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Sequential click synthesis of hyperbranched polymers *via* the A_2 + CB_2 approach†

Jin Han, Bo Zhao, Yanqin Gao, Aijin Tang and Chao Gao*

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Sequential thiol–ene and thiol–yne click chemistry *via* the A_2 + CB_2 protocol is presented for simple, rapid, and scalable production of hyperbranched polymers, affording hyperbranched polythioether–ynes with high molecular weight and high degree of branching.

Hyperbranched polymers (HPs) possess unique structural attributes as well as special chemical and physical properties, enabling them to be used in coating, processing additives, nanocarriers for dyes and drugs, nanotemplates for metal catalysts, and so on.[1] These tremendous applications are urgently calling for HP synthesis developing towards rapidness, mildness, high-yield and scale-up.[2] Several synthesis strategies have been developed. Unlike conventional single-monomer (AB_2) and symmetric monomer pair (A_2 + B_3) strategies, the newly developed couple-monomer methodology (CMM) including A_2 + CB_2, A_2 + BB'_2, AB + CD_2, and A* + CB_2 approaches employs asymmetric monomer pair that can mainly *in situ* form AB_2-type intermediate for polymerization instead of purified AB_2 or A_2 + B_3 monomer, saves much effort on precursor purification and allows one-pot simple acquisition of HPs with low gelation risk.[2,3] However, the utilized conventional reactions are relatively slow,[3] posing a challenge of how to rapidly prepare HPs while keeping the advantages of CMM.

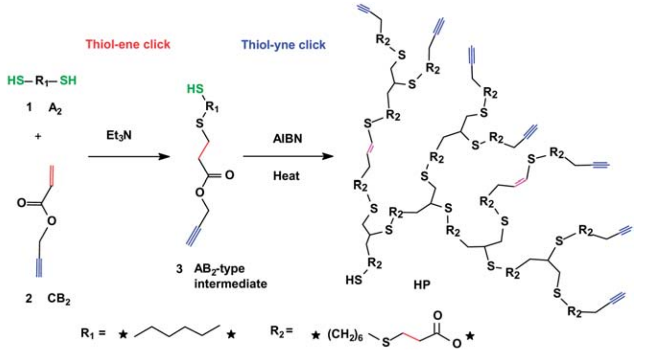
Herein, we represent a sequential click chemistry (SCC) approach to fast production of HPs from commercial monomer pairs.[4] Click chemistry has been widely demonstrated as a versatile tool for construction of complex macromolecules since its first definition in 2004 by Sharpless *et al.*[5] Hence, our synthesis approach holds both merits of CMM and click chemistry: simplicity, low risk of gelation, scalability, fastness, mildness, and modularity. Notably, single click chemistry such as thiol–yne or azide–alkyne reaction has been used for the preparation of HPs in the final polymerization step,[6,7] whereas no report has been published to employ click chemistry in all of the reaction steps including the synthesis of precursor and formation of HPs.

As shown in Scheme 1, di-thiols and propargyl acrylate are selected as A_2 and CB_2 monomers, respectively. In the presence of triethylamine (Et_3N), a thiol group of di-thiol can react with C=C bond of propargyl acrylate *via* Michael addition thiol–ene click chemistry,[8,9] mainly affording an AB_2-type intermediate of "thiol–alkyne"; the following thiol–yne click polymerization yields HP.[6,8]

Clearly, the AB_2-type intermediate is *in situ* formed in our approach and subsequently used for direct polymerization without further isolation of AB_2 monomer. Thus, our approach is essentially different from the classic AB_2 approach that needs the synthesis and purification of precursor through conventional reaction with a low efficiency (*e.g.*, 13%) even though thiol–yne click polymerization could be used in the final step.[6] Moreover, we employ thermal initiating rather than the generally used UV-light irradiation for the thiol–yne polymerization in order to make the process more straightforward and easily accessible in a large-scale.

Typically, propargyl acrylate **2** was added dropwise to a THF solution of 1,6-hexanedithiol **1** under N_2 in the presence of Et_3N as a catalyst. After reaction at 35 °C for 6 h till the reaction completion, THF and Et_3N were removed under reduced pressure. Toluene containing 2,2′-azobisisobutyronitrile (AIBN) initiator was added subsequently. Further thermo-initiated thiol–yne polymerization was conducted at 65 °C for given times. The whole process was accomplished within 12 h, declaring the high efficiency and cost effectiveness of our new approach indeed.

^1H NMR spectra of precursor and HPs are shown in Fig. 1. ^{13}C NMR spectra of precursor and HP are shown in Fig. S1 and S3†, respectively. In the ^1H NMR spectrum of precursor, the proton signals at 5.8–6.6 ppm ascribed to the CH_2=CH moiety of acrylate totally vanished due to the thiol–ene addition,[10] new signals at 2.6–2.8 ppm assigned to the resulted CH_2CH_2 bonds emerged and the



Scheme 1 Sequential thiol–ene and thiol–yne click chemistry approach to rapid, easy synthesis of HPs *via* the A_2 + CB_2 framework.

