Novel (Trimethylgermyl)copper(I) Reagents: Preparation and Addition to α,β-Unsaturated Ketones and α,β-Alkynic Esters

Edward Piers* and René M. Lemieux

Department of Chemistry, University of British Columbia, 2036 Main Mall, University Campus, Vancouver, British Columbia, Canada V6T 1Z1

Received June 24, 1998

The preparation of the novel (trimethylgermyl)cuprates $(Me_3Ge)_2CuLi$ (**2**), $Me_3GeCu(CN)Li$ (**3**), $(Me_3Ge)_2Cu(CN)Li_2$ (**4**), and $Me_3Ge(Me)Cu(CN)Li_2$ (**5**) is described. (Trimethylgermyl)copper(I) reagents add, in a 1,4-fashion, to α,β-unsaturated ketones and α,β-alkynic esters.

Introduction

In connection with an ongoing research program directed at developing the use of organogermane reagents for organic synthesis,[1] we recently described the use of a (trimethylgermyl)copper(I) reagent, namely $Me_3GeCu{\cdot}Me_2S$ (**1**), for the preparation of functionalized acyltrimethylgermanes from acyl chlorides.[2] As an extension to this work, it was of interest to undertake a short investigation into the preparation and chemical reactivity of additional (trimethylgermyl)copper(I) reagents. A perusal of the chemical literature revealed that this type of organometallic species has been the subject of only a small number of reports and these have been limited to the preparation and use of (tri*phenyl*germyl)- and (tri*ethyl*germyl)copper(I) reagents.[3−5] We report herein the results of a brief study on (a) the preparation of the novel (trimethylgermyl)cuprates **2**−**5**[6] and (b) the reactions of one or more of the reagents **1**−**5** with selected α,β-unsaturated ketones and alkyl alk-2-ynoates.

Results and Discussion

Lithium bis(trimethylgermyl)cuprate (**2**; Chart 1) was easily prepared by treatment of a suspension of $CuBr{\cdot}Me_2S$ (1 equiv) in dry tetrahydrofuran (THF) at −78 °C with a THF solution of Me_3GeLi[2] (2 equiv). Similarly, reagents **3** and **4** were obtained by adding a solution of Me_3GeLi (1 and 2 equiv, respectively) to a suspension of CuCN (1 equiv) in dry THF (−78 °C). Finally, the mixed "higher order" cuprate **5** was obtained by treatment of a suspension of CuCN (1 equiv) in dry THF with a THF solution containing 1 equiv of each of Me_3GeLi and MeLi. In each of these preparations, the mixture was stirred at −78 °C for 1 h to afford a THF solution of the desired reagent, which was then ready for use.

Chart 1

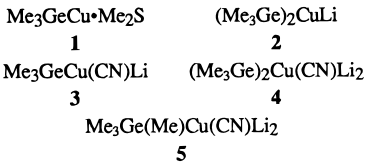
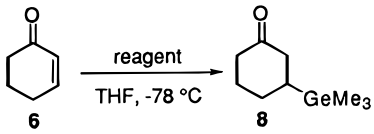


Table 1. Conjugate Addition of Reagents 1−5 to Cyclohex-2-en-1-one (6)



entry no.	reagent[a]	amt of **8** (%)[b]
1	**1**	77
2[c]	**2**	86
3	**3**	90
4[c]	**4**	85
5	**5**	87

[a] 1.3 equiv of reagent was used unless otherwise stated. [b] Yield of isolated and purified product. [c] 0.65 equiv of reagent was used.

To evaluate the efficacy of $Me_3GeCu{\cdot}Me_2S$ (**1**) and the cuprate reagents **2**−**5** to transfer, in a conjugate sense, the Me_3Ge function to α,β-unsaturated ketones, cyclohex-2-en-1-one (**6**) and isophorone (**7**) were chosen as substrates. The results of experiments performed using the enone **6** as substrate are summarized in Table 1.

The conjugate addition reactions involving reagents **1**−**5** and the substrate **6** were carried out under mild

* To whom correspondence should be directed. Fax number: 1-604-822-2847. E-mail: epier@unixg.ubc.ca.

(1) (a) Piers, E.; Marais, P. C. *J. Chem. Soc., Chem. Commun.* **1989**, 1222. (b) Piers, E.; Marais, P. C. *J. Org. Chem.* **1990**, *55*, 3454. (c) Piers, E.; Renaud, J. *J. Org. Chem.* **1993**, *58*, 11. (d) Piers, E.; Oballa, R. M. *Tetrahedron Lett.* **1995**, *36*, 5857. (e) Piers, E.; Kaller, A. M. *Synlett* **1996**, 549.

(2) Piers, E.; Lemieux, R. *Organometallics* **1995**, *14*, 5011.

(3) Oda, H.; Morizawa, Y.; Oshima, K.; Nozaki, H. *Tetrahedron Lett.* **1984**, *25*, 3217.

