Synthesis of β -cyclodextrin-based star polymers *via* a simplified electrochemically mediated ATRP

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ABSTRACT

Cyclodextrin-based star polymers were synthesized using functionalized β -cyclodextrin (β -CD) core, and *n*-butyl acrylate (BA) as hydrophobic arms. The β -CD core macroinitiator was prepared by the transesterification reaction of β -CD with 2-bromoisobutyryl bromide. The core-first method was chosen as the synthetic strategy as it allows good control over the polymer architecture. Star-shaped amphiphilic polymers were prepared *via* a simplified electrochemically mediated ATRP (*se*ATRP) procedure under both potentiostatic and pseudo-galvanostatic conditions, utilizing only 50 ppm (40 ppm by weight (wt)) of Cu^{II} complex, much less than previously reported concentrations of catalyst of *ca.* 4,000–130,000 ppm (590–19,000 ppm (by wt)). The rate of the polymerizations (R_p) was controlled by applying different potentials E_{app} , with slower R_p observed using more positive E_{app} values thereby suppressing intermolecular termination reactions between growing arms, and subsequent star-star coupling. The polymerization results showed molecular weight evolution close to theoretical values while maintaining a narrow molecular weight distribution for the growing star polymer throughout the reaction. The differences between theoretical and measured MW originate in different hydrodynamic radii of stars and linear polymers used as standards for gel-permeation chromatography (GPC). Successful chain extension of the ω -functional arms with *tert*-butyl acrylate (*t*BA) resulted in star block copolymers and confirmed the living nature of the β -CD-PBA star polymers prepared by *se*ATRP. Moreover, the absence of radical coupling reactions during *se*ATRP synthesis was confirmed by GPC analyses of the actual arm length of obtained star polymers and copolymers.

KEYWORDS

poly(*n*-butyl acrylate), cyclodextrin-based star polymers, simplified electrochemically mediated ATRP

INTRODUCTION

Atom transfer radical polymerization (ATRP) is one of the most versatile reversible deactivation radical polymerization (RDRP) methods, permitting control over macromolecular topology.[1-21] During the past few years, various poly(meth)acrylates, poly(meth)acrylamides, polystyrenes, and polyacrylonitrile were successfully prepared by ATRP with relatively narrow molecular weight distribution (M_w/M_n , MWD) and targeted degrees of polymerization (DP).[2, 18, 22-34]

Star polymers, consisting of multiple arms linked to a central core, have attracted significant attention, because of their branched architecture, globular shape, and chemically crosslinked structure.[35-42] One approach to prepare star polymers *via* ATRP is the core-first technique, which involves the use of a multifunctional initiator, which predetermines the number of arms in the star polymer by the number of initiating sites on the initiator. In addition, the star polymers can easily introduce next segment by chain extension of ω -chain ends (at periphery of the stars) and the final products can be easily purified.[38, 43-46] β -Cyclodextrin (β -CD) is a cyclic oligosaccharide consisting of seven glucose units linked by α -1,4-glucosidic bonds with seven primary and fourteen secondary hydroxyl groups.[47] The core can be used for selective modification of the hydroxyl groups. Therefore β -CD is an excellent candidate, among molecules of cyclical structure, for synthesis of star polymers *via* the core-first approach.[47-59]

Amphiphilic star polymers composed of poly(*n*-butyl acrylate) (PBA) arms covalently linked to a β -CD core are especially interesting, because they can be potentially used in

biomedical applications, such as target drug delivery system. PBA is an industrially important polymer because of its low glass-transition temperature, durability, and potential use as a soft segment in thermoplastic elastomers.[60, 61]

