Hyperbranched polymers with high degrees of branching and low dispersity values: Pushing the limits of thiol–yne chemistry

Alexander B. Cook,[1] Raphael Barbey,[2] James A. Burns,[3] and Sébastien Perrier[1,4]*

[1] Department of Chemistry, The University of Warwick, Coventry, CV4 7AL, UK

[2] Key Centre for Polymers & Colloids, School of Chemistry, Building F11, The University of Sydney, NSW 2006, Australia

[3] Syngenta, Jealott's Hill International Research Centre, Bracknell, Berkshire, RG42 6EY, UK

[4] Faculty of Pharmacy and Pharmaceutical Sciences, Monash University, 381 Royal Parade, Parkville, Victoria 3052, Australia

*Corresponding author: Email: s.perrier@warwick.ac.uk; Tel: +44 2476 528 085

Abstract

We propose a versatile approach to the production of hyperbranched polymers with high degrees of branching and low dispersity values ($Đ$), involving slow monomer addition of a thiol/yne monomer to multifunctional core molecules in the presence of photoinitiator and under UV irradiation. The small thiol/yne monomer was synthesized via 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (EDC.HCl) esterification and batch polymerizations were performed at varying concentrations. The batch thiol–yne polymerizations had fast reaction kinetics and large dispersity values that increased with increasing concentration. Introduction of monomer by slow addition to a multifunctional alkyne core (tri(prop-2-yn-1-yl) 1,3,5-benzenetricarboxylate) or alkene core (triallyl 1,3,5-benzenetricarboxylate) was found to lower dispersity at monomer concentrations of 0.5 M to 2.0 M. Degrees of branching were determined by ^{1}H NMR spectroscopy to be greater than

0.8 in most cases. Increasing the fraction of core molecule was found to decrease dispersity to values as low as 1.26 and 1.38 for the alkene core and alkyne core respectively, for monomer concentrations of 0.5 M with 10 mol% core molecule. Molecular weights of the hyperbranched structures were also determined by light scattering size exclusion chromatography (SEC) detection, and intrinsic viscosities determined by viscometry SEC detection. The Kuhn-Mark-Houwink-Sakurada α parameter decreased from 0.35 for the batch process to values as low as 0.21 (10 mol% alkene core) or 0.16 (10 mol% alkyne core), indicating that the thiol–yne structures became more globular and dense with the slow monomer addition strategy. This simple and versatile approach is a promising new development for the design of hyperbranched polymers of well-controlled molecular weight and molecular weight distributions, with very high degrees of branching.

Introduction

Highly branched and three dimensional macromolecular structures, or dendritic polymers, have become an important class of materials over recent decades.[1,2] These structures, including dendrimers and hyperbranched polymers, have received increasing interest due to their unique properties including large number of terminal functional groups, globular three dimensional structures, and low intrinsic viscosities.[3,4] Dendrimers were first reported in the late 1970's and early 1980's, and were synthesized *via* a divergent approach which involves many synthetic steps and tends to lead to branching irregularities at higher generations.[5,6] The convergent approach to dendrimer synthesis was introduced in pioneering work by Fréchet and Hawker in the early 1990's and can lead to higher purity.[7] While perfectly branched dendrimers with degrees of branching (DB) of 1 are very promising structures, the sometimes complicated synthetic and purification steps have led to attempts to replicate their structural properties *via* synthesis of hyperbranched polymers with high degrees of branching in one pot processes.

Flory established the theory of AB$_2$ hyperbranched polymers that could be prepared without gelation in 1952,[8] but it wasn't until 1988 that AB$_2$ hyperbranched polymers were synthesized for the first time in practice.[9-11] Traditional AB$_2$ hyperbranched polymers where both B groups have the same reactivity have a maximum degree of branching of 0.5 due to the statistical nature of the reaction.[12] But by designing monomers where the second B group reacts at a faster rate, DB can be dramatically increased producing hyperbranched polymers with degrees of branching in the region of dendrimers.[13] An interesting chemistry that shows

this enhanced reactivity are radical-mediated thiol–yne additions, which were re-introduced by the group of Bowman in 2009,[14] and applied in the synthesis of hyperbranched polymers with high degrees of branching by our group.[15-18] Another recent example involves copper-catalyzed azide–alkyne click chemistry, where the second B group reacts at a faster rate, due to the first triazole formed complexing the copper catalyst and causing faster reaction of the second moiety.[19]

Accelerated strategies to dendrimer synthesis using orthogonal click chemistry have greatly improved applications of dendrimers and increased their availability to the scientific community, by reducing number of reaction steps and need for demanding purifications.[20-23] Further to this, the development of methods to produce hyperbranched polymers with narrow molecular weight distributions is an important target as it would allow the preparation of materials with greater control and more similarities to dendrimers, in a convenient manner. This could improve the application of hyperbranched polymers in a number of areas including biological systems, and as rheology additives. A number of strategies have been employed to control the molecular weight and dispersity of hyperbranched polymers including polymerization of inimers in confined space;[24,25] however this has yet to be used to produce polymers with degrees of branching higher than 0.5. Slow feeding of AB_2 monomer to multifunctional core has been described previously theoretically,[26,27] and in practice,[28] as another method to control molecular weight and dispersity of hyperbranched polymers. Further to this, increasing the reactivity of the core molecule has been shown to have a greater effect on the narrowing of hyperbranched polymer dispersity.[29-31]

In this article, we report a new strategy to generate hyperbranched polymers via radical thiol–yne chemistry. We dramatically improve our previously published procedure by producing hyperbranched polymers with high degrees of branching and remarkably low dispersity values, *via* slow addition of the thiol/yne monomer to a trifunctional alkyne core and a trifunctional alkene core, tri(prop-2-yn-1-yl) 1,3,5-benzenetricarboxylate and triallyl 1,3,5-benzenetricarboxylate, respectively. The first part of this contribution involves the investigation of the effect of concentration and reactivity of the core molecule on the hyperbranched structure formed with slow monomer addition. The degree of branching for this system and also the kinetics of the thiol–yne batch polymerization were studied in order to establish appropriate slow monomer addition parameters. The second part of this report discusses the effect of the type and amount of core molecules on the production of hyperbranched structures. The molecular weight distributions of the hyperbranched polymers,

their molecular weight and dendritic conformation in solution were determined by multidetector SEC, and the degrees of branching by nuclear magnetic resonance (NMR) spectroscopy.

Experimental

Materials

Propargyl alcohol, 1,3,5-benzenetricarboxylic acid, 3,3-dithiodipropionic acid, dithiothreitol (DTT), 4-dimethylaminopyridine (DMAP), and 2,2-dimethoxy-2-phenylacetophenone (DMPA) were all purchased from Sigma Aldrich. 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (EDC.HCl) was purchased from Iris Biotech. Triethylamine was purchased from Fischer Scientific. Triallyl 1,3,5-benzenetricarboxylate was purchased from Acros. All other materials were purchased from Fisher Scientific or Sigma Aldrich.