MOE Key Laboratory of Macromolecular Synthesis and Functionalization, Department of Polymer Science and Engineering, Zhejiang University, Hangzhou, P. R. China. E-mail: chaogao@zju.edu.cn

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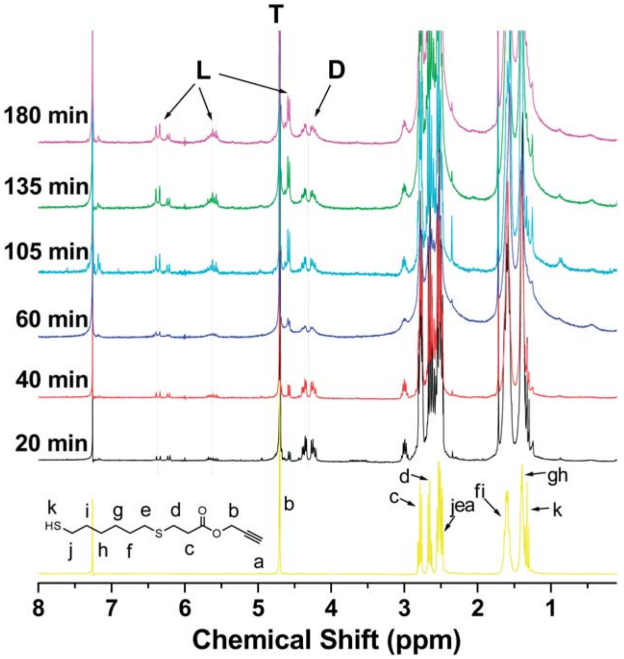

Fig. 1 ^{1}H NMR spectra of precursor obtained by thiol–ene reaction and corresponding HPs at different polymerization times before precipitation. Here, 6.3, 5.6 and 4.58 ppm, CH=CH–CH_2OOC moiety of **L**; 4.7 ppm, CH_2OOC moiety of **T**; 4.2–4.4 ppm, CH_2OOC moiety of **D**.

ratio of the integration of the proton signals labeled with "b" to the integration sum of the proton signals labeled with "f" and "i" was 1:2, indicating that the precursor was successfully prepared and contained equal amount of thiol groups and alkyne groups. Mass spectroscopy analysis revealed that the precursor comprised of three components: unreacted dithiols, AB_2 monomer and di-ynes (Fig. S2†). HPLC measurements revealed that the precursor contained ~56% of AB_2 monomer, ~22% of di-thiols and ~22% of di-ynes. In the ^{1}H NMR spectrum of HPs, the proton signal of CH_2 moiety in the propargyl group at 4.7 ppm gradually weakened and the signals at 2.5–2.8 ppm assigned to the protons of CH_2SCH_2 moiety gradually increased upon reaction time, implying the proceeding of polymerization. The emerging proton signals at 6.1 and 5.6 ppm and the emerging vinyl carbon signals at 119–132 ppm (Fig. S3†) implied the formation of vinyl sulfides generated by monoaddition of thiol to alkyne, indicating the generation of linear units (**L**).[6]

In order to detect the conversion of thiol groups and probe the structure of the HPs, model compounds were elaborated: **Ter** was synthesized by thiol–ene addition of 1-propanethiol to propargyl acrylate to mimic the terminal unit (**T**); **Den** was prepared by thiol–yne bisaddition of 1-propanethiol to **Ter** to mimic the dendritic unit (**D**); two mixtures comprised of **Ter**, **Den** and **Lin**, **Mix₁** and **Mix₂** were prepared to mimic the unit structure of HP by inadequate additions of 1.8 and 0.5 equivalent of 1-propanethiol to **Ter**, respectively (see ESI† for preparation details). Their ^{1}H NMR spectra are shown in Fig. 2. Differences are observed: in the spectrum of **Ter**, the proton signal of CH_2 moiety in the propargyl group is located at 4.7 ppm; in the spectrum of **Den**, the double peak of the propargyl CH_2 moiety originally appearing at 4.7 ppm is converted into the multiple peak at 4.2–4.4 ppm by bisaddition; in the spectrum of **Mix_1** and **Mix_2**, the vinyl group of **Lin** formed by monoaddition displays its proton signals at 5.6 and 6.3 ppm, and the adjacent CH_2 moiety shows its signal at 4.58 ppm. All these proton signals mentioned here can be seen in the ^{1}H NMR spectra of HPs, justifying that the model compounds can be used to examine the conversion of thiol groups and the unit structure of HP accurately.