Previously using a β -CD macroinitiator, star polymers composed of poly(methyl methacrylate),[44, 62] poly(*tert*-butyl acrylate) (PtBA) ,[50, 63-67] poly(2-(dimethylamino)ethyl methacrylate),[53, 55, 57] poly((2-hydroxy-3-(2-aminoethyl) amino)propyl methacrylate),[55] polyacrylamide,[47] poly(*N*-isopropylacrylamide),[56] poly(*N*-(3-(dimethylamino)propyl) methacrylamide),[55] or poly((2-(methacryloyloxy)ethyl trimethyl ammonium)[48, 55, 68] were synthesized using ATRP, but synthesis of β -CD-PBA has not yet been reported. Furthermore, in all cases rather high catalyst loadings, *ca.* 4,000–130,000 ppm as a molar ratio of catalysts to monomer (590–19,000 ppm (by wt)), were used for the star synthesis.[44, 47, 48, 50, 53, 55-57, 62, 68]

The advent of new low catalyst ATRP systems, that use parts per million (ppm) concentrations of catalyst, such as activators regenerated by electron transfer (ARGET) ATRP,[69] initiators for continuous activator regeneration (ICAR) ATRP,[70] supplemental activator and reducing agent (SARA) ATRP[71] and photoinduced ATRP[72] offer more environmentally benign and industrially scalable reaction conditions for the synthesis of polymers prepared by ATRP, but also provides an option to prepare polymers with designed dispersity, defined by the catalyst concentration.[18]

More recently, a novel ATRP process termed electrochemically mediated ATRP (*e*ATRP) was developed.[34, 73-82] It has some advantages for synthesis of complex polymeric architectures, for example star polymers.[77] Based on the mechanism of *e*ATRP, the ratio of the concentration of $\text{Cu}^{\text{I}}/\text{L}$ to $\text{X-Cu}^{\text{II}}/\text{L}$ can be precisely controlled by the applied current (*I*), and potential (*E*) at the electrode surface.[75] Consequently, the concentration of the radical species required to propagate and form polymeric chains by reacting with

monomers (M), and the efficiency of deactivation back to the dormant species (P_n-X) can be controlled, **Scheme 1**.^[81]

Scheme 1. Mechanism of *e*ATRP. Reprinted with permission from reference [75]. Copyright 2013 American Chemical Society.

However, there are some intrinsic limitations related to the reaction setup of the initial *e*ATRP procedure. Recently,^[81] significant simplifications of the procedures used for an *e*ATRP were reported: the use of a sacrificial counter electrode that allowed elimination of the requirement for separation of electrode compartments and the polymerization under either potentiostatic and galvanostatic conditions.

Here, we report the first example of the preparation of both 14-arm and 21-arm β -cyclodextrin based PBA stars by *e*ATRP using simplified electrochemically mediated ATRP (*se*ATRP), under both potentiostatic and pseudo-galvanostatic conditions (**Scheme 2**). Polymerization conditions were optimized to provide fast reactions while employing low catalyst concentrations and preparation of polymers with narrow molecular weight distributions. In addition, utilizing high ω -chain end functionalities of the star polymers (at the star periphery), well-defined block star copolymers (β -CD-PBA-*Pt*BA) were successfully prepared by *se*ATRP (**Scheme 3**).

Scheme 2. Synthesis of β -CD-PBA star polymers *via seATRP*.

Scheme 3. Synthesis of β -CD-(PBA-*b*-PtBA) star block copolymers *via seATRP*.

RESULTS AND DISCUSSION

Motivated by the excellent control of various β -CD star polymers prepared by ATRP with high amounts of Cu catalyst complexes (typically > 4,000 ppm), we aimed to achieve similar levels of control using only 50 ppm (40 ppm (wt)) of X-Cu^{II}/L in solution, following the *seATRP* procedure under potentiostatic or pseudo-galvanostatic conditions. First, a β -CD-Br ATRP initiator with 14 -Br atoms tethered to the core was synthesized by esterification of

a fraction of the hydroxyl groups on β -CD with BriBBR (**Scheme S1**), according to the procedures reported by Zhang et al.[83] The composition was confirmed by ^1H NMR (**Figure S1**). Additionally, a β -CD-Br₂₁ initiator was prepared according to the procedure reported by Li et al.[84] (**Scheme S2**), and the composition was also confirmed by ^1H NMR (**Figure S2**). The use of the functionalized β -CD's as core molecules, with a well-defined number of initiating groups, allows predetermination of the number of arms in star polymers. All experimental procedures and compound characterization data are included in the manuscript's Supporting Information.