Characterization

Size Exclusion Chromatography (SEC) was performed in DMF, using an Agilent 390-LC MDS instrument equipped with differential refractive index (DRI), viscometry, dual angle light scattering, and dual wavelength UV detectors. The system was equipped with 2 x PLgel Mixed D columns (300 x 7.5 mm) and a PLgel 5 μm guard column. The eluent was DMF with 5 mmol NH_4BF_4 additive, and samples were run at 1 mL/min at 50 °C. Analyte samples were filtered through a nylon membrane with 0.22 μm pore size before injection. Apparent molar mass values ($M_{n,SEC}$ and $M_{w,SEC}$) and dispersity ($Đ$) of synthesized polymers were determined by DRI detector and conventional calibration using Agilent SEC software. Poly(methyl methacrylate) (PMMA) standards (Agilent EasyVials) were used for calibration. Molar mass ($M_{w,MALLS}$) was determined on Agilent SEC software using a dual angle light scattering detector, and also DRI detector to determine the incremental refractive index dn/dc. The Kuhn-Mark-Houwink-Sakurada parameter α, relating to polymer conformation in solution was determined from the gradient of the double logarithmic plot of intrinsic viscosity as a function of molecular weight, using the SEC viscometry detector and Agilent SEC software. Proton nuclear magnetic resonance spectra (^{1}H NMR) were recorded on a Bruker Advance 400 or 500 spectrometer (400 MHz or 500 MHz) at 27 °C in CDCl$_3$, with chemical shift values (δ) reported in ppm, and the residual proton signal of the solvent used as internal standard (δH 7.26). Proton-decoupled carbon nuclear magnetic resonance spectra (^{13}C NMR) were recorded on a Bruker Advance 400 or 500 spectrometer (100 MHz or 125 MHz) at 27

°C in CDCl$_3$, with chemical shift values (δ) reported in ppm, and the residual proton signal of the solvent used as internal standard (δC 77.16). Fourier transform infrared spectra (FTIR) were recorded on a Bruker Vector 22 FTIR spectrometer. Electrospray ionisation mass spectra (ESI-MS) were recorded using an Agilent 6130B single Quad mass spectrometer or an Apex Ultra 7T Fourier transform ion cyclotron resonance (FTICR) from Bruker Daltonics.

Preparation of tri(prop-2-yn-1-yl) 1,3,5-benzenetricarboxylate (trialkyne core)

1,3,5-benzenetricarboxylic acid (5.00 g, 23.8 mmol) in 100 mL of DCM, in a round bottomed flask was cooled to 0 ˚C. 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (EDC.HCl) (16.47 g, 85.9 mmol) and 4-dimethylaminopyridine (DMAP) (1.08 g, 8.8 mmol) were dissolved in 100 mL DCM and added to the round bottomed flask under vigorous stirring. Propargyl alcohol (5.30 g, 94.5 mmol) was then added over 1 minute; the reaction mixture was allowed to reach room temperature and stirred for 24 hours. The DCM phase was washed with MilliQ water (2 × 150 mL, 2 × 100 mL), dried with MgSO$_4$, filtered, and the solvent was removed by rotary evaporation. The light brown solid was purified over a short silica column with DCM as the eluent, and the solvent removed by rotary evaporation to give a white powder (5.83 g, 76% yield). ^{1}H NMR (CDCl$_3$, 500 MHz), δ ppm: 8.93 (s, 3H, **CH** phenyl) 4.99 (s, 6H, O-**CH$_2$**-C≡), 2.56 (s, 3H, C≡**CH**). ^{13}C NMR (CDCl$_3$, 125 MHz), δ ppm: 164.06 (**C**=O), 135.36 (**CH** phenyl), 130.87 (**C** phenyl), 77.24 (CH$_2$-**C**≡CH), 75.76 (C≡**C**H), 53.24 (O-**C**H$_2$-C≡). High resolution ESI-MS, expected: *m/z* 347.05 [M+Na]$^+$, found: *m/z* 347.0526 [M+Na]$^+$. ^{1}H and ^{13}C NMR spectra can be found in the Supporting Information (Figure S1 and S2).

Preparation of di(prop-2-yn-1-yl) 3,3'-disulfanediyldipropionate (protected thiol/yne monomer)

1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (EDC.HCl) (21.88 g, 114.14 mol), 3,3-dithiodipropionic acid (10.0 g, 47.56 mol), and 4-dimethylaminopyridine (DMAP) (1.14 g, 9.52 mol) were dissolved in 250 mL of DMF and cooled in an ice bath under stirring. Propargyl alcohol (6.4 g, 114.14 mol) was added; the reaction was allowed to reach room temperature and stirred for 24 hours. The reaction mixture was concentrated via rotary evaporation to yield a yellow oil which was redissolved in DCM, and washed with

water (3 × 100 mL) to remove trace DMF. The DCM phase was then washed with HCl (1 M, 1 × 100 mL), NaOH (1 M, 1 × 100 mL), and water (1 × 100 mL), then dried with Na_2SO_4, filtered and the solvent removed by rotary evaporation. The product was purified by column chromatography (eluent: DCM with 2.5% MeOH), and the resulting viscous liquid (10.3 g, 87% yield) crystallized at 4 °C. ^{1}H-NMR (CDCl$_3$, 400 MHz) δ ppm: 4.71 (s, 2H, O-CH$_2$-C≡), 2.94 (t, 2H, C(O)-CH$_2$-CH$_2$), 2.80 (t, 2H, CH$_2$-CH$_2$-S), 2.49 (s, 1H, C≡CH). ^{13}C-NMR (CDCl$_3$, 100 MHz) δ ppm: 170.91 (**C**=O), 76.84 (CH$_2$-**C**≡CH), 75.25 (C≡**C**H), 52.32 (O-**C**H$_2$-C≡), 33.86 (C(O)-**C**H$_2$-CH$_2$), 32.79 (CH$_2$-**C**H$_2$-S). FTIR v cm^{-1}: 3240-3270 (≡C-H), 2125 (C≡C), 1732 (C(O)=O), 561 (S-S). ESI-MS, expected: m/z 309.02 [M+Na]$^+$, found: m/z 309.0 [M+Na]$^+$. Characterisation data agree with literature.[32] The different spectra are available in the Supporting Information (Figure S3–S5).

Preparation of prop-2-yn-1-yl 3-mercaptopropanoate (monomer deprotection)

Disulfide protected thiol/yne monomer (0.79 g, 5.5 mmol) was dissolved in DCM (10 mL), DTT (1.85 g, 12.1 mmol) and triethylamine (1.75 mL, 12.5 mmol) were added and solution deoxygenated with nitrogen bubbling for 10 min. The solution was stirred at room temperature for 2 hours. The organic layer was washed with 1 M HCl (1 × 20 mL) and water (2 × 20 mL), dried with Na_2SO_4, and solvent removed by rotary evaporation. The resulting viscous liquid (0.73 g, 92% yield) was stored under nitrogen, to prevent disulfide formation. Characterization data agrees with previously published synthetic method.[15] ^{1}H-NMR (CDCl$_3$, 400 MHz) δ ppm: 4.71 (s, 2H, O-CH$_2$-C≡), 2.79 (m, 2H, C(O)-CH$_2$-CH$_2$), 2.71 (m, 2H, CH$_2$-CH$_2$-SH), 2.49 (s, 1H, C≡CH), 1.66 (t, 1H, CH$_2$-SH). ^{13}C-NMR (CDCl$_3$, 100 MHz) δ ppm: 170.81 (**C**=O), 76.84 (CH$_2$-**C**≡CH), 75.20 (C≡**C**H), 52.15 (O-**C**H$_2$-C≡), 38.16 (C(O)-**C**H$_2$-CH$_2$), 19.56 (CH$_2$-**C**H$_2$-SH). FTIR v cm^{-1}: 3270-3290 (≡C-H), 2565-2570 (S-H), 2127 (C≡C), 1732 (C(O)=O). ESI-MS, expected: m/z 311.04 [2M+Na]$^+$, found: m/z 311.0 [2M+Na]$^+$. The spectra are reported in the Supporting Information as Figures S6–S8.

