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Terminal-Selective Transesterification of Chlorine-Capped Poly(Methyl Methacrylate)s: A Modular Approach to Telechelic and Pinpoint-Functionalized Polymers

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Supporting Information

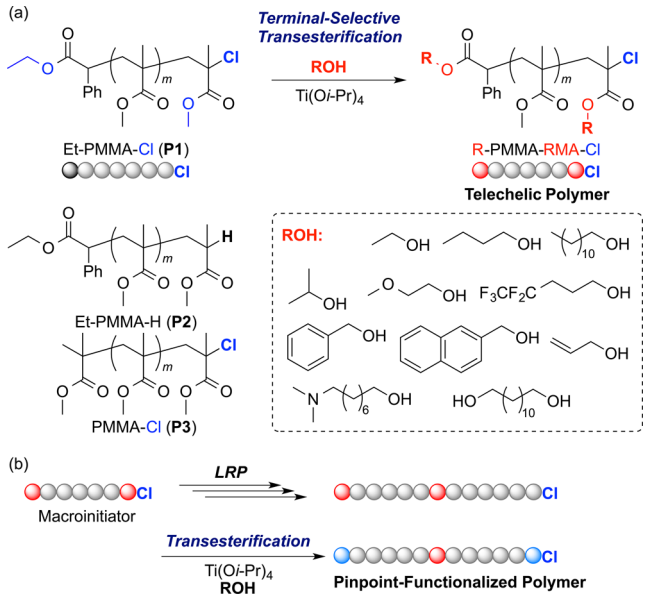
ABSTRACT: Terminal-selective transesterification of chlorine-capped poly(methyl methacrylate)s (PMMA-Cl) with alcohols was developed as a modular approach to create telechelic and pinpoint-functionalized polymers. Being sterically less hindered and electronically activated, both the α-end ethyl ester and ω-end methyl ester of PMMA-Cl were efficiently and selectively transesterified with diverse alcohols in the presence of a titanium alkoxide catalyst, while retaining the pendent esters intact, to almost quantitatively give various chlorine-capped telechelic PMMAs. In sharp contrast to conventional telechelic counterparts, the telechelic polymers obtained herein yet carry a chlorine atom at the ω-terminal to further work as a macroinitiator in living radical polymerization. The iterative process of living radical polymerization and terminal-selective transesterification successfully afforded unique pinpoint-functionalized polymers where a single functional monomer unit was introduced into the desired site of the polymer chains.

Precision functionalization of synthetic macromolecules is a key to create unique and selective functions therefrom.[1] Recent advances in precision polymerization including living radical polymerization[2−4] has allowed the synthesis of various functional polymers with a precision primary structure (e.g., molecular weight, terminal structure) and three-dimensional architectures (e.g., star and folding polymers). In particular, the selective and pinpoint functionalization of desired positions and the sequence control of monomers (functional groups) are important for site-specific functionalization;[1,4,5] the former is typically achieved via living anionic polymerization with nonhomopolymerizable 1,1-diphenylethylene derivatives.[4] As versatile and accessible approaches, the combination of selective and efficient organic reactions and precision polymerization would be promising, because they can play different roles as follows: the former may selectively modify the target segments and/or compounds, while the latter can control the molecular weight and terminal structure.[6−10]

In fact, we have originally developed concurrent tandem catalysis of living radical polymerization and metal alkoxide-mediated transesterification of methacrylates (e.g., methyl methacrylate: MMA) with alcohols (ROH) as a versatile synthetic strategy of gradient copolymers and their related sequence-regulated copolymers.[10] The key is the transesterification selective for the monomer (e.g., MMA) into RMA; uniquely, the resulting polymethacrylates comprising quaternary carbons in main chains are hardly transesterified, though polyacrylates comprising tertiary carbons (without α-methyl groups) are transesterifed.[10a] This importantly suggests that the bulky substituents adjacent to esters sterically hinder metal alkoxide catalysts from activating the carbonyl groups.[10a,11]

