Supporting Information

Selective Radical Addition with Designed Hetero-Bifunctional Halide: A Primary Study toward Sequence-Controlled Polymerization upon Template Effect

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Experimental

Materials

2-Hydroxybenzyl alcohol (2-HBA; Aldrich; 99%), 2-chloroethyl vinyl ether (CEVE; Tokyo Kasei; >97%), potassium hydroxide (Wako; >85%), and *n*-Bu_4NBr (Tokyo Kasei; >99%) were used as received. α-Chlorophenyl acetyl chloride (Aldrich; 90%) was distilled under reduced pressure before use. Triethylamine was dried overnight over calcium chloride and distilled before use.

Di-*tert*-butyl {*N*-[2-(vinyloxy)ethyl]imido}dicarboxylate (BocVE) was prepared according to literature.[1] Chromatography-grade dichloromethane (CH_2Cl_2; solvent) and toluene (solvent) were purified to moisture- and oxygen-free by passing through a purification column (Solvent Dispensing System; Glass Contour) before use. $SnCl_4$ (1.0 M in CH_2Cl_2; Aldrich), *n*-Bu_4NCl (Tokyo Kasei; >98%), $LiBH_4$ (2.0 M in THF; Aldrich), and HCl (4.0 M in 1,4-dioxane) were used as received.

Methacrylic acid (MAA; Tokyo Kasei; >99%) was dried overnight over calcium chloride and distilled under reduced pressure before use. Methyl methacrylate (MMA; Tokyo Kasei; >99%) was dried overnight over calcium chloride and distilled twice from calcium hydride under reduced pressure before use. $RuCl(Ind)(PPh_3)_2$ (Strem; >98%) was used as received and handled in a glove box under a moisture- and oxygen-free argon atmosphere (H_2O < 1 ppm; O_2 < 1 ppm). Ethyl 2-chloro-2-phenylacetate (ECPA; Aldrich; >97%) was distilled under reduced pressure before use. Butylamine (*n*-$BuNH_2$; Tokyo Kasei; >99%) was degassed by bubbling dry nitrogen for more than 15 min before use. Tetralin (1,2,3,4-tetrahydronaphtalene; ^1H NMR internal standard for MAA and MMA) was dried overnight over calcium chloride and doubly distilled from calcium hydride under reduced pressure before use.

{2-[2-(Vinyloxy)ethoxy]phenyl}methanol (**3**)

2-HBA (10 g, 80 mmol) was dissolved in 15 ml of KOHaq (22 wt%). To the solution were added CEVE (12.2 mL, 120 mmol) and *n*-Bu_4NBr (0.54 g; 1.66 mmol), and the mixture was heated to reflux for 24 h. The reaction mixture was diluted with CH_2Cl_2 (100 mL), washed with water for three times, and evaporated to dryness under reduced pressure. The crude product was purified by silica-gel column chromatography [eluent: chloroform/MeOH, 100/3(v/v)]. The isolated product was dissolved in CH_2Cl_2 (300 mL), dried with $NaSO_4$

overnight, and evaporated to dryness under reduced pressure to give **3**: yield, 68 %. ^{1}H NMR ($CDCl_3$): δ 7.26 (m, 2H, Ar-*H*), 6.96 (t, 1H, Ar-*H*), 6.90 (d, 1H, Ar-*H*), 6.52 (dd, 1H, CH_2=C*H*-), 4.67 (d, 2H, Ar-CH_2-OH), 4.25-4.06 (m, 6H, CH_2=CH-O-CH_2-CH_2-), 2.75 (t, 1H, -O*H*). ^{13}C NMR ($CDCl_3$): δ 156.62, 129.84, 129.03, 128.89, 121.29, 111.77 (-O-C_6H_4-CH_2-), 151.73 (CH_2=*C*H-O-), 87.38 (*C*H_2=CH-), 66.78 (CH_2=CH-O-CH_2-*C*H_2-O-), 66.33 (CH_2=CH-O-*C*H_2-CH_2-O-), 62.16 (Ar-*C*H_2-OH).

