Thiol-ene Clickable Hyperscaffolds Bearing Peripheral Allyl Groups

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ABSTRACT: Radical catalyzed thiol-ene reaction has become a useful alternative to the Huisgen-type click reaction as it helps to expand the variability in reaction conditions as well as the range of clickable entities. Thus, direct generation of hyperbranched polymers bearing peripheral allyl groups that could be clicked using a variety of functional thiols would be of immense value. A specifically designed AB₂ type monomer, that carries two allyl benzyl ethers groups and one alcohol functionality, was shown to undergo self-condensation under acid-catalyzed melt-transetherification to yield a hyperbranched polyether that carries numerous allyl end-groups. Importantly, it was shown that the kinetics of polymerization is not dramatically affected by the change of the ether unit from previously studied methyl benzyl ether to an allyl benzyl ether. The peripheral allyl groups were readily clicked quantitatively, using a variety of thiols, to generate an hydrocarbon-soluble octadecyl-derivative, amphiphilic systems using 2-mercaptoethanol and chiral amino acid (*N*-benzoyl cystine) derivatized hyperbranched structures; thus demonstrating the versatility of this novel class of clickable *hyperscaffolds*. © 2011 Wiley Periodicals, Inc. J Polym Sci Part A: Polym Chem 49:1735–1744, 2011

KEYWORDS: functionalization of polymers; glass transition; hyperbranched; kinetics (polym.); polyethers; thermogravimetric analysis (TGA)

INTRODUCTION Hyperbranched polymers, prepared via the self-condensation of an AB₂ type monomer, yields polymers with large number of B groups at the periphery.¹ The numerous end-groups present in hyperbranched polymers make them potentially useful as crosslinkers, scaffolds for preparing core-shell type polymers, and so forth. Typically, the end-groups in hyperbranched polymers which are readily amenable to further functionalization are amines, alcohols or carboxylic acids. These functional groups can be modified under standard conditions to generate a wide range of peripherally functionalized polymers, although it is often difficult to achieve high conversions.² A few years ago, we demonstrated an alternate straightforward approach that utilized the copolymerization of an AB₂ monomer with a A-R type molecule to generate peripherally modified hyperbanched systems in a single step; however, this approach also had the limitation of incomplete conversion.³ Despite these limitations, peripherally functionalized hyperbranched polymers, such as hyperbranched polyglycerols, have been extensively explored to yield a variety of interesting structures.⁴

We have been interested in developing simple and straightforward approaches for the preparation of hyperbranched polymers that carry quantitatively functionalizable endgroups. To this end, we recently developed a novel strategy to prepare peripherally "clickable" hyperbranched polyethers in a single step using a suitably designed AB₂ type monomer

that carries two propargylbenzyl ether groups and one hydroxyl group; acid-catalyzed melt-transetherification of this monomer yielded a hyperbranched polymer bearing a large number of peripheral propargyl groups, which could in turn be quantitatively functionalized under mild conditions via the Cu-catalyzed click reaction with a variety of organic azides.⁵ Later we also showed that hyperbranched polyesters can be similarly prepared under standard melt transesterification process of a suitably designed hydroxy bis(propargyl ester) monomer.⁶ This was an important finding because it demonstrated for the first time that propargyl ester groups can be trans-esterified just like any other simple methyl or ethyl esters, which are typically the basic monomers for commercial production of polyesters. Although alkyne-azide click reactions have their own merits, search for alternate reactions that proceed quantitatively under mild conditions has lead to the identification of several other potentially useful approaches; of these the most extensively studied is the thiol-ene reaction.⁷ The thiol-ene reaction, which is the century-old radical-catalyzed addition of a thiol to an alkene, exhibits several of the important characteristics to qualify being termed a click reaction, as delineated by Sharpless;⁸ the reactions occur quantitatively under very mild conditions, generates no side products and, importantly, it can be carried out under biologically benign conditions. Some of the advantages of the thiol-ene reaction over the Cu-catalyzed 1,3-dipolar cycloaddition based click reaction is that it can

