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Synthesis of Dendrimer-Like Star-Branched Poly(methyl methacrylate)s of Generations Consisting of Four Branched Polymer Chains at Each Junction by Iterative Methodology Involving Coupling and Transformation Reactions

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Summary: A series of dendrimer-like star-branched poly(methyl methacrylate)s (PMMA)s of generations consisting of four branched segments at each junction have been successfully synthesized by developing an iterative methodology. It involves two reaction steps in each iterative reaction sequence, (a) a coupling reaction of the α-functionalized living anionic PMMA with four *tert*-butyldimethylsilyloxymethylphenyl (SMP) groups with benzy bromide (BnBr)-chain-functionalized PMMA and (b) a transformation of SMP group into BnBr functionality. By repeating the reaction sequence thrice, the above-mentioned dendrimer-like star-branched (PMMA)s of up to third-generation made up of 4, 20, and 84 PMMA segments and 16, 64, and 256 BnBr termini were synthesized by the first, second, and third iterative processes, respectively. The resulting polymers all were well-defined in branched architecture and precisely controlled in chain length.

Keywords: dendrimer-like star-branched polymer; hyperbranched poly(methyl methacrylte); iterative methodology; living anionic polymerization

Introduction

Dendrimer-like star-branched polymers have recently appeared as a new class of hyperbranched polymers. Although such polymers are analogous in branched architecture to well-known dendrimers, they are constructed from generations of high molecular weight polymer chains between branching junctions and, accordingly, much higher in molecular weight and larger in molecular size than dendrimers. Therefore, these polymers are of particular interest as nano-size functional polymers, because of the unique topological hyperbranched architecture, the high functionality resulting from many chain-ends, the different branched density between core and outside shell, the possible formation of several layered structures with different characters, and the possible fabrication of periodic mesoscopic objects with sepcially shaped suprastructures.

Since the first successful syntheis of dendrimer-like star-branched polymers in 1998 by Hedrick et al, the synthesis of similar hyperbranched polymers have been reported by repeating living polymerization from multifunctional precursors and chain-end-functionalization reaction to increase the initiating reaction sites.[1–6] Not only regular type, but also amphiphilic block copolymers were also synthesized.[7–11] Very recently, Gnanou et al have reported the synthesis of polymers of very high generation up to eighth.[12] Although the resulting polymers were considered to possess controlled architectures by several analyses, the uniformity of all polymer segments starting from

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multifunctional initiators remains a question. Alternatively, Hadjichristidis and Chalari have synthesized a series of dendrimer-like star-branched block copolymers of second generation by coupling the off-center living anionic polymers with CH_3SiCl_3 or $SiCl_4$.[13] The methodology has recently been extended to the synthesis of the third-generation copolymers.[14] Since the resulting copolymers were synthesized by the methodology based on "arm-first" termination method using pre-made living polymers, they possessed a high molecular and compositional homogeneity. Hutchings et al have proposed a step-wise convergent coupling method using an AB_2 macromonomer as a building block for the synthesis of dendrimer-like star-branched polymers.[15] Unfortunately, the coupling efficiency was not high enough to the synthesis of polymers of high generations. Knauss and his coworkers have demonstrated the convenient procedure for the synthesis of hyperbranched polymers structurally analogous to the dendrimer-like star-branched polymers by the convergent living anionic polymerization involving successive linking reaction and living anionic polymerization.[16] The resulting polymers have a less perfect structure, but offer the advantage of a convenient one-pot synthesis.

Recently, we have synthesized a series of dendrimer-like star-branched poly(methyl methacrylate)s (PMMA)s by developing a novel iterative methodology.[17,18] It involves only two reaction steps for the entire iterative reaction sequence: (a) a coupling reaction between the α-functionalized living anionic PMMA with two *tert*-butyldimethylsilyloxymethylphenyl (SMP) groups and chain-functionalized PMMA having two benzyl bromide (BnBr) termini and (b) a transformation reaction of the introduced SMP group into BnBr functionality. Since the two reactions proceeded cleanly and quantitatively, the above reaction sequence could be repeated thrice to result in the formation of dendrimer-like star-branched PMMA of third-generation. Furthermore, we have recently succeeded in synthesizing the similar dendrimer-like star-branched (PMMA) of seventh generation that is a huge macromolecule made up of 508 PMMA segments and possessing 512 SMP termini.[19] By utilizing the same methodology, structurally similar hyperbranched block copolymers comprising PMMA segments and either poly(2-hydroxyethyl methacrylate) or poly(2-(4-perfluorobutyl)ethyl methacrylate) segments could also be synthesized.[17,20] Since the synthetic procedure is based on an "arm-first" termination methodology using pre-made α-functionalized living (PMMA)s and quantitative two reactions, the resulting polymers all are well-defined in branched architecture and precisely controlled in chain length.