Typical thiol–yne batch polymerization procedure

A typical polymerization is as follows: deprotected thiol/yne monomer (50 mg, 0.347 mmol) was dissolved with DMPA (2 mg, 0.195 mmol) in DMF (300 mg) in a 1.5 mL vial equipped with a small stirrer bar and a rubber septum screw cap. Monomer to initiator ratio

was kept the same for all polymerizations. The vial was wrapped in aluminium foil and deoxygenated with nitrogen for 5 min. The vial was placed under a 365 nm UV lamp (UVP, UVGL-55, 6 watt, 365 nm) in an aluminium foil lined dark box over a magnetic stirrer plate. For the kinetic samples, each time point corresponds to a separate vial removed after the allocated polymerization time. After the predetermined reaction time the vial was removed and analyzed by NMR spectroscopy and SEC. Polymer reaction mixture was precipitated in diethyl ether and the polymer recovered by centrifugation. Conversion was determined by disappearance of thiol peak at ~1.7 ppm, compared to total polymer. The monomer contribution to the integral of the terminal polymer CH_2 next to the alkyne (4.7 ppm) was subtracted.

**Typical thiol–yne polymerization procedure with slow monomer addition**

A typical polymerization is as follows: a solution of deprotected thiol/yne monomer (50 mg, 0.347 mmol) was dissolved with DMPA (1 mg, 0.0975 mmol) in DMF (150 mg) and deoxygenated by bubbling with nitrogen. This was then added to a 250 μL Hamilton gastight glass syringe fitted with stainless steel cannula, and wrapped in aluminium foil and placed on syringe pump. Trialkyne core molecule (11.25 mg, 0.0347 mmol) and DMPA (1 mg, 0.0975 mmol) were dissolved in DMF (150 mg) with a small stirrer in a 1.5 mL vial with a rubber septum screw cap. The vial was wrapped in aluminium foil and deoxygenated with nitrogen for 5 min. Initiator was split between feed syringe and reaction vessel to keep rate of radical formation high and approximately constant, after preliminary experiments showed having all the initiator in the syringe led to slower polymerization due to low concentration of radicals in the reaction vessel. Monomer and initiator concentrations were chosen to keep final concentrations after feeding period the same as the batch polymerizations to enable comparison of results. The vial was placed under a 365nm UV lamp (UVP, UVGL-55, 6 watt) in an aluminium foil lined dark box over a magnetic stirrer plate and feeding started at the same time as irradiation. The feeding was performed over a period of 20 min. For thiol/yne monomer feeding to trialkene core the procedure was the same. After the predetermined reaction time the vial was removed, exposed to air, and analyzed by NMR spectroscopy and SEC. Polymer reaction mixture was precipitated in diethyl ether and the polymer recovered by centrifugation. After a maximum of 80 min, the reaction was stopped.

Results and Discussion

Preparation of thiol/yne monomer and batch thiol–yne photopolymerization

The traditional batch polymerization of AB_2 monomers typically gives hyperbranched polymers with poor control and broad molecular weight distributions. Batch copolymerization of AB_2 and B_f (core molecule with f number of B functionalities) monomers in the molten state was first shown to decrease dispersity in 1995, with a degree of control over molecular weight achieved by varying the core to monomer ratio.[33-38] In 1998, the theory and computational studies of slow monomer addition to multifunctional core were developed by Frey and Müller,[26,27] which showed that the slow monomer addition method could be used to lower dispersity further. The slow monomer addition to multifunctional core strategy was employed to control the synthesis of hyperbranched polymers by Moore *et al.* for the preparation of hyperbranched phenylacetylenes with low dispersity values, however the degree of branching was not determined.[28] Frey *et al.* used slow monomer addition to a core initiator in the synthesis of polyglycerols by ring-opening polymerization, to give hyperbranched polymers with low dispersity values and DB's of ~0.55.[39] Thus, in order to determine appropriate slow addition parameters for the thiol–yne system, an initial set of experiments was conducted in which thiol/yne monomer was polymerized in a batch system allowing characterization of the kinetics of the reaction and degree of branching.

Scheme 1. *Preparation of thiol/yne monomer and batch photopolymerization to form hyperbranched thiol–yne polymers.*
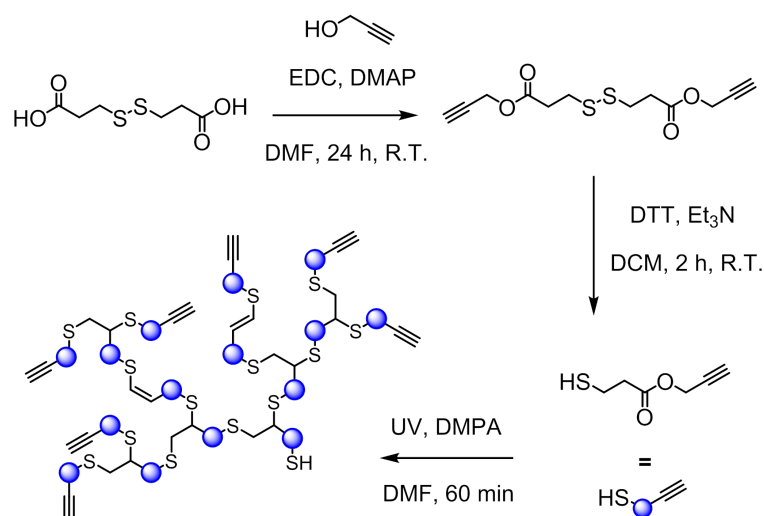
The thiol/yne monomer used in this study was synthesized via a two-step procedure, as shown in Scheme 1. The first step involved the esterification of propargyl alcohol with 3,3-dithiodipropionic acid. This reaction procedure allows large scale synthesis and convenient storage of thiols in their disulfide form, compared to the reduced form, which is subject to reasonably fast oxidation under air. However, storage of the reduced thiol form of the monomer under inert atmosphere is also possible for periods of up to a week and subsequent polymerisations showing no effect on polymer characteristics. Facile reduction of the disulfide (i.e., thiol-protected) monomer was achieved using dithiothreitol (DTT) over 2 hours, and extraction of the DTT with water, to give the pure thiol/yne monomer, prop-2-ynyl 3-mercaptopropanoate, in good yields. The monomer was polymerized under UV light (365 nm) with the radical photoinitiator 2,2-dimethoxy-2-phenylacetophenone (DMPA) in a 1.1 M solution in DMF, following a method similar to that previously published by our group.[15,17,18] A summary of the results is shown in Table 1. The reaction proceeds through the radical-mediated addition of a thiol to an alkyne followed by the addition of a second thiol to the formed vinylthioether to give a dendritic unit. The rate of the second addition is much faster than the first addition, which leads to hyperbranched polymers with very high degrees of branching.

Table 1. *Conversions, molecular weights, dispersity, and degree of branching values for hyperbranched thiol–yne polymers prepared by batch process.*

Time (min)	Conv. [a]	$M_{n,SEC}$ (g/mol) [b]	$M_{w,SEC}$ (g/mol) [b]	$Đ$ [b]	DB [c]
2	35%	1600	2400	1.50	0.84
5	61%	2300	3900	1.66	0.89
10	86%	3400	6500	1.89	0.87
20	98%	4700	10900	2.30	0.84
30	> 99%	5400	14400	2.67	0.83
60	> 99%	5600	16100	2.88	0.84
60 (ppt)	-	9500	19900	2.09	0.85

[a] Determined by ^{1}H NMR spectroscopy, from disappearance of thiol triplet at 1.7 ppm. [b] From DMF SEC with DRI detector and PMMA standard, [c] DB = degree of branching, following equation DB = (D+T)/(D+T+L).[40]

Figure 1a shows the conversion of the thiol/yne monomer over time. Conversion was monitored by ^{1}H NMR spectroscopy, by comparing the integral of the thiol triplet at 1.7 ppm to the integrals corresponding to the dendritic monomer units at 4.3 ppm, the terminal monomer units at 4.7 ppm, and the linear monomer units at 6.4 ppm (see Figure S9 in the