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HBP-Me

SCHEME 1 Synthesis of hyperbranched polyether with methoxy endgroups.

be done in the absence of a metal ion and can also be initiated photochemically in the absence of any radical initiator.⁹ Given the merits of the thiol-ene reaction and its wide ranging application potential, it would be useful to develop simple strategies to synthesize hyperbranched polymers that carry numerous peripheral allyl groups, in a single step. Dendrimers carrying numerous allyl groups at their periphery have been synthesized and utilized to access a wide range of structures using the thiol-ene click process.¹⁰ While dendrimers provide structurally perfect scaffolds for building variety of interesting nano-dimensional systems, they require tedious step-wise synthesis; a notable recent exception is the use of the thiol-ene reaction itself for the construction of the dendrimer, which has simplified the procedure considerably.¹¹ In this article, we describe a single-step process for the preparation of clickable hyperbranched polyethers from an AB_2 type monomer and demonstrate that these polymers can be readily transformed to interesting functional systems by clicking with different thiols, thereby making them potentially useful as nano-dimensional *hyperscaffolds* for a variety of applications.

RESULTS AND DISCUSSION

Some years ago, we developed an interesting melt transetherification polymerization process wherein a monomer carrying two benzylmethyl ether groups when reacted with an aliphatic diol at 150 °C in the presence of an acid catalyst, like PTSA, yielded a polyether with the exclusion of low boiling methanol.¹² This process was later optimized and extended for the preparation of hyperbranched polyethers using a suitably designed AB_2 monomer (A) (Scheme 1), which in turn was prepared from Mesitol.¹³ Recently we showed that, if instead of the benzylmethyl ether a benzylpropargyl ether were used, a hyperbranched polyether bearing numerous terminal propargyl groups was formed.⁵ Click reaction of the propargyl groups with a variety of organic azides permitted the generation of a variety of peripherally funtionalized hyperbranched polymers. As the thiol-ene click reaction often complements the alkyne-azide process, we designed alternate AB₂ monomer (3) bearing two benzylallyl ethers and one hydroxyl group, which can undergo a similar transetherification polycondensation. The monomer was prepared starting from Mesitol in three steps as depicted in Scheme 2. A fully substituted aromatic nucleus is used to preclude electrophilic aromatic substitution that could occur during the acid-catalyzed melt condensation.¹² Melt polymerization of this monomer in the presence of 2 mol % of pyridinium camphor sulphonate (PCS)^{13(b)} proceeded smoothly at 150 °C with rapid evolution of allyl alcohol. The



SCHEME 2 Synthesis and polymerization of the bis-allyloxy AB₂ monomer.



SCHEME 3 Thiol-ene click reaction of the allyl-terminated HBP with a variety of thiols.

polymerization was done in two steps—in the first step a slow purge of dry nitrogen was used to remove the allyl alcohol that was formed and the second step was done under reduced pressure to drive the reaction to completion.

The proton NMR spectra of the monomer **3** and the hyperbranched polymer (HBP-Allyl) are shown in Figure 1, along with the peak assignments. The main difference in the spectra is the decrease in the relative intensity of the peaks belonging to the allyl unit; the ratio of the allyl methylene protons (peak **d**) to the benzylic protons (peak **c** and **c'**) changes from 1:1 to nearly 0.5:1, which is expected at high conversions. Unlike in the **HBP-Me** polymer (see Scheme 1),¹⁴ in the allyl polymer the benzylic proton peaks do not resolve adequately to permit the direct determination of the degree of branching (DB). However, using previously established spectral assignment of the aromatic methyl protons (the seven peaks in the region 2.2–2.5 ppm),¹⁴ the DB was estimated to be around 0.45, which is in reasonable accordance with the statistically expected value of $0.5.^{15}$ The molecular weight of the polymer was determined using GPC, which was coupled to a triple detector systems and the M_w was estimated to be around 15,000 (PDI = 2.3) based on the Universal calibration method.