Herein, we propose the extension of the above-mentioned iterative methodology to the synthesis of dendrimer-like star-branched (PMMA)s of generations consisting of four branched PMMA chains at each junction. The resulting polymers will possess higher branch segment densities than those of the polymers previously reported. The effectiveness, versatity, and generality of the iterative methodology so far developed will be examined throughout the synthesis.

Experimental

Materials

All chemicals (>98% purities) were purchased from Aldrich, Japan, and used as received unless otherwise stated. Dichloromethane, acetone, MMA, THF, heptane, acetonitrile, $(CH_3)_3SiCl$, LiCl, and LiBr were purified according to the reported procedures described elsewhere.[19,21] 1,1-Bis(3-hydroxymethylphenyl)ethylene, 1,1-bis(3-*tert*-butyldimethylsilyloxymethylphenyl)ethylene (**1**), and 1,1,4,4-tetra(3-bromomethylphenyl)butane were synthesized according to our procedures previously reported.[19,22]

Mesurement

Both ^1H and ^{13}C NMR spectra were measured on a Bruker DPX300 (300 MHz for ^1H and 75 MHz for ^{13}C) in $CDCl_3$. Sice-exclusion chromatograms (SEC) were measured in THF with a TOSOH HLC-8020 at 40 °C with UV (254 nm) or refractive index detection. A calibration curve was made with six PMMA standard samples. The measurements for static light scattering (SLS) were performed with an Ohtsuka Electronics Photal SLS-600R instrument equipped with a He-Ne laser (632.8 nm) in THF at 25 °C. Berry plots were used to determine M_w values of the dendrimer-like star-branched PMMAs herein synthesized. MALDI-TOF MASS spectra were taken on a Shimazu AXIMA-CFR mass spectrometer. The sample solution (1 g/L) was prepared in THF. The matrix, 2,5-dihydroxybenzoic acid (Aldrich) (10 mg), and sodium trifluoroacetate (Aldrich) (1 mg) were dissolved in THF (1 mL). The sample solution was then mixed with 50 μL of the matrix solution.

Synthesis of 1,1-Bis(3-bromomethylphenyl)ethylene (2)

Under nitrogen, to a CH_2Cl_2 (40 mL) solution of 1,1-bis(3-hydroxymethylphenyl)ethylene (22.5 mmol) was added PBr_3 (35.0 mmol) in CH_2Cl_2 (10 mL) dropwise at 0 °C. The reaction mixture was allowed to stir at 25 °C for 1 h. After quenching with water at 0 °C and the usual work-up, flash column chromatography on silica gel (hexane/ethyl acetate, 40/1, v/v), followed by recrystallization from hexane afforded 5.60 g (15.3 mmol, 68%) of **2** as a white solid. ^1H NMR: δ 7.39–7.26 (m, 8H, aromatic), 5.51 (s, 2H, $=CH_2$), 4.49 (s, 4H, $-CH_2-Br$). ^{13}C NMR: δ 148.9, 141.8, 137.9, 128.9, 128.8, 128.6, 128.4, 115.4, 33.5.

