

Highly Controlled Living Radical Polymerization through Dual Activation of Organobismuthines**

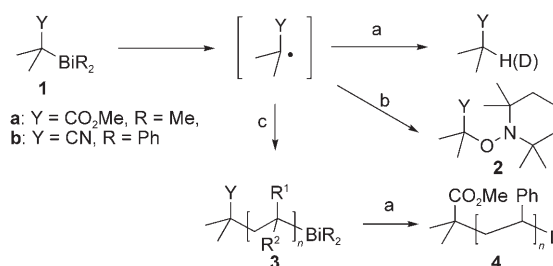
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Synthetic radical chemistry of Group 16 and 17 heteroatom compounds, such as organoselenides, tellurides, bromides, and iodides, has been the subject of intensive research because of their ability to generate carbon-centered radicals under mild conditions.^[1] In contrast, the synthetic radical chemistry of Group 15 heteroatom compounds is virtually unknown. We recently reported that organostibines are excellent precursors for carbon-centered radicals and promote highly controlled living radical polymerization.^[2–4] The results prompted us to examine radical reactions involving Group 15 heteroatom compounds other than organostibines.

The key feature of organostibines in radical chemistry is their ability to undergo organostibanyl group-transfer (GT) reactions with radicals to generate new carbon-centered radicals.^[3a,b] Although organotellurides and iodides have been reported as being the most reactive heteroatoms towards the GT and atom-transfer (AT) reactions so far,^[5–7] our results show that organostibines are more reactive than these heteroatom compounds. The superior transfer ability leads to higher reaction efficiencies and controls in GT and AT additions to alkynes and alkenes,^[5a] such as living radical polymerization.^[8] Furthermore, GT and AT reactions are faster with heteroatoms lower on the periodic table.^[6a] Therefore, we have been interested in the reactivity of organobismuthines. We report herein that organobismuthines are indeed excellent precursors for carbon-centered radicals

and promote highly controlled living radical polymerization; the level of control in organobismuthine-mediated living radical polymerization (BIRP) is considerably higher than that in organostibine-, tellurium-, and iodine-mediated radical polymerizations (SBRP,^[3] TERP,^[9] and IRP,^[10] respectively). Although several examples involving the generation of radicals from organobismuthines have been reported,^[11] this is the first example of the use of them in synthetic radical chemistry.

A carbon-centered radical was generated from **1a** (Y = CO₂Me, R = Me) through a tributyltin hydride mediated reduction, which was performed at 80 °C for 1 hour to give methyl 2-methylpropionate in quantitative yield (Scheme 1).



Scheme 1. Reactivities of organobismuthine **1**. a) Bu₃SnH(D) (1.1 equiv), C₆D₆, 80 °C, 1 h, 100%. b) TEMPO (1.0 equiv), C₆D₆, 80 °C, 1 h, 83% (92% based on conversion). c) See Table 1 and main text.

When tributyltin deuteride was used, the corresponding deuterated product was formed. The rates of the reduction were not affected much by the presence of 0.1 equivalents of 2,2'-azobisisobutyronitrile (AIBN, a radical initiator) or 2,2,6,6-tetramethylpiperidinyloxy free radical (TEMPO, a radical inhibitor). When a stoichiometric amount of TEMPO was used, the corresponding TEMPO adduct **2a** was formed in 92% conversion. These results indicate that the corresponding carbon-centered radical is generated from **1a** by C–Bi-bond homolysis under mild thermal conditions.

The bulk polymerization of styrene was next examined by heating a solution of **1a** and styrene (100 equiv) at 100 °C for 4 hours. Polystyrene with a predetermined number-average molecular weight (M_n [exptl] = 10 500, M_n [theor] = 10 100 from the ratio of styrene/**1a**) and a low polydispersity index (PDI = M_w/M_n = 1.07) was obtained in quantitative yield (Table 1, entry 1). This result is in sharp contrast to those of TERP^[9a] and SBRP^[2a] which require 15–48 h at 100–110 °C and give PDI values of 1.14–1.15. Mediator **1b** also sufficiently controlled the polymerization (Table 1, entry 2). Polymerization occurred at 60 °C in the presence of AIBN

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Table 1: Organobismuthine-mediated living radical polymerization.^[a]