Kinetics of Polymerization

The rate of the transetherification process would expectedly depend on ether linkage that is being cleaved, both because of the difference in intrinsic susceptibility of the ether linkage as well as due to the difference in volatility of the liberated alcohol; the removal of which drives the equilibrium towards polymer formation. To study the rate of polycondensation, we chose to directly use thermogravimetric analysis (TGA); because the volatility of the monomer at the polymerization temperature of 150 °C was small, the weight loss during the analysis may be ascribed primarily to the loss of the condensate alcohol alone. TGA has been very seldom used to follow the kinetics of polycondensation and, to the best of our knowledge, there is only one report that has done so, ¹⁶ even though it is evident that TGA would be one



FIGURE 1 ¹H NMR spectra of monomer **3** and the hyperbranched polymer; the spectrum of the polymer was recorded in C_6D_6 to provide improved spectral resolution. Peaks marked by an * are due to either solvent or inadvertent water contamination. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

of the quickest ways to obtain kinetic information and, importantly, it would require only very little sample. To obtain meaningful data from the TGA runs, however, one needs to ensure that the purge rate of the career gas is adequate to rapidly carry the volatile condensate; this will ensure that the weight loss is indeed a direct reflection of the condensation rate.

Firstly, to gain a quick estimate of the relative of the rates of polymerization, the TGA thermograms of both the monomers, namely the bis-allyl ether monomer (**3**) and the bismethyl ether monomer (**A**), were carried out under a fixed nitrogen purge rate 20 mL/min in the presence of 2 mol % of the catalyst, pyridinium camphorsulfonate, PCS (Supporting Information Fig. S2). At first sight, it appeared that the weight-loss in the case of monomer **3** begins at a slightly lower temperature suggesting greater ease of polymerization in this case. However, careful examination revealed that the difference is more a reflection of the higher molecular weight of the evolved fragment in the case of the allyl ether monomer. Additionally, it was also noticed that a gradual weight loss began right from the beginning of the run suggesting the presence of some volatile species, like a solvent.

In an effort to gain a more quantitative assessment of the relative rates of polycondensation, we carried out isothermal TGA experiments. Here the monomer with the required amount of PCS was heated rapidly to 100 $^\circ$ C, held at this temperature for 3 min and then heated at 10 deg/min to

150 °C; the temperature was then held constant and the weight-loss was monitored as a function of time. The first isothermal segment (3 mins at 100 °C) was to ensure that



FIGURE 2 Isothermal TGA scans of the two monomers, in the presence of 2 mol % PCS at 150 °C; Inset shows a plot of percent conversion versus time for the two monomers. The plateau value of the weight loss for the two monomers (monomer **A**-red and **3**-black) are different reflecting the loss of higher molecular weight, allyl alcohol, in case of monomer **3**.



FIGURE 3 Stack plot of the ¹H NMR spectra of aliquots taken after different time intervals during the polymerization of monomer **3**. The polymerization times are listed on the right, while the numbers on top of the peaks reflect their relative intensities; the set of peaks between 2.2 and 2.5 ppm have been normalized in all the spectra to reflect 9 protons.

any weight loss due to the inadvertent presence of volatiles is accounted for and, secondly, this permitted the heating to $150 \,^{\circ}$ C to be carried out in a relatively short time before beginning the isothermal segment. This ensured that minimum weight loss (due to condensation) occurs during the temperature ramp segment. The flow rate of the purge gas was maintained at 20 mL/min to ensure that the weight loss does reflect the rate of polycondensation. Figure 2 shows the isothermal scans of the two monomers; here again the relative slopes appear to suggest that polymerization of the allyl monomer **3** may be faster. However, further analysis of the data, wherein the percent conversion is estimated from the percent weight loss in each case, shows that the two monomers appear to polymerize at roughly similar rates (see Fig. 2 inset); this is evident from the near overlapping of the two curves and the similar slopes exhibited for the linear segment after the apparent induction period. This study confirms that replacing the methyl groups in monomer **A** with allyl groups does not change the rate of polycondensation significantly.

