A Thiol-ene Clickable Hyperbranched Polyester via a Simple Single-Step Melt Trans-Esterification Process

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ABSTRACT: Self-condensation of AB_2 type monomers (containing one A-type and two B-type functional groups) generates hyperbranched (HB) polymers that carry numerous **B**-type end-groups at their molecular periphery; thus, development of synthetic methods that directly provide quantitatively transformable peripheral **B** groups would be of immense value as this would provide easy access to multiply functionalized HB systems. A readily accessible AB_2 monomer, namely diallyl, 5-(4-hydroxybutoxy)isophthalate was synthesized, which on polymerization under standard melt-transesterfication conditions yielded a *peripherally clickable HB polyester* in a single step; the allyl groups were quantitatively reacted with a variety of thiols using the facile photoinitiated "thiol-ene" reaction to generate a wide range of derivatives, with varying solubility and thermal properties. Furthermore, it is shown that the peripheral allyl double bonds can also be readily epoxidized using meta-chloroperoxybenzoic acid to yield interesting HB systems, which could potentially serve as a multifunctional cross-linking agent in epoxy formulations. © 2013 Wiley Periodicals, Inc. J. Appl. Polym. Sci. **2014**, *131*, 40248.

INTRODUCTION

Hyperbranched (HB) polymers (HBPs) exhibit several of the functional properties that are typically associated with the structurally perfect dendrimeric analogues; however, they are a lot easier to prepare and, therefore, are more attractive from the applications viewpoint, especially in situations where high polydispersity, which is an intrinsic feature of HBPs, is not a major drawback.[1–3] The main similarity between dendrimers and HB polymers is that both of them adopt compact conformations and, when suitably functionalized at the periphery, can be viewed as dense nanoscale molecular entities that could function as drug delivery vehicles,[4,5] imaging agents,[6,7] nanocontainers,[8] and so on. One of the important strategies to expand the scope of potential applications of these systems is to impart multiple functions by suitable modifications of their molecular periphery. Extensive studies have explored this strategy using dendrimers to create systems for targeted drug delivery.[9] Thus, it is evident that the development of new synthetic methodologies to directly access HBPs that could be readily functionalized at their periphery, using simple and quantitative reaction schemes, would add substantial value to this class of polymers.

During the past decade, a class of reactions that occur under mild conditions, in a quantitative fashion, has been termed as *click*

reactions; this term initially referred to the Cu(I)-catalyzed 1,3-dipolar cycloadditon reaction between an organic azide and an alkyne developed by Rostovtsev et al.[10] but was later generalized to include other reactions, such as the thiol-ene reaction, thiol-yne reaction, and so on.[11,12] Recently, we described some novel synthetic strategies for the preparation of *azide-yne clickable* polyethers[13] and polyesters[14] using simple melt polycondensation; we also demonstrated that the peripheral groups can be readily transformed to impart a variety of different properties. Furthermore, we showed that the clickable polyesters can be functionalized with both hydrophobic and hydrophilic segments; such systems were shown to reconfigure and segregate the two segments and form Janus structures,[15] wherein the peripheral molecular surface of the HBP carries two different types of moieties (*Janus* comes from the Greek god with two different faces). This observation clearly demonstrated the remarkable ability of the branched polymer backbone to undergo conformational reorganization. To further expand the scope of the click-based functionalization, it would be very useful to design HB scaffolds onto which *thiol-ene click reactions* can be performed; this obviously enriches the area by providing a greater choice of functionalities that can be clicked and it also widens the range of conditions under which the reaction can be performed, such as under metal-free photo-initiated

reaction conditions. Keeping this in view, we had recently reported a simple process to prepare HB polyethers that carry allyl groups on their periphery using the melt transetherification process and demonstrated quantitative transformation of the peripheral allyl groups.[16] Dendrimers[17] and HBPs[18] carrying allyl groups at the periphery have been prepared earlier primarily using a post-polymerization functionalization step, typically by transforming the peripheral hydroxyl groups by coupling with allyl bromide; this approach, apart from requiring an additional step, also often leads to incomplete conversion. Subsequently, these HB polymers carrying terminal allyl groups have been used as multivalent cross-linkers for the preparation of thermosets using thiol-ene reaction.[19] In this study, we describe a simple approach for the preparation of HB polyesters that carry clickable peripheral allyl groups; the most important advantage of this approach is that the AB_2 monomer can be easily prepared from a readily available starting material, namely 5-hydroxy isophthalic acid, and the HBP carrying peripheral allyl groups can be prepared in a single step using a solvent-free melt polymerization, which should make them more commercially valuable. Furthermore, unlike the previously reported polyethers,[20] which were limited to benzylic-type polyethers that are susceptible to acid-hydrolysis,[21] polyesters are relatively more stable and possess distinctly different properties. Importantly, polyesters have a greater potential for commercial adaptation, either directly or via a copolymerization approach. To demonstrate the versatility of the peripheral functionalization process, a variety of segments have been installed onto the periphery of the HB polyester to impart hydrocarbon-solubility, water-solubility, pH-dependant solubility, and so on.

MATERIALS AND METHODS

All solvents for synthesis were purified before use using standard procedures.[22] 5-Hydroxy isophthalic acid, magnesium turnings, allyl bromide, hexadecane thiol, mercaptosuccinic acid (thiomalic acid), mercaptoethanol, tetraethylene glycol monomethyl ether (TEG), and benzyl alcohol were purchased from Aldrich Chemical Company and used directly. The proton nuclear magnetic resonance (^{1}H NMR) spectra were recorded in a Bruker AV 400 MHz spectrometer using a suitable deuterated solvent; tetramethyl silane was used as an internal standard. Gel permeation chromatography (GPC) measurements were carried out in Viscotek triple detector analyzer model 300 system, with refractive index (RI), differential viscometer (DV), and light scattering detectors, which are connected in series with each other. The separation was affected with the help of two polymer laboratories (PL) gel-mixed bed columns (300 × 7.5 mm) operated at 30°C using tetrahydrofuran (THF)/CHCl$_3$ as the eluent. Universal calibration curve based on the data from the RI and DV detectors, using narrow polystyrene standards, was used to estimate the molecular weights. The thermal analysis was performed using a Mettler Toledo differential scanning calorimetric (DSC) instrument at a heating rate of 10°C/min under a dry nitrogen (N_2) atmosphere. The sample of 2–3 mg was initially heated to a temperature above its melting point (to make sure that, the sample flows and makes good contact with the pan) and then cooled; two subsequent heating and cooling runs were performed to ensure reproducibility.