Entry	Monomer ^[b] (equiv)	Promoter	Conditions [°C/h]	Conv. ^[c] [%]	M_n ^[d]	PDI ^[d]
1	St (100)	1a	100/4	99	10500	1.07
2	St (100)	1b	100/1	85	10900	1.08
3	St (100)	1a ^[e]	60/18	100	10500	1.09
4	St (200)	1a	100/8	96	20100	1.09
5	St (500)	1a	100/16	97	49500	1.12
6	St (1000)	1a	100/24	98	86900	1.21
7	MMA (100)	1a	100/3	99	10800	1.10
8	MMA (500)	1a	100/4	93	54300	1.11
9	MMA (1000)	1a	100/5	100	107200	1.14
10	BA (100)	1a ^[e]	60/3	97	11000	1.10
11	BA (500)	1a ^[e]	60/8	95	52000	1.11
12	BA (1000)	1a ^[e]	60/8	98	121900	1.20
13 ^[f]	NIPAM (100)	1a ^[e]	60/2	94	12200	1.10
14 ^[f]	NIPAM (500)	1a ^[e]	60/8	94	62000	1.10
15 ^[f]	NIPAM (1000)	1a ^[e]	60/16	93	98700	1.15
16	NVP (100)	1a ^[e]	60/1	94	11100	1.06
17	NVP (500)	1a ^[e]	60/2	100	60000	1.12

[a] A mixture of **1** and monomer was heated under a nitrogen atmosphere. [b] St = styrene, MMA = methyl methacrylate, BA = *n*-butyl acrylate, NIPAM = *N*-isopropyl acrylamide, NVP = *N*-vinylpyrrolidone. [c] Monomer conversion was determined by ¹H NMR. [d] The number-average molecular weight (M_n) and polydispersity index ($PDI = M_w/M_n$) were obtained by size-exclusion chromatography calibrated by polystyrene standards for entries 1–6 and poly(methyl methacrylate) standards for other entries. [e] AIBN (0.2 equiv) was added. [f] Reaction was carried out in DMF.

to give well-controlled polystyrene (Table 1, entry 3). The M_n value of polystyrene increased linearly with an increase of the styrene/**1a** ratio, and the desired high- M_n polystyrenes with low PDI values were obtained in all cases (Table 1, entries 4–6, and Figure 1). Although the M_n value deviated slightly from the theoretical value and the PDI value increased as the targeted M_n value increased, a sufficiently high level of control was obtained.

The synthetic scope of the current polymerization reaction was examined with various vinyl monomers (Table 1, entries 7–17). Organobismuthine mediators were highly versatile and promoted controlled polymerization of both conjugated monomers [e.g., methyl methacrylate (MMA,

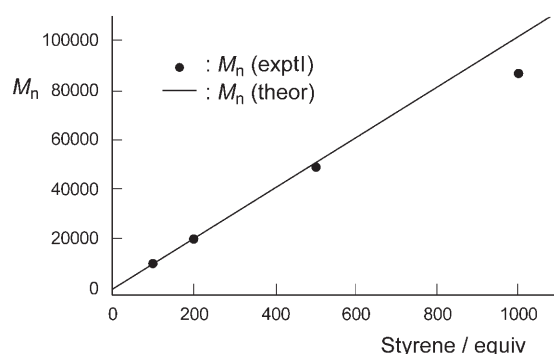
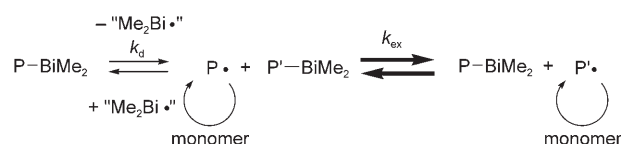


Figure 1. Correlation of experimental and theoretical number-average molecular weight (M_n) of polystyrene in the bulk polymerization of styrene with **1a** as a function of the amount of styrene used (100–1000 equiv).

Table 1, entries 7–9), *n*-butyl acrylate (BA, Table 1, entries 10–12), and *N*-isopropyl acrylamide (NIPAM, Table 1, entries 13–15)] and nonconjugated monomers [e.g., *N*-vinylpyrrolidone (NVP, Table 1, entries 16 and 17)].^[2c] In all cases, the desired polymers formed with high monomer conversion and excellent control of the M_n and PDI values, the level of which was considerably higher than with SBRP, TERP, and IRP. High- M_n polymers ($M_n \approx 100\,000$) were synthesized in a controlled manner in all cases (Table 1, entries 9, 12, and 15). Polymerization of BA, NIPAM, and NVP proceeded smoothly at 60 °C in the presence of AIBN, whereas it did not proceed efficiently without AIBN at 100 °C (Table 1, entries 10–17).^[6a] This result is attributed to the strong C–Bi bond of the corresponding dormant polymer species,^[12] from which the radical was not generated efficiently at this temperature.

Several control experiments confirmed unambiguously the living character of the current polymerization. Firstly, the M_n value increased linearly with an increase in the amount of monomer used in all cases (Figure 1). Secondly, a block copolymer was successfully synthesized by using the living polymer end. Thus, the treatment of a polystyrene macro-mediator (**3a**, Y = CO₂Me, R = Me, R¹ = Ph, R² = H, M_n = 6000, PDI = 1.07) with NVP (100 equiv) in the presence of AIBN (0.2 equiv) in DMF at 60 °C afforded the corresponding diblock copolymer in 93 % yield (M_n = 15 100, PDI = 1.16). Furthermore, the molecular structure of **3a** was determined by MALDI-TOF mass spectroscopy as the end-deuterated polystyrene **4** after treatment of **3a** with tributyltin deuteride (see the Supporting Information).