2-[2-(Vinyloxy)ethoxy]benzyl 2-chloro-2-phenylacetate (4)

To a solution of **3** (10.5 g, 54.3 mmol) and triethylamine (9.86 mL, 81.4 mmol) in dry THF (280 mL) at 0 °C was slowly added α-chlorophenyl acetyl chloride (8.14 ml, 51.5 mmol) dropwise under dry argon. The solution was stirred at 0 °C for 30 min and then at room temperature for an additional 3 h. The reaction was quenched with 250 mL of water. The quenched solution was diluted with CH_2Cl_2 (500 mL), washed with water for three times, and evaporated under reduced pressure. The crude product was purified by silica-gel column chromatography (eluent: chloroform). The product was dissolved in CH_2Cl_2 (300 mL), dried with $NaSO_4$ overnight, and evaporated to dryness under reduced pressure to give **4**: yield, 73 %. ^{1}H NMR ($CDCl_3$): δ 7.50 (m, 2H, Ar-*H*), 7.36 (m, 3H, Ar-*H*), 7.30-7.22 (m, 2H, Ar-*H*), 6.94-6.88 (m, 2H, Ar-*H*), 6.48 (dd, 1H, CH_2=C*H*-), 5.41 [s, 1H, Ar-C*H*(Cl)-CO], 5.28 (q, 2H, Ar-CH_2-O), 4.23 (dd, 1H, *cis*CH_2=CH-), 4.15 (t, 2H, Ar-O-CH_2-), 4.06 (dd, 1H, *trans*CH_2=CH-), 3.94 (t, 2H, CH_2=CH-O-CH_2-). ^{13}C NMR ($CDCl_3$): δ 168.1 [-O-*C*O-CH(Cl)-], 156.5, 135.8, 129.8, 129.7, 129.2, 128.7, 128.0, 123.8, 120.9, 111.7 (-C_6H_4-O-CO-CH(Cl)-C_6H_5), 151.7 (CH_2=*C*H-O-), 87.1 (*C*H_2=CH-), 66.8 (-CH_2-*C*H_2-O-C_6H_4-), 66.4 (CH_2=CH-O-*C*H_2-), 63.6 [-CO-*C*H(Cl)-C_6H_5], 59.1 (-C_6H_4-*C*H_2-O-).

2-[2-(1-Chloroethoxy)ethoxy]benzyl 2-chloro-2-phenylacetate (1)

Compound **1** was prepared by bubbling dry HCl gas into a CH_2Cl_2 solution of **4**, as reported.[2]

Precursor (5) of the Template Initiator

Living cationic "addition" of BocVE was carried out under dry argon in baked glass flasks equipped with a three-way stopcock. The reaction was initiated by adding a solution of $SnCl_4$/*n*-Bu_4NCl (in CH_2Cl_2) into a mixture of **1** and BocVE in CH_2Cl_2 at -78 °C by a dry syringe ($[\mathbf{1}]_0$ = 10 mM; $[BocVE]_0$ = 50 mM; $[SnCl_4]_0$ = 10 mM; $[n\text{-}Bu_4NCl]_0$ = 5.0 mM). After an hour, $LiBH_4$ (3 equiv. for **1**) was added, and the reaction mixture was stirred at room temperature for an additional 30 min, followed by addition of water was to decompose the residual $LiBH_4$. The quenched reaction mixture was diluted with *n*-hexane, washed with water, evaporated under reduced pressure, and finally vacuum dried: crude **5** (100% conversion). The crude product was further purified by preparative size-exclusion chromatography (column, Shodex KF-5001; eluent, THF): isolated yield, 60 %. ^{1}H NMR ($CDCl_3$): δ 7.48 (m, 2H), 7.36 (m, 3H), 7.30-7.18 (m, 2H), 6.89 (m, 2H), 5.39 (s, 1H), 5.24 (q, 2H), 4.03 (m, 2H), 3.75-3.50 (m, 9H), 1.74-1.63 (m, 2H), 1.48 (s, 18H), 1.15 (d, 3H). ^{13}C NMR ($CDCl_3$): δ 168.30, 156.87, 152.81, 136.00, 129.87, 129.59, 129.35, 128.92, 128.16, 123.77, 120.72, 111.75, 82.33, 73.22, 69.05, 67.98, 67.70, 66.98, 63.77, 59.26, 45.57, 36.95, 28.19, 19.94. A representative ^{1}H NMR spectrum is shown in Figure S1.