A similar kinetics study was carried out by taking aliquots from the polymerization mixture after different time intervals and recording their NMR spectrum. A stack plot showing the spectral evolution as a function of polymerization time is shown in Figure 3. The intensity of an invariant set of peaks, such as those due to the three aromatic methyl groups at 2.3-2.4 ppm, was normalized to reflect nine protons; this permitted the direct comparison of the peaks due to the allyl unit (for instance, the peak at 5.3 ppm), as indicative of the percent conversion. The intensity of this peak (at 5.3 ppm) clearly decreases with polymerization time; the percent conversion can be readily estimated from this variation in relative intensities, and the values thus obtained are plotted as a function of polymerization time in Figure 4. Here again, the comparison of the initial polymerization rates (up to 40 min, after which the polymerization is carried out under a reduced pressure of 2 torr) of monomers 3 and A suggests that the rates are not significantly different; although the allyl monomer appears to polymerize marginally faster.

Overall, the NMR studies are broadly in concurrence with the TGA analysis suggesting that simple TGA analysis could serve as a quick and easy method for assessing the relative polymerization rates of a variety of melt polymerizations, especially when relatively nonvolatile monomers are used.

Clicking the Hyperscaffold with Various Thiols

One of the virtues of generating hyperbranched polymers that carry terminal allyl groups is the opportunity to generate a wide range of polymers with very distinct properties by using different organic thiols. Of the various approaches to carry out thiol-ene reactions, the photochemically initiated approach, using 2,2-dimethoxy 2-phenyl acetophenone as the initiator, is often the method of choice.⁹ Hence, in the present studies, a solution of the hyperbranched polymer (HBP-allyl) and the required thiol was taken along with the initiator in THF and irradiated using a Hg-vapor lamp for about 4 h. The isolated polymers were analyzed using ¹H NMR and GPC. Four different thiols were used for this study: benzyl thiol as a control, octadecane thiol to induce hydrocarbon solubility, 2-mercaptoethanol to impart hydrophilicity and N-benzoyl cystine to demonstrate the potential for bioconjugation; the structures of these clicked hyperbranched polymers are shown in Scheme 3.

The ¹H NMR spectra of the homopolymer, along with those of the clicked polymers are shown in Figure 5; the region where the allyl proton signals is expected has been yexpanded to reveal the absence of residual allyl groups in the polymer, thereby confirming that the click reaction has proceeded to near completion in all the cases. In addition to the disappearance of the allyl proton signals, the relative intensities of the signals arising from the clicked moiety also tallies well with the expected values for quantitative conversion. These experiments clearly suggest that the allylterminated hyperbranched polyethers can indeed serve as compact hyperscaffolds onto which a variety of function-performing units could be ligated under fairly benign conditions; this should make these polymers interesting and amenable to facile anchoring of biologically interesting subunits. The molecular weights of the clicked polymers typically

increased slightly, except in the case of 2-mercaptoethanol where a small apparent reduction was noticed; this we believe is more a reflection of chain compaction due to intramolecular H-bonding (see Supporting Information).

Thermal Properties of Clicked Hyperbranched Polymers

It is well-known that the thermal properties of hyperbranched polymers depend strongly on the nature of terminal groups.¹⁷ The DSC thermograms of the various clicked polymer samples along with that of the pristine hyperbranched polyether (HBP-allyl) are shown in Figure 6. All the hyperbranched polymers, except **HBP-SC18** that carries long alkyl chains (C-18) at the periphery, are amorphous as expected and exhibit only a glass transition. The T_g of the parent polymer was at -13 °C, while those clicked with benzylthiol (**HBP-SBz**) and 2-mercapto ethanol (**HBP-SC20H**) were at -4 °C and -11 °C, respectively. The very small difference between the parent polymer and **HBP-SC20H** is a bit surprising as one may have expected that the H-bonding between the peripheral hydroxyl groups would increase the T_g of the sample.