Supporting Information). The reaction proceeds very rapidly and reaches 98% conversion after 20 minutes, with no observable monomer peaks remaining in the ^{1}H NMR spectrum after 60 minutes. The molecular weight increases in a linear fashion until high conversion, where above 90% conversion, polymer–polymer coupling is observed as expected from a step growth hyperbranched polymer synthesis (Figure 1b). The step growth nature of the thiol–yne hyperbranched system also leads to broadening of the molecular weight distribution as conversion increases, as seen in Figure 1c. Note that purification by precipitation removes the smallest hyperbranched oligomers thus leading to a small decrease in the dispersity (Figure 1c).
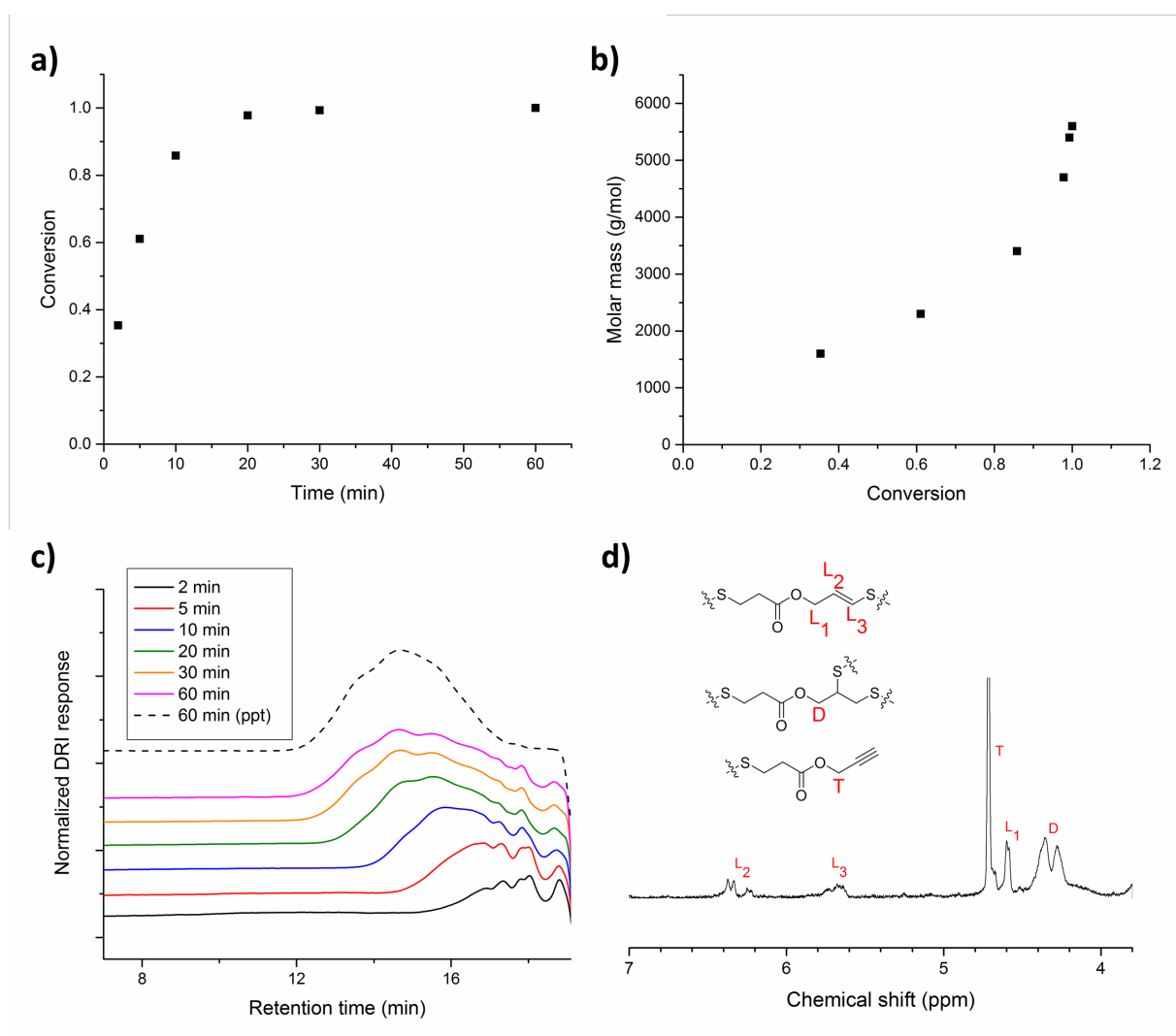

Figure 1. a) *Conversion of thiol/yne monomer as a function of time,* *b)* *Number average molecular weight as a function of conversion,* *c)* *SEC chromatograms of polymer samples at different times during the polymerization,* *d)* *^{1}H NMR spectrum of the precipitated hyperbranched thiol–yne polymer showing peaks corresponding to dendritic, linear, and terminal units for calculation of degree of branching (see SI).*

The concept of 'degree of branching' (DB) was introduced by Flory in the 1940's with polymers in the state of gelation,[41] and expanded to highly-branched polymers in solution with the theory of AB$_2$ polymerizations in 1952.[8] An important associated equation for the characterization degree of branching in hyperbranched polymers was proposed by Hawker and Fréchet in 1991.[40] The polymerization of the thiol/yne monomer allows for easy determination of the degree of branching by ^{1}H NMR spectroscopy, as the peaks for terminal, dendritic, and linear units appear at distinct chemical shifts.[42] For batch polymerization of thiol/yne monomer at 1.1 M concentration, the precipitated polymer had a degree of branching of 0.85 (Figure S11), which corresponds to 15% linear units. It is remarkable to achieve such a high degree of branching for hyperbranched polymers, especially considering the simplicity and versatility of the process, although the final materials exhibit relatively high dispersity.

