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Site-Specific Functionalization of Hyperbranched Polymers Using "Click" Chemistry

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ABSTRACT: Different strategies for functionalization of the core region and periphery of core−shell type hyperbranched polymers (HBP) using the "click" reaction have been explored. For achieving peripheral functionalization, an AB_2 + $A-R_1$ + $A-R_2$ type copolymerization approach was used, where $A-R_1$ is heptaethylene glycol monomethyl ether (**HPEG-M**) and $A-R_2$ is tetraethylene glycol monopropargyl ether (**TEG-P**). A very small mole fraction of the propargyl containing monomer, **TEG-P**, was used to ensure that the water-solubility of the hyperbranched polymer is minimally affected. Similarly, to incorporate propargyl groups in the core region, a new propargyl group bearing B_2-type monomer was designed and utilized in an AB_2 + A_2 + B_2 + $A-R_1$ type copolymerization, such that the total mole fraction of B_2 + A_2 is small and their mole-ratio is 1:1. Further, using a combination of both the above approaches, namely AB_2 + A_2 + B_2 + $A-R_1$ + $A-R_2$, hyperbranched structures that incorporate propargyl groups both at the periphery and within the core were synthesized. Since the AB_2 monomer carries a hexamethylene spacer (C-6) and the periphery is PEGylated, all the derivatized polymers form core−shell type structures in aqueous solutions. Attempts were made to ascertain and probe the location of the propargyl groups in these HBP's, by "clicking" azidomethylpyrene, onto them. However, the fluorescence spectra of aqueous solutions of the pyrene derivatized polymers were unable to discriminate between the various locations, possibly because the relatively hydrophobic pyrene units insert themselves into the core region to minimize exposure to water.

Introduction

Site-specific incorporation of functionality onto dendrimers and hyperbranched polymers is of interest owing to their potentially interesting properties, such as their use for encapsulation of dyes and metal nanoparticles,[1] as scaffolds for catalysis,[2] as drug delivery vehicles,[3] for light harvesting,[4] etc. In the case of dendrimers, functionality can be selectively incorporated at various sites, such as the core[5] or the periphery,[6] as a pendant unit within the internal layers,[7] or even directly within the backbone segment,[8] owing to the stepwise synthesis procedure usually adopted. Hyperbranched polymers, on the other hand, are randomly branched structures devoid of a distinct core or discrete generations, and therefore, most efforts in this area have focused on terminal functionalization,[9] wherein the end groups present at the linear and terminal units get nonselectively functionalized. Haag et al. addressed this limitation in the case of hyperbranched polyglycerols using a clever strategy that helped discriminate between the terminal vicinal diol groups and the isolated hydroxyl groups present at the linear defect locations. Using the selective formation of cyclic ketals/acetals at the terminal locations, they were able to create hyperbranched polymers that were selectively functionalized either at the periphery or within the core region of the hyperbranched polyglycerol.[10] They also showed that this approach can be used to create core−shell type systems as well as pseudodendrimers by a suitable postfunctionalization of the hyperbranched polyglycerol.[10,11] In another interesting report, Ambade et al. have generated internally functionalizable *N*-allyl hyperbranched polyurea from a suitably designed carbonyl azide based AB_2 monomer.[12] In a more recent report, Gittins et al. functionalized the so-called focal point (i.e., the single residual A group) of a hyperbranched polymer with a *p*-nitrophenyl ester unit in a single-step process, and subsequently modified this site with isobutyl amine very rapidly at room temperature in a postsynthetic step.[14]

Click reaction, which most widely refers to the 1,3-dipolar cycloaddition between an organic azide and a acetylenic unit, has become an exceedingly popular method for the incorporation of a wide range of functionality onto polymeric systems.[15] Consequently, simple strategies to incorporate either azide or acetylenic units in polymeric structures have become increasingly important. Clickable propargyl groups have been incorporated into hyperbranched polymers[16] by Haag and co-workers, and these were used to generate intramolecularly cross-linked polymeric nanoparticles by the use of an organic diazide.[17] In the context of linear polymers, Du Prez and co-workers have recently explored the *direct* incorporation of clickable propargyl groups into linear aliphatic polyesters using a suitably propargylated monomer.[18] Click reaction has also been used for the preparation of block copolymers,[19] polymer surface modification[20] and even as the polymer forming reaction.[21] Given the remarkable versatility of click reaction, development of simple strategies for the *direct* inclusion of clickable units at various locations in HBPs would be an attractive objective. Thus, the aim of the present investigation is 2-fold: (1) to incorporate clickable functionality at specific sites in hyperbranched polymers directly during the polymerization process and (2) to demonstrate quantitative inclusion of functional units at these specific locations using the click reaction.

AB_2 + AR type polycondensation was developed in our laboratory several years ago as an approach to incorporate mesogenic units at the periphery of hyperbranched polyurethanes.[22] Since, the AB_2 monomer carries one equivalent excess of B-type functionality, it can be copolymerized with up to one-equivalent of a molecule carrying a single A-functionality without

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affecting the polymer molecular weight. Thus, the copolymerization of AB_2 with an A−R monomer serves as a straightforward approach to generate peripherally functionalized HBPs. Recently, we used such a copolymerization approach to directly prepare core−shell type hyperbranched polyethers using the melt-transetherification process[23] and have examined their unimolecular micellar properties[24] and their LCST behavior.[25] For water-soluble unimolecular micelle-forming systems, we copolymerized AB_2 monomers that carry hydrophobic alkylene spacers along with a hydrophilic heptaethylene glycol monomethyl ether (HPEG-M) as the A−R monomer. In the present study, we have extended this approach by first utilizing tetraethyleneglycol monopropargyl ether (TEG-P) as an additional A−R type comonomer in an $AB_2 + A-R_1 + A-R_2$ type copolymerization. Furthermore, using a small amount of $A_2 + B_2$ (that carries a pendant propargyl group) in an $AB_2 + A_2 + B_2 + A-R_1$ copolymerization, clickable units were incorporated within the core region. Finally, we also show that, using both components in an $AB_2 + A_2 + B_2 + A-R_1 + A-R_2$ type copolymerization, propargyl groups can be incorporated both in the core region as well as at the periphery of hyperbranched polymers.