The $T_{\rm g}$ of the *N*-benzoyl cystine clicked polymer (HBP-NBC), on the other hand, was significantly higher (57 °C) reflecting the presence of strong H-bonding interactions between the pendant carboxylic acid groups as well as between the amide units. Polymer HBP-NBC was also soluble in aqueous bicarbonate solution due to the presence of numerous pendant carboxylic acid groups. The octadecyl clicked polymer **HBP-SC18** was the only sample that was crystalline and exhibited a clear melting transition around 33 °C, reflecting the strong tendency of the long paraffinic chains to crystallize despite being present on a hyperbranched core that contains a substantial number of linear defects.



FIGURE 4 Plot of percent conversion of monomers **3** and **A** as a function of polymerization time; the percent conversion was estimated by ¹H NMR spectroscopy. The first stage of polymerization was carried out under dry N₂ purge for 40 mins, after which the polymerization was carried out under reduced pressure (~2Torr). [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]



FIGURE 5 ¹H NMR spectra of the pristine hyperbranched polymer (a), the polymer clicked with benzylthiol –HBP-SBz (b), with hexadecylthiol HBP-SC18 (c), with 2-mercaptoethanol HBP-S-C2-OH (d), and with *N*-benzoyl cystine HBP-NBC (e). The spectra of all the polymers were recorded in CDCl₃. Peaks marked by an * are due to either solvent or inadvertent water contamination. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

This confirms the ability of the flexible core to adapt to permit the crystallization of the peripheral alkyl groups; a similar conclusion regarding the conformational adaptability of the core was also inferred in the case of PEGylated hyperbranched polymers that readily formed core-shell type structures in aqueous solutions.^{3(a)}

CONCLUSIONS

We have demonstrated that the transetherification polycondensation is an effective strategy for the preparation of hyperbranched polymers carrying numerous terminal allyl groups. The polymerization proceeded by the self-condensation of an AB_2 monomer that carries two allylbenzyl ether groups and an aliphatic —OH group; the polymerization proceeds by the exclusion of one mole of allyl alcohol, while the second mole of allyl groups decorates the periphery of the hyperbranched polymer. TGA and NMR studies revealed that the kinetics of polymerization is not significantly altered when the methyl benzyl ether groups in the AB₂ monomer is replaced by allyl benzyl ether groups. NMR structural studies also confirm that the terminal allyl units can be quantitatively clicked using the thiol-ene reaction under photochemically initiated conditions. DSC studies clearly reveal the strong influence of the nature on the terminal groups on the $T_{\rm g}$ of hyperbanched polymers; the *N*-benzoyl cystine clicked polymers exhibited a T_{g} about 70 degrees higher than the parent polymer because of the strong H-bonding interactions between the numerous terminal carboxylic acid groups. When the HBP's are clicked with long chain alkyl groups, such as an octadecyl group, the polymer exhibits a clear melting transition that reflects the very strong tendency of long paraffinic chains to independently crystallize despite their fairly irregular placement on a defective hyperbranched framework indicating the adaptability of the relatively flexible core. Recent studies have revealed that diallylesters of 5-



FIGURE 6 DSC thermograms of the pristine HBP and the various thiol-ene clicked derivatives. The studies were carried out under a dry nitrogen purge at a heating rate of 5 deg/min. Reproducibility of all the scan were checked by carrying out sequential heating-cooling-heating cycles and the reported scans are the 2nd heating runs.

hydroxy-isophthalic acid also undergoes facile melt transesterification polycondensation to yield similarly clickable hyperbranched polyesters;¹⁸ this should make clickable hyperbranched polymeric scaffolds more readily accessible, given the ready availability of the starting material and simplicity of the monomer synthesis. Presently, we are exploring various applications of such clickable HBP's that involve simultaneous, and often orthogonal, clicking of multiple units on to a single scaffold for introduction of multiple functions.