5-Hydroxy isophthalic methyl ester (1)
5-Hydroxy isophthalic acid (15 g, 82.4 mmol) was taken in 150 mL of methanol, along with a catalytic amount of H_2SO_4, and refluxed for 12 h. The reaction mixture was concentrated, water was added, and the contents were extracted with ethyl acetate; the organic layer was washed with aqueous NaHCO$_3$ solution, dried using anhydrous Na$_2$SO$_4$, and concentrated to give the product. Yield was 98%. Melting point (Mp): 160°C.

^{1}H NMR (CDCl$_3$, δ ppm): 8.2 (s, 1H, Ar**CH**); 7.76 (d, 2H, Ar**CH**); 6.28 (s, 1H, Ar**OH**); 3.94 (s, 6H, ArO**CH$_3$**).

4-Bromobutylacetate (2)[23]
1,2-Dibromoethane (92.74 g, 493 mmol) and Mg turnings (12 g, 493 mmol) were taken in 300 mL dry diethyl ether and stirred for 3 h at room temperature (RT) under N_2 atmosphere. Once the evolution of ethylene gas ceases, indicating complete formation of MgBr$_2$, the excess ether was removed under reduced pressure and 200 mL of dry acetonitrile was added, along with 40 mL of dry THF and 51 mL of acetic anhydride. The mixture was stirred for 16 h at RT, neutralized with NaHCO$_3$ solution, and extracted with ethyl acetate; the organic layer was dried over anhydrous Na$_2$SO$_4$, concentrated, and distilled under reduced pressure (at 120°C/2.0 mm of Hg) to get the desired product. Yield = 95%.

^{1}H NMR (CDCl$_3$, δ ppm): 4.0 (t, 2H, BrCH$_2$CH$_2$CH$_2$**CH$_2$**O COCH$_3$); 3.42 (t, 2H, Br**CH$_2$**CH$_2$CH$_2$CH$_2$OCOCH$_3$); 2.0 (s, 3H, BrCH$_2$CH$_2$CH$_2$CH$_2$OCO**CH$_3$**); 1.88–1.94 (m, 2H, Br CH$_2$**CH$_2$**CH$_2$CH$_2$OCOCH$_3$); 1.75–1.79 (m, 1H, BrCH$_2$CH$_2$ **CH$_2$**CH$_2$OCOCH$_3$).

5-(4-Hydroxybutoxy) benzene-1,3-dioic acid (3)
A mixture of **1** (10 g, 47.62 mmol), **2** (13.9 g, 71.43 mmol), K$_2$CO$_3$ (39.5 g, 285.7 m mol), and catalytic amount of KI potassium iodide were taken in 200 mL methyl ethyl ketone and refluxed at 80°C under N_2 atmosphere for 12 h. The completion of the reaction was confirmed by thin layer chromatography (TLC). After the reaction was complete, excess solvent was removed and the residue was extracted with ethyl acetate; the extract was dried over anhydrous Na$_2$SO$_4$ and concentrated under reduced pressure. The excess of **2** could be removed by washing the residue twice with pet ether. The crude ester was taken in methanol and refluxed for 12 h in the presence of NaOH (10.4 g, 262.24 mmol) to affect hydrolysis. After removal of the solvent, the residue was neutralized with dilute HCl and the white precipitate obtained was filtered and dried. Overall yield was 90%. Mp: 184°C.

^{1}H NMR (CD$_3$OD, δ ppm): 8.2(t, 1H, Ar**CH**); 7.7(d, 2H, Ar**CH**); 4.1(t, 2H, Ar**CH$_2$**CH$_2$CH$_2$CH$_2$OH); 3.64(t, 2H, ArCH$_2$CH$_2$CH$_2$**CH$_2$**OH); 1.86–1.93(m, 2H, ArCH$_2$**CH$_2$**CH$_2$CH$_2$OH); 1.7–1.77(m, 2H, ArCH$_2$CH$_2$**CH$_2$**CH$_2$OH).

Diallyl 5-(4-hydroxybutoxy) benzene-1,3-dioate
Compound **3** (5 g, 19.6 mmol) was taken in dimethyl sulfoxide along with NaHCO$_3$ (3.29 g, 39.2 mmol) and allyl bromide (4.7 g, 39.2 mmol); the mixture was stirred at RT for 36 h. The completion of the reaction was confirmed by TLC. Water was added to the reaction mixture and the product was extracted with ethyl acetate; the organic layer was dried over anhydrous
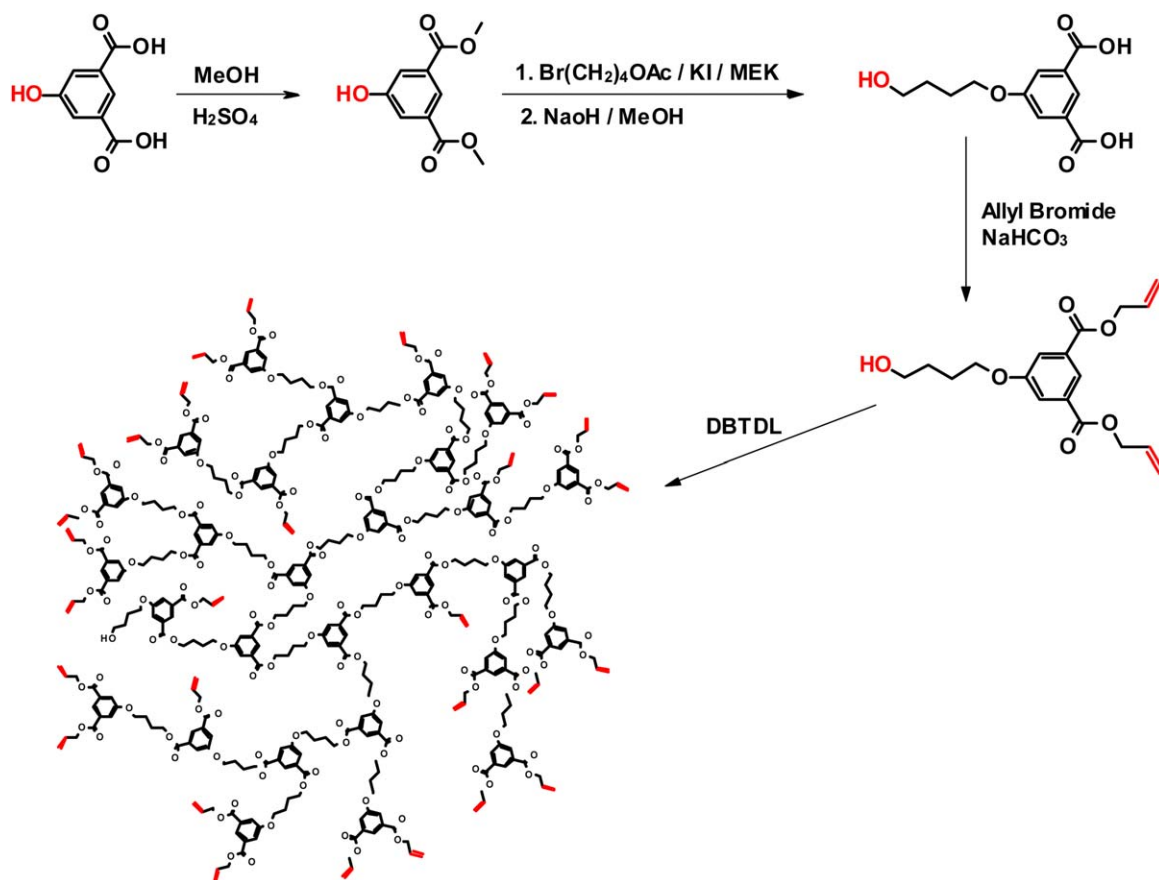
Scheme 1. Synthesis of the AB$_2$ monomer and its polymerization. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