Experimental Section

2,4,6-Trimethylphenol (Mesitol), 1,6-hexanediol, tetraethylene glycol, triethylene glycol monomethyl ether, propargyl alcohol, p-toluene sulfonyl chloride and 1-pyrenecarboxaldehyde were purchased from Aldrich Chemical Co. Mesyl chloride and dichloromethane (DCM) was dried over P_2O_5 and distilled. Et_3N was refluxed over KOH followed by distillation. Monomers **AB2-C6** and heptaethylene glycol monomethyl ether (**HPEG-M**) were synthesized according to the procedure described in our earlier paper.[26] 1-Azidomethylpyrene (**F**) was synthesized from pyrenecarboxaldehyde according to a reported procedure,[27] details of which are given in the Supporting Information. Structures of all intermediates, monomers and polymers were confirmed by ^{1}H NMR spectroscopy. NMR spectra were recorded on a Bruker AV400 MHz spectrometer, using $CDCl_3$ or C_6D_6 as the solvent and TMS as reference. GPC measurements were carried out using Viscotek TDA model 300 system, coupled to a refractive index (RI), differential viscometer (DV) and light scattering (LS) detectors in series. The separation was achieved using a series of two PLgel mixed bed columns (300 × 7.5 mm) operated at 30 °C using THF as the eluent. Molecular weights were determined using a universal calibration curve based on the data from the refractive index (RI) and differential viscometric (DV) detectors using narrow polystyrene standards. The UV−visible spectra were recorded using a Varian 300 spectrophotometer. Steady state fluorescence measurements were done using a Fluorolog instrument.

TEG-P. Tetraethylene glycol (4.35 g, 22.3 mmol) was taken in 15 mL of dry THF. Na (0.34 g, 14.9 mmol) was added in pieces. Propargyl mesylate (2.0 g, 14.9 mmol) taken in 10 mL of dry THF, was then added to it dropwise at 0 °C under N_2. The contents were stirred for 12 h at room temperature under N_2. After the reaction was complete, the contents were filtered and purified by silica column using petroleum ether and EtOAc as the eluent to get a liquid product (2.65 g, yield = 51%). ^{1}H NMR (δ, ppm, $CDCl_3$): 2.43−2.44 (t, 1H, **CH**); 3.6−3.73 (m, 16H, glycol); 4.20−4.21 (d, 2H, **CH_2**-triple bond).

B2 Monomer. Compound **AB2-C0**[26] (see Scheme 1) (1.0 g, 4.46 mmol) and propargyl mesylate (0.89 g, 6.69 mmol) were dissolved in 50 mL of dry CH_3CN. Then K_2CO_3 (3.5 g, 25.3 mmol) and catalytic amount of KI was added to it and the contents were refluxed for 3 days under N_2. After the reaction was completed, CH_3CN was removed and 20 mL of H_2O was added to it. After extraction, the DCM layer was washed with brine and passed over Na_2SO_4. The product was purified over a silica column using petroleum ether and EtOAc as the eluent to get the white solid product (0.83 g, yield = 71%). M.P. = 109−110 °C. ^{1}H NMR (δ, ppm, $CDCl_3$): 2.36−2.37 (s, two peaks merged, 9H, Ar**CH_3**); 2.51−2.52 (t, 1H, **CH**); 3.41 (s, 6H, **OCH_3**); 4.37−4.38 (d, 2H, Ar**OCH_2**); 4.46 (s, 4H, Ar**CH_2**).

Synthesis of the Polymers. *Polymer **P1***. Monomer **AB2-C6** (see Scheme 1) (618 mg, 1.9 mmol), along with **TEG-P** (434 mg, 1.86 mmol) and pyridinium camphorsulfonate (PCS)[23d] (11.8 mg, 0.037 mmol) were taken in the polymerization vessel. It was stirred at a temperature of 110 °C for 10 min under continuous N_2 purge, to ensure homogeneous mixing of catalyst and the monomers in the melt. Then the polymerization was carried out at 150 °C under N_2 purge for 5 h with constant stirring. Subsequently, using a Kugelrohr apparatus, the polymerization was continued for an additional period (1 h) at 150 °C under reduced pressure (100 Torr), with continuous mixing of the melt by rotation. The resultant polymer was dissolved in THF, treated with solid $NaHCO_3$ to neutralize PCS and filtered. The filtrate was concentrated and poured into petroleum ether to get the polymer **P1** (yield = 61%).

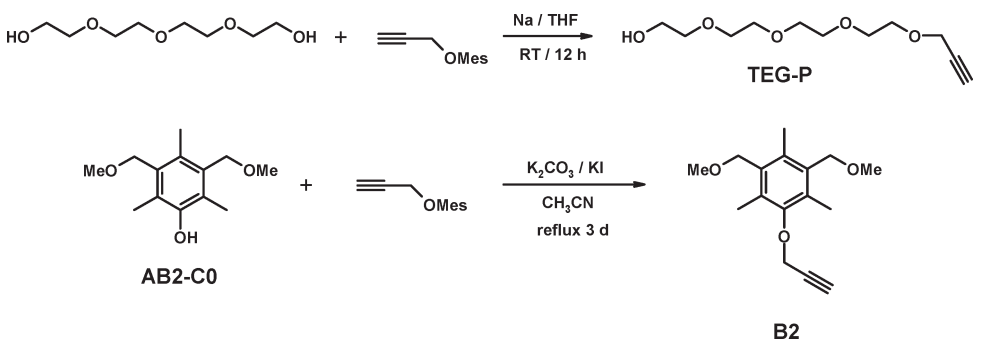
*Polymer **P2***. Polymerization was done as before using monomer **AB2-C6** (1.5 g, 4.62 mmol), along with **TEG-P** (107.5 mg, 0.462 mmol), **HPEG-M** (1.41 g, 4.15 mmol) and PCS (28.7 mg, 0.092 mmol). The polymer **P2** was obtained in 55% yield, after purification by reprecipitation from THF−petroleum ether.

*Polymer **P4***. Similarly, using monomer **AB2-C6** (1.5 g, 4.62 mmol), along with **B2** (77.4 mg, 0.295 mmol), **A2** (34.9 mg, 0.295 mmol), **HPEG-M** (1.54 g, 4.52 mmol), and PCS (28.7 mg, 0.092 mmol), polymer **P4** was obtained in 48% yield after purification from THF−petroleum ether.

*Polymer **P6***. Polymer **P6** was obtained similarly using monomer **AB2-C6** (3.0 g, 9.25 mmol), along with **B2** (154.8 mg, 0.59 mmol), **A2** (69.8 mg, 0.59 mmol), **TEG-P** (182.9 mg, 0.78 mmol), **HPEG-M** (2.81 g, 8.25 mmol), and PCS (57.5 mg, 0.18 mmol). Yield after purification from THF−petroleum ether was 47%.

Click Reaction with the Polymers. *Polymer **P3***. Polymer **P2** (348.0 mg, 0.71 mmol) and 1-azidomethylpyrene (20 mg, 0.07 mmol) was dissolved in 4 mL of THF. Then $CuSO_4.5H_2O$

Scheme 1. Synthesis of the Monomers



(1.2 mg, 0.005 mmol) dissolved in 0.3 mL of H_2O was added to it, followed by the addition of 0.3 mL of aqueous sodium ascorbate (2.0 mg, 0.01 mmol) solution. Immediately, after the addition of sodium ascorbate, the reaction flask was flushed with N_2 and the contents were stirred for 3 days at 50 °C. After the reaction was complete, the reaction mixture was dried over anhydrous Na_2SO_4 and filtered. The filtrate was concentrated and poured into petroleum ether. The polymer was purified twice by dissolution-reprecipitation using THF−petroleum ether and finally dried to obtain a tacky polymer **P3**. Yield = 76%.

