Synthetic Radical Reactions Using Dibutylchlorogermane and Dibutylethoxygermane as Radical Mediators

Katsukiyo Miura,*[a] Kazunori Ootsuka,[a] Akira Hosomi*[a,b]

[a] Department of Chemistry, 21st Century COE, Graduate School of Pure and Applied Sciences, University of Tsukuba, and CREST, Japan Science and Technology Corporation (JST), Tsukuba, Ibaraki 305-8571, Japan
Fax +81(29)8536503; E-mail: miura@chem.tsukuba.ac.jp; E-mail: hosomi@chem.tsukuba.ac.jp

[b] Faculty of University Evaluation and Research, National Institution for Academic Degrees and University Evaluation, Kodaira, Tokyo 187-8587, Japan

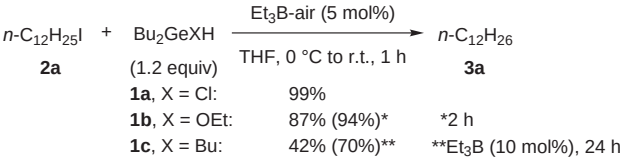
Received 28 September 2005

Abstract: In the presence of Et_3B as radical initiator, dibutylchlorogermane (**1a**) and dibutylethoxygermane (**1b**) reacted with bromo- and iodoalkanes at room temperature to give the corresponding alkanes in high yields. Hydrogermane **1a** was more reactive than **1b**. However, **1b** worked as a better radical mediator in intermolecular radical addition of haloalkanes to electron-deficient alkenes.

Key words: addition reactions, halides, organometallic reagents, radical reactions, reductions

Radical chemistry directed toward fine organic synthesis has rapidly been advanced in the last four decades.[1] At present radical reactions involving carbon radical species are recognized as being valuable for highly selective, efficient transformations of organic molecules. Triorganostannanes such as Bu_3SnH and Ph_3SnH have frequently been used as efficient radical mediators for synthetic radical reactions.[1] Unfortunately, their use has two critical drawbacks, that is, the toxicity of organostannanes and the difficulty of product purification.[2,3] A number of radical mediators have been developed as substitutes for triorganostannanes so far.[3–8] These new mediators are very effective in radical reduction and intramolecular radical addition of organic halides and pseudohalides. In contrast, their utility for efficient intermolecular radical addition is rather limited.[4,6,7] Triorganogermanes are usable for synthetic radical reactions including the intermolecular reaction; however, they are not necessarily as efficient as triorganostannanes and have much room for improvement. We herein report the utility of heteroatom-substituted hydrogermanes, Bu_2GeClH (**1a**) and $Bu_2Ge(OEt)H$ (**1b**), as radical mediators.

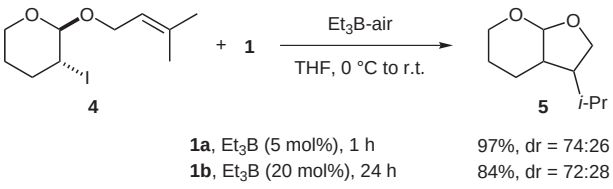
Hydrogermane **1a** was prepared from $GeCl_4$ by four steps without difficulty.[9] The reaction of **1a** with EtOLi gave the ethoxy analogue **1b**. Initially, we examined homolytic reduction of 1-iododododecane (**2a**) with these hydrogermanes and Bu_3GeH (**1c**, Scheme 1). In the presence of 5 mol% Et_3B and dry air, **1a** reacted smoothly with **2a** at room temperature to give dodecane (**3a**) in a quantitative yield. The reduction with **1b** was slightly slower than that with **1a**; however, a prolonged reaction achieved a high yield of **3a**. In contrast, **1c** showed much lower reactivity under the same conditions.[10]