Synthesis of DPE Derivative with Four SMP Groups, 3

Under high vacuum conditions (10^{-6} torr), a THF (29.5 mL) solution of **1** (17.8 mmol) was added to *sec*-BuLi (14.6 mmol) in heptane (14.6 mL) at −78 °C and the mixture was allowed to stand for 20 min. Then, a THF (19.7 mL) solution of **2** (6.58 mmol) was added and the reaction mixture was allowed to stand at −78 °C for 1 h. After quenching with degassed methanol, followed by removal of the solvents, the residue was purified by flash column chromatography on silica gel pre-treated with triethylamine (hexane/benzene, 50/1 ∼ 5/1, v/v) to give 8.28 g (6.57 mmol, 98%) of **3** as a colorless syrup. ^1H NMR: δ 7.38–6.41 (m, 24H, aromatic), 5.00 (s, 2H, $=CH_2$), 4.74 (s, 8H, $-CH_2-O-$), 3.46 (s, 4H, $Ph-CH_2-C-$), 1.89 (m, $-C-CH_2-CH-$), 1.49 (broad, 2H, $-CH-$), 0.91 (m, 40H, $-Si-C-(CH_3)_3$ and $-CH_2-CH_3$), 0.67 (t, 6H, $-CH_2-CH_3$), 0.40 (d, 6H, $-CH-CH_3$), 0.03 (s, 24H, $-Si-(CH_3)_2$). ^{13}C NMR: δ 150.2, 148.8, 148.7, 140.7, 140.6, 138.0, 130.8, 130.0, 127.5, 126.8, 126.5, 126.0, 123.5, 113.6, 65.2, 51.1, 45.1, 44.1, 31.1, 30.3, 26.0, 20.4, 18.4, 11.2, −5.1. MALDI-TOF-MASS: calcd for $C_{40}H_{80}O_4Si_4$, 1258.2 Da; found at 1281.8 Da ($M-Na^+$).

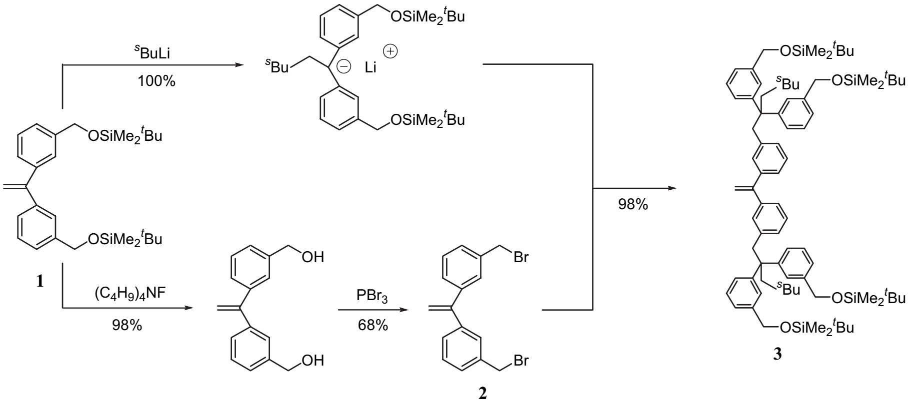
Synthesis of Dendrimer-Like Star-Branched (PMMA)s by Iterative Methodology

All the polymerizations and coupling reactions were carried out under high-vacuum conditions (10^{-6} torr) in sealed glass reactors equipped with break-seals. The transformation and re-transformation reactions were carefully performed under nitrogen. The methodology was carried out by the same procedures as those previously reported.[19] Only the difference is to use the α-functionalized living PMMA with four SMP group was always used instead of that with two SMP groups in the coupling reaction. The objective coupled polymers were isolated by fractional precipitation using benzene and methanol.

Results and Discussion

Synthesis of α-Functionalized Living PMMA with Four SMP Groups

In order to synthesize dendrimer-like star-branched polymers of generations consisting of four branched polymer chains at each junction, an α-functionalized living anionic PMMA with four SMP groups is required as a new building block in the methodology so far developed. For this synthesis, we have newly prepared a tetra-substituted DPE



Scheme 1.
Synthesis of DPE derivatives with four SMP groups.