*Polymer **P5***. Polymer **P5** was prepared following the same procedure as that of polymer **P3**. Polymer **P4** (1.2 g, 2.5 mmol) and 1-azidomethylpyrene (69.6 mg, 0.26 mmol) was dissolved in 4 mL of THF. Then $CuSO_4.5H_2O$ (2.2 mg, 0.008 mmol) dissolved in 0.1 mL of H_2O was added to it, followed by the addition of sodium ascorbate (3.5 mg, 0.017 mmol) dissolved in 0.1 mL of H_2O. Yield after purification from THF−petroleum ether was 71%.

*Polymer **P7***. Similarly, polymer **P6** (485 mg, 0.99 mmol) and 1-azidomethylpyrene (70 mg, 0.26 mmol) was dissolved in 4 mL of THF. Then $CuSO_4.5H_2O$ (2 mg, 0.008 mmol) dissolved in 0.1 mL of H_2O was added to it, followed by the addition of sodium ascorbate (3 mg, 0.015 mmol) dissolved in 0.1 mL of H_2O. Polymer **P7** obtained in 81% yield after purification from THF−petroleum ether.

Results and Discussion

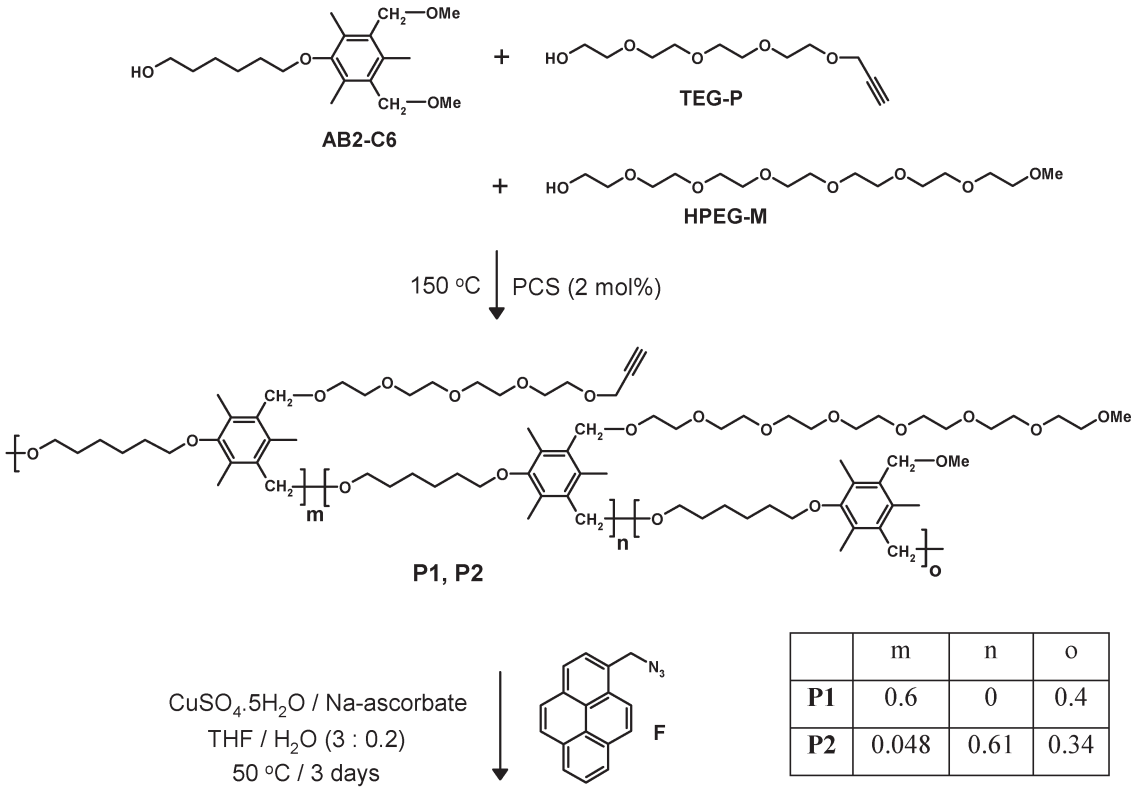
Synthesis of Monomers. As mentioned in the introduction the main objective of this study was to devise simple approaches to incorporate propargyl groups at different locations in a hyperbranched polymer (HBP). These propargyl groups could subsequently be linked to a variety of functional units quantitatively under mild conditions using Sharpless-modified Huisgen-type 1,3-dipolar cycloaddition, popularly known as the "click" reaction.[15a] We had earlier shown that core−shell type hyperbranched polymers can be readily prepared by the copolymerization of an appropriately designed AB_2 monomer, that carries a hydrophobic hexamethylene spacer (C-6), and a water-soluble A−R type comonomer, such as heptaethylene glycol monomethyl ether (**HPEG-M**), under melt-transetherification conditions.[24] Aqueous solutions of such core−shell type HBPs exhibited the capacity to take-up hydrophobic dyes into their core and thereby served as unimolecular micelles. In an effort to develop methods to introduce functionality into HBPs while retaining the ability to form such core−shell structures in water, an alternate A−R type monomer, namely tetraethylene glycol monopropargyl ether (**TEG-P**) was synthesized. The presence of an oxyethylene oxide segment in **TEG-P** would render it some hydrophilicity and hence is expected not to hinder the formation of core−shell type structures in water. **TEG-P** was readily synthesized by coupling tetraethylene glycol (used in 1.5 fold excess) with propargyl mesylate as shown in Scheme 1. Similarly, to incorporate propargyl groups within the core, a new $\mathbf{B_2}$ type monomer carrying a propargyl group was synthesized by capping the A-group in the conventional parent AB_2 monomer, **AB2-C0** using propargyl mesylate. The structures of the monomers were confirmed by their ^{1}H NMR spectra. The synthesis of the parent **AB2-C0** monomer and the **AB2-C6** monomer having a hexamethylene spacer were described earlier.[26]

Synthesis and Structural Elucidation of Propargyl Group Bearing HBPs. An AB_2 monomer carries one equivalent excess of B-type functionality and hence can be copolymerized with up to 1 equiv of a molecule carrying a single A-functionality to generate peripherally functionalized HBPs. To confirm that the propargyl group is unaffected during the melt-transetherification polymerization, the AB_2 monomer (**AB2-C6**) was first copolymerized with **TEG-P**, in a 1:0.98 ratio under standard transetherification conditions, to generate a HBP **P1** carrying a large number of propargyl groups at the periphery as shown in Scheme 2.