Table 1 summarizes the results of the star polymers synthesis using the β -CD based macroinitiators (β -CD-Br₁₄: $M_n = 3,230$ and $M_w/M_n = 1.05$; β -CD-Br₂₁: $M_n = 4,260$ and $M_w/M_n = 1.06$ (M_w/M_n values were determined by GPC)) under both potentiostatic and pseudo-galvanostatic conditions.

Table 1. Summary of β -CD-PBA synthesis by *e*ATRP and *se*ATRP.

entry	[M]/[I]/ [Cu ^{II} Br ₂ /2TPMA]	E_{app} ^a	k_p^{app} (h ⁻¹) ^b	conv (%) ^b	$\text{DP}_{n,\text{theo}}$ (per arm) ^b	$M_{n,\text{theo}}$ ($\times 10^{-3}$) ^c	M_n^{app} ($\times 10^{-3}$) ^d	M_w/M_n^{d}
1	85/1 ^e /0.0085	E_{pc} -80 mV	0.412	71	60	111.8	86.2	1.10
2	85/1 ^e /0.0085	<i>Pseudo-galvanostatic Conditions</i> ^f	0.380	68	58	107.6	84.0	1.11
3	85/1 ^e /0.0085	E_{pc} -80 mV	0.551	81	69	126.3	97.2	1.09
4	85/1 ^e /0.0085	<i>Pseudo-galvanostatic Conditions</i> ^g	0.547	80	68	124.7	99.7	1.10
5	85/1 ^e /0.0064	E_{pc} -80 mV	0.377	67	57	105.6	80.2	1.08
6	85/1 ^e /0.0043	E_{pc} -80 mV	0.236	51	43	80.7	64.2	1.07

7	85/1 ^c /0.0021	E_{pc} -80 mV	0.098	25	22	42.0	31.2	1.09
8	85/1 ^h /0.0043	E_{pc} -80 mV	0.279	57	49	135.0	169.5	2.93
9	85/1 ^h /0.0043	E_{pc} -50 mV	0.251	54	46	128.4	89.5	1.27
10	85/1 ^h /0.0043	E_{pc} -20 mV	0.230	50	43	118.8	86.2	1.18
11	85/1 ^h /0.0043	<i>Pseudo-galvanostatic Conditionsⁱ</i>	0.219	48	41	115.0	84.3	1.18
12	60/1 ^j /0.0030	E_{pc} -35 mV	0.511	64	38	218.4	148.1	1.24
13	60/1 ^j /0.0030	<i>Pseudo-galvanostatic Conditions^k</i>	0.466	61	36	212.9	140.2	1.23