Given these features, we herein report terminal-selective transesterification of chlorine-capped poly(MMA)s (Et-PMMA-Cl) with a titanium alkoxide catalyst and alcohols; this serves as a novel modular approach to synthesize telechelic and pinpoint-functionalized polymers (Scheme 1). The selective functionalization is achieved without any specific functional units (e.g., activated esters or protecting groups),[12,13] due to the fact that these terminals are far less sterically hindered than the pendent esters and the ω-end terminal would be also electronically activated by the chlorine atom. It should be noted that the transesterification of Et-PMMA-Cl almost quantitatively pro-

Scheme 1. (a) Chlorine-Capped Telechelic and (b) Pinpoint-Functionalized Polymers via Terminal-Selective Transesterification of Chlorine-Capped PMMAs with Living Radical Polymerization (LRP)



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vides "chlorine-capped" telechelic poly(MMA)s (R-PMMA-RMA-Cl), in sharp contrast to the conventional telechelic polymers obtained from the transformation of an active polymer terminal via living polymerization.[14−17] Thus, the chlorine-capped telechelic polymers work as a macroinitiator in living radical polymerization. The iterative process of living radical polymerization and terminal-selective transesterification thereby affords "pinpoint-functionalized" polymers, where a single functionality may precisely be introduced into a specific site (terminal, center, midchain unit, etc.) in a macromolecule. Obviously, such a precision "pinpoint" (or position-specific) functionalization is generally difficult in radical polymerization.[1] This strategy would be further applicable to the design of various functional polymers with a precise and complex repeat-unit and functionality sequence such as periodic sequence-regulated copolymers.

A chlorine-capped PMMA [Et-PMMA-Cl (**P1**): M_n = 4200, M_w/M_n = 1.13 by size exclusion chromatography (SEC)] was first synthesized by Ru-catalyzed living radical polymerization of MMA with a ruthenium catalytic system [Ru(Ind)Cl$(PPh_3)_2$/*n*-Bu_3N] and a chloride initiator [ethyl 2-chloro-2-phenylacetate (ECPA)] in toluene at 80 °C. Confirmed by proton nuclear magnetic resonance (^{1}H NMR, Figure 1a), the PMMA almost

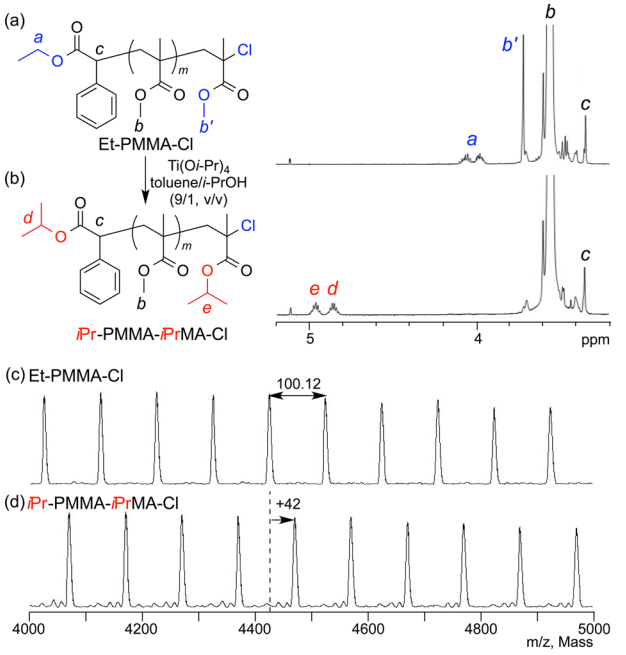

Figure 1. Terminal-selective transesterification of Et-PMMA-Cl with Ti(O*i*-Pr)$_4$ and isopropanol (*i*-PrOH): [Et-PMMA-Cl]/[Ti(O*i*-Pr)$_4$] = 30/80 mM in toluene/isopropanol (9/1, v/v) at 80 °C. ^{1}H NMR (a, b, in CD_2Cl_2 at rt) and MALDI-TOF-MS (c, d) spectra of Et-PMMA-Cl (a, c) and the product (b, d) obtained after the transesterification.

quantitatively has an α-end ethyl group (*a*: 4.1−3.9 ppm) and an ω-end chlorine (*b*′: 3.7 ppm), originating from the initiator [M_n (NMR, α) = 3800, M_n (NMR, ω) = 4000].