The ^{1}H NMR spectra of the resulting polymer **P1** is presented along with those of the two monomers in Figure 1. The various peaks have been assigned as shown in the figure. A few crucial features in the spectra are worthy of mention: (i) the single peak due to benzylic protons (peak a) in the AB_2 monomer splits into three peaks in the polymer reflecting the three different types of benzylic environments in the polymer, as labeled in the figure; (ii) the propargyl methylene protons (peak 1) and the acetylenic proton (peak 2) are clearly seen in the polymer; (iii) from the relative intensities of the peaks belonging to the propargyl group (peak 1) and that due to the methoxy protons (peak c), the level of **TEG-P** incorporation was estimated to be ∼60 mol %, which is comparable to the values typically obtained in our earlier studies dealing with PEGylated HBPs.[24,25] From these observations it is clear that the propargyl group remains intact even under the harsh melt polymerization process that was carried out at 150 °C in the presence of an acidic catalyst, like pyridinium camphorsulfonate.

By the use of two A−R type monomers, namely **HPEG-M** and **TEG-P**, one that carries a terminal methyl and the other a terminal propargyl group, HBPs that bear varying levels of functionalizable propargyl groups at their molecular periphery can be readily prepared. In this study, we limited the level of propargyl-group incorporation to low values so that subsequent click reaction with a fluorescent azide can be done without concern for intrachain fluorophore interactions. Thus, the copolymerization of the type $AB_2 + A{-}R_1 + A{-}R_2$ was done using a ratio of $A{-}R_1$:$A{-}R_2$ of 9:1 as depicted in Scheme 2. The ^{1}H NMR spectra of the resulting copolymer **P2** is shown in Figure 2A. The overall efficacy of direct end-capping using the AB_2 + A−R approach, as seen earlier, was around 60−70%, as roughly confirmed in this case from the relative intensities of the two types of methoxy protons (labeled 5 and 6). Since the level of incorporation of the propargyl-containing monomer is very low, its presence is not readily evident in the spectra. In order to ascertain and quantify the level of propargyl incorporation, the region where the methylene protons of the propargyl ether group is expected (4.0−5.0 ppm) has been expanded; the peak at 4.18 ppm that corresponds to the propargyl methylene protons (labeled 11), is clearly seen in the copolymer confirming the incorporation of the propargyl terminated **TEG-P** segment. From the relative integral intensities of peak 11 (at 4.18 ppm) and the total benzylic protons Ar−$\mathbf{CH_2}$− between 4.45 and 4.55 ppm (labeled 1, 2, and 3), the level of $A{-}R_2$ (**TEG-P**) incorporation was calculated to be 4.8 mol %. However, the incorporation of $A{-}R_1$ (**HPEG-M**) could not be calculated accurately from the spectrum recorded in $CDCl_3$ because the peaks corresponding to terminal methoxy protons of heptaethylene glycol monomethyl ether (6) and the residual methoxymethyl protons $ArCH_2$**OMe** (5) at around 3.39 ppm were not well-resolved. We had shown earlier,[28] that when the spectra of the hyperbranched polymers are recorded in an aromatic solvent, like benzene, a dramatic enhancement in peak separation is seen due to aromatic solvent induced shift (ASIS).[29] Thus the spectrum in a $CDCl_3{-}C_6D_6$ (1:1 v/v) mixture, showed two well-resolved peaks (not shown); from the relative intensities of which the exact level of $A{-}R_1$ incorporation was calculated to be 61 mol %.

Scheme 2. Synthesis of the Hyperbranched Polymers (P1 and P2) Having Propargyl Groups at the Molecular Periphery and the Subsequent Click Reaction of P2 with Fluorophore To Generate Polymer P3[a]



	m	n	o
P1	0.6	0	0.4
P2	0.048	0.61	0.34

	m	n	o
P3	0.048	0.61	0.34

[a] The tables indicate the relative mole fractions of various repeat units in the copolymer.

In order to incorporate propargyl groups within the core region of the hyperbranched polymer, an alternate strategy was developed, wherein the AB_2 monomer is copolymerized with equimolar amounts of B_2 and A_2 monomers, where B_2 carries a pendant propargyl group. At low levels of incorporation of the latter two monomers, they would behave as linear defects within the hyperbranched structure. This strategy has one limitation and that is it could lead to cross-linking at higher levels of $B_2 + A_2$, but at the very low levels employed in the present study it does not pose a problem.[30] An extension of this idea is the copolymerization: $AB_2 + B_2 + A_2 + A-R_1$, where the end-capping with **HPEG-M** yields the required water-soluble core−shell type polymer (**P4**), as shown in scheme 3. The use of $A-R_1$ type comonomer for capping also serves to decrease the probability of cross-linking even further, as was demonstrated by Long and co-workers in the case of $A_3 + B_2$ type approach.[31] Copolymerization using the four monomers was carried out under standard melt-transetherification conditions and the polymer obtained was found to be readily soluble in water as well as in several organic solvents. The ^{1}H NMR spectra of the polymer **P4** is shown in Figure 2B. In the expanded spectrum, the methylene protons of the propargyl unit (peak 13) is seen to appear slightly downfield shifted at ~4.36 ppm compared to peak 11. From the relative intensity of peak 13 with respect to all the benzylic protons, the extent of its

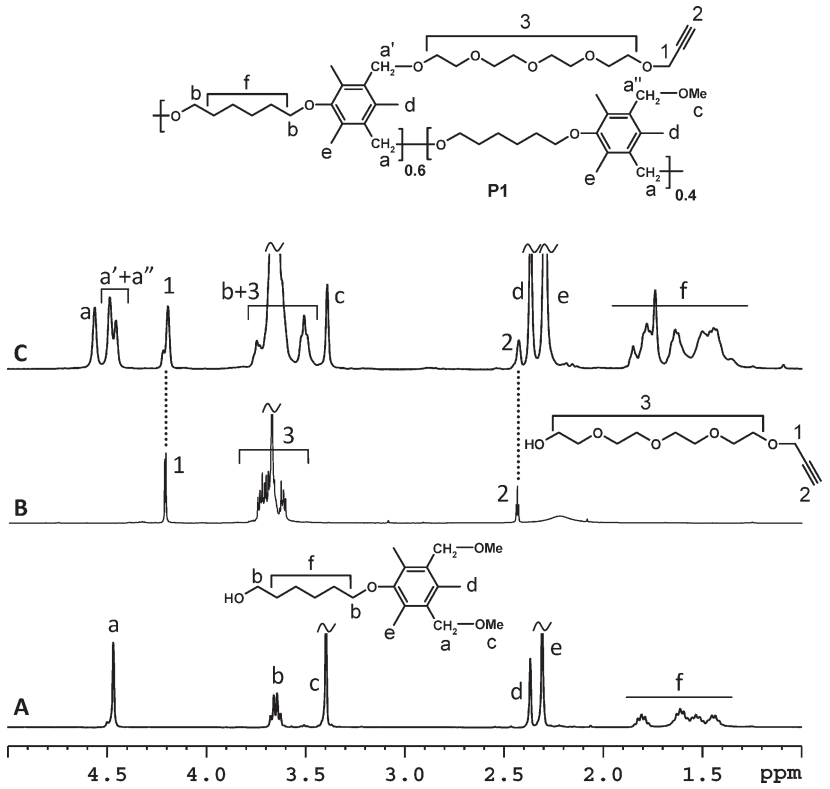


Figure 1. ^{1}H NMR spectra of the monomers **AB2-C6** (A) and **TEG-P** (B), along with the polymer **P1** (C) recorded in $CDCl_3$.

