## Novel Diastereoselective Synthesis of (*E*)-*gem*-Dimetalloalkenes Containing Boron and Germanium: An Easy Access to Alkyl Trimethylgermyl Ketones and Carboxylic Acids

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Abstract: A convenient, novel synthesis of (E)-gem-dimetalloalkenes containing boron and germanium from the (Z)-1-bromo-1-alkenylboronate esters has been developed. α-Bromo-(Z)-1alkenylboronate esters readily prepared from the literature procedures smoothly underwent a reaction with freshly generated trimethylgermyllithium in hexamethylphosphoramide (HMPA) from the hexamethyldigermanium at -78 °C to provide the corresponding 'ate' complexes. These 'ate' complexes underwent intramolecular nucleophilic substitution reaction to provide the corresponding (E)-1-alkenylboronate esters containing trimethylgermyl moiety. These intermediates were isolated in good yields (72-81%) and were characterized by the spectral data (<sup>1</sup>H NMR and <sup>13</sup>C NMR). Upon oxidation of these intermediates with trimethylamine-Noxide, the corresponding alkyl trimethylgermyl ketones were prepared in good yields (78-86%). Oxidation with alkaline hydrogen peroxide followed by acidification afforded the corresponding carboxylic acids in good yields (82-88%).

Key words: *gem*-dimetalloalkanes, trimethylgermyllithium, hexamethylphosphoramide

The acylgermanes are important intermediates<sup>1</sup> in organic synthesis. They are potential prochiral ketones for asymmetric reduction reactions. In view of the synthetic importance of alkyl trimethylgermyl ketones, it was desirable to have a general and convenient methodology for their synthesis, especially from readily available organoborane reagents.

In a previous study, a stereoselective preparation of the (Z)-1-bromo-1-alkenylboronate esters via the hydroboration of 1-bromo-1-alkynes followed by treatment with

1,3-propane diol has been reported.<sup>2</sup> It should be noted that these  $\alpha$ -halo-(*Z*)-1-alkyenylboronate esters are known to undergo intramolecular nucleophilic substitution reactions<sup>3-6</sup> with nucleophiles such as hydrides,<sup>7</sup> Grignard reagents,<sup>8</sup> organolithium reagents<sup>8</sup>, allylmagnesium bromide,<sup>9</sup> trimethylsilylmethyllithium,<sup>10</sup> and trimethylsilyllithium.<sup>11</sup>

In this report, we reacted 1-bromo-(*Z*)-1-hexenylboronate esters with a nucleophilic reagent such as freshly prepared trimethylgermyllithium in hexamethylphosphoramide followed by oxidation with hydrogen peroxide and sodium acetate (Scheme 1). Consequently, we describe a facile general synthesis of (*E*)-*gem*-dimetalloalkenes containing boron and germanium and their oxidation to alkyl trimethylgermyl ketones and carboxylic acids based on versatile intermediates such as  $\alpha$ -bromo-(*Z*)-1-alkenylboronate esters.

The required starting materials such as 1-bromo-1alkynes and  $\alpha$ -bromo-(Z)-1-alkenylboronate esters were prepared using literature procedures.<sup>2</sup> In a typical experiment,  $\alpha$ -bromo-(Z)-1-hexenylboronate ester was reacted with trimethylgermylllithium in hexamethylphosphoramide (easily generated by reacting hexamethyldigermanium with methyllithium<sup>12a</sup> at 0 °C for 0.5 h) at -78 °C under an inert atmosphere and the reaction mixture was stirred at -78 °C for two hours followed by stirring overnight at room temperature. The resulting product (entry 1 in Table 1, 81% yield) was isolated and purified by column chromatography over silica gel. It was then subjected



## Scheme 1

SYNLETT 2007, No. 13, pp 2023–2024 Advanced online publication: 27.06.2007 DOI: 10.1055/s-2007-984542; Art ID: S01507ST © Georg Thieme Verlag Stuttgart · New York to oxidation using trimethylamine-*N*-oxide (TMANO)<sup>12b</sup> in tetrahydrofuran at room temperature for 12 hours. After workup, the reaction provided *n*-pentyl trimethylgermyl ketone in 80% isolated yield. Using the above procedure, the representative alkyl trimethylgermyl ketones were prepared. Oxidation of the resulting (*E*)-1-trimethylgermyl-1-alkenylboronate esters (Table 1) with alkaline peroxide followed by acidic workup provided the corresponding carboxylic acids (Scheme 1).

Presumably, the starting  $\alpha$ -bromo-(*Z*)-1-alkenylboronate ester could form an 'ate' complex as a result of a reaction with trimethylgermyllithium. This would further undergo an anionotropic rearrangement involving the migration of the trimethylgermyl group from boron to the adjacent alkenyl carbon with inversion of configuration to provide *E*-trisubstituted boron intermediate containing trimethylgermyl moiety, the oxidation of which would provide alkyl trimethylgermyl ketones and carboxylic acids under different oxidation conditions (Scheme 1).