Conventional *e*ATRP under potentiostatic conditions (WE = Pt mesh, CE = Pt mesh separated from the reaction solution by the supporting electrolyte saturated Tylose gel placed in a glass tube equipped with a glass frit, RE = saturated calomel electrode (SCE)): entry 1; *e*ATRP under pseudo-galvanostatic conditions (WE and CE without RE): entry 2; *se*ATRP under potentiostatic conditions (WE = Pt mesh, CE = Al wire ($l = 10$ cm, $d = 1$ mm), RE = SCE): entries 3, 5–10, and 12; *se*ATRP under pseudo-galvanostatic conditions: entry 4, 11, and 13. ^a E_{app} were selected based on CV analysis of Cu/L ($v = 100$ mV/s); ^bMonomer conversion, apparent propagation rate constants (k_p^{app}), and *theoretical* degree of polymerization of monomer unit per arm ($DP_{n,theo}$) were determined by NMR, k_p^{app} values were calculated from the slope of the $\ln([M]_0/[M])$ -time graphs; ^c $M_{n,theo} = ([M]_0/[MI]_0) \times \text{conversion} \times M_{monomer} + M_{initiator}$; ^dapparent M_n and MWD were determined by THF GPC with PS standard curves; ^eI = β -CD-Br₁₄ (calculated per -Br); ^f $I_{app} = -0.14, -0.08, \text{ and } -0.07$ mA for each steps; ^g $I_{app} = -0.28, -0.15, -0.78, \text{ and } -0.06$ mA for each steps; ^hI = β -CD-Br₂₁ (calculated per -Br); ⁱ $I_{app} = -0.31, -0.11, -0.06, \text{ and } -0.04$ mA for each steps; ^jI = β -CD-(PBA-Br)₂₁ (calculated per -Br); ^k $I_{app} = -0.23, -0.12, -0.05, \text{ and } -0.03$ mA for each steps. General reaction conditions: $T = 50$ °C; $V_{tot} = 20$ mL; [BA] = 3.6 M (except entries 12–13: [tBA] = 3.4 M); [β -CD-Br₁₄] = 3.1 mM, [β -CD-Br₂₁] = 2.0 mM, [β -CD-(PBA-Br)₂₁] = 2.7 mM; [Cu^{II}Br₂/2TPMA] = 0.36 mM for entries 1-4, 0.27 mM (entry 5), 0.18 mM (entries 6, 8–11), 0.09 mM (entry 7), and 0.17 mM (entries 12–13). Supporting electrolyte concentration (tetrabutylammonium perchlorate, TBAP) = 0.2 M.

Star synthesis by conventional and simplified *e*ATRP. Conventional *e*ATRP was carried out under potentiostatic conditions with a Pt mesh WE, Pt mesh CE, and SCE RE (**Table 1, entry 1, Figures 1a,b, S3, S4a, and S5**). Prior to conducting a polymerization, the $E_{1/2}$ values for $\text{Cu}^{\text{II}}\text{Br}_2/\text{TPMA}$ complex (which are reported in the Supporting Information (**Figure S3**)), were determined in the absence and presence of the $\beta\text{-CD-Br}_{14}$ multifunctional initiator. On the basis of these results, the applied potential (E_{app}) was selected as $E_{\text{app}} = \text{cathodic peak potential } (E_{\text{pc}}) - 80 \text{ mV}$. The polymerization of BA by *e*ATRP showed good evolution of molecular weight (MW), close to theoretical values, while maintaining narrow molecular weight distributions (**Figures 1b and S4a**). The differences between theoretical and measured MW originate the differences in hydrodynamic radius of star and linear polymer standards for GPC.

The preparation of star homopolymers with PBA arms under pseudo-galvanostatic conditions was also carried out and the results are reported in **Table 1, entry 2, Figures 1a,b, S4b, and S5**. The applied currents (I_{app}) were determined by the polymerizations conducted under potentiostatic conditions (**Table 1, entry 1**). On the basis of the preparative electrolysis results (**Figure 1a**), the total charge passed was calculated according to a previously published procedure.[81] It was observed that in Figure 1a the current decreased; it was probably caused by the formation of an oxidized species. The most probable explanation is to assumed, that the traces of oxygen were leaked throught the glass frit of Pt mesh counter electrode in to the reaction mixture. The increase of the current was so small, that it did not influenced the main reaction. The rate of polymerization (R_p) showed a slight decrease from values observed under potentiostatic conditions, cf. values of k_p^{app} ; **Table 1, entries 2 vs. 1**. However, nearly identical first-order kinetic plots were observed (**Figure S5**), and GPC analysis indicated similar MW evolution, indicating similar initiation efficiency, and

formation of uniform star molecules (narrow MWD, **Figure 1b**). Therefore it can be stated that the potentiostatic mode can be well mimicked by the pseudo-galvanostatic mode.

Fig. 1. Conventional *e*ATRP with potentiostatic or pseudo-galvanostatic conditions; (a) preparative electrolysis results from potentiostatic conditions (grey line) and applied current (red line), and (b) M_n and M_w/M_n versus monomer conversion by potentiostatic and pseudo-galvanostatic conditions.