Template Initiator (2).

The precursor **5** was treated with HCl (4 M in 1,4-dioxane; 200 equiv. to the Boc group in **5**) for 24 h at room

temperature with stirring. The product was isolated by evaporation, dissolved in 1,4-dioxane, treated with $NaHCO_3$ aqueous solution for neutralization, and then isolated by evaporation. Chloroform was added to the product and the soluble part was isolated by filtration. Then the filtrate was evaporated to dryness to obtain **2**: yield, 89 %. ^{1}H NMR ($CDCl_3$): δ 7.48 (m, 2H), 7.34-7.18 (m, 5H), 6.89 (m, 2H), 5.40 (s, 1H), 5.30 (m, 2H), 4.01(m, 2H), 3.72-3.48 (m, 7H), 2.98 (s, 2H), 1.69 (m, 2H), 1.13 (m, 3H). ^{1}H NMR spectrum was shown in Figure S1. LR MS (ESI) (*m/z*): $[M + H]^+$ calcd for $C_{23}H_{30}ClNO_5$, 436.18; found, 436.0.

Radical Addition

The reaction was carried out under dry argon in baked and sealed glass tubes. A typical example with the template initiator **2** is given below: In a 50-mL round-bottomed flask was placed **2** (0.085 g), and toluene (3.42 mL), tetralin (0.100 mL), solutions of MAA (1 M in toluene; 0.195 mL) and MMA (1 M in toluene; 0.195 mL) were added sequentially in this order at room temperature under dry argon. The resulting mixture was totally transferred by syringe under dry argon to a 50-mL round-bottomed flask containing RuCl(Ind)(PPh_3) (12.1 mg). The total volume of the reaction mixture was thus 3.90 mL. Immediately after mixing, aliquots (0.40 mL each) of the solution were injected into baked glass tubes, which were then sealed and placed in an oil bath kept at 80 °C. At predetermined intervals, the reaction was terminated by cooling the reaction mixtures to –78 °C. Monomer conversion was determined from the concentration of residual monomer measured by ^{1}H NMR with tetralin as an internal standard.

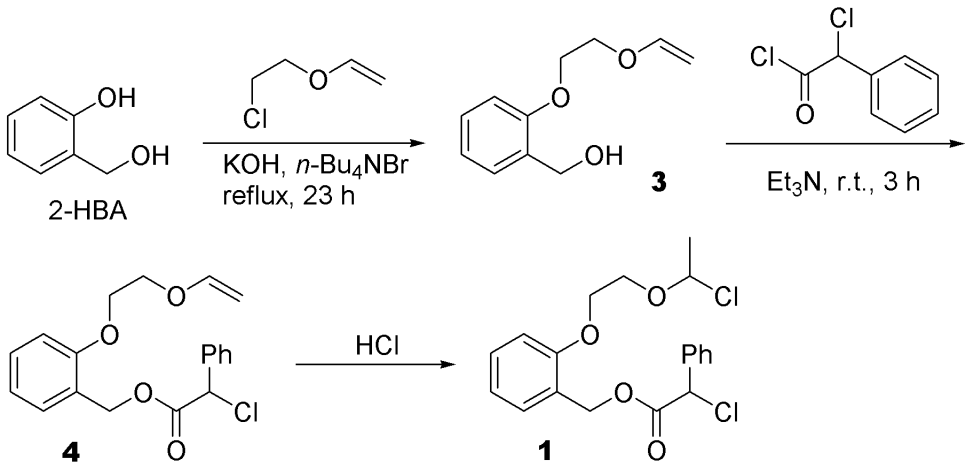
Measurements

^{1}H NMR spectra were recorded in $CDCl_3$ at room temperature on a JEOL JNM-LA500 spectrometer, operating at 500.16 MHz. Electrospray-ionization mass spectra (ESI-MS) were measured on a Waters Quattro micro API.