EXPERIMENTAL

Materials and Methods

2,4,6-Trimethyl phenol, octadecanthiol, 2-mecaptoethanol, trioxane and camphor sulfonic acid were purchased from Sigma-Aldrich chemical company and used directly. Allyl alcohol, metallic sodium, benzyl chloride, pyridine and 33% acetic acid solution of HBr were purchased from Spectrochem and used directly. Common organic solvents were purchased locally and distilled before use. ¹H NMR spectrum was recorded using a 400 MHz Bruker spectrometer using CDCl₃ as solvent, unless mentioned otherwise. DSC measurements were carried out using a TA DSC-Q10 instrument. Gel permeation chromatography (GPC) was carried out using a Viscotek TDA model 300 system, which is coupled to refractive-index, differential viscometer and light scattering detectors in series. The separation was achieved using two mixedbed PLgel columns (5 μ m, mixed C) maintained at 35 °C; tetrahydrofuran (THF) was used as the eluent. The molecular weights were estimated using a universal calibration curve based on polystyrene standards.

3,5-Bisbromomethyl-2,4,6-trimethylphenol (1)¹⁹

One-hundred milliliter of HBr in AcOH (33%) was added to a mixture of trioxane (6.61 g, 73.5 mmol) and 2,4,6-trimethyl

phenol (10 g, 73.5 mmol). The reaction mixture was refluxed for 3 h, cooled to room temperature and poured into icecold water. The residue was filtered through suction and washed with saturated solution of NaHCO₃ to ensure it is acid free and then dried under vacuum (22.4 g, 95%, mp = 136 °C).

¹H NMR (δ, ppm, CDCl₃): 2.31 (s, 6H, Ar-**CH**₃); 2.39 (s, 3H, Ar-**CH**₃); 4.57 (s, 4H, Ar-CH₂Br).

3,5-Bis(allyloxymethyl)-2,4,6-trimethyl phenol (2)

Sodium metal (4.2 g, 182.6 mmol) was added in small pieces to 150 mL of dry allyl alcohol. Compound **1** (10 g, 31 mmol) was dissolved in allyl alcohol (~50 mL) and added dropwise to the degassed sodium alkoxide solution. The reaction mixture was refluxed for 18 h under N₂ atmosphere and then cooled to room temperature. Excess allyl alcohol was removed under reduced pressure and 100 mL of ice-cold water was added to the residue, which was then acidified using 10% HCl (v/v). The precipitate formed was extracted with CHCl₃ (2 × 100 mL) and the combined organic extract was dried using anhydrous sodium sulphate. Chloroform was removed under reduced pressure and the residue was distilled (220 °C/2 Torr) in Kugelröhr apparatus (Yield = 33%).

¹H NMR (δ, ppm, CDCl₃): 2.27 (s, 6H, Ar-**CH**₃); 2.36 (s, 3H, Ar-**CH**₃); 4.04 (d, 4H, Ar-O**CH**₂CHCH₂); 4.52 (s, 4H, Ar-**CH**₂O-); 4.60 (s, 1H, Ar-**OH**); 5.25 (m, 4H, ArOCH₂CH**CH**₂); 5.97 (m, 2H, ArOCH₂**CH**CH₂).

4-Bromobutylacetate (3)²⁰

2.16 g (26.0 mmol) 1,2-dibromoethane was added to 0.63 g (26 mmol) of Mg turnings in 25 mL of dry ether under N₂ atmosphere and the mixture was stirred for 3 h at RT until evolution ethylene gas ceases, suggesting complete formation of MgBr₂. The excess ether was removed under reduced pressure and 25 mL of dry acetonitrile was added to the solid mass followed by addition of 2.05 mL of dry THF and 5.20 mL of acetic anhydride. The mixture was stirred for 16 h at room temperature, neutralized with NaHCO₃ solution and then extracted with (3 × 50 mL) of diethyl ether. The ether layer was dried over anhydrous Na₂SO₄, concentrated and distilled in a Kugelröhr (87 °C/2.0) torr to get desired product (Yield = 90%).

¹H NMR (δ, ppm, CDCl₃): 1.74-1.81 (m, 2H, -BrCH₂CH₂-); 1.88-1.95 (m, 2H, -CH₂CH₂OAc-); 2.03 (s, 3H, -OCOCH₃); 3.42 (t, 3H, -CH₂CH₂Br); 4.07 (t, 2H, -CH₂CH₂OAc).