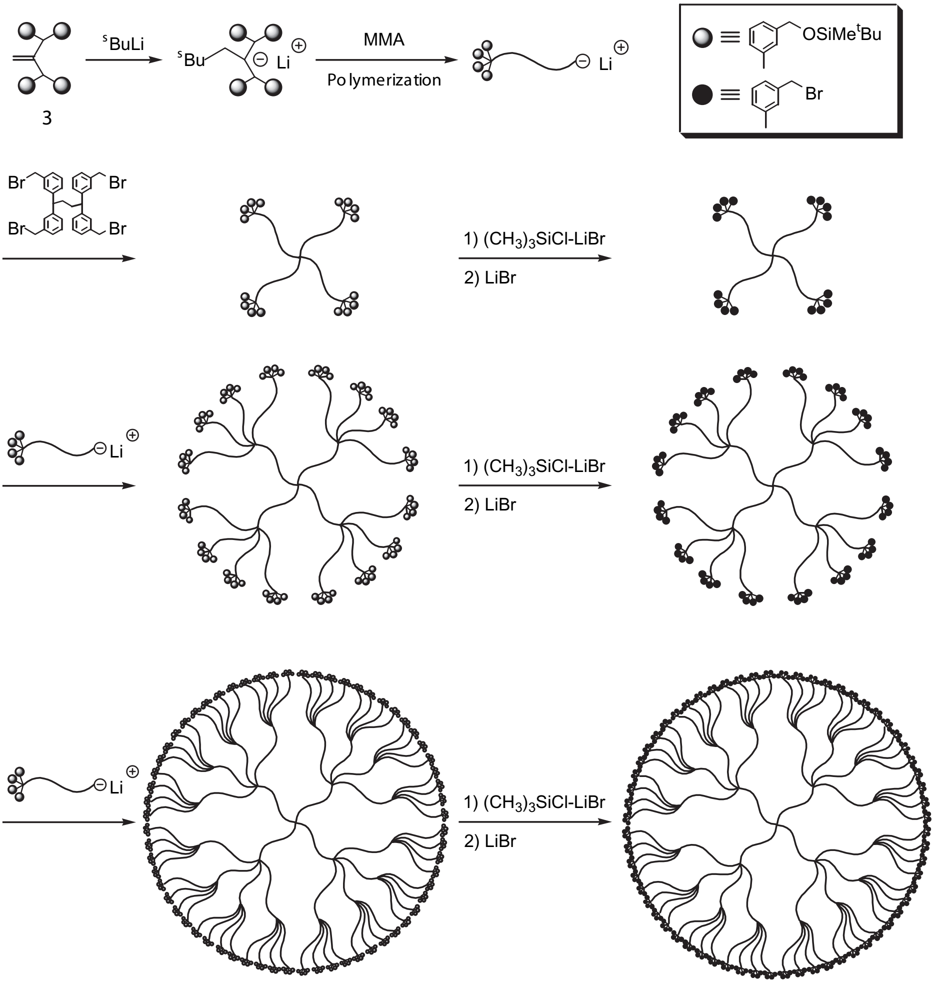
derivative with SMP groups. As illustrated in Scheme 1, 1,1-bis(3-bromomethylphenyl)ethylene (**2**) was prepared in 68% isolated yield by deprotection of **1** with $(C_4H_9)_4NF$, followed by treatment with PBr_3. At the same time, **1** was reacted with *sec*-BuLi to convert to its 1:1 adduct anion, followed by coupling with **2** to quantitatively afford the requisite DPE derivative with four SMP groups, **3**. Thus importantly, **3** could be synthesized from **1** used as a key functional material in the previous synthetic methodology.[17–20]

The **3** thus synthesized was reacted with *sec*-BuLi to convert to a 1:1 adduct anion, with which the living anionic polymerization of MMA was carried out in THF at −78 °C for 1 h. Prior to the polymerization, a 5-fold excess of LiCl was added to narrow the molecular weight distribution. A polymer yield was quantitative. SEC profile of the resulting polymer shows a sharp monomodal distribution, the M_w/M_n value being 1.02. The M_n value (10.3 K) observed by SEC is in good agreement with that calculated (10.5 K). The degree of SMP-end-functionalization measured by ^1H NMR was 4.0_1. All of the analtical results clearly show that the polymerization proceed as expected to give an α-functionalized living PMMA with four SMP groups.

Synthesis of Dendrimer-Like Star-Branched (PMMA)s of Generations Consisting of Four Branched Segments at Each Junction

The synthetic outline is illustrated in Scheme 2. In the first iteration, the α-functionalized living PMMA with four SMP groups was prepared by the above-mentioned process and coupled with 1,1,4,4-tetra(3-bromomethyphenyl)butane to afford a 4-arm star-branched PMMA functionalized with four SMP groups at each chain-end. A 2.0-fold excess of living PMMA toward each BnBr moiety was used to complete the reaction. SEC profile of the reaction mixture exhibited two sharp distinct peaks corresponding to the coupled polymer and the deactivated living PMMA used in excess. The coupling efficiency was estimated to be quantitative by comparing the two peak areas. The coupled polymer was isolated in 80% yield by fractional precipitation. It was purified by reprecipitation twice and freeze-drying and characterized by ^1H NMR, SEC, and SLS, respectively. The results are summarized in Table 1.