References

(1) Shohi, H.; Sawamoto, M.; Higashimura, T. *Macromolecules* **1992,** *25,* 58.

(2) Higashimura, T.; Kamigaito, M.; Kato, M.; Hasebe, T.; Sawamoto, M. *Macromolecules* **1993,** *26,* 2670.



Scheme S1. Synthesis of a hetero bifunctional halide, **1.**

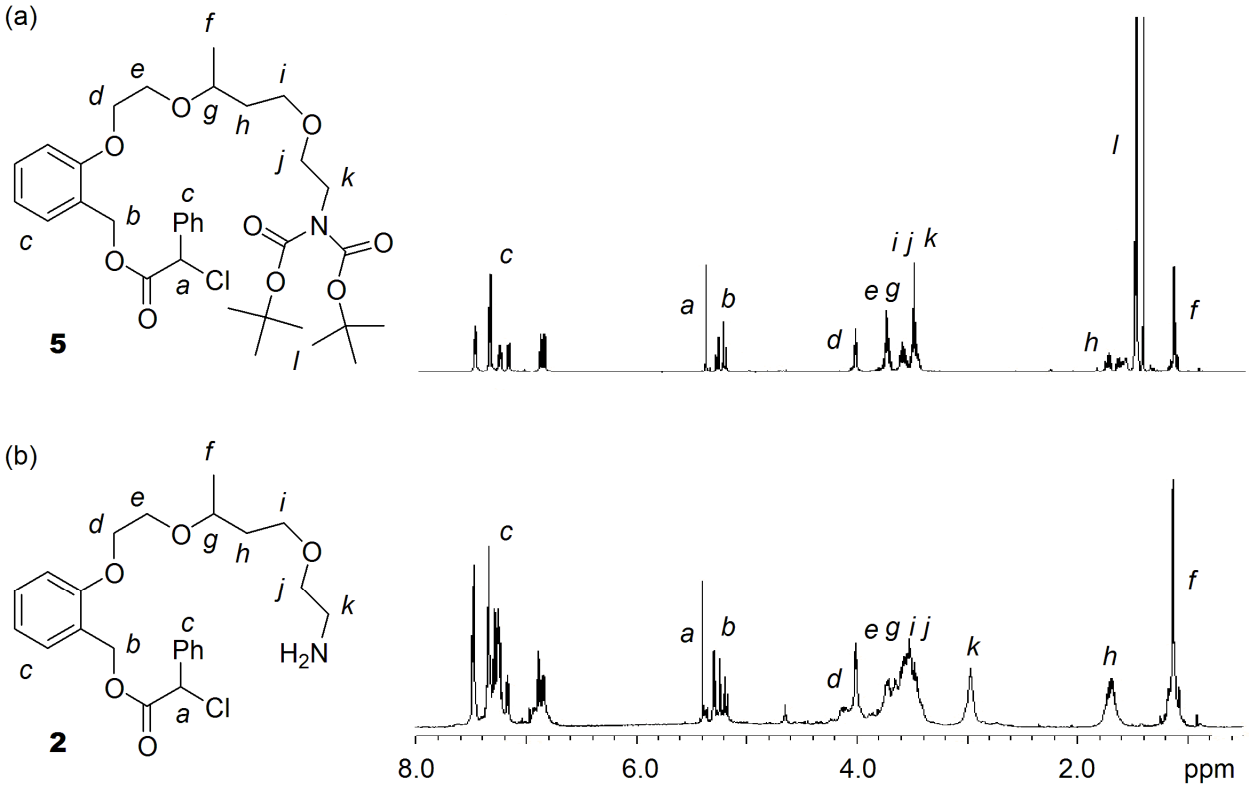


Figure S1. ^{1}H NMR spectra (in $CDCl_3$) of (a) the precursor halide, **5**, and (b) the template halide, **2**.