Then, transesterification of Et-PMMA-Cl was examined with Ti(O*i*-Pr)$_4$ in an isopropanol (*i*-PrOH)/toluene (1/9, v/v) mixture at 80 °C ([Et-PMMA-Cl]$_0$/[Ti(O*i*-Pr)$_4$]$_0$ = 30/80 mM). After 47 h, the product was analyzed by ^{1}H NMR spectroscopy and matrix assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF-MS) (Figure 1). As shown in Figure 1b, both the α-end methylene protons (*a*) and the ω-end methoxy protons adjacent to the chlorine terminal (*b*′) completely disappeared, while two kinds of isopropyl methine protons (*d*, *e*: 5.0−4.8 ppm) newly appeared. The signal intensity ratio of the isopropyl protons (*d*, *e*) to the α-end aromatic protons (7.15−7.3 ppm) was close to the calculated values, assuming that a single isopropyl unit was incorporated into both α- and ω-terminals of the PMMA chain [Yield (α-end/ω-end) = 95%/96%].

Confirmed by MALDI-TOF-MS, the product exhibited single series signals, regularly separated by the molar mass of MMA (100.12) (Figure 1d). The absolute mass of each peak was equal to that expected for the PMMA bearing an isopropyl ester at the α-end and an isopropyl methacrylate unit capped with one chlorine atom at the ω-end (*i*-Pr-PMMA-*i*-PrMA-Cl), plus a sodium ion from externally added salt for ionization. It should be noted that the product yet quantitatively carries a chlorine terminal. The mass difference between Et-PMMA-Cl (Figure 1c) and the product (Figure 1d) was 42, fully consistent with the selective transformation of the α-end ethyl and ω-end methyl groups into two isopropyl groups [mass increase: +14 (Et → *i*-Pr); +28 (MMA-Cl → *i*-PrMA-Cl)]. These results demonstrate that both α- and ω-terminal esters of Et-PMMA-Cl can be selectively transesterified to yield a chlorine-capped telechelic polymer.

For such efficient and selective terminal transesterification, it was quite important to control isopropanol content in the mixed solvents (*i*-PrOH/toluene). Over 30 vol % isopropanol mixtures with Ti(O*i*-Pr)$_4$ induced terminal cyclization via the elimination of the chlorine terminal,[18] in addition to terminal-selective transesterification, to give *i*-Pr-PMMA-*i*-PrMA with a five-membered ring terminal as a byproduct (Figure S2). The byproduct increased with increasing content of isopropanol (*i*-PrOH/toluene =3/7, 5/5, 7/3, v/v, Table 1, entries 2−4).

Effects of the terminal structures of PMMAs on Ti(O*i*-Pr)$_4$-mediated transesterification with isopropanol were investigated with three kinds of poly(MMA)s with different terminal structures: Et-PMMA-Cl (**P1**), terminal-hydrogenated Et-PMMA-H (**P2**: M_n = 6200, M_w/M_n = 1.27),[7] and PMMA-Cl with a MMA-type methyl ester α-end (**P3**: M_n = 4100, M_w/M_n = 1.11). Monitored by ^{1}H NMR, Et-PMMA-Cl and Et-PMMA-H underwent simultaneous and almost quantitative transesterification of both the α-end ethyl ester and ω-end methyl ester to give corresponding telechelic PMMAs (Figures S3 and S4, Table 1, entries 1 and 5); all of the terminal units were transesterified at equal speed. However, PMMA-Cl underwent much slower transesterification of the α-end methyl ester adjacent to the nonchlorinated quaternary carbon atom [ester-C$(CH_3)_2CH_2$−: 22% in 47 h] than that of the ω-end methyl ester (Figure S3, Table 1, entry 6). This result suggests that the efficient and selective terminal-unit transesterification of **P1** and **P2** is due to both the less steric hindrance around the α- and ω-end esters by adjacent tertiary carbons and the activation of the ω-end ester by the chlorine atom. For the α-end methyl ester in **P3**, an adjacent quaternary carbon substituent would sterically hinder the Ti(O*i*-Pr)$_4$ catalyst from activating the carbonyl oxygen, thereby reducing the reactivity of the transesterification. A similar steric effect has been reported for tertiary butyl esters:[11] e.g., *tert*-butyl methacrylate is not transesterified with Al(O*i*-Pr)$_3$,[10b] while the activation effect was in turn observed for an MMA dimer carrying one chlorine atom [H-$(MMA)_2$-Cl] (Figure S5).