Since the M_n value estimated by SEC was not realiable due to its branched structure, it was determined by ^1H NMR using two resonances at 3.6 ppm for methoxy protons of the PMMA side chain



Scheme 2.
Synthesis of dendrimer-like star-branched (PMMA)s.

Table 1.
Synthesis of dendrimer-like star-branched (PMMA)s.

Type	$M_n \times 10^{-3}$			$M_w \times 10^{-3}$		M_w/M_n	Functionality[a)]		
	calcd	SEC	^{1}H NMR	calcd	SLS		calcd	SMP	BnBr
A_4	52.8	46.5	52.2	53.9	51.6	1.02	16	15.8	
$((Br)_4A)_4$	52.0	45.5	51.4			1.02	16		16.0
$(A_4\text{-}A)_4$	260	156	263	268	272	1.03	64	64.8	
$(((Br_4)A)_4\text{-}A)_4$	257	152	260			1.03	64		63.9
$(A_{16}\text{-}A_4\text{-}A)_4$	1300	522	1340	1340	1390	1.03	256	265	
$(((Br)_4A)_{16}\text{-}A_4\text{-}A)_4$	1290	510	1330			1.02	256		256

a) Estimated by ^{1}H NMR.

and 0.04 ppm for silylmethyl protons of the *tert*-butyldimethylsilyl group, respectively. The absolute M_w value was directly determined by SLS. The both values were in good agreement with those expected. Furthermore, the degree of SMP-end-functionality measured by ^1H NMR was consistent with that predicted. These results clearly indicate that the α-functionalized living PMMA with four SMP groups is coupled quantitatively with the terminator to afford the first-generation polymer referred to as **A$_4$**. It should be mentioned that **A$_4$** is actually a 4-arm star-branched PMMA, but not have a dendrimer-like star-branched architecture.

The SMP groups introduced into **A$_4$** were transformed into BnBr functionalities by treatment with $(CH_3)_3SiCl$-LiBr. Three ^1H NMR resonances at 4.66, 0.90, and 0.04 ppm characteristic to benzyl methylene protons of the silyl ether and two different methyl protons of the *tert*-butyldimethylsilyl group completely disappeared. Instead, a new resonance at 4.45 ppm for the BnBr methylene protons appeared along with a small peak (*ca.* 5%) at 4.53 ppm assignable to benzyl methylene protons of the benzyl chloride (BnCl) functionality. The BnCl was readily re-transformed into BnBr moiety by treatment with a 50-fold excess of LiBr in acetone. The SEC peak of the polymer recovered after this treatment remained unchanged in shape.

By using the **A$_4$** as a starting material, the second iterative reaction sequence was conducted under the identical conditions. A 2.0-fold excess of the α-functionalized living PMMA was coupled with **A$_4$** in THF at −40 °C for 24 h. Only two sharp SEC peaks for the coupled product and the deactivated living PMMA used in excess were observed. Neither intermediate polymer nor high molecular weight shoulder was present at all. The coupling efficiency was virtually quantitative on the basis of the two peak areas. The higher molecular weight fraction was isolated in 85% yield by fractional precipitation. The M_n and M_w values determined by ^1H NMR and SLS agreed well with those predicted (Table 1). The resulting polymer was found to have 64.4 SMP groups very close to the expected value of 64. Thus, we were successful in synthesizing the second-generation polymer, **(A$_4$-A)$_4$**, that possessed a dendrimer-like star-branched architecture comprising 20 PMMA segments and 64 SMP termini. The SMP groups were again transformed into BnBr functionalities by treatment with $(CH_3)_3SiCl$-LiBr and subsequently with LiBr under the same conditions.