The results of a simplified polymerization under potentiostatic conditions with a Pt mesh WE, a sacrificial Al CE, and SCE RE are shown in **Table 1, entry 3**, and in **Figures 2a,b, and S3c, and S6**. A first-order kinetic plot was also observed (**Figure S6**), with linear MW evolution and even narrower MWD (**Figure 2b**). Four constant I_{app} values were used for the polymerization under pseudo-galvanostatic conditions; $I_{app,1} = (-) 0.28$ mA (for 0 to 0.13 h), $I_{app,2} = (-) 0.15$ mA (for 0.13 to 0.88 h), $I_{app,3} = (-) 0.08$ mA (for 0.88 to 1.63 h), and $I_{app,4} = (-) 0.06$ mA (for 1.63 to 3 h) where negative values indicate the cathodic currents (**Table 1, entry 4, Figures 2a,b, S4d, S6, and S7**). The values for MW evolution and MWD observed for *se*ATRP under pseudo-galvanostatic conditions as compared to polymerizations conducted under potentiostatic conditions, **Figure 2b**, and were similar. The ^1H NMR spectrum shown in **Figure S7** confirms the structure of β -CD-PBA star polymer obtained through *se*ATRP under pseudo-galvanostatic conditions (**Table 1, entry 4**).

Fig. 2. PBA star polymers by *se*ATRP under potentiostatic and pseudo-galvanostatic conditions; (a) preparative electrolysis results from potentiostatic conditions (grey line) and applied current (red line), and (b) M_n and M_w/M_n versus monomer conversion by potentiostatic and pseudo-galvanostatic conditions.

Influence of the concentration of the catalyst complex. The next series of polymerizations were designed to examine the influence of the concentration of Cu/TPMA within *se*ATRP. Three polymerizations were conducted using different $[X-Cu^{II}/L]_0$, ranging from 100 to 25 ppm (as a molar ratio to $[M]$, **Table 1**, **entries 3,5–7**, **Figure 3a,b**, **S4c,e,f,g** and **S8a,b**). Higher concentrations of copper catalyst should yield faster R_p in electrochemically mediated ATRP methods, because R_p is proportion to the square root of $[X-Cu^{II}/L]$ according to the equation defined as $R_p = k_p[M][P\cdot] = k_p[M]K_{ATRP} \frac{[P-X][Cu^I/L]}{[X-Cu^{II}/L]}$, [75] where $[P\cdot] = \sqrt{\frac{k_{red}[X-Cu^{II}/L]}{k_t}}$ [75, 85, 86] (k_{red} denote reduction rate constant). Similar to literature accounts,[85, 86] it was observed that as the initial $[X-Cu^{II}/L]_0$ increases, the rate of polymerization increases with an approximately square root dependence on the catalyst concentration (**Figure S8b**). Briefly, a polymerization with 100 ppm catalyst concentration was 1.5 times faster (compare k_p^{app} ; **Table 1**, **entry 3 vs. 5**) than with 75 ppm catalyst, 2.3 times faster than with 50 ppm catalyst (compare k_p^{app} ; **Table 1**, **entry 3 vs. 6**) and 5.6 times faster than with 25 ppm catalyst (compare k_p^{app} ; **Table 1**, **entry 3**

vs. 7). An increase in R_p reflects a higher $[P^*]$, which is a result of faster reduction rates generating more $\text{Cu}^{\text{I}}/\text{L}$. Moreover, as **Figure 3b** illustrates, there is an almost linear increase in MW with respect to conversion for all reactions and a slight decrease in the MWDs with lower $[\text{X}-\text{Cu}^{\text{II}}/\text{L}]_0$ (compare M_w/M_n ; **Table 1**, entries **3**, **5**, and **6**). This observation is opposite to that supported by the equation describing the distribution of molecular weights of polymer: $\frac{M_w}{M_n} = 1 + \left(\frac{k_p[\text{P-X}]}{k_{\text{da}}[\text{Cu}^{\text{II}}]} \right) \left(\frac{2}{p} - 1 \right)$ [75] (where p denotes monomer conversion), which indicates higher $[\text{X}-\text{Cu}^{\text{II}}/\text{L}]$ should produce polymers with lower M_w/M_n values from an increased rate of deactivation and fewer monomer additions within each activation–deactivation cycle.