We further applied various alcohols (ROH: ethanol, 1-butanol, 1-dodecanol, benzyl alcohol, 2-naphthalene methanol, 4,4,5,5,5-pentafluoro-1-pentanol, 2-methoxy ethanol, allyl alcohol, 8-

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Table 1. Terminal Transesterification with Various Alcohols[a]

entry	PMMA	alcohol	alcohol (mM)	time (h)	α-end yield[b] (%)	ω-end yield[b] (%)
1	**P1**	isopropanol	1300	47	95	96
2	**P1**	isopropanol	3900	47	>99	>99 (11)
3	**P1**	isopropanol	6500	47	>99	>99 (22)
4	**P1**	isopropanol	9100	47	>99	>99 (33)
5	**P2**	isopropanol	1300	47	91	94
6	**P3**	isopropanol	1300	47	22	90
7	**P1**	ethanol	1720	24	n.d.	>99
8	**P1**	1-butanol	1090	24	>99	>99
9	**P1**	1-dodecanol	450	24	>99	>99
10	**P1**	2-methoxy ethanol	1270	47	95	96
11	**P1**	4,4,5,5,5-pentafluoro-1-pentanol	760	47	97	98
12	**P1**	benzyl alcohol	970	47	91	92
13	**P1**	2-naphthalene methanol	1000	47	94	96
14	**P1**	allyl alcohol	1460	24	97	>99
15[c]	**P1**	8-dimethylamino-1-octanol	500	60	58	>99
16[c]	**P1**	1,12-dodecanediol	1000	60	n.d.	83

[a][PMMA]/[Ti(O*i*-Pr)$_4$] = 30/80 (entries 1−10, 12, 14) or 160 (entries 11, 13, 15, 16) mM in toluene/alcohol at 80 °C: Et-PMMA-Cl (**P1**); Et-PMMA-H (**P2**); PMMA-Cl (**P3**). [b]Yield or conversion (entry 16) determined by ^{1}H NMR. The value in parentheses: cyclized terminal. n.d.: not determined. [c]Reactions were conducted with molecular sieves 4A (0.33 g/mL in solution).

dimethylamino-1-octanol, 1,12-dodecanediol) to the terminal-selective transesterification of Et-PMMA-Cl to synthesize corresponding chlorine-capped telechelic polymers (Table 1, entries 7−16, Figures 2, S6−S8). Here, prior to the transesterification, Ti(O*i*-Pr)$_4$ was first mixed with the alcohols (ROH) at 80 °C for 1 h and the mixture was evaporated in situ to form the corresponding Ti(OR)$_n$. The Ti(OR)$_n$ (80−160 mM) was utilized for the transesterification of Et-PMMA-Cl in ROH/toluene (1/9, v/v) at 80 °C.

Confirmed by ^{1}H NMR and MALDI-TOF-MS, ethanol, 1-butanol, 1-dodecanol, benzyl alcohol, 2-naphthalene methanol, 4,4,5,5,5-pentafluoro-1-pentanol, 2-methoxy ethanol, and allyl alcohol efficiently gave the corresponding chlorine-capped telechelic PMMAs (R-PMMA-RMA-Cl) in high yield (>90%). 8-Dimethylamino-1-octanol and 1,12-dodecanediol also induced terminal-selective transesterification, though the yield of the telechelic PMMAs was lower than that of the others probably owing to the interaction of the amino group to the Ti catalyst and low solubility of alcohol (1,12-dodecanediol). The preferential ω-end transesterification with these alcohols would be due to the activation by the terminal chlorine. The titanium-catalyzed transesterification of Et-PMMA-Cl is thus quite efficient and versatile to produce chlorine-capped telechelic polymers.