Scheme 1

The results of the Et_3B-initiated reduction of several haloalkanes **2** with **1a** and **1b** are summarized in Table 1. Simple iodo- and bromoalkanes were efficiently reduced to the corresponding alkanes although the reduction with **1b** required elongation of the reaction time and increased amounts of Et_3B and **1b** for complete conversion of **2** (entries 1–4). The difference between **1a** and **1b** in reactivity became more distinct in the reduction of bromoalkanes. For example, the Et_3B-initiated reaction of bromododecane (**2c**) with **1a** went to completion within 1 hour, while the reduction using **1b** and 5 mol% Et_3B stopped before reaching completion (entry 3). In addition, the reaction of **2c** revealed the rather low reactivity of **1c** in agreement with the result shown in Scheme 1. Hydrogermane **1a** was quite valuable also for the reduction of functionalized bromoalkanes (entries 5 and 6). Chloroalkanes were hardly reduced with **1a**,**b** as expected from their low reactivity toward homolytic reduction using other hydrogermanes (entries 7 and 8).[5a,c]

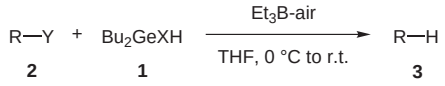
Hydrogermanes **1a**,**b** are applicable to radical cyclization. Thus, the reaction of iodoalkene **4** with **1a**,**b** gave the cyclized product **5** in high yields (Scheme 2). Also in this case, **1a** was more reactive than **1b**.



Scheme 2

SYNLETT 2005, No. 20, pp 3151–3153
Advanced online publication: 28.11.2005
DOI: 10.1055/s-2005-921927; Art ID: U28405ST

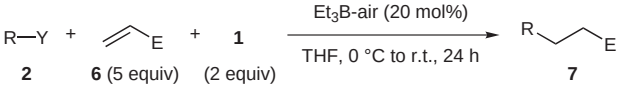
Table 1 Reduction of Haloalkanes **2** with Hydrogermanes **1**[a]



Entry	RY	Yield (%)[b] With **1a**[c]	With **1b**[d]
1	*n*-$C_{12}H_{25}I$ (**2a**)	99	97
2	*c*-$C_{12}H_{23}I$ (**2b**)	97	99[e]
3	*n*-$C_{12}H_{25}Br$ (**2c**)	99	99 (72)[f] (31)[g]
4	*c*-$C_{12}H_{23}Br$ (**2d**)	91	99[e] (86)[f]
5	$PhC(O)(CH_2)_5Br$	92	–
6	$PhC(O)O(CH_2)_3Br$	99	–
7	*n*-$C_{12}H_{25}Cl$	Trace	16[e]
8	*c*-$C_{12}H_{23}Cl$	0	12[e]

[a] Unless otherwise noted, all reactions were carried out with **2** (0.50 mmol), **1** (0.60 mmol), Et_3B, and dry air in THF (1.0 mL) at 0 °C to r.t.
[b] Determined by GC analysis in entries 1–4, 7, and 8. Isolated yields are shown in entries 5 and 6.
[c] Et_3B (1 M in hexane, 0.025 mmol), dry air (2.5 mL), 1 h.
[d] Et_3B (0.05 mmol), dry air (5 mL), 15–24 h.
[e] Hydrostannane **1b** (0.70 mmol).
[f] Et_3B (0.025 mmol), dry air (2.5 mL), 72 h.
[g] Hydrostannane **1c** was used instead of **1b** under the conditions shown in footnotes a and d.