sodium sulphate and the solvent was removed under reduced pressure to give the product in 90% yield.

^{1}H NMR (CDCl$_3$, δ ppm): 8.29 (d, 1H, Ar**CH**); 7.74 (d, 2H, Ar**CH**); 5.9–6.0 (m, 2H, ArOCH$_2$**CH**CH$_2$); 5.2–5.4 (m, 4H, ArO CH$_2$CH**CH$_2$**); 4.8 (m, 4H, ArO**CH$_2$**CHCH$_2$); 4.08 (t, 2H, ArO **CH$_2$**CH$_2$CH$_2$CH$_2$OH); 3.7 (t, 2H, ArOCH$_2$CH$_2$CH$_2$**CH$_2$**OH); 1.78 (m, 4H, ArOCH$_2$**CH$_2$CH$_2$**CH$_2$OH); 1.97 (s, 1H, ArO CH$_2$CH$_2$CH$_2$CH$_2$**OH**).

Melt Polymerization

The **AB$_2$** monomer (1.5g, 4.48 mmol) along with 2 mol % of dibutyl tin dilaurate (DBTDL) was taken in a test tube shaped polymerization vessel. The mixture was degassed for about 10 min and maintained at 110°C under continuous N$_2$ purge to attain the homogeneous mixture of the monomer and the catalyst. The polymerization was first carried out at 150°C under continuous N$_2$ purge for about 45 min with constant stirring; subsequently, the polymerization was continued in Kugelrohr for a period of 45 min under reduced pressure (2 Torr) at 150°C, with the continuous mixing of the melt through rotation. The polymer obtained was dissolved in CHCl$_3$ and precipitated in methanol; it was further purified by one additional dissolution and precipitation to give the product **HBP-Allyl** in 80% yield.

^{1}H NMR (CDCl$_3$, δ ppm): 8.26(s, 1H, Ar**CH**); 7.72(s, 2H, Ar**CH**); 6.0(t, 1H, ArOCH$_2$**CH**CH$_2$); 5.2–5.4(m, 2H, ArOCH$_2$CH**CH$_2$**);

4.8(s, 2H, ArO**CH$_2$**CHCH$_2$); 4.41(s, 2H, Ar**CH$_2$**CH$_2$CH$_2$CH$_2$—); 4.1(s, 2H, ArCH$_2$CH$_2$CH$_2$**CH$_2$**—); 1.98(s, 4H, ArCH$_2$**CH$_2$ CH$_2$**CH$_2$—).

Clicking with Various Thiols

A mixture of the polymer, **HBP-Allyl** (500 mg, 1.81 mmol), and mercaptoethanol (252.8 mg, 3.62 mmol) were dissolved in 10 mL of CHCl$_3$ in a quartz test tube, along with the photoinitiator 2,2-di-methoxy 2-phenyl acetophenone (46.39 mg, 0.18 mmol); the contents were then irradiated with ultraviolet light (250 W Hg vapor lamp) for 8 h. The polymer solution was concentrated and precipitated in methanol; one additional dissolution/reprecipitation was carried out to purify the sample.

The thiol-ene reaction with all other thiols namely hexadecane thiol, mercapto succinic acid, tetraethylene thioglycol monomethyl ether, benzyl thiol, and mercaptoethanol were carried out under similar conditions to give respective thiol-clicked product. In the case of the mercaptosuccinic acid clicked product **HBP-TSA**, the product was precipitated in water instead of methanol. The typical yields of the product ranged from 60 to 70%.