Pinpoint-functionalized polymers can be obtained with chlorine-capped telechelic PMMAs. Typically, Et-PMMA-EMA-Cl (M_n = 2700, M_w/M_n = 1.14), obtained from the transesterification of Et-PMMA-Cl with ethanol, was employed as a macroinitiator for the Ru(Ind)Cl(PPh$_3$)$_2$/*n*-Bu$_3$N-catalyzed living radical polymerization of MMA to give well-controlled Et-PMMA-EMA-PMMA-Cl (M_n = 5800, M_w/M_n = 1.08, Figure S9a). The ^{1}H NMR spectrum of the product clearly showed the

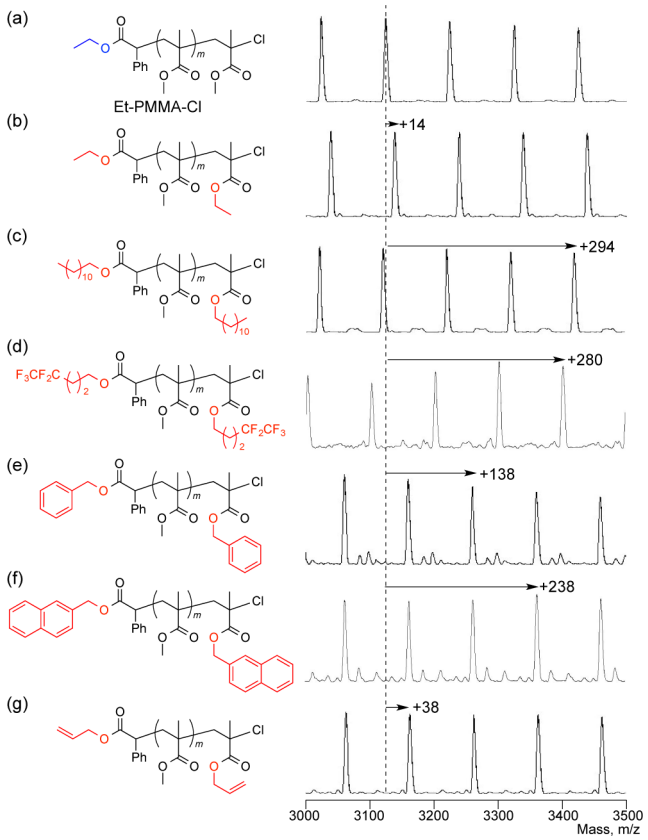

Figure 2. MALDI-TOF-MS spectra of chlorine-capped telechelic polymers (R-PMMA-RMA-Cl) obtained from the transesterification of Et-PMMA-Cl (a) with alcohols [ROH: (b) EtOH; (c) 1-dodecanol; (d) 4,4,5,5,5-pentafluoro-1-pentanol; (e) benzyl alcohol; (f) 2-naphthalene methanol; (g) allyl alcohol]: [Et-PMMA-Cl]/[Ti(O*i*-Pr)$_4$] = 30/80 or 160 (d, f) mM in toluene/ROH (9/1, v/v) at 80 °C.

ω-end methyl ester protons (c′) adjacent to the chlorine atom (Figure 3b). The subsequent titanium-mediated transesterification of the product with allyl alcohol successfully yielded the pinpoint-functionalized telechelic polymers carrying an olefin at the α-end, a single ethyl pendant at the middle point, and a chlorine-capped allyl methacrylate unit (olefin) at the ω-end (olefin-PMMA-EMA-PMMA-Allyl MA-Cl: M_n = 5900, M_w/M_n = 1.09, Figures 3 and S9b).

In addition, various pinpoint-functionalized block copolymers were also efficiently obtained from the polymerization of dodecyl methacrylate (DMA), poly(ethylene glycol) methyl ether methacrylate (PEGMA), and a perfluoroalkyl methacrylate (13FOMA) with a chlorine-capped telechelic PMMA (*i*-Pr-PMMA-*i*-PrMA-Cl, Chart 1, Figure S11). Such block copolymers would be quite useful for the selective interface functionalization of the microphase-separated materials and core−shell nanocapsules.