Fig. 3. Synthesis of β -CD-PBA star polymers as a function of $[\text{Br}-\text{Cu}^{\text{II}}/2\text{TPMA}]$. (a) First-order kinetic plot of monomer conversion versus time, and (b) evolution of M_n and M_w/M_n versus monomer conversion. Reaction conditions: $[\text{BA}]/[\beta\text{-CD-Br}_{14} \text{ (per -Br)}]/[\text{Cu}^{\text{II}}\text{Br}_2/2\text{TPMA}] = 85/1/x$, $[\text{BA}] = 3.6 \text{ M}$, $T = 50 \text{ }^\circ\text{C}$, $[\text{TBAP}]_0 = 0.2 \text{ M}$, $V_{\text{tot}} = 20 \text{ mL}$, $E_{\text{app}} = E_{\text{pc}} - 80 \text{ mV (vs. SCE)}$, $x = 0.0085, 0.0064, 0.0043$, and 0.0021 corresponding to 100, 75, 50, and 25 ppm, respectively.

Furthermore, 40 ppm (by wt) concentration of catalyst complex generated transparent solutions and represents a 15–475 fold decrease in total Cu catalysts relative to previous

reports where the concentration of Cu/L used in ATRP varied between *ca.* 590–19,000 ppm (by wt).

Influence of applied potential. After establishment of the optimal catalyst complex concentration, a series of polymerizations were carried out to examine the influence of the applied overpotential [$\eta = E_{\text{app}} - E_{1/2}$; $E_{1/2} = (E_{\text{pc}} + E_{\text{pa}})/2$] on the polymerization behavior (**Table 1**, entries 8–10, **Figure 4a, b**, **S4h–j** and **S9a–c**). Control over the rate of polymerization was evaluated by applying different constant potentials E_{app} . Three E_{app} values were selected: $E_{\text{pc}} - 80$ mV, $E_{\text{pc}} - 50$ mV, and $E_{\text{pc}} - 20$ mV (**Figure 4a**). Faster R_p was observed when more negative potentials were applied. The fastest apparent propagation rate constant was observed for 0.279 h^{-1} ($E_{\text{pc}} - 80$ mV). The R_p was 1.2 times faster than when $E_{\text{pc}} - 20$ mV was applied, **Figure 4b**.

Fig. 4. R_p as a function of applied potential during synthesis of $\beta\text{-CD-PBA}$ star polymers. (a) Cyclic voltammetry of $\text{Cu}^{\text{II}}\text{Br}_2/2\text{TPMA}$ with and without initiator (lines indicate E_{app}), and (b) first-order kinetic plots for different E_{app} values. Reaction conditions: $[\text{BA}]/[\beta\text{-CD-Br}_{21} \text{ (per -Br)}]/[\text{Cu}^{\text{II}}\text{Br}_2/2\text{TPMA}] = 85/1/0.0043$, $[\text{BA}] = 3.6 \text{ M}$, $[\text{Cu}^{\text{II}}\text{Br}_2/2\text{TPMA}] = 0.18 \text{ mM}$, $T = 50 \text{ }^\circ\text{C}$, $[\text{TBAP}]_0 = 0.2 \text{ M}$, $V_{\text{tot}} = 20 \text{ mL}$, $E_{\text{app}} = E_{\text{pc}} - 80 \text{ mV}$, $E_{\text{app}} = E_{\text{pc}} - 50 \text{ mV}$, $E_{\text{app}} = E_{\text{pc}} - 20 \text{ mV}$ (vs. SCE).