HBP-TSA. ^{1}H NMR (CD$_3$OD, δ ppm): 8.1(s, 1H, Ar**CH**); 7.68(t, 2H, Ar**CH**); 4.3(s, 4H, —**CH$_2$**CH$_2$CH$_2$CH$_2$OArO**CH$_2$**—); 3.9(s, 2H, —CH$_2$CH$_2$CH$_2$**CH$_2$**OArOCH$_2$—); 3.65(t, 1H, ArOCH$_2$CH$_2$ CH$_2$S**CH**—); 2.6–3.0(m, 4H, ArOCH$_2$CH$_2$**CH$_2$**SCH**CH$_2$**—); 2.25(s,
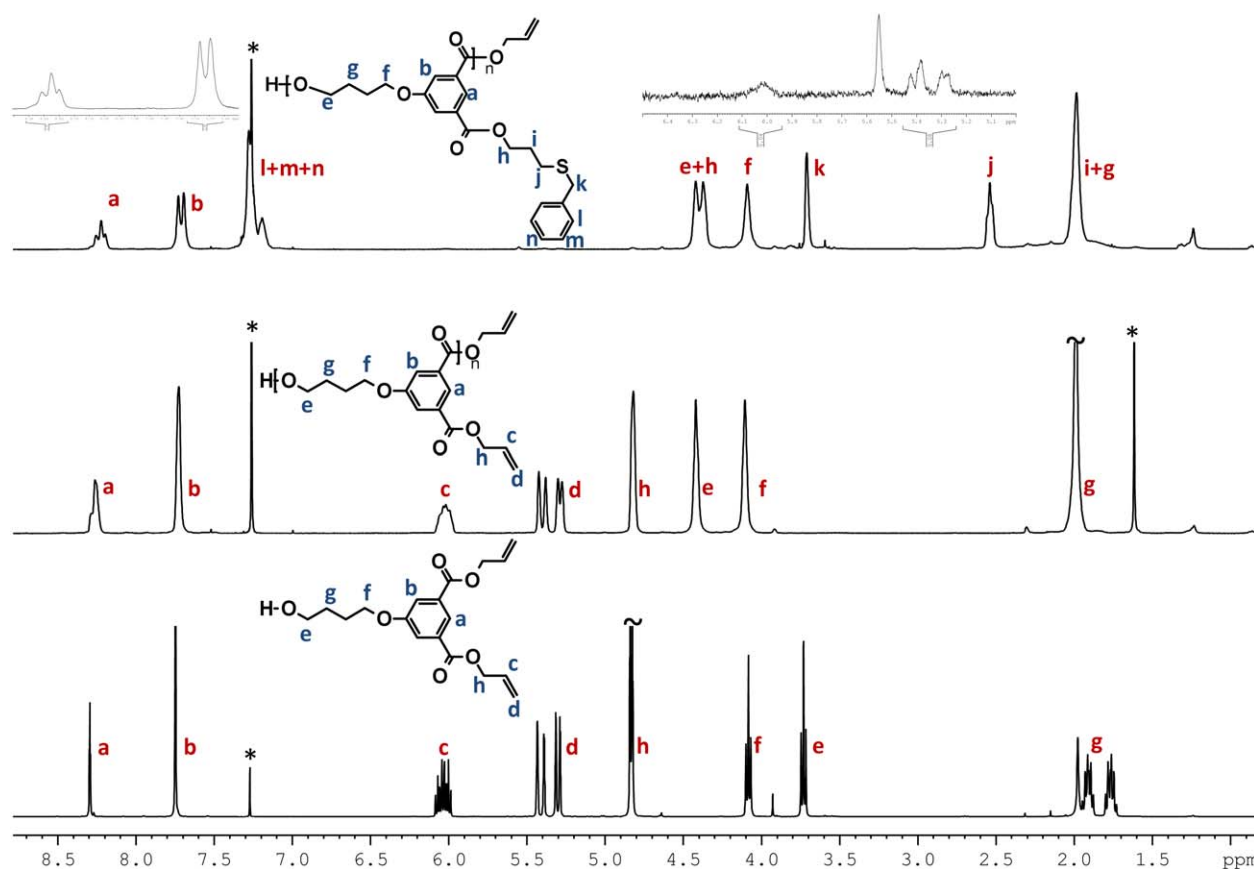
Figure 1. ¹H NMR spectra of the AB₂ monomer, the parent HBP and the benzylthiol clicked polymer; the spectra were recorded using CDCl₃ as the solvent. The two expanded spectra show peaks due to the presence of residual unreacted allyl groups (<5%) and the splitting of the aromatic peaks due to the *internal aromatic solvent effect*. The sharp peaks marked with an asterisk are due to chloroform or water. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

2H, ArOCH$_2$**CH$_2$**CH$_2$CH$_2$SCHCH$_2$—); 2.0(s, 4H, —CH$_2$**CH$_2$CH$_2$** CH$_2$OArOCH$_2$—).

HBP-ME. ¹H NMR (CDCl₃, δ ppm): 8.2(s, 1H, Ar**CH**); 7.7(m,2H, Ar**CH**); 4.41(s, 4H, —**CH$_2$**CH$_2$CH$_2$CH$_2$OArO**CH$_2$**—); 4.1(s, 2H, —CH$_2$CH$_2$CH$_2$**CH$_2$**OArOCH$_2$—); 3.75(s, 2H, ArOH$_2$CH$_2$CH$_2$SCH$_2$**CH$_2$**OH); 2.69–2.74 (d, 4H, ArOCH$_2$CH$_2$**CH$_2$**S**CH$_2$**CH$_2$OH); 1.98–2.05(m, 6H, —CH$_2$**CH$_2$CH$_2$**CH$_2$OArO CH$_2$**CH$_2$**CH$_2$S—).

HBP-Bz. ¹H NMR (CDCl₃, δ ppm): 8.2(t, 1H, Ar**CH**); 7.69(m, 2H, Ar**CH**); 7.19(m, 5H, ArOCH2CH2CH2SCh2Ar**CH**); 4.37 (m, 4H, —O**CH$_2$**CH$_2$CH$_2$CH$_2$OArO**CH$_2$**—); 4.09(s, 2H, —OCH$_2$CH$_2$CH$_2$**CH$_2$**OAr—); 3.71(s, 2H, —ArO CH$_2$CH$_2$CH$_2$S**CH$_2$**Ar); 2.5(s, 2H, —ArOCH$_2$CH$_2$**CH$_2$**SCH$_2$Ar); 1.984(s, 6H, —CH$_2$**CH$_2$CH$_2$**CH$_2$OArO CH$_2$**CH$_2$**—).

HBP-TEG. ¹H NMR (CDCl₃, δ ppm): 8.2(d, 1H, Ar**CH**); 7.7(s, 2H, Ar**CH**); 4.4(s, 4H, —**CH$_2$**CH$_2$CH$_2$CH$_2$OArO**CH$_2$**—); 4.1(s, 2H, —CH$_2$CH$_2$CH$_2$**CH$_2$**OAr—); 3.5–3.6(m, 8H, —ArOCH$_2$CH$_2$CH$_2$S—**CH$_2$CH$_2$O**—); 2.68–2.72(m, 4H, —ArOCH$_2$CH$_2$**CH$_2$**S**CH$_2$**—); 2.02–2.04(m, 6H, —CH$_2$**CH$_2$CH$_2$**CH$_2$OArOCH$_2$**CH$_2$**—).