**Table 1** Stereoselective Synthesis of (E)-gem-Dimetalloalkenes

 Containing Boron and Germanium

Entry <sup>a</sup>	R	Isolated yield <sup>b,c</sup>	Germyl ketones	Carboxylic acids
1	<i>n</i> -Bu	81%	80%	82%
2	$n-C_5H_{11}$	80%	86%	88%
3	$n - C_6 H_{13}$	78%	84%	85%
4	Cl(CH <sub>2</sub> ) <sub>3</sub>	78%	78%	84%
5	<i>t</i> -Bu	72%	82%	82%
6	CH <sub>2</sub> CH <sub>2</sub> CHMe <sub>2</sub>	74%	78%	80%
7	CH <sub>2</sub> CH <sub>2</sub> Ph	80%	82%	82%

<sup>a</sup> All compounds were oxidized with trimethylamine-N-oxide

(TMANO) to the corresponding alkyl trimethylgermyl ketones in >78% isolated yields. Oxidation with alkaline hydrogen peroxide followed by acidification provided the corresponding carboxylic acids in high yields (82–88%). They were characterized by spectral data (IR, <sup>1</sup>H NMR, and <sup>13</sup>C NMR).

<sup>b</sup> All reactions were carried out on a 5-mmol scale. The yields are based on the corresponding α-bromo-(*Z*)-1-alkenylboronate esters. <sup>c</sup> All compounds were isolated by column chromatography over silica gel and were characterized by IR and NMR spectral data. The stereochemical purities<sup>13</sup> of these intermediates were confirmed by <sup>1</sup>H NMR and <sup>13</sup>C NMR.

In summation, we have developed a novel synthetic route for the preparation of alkyl trimethylgermyl ketones and carboxylic acids<sup>14</sup> based on the reactions of trimethylgermyllithium with  $\alpha$ -bromo-(*Z*)-1-alkenylboronate esters followed by oxidation studies. The representative synthetic applications of these *E*-trisubstituted organoLETTER

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## **References and Notes**

- (1) Curran, D. P.; Diederichsen, U.; Palovich, M. J. Am. Chem. Soc. **1997**, 119, 4797; and references cited therein.
- (2) Brown, H. C.; Bhat, N. G.; Somayaji, V. Organometallics 1983, 2, 1311.
- (3) Matteson, D. S.; Majumdar, D. *Organometallics* **1983**, *2*, 1529; and references cited therein.
- (4) Tsai, D. J. S.; Jesthi, P. K.; Matteson, D. S. Organometallics 1983, 2, 1543.
- (5) Brown, H. C.; De Lue, N. R.; Yamamoto, Y.; Maruyama, K.; Kasahara, T.; Murahashi, S.; Sonoda, A. J. Org. Chem. 1977, 42, 4088.
- (6) Rathke, M. W.; Chao, E.; Wu, G. J. Organomet. Chem. 1976, 122, 145.
- (7) Brown, H. C.; Imai, T. Organometallics 1984, 3, 1293.
- (8) Brown, H. C.; Imai, T.; Bhat, N. G. J. Org. Chem. 1986, 51, 5277.
- (9) Brown, H. C.; Soundararajan, R. *Tetrahedron Lett.* **1994**, *35*, 6963.
- (10) Bhat, N. G.; Martinez, C.; De Los Santos, J. *Tetrahedron Lett.* 2000, *41*, 6541.
- (11) Bhat, N. G.; Tamm, A.; Gorena, A. Synlett 2004, 297.
- (12) (a) Still, W. C. J. Org. Chem. 1976, 41, 3063.
  (b) Soderquist, J. A.; Hassner, A. J. Am. Chem. Soc. 1980, 102, 1577.
- (13) In a mixture of isomers, the vinylic carbons of the Z alkenes can be distinguished from the corresponding carbons of *E*alkenes: Dorman, D. E.; Jautelat, M.; Roberts, J. D. J. Org. *Chem.* **1971**, *36*, 2757.
- (14) The preparation of *n*-hexanoic acid from the (E)-2-(1-trimethylgermyl-1-hexenyl)-1,3,2-dioxaborinane is representative: To a solution of (E)-2-(1-trimethylgermyl-1hexenyl)-1,3,2-dioxaborinane (10 mmol, 2.85 g) in THF (10 mL) was added MeOH (5 mL). It was then cooled to 0  $^\circ\mathrm{C}$ and NaOH (3 M, 5 mL) was added followed by the slow addition of 30% H<sub>2</sub>O<sub>2</sub> (25 mmol, 2.5 mL). The reaction mixture was allowed to come to r.t. and the stirring was continued for 4 h at r.t. Also, 3 M NaOH (5 mL) was added. The reaction mixture was washed with  $Et_2O$  (2 × 30 mL). Acidification of the aqueous phase was performed with concd HCl acid. It was then extracted with  $Et_2O(2 \times 30 \text{ mL})$ , which was then removed via evaporation to provide nhexanoic acid in 82% (0.95 g) isolated yield. IR, <sup>1</sup>H NMR, and <sup>13</sup>C NMR spectral data were used characterize the compound. IR (neat): <2926, 1718 cm<sup>-1</sup>. <sup>1</sup>H NMR (CDCl<sub>3</sub>/ without TMS):  $\delta = 0.8 \text{ (m, 3 H)}, 1.28 - 1.57 \text{ (m, 6 H)}, 2.30 \text{ (m, }$ 2 H), 11.75 (s, 1 H). CMR (CDCl<sub>3</sub>/without TMS):  $\delta = 13.79$ , 22.31, 24.37, 31.24, 34.11, 180.74.

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