Table 2 Intermolecular Addition of Haloalkanes to Alkenes[a]

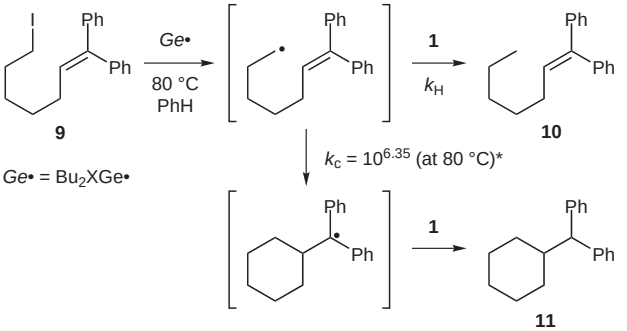


Entry	RY	E in **6**	**1**	Isolated yield (%)
1	**2a**	CO_2t-Bu (**6a**)	**1a**	55[b]
2	**2a**	CO_2t-Bu	**1b**	97
3	**2a**	CO_2t-Bu	**1c**	38[c]
4	**2b**	CO_2t-Bu	**1b**	81
5	**2a**	CO_2Me (**6b**)	**1b**	89
6	**2a**	CN (**6c**)	**1b**	99
7	**2b**	CN	**1b**	99
8	**2c**	CO_2t-Bu	**1b**	8
9	**2d**	CO_2t-Bu	**1b**	10

[a] All reactions were carried out with **2** (0.50 mmol), **6** (2.50 mmol), **1** (1.00 mmol), Et_3B (1.0 M in hexane, 0.10 mmol), and dry air (10 mL) in THF (1.0 mL) at 0 °C to r.t.
[b] Dodecane (**3a**) was obtained in 39% GC yield.
[c] β-Germylester **8c** was obtained in 27% yield (based on the amount of **1c**). See Scheme 4.

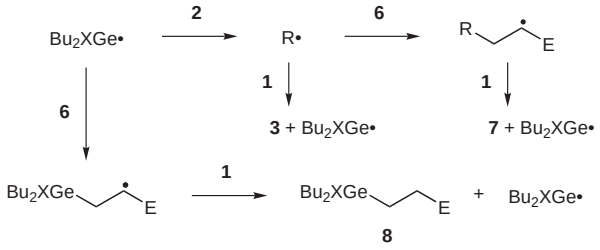
We next examined intermolecular radical addition of haloalkanes to electron-deficient alkenes using **1** as radical mediators (Table 2). The Et_3B-initiated reaction among **2a**, *tert*-butyl acrylate (**6a**), and **1a** (**2a**:**6a**:**1a**:Et_3B = 1:5:2:0.2) gave the desired adduct **7a** in a moderate yield with competitive reduction of **2a** (entry 1). Under the same conditions, the use of **1b** instead of **1a** achieved a higher yield of **7a** (entry 2). The reaction with **1c** resulted in low efficiency, and a significant amount of hydrogermylation product **8c** (X = Bu) was formed (entry 3). The **1b**-mediated radical addition of iodocyclododecane (**2b**) to **6a** proceeded efficiently (entry 4). Methyl acrylate (**6b**) and acrylonitrile (**6c**) as well underwent the **1b**-mediated addition of these iodoalkanes in high yields (entries 5–7). Unfortunately, bromoalkanes were not suitable for the intermolecular addition (entries 8 and 9).

To determine the hydrogen-donating ability of **1**, we performed radical clock experiments using iodoalkene **9**.[11,12] As shown in Scheme 3, it was found that **1a** has higher hydrogen-donating ability than **1b**,**c**.[13] This result provides a reasonable explanation for the competitive reduction with **1a** (entry 1 in Table 2). The successful intermolecular addition with **1b** is attributable to its moderate hydrogen-donating ability, which decelerates hydrogen abstraction of the carbon radical intermediate (R•) and allows efficient quenching of the adduct radical [RCH_2C•(E)H, Scheme 4]. Hydrogermanes **1b**,**c** have similar hydrogen-donating abilities (Scheme 3); however, **1b** is a better radical mediator than **1c** as described above. Judging from the formation of **8c** in the **1c**-mediated reaction (entry 3 in Table 2), an additional reason for the efficient reaction with **1b** is probably that the addition of Bu_2(EtO)Ge• to **6** is slower than that of Bu_3Ge•, a more electron-rich (nucleophilic) germyl radical (Scheme 4). The low reactivity of Bu_2(EtO)Ge• would bring efficient iodine-abstraction from **2** (Y = I).