Kinetic experiments were carried out by using the same protocol as described previously.^[13] The results suggested that BIRP, like SBRP,^[2b] TERP,^[6a] and IRP,^[8] proceeded mainly through a degenerative transfer mechanism together with a small contribution from a thermal dissociation mechanism (Scheme 2). The rate constant k_{ex} for dimethylbismutanyl GT



Scheme 2. Reaction mechanism of BIRP.

in styrene polymerization at 100 °C was determined to be $4.6 \times 10^4 \text{ M}^{-1} \text{ s}^{-1}$, which is around 2, 3, and 12 times faster than dimethylstibanyl GT, methyltellanyl GT, and iodine AT reactions, respectively. As the faster degenerative transfer leads to greater PDI control,^[8,14] the kinetic data are consistent with the polymerization results. Because the organobismutanyl GT reaction is the fastest among the GT and AT reactions involving Group 15, 16, and 17 heteroatoms reported so far, BIRP has, in principle, the best PDI control among the living radical polymerization methods using heteroatom compounds.

The rate constant k_d for the thermal dissociation step was determined to be $1.2 \times 10^{-4} \text{ s}^{-1}$ (100 °C), which is at least 2

times faster than that in SBRP, TERP, and IRP. The result indicates that organobismuthines are also the best radical initiators among the heteroatom compounds. Azo initiators cause the formation of the corresponding radical-initiated polymer upon its consumption and increase the formation of “dead” polymers. Therefore, the controllability of the polymerization decreases in the presence of azo initiators. In this respect, efficient thermal generation contributed considerably to the precise control in styrene and MMA polymerizations.

In summary, we have demonstrated that organobismuthines are excellent initiators and mediators for the highly controlled living radical polymerization. The results clearly open the possibility of the use of organobismuthines in controlled radical reactions. Furthermore, the excellent controllability and versatility of BIRP would be highly attractive for the synthesis of a variety of functional nanomaterials.^[16]

Experimental Section

1a: Lithium diisopropylamide (14.0 mL, 2.0 M in heptane, THF, and ethylbenzene, 28 mmol) was slowly added to a solution of methyl isobutyrate (2.86 g, 28 mmol) in THF (25 mL) at -78°C . The resulting mixture was stirred for 10 min at this temperature, and was slowly warmed to -30°C over 1 h. Dimethylbismuthanyl bromide^[15] (8.9 g) in THF (25 mL) was added to the reaction mixture, and the solution was slowly warmed to 0°C over 1 h. The precipitate was filtered off by passing the mixture through glass wool under a nitrogen atmosphere, and the filtrate was evaporated under reduced pressure and then distilled under reduced pressure (b.p. $32^{\circ}\text{C}/1.5\text{ mmHg}$) to give **1a** as a slightly yellow oil (4.45 g, 47%). This compound is sensitive to oxygen, but can be stored for a long period under an inert atmosphere. ^1H NMR (400 MHz, CDCl_3): $\delta = 1.08$ (s, 6H, $\text{Bi}(\text{CH}_3)_2$), 1.77 (s, 6H, $\text{C}(\text{CH}_3)_2$), 3.72 ppm (s, 3H, OCH_3); ^{13}C NMR (100 MHz, CDCl_3): $\delta = 10.12$, 21.84, 24.12, 50.68, 178.28 ppm; HRMS (EI) m/z : Calcd for $\text{C}_7\text{H}_{15}\text{O}_2\text{Bi}$ $[M]^+$ 340.0875; found 340.0871; IR (neat): $\tilde{\nu} = 815$, 1135, 1185, 1270, 1460, 1695, 2940 cm^{-1} .

Typical procedure of polymerization of styrene: A solution of styrene (1.04 g, 10 mmol) and **1a** (41 μL , 0.1 mmol) was heated at 100°C for 4 h with stirring under a nitrogen atmosphere in a glove box. A small portion of the reaction mixture was taken and dissolved in CDCl_3 . The conversion of monomer (96%) was determined by ^1H NMR spectroscopy. The rest of reaction mixture was dissolved in CHCl_3 (4 mL) and poured into vigorously stirred methanol (200 mL). The product was collected by filtration and dried under reduced pressure at 40°C to give 1.01 g of polystyrene. The M_n value (10500) and PDI value (1.07) were determined by size-exclusion chromatography calibrated with polystyrene standards.

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- [16] The toxicity of organobismuthines is not clear. Hence, they should be handled with care.