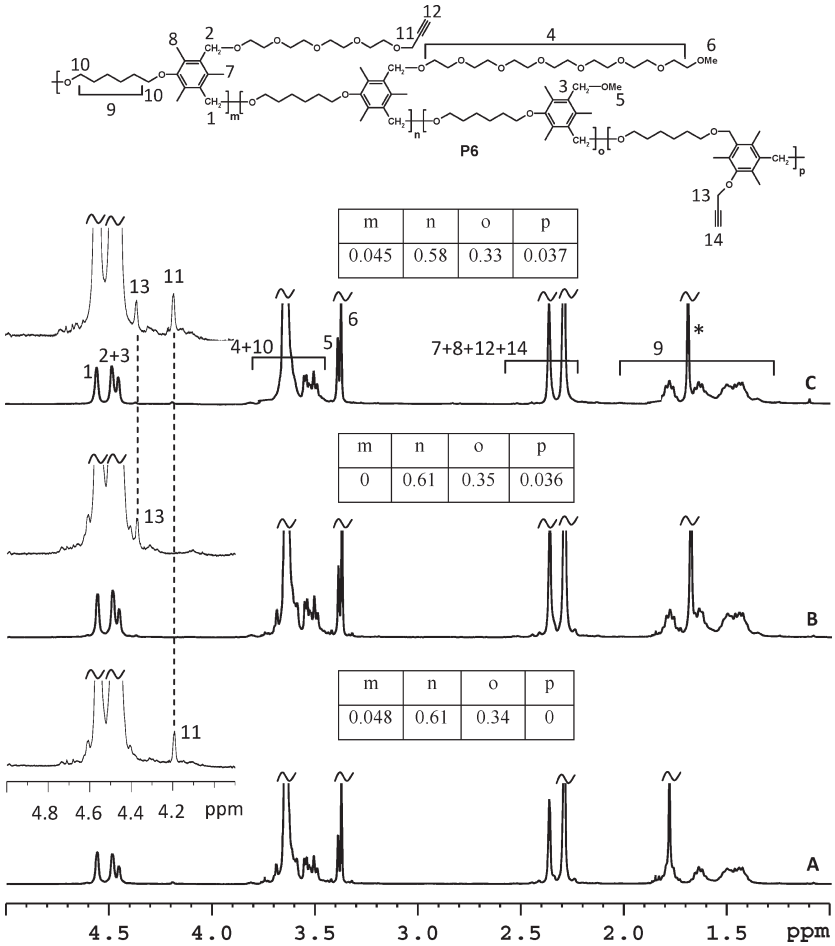
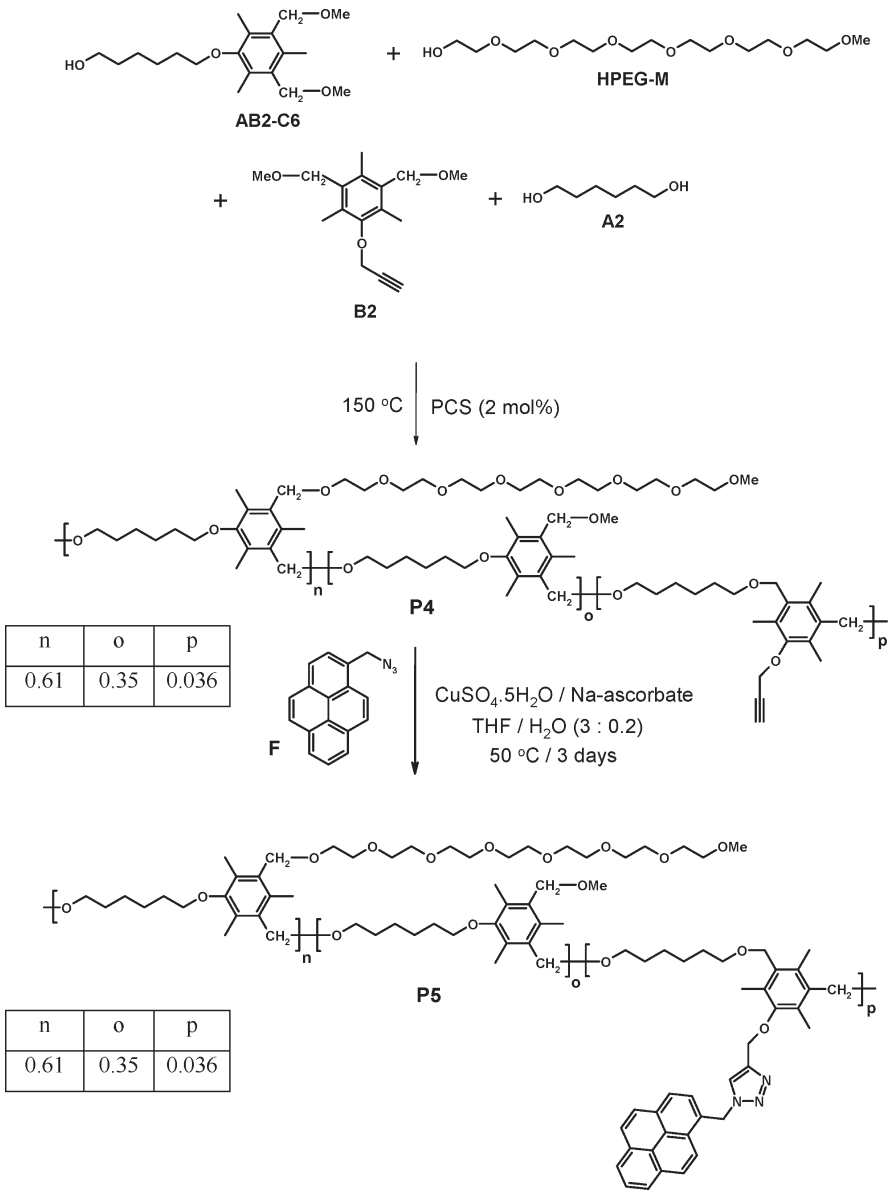


Figure 2. ^{1}H NMR spectra of the (A) hyperbranched polymer **P2** having propargyl groups at the molecular periphery, (B) hyperbranched polymer **P4** having propargyl groups within the core, and (C) hyperbranched polymer **P6** having propargyl groups both at the molecular periphery as well as within the core, recorded in $CDCl_3$. The tables indicate the relative mole fractions of various repeat units in the copolymer.