[**1a**]$_0$ = 0.23, [**10**]/[**11**] = 0.23: k_H (**1a**) = 2.2 x 10^6
[**1b**]$_0$ = 0.23, [**10**]/[**11**] = 0.056: k_H (**1b**) = 5.4 x 10^5
[**1c**]$_0$ = 0.21, [**10**]/[**11**] = 0.040: k_H (**1c**) = 4.3 x 10^5
k_H (**1**) = (k_c/[**1**]$_0$) x ([**10**]/[**11**]) (pseudo-first order conditions).
*See ref. 11.

Scheme 3



Scheme 4

In conclusion, hydrogermanes **1a** and **1b** are valuable as radical mediators not only for reduction of haloalkanes but also for intra- and intermolecular addition of haloalkanes to alkenes. We have demonstrated that elaboration of the substituent on germanium enables fine control of the reactivity of hydrogermanes.

Typical Procedure

Under a nitrogen atmosphere, Et_3B (1.0 M in hexane, 0.10 mL, 0.10 mmol) and dry air (10 mL) were added to a stirred solution of **2a** (148 mg, 0.50 mmol), **6a** (320 mg, 2.50 mmol), and **1b** (233 mg, 1.00 mmol) in THF (1.0 mL) at 0 °C. After being stirred for 10 min, the mixture was warmed to r.t. and stirred for 24 h. The reaction mixture was treated with sat. aq $NaHCO_3$ (5 mL) and extracted with *t*-BuOMe (3 × 10 mL). The extract was dried over Na_2SO_4 and evaporated. Purification of the residual oil by silica gel column chromatography gave *tert*-butyl pentadecanoate (**7a**) in 97% yield (145 mg, 0.485 mmol).

Compound 7a

IR (neat): 2925, 1733, 1153 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 0.88 (t, *J* = 6.3 Hz, 3 H), 1.20–1.30 (m, 24 H), 1.44 (s, 9 H), 2.19 (t, *J* = 7.5 Hz, 2 H). ^{13}C NMR ($CDCl_3$): δ = 14.10 (CH_3), 22.67 (CH_2), 25.10 (CH_2), 28.09 (3 × CH_3), 29.09 (CH_2), 29.29 (CH_2), 29.35 (CH_2), 29.47 (CH_2), 29.60 (CH_2), 29.64 (2 × CH_2), 29.67 (2 × CH_2), 31.91 (CH_2), 35.61 (CH_2), 79.84 (C), 173.34 (C). MS: *m/z* (relative intensity) = 243 (9.5) [$M^+ - C_4H_7$], 242 (4.7) [$M^+ - C_4H_8$], 57 (100).

Acknowledgment

This work was partly supported by Grants-in-Aid for Scientific Research from the Ministry of Education, Culture, Sports, Science, and Technology, Government of Japan.

References

(1) (a) Renaud, P.; Sibi, M. P. *Radicals in Organic Synthesis*; Wiley-VCH: Weinheim, **2001**. (b) Curran, D. P.; Porter, N. A.; Giese, B. *Stereochemistry of Radical Reactions*; VCH: Weinheim, **1996**. (c) Curran, D. P. In *Comprehensive Organic Synthesis*, Vol. 4; Trost, B. M.; Fleming, I., Eds.; Pergamon Press: Oxford, **1991**, Chap. 4.1 and 4.2, 715. (d) Giese, B. *Radicals in Organic Synthesis: Formation of Carbon–Carbon Bonds*; Pergamon Press: Oxford, **1986**.

(2) Boyer, I. J. *Toxicology* **1989**, *55*, 253.

(3) Baguley, P. A.; Walton, J. C. *Angew. Chem. Int. Ed.* **1998**, *37*, 3073; and references therein.