1-(4-Hydroxybutyloxy)-3,5-bis(allyloxymethyl)-2,4, 6-trimethylbenzene (4)

A mixture of K_2CO_3 (15 g, 108.6 mmol) and catalytic amount of KI were taken in dry acetonitrile (120 mL). The mixture was degassed for 20 min by purging with nitrogen after which **3** (5.3 g, 27.17 mmol) and **2** (5.0 g, 18.1 mmol) were added to the solution. The reaction mixture was degassed for further 20 min and then refluxed for 72 h under N_2 atmosphere. The solvent was them removed under reduced pressure and 50 mL of ice-cold water was added to it. The resulting solution was extracted with 150 mL (2 × 75 mL) diethyl ether; the ether layer was washed with 120 mL (4 \times 30 mL) 10% aq. NaOH solution followed by water (30 mL) and brine solution (30 mL). The ether layer was dried over anhydrous sodium sulphate and concentrated under reduced pressure. The acetate derivative (without any further purification) along with 50 mL of 10% aq. NaOH and equal amount of ethanol were refluxed overnight and cooled to RT. The product was extracted into diethyl ether (2 \times 50 mL), dried over anhydrous Na₂SO₄, and concentrated. The crude product was purified on a silica-gel column using ethyl acetate-Pet. ether (35:65 v/v) as the eluent. (Yield = 60%).

¹H NMR (δ , ppm, CDCl₃): 1.81 (m, 2H, ArOCH₂CH₂CH₂. CH₂OH); 1.90 (m, 2H, ArOCH₂CH₂CH₂CH₂OH); 2.30 (s, 6H, Ar-CH₃); 2.36 (s, 3H, Ar-CH₃); 3.68 (t, 2H, ArOCH₂CH₂CH₂CH₂CH₂CH₂CH); 3.74 (t, 2H, ArOCH₂CH₂CH₂CH₂CH₂OH); 4.05 (d, 4H, Ar-CH₂OCH₂CHCH₂); 4.51 (s, 4H, Ar-CH₂O-); 5.25 (m, 4H, ArCH₂OCH₂CHCH₂); 5.97 (m, 2H, ArCH₂OCH₂CHCH₂).

Polymerization

Monomer 4 (1.5 g, 4.31 mmol) along with 2 mol % of pyridinium camphorsulfonate (PCS)^{13(b)} was taken in a test-tube shaped polymerization vessel. The mixture was degassed for 10 min and maintained at a temperature of 110 °C under continuous N2 purge, to ensure homogeneous mixing of catalyst and monomers. The polymerization was then carried out at 150 °C under N₂ for 1 h with constant stirring. Subsequently, using a Kugelröhr apparatus, the polymerization was continued for an additional period of 45 min at 150 $^\circ\text{C}$ under reduced pressure (2 Torr), with continuous mixing of the melt by rotation. The resultant polymer was dissolved in THF, the acid-catalyst was neutralized with solid NaHCO₃ and then the solution was filtered. The filtrate was concentrated under reduced pressure to a viscous solution and precipitated in methanol. The polymer was further purified twice by dissolution in THF and reprecipitation into methanol (Yield = 70%).

¹H NMR (δ , ppm, CDCl₃): 1.85 (m, 4H, ArOCH₂CH₂CH₂. CH₂OH); 2.30 (m, 6H, Ar-CH₃); 2.37 (m, 3H, Ar-CH₃); 3.57 (t, 2H, ArOCH₂CH₂CH₂CH₂OH); 3.63 (t, 2H, ArOCH₂CH₂CH₂CH₂CH₂CH₂OH); 4.03 (d, 2H, ArCH₂OCH₂CHCH₂); 4.49 (s, 4H, Ar-CH₂O-); 5.25 (m, 2H, ArCH₂OCH₂CHCH₂); 5.97 (m, 1H, ArCH₂OCH₂CHCH₂).