With use of the second-generation brominated PMMA, **((Br)$_4$A)$_4$-A)$_4$** as a starting polymer, the third iterative process was conducted. In this synthesis, a 4.0-fold excess of the α-functionalized living PMMA was used taking the steric hindrance into consideration. After the coupling reaction was carried out in THF at −40 °C for 24 h, the reaction was terminated to precipitate the polymers in methanol. Based on the SEC trace of the polymers shown in Figure 1(A), the coupling reaction proceeded cleanly and quantitatively. The coupled polymer was isolated in 80% yield by fractional precipitation. Agreement of the molecular weights (both M_n and M_w) of the isolated polymer between predicted and measured is satisfactory as listed in Table 1. Comparison of the degrees of SMP-end-functionality expected and observed by ^1H NMR gave excellent agreement. Thus, the synthesis of the third-generation PMMA was also successful. The resulting polymer referred to as **(A$_{16}$-A$_4$-A)$_4$** is well-defined hyperbranched architecture and precisely controlled in chain length and made up of 84 PMMA segments and 256 SMP termin. Surpringly, the coupling reaction proceeded effectively and completely to link 64 PMMA segments on the second-generation PMMA.

The quantitative transformation of the SMP groups introduced into **(A$_{16}$-A$_4$-A)$_4$** to BnBr functions was required by using a 250-fold excess of $(CH_3)_3SiCl$-LiBr, followed by treatment with a 50-fold excess of LiBr. Since the resulting brominated polymer, **((Br)$_4$A)$_{16}$-A$_4$-A)$_4$**, has the same BnBr functionalities, the iterative process

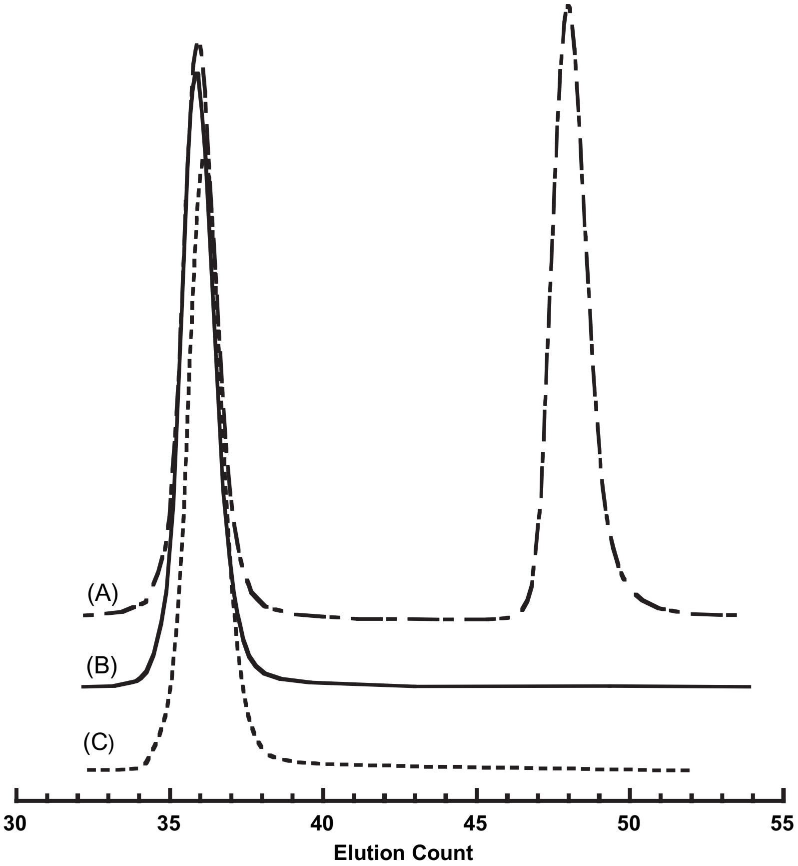


Figure 1.
SEC profiles of the reaction mixture (A), **$(A_{16}$-A_4-$A)_4$** obtained after fractional precipitation (B), and **$(((Br)_4A)_{16}$-A_4-$A)_4$** obtained after transformation reaction (C).

will be repeated to synthesize higher generation polymers, although the steric hindrance in the coupling reaction appears to become more significant even in the next fourth iterative process. The synthesis of higher generation polymers by the iterative methodology developed herein is now under investigation and the results will be reported in a forthcoming paper.

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