Slow addition of thiol/yne monomer to multifunctional core

In order to lower this dispersity, the thiol/yne monomer was fed to a trifunctional alkyne core, tri(prop-2-yn-1-yl) 1,3,5-benzenetricarboxylate, at varying concentrations. The proportion of core molecule was chosen to be 10 mol% core for an initial series of feeding experiments. Thiol/yne monomer was introduced gradually into the reaction vessel at a rate that allows the majority of monomer to react with the core before more monomer is added, thus limiting monomer–monomer reactions and promoting monomer–polymer reactions, ie. polymerization from core. This process creates a core region of the hyperbranched polymers analogous to dendrimers, and indicates that there are no thiol focal points which could cause polymer–polymer coupling at high conversions and broaden the molecular weight distribution. Based on the initial thiol–yne batch polymerization kinetic experiments (with 98% conversion after 20 minutes) and previous studies,[15,17] slow monomer addition conditions were employed with the monomer fed over 20 minutes. The matching of the rate of feeding to rate of polymerization means there is always a low concentration of unreacted AB$_2$ in the reaction vessel.
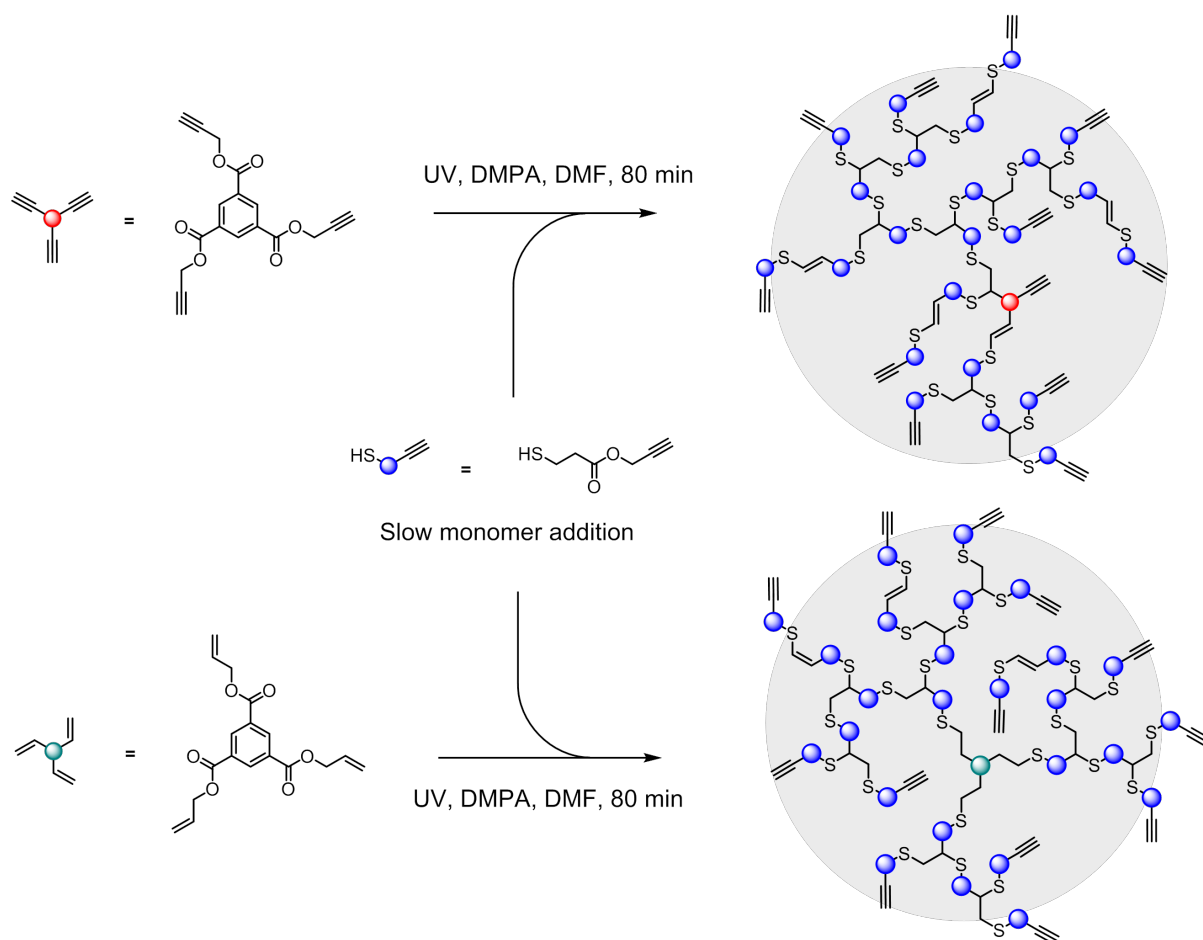
Figure 2 shows the SEC chromatograms of hyperbranched thiol–yne polymers prepared at varying concentrations either by slow monomer addition or in a batch process. Molecular weights and dispersity values are shown in Table 2, and were determined using a conventional calibration with PMMA standards and also multi angle light scattering (MALLS) SEC detection. With increasing concentration the batch thiol–yne hyperbranched polymers have higher molecular weights and broader molecular weight distributions, with the batch polymerization at 2.0 M having a very high apparent molecular weight and large dispersity values. At 0.5 M the use of slow monomer addition to multifunctional alkyne core allows the reduction of the molecular weight to $M_{w,MALLS} = 13300$ g/mol and the molecular weight distribution is narrowed to 1.38. Using the slow monomer addition strategy with the alkyne core, and with careful choice of monomer concentration, the molecular weight can be

targeted to between 13300 g/mol and 77700 g/mol with considerably lower dispersity values than the equivalent batch polymerization.
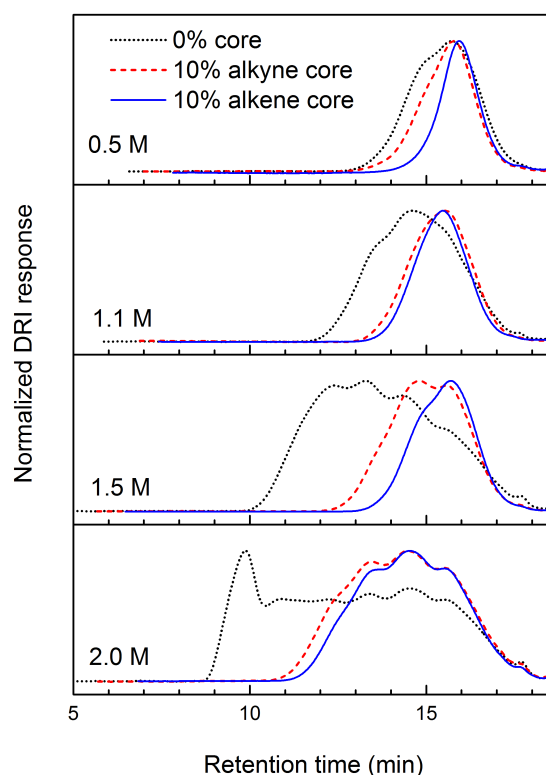

Figure 2. Normalized DRI response SEC chromatograms of hyperbranched thiol–yne polymers prepared by both batch and slow monomer addition process to multifunctional alkyne and alkene core molecules at varying concentrations.

Increasing the reactivity of the core functional groups compared to the monomer can further enhance control and lower dispersity.[43-46] This approach has been used in batch polymerizations to reasonable effect. Fossum *et al*. have shown that copolymerization of an AB_2 monomer with multifunctional C_f cores, where the reactivity towards A of the C group is higher than that of the B group, permits to reduce dispersity of the resulting hyperbranched polymers.[29] Similar results were obtained by Ramakrishnan *et al*. for the copolymerization of AB_2 with a higher reactivity core molecule.[30] In an attempt to reduce dispersity further, use of slow feeding combined with higher reactivity core can be used.[31] Since alkenes are usually more reactive in radical thiol yne/ene reactions,[47] thiol/yne monomer was fed to a trifunctional alkene core, triallyl 1,3,5-benzenetricarboxylate, at varying concentrations.

Use of the alkene core gave narrower molecular weight distributions compared to the same polymerization protocols using the alkyne core. The most remarkable results were obtained with reducing monomer concentration, leading to dispersity as low as 1.26 – a value close to that expected from controlled polymer synthesis techniques such as controlled radical polymerizations – whilst keeping very high degrees of branching (above 0.8).

Molecular weights can also be relatively well-controlled, with lower M_w obtained at lower monomer concentrations. Note that increasing molecular weight by increasing monomer concentration leads to higher $Đ$, as expected from theory and previous reports in the literature.[17,28,29,39] A monomer concentration of 1.1 M was found to give a good combination of control over molecular weight and molecular weight distribution, with very high degree of branching. These conditions were used to investigate the effect of mole fraction core molecule, and conduct a more detailed study of polymer conformation and molecular weight using multidetector SEC.