Scheme 3. Synthesis of the Hyperbranched Polymer P4 Having a Few Percent of the Propargyl Groups within the Core Region and the Subsequent Click Reaction with Fluorophore To Generate Polymer P5[a]



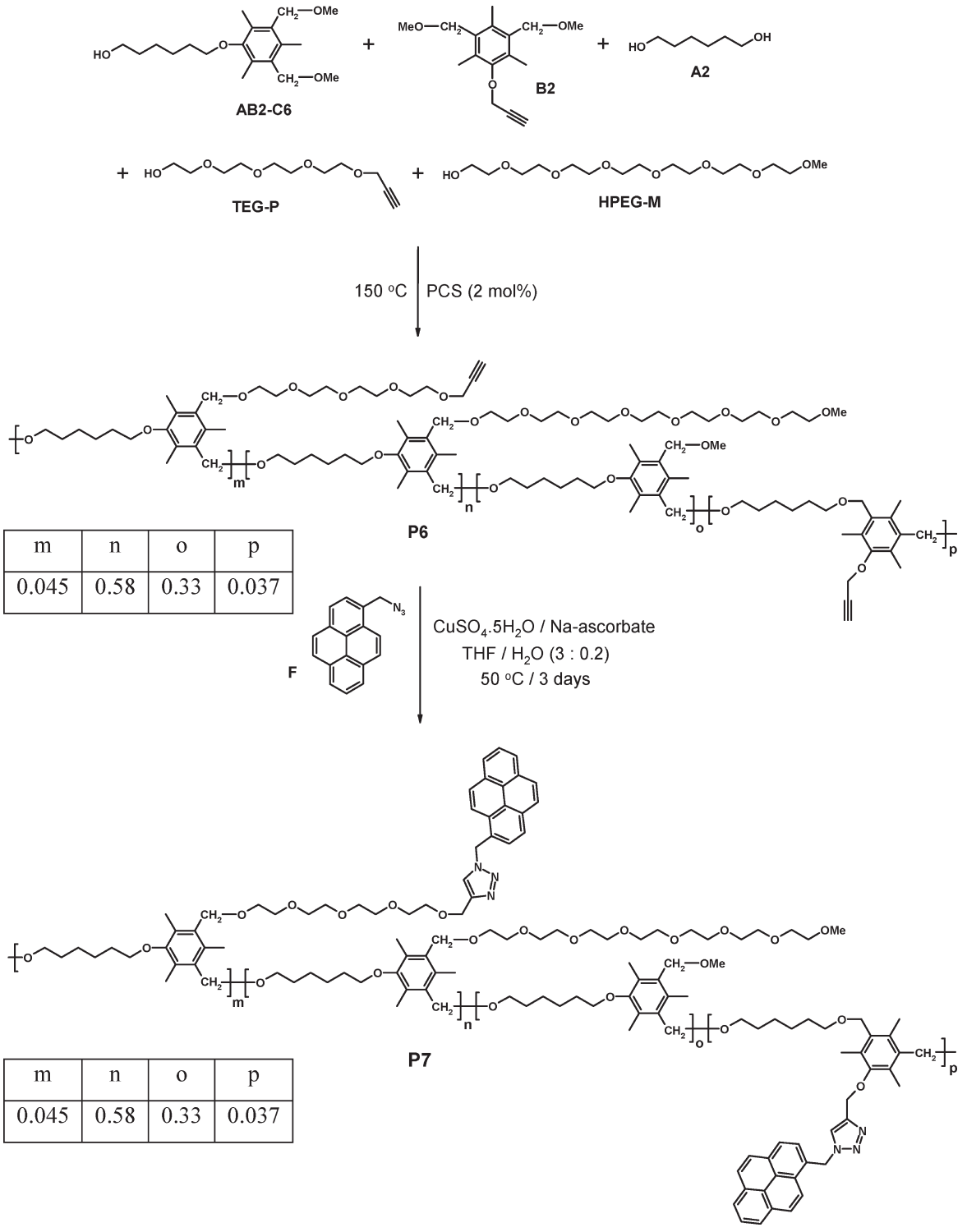
[a] The tables indicate the relative mole fractions of various repeat units in the copolymer.

incorporation was estimated to be about 3.6 mol % and the extent of $A-R_1$ incorporation was calculated to be around 61 mol %, as was done earlier. Similarly, a third polymerization was carried out using monomers that permit the incorporation of the propargyl groups both within the core region as well as at the molecular periphery; in this case two types of A−R monomers are used in a five component polymerization, namely $AB_2 + B_2 + A_2 + A-R_1 + A-R_2$, to generate the polymer **P6** as shown in Scheme 4. From the expanded spectrum in Figure 2C, the relative levels of the incorporation within the core and at the periphery could be independently quantified and was found to be 3.7 and 4.5 mol %, respectively, and the level of $A-R_1$ incorporation was calculated to be around 58 mol %. These spectra unequivocally confirm the incorporation of the propargyl unit in all the three cases and importantly the presence of both types of propargyl units is clearly evident in polymer **P6**. It is important to mention here that for the calculation of $A-R_1$ incorporation, all the spectra were rerecorded in a mixture of $CDCl_3 + C_6D_6$ (1:1) to ensure enhanced peak separation (see Supporting Information).

Clicking fluorophores onto the propargylated HBPs. Having incorporated propargyl groups at various sites in the hyperbranched polymer, it is important to demonstrate their accessibility to click reaction. A fluorescent azide, namely 1-azidomethylpyrene **F**, was used for this purpose both because it can be readily observable by fluorescence spectroscopy and additionally we expected that it would provide us a potential handle to examine the immediate environment around the fluorophore, as pyrene is well-known to be a sensitive probe of its environment. The click reaction was done under standard conditions using $CuSO_4$ and Na-ascorbate at 50 °C in an optimized solvent mixture (15:1 v/v $THF:H_2O$), as depicted in schemes 2, 3 and 4.