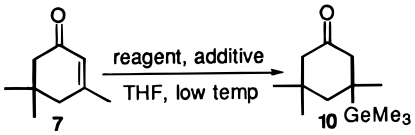
(4) Bravo-Zhivotovskii, D. A.; Pigarev, S. D.; Kalikhman, I. D.; Vyazankina, O. A.; Vyazankin, N. S. *J. Organomet. Chem.* **1983**, *248*, 51.

(5) Yamaguchi, J.-i.; Tamada, Y.; Takeda, T. *Bull. Chem. Soc. Jpn.* **1993**, *66*, 607.

(6) The formulas **2**−**5** are not meant to portray actual structures but are based on the relative amounts of reactants employed in the preparation of the reagents and on the "traditional" protocol employed to represent cuprates. See: (a) Lipshutz, B. H.; Sengupta, S. *Org. React.* **1992**, *41*, 135. (b) Lipshutz, B. H. *Acc. Chem. Res.* **1997**, *30*, 277. (c) Nakamura, E.; Mori, S.; Nakamura, M.; Morokuma, K. *J. Am. Chem. Soc.* **1997**, *119*, 4887 and references therein. (d) Bertz, S. H.; Nilsson, K.; Davidsson, O.; Snyder, J. P. *Angew. Chem., Int. Ed. Engl.* **1998**, *37*, 314 and references therein.

S0276-7333(98)00537-8 CCC: $15.00
Publication on Web 08/27/1998

Table 2. Conjugate Addition of Reagents 4 and 5 to Isophorone (7)

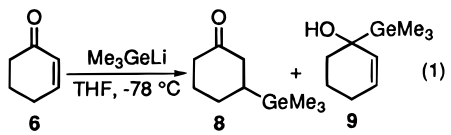


entry no.	reagent[a]	additive	yield (%)[b]
1[c]	**4**	HMPA (2.6 equiv)	42
2[d]	**5**	none	33
3[e]	**5**	TMSCl (1.5 equiv)	33
4[f]	**5**	TMSBr (4 equiv)	66

[a] 0.64 equiv and 1.2 equiv of reagents **4** and **5**, respectively, were employed. [b] Yield of isolated, purified product. [c] Conditions: −78 °C, 1 h, then HMPA, −78 to 0 °C. [d] Conditions: −78 to 0 °C. [e] Conditions: −78 to −30 °C. [f] Conditions: −78 to −15 °C.

conditions (−78 °C, 0.5 h) and produced 3-(trimethylgermyl)cyclohexanone (**8**) in very good to excellent yields. It is noteworthy that the transformations carried out with reagents that possess two Me_3Ge groups (**2**, Table 1, entry 2; **4**, entry 4) provided the adduct **8** in high yields (86 and 85%, respectively) even though, in each case, only 0.65 equiv of reagent was employed. These results demonstrate that for each of the cuprates **2** and **4**, *both* of the germane ligands are transferable and, thus, "throwing away" a valuable Me_3Ge moiety is precluded. Similarly, this concept of "ligand economy" instigated the preparation of reagent **5**, which possesses an expendable nontransferable group (Me).[6a] Thus, when 1 equiv of the enone **6** was allowed to react with 1.3 equiv of the cuprate **5**, the conjugate addition product **8** was obtained in 87% yield (entry 5).

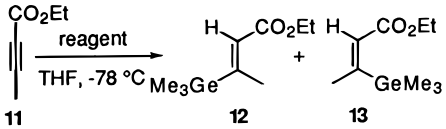
It has been shown[7] that Me_3SnLi reacts with cyclohex-2-en-1-one (**6**) in THF (−78 °C, 5 min) to produce only (96% yield) the conjugate addition product related in structure to **8** ($SnMe_3$ in place of $GeMe_3$). Therefore, it might be expected that Me_3GeLi would also add in a 1,4-fashion to the enone **6** in THF solution. However, when substrate **6** was allowed to react with Me_3GeLi in THF at −78 °C for 5 min, a mixture of two compounds was obtained in a ratio of ∼1:3.8 (GLC analysis). Separation of the two products by chromatography on silica gel afforded the ketone **8** in 20% yield and the alcohol **9** in 59% yield (eq 1). Thus, under identical experimental conditions, Me_3SnLi undergoes exclusive conjugate addition to **6**, while Me_3GeLi reacts with **6** to afford primarily the 1,2-addition product **9** (eq 1). On the other hand, addition of reagents **1**−**5** to **6** results in the exclusive formation of the conjugate addition product **8** (Table 1).



It is well-known that isophorone (**7**) is generally a poor substrate for conjugate addition reactions with cuprate reagents.[6] Consequently, it was of interest to determine whether the (trimethylgermyl)cuprates would be capable of transferring, in a 1,4-sense, the Me_3Ge group to **7**. Reagents **4** and **5** were selected for this purpose, and the results are summarized in Table 2.

(7) Still, W. C. *J. Am. Chem. Soc.* