in a thermostatic oil bath to initiate the polymerization. The reaction was stopped after 96 h, the solvent was evaporated under reduced pressure and the crude product was purified by dissolving it in the minimum amount of tetrahydrofuran and precipitating it in hexane (THF:hexane, 1:30, v:v). The hyperbranched polymers **HP11a-d** were obtained as white powders with different yields in different conditions and at different reagent ratios (see Table 1). ^{1}H-NMR (**HP11a**, DMSO-d_6, 300 MHz): δ (ppm) = 8.13 (s, 1H, C$\underline{H}$ triazole), 5.41 (s, 2H, —$COOC\underline{H_2}ArH$), 5.21 (s, 4H, —$OCOC\underline{H_2}ArH$), 4.27 (s, 4H, —$C\underline{H_2}OCOCH_2ArH$), 4.24 (s, 2H, —$C\underline{H_2}OCOCH_2N_3$), 4.06 (s, 2H, —$CH_2OCOC\underline{H_2}N_3$), 1.16 (m, 3H, —$C\underline{H_3}$). ^{13}C-NMR (**HP11a**, DMSO-d_6, 300 MHz): δ (ppm) = 171.7–166.7 (m, —$\underline{C}OOCH_2$), 141.6 (triazole), 126.1 (triazole), 66.0–65.8, 58.0 and 45.9 (—$\underline{C}H_2$ triazole), 50.1 (—$CO\underline{C}H_2N_3$), 49.3 ($CH_3\underline{C}$—), 17.0–16.9 (—$\underline{C}H_3$).

4.11 | Polymers HP12a-b

The same method used to synthesize polymers **HP11a-d** was repeated to produce polymers **HP12a-b**, obtained as white powders after purification starting from monomer **10** (150–170 mg, 0.42–0.48 mmol). ^{1}H-NMR (DMSO-d_6, 300 MHz): δ (ppm) = 7.90 (s, 1H, C$\underline{H}$ triazole), 5.37 (s, 6H, —$COOCH_2C\underline{H_2}ArH$, —$OCOC\underline{H_2}ArH$), 4.29 (s, 4H, —$C\underline{H_2}OCOCH_2ArH$), 4.25 (s, 2H, —$C\underline{H_2}OCOCH_2N_3$), 4.11 (s, 2H, —$CH_2OCOC\underline{H_2}N_3$), 2.87 (broad, 2H, —$COOC\underline{H_2}CH_2ArH$), 1.20 (m, 3H, —$C\underline{H_3}$). ^{13}C-NMR (**HP12a**, DMSO-d_6, 300 MHz): δ (ppm) = 171.8–166.9 (m, —$\underline{C}OOCH_2$), 143.0 (triazole), 124.0 (triazole), 80.5, 72.4, 66.0–65.8, 58.0 and 45.9 (—$\underline{C}H_2$ triazole), 50.1 (—$CO\underline{C}H_2N_3$), 49.3 ($CH_3\underline{C}$—), 25.1, 17.0–16.9 (—$\underline{C}H_3$).

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