More negative η values produced larger initial currents, indicative of a faster rate of reduction. In essence, faster rates of reduction provide a higher $[\text{Cu}^{\text{I}}/\text{L}]$ and, therefore, faster polymerization, due to higher $[\text{P}^*]$. The magnitude of stationary current values, reflect the

relative activator regeneration rates and hence termination rates, therefore, a more negative η leads to a higher R_p and stationary current, resulting in more termination.[75] Controlled polymerization behavior was confirmed in case of more positive applied potentials (E_{pc} -50 mV and E_{pc} -20 mV) by a linear increase of M_n with conversion, while producing a monomodal population of polymers with relatively low M_w/M_n values (**Table 1, entries 9,10** and **Figure S4i,j**). Significantly higher M_w/M_n values were observed at the most negative applied potential (E_{pc} -80 mV, **Table 1, entry 8, Figure S4h**). The observed increase in M_w/M_n can be related to a more pronounced star-star coupling. Comparing polymerization using β -CD-Br₁₄ with polymerization using β -CD-Br₂₁ initiator (compare M_w/M_n ; **Table 1, entry 6 vs. 8**), the coupling reaction was observed in case of the second one, which is caused by sterically congestion of growing chains and might have on account of higher change to star-star intermolecular X-linking. Termination between growing arms can happen in the intermolecular and intramolecular mode. The former will lead to star-star coupling, the latter to less uniform growth of arms. Intramolecular coupling was mainly diminished by low radical concentration. Usually it can be evidenced by bimodal MWD of arms of stars.[7] In the case of presented results the % of chains terminated by radical means could be estimated according to the formulae (Dead Chain Fraction defined as $DCF = \left(\frac{[D]}{[P-X]_0} \right) \cdot 100\%$ [87] where $[D] = k_t[P \cdot]^2 t$ ($[D]$ denotes concentration of terminated chains, t denote reaction time), $k_t = 1.0 \cdot 10^8 \text{ M}^{-1}\text{s}^{-1}$, [88, 89] $[P \cdot] = \left(\frac{d\ln[M]}{dt} \right) (k_p)^{-1}$, $k_p = 2.77 \cdot 10^4 \text{ M}^{-1}\text{s}^{-1}$ [90]). The calculated values are well below 1% (**Table S1, entry 7**), so the bimodality cannot be detected by GPC, even if termination will be 100% of coupling. It is also possible that there would be even less coupling and the disproportionation could not be detected by GPC.[91] Probability of the intramolecular termination of acrylates can be enhanced due to a close proximity of radicals but also can be diminished due to radical segregation.[92] Therefore subsequent reactions were performed with less negative E_{app} (E_{pc} -50 mV and E_{pc} -20 mV

respectively) while targeting polymerizations with limited monomer conversion, thereby further suppressing the intermolecular termination reactions between growing arms, and subsequent star-star coupling.

Chain extension from PBA star polymers. The preparation of CD star homopolymers with 21 arms of PBA under pseudo-galvanostatic conditions was carried out and the results are reported in **Table 1, entry 11, Figure 5, S4k and S10a–c**. Nearly identical first-order kinetic plots were observed, and GPC analysis indicated narrow MWD (**Figure S10 b, and c**). The ^1H NMR spectrum, shown in **Figure 5**, confirms the structure of β -CD-PBA star polymer obtained through *se*ATRP under pseudo-galvanostatic conditions (**Table 1, entry 11**). The chemical shifts, 0.80–1.03 ppm, 1.34–2.00 ppm, 2.16–2.55 ppm, and 3.75–4.30 ppm, are mainly attributed by the $-\text{CH}_3$ (d), $-\text{CH}_2-$ (β +b+c), $-\text{CH}-$ (α), and $-\text{OCH}_2-$ (a) groups of the PBA units in the arms, respectively, indicating the presence of PBA chains.

Fig. 5. ^1H -NMR spectrum of CD star homopolymers with PBA arms (β -CD-(PBA₄₁)₂₁); $M_n = 115,000$, $D = 1.18$) after purification (in CDCl_3). Table 1, entry 11.