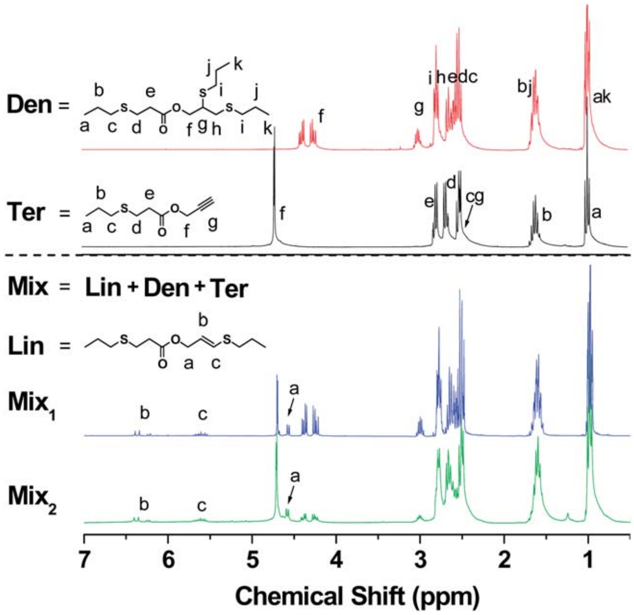

Fig. 2 ^{1}H NMR spectra of model compounds. **Den**, model for the dendritic units; **Ter**, model for the terminal units; **Lin**, model for the linear units; **Mix_1** and **Mix_2**, models for the **HP**.

The conversion of thiol groups and the degree of branching (DB) were calculated according to the following two formulas, respectively.

$$\text{Conversion} = \frac{\text{L} + 2\text{D}}{\text{D} + \text{T} + \text{L}} \tag{1}$$

$$\text{DB} = \frac{\text{D} + \text{T}}{\text{D} + \text{T} + \text{L}} \tag{2}$$

As a result, the conversion of thiol groups reached 95.4% in 3 h, indicating that the polymerization proceeds very fast. All the DB values are higher than 0.5 (the maximum value for a HP made from AB_2 monomer without substitution effect) due to that the first addition of thiol to alkyne (r_1) is much slower than the second

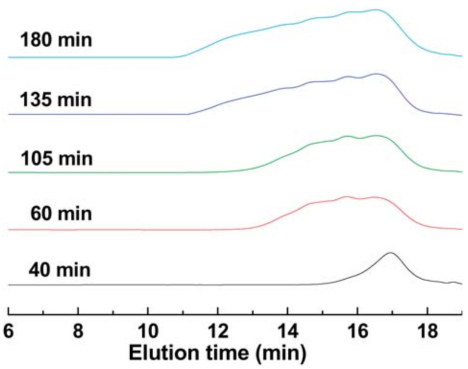

Fig. 3 GPC curves of HPs at different polymerization times.

Table 1 Reaction conditions and results for the HPs (D, T, and L denote the relative integration of dendritic, terminal and linear units, respectively)

Sample	Time/min	Conv^a (%)	M_n (k)	M_w (k)	PDI^b	DB	**D**	**T**	**L**
HP-A	20	55.4	—	—	—	0.98	0.27	0.71	0.02
HP-B	40	67.9	2.3	3.4	1.48	0.91	0.29	0.62	0.09
HP-C	60	72.3	5.1	20.7	4.06	0.87	0.30	0.57	0.13
HP-D	105	81.5	5.3	26.3	4.96	0.82	0.32	0.50	0.18
HP-E	135	92.2	6.8	87.9	12.93	0.80	0.36	0.44	0.20
HP-F	180	95.4	7.2	104.8	14.56	0.76	0.36	0.40	0.24

^{a} Conversion of thiol groups. ^{b} Polydispersity index (M_w/M_n).

addition of thiol to vinyl sulfide (r_2) and thus the reactivity ratio (γ) of r_2 to r_1 is generally larger than 1.[11] In the kinetics theory with substitution effect, if $\gamma \geq 10$, DB will be close to or even higher than 0.7 at conversion of 70%.[12]

The molecular weights and polydispersity indices (PDIs) of HPs precipitated from methanol were determined by gel permeation chromatography (GPC). HP at 0.33 h of polymerization cannot be precipitated out because of its low molecular weight. GPC curves and polymerization data are presented in Fig. 3 and Table 1, respectively. It can be seen that the elution peaks come out earlier and the curves become broader with increasing the polymerization time. Both M_n (number-average molecular weight) and M_w (weight-average molecular weight) increase rapidly with conversion, with M_w growing much faster than M_n, resulting in higher and higher PDI. This phenomenon could also be seen in the reported preparations of other HPs.[2,6] Polymerization for 3 h afforded the HP with M_n of 7200, M_w of 10 4800 and DP_w (weight-average degree of polymerization) of 402. It should be pointed out that at the high conversion up to 95.4%, no gelation occurred, implying that the reaction between 22% of di-thiol and 22% of di-yne which has the potential to cause crosslinking at low conversion cannot impose remarkable impact in the presence of 56% of AB_2 monomer. This confirms the validity of the $A_2 + CB_2$ approach that differs from the conventional AB_2 or $A_2 + B_3$ approaches in essence.