HBP-C16. ¹H NMR (CDCl₃, δ ppm): 8.2(d, 1H, AR**CH**); 7.7(s, 2H, Ar**CH**); 4.4(D, 4H, —**CH$_2$**CH$_2$CH$_2$CH$_2$OArO**CH$_2$**—); 4.1(s, 2H, —CH$_2$CH$_2$CH$_2$**CH$_2$**OAr—); 2.6(m, 2H, —ArOCH$_2$CH$_2$**CH$_2$**—);

2.5(s, 2H, —ArOCH$_2$CH$_2$**CH$_2$**S**CH$_2$**—); 1.99–2.05(m, 6H, —CH$_2$**CH$_2$CH$_2$**CH$_2$OArO OCH$_2$**CH$_2$**—); 1.23–1.57(m, 28H, —SCH$_2$**(CH$_2$)$_{14}$**CH$_3$);0.86(t, 3H, —SCH2(CH2)$_{14}$**CH$_3$**).

Epoxidation of HBP-Allyl

The polymer (500 mg, 1.81 mmol) was taken along with meta-chloroperoxybenzoic acid (MCPBA) (0.935 mg, 5.41 mmol), NaHCO₃ (152 mg, 1.81 mmol), and CHCl₃ as solvent. The reaction mixture was stirred at RT for 3 days. The mixture was filtered and the organic layer was concentrated and precipitated into methanol; it was further purified by dissolution in chloroform and precipitation into diethyl ether. Yield = 66%.

¹H NMR (CDCl₃, δ ppm): 8.21(s, 1H, Ar**CH**); 7.70(s, 2H, Ar**CH**); 4.64(s, 2H, ArOCH2—); 4.40(s, 2H, —OCH2CH2CH2CH2OAr—); 4.09(s, 2H, —OCH2CH2CH2CH2OAr—); 3.34(s, 1H, —O**H**CHCHCH2OAr—); 2.89(s, 1H, —OHC**H**CHCH2OAr—); 2.72(s, 1H, —OHCHC**H**CH2OAr—).

RESULTS AND DISCUSSION

The AB₂ monomer was synthesized in two steps starting from dimethyl, 5-hydroxy-isophthalate, as depicted in Scheme 1; coupling with 4-bromobutylacetate followed by hydrolysis yielded the intermediate, 5-(4-hydroxybutoxy)-isophthalic acid, which on treatment with allyl bromide under basic conditions yielded
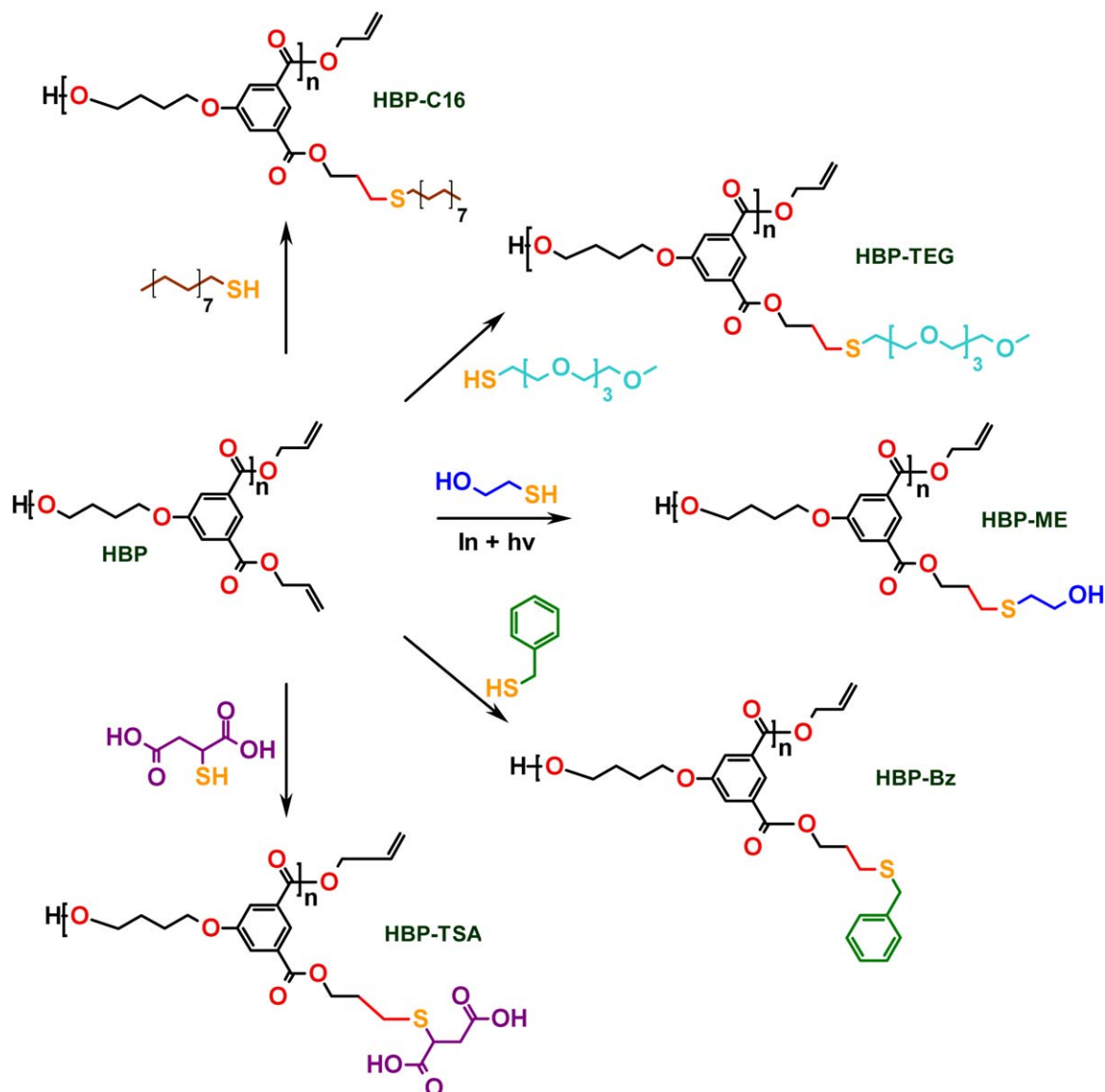
Scheme 2. Peripheral functionalization of the HB polyester using a variety of different thiols. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

the required diallyl ester monomer in excellent yield. This AB_2 monomer was readily polymerized at 150°C under melt transesterification conditions using DBTDL as catalyst to yield the required HB polyester (**HBP-Allyl**) as a clear tough solid; the polymerization is driven to completion by continuous removal of the condensate, namely allyl alcohol. The GPC molecular weight of the parent HBP was found to be moderately high; M_w was around 12,700.