(4) (a) Giese, B.; Kopping, B.; Chatgilialoglu, C. *Tetrahedron Lett.* **1989**, *30*, 681. (b) Chatgilialoglu, C. *Acc. Chem. Res.* **1992**, *25*, 188. (c) Chatgilialoglu, C.; Guerra, M.; Guerrini, A.; Seconi, G. *J. Org. Chem.* **1992**, *57*, 2427. (d) Yamazaki, O.; Togo, H.; Matsubayashi, S.; Yokoyama, M. *Tetrahedron* **1999**, *55*, 3735. (e) Studer, A.; Amrein, S.; Schleth, F.; Schulte, T.; Walton, J. C. *J. Am. Chem. Soc.* **2003**, *125*, 5726.

(5) (a) Sakurai, H.; Mochida, K.; Hosomi, A.; Mita, F. *J. Organomet. Chem.* **1972**, *38*, 275. (b) Chatgilialoglu, C.; Ballestri, M. *Organometallics* **1995**, *14*, 5017. (c) Nakamura, T.; Yorimitsu, H.; Shinokubo, H.; Oshima, K. *Bull. Chem. Soc. Jpn.* **2001**, *74*, 747.

(6) For the hydrogermane-mediated intermolecular radical addition of iodoalkanes, see: (a) Pike, P.; Hershberger, S.; Hershberger, J. *Tetrahedron Lett.* **1985**, *26*, 6289. (b) Pike, P.; Hershberger, S.; Hershberger, J. *Tetrahedron* **1988**, *44*, 6295.

(7) (a) Inoue, K.; Sawada, A.; Shibata, I.; Baba, A. *J. Am. Chem. Soc.* **2002**, *124*, 906. (b) Hayashi, N.; Shibata, I.; Baba, A. *Org. Lett.* **2005**, *7*, 3093. (c) Takami, K.; Mikami, S.; Yorimitsu, H.; Shinokubo, H.; Oshima, K. *Tetrahedron* **2003**, *59*, 6627; and references therein.

(8) Barton, D. H. R.; Jang, D. O.; Jaszberenyi, J. C. *J. Org. Chem.* **1993**, *58*, 6838; and references therein.

(9) (a) The preparation of **1a** was carried out by the following steps: butylation of $GeCl_4$ with BuMgBr, dealkylative dichlorination of Bu_4Ge with $AlCl_3$ and AcCl, reduction of Bu_2GeCl_2 with $LiAlH_4$, and chlorination of Bu_2GeH_2 with $CuCl_2$. For the last step, see: Ohshita, J.; Toyoshima, Y.; Iwata, A.; Tang, H.; Kunai, A. *Chem. Lett.* **2001**, 886. (b) For the preparation of **1a**, see also: Satge, J. *Ann. Chim.* **1961**, *6*, 519.

(10) The use of Bu_2SnH_2 as reducing agent was also attempted for the reduction of **2a**. The Et_3B-initiated reaction with Bu_2SnH_2 (1.2 equiv) for 24 h gave **3a** in 34% yield with recovery of **2a** (ca. 50%).

(11) (a) Newcomb, M.; Horner, J. H.; Filipkowski, M. A.; Ha, C.; Park, S.-U. *J. Am. Chem. Soc.* **1995**, *117*, 3674. (b) Gualtieri, G.; Geib, S. J.; Curran, D. P. *J. Org. Chem.* **2003**, *68*, 5013.

(12) Newcomb, M. In *Radicals in Organic Synthesis*, Vol. 1; Renaud, P.; Sibi, M. P., Eds.; Wiley-VCH: Weinheim, **2001**, Chap. 3.1, 317.

(13) The reported value for k_H(**1c**) at 80 °C is 3.8×10^5 $M^{-1}s^{-1}$. See: Chatgilialoglu, C.; Ballestri, M.; Escudié, J.; Pailhous, I. *Organometallics* **1999**, *18*, 2395.