The synthesis of star block copolymers under potentiostatic and pseudo-galvanostatic conditions was carried out (**Table 1, entries 12 and 13, Figure 6, S4l,m, and S11a–c**). Close

to identical first-order kinetic plots were observed, and GPC analysis indicated narrow MWD (**Figure S11b** and **c**) confirming that the halogen end groups were preserved during the *se*ATRP of BA. The ^1H NMR spectrum shown in **Figure 6** confirms the structure of β -CD-PBA-*Pt*BA star block copolymer obtained through *se*ATRP under pseudo-galvanostatic conditions (**Table 1, entry 13**). The chemical shifts, 1.34–2.00 ppm, and 2.16–2.55 ppm, are mainly attributed to the $-\text{CH}_2-$ (β'), $-\text{CH}_3$ (e), and $-\text{CH}-$ (α') groups of the *Pt*BA units in the arms, respectively, indicating the presence of *Pt*BA chains.[93]

Fig. 6. ^1H -NMR spectrum of star block copolymer (β -CD-(PBA₄₁-*Pt*BA₃₅)₂₁); $M_n = 212,900$, $D = 1.23$) after purification (in CDCl_3). Table 1, entry 13.

Analysis of the arm length of star (co)polymers. In order to determine the actual arm length of obtained star polymers and copolymers, and thus the initiation efficiency (f_i), the arms were cleaved from the core by acid solvolysis of the ester groups.[94, 95] The results of the molecular weight determinations and the comparison with the expected values are summarized in **Table S2**. The obtained polymer stars with homopolymer or di-block copolymer arms showed monomodal GPC eluograms (**Figures S12a–c**) and their molecular weight distributions are narrow ($D < 1.32$; **Table S2, entries 4, 11 and 13**), indicating that

radical coupling reactions are negligible. These results confirm the well-controlled *se*ATRP of BA/*t*BA as well as the formation of a well-defined (co)polymer stars. As expected, the initiation efficiency (and blocking efficiency) of analysed acrylates were close to 100% (Table S2, entries 4, 11 and 13).[96]

CONCLUSIONS

β -Cyclodextrin (β -CD) core macroinitiators were synthesized and employed for the preparation of well-defined star polymers with poly(*n*-butyl acrylate) (PBA) arms utilizing a simplified electrochemically mediated atom transfer radical polymerization (*se*ATRP) procedure with low concentrations of catalyst, as low as 50 ppm of added Cu^{II} species. This appears to be the first report using *se*ATRP for the polymerization of *n*-butyl acrylate as hydrophobic arms from a modified β -CD as the hydrophilic macroinitiator. The use of a simplified multi-step current pseudo-galvanostatic technique provided identical results to polymerizations carried out under potentiostatic conditions, providing star-shaped polymers with molecular weight evolution close to theoretical values while generating stars with narrow molecular weight distribution. The rate of the polymerizations (R_p) under pseudo-galvanostatic conditions was controlled by applying less negative E_{app} , thereby suppressing intermolecular termination *via* a chain coupling process, and subsequent star-star coupling. Chain extension of the initially formed star polymer with *t*BA, confirmed the preservation of terminal halogen end group during the *se*ATRP of acrylates. The readily purified star polymers obtained by this procedure had a hydrophilic β -CD core with the potential to form inclusion complexes with small organic compounds. These new amphiphilic star polymers are promising precursors for polyelectrolyte star polymers, with potential application in biomedical application field.

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Associated Content

Supporting Information – Experimental conditions, figures showing GPC traces of polymers, NMR spectrum, CV and CA results.

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Notes: The authors declare no competing financial interest.

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Synthesis of β -cyclodextrin-based star polymers via a simplified electrochemically mediated ATRP

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Star polymers were synthesized by a simplified electrochemically mediated ATRP (*se*ATRP) of *n*-butyl acrylate using β -cyclodextrin macroinitiators with 14- and 21-active sites. Polymerizations were well controlled with low concentration of $\text{Cu}^{\text{II}}\text{Br}_2/2\text{TPMA}$ complex under either potentiostatic or pseudo-galvanostatic conditions. The synthesis of β -CD-PBA-PtBA star shaped block copolymers was successfully carried out with the formed β -CD-PBA star polymers as macroinitiators.

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