Postpolymerization Modification: Thiol-ene Click with Benzylthiol

A mixture of the polymer, HBP-allyl (60 mg, 0.206 mmol) and benzyl thiol (80 mg, 0.62 mmol) were taken in 5 mL THF. To the reaction mixture, the photo-initiator 2,2-dimethoxy 2-phenyl acetophenone (2 mg, 0.08 mmol), was added. The content was irradiated with UV light for 4 h. The polymer solution was concentrated under reduced pressure to a viscous solution and precipitated in methanol; the polymer was further purified twice by dissolution in THF and reprecipitation into methanol to yield the polymer, **HBP-SBz**.

1H NMR (δ, ppm, CDCl₃): 1.85 (m, 6H, ArOCH₂CH₂CH₂. CH₂OH, ArCH₂OCH₂CH₂CH₂S-); 2.25-2.38 (m, 9H, Ar-CH₃); 2.49 (t, 2H, -CH₂CH₂SCH₂Ph); 3.52-3.57 (m, 4H, ArOCH₂CH₂ CH₂CH₂OH); 3.62 (t, 2H, ArCH₂OCH₂CH₂CH₂SCH₂Ph); 3.67 (s, 2H, ArSCH₂Ph); 4.49 (m, 4H, Ar-CH₂O-); 7.25 (m, 5H, -SCH₂Ph)

Clicking with all other thiols, namely 2-mercaptoethanol, 1octadecane thiol and *N*-benzoyl cystine, were carried out using a similar procedure to give -**HBP-SC2OH**, **HBP-SC18** and HBP-NBC, respectively, in yields ranging from 60 to 70%, after two reprecipitations.

HBP-SC2OH

¹H NMR (δ , ppm, CDCl₃): 1.85 (m, 6H, ArOCH₂CH₂CH₂. CH₂OH, ArCH₂OCH₂CH₂CH₂S-); 2.25-2.38 (m, 9H, Ar-CH₃); 2.59 (t, 2H, -ArCH₂CH₂SCH₂CH₂OH); 2.65 (t, 2H, -ArCH₂. SCH₂CH₂OH); 3.59-3.64 (m, 8H, ArOCH₂CH₂CH₂CH₂CH₂OH, ArCH₂OCH₂-, ArSCH₂CH₂OH); 4.49 (m, 4H, Ar-CH₂O-).

HBP-SC18

¹H NMR (δ , ppm, CDCl₃): 0.88 (t, 3H, ArS(CH₂)₁₇CH₃); 1.25-1.60 (m, 32H, ArSCH₂(CH₂)₁₆CH₃); 1.85 (m, 6H, ArOCH₂ CH₂CH₂CH₂OH, ArOCH₂CH₂CH₂S-); 2.25-2.38 (m, 9H, Ar-CH₃); 2.50 (t, 2H, ArSCH₂(CH₂)₁₆CH₃); 2.59 (t, 2H, -ArCH₂ CH₂SCH₂(CH₂)₁₆CH₃); 3.59-3.64 (m, 6H, ArOCH₂CH₂CH₂CH₂ CH₂OH, ArCH₂OCH₂-); 4.49 (m, 4H, Ar-CH₂O-).

HBP-NBC

¹H NMR (*δ*, ppm, CDCl₃): 1.85 (m, 6H, ArOCH₂CH₂CH₂-CH₂OH, ArOCH₂CH₂CH₂S-); 2.25-2.38 (m, 9H, Ar-CH₃); 2.59 (t, 2H, ArCH₂CH₂SCH₂CH₂OH); 3.59-3.64 (m, 8H, ArOCH₂-CH₂CH₂CH₂OH, ArCH₂OCH₂-, ArSCH₂CH(CO₂H)NHCOPh); 4.49 (m, 4H, Ar-CH₂O-); 5.01 (m, 1H, ArSCH₂CH(CO₂H)NHCOPh); 6.9-7.7 (m, 5H, ArNHCOPh).

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