The ^{1}H NMR spectra of the monomer and the HB polyester are shown in Figure 1; the first important observation is that the spectra reveal that allyl groups are stable under the melt polymerization conditions. The other salient changes in the polymer spectra are: (i) all the peaks are considerably broadened as expected for high-molecular-weight polymers; (ii) there is a considerable down-field shift in the methylene protons (peak **e**) adjacent to the OH group upon ester formation; (iii) the rela-

tive intensity of any of the allyl proton peaks with respect to those of the spacer segment reflects the loss of one of the allyl groups (**h:e** goes from 2:1 in the monomer to 1:1 in the polymer); and (iv) the two internal methylene proton peaks of the butylene spacer (1.7–2.0 ppm) have merged in the polymer spectrum. The various peaks have been completely assigned, as shown in the figure, and their relative intensities are consistent with the expected polymer structure.

Thiol-ene Click Reaction
Thiol-ene click reaction has become an excellent alternative to the Cu-catalyzed azide-yne reaction, and it has opened the click strategy to a variety of other functional entities and reaction conditions; these reactions also tend to be nearly quantitative and can be performed under mild reaction conditions. Importantly, the thiol-ene reaction does not require a metal catalyst and can be performed under photoinitiated reaction conditions,
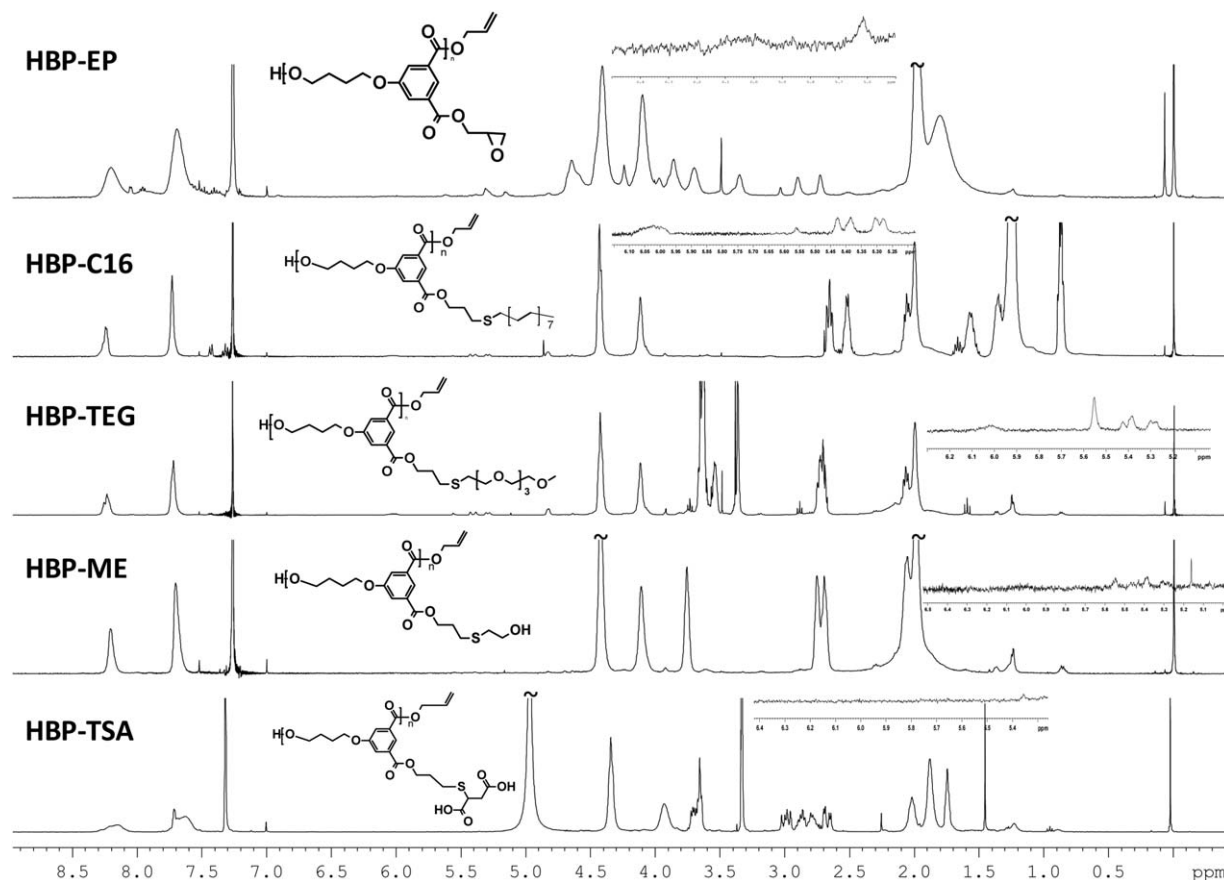
Figure 2. ^{1}H NMR spectra of various peripherally functionalized derivatives; the spectra were recorded in CDCl$_3$ (HBP-TSA in CD$_3$OD). The inset shows the y-expanded (10×) region revealing the presence of small amounts of residual allyl peaks; in all cases, however, the extent of reaction was estimated to be around 90–99%.

which offers it several advantages.[16] In this study, the HB polyester carrying numerous allyl groups at their periphery was reacted with a variety of thiols (Scheme 2), in the presence of a radical photoinitiator; the reaction was typically conducted by irradiating a solution containing the HB polyester, the required thiol and 10 mol % of 2,2-dimethoxy-2-phenyl acetophenone, which served as the photoinitiator. As a test case, the parent HBP was clicked with benzylthiol to generate the sample **HBP-Bz**; the NMR spectrum of this sample is also shown in Figure 1, along with the peak assignments. It is evident from the spectrum that the allyl protons have nearly completely disappeared; the expanded region is also shown in the figure, from which the extent of click reaction was estimated to be around 95%. Careful examination of the spectrum of **HBP-Bz** revealed another interesting feature; both the aromatic proton peaks appear as multiplets, as evident from the expansion of this region. By carrying out selective irradiation experiments, it was established that this multiplicity is clearly not due to scalar coupling, but due to chemical shift differences arising from different types of repeat units. It is interesting that such clear discrimination is not seen in the parent polymer and neither is it seen all the other clicked derivatives (Figure 2); benzylthiol being the only clicked entity that carries an aromatic unit, it is indeed possible that it behaves like an internal aromatic solvent.[24–26] We had earlier shown that addition of an aromatic solvent, like benzene,

leads to a very dramatic separation of peaks in the ^{1}H NMR spectra of HBPs, which in turn permitted one to distinguish between the different types of units, namely dendritic, linear defects, and terminal units.[27] Therefore, in this case, it appears that the clicked benzyl unit serves as an internal aromatic solvent that leads to a similar effect due to the diamagnetic anisotropic effect of the aromatic ring; assuming that one of the peaks in the doublet at approximately 7.7 ppm is due to the linear defect, the rough estimate of the degree of branching was found to be around 50%, which is along expected lines for a statistically random growth process of AB$_2$ type monomers.[28,29]