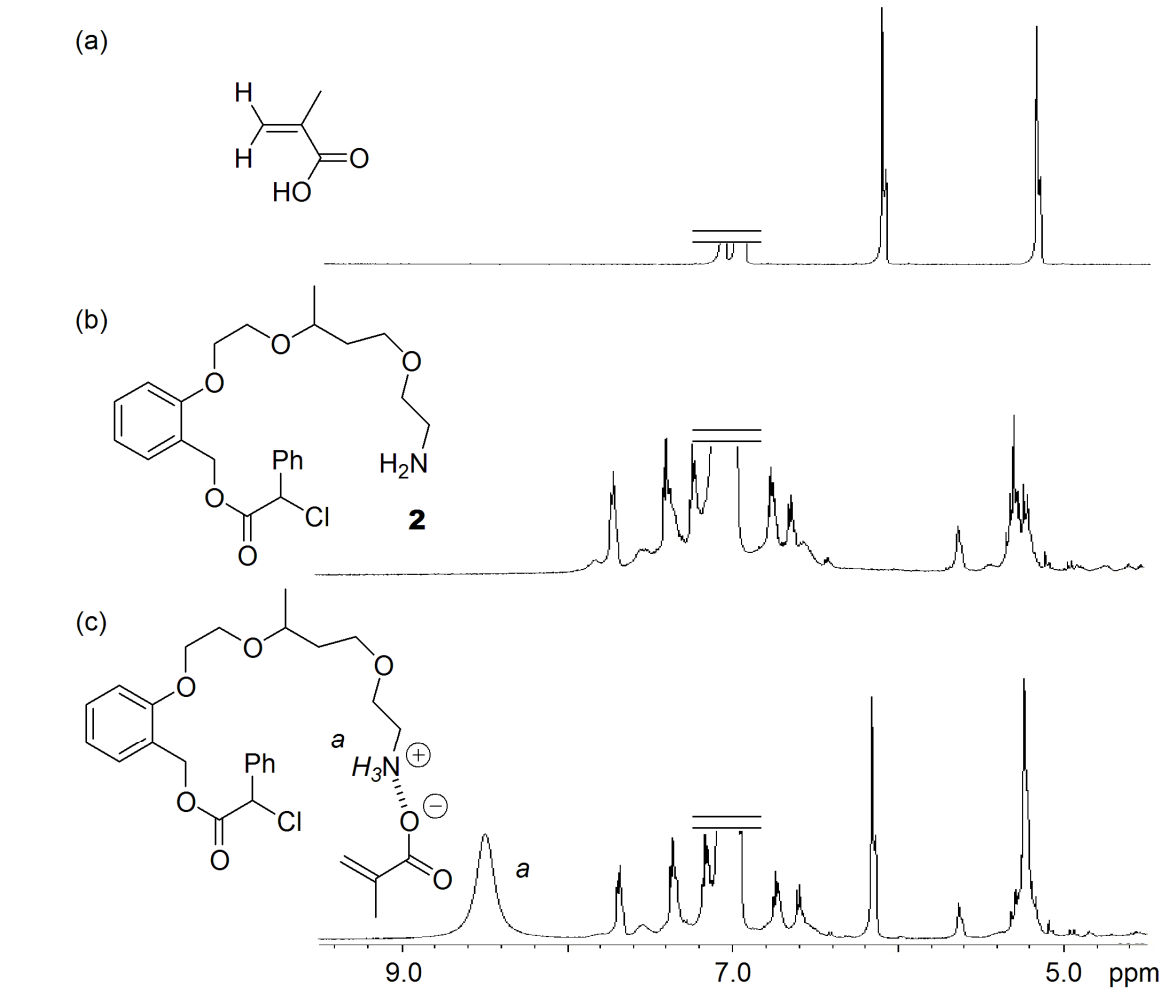


Figure S2. ^{1}H NMR spectra of MAA with amine-template halide (**2**) in toluene-d_8 at room temperature: [pendent amine] = [MAA] = 100 mM.