The ^1H NMR spectra of all three polymers (**P3**, **P5**, **P7**) after clicking with azidomethylpyrene are shown in Figure 3. Since the level of pyrene incorporation is very low (< 5 mol %) the spectral signatures were clearly seen only in

Scheme 4. Synthesis of the Hyperbranched Polymer P6 Having a Few Percent of the Propargyl Groups within the Core and at the Molecular Periphery, and the Subsequent Click Reaction with Fluorophore To Generate Polymer P7[a]



[a] The tables indicate the relative mole fractions of various repeat units in the copolymer.

the expanded spectra, which are also presented in the figure. We note two important points: (i) a new peak due to the methylene protons adjacent to the pyrene unit (~6.2−6.5 ppm) is seen in the clicked polymer along with the complete disappearance of the propargyl methylene protons (between 4.2 and 4.4 ppm), suggesting that the click reaction has occurred to near completion; (ii) the methylene proton adjacent to the pyrene unit occurs at different chemical shifts when incorporated at the core region (peak 19) and the periphery (peak 16). Both peaks are seen in the polymer **P7,** thereby confirming the occurrence of the click reaction at both the sites.[32] Similarly, the triazole ring proton also shows the presence of both types of clicked units (peaks 15 and 18) in polymer **P7**. Additionally, the aromatic peaks due to pyrene are also seen in the expanded spectra between 7.9 and 8.3 ppm.

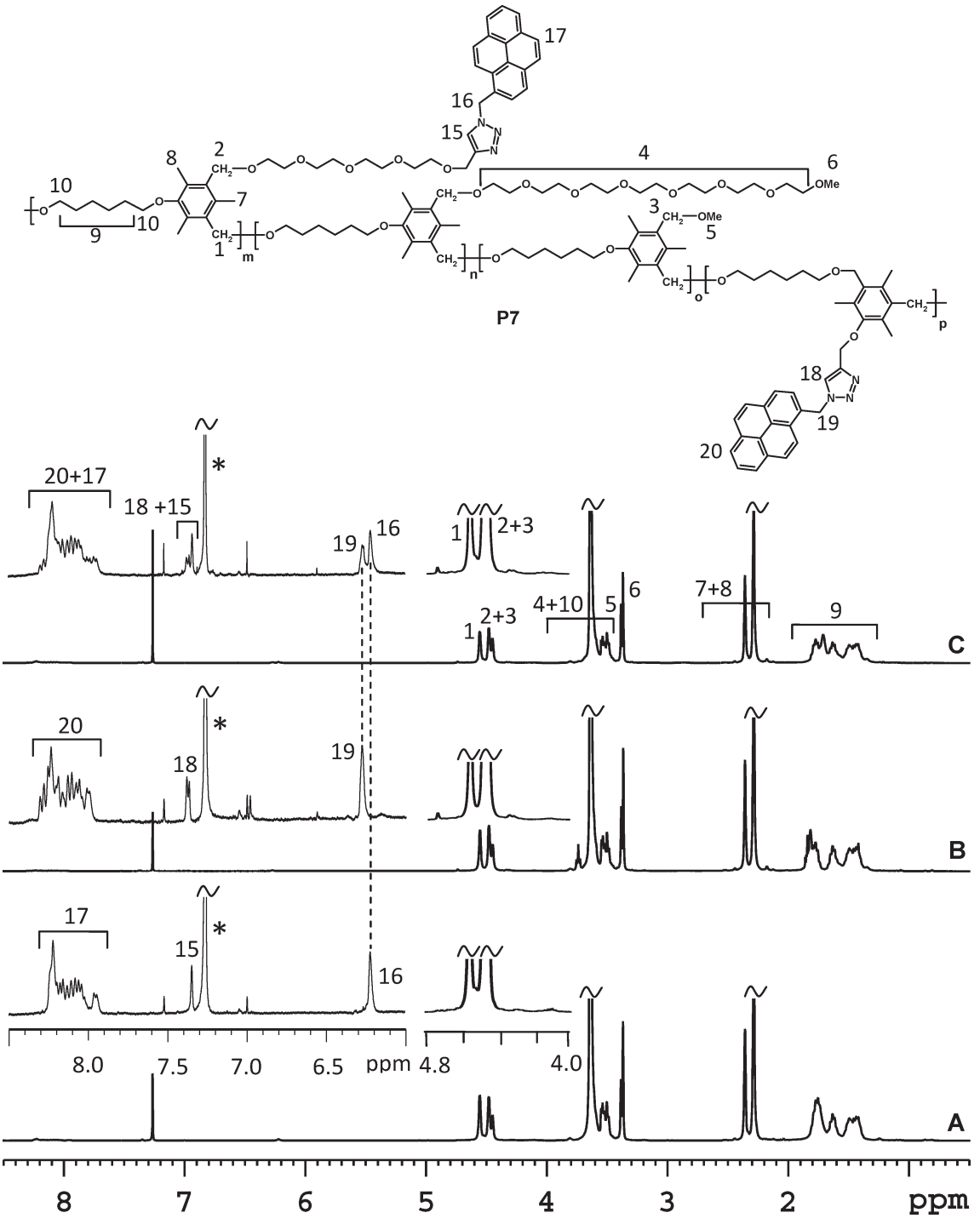


Figure 3. ^{1}H NMR spectra of the (A) hyperbranched polymer **P3** having pyrene at the molecular periphery, (B) hyperbranched polymer **P5** having pyrene within the core, and (C) hyperbranched polymer **P7** having pyrene both at the molecular periphery as well as within the core, recorded in $CDCl_3$.

The molecular weights of all the polymers before and after the click reaction were determined by GPC using a triple detector system in order to minimize underestimation that is typical for highly branched polymers that adopt very compact structures.[26] The values obtained are shown in Table 1. Typically, the molecular weights are moderate and very little change is observed after the click reaction. This is not surprising as the level of functionalization is very small, although in two of the samples a small increase is noticed, which could be more due to the fractionation that could have occurred during the isolation process. This is also reflected in a small decrease in their PDI. The Mark−Houwink exponents "*a*" in all cases are small reflecting the rather compact structures that are typical of HBPs.

Fluorescence Spectroscopic Studies of Pyrene-Clicked Polymers. The fluorescence spectra of all three HBPs bearing pyrene units were measured in two different solvents—in THF wherein the entire polymer is expected to be well-solvated and in water wherein the core would be collapsed while the shell would remain solvated. In Figure 4, we have plotted the normalized fluorescence spectra of two of the polymers, **P3** and **P5** that carry the pyrene units either at the periphery or in the core region, recorded in water and THF. In water, the spectra of both the polymers match almost

Table 1. Structural characteristics and properties of the hyperbranched polymers.

polymer	feed composition *or* polymer description	M_n	M_w	PDI	M−H constant (*a*)
P1	AB_2:**TEG-P** = 1:0.98	5400	22100	4.1	0.31
P2	AB_2:**TEG-P**:**HPEG-M** = 1:0.1:0.9	4000	20100	5.0	0.30
P3	polymer **P2** after click	5300	24600	4.6	0.36
P4	AB_2:A_2:B_2:**HPEG-M** = 1:0.06:0.06:0.98	5200	54100	10.4	0.30
P5	polymer **P4** after click	4900	54700	11.1	0.27
P6	AB_2:A_2:B_2:**TEG-P**:**HPEG-M** = 1:0.06:0.06:0.08:0.9	4800	16200	3.3	0.33
P7	polymer **P6** after click	5500	17800	3.2	0.30