The molecular weights of the clicked polymers, as expected, were substantially higher, with M_w ranging from 35,000 to 53,000; except in the case of the sample clicked with mercaptosuccinic acid, **HBP-TSA**, for which there was a decrease and M_w was around 5500. One possible explanation for this observation is that intramolecular H-bonding between the numerous carboxylic acid groups could cause the compaction of the polymer chain leading to a reduction in the hydrodynamic volume, and, consequently, an apparently lowering of its molecular weight. The ^{1}H NMR spectra of the parent HBP and those of the remaining clicked derivatives are shown in Figure 2. It is clear from the spectra that the reaction is nearly quantitative in most of the cases; the allyl proton region has been y-expanded and in
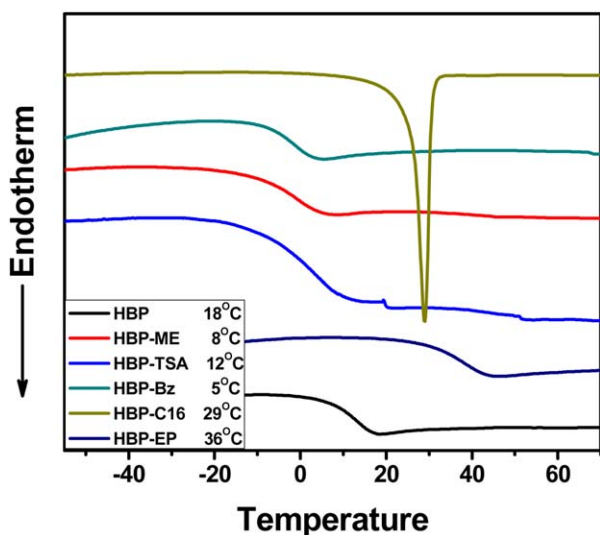
Figure 3. DSC thermograms of the parent HBP and the various peripherally functionalized derivatives. The T_g's of the samples are indicated against the labels in the legend, except in the case of **HBP-C16** where the number indicates T_m. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

some cases they show small amounts of residual allyl peaks, which normally is less than 5 %. In the cases of **HBP-TEG** and **HBP-C16,** the extent of conversion is a little lower; the residual allyl peaks accounts for about 11% and 8%, respectively, for these samples. The spectra of all the derivatives were fully assigned, and they were in accordance with the expected structure (see Supporting Information for more details). To demonstrate the versatility of the thiol-ene click reaction, a wide variety of thiols were clicked, ranging from simple benzyl mercaptan to thiosuccinic acid and from long chain alkanethiols to TEG thiols. The properties of these different derivatives were distinctly different; it is well-known that in these highly branched structures the solubility characteristics are largely governed by the nature of the peripheral groups.[30–34] Thus, the thiosuccinic acid, mercaptoethanol, and TEG-derivatized systems were soluble in polar solvents, while the other two polymers clicked with benzyl and cetyl units were soluble only in nonpolar solvents. In principle, these clickable HB precursors can be clicked with any combination of these thiols in any required composition to generate multiply functionalized HBPs or *hetero-functionalized HBPs*. Preliminary experiments have shown that clicking with long chain alkane thiol and a thiocarboxylic acid can lead to amphiphilic HBPs that exhibit surfactant-type behavior; detailed properties of this novel class of amphiphiles, which we have termed *hypersurfs*, are currently being examined.[35] Other derivatives based on this readily accessible polyester are being contemplated wherein several different segments are placed on this hyperscaffold to impart multiple properties to these compact molecular entities. The terminal allyl groups of the parent polymer **HBP-Allyl** were also readily epoxidized under standard conditions using MCPBA. The ^{1}H NMR spectrum of the epoxidized polymer, **HBP-EP**, clearly reveals that the transformation is nearly complete; the residual allyl protons signals account for only about 5%, as evident from the

expanded region of the spectrum. This HBP carrying numerous peripheral epoxy groups could be potentially useful as a multifunctional cross-linker.[36]

DSC measurements of the parent HBP and the various derivatives were performed and the thermograms are shown in Figure 3; all the samples were first heated to about 100°C before recording the scans to ensure complete erasure of any thermal history, and all the runs were repeated to confirm reproducibility. Most of the peripherally functionalized HB polyesters appear to be amorphous and exhibit a clear glass transition temperature (T_g); interestingly, in most cases, the T_g of the derivatives is lower than that of the parent polymer, except in the epoxy-derivative **HBP-EP**. This is bit surprising, given that one might expect both the mercaptosuccinic acid and mercaptoethanol-derivatized samples to exhibit higher T_g values due to the possible presence of H-bonding between the terminal groups. The thermograms of all the samples are reproducible and they exhibit a clear T_g; the exact origin for this unusually low value of T_g for these samples is not apparent. The sample **HBP-C16** is the only sample that exhibited a melting point and no clear T_g; this is evidently due to the crystallization of the peripheral C-16 alkyl segments into a paraffinic lattice, a feature that has been often observed in a variety of polymers that carry long (>C12) pendant alkyl segments.[37] The sample **HBP-TEG**, on the other hand, does not exhibit a clear T_g despite several attempts, even after rapid quenching.