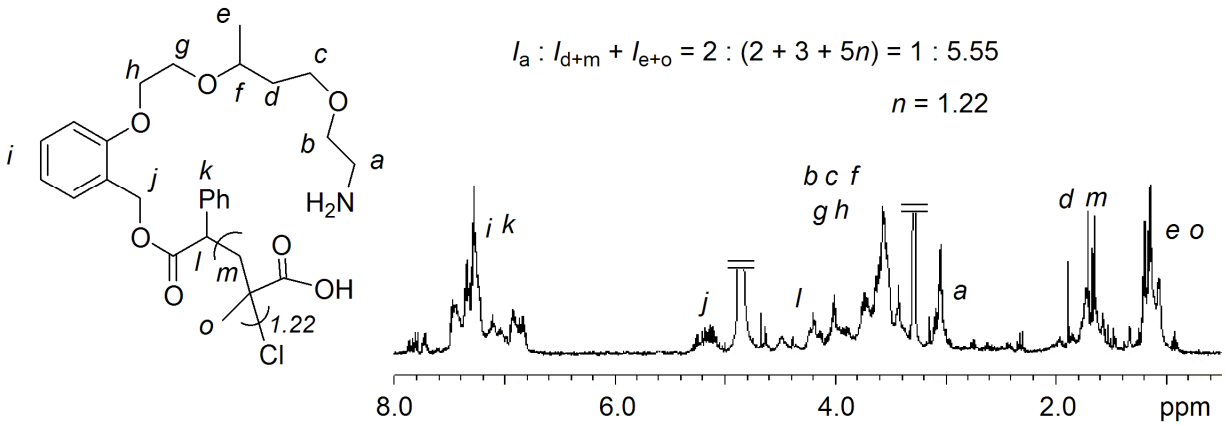


Figure S3. ^{1}H NMR spectra (in CD_3OD) of the product obtained by template initiator-assisted radical addition of MAA in toluene at 80 °C: $[MAA]_0$ = 100 mM; $[\mathbf{2}]_0$ = 100 mM; $[RuCl(Ind)(PPh_3)_2]_0$ = 4.0 mM. The average number of MAA units per halide was calculated from the integral ratio of *a*, *d*, *e*, *m*, and *o*.

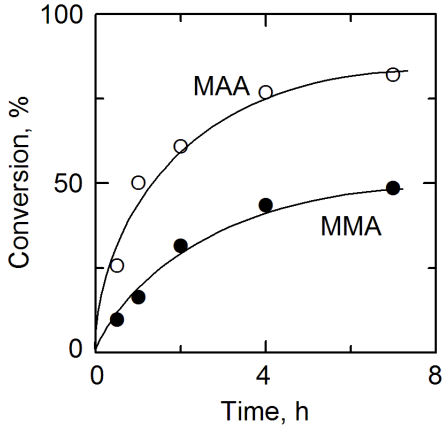


Figure S4. Time-conversion curve of competing radical addition of MAA and MMA with a non-template initiator (ECPA) in toluene at 80 °C: $[MAA]_0$ = 50 mM; $[MMA]_0$ = 50 mM; $[ECPA]_0$ = 50 mM; $[n\text{-}BuNH_2]_0$ = 50 mM; $[RuCl(Ind)(PPh_3)_2]_0$ = 4.0 mM.