This iterative strategy is applicable to the design of many kinds of pinpoint-functionalized and periodic sequence-regulated polymers (Figures S10, 11) with the following advantages: (1) versatile and easy design of functional units with diverse alcohols; (2) precision, on-demand, and site-specific functionalization of polymer chains via living radical polymerization.

In conclusion, we created a modular approach to synthesize chlorine-capped telechelic and pinpoint-functionalized polymers via the Ti-mediated terminal-selective transesterification of chlorine-capped PMMAs in conjunction with ruthenium-

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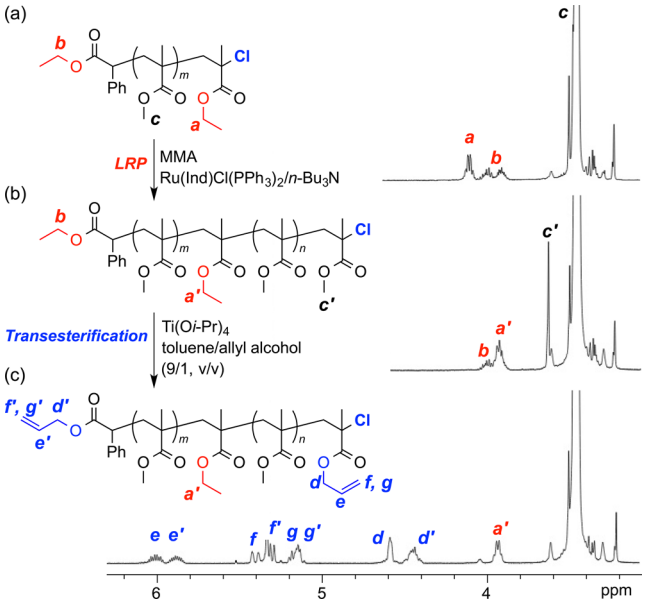
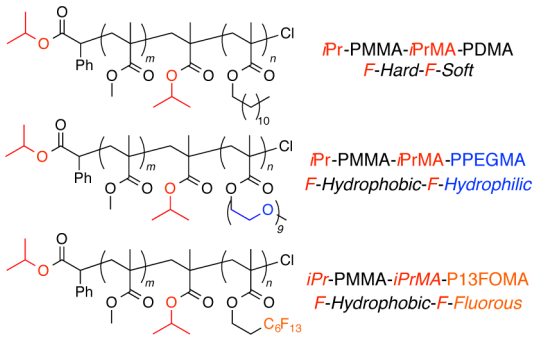


Figure 3. A pinpoint-functionalized telechelic polymer (olefin-PMMA-EMA-PMMA-Allyl MA-Cl) via the iterative process of living radical polymerization (LRP) and terminal-selective transesterification. LRP: [MMA]/[Et-PMMA-EMA-Cl]/[Ru(Ind)Cl(PPh_3)$_2$]/[n-Bu_3N] = 2000/10/1/10 mM in toluene at 80 °C. Transesterification: [Et-PMMA-EMA-PMMA-Cl]/[Ti(Oi-Pr)$_4$] = 10/80 mM in toluene/allyl alcohol (9/1, v/v) at 80 °C.

Chart 1. Pinpoint-Functionalized Block Copolymers



catalyzed living radical polymerization. With common and diverse alcohols, various functional groups can be efficiently and easily introduced into the desired position of polymethacrylates. Importantly, chlorine-capped telechelic polymers worked as a macroinitiator in living radical polymerization, opening a new avenue to pinpoint-functionalized polymers. Therefore, the terminal-selective transesterification developed herein would be one of the most innovative strategies to design functional polymeric materials with a precision primary structure toward intriguing functions.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/jacs.6b01239.

Experimental details, SEC curves, NMR spectra, and MALDI-TOF-MS spectra of products (PDF)

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Notes

The authors declare no competing financial interest.

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