CONCLUSIONS

In conclusion, we have developed a simple approach to prepare HB polyesters that carry numerous allyl groups on their periphery; the starting AB$_2$ monomer is readily prepared in a few steps from commercially available 5-hydroxyisophthalic acid. The hydroxyl allyl ester monomer undergoes polymerization under standard melt transesterification conditions; importantly, the allyl ester groups were shown to be stable under the high temperature polymerization conditions. The peripheral allyl groups was quantitatively clicked using the thiol-ene reaction to install a variety of functional groups, such as carboxylic acid, hydroxyl, polyethylene glycol (PEG), long alkyl segments, and so on; this dramatically modified their solubility characteristics. Furthermore, the allyl groups were also easily transformed to epoxy groups, which could make these HBPs useful as multifunctional cross-linkers. In summary, this study has clearly demonstrates a simple route to access peripherally clickable HB polyesters; an obvious next step would be to use these interesting globular molecular entities as scaffolds for anchoring multiple functions, such as fluorophores, drugs, catalysts, and so on., which could then serve as nanocarriers for selected applications.

REFERENCES

1. Voit, B. I.; Lederer, A. *Chem. Rev.* **2009**, *109*, 5924.

2. Gao, C.; Yan, D. *Prog. Polym. Sci.* **2004**, *29*, 183.

3. Yan, D.; Gao, C.; Frey, H. Hyperbranched Polymers: Synthesis, Properties and Applications; John Wiley & Sons, Hoboken, **2011**.

4. Chen, S.; Zhang, X.-Z.; Cheng, S.-X.; Zhuo, R.-X.; Gu, Z.-W. *Biomacromolecules* **2008**, *9*, 2578.

5. Ye, L.; Letchford, K.; Heller, M.; Liggins, R.; Guan, D.; Kizhakkedathu, J. N.; Brooks, D. E.; Jackson, J. K.; Burt, H. M. *Biomacromolecules* **2011**, *12*, 145.

6. Zhu, Q.; Qiu, F.; Zhu, B.; Zhu, X. *RSC Advances* **2013**, *3*, 2071.

7. Saatchi, K.; Soema, P.; Gelder, N.; Misri, R.; McPhee, K.; Baker, J. H.; Reinsberg, S. A.; Brooks, D. E.; Häfeli, U.O. *Bioconjug. Chem.* **2012**, *23*, 372.

8. Picco, A. S.; Yameen, B.; Azzaroni, O.; Ceolín, M. *Chem. Commun.* **2011**, *47*, 3802.

9. Patri, A. K.; Kukowska-Latallo, J. F.; Baker, J. R. *Adv. Drug Deliv. Rev.* **2005**, *57*, 2203.

10. Rostovtsev, V. V.; Green, L. G.; Fokin, V. V.; Sharpless, K. B. *Angew. Chem. Int. Ed.* **2002**, *41*, 2596.

11. Kade, M. J.; Burke, D. J.; Hawker, C. J. *J. Polym. Sci. Polym. Chem.* **2010**, *48*, 743.

12. Binder, W. H.; Sachsenhofer, R. *Macromol. Rapid Commun.* **2008**, *29*, 952.

13. Saha, A.; Ramakrishnan, S. *Macromolecules* **2009**, *42*, 4956.

14. Ramkumar, S. G.; Rose, K. A. A.; Ramakrishnan, S. *J. Polym. Sci. Polym. Chem.* **2010**, *48*, 3200.

15. Samuel, A. Z.; Ramakrishnan, S. *Macromolecules* **2012**, *45*, 2348.

16. Roy, R. K.; Ramakrishnan, S. *J. Polym. Sci. Chem. Ed.* **2011**, *49*, 1735.

17. Nilsson, C.; Malmstrom, E.; Johansson, M.; Trey, S. M. *J. Polym. Sci. Part A. Polym. Chem.* **2009**, *47*, 589.

18. Tomuta, A.; Ferrando, F.; Serra, A.; Ramis, X. *React. Funct. Polym.* **2012**, *72*, 556.

19. Flores, M.; Tomuta, A. M.; Fernandez-Francos, X.; Ramis, X.; Sangermano, M.; Serra, A. *Polymer* **2013**, *54*, 5473.

20. Jayakannan, M.; Ramakrishnan, S. *J. Polym. Sci. Part A. Polym. Chem.* **2001**, *39*, 1615.

21. Iha, R. K.; Wooley, K. L.; Nystrom, A. M.; Burke, D. J.; Kade, M. J.; Hawker, C. *J. Chem. Rev.* **2009**, *109*, 5620.

22. Armarego, W. L. F.; Perrin, D. D. Purification of Laboratory Chemicals, 4th ed.; Butterworth-Heinemann (Oxford), **2000**.

23. Goldsmith, D. J.; Kennedy, E.; Campbell, R. G. *J. Org. Chem.* **1975**, *40*, 3571.

24. Stamm, H.; Jäckel, H. *J. Am. Chem. Soc.* **1989**, *111*, 6544.

25. Henderson, W. G.; Mooney, E. F. In Annual Review of NMR Spectroscopy, Mooney, E. F. (ed.), Academic Press: London, **1969**; Vol. *2*, p 83.

26. Emsley, W.; Feeney, J.; Sutcliffe, L. Progress in Nuclear Magnetic Resonance Spectroscopy; Pergamon Press: Oxford, **1967**, Vol. *3*, Chapter 6, p 231.

27. Behera, G.; Ramakrishnan, S. *J. Polym. Sci. Polym. Chem.* **2007**, *45*, 1474.

28. Holter, D.; Burgath, A.; Frey, H. *Acta. Polym.* **1997**, *48*, 30.

29. Hölter, D.; Burgath, A.; Frey, H. *Acta Polym.* **1997**, *48*, 298.

30. Kim, Y. H.; Webster, O. W. *Macromolecules* **1992**, *25*, 5561.

31. Wooley, K. L.; Frechet, J. M. J.; Hawker, C. J. *Polymer* **1994**, *35*, 4489.

32. Uhrich, K. E.; Hawker, C. J.; Frechet, J. M. J. Turner, S. R. *Macromolecules* **1992**, *25*, 4583.

33. Miravet, J. F.; Frechet, J. M. J. *Macromolecules* **1998**, *31*, 3461.

34. Ishizu, K.; Tsubaki, K.; Mori, A.; Uchida, S. *Prog. Polym. Sci.* **2003**, *28*, 27.

35. Shree Varaprasad, N. S.; Ramakrishnan, S. unpublished results.

36. Fernández-Francos, X.; Foix, D.; Serra, À.; Salla, J. M.; Ramis, X. *React. Funct. Polym.* **2010**, *70*, 798.

37. Kim, Y. H.; Beckerbauer, R. *Macromolecules* **1994**, *27*, 1968.