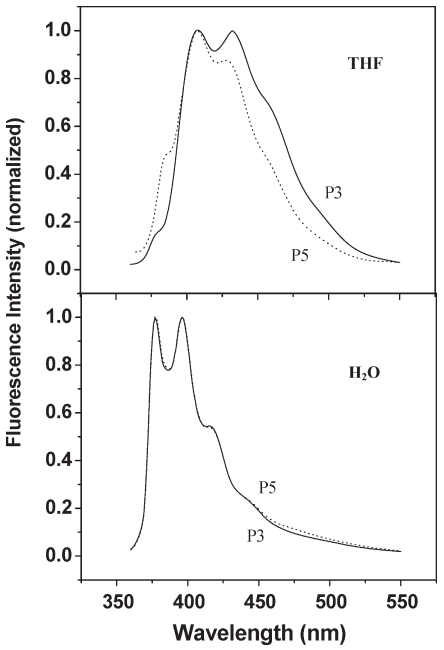


Figure 4. Normalized fluorescence spectra of polymer **P3** and **P5** in two different solvents, THF and H_2O. In THF (λ_{ex} = 343 nm): [polymer **P3**] = 2×10^{-6} M; [polymer **P5**] = 7×10^{-7} M. In H_2O (λ_{ex} = 346 nm): [polymer **P3**] = 4.2×10^{-6} M; [polymer **P5**] = 1×10^{-5} M. In both cases, the concentration has been calculated with respect to the molecular weight of the repeat unit.

exactly while in THF some clear differences are evident. At first sight this was a bit surprising as we expected the pyrene at the periphery to experience a distinctly different polarity as compared to the one within the core. However, considering the fact that pyrene is tagged onto a long flexible oxyethylene tether, we can rationalize this behavior as being due to the insertion of the pyrene chromophore into the hydrophobic core, which would be collapsed when the HBP is dissolved in water. Therefore, in both polymers, **P3** and **P5**, the pyrene appears to be experiencing the relatively hydrophobic core environment when the HBPs are dissolved in water. This fact is also borne out in the ^{1}H NMR spectra recorded of such core−shell HBPs in D_2O, wherein the core protons appear very broad while the peripheral HPEG protons are sharp suggesting the presence of a rather collapsed solid-like core in water.[33] However, when the polymer is dissolved in a relatively good solvent that solvates both the core and the shell region, differences in the spectra probably reflect the true differences in the environments of the two chromophores, the extent of solvation being different in both regions. Fluorescence spectrum of **P7** in water exhibited small differences compared to **P3** and **P5**, the reasons for which were not clear (See Supporting Information). Further studies are required to explore these differences in greater detail.

At this point, we would like to highlight the fact that the demarcation of core and shell regions in hyperbranched polymers could be viewed either from a structural and/or a functional standpoint. While in most dendrimers, the core and shell regions are structurally separated, in hyperbranched polymers the presence of numerous linear defects (typically close to 50%), make such a structural demarcation difficult. However, when the interior and the terminal groups of hyperbranched polymers possess distinctly different solubility characteristics, the polymer will adopt a conformation that pushes the solvophilic segments to the outside while retaining the solvophobic ones within the core (or interior). Such a conformational reorganization will generate *functional* core−shell structures in solvents that selectively dissolve the peripheral segments. Thus, in our case, the presence of a long hydrophobic spacer in the AB_2 monomer makes the *interior hydrophobic* while the PEG terminal groups make the *periphery hydrophilic*, and therefore, in an aqueous medium, the chain adopts a *core−shell type structure*. Such conformational reorganization is precisely what enables such core−shell type hyperbranched polymers to act as unimolecular micelles and reverse micelles, as confirmed by dye-uptake studies.[9,24] Thus, despite the presence of a large number of defects in hyperbranched polymers, when appropriately modified, these polymers can adopt conformations that permit them to function as core−shell type systems in suitable (selective) solvents.

Conclusions

In conclusion, we have demonstrated that the copolymerization of a suitable AB_2 monomer, bearing a hydrophobic hexamethylene (C-6) spacer, with two different hydrophilic (PEG containing) A−R type monomers, one that carries a terminal methyl group while the other a terminal propargyl group, generates core−shell type hyperbranched polymers bearing controllable amounts of "clickable" groups at the molecular periphery. Similarly, the use of equimolar amounts of B_2 and A_2 monomers (at low levels), one of which carries a pendant propargyl group, serves as a good strategy to incorporate "clickable" functionalities within the core region of hyperbranched structures. Simultaneous use of both the propargyl bearing B_2 and A−R type monomers in a five component copolymerization permitted their incorporation both within the core as well as at the periphery. Further, we demonstrated that these propargyl groups can be quantitatively clicked using 1-azidomethylpyrene to generate core−shell type hyperbranched polymers that carry fluorophores at specific locations. Steady state fluorescence spectral studies in water, however, were unable to differentiate between the fluorophores present at different locations suggesting that pyrene, tethered at the end of a flexible oligoethylene oxide unit, is probably tucked within the core region because of its intrinsic hydrophobic nature. In summary, it is evident that these copolymerization approaches using an AB_2 monomer along with other types of comonomers, such as A−R or A_2 + B_2, can be readily extended to prepare other classes of hyperbranched polymers, such as polyesters, polyurethanes, polyimides, etc., wherein potentially derivatizable functionality can be placed at different locations of the highly branched scaffold.

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Supporting Information Available: Figures showing ^{1}H NMR spectra of the monomers, schemes showing the synthesis of the model compound, text discussing the experimental preparations, and figures showing comparison of the ^{1}H NMR spectra of the model compound with the polymer, size exclusion chromatograms of the polymers, and ^{1}H NMR spectra of the PEGylated polymer in different solvents. This material is available free of charge via the Internet at http://pubs.acs.org.

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(30) The use of $A_2 + B_2$ in presence of an AB_2 monomer could lead to the formation of an A_3 type species; for instance, by the condensation of two molecules of A_2 with AB_2. This could thus lead to the formation of cross-linked products.

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(32) A model compound was prepared by the click reaction between the propargyl bearing **B2** monomer and azidomethylpyrene (**F**). The methylene proton adjacent to the pyrene unit in this model compound occurs at exactly the same chemical shift as in the polymer. This confirms that the difference in chemical shift is intrinsic to the nature of the compound (repeat unit) and is not a reflection of the location of the unit in the polymer. See Supporting Information (Figure S5) for spectral comparison.

(33) The ^{1}H NMR spectra of a PEGylated HBP bearing a C-10 spacer was recorded in $CDCl_3$, D_2O and D_2O + $CDCl_3$; it is seen that the core protons are very broad in D_2O but in the presence of a small amount of $CDCl_3$, solvation of the core leads the reappearance of the core proton peaks. See the Supporting Information for an overlay of these spectra (Figure S9).