Table 2. *Conversions, molecular weights, dispersity, and degree of branching values for hyperbranched thiol–yne polymers prepared by batch polymerization or by slow monomer addition process to multifunctional alkyne and alkene core molecules at varying concentrations.*

Conc. (M)	Core mol%	Conv. [a]	$M_{n,SEC}$ (g/mol) [b]	$M_{w,SEC}$ (g/mol) [b]	$Đ$ [b]	$M_{w,MALLS}$ (g/mol) [c]	DB [d]
	0%	> 99%	6700	10300	1.53	17100	0.80
0.5	10% yne	> 99%	6700	9200	1.38	13300	0.79
	10% ene	> 99%	5400	6800	1.26	12100	0.82
	0%	> 99%	9500	19900	2.09	46800	0.85
1.1	10% yne	> 99%	7200	10400	1.44	19600	0.82
	10% ene	> 99%	7200	9700	1.35	13600	0.82
	0%	> 99%	13800	73400	5.30	175400	0.86
1.5	10% yne	> 99%	8100	16800	2.07	25700	0.83
	10% ene	> 99%	6300	10300	1.62	16500	0.84
	0%	> 99%	13900	291600	21.0	1698000	0.87
2.0	10% yne	> 99%	9600	42600	4.44	77700	0.88
	10% ene	> 99%	9400	33500	3.55	54000	0.86

[a] Determined by ^{1}H NMR spectroscopy, from disappearance of thiol triplet at 1.7 ppm. [b] From DMF SEC with DRI detector and PMMA standard. [c] From DMF SEC, MALLS detector. [d] DB = degree of branching, following equation DB = (D+T)/(D+T+L).[40]

Variation of amounts of multifunctional core

The thiol/yne monomer was slowly fed to multifunctional core alkyne and core alkene at 1.1 M final monomer concentrations, with the fraction of core molecule ranging from 2 mol% to 20 mol% (Table 3). The molecular weights of the resulting hyperbranched structures were determined by SEC using a DRI detector and comparing retention time to retention time of PMMA. As retention time is based on hydrodynamic volume, the molecular weight determined by this conventional calibration is significantly underestimated, hyperbranched polymers having a smaller hydrodynamic volume than their linear counterparts, at equivalent molecular weight.[48] For this reason molecular weight was also determined by MALLS SEC detection which determines molecular weight based on scattered light of the polymer.

Figures 3a and 3b show the ^{1}H NMR spectra of the hyperbranched polymers synthesized by both batch and slow monomer addition to core molecules. The degrees of branching and also the extent to which the core molecule functional groups have reacted were calculated. For the polymers synthesized with slow monomer addition, the degrees of branching are all ~0.82 (Table 3), which corresponds to ~18% linear units in the main structure of the hyperbranched polymers. For the hyperbranched polymers specifically with trifunctional alkyne core, the fraction of core alkyne functional groups and core thiovinylether groups remaining after polymerization is the same for all initial core ratios. These remaining core functionalities are ~19% vinylthioether groups, and 40% alkyne groups. In the case of slow monomer addition to alkene core the polymers have 30% alkene functionality remaining on the core after polymerization, with very similar degrees of branching for the main thiol–yne polymer structure as expected. This fraction of residual functionality located on the core molecule after polymerization is the same for all initial core ratios, and is most likely due to steric hindrance around the core as the hyperbranched polymer grows.
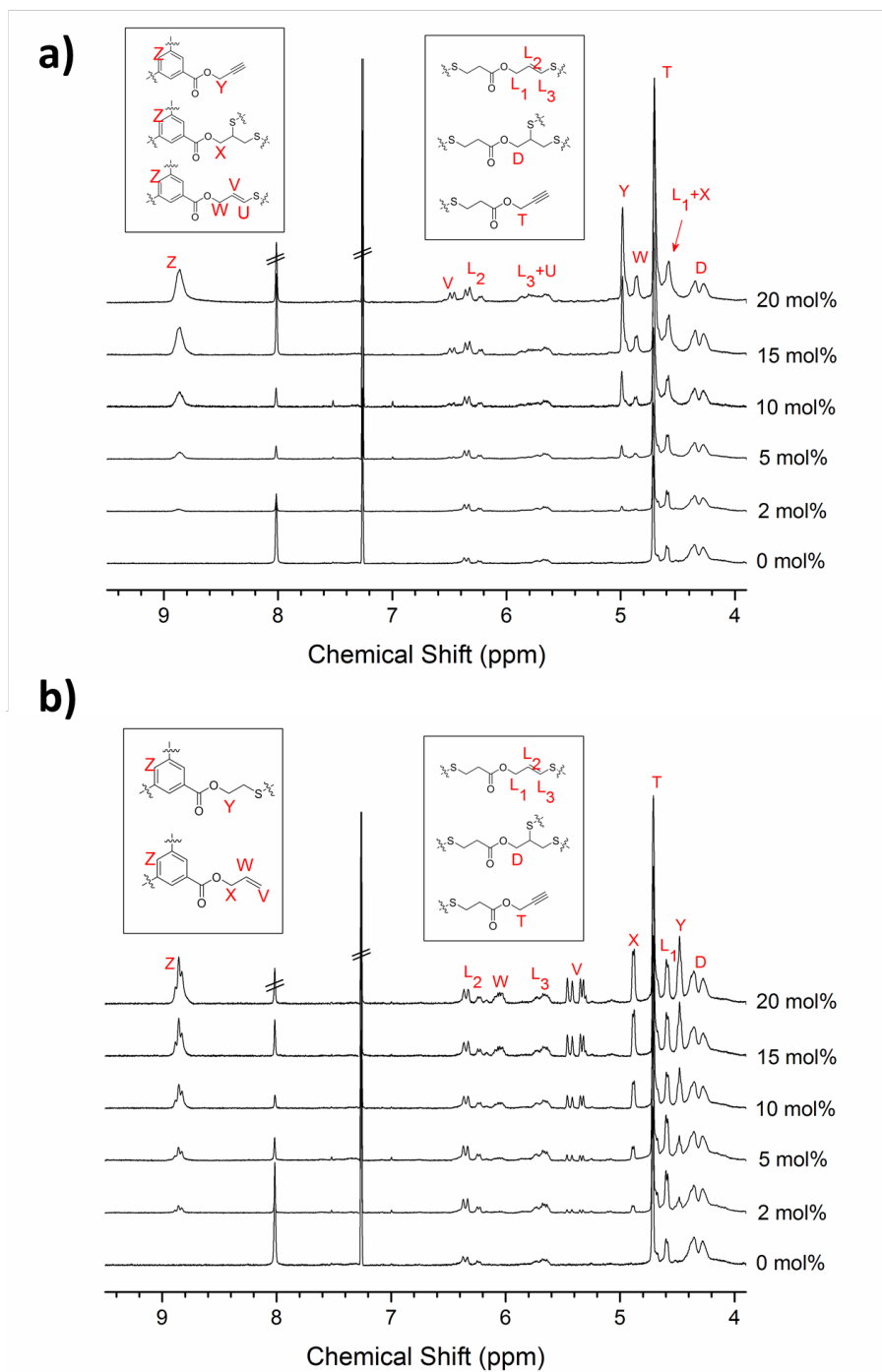
Figure 3. *^{1}H NMR spectra of hyperbranched thiol–yne polymers prepared by both batch and slow monomer addition process to varying amounts of multifunctional **a)** alkyne and **b)** alkene core molecules at 1.1 M concentration.*

Table 3. *Conversions, molecular weights, dispersity, degree of branching values, and KMHS parameter α, for hyperbranched thiol–yne polymers prepared by slow monomer addition process to varying amounts of multifunctional alkyne and alkene core molecules at 1.1 M concentration.*

	Core mol%	Conv. [a]	$M_{n,SEC}$ (g/mol) [b]	$M_{w,SEC}$ (g/mol) [b]	$Đ$ [b]	$M_{w,MALLS}$ (g/mol) [c]	DB [d]	$α$ [e]
	0%	> 99%	9500	19900	2.09	46800	0.85	0.35
Alkyne Core	2%	> 99%	8500	15100	1.79	34200	0.81	0.32
	5%	> 99%	8200	12800	1.56	24600	0.81	0.27
	10%	> 99%	7200	10400	1.44	19600	0.82	0.21
	15%	98%	6300	9000	1.42	14200	0.79	0.35
	20%	97%	6100	8600	1.43	12600	0.73	0.40
Alkene Core	2%	> 99%	9400	16200	1.72	29400	0.82	0.34
	5%	> 99%	7900	11900	1.52	23000	0.81	0.20
	10%	> 99%	7200	9700	1.35	13600	0.82	0.16
	15%	99%	6500	8800	1.36	13400	0.82	0.31
	20%	97%	6300	8300	1.31	12400	0.82	0.34

[a] Determined by ^{1}H NMR spectroscopy, from disappearance of thiol triplet at 1.7 ppm. [b] From DMF SEC, DRI detector, PMMA standard. [c] From DMF SEC, MALLS detector. [d] DB = degree of branching, following equation DB = (D+T)/(D+T+L)[40]. [e] α = Kuhn-Mark-Houwink-Sakurada parameter, from DMF SEC viscometry detector.