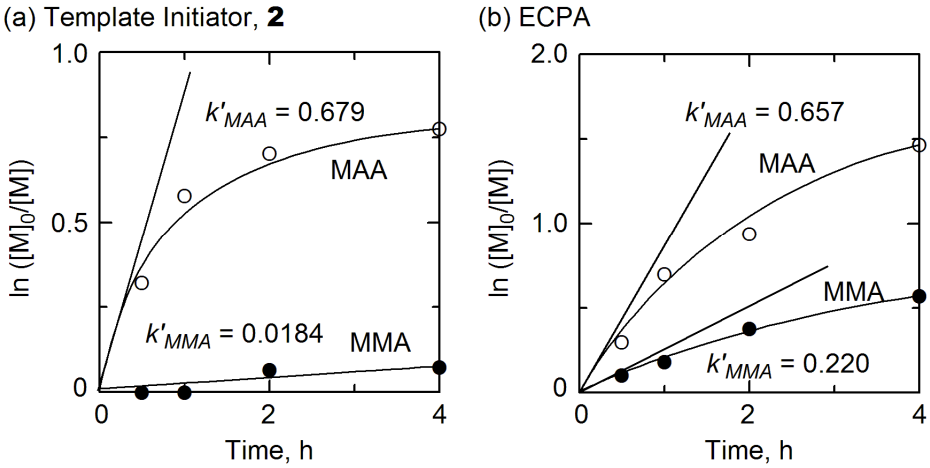


Figure S5. Kinetic analysis of competing radical addition of MAA and MMA in toluene at 80 °C: $[MAA]_0$ = 50 mM; $[MMA]_0$ = 50 mM; $[RuCl(Ind)(PPh_3)_2]_0$ = 4.0 mM; (a) [**2**]$_0$ = 50 mM, (b) $[ECPA]_0$ = 50 mM; $[n\text{-}BuNH_2]_0$ = 50 mM.

Table S1. Template-assisted competing radical addition of MAA and MMA with concentration of 100 mM.[a]

entry	halide/additive	solvent	k'_{MAA} (h^{-1})	k'_{MMA} (h^{-1})	Selectivity[b]	template effect[c]
1	**2**	toluene	0.857	0.172	4.98	1.49
2	ECPA/*n*-$BuNH_2$		1.62	0.485	3.34	
3	**2**	THF	0.251	0.0897	2.80	2.15
4	ECPA/*n*-$BuNH_2$		0.463	0.357	1.30	
5	**2**	dichloroethane	0.254	0.0781	3.25	1.43
6	ECPA/*n*-$BuNH_2$		0.862	0.379	2.27	
7	**2**	EtOH	0.324	0.183	1.77	1.95
8	ECPA/*n*-$BuNH_2$		0.454	0.500	0.908	

[a] Reaction conditions: $[MAA]_0$ = 100 mM, $[MMA]_0$ = 100 mM, $[halide]_0$ = 100 mM $[n\text{-}BuNH_2]_0$ = 0 or 100 mM, $[RuCl(Ind)(PPh_3)_2]_0$ = 4.0 mM at 80 °C. [b] [Selectivity] = k'_{MAA}/k'_{MMA}. [c] The ratio of Selectivity between the template system and the corresponding non-template one; [Template Effect] = $[Selectivity]_{\mathbf{2}}/[Selectivity]_{ECPA}$.

Table S2. Template-assisted competing radical addition of MAA and MMA with concentration of 50 mM.[a]

entry	initiator/additive	solvent	k'_{MAA} (h^{-1})	k'_{MMA} (h^{-1})	Selectivity[b]	Template Effect[c]
1	**2**	toluene	0.679	0.0184	36.9	12.3
2	ECPA/*n*-$BuNH_2$		0.657	0.220	2.99	
3	**2**	THF	0.182	0.0375	4.85	4.11
4	ECPA/*n*-$BuNH_2$		0.511	0.430	1.18	
5	**2**	dichloroethane	0.575	0.338	1.70	1.34
6	ECPA/*n*-$BuNH_2$		0.481	0.378	1.27	
7	**2**	EtOH	0.365	0.332	1.10	1.28
8	ECPA/*n*-$BuNH_2$		0.570	0.663	0.859	

[a] Reaction conditions: $[MAA]_0$ = 50 mM, $[MMA]_0$ = 50 mM, $[halide]_0$ = 50 mM $[n\text{-}BuNH_2]_0$ = 0 or 50 mM, $[RuCl(Ind)(PPh_3)_2]_0$ = 4.0 mM at 80 °C. [b] [Selectivity] = k'_{MAA}/k'_{MMA}. [c] The ratio of Selectivity between the template system and the corresponding non-template one; [Template Effect] = $[Selectivity]_{\mathbf{2}}/[Selectivity]_{ECPA}$.