Polymerization under UV irradiation in the presence of 2,2-dimethoxy-2-phenyl-acetophenone (DMPA) was also attempted,[6] and yielded HP with M_n of 4500 and M_w of 34 300 after irradiation for only 30 min. 3,6-Dioxaoctane-1,8-dithiol was also employed to test the modularity of this SCC procedure, affording HP with M_n of 6300 and M_w of 19 300.

Conclusions

In summary, sequential thiol–ene and thiol–yne click chemistry has achieved the rapidness, simplicity and high efficiency during the process from commercial starting materials to final HP product. HPs with high molecular weights and high DBs which both can be adjusted through the reaction time or conversion have been readily prepared from commercial monomers within 12 h in high yield. Both thermo-initiated and UV-initiated thiol–yne polymerizations are available. Currently, employing various functional monomers to create versatile HPs and investigating their applications are in progress in our laboratory. Thiol–halogen click-like and thiol–yne click reactions are successfully combined *via* the SCC strategy to create HPs with high molecular weights and high DBs, and the results will be published elsewhere. Other click reactions, such as thiol–epoxy, thiol–isocyanate, thiol–ene, azide–alkyne and so on, will also be applied in this sequential procedure, opening an avenue to fast, easy, scalable production of HPs.

The prepared hyperbranched polythioether–ynes also have big potential in many applications due to its chemical features, internal thioether groups and peripheral alkyne groups, and dendritic architecture. The sulfur-rich feature benefits the application of the HPs in metal ion absorption, oil resistance, anti-oxidation, and so on. The alkyne groups at the periphery can facilitate the modification of HPs *via* highly efficient thiol–yne and azide–alkyne click chemistry techniques.

Experimental

The whole preparation procedure for HP can be completed within 12 h. Typically, 1,6-hexanedithiol (1.51 g, 10 mmol) and Et_3N (1.01 g, 10 mmol) were dissolved in THF (4 mL) in a 50 mL flask placed in a water bath. The solution was purged with N_2 for 10 min to eliminate oxygen and then added dropwise a THF (2 mL) solution of propargyl acrylate (1.10 g, 10 mmol) over 30 min with vigorous stirring. The reaction system was kept at 35 °C and monitored with ^{1}H NMR spectroscopy. It was found that proton signals of the $CH_2{=}CH$ moiety of acrylate totally disappeared 6 h later. Then a vacuum pump was connected with the flask to remove THF and Et_3N, affording colourless liquid (2.59 g) containing equal amounts of thiol and propargyl groups. ^{1}H NMR (300 MHz, $CDCl_3$): 4.7 (d, 2H, $CH{\equiv}CC\mathit{H}_2O$), 2.82–2.6 (m, 4H, $OCC\mathit{H}_2C\mathit{H}_2S$), 2.58–2.49 (m, 4H, $HSC\mathit{H}_2CH_2CH_2CH_2CH_2C\mathit{H}_2S$), 2.48 (t, 1H, $C\mathit{H}{\equiv}C$), 1.52–1.68 (m, 4H, $HSCH_2C\mathit{H}_2CH_2CH_2\ C\mathit{H}_2CH_2S$), 1.46–1.35 (m, 4H, $HSCH_2CH_2C\mathit{H}_2C\mathit{H}_2CH_2CH_2S$), 1.33 (t, 1H, $\mathit{H}SCH_2$). ^{13}C NMR (125MHz, $CDCl_3$): 171.2, 77.8, 75.4, 52.2, 34.8, 33.9, 32.1, 29.5, 28.4, 28.0, 26.9, 24.6. GC-MS: 150.0 g mol^{-1} for dithiols, 260.1 g mol^{-1} for AB_2 monomer, 371.2 g mol^{-1} for di-ynes (calculated 150.31 g mol^{-1}, 260.42 g mol^{-1}, and 370.53 g mol^{-1}).

The resulting liquid was diluted with toluene to 0.5 M and mixed with AIBN (32.8 mg, 0.2 mmol). After purging N_2 to the flask for 10 min, the temperature was elevated to 65 °C to start the polymerization. Samples were collected in given reaction time through air-tight syringe and analyzed by ^{1}H NMR spectroscopy. The polymer was precipitated out by pouring the polymer solution into methanol and characterized by GPC. The polymer irradiated for 3 h was characterized by ^{13}C NMR spectroscopy (Fig. S3†).

UV irradiation initiated polymerization was also attempted by employing 2 mol% of DMPA as photoinitiator instead of AIBN.

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