Figures 4a and 4b show that as the proportion of multifunctional alkyne core is increased the molecular weight distribution becomes narrower. As previously discussed the batch polymerization has a broad dispersity of over 2, with 2 mol% core this decreases to 1.7-1.8 for both core molecules. For 5 mol% this is reduced further to around 1.5 for both core molecules. At 10 mol% the dispersity reaches 1.35 for alkene core and 1.44 for the alkyne core, with higher core ratios not having a significant further effect on the dispersity. High molar ratios of 20% core did however reduce the molecular weight further, and cause a reduction in the degree of branching most notable for the alkyne core. The distributions also become monomodal due to reduction in polymer–polymer coupling with higher amounts of core.

Lack of entanglements in hyperbranched polymers leads to lower solution viscosities compared to their linear analogues.[48] Figure 4c and 4d show the Kuhn-Mark-Houwink-Sakurada (KMHS) plots of intrinsic viscosity as a function of molecular weight, which

describe polymer conformation in solution, obtained using a viscometry detector on the SEC. KMHS α values, which correspond to the gradient of these plots, are 0 for a hard sphere, 2 for a rigid rod and ~0.7 for linear polymers.[49] An α of between $0.2 - 0.4$ corresponds to globular structures with a high degree of branching, consistent with hyperbranched polymers.[2,50] For the batch polymerization of thiol–yne hyperbranched structures the α value was 0.35, indicating globular hyperbranched polymer structures. With increasing core fraction the α value decreases to 0.21 for the 10% alkyne core hyperbranched polymer and 0.16 for the 10% alkene core hyperbranched polymer, as the structures become more uniform in size and more dense, consistent with the molecular weight distribution traces. Intrinsic viscosity decreases for the alkene core compared to the alkyne core as seen in Figure 4c and 4d, which also indicates a more uniform structure with fewer entanglements, as expected from a more reactive core.
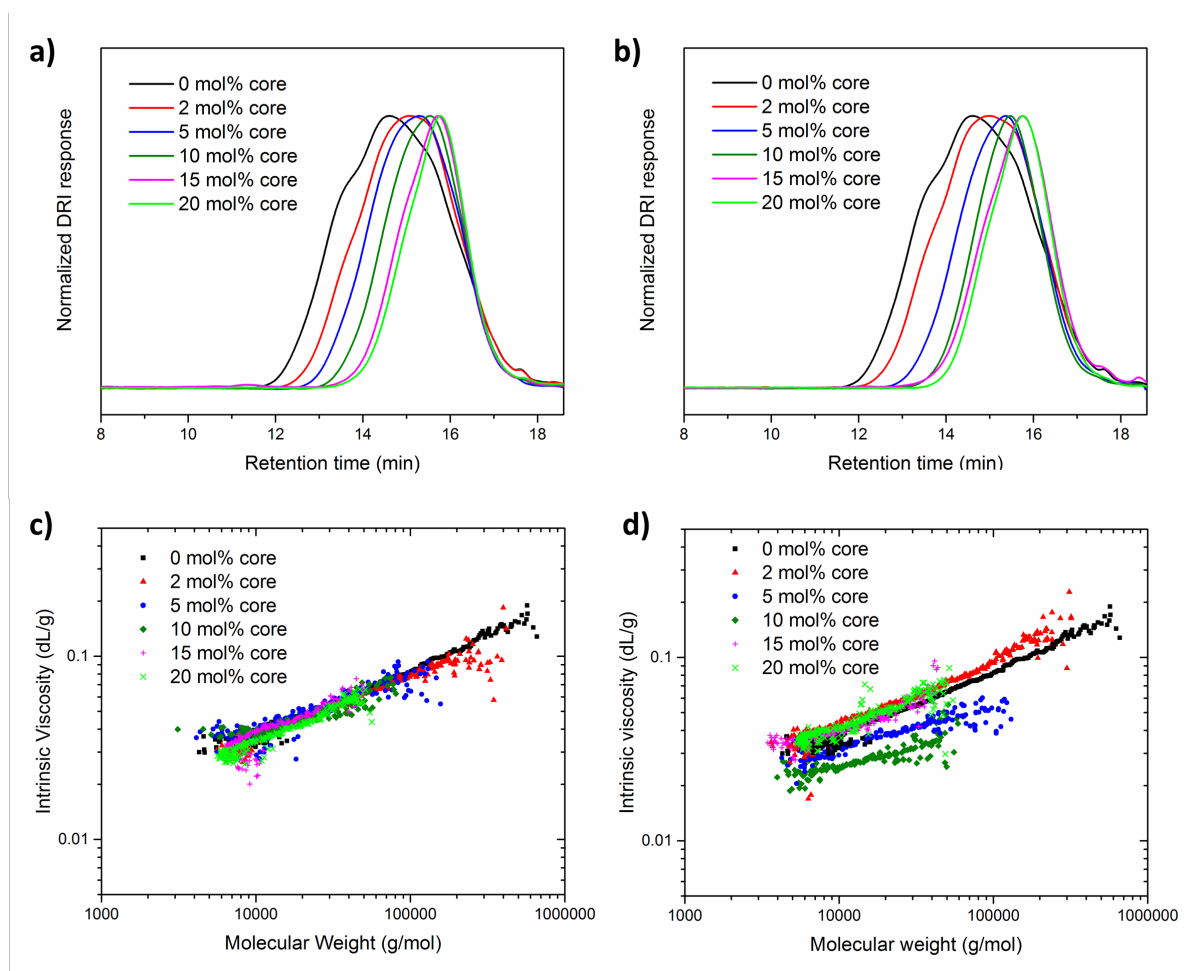

Figure 4. *Normalized DRI response SEC chromatograms of hyperbranched thiol–yne polymers prepared by both batch and slow monomer addition process to varying amounts of*

*multifunctional **a)** alkyne and **b)** alkene core molecules at 1.1 M concentration. Kuhn-Mark-Houwink-Sakurada plots of intrinsic viscosity as a function of molecular weight, determined by viscometry detector on DMF SEC, for hyperbranched thiol–yne polymers prepared by both batch and slow monomer addition process to varying amounts of multifunctional **c)** alkyne and **d)** alkene core molecules at 1.1 M concentration.*

Conclusions

A method for the preparation of hyperbranched polymers with high degrees of branching, predictable molecular weights and narrow molecular weight distributions has been described, involving slow monomer addition of a thiol/yne monomer to multifunctional core molecules in the presence of photoinitiator and UV irradiation. A small thiol/yne monomer was synthesized via simple esterification, giving a route to high purity monomers. Addition of the thiol/yne monomer to multifunctional alkyne and alkene cores was found to lower dispersity of the resulting hyperbranched polymers, whilst maintaining very high degrees of branching. Increasing the fraction of core molecule was found to decrease dispersity, with the ideal value being approximately 10 mol% core molecule. Molecular weights of the hyperbranched structures were determined by conventional calibration SEC and also light scattering SEC detection, and intrinsic viscosities determined by viscometry SEC detection. The KMHS α parameter was found to be below 0.4 in all cases indicating dense and highly branched structures. Using the slow monomer addition strategy reduced the α value to 0.16 in the case of 10% the alkene core molecule, and 0.21 when using 10% alkyne core. In summary, this approach proves to be a simple and versatile process for the synthesis of hyperbranched polymers of remarkably well-controlled molecular weight and molecular weight distributions, with very high degrees of branching.

Acknowledgments

Supporting information

FTIR spectroscopy spectra, ^{1}H and ^{13}C NMR spectroscopy spectra, representative conversion and degree of branching calculations, representative multidetector SEC chromatograms, and polymerisation kinetics of slow monomer addition.

References

(1)   Gao, C.; Yan, D. *Prog. Polym. Sci.* **2004**, *29*, 183.

(2)   Jikei, M.; Kakimoto, M. *Prog. Polym. Sci.* **2001**, *26*, 1233.

(3)   Frechet, J. M. J.; Hawker, C. J.; Gitsov, I.; Leon, J. W. *J. Macromol. Sci., Pure Appl. Chem.* **1996**, *A33*, 1399.

(4)   Voit, B. *J. Polym. Sci., Part A: Polym. Chem.* **2000**, *38*, 2505.

(5)   Tomalia, D. A.; Baker, H.; Dewald, J.; Hall, M.; Kallos, G.; Martin, S.; Roeck, J.; Ryder, J.; Smith, P. *Polym. J.* **1985**, *17*, 117.

(6)   Buhleier, E.; Wehner, W.; Vogtle, F. *Synthesis-Stuttgart* **1978**, 155.

(7)   Hawker, C. J.; Frechet, J. M. J. *J. Am. Chem. Soc.* **1990**, *112*, 7638.

(8)   Flory, P. J. *J. Am. Chem. Soc.* **1952**, *74*, 2718.

(9)   Kim, Y. H.; Webster, O. W. *Polym. Prepr. (Am. Chem. Soc., Div. Polym. Chem.)* **1988**, *29*, 310.

(10)   Kim, Y. H.; Webster, O. W. *Macromolecules* **1992**, *25*, 5561.

(11)   Kim, Y. H.; Webster, O. W. *J. Am. Chem. Soc.* **1990**, *112*, 4592.

(12)   Holter, D.; Burgath, A.; Frey, H. *Acta Polym.* **1997**, *48*, 30.

(13)   Holter, D.; Frey, H. *Acta Polym.* **1997**, *48*, 298.

(14)   Fairbanks, B. D.; Scott, T. F.; Kloxin, C. J.; Anseth, K. S.; Bowman, C. N. *Macromolecules* **2009**, *42*, 211.

(15)   Konkolewicz, D.; Gray-Weale, A.; Perrier, S. *J. Am. Chem. Soc.* **2009**, *131*, 18075.

(16)   Konkolewicz, D.; Poon, C. K.; Gray-Weale, A.; Perrier, S. *Chem. Commun.* **2011**, *47*, 239.

(17)   Barbey, R.; Perrier, S. *Macromolecules* **2014**, *47*, 6697.

(18)   Barbey, R.; Perrier, S. *ACS Macro Lett.* **2013**, *2*, 366.

(19)   Shi, Y.; Graff, R. W.; Cao, X.; Wang, X.; Gao, H. *Angew. Chem. Int. Ed.* **2015**, *54*, 7631.

(20)   Killops, K. L.; Campos, L. M.; Hawker, C. J. *J. Am. Chem. Soc.* **2008**, *130*, 5062.

(21)   Malkoch, M.; Schleicher, K.; Drockenmuller, E.; Hawker, C. J.; Russell, T. P.; Wu, P.; Fokin, V. V. *Macromolecules* **2005**, *38*, 3663.

(22)   Wu, P.; Feldman, A. K.; Nugent, A. K.; Hawker, C. J.; Scheel, A.; Voit, B.; Pyun, J.; Frechet, J. M. J.; Sharpless, K. B.; Fokin, V. V. *Angew. Chem. Int. Ed.* **2004**, *43*, 3928.

(23)   Walter, M. V.; Malkoch, M. *Chem. Soc. Rev.* **2012**, *41*, 4593.

(24)   Graff, R. W.; Wang, X.; Gao, H. *Macromolecules* **2015**, *48*, 2118.

(25)   Min, K.; Gao, H. *J. Am. Chem. Soc.* **2012**, *134*, 15680.

(26)   Hanselmann, R.; Holter, D.; Frey, H. *Macromolecules* **1998**, *31*, 3790.

(27)   Radke, W.; Litvinenko, G.; Muller, A. H. E. *Macromolecules* **1998**, *31*, 239.

(28)   Bharathi, P.; Moore, J. S. *Macromolecules* **2000**, *33*, 3212.

(29)   Bernal, D. P.; Bedrossian, L.; Collins, K.; Fossum, E. *Macromolecules* **2003**, *36*, 333.

(30)   Roy, R. K.; Ramakrishnan, S. *Macromolecules* **2011**, *44*, 8398.

(31)   Chen, J.-Y.; Smet, M.; Zhang, J.-C.; Shao, W.-K.; Li, X.; Zhang, K.; Fu, Y.; Jiao, Y.-H.; Sun, T.; Dehaen, W.; Liu, F.-C.; Han, E.-H. *Polymer Chemistry* **2014**, *5*, 2401.

(32)   Willenbacher, J.; Schmidt, B.; Schulze-Suenninghausen, D.; Altintas, O.; Luy, B.; Delaittre, G.; Barner-Kowollik, C. *Chem. Commun.* **2014**, *50*, 7056.

(33)   Malmstrom, E.; Johansson, M.; Hult, A. *Macromolecules* **1995**, *28*, 1698.

(34)   Feast, W. J.; Stainton, N. M. *J. Mater. Chem.* **1995**, *5*, 405.

(35)   Lach, C.; Muller, P.; Frey, H.; Mulhaupt, R. *Macromol. Rapid Commun.* **1997**, *18*, 253.

(36)   Parker, D.; Feast, W. J. *Macromolecules* **2001**, *34*, 5792.

(37)   Hobson, L. J.; Feast, W. J. *Polymer* **1999**, *40*, 1279.

(38)   Hobson, L. J.; Feast, W. J. *Chem. Commun.* **1997**, 2067.

(39)   Sunder, A.; Hanselmann, R.; Frey, H.; Mulhaupt, R. *Macromolecules* **1999**, *32*, 4240.

(40)   Hawker, C. J.; Lee, R.; Frechet, J. M. J. *J. Am. Chem. Soc.* **1991**, *113*, 4583.

(41)   Flory, P. J. *J. Am. Chem. Soc.* **1941**, *63*, 3083.

(42)   Han, J.; Zhao, B.; Gao, Y. Q.; Tang, A. J.; Gao, C. *Polymer Chemistry* **2011**, *2*, 2175.

(43)   Cheng, K. C.; Wang, L. Y. *Macromolecules* **2002**, *35*, 5657.

(44)   Zhou, Z.; Jia, Z.; Yan, D. *Polymer* **2012**, *53*, 3386.

(45)   Ohta, Y.; Kamijyo, Y.; Fujii, S.; Yokoyama, A.; Yokozawa, T. *Macromolecules* **2011**, *44*, 5112.

(46)   Ohta, Y.; Fujii, S.; Yokoyama, A.; Furuyama, T.; Uchiyama, M.; Yokozawa, T. *Angew. Chem. Int. Ed.* **2009**, *48*, 5942.

(47)   Lowe, A. B.; Hoyle, C. E.; Bowman, C. N. *J. Mater. Chem.* **2010**, *20*, 4745.

(48)   Voit, B. I.; Lederer, A. *Chem. Rev.* **2009**, *109*, 5924.

(49)   Hiemenz, P. C.; Lodge, T. P. *Polymer Chemistry, Second Edition*; Taylor & Francis, 2007.

(50)   Striegel, A. M. *Anal. Chem.* **2005**, *77*, 104 A.

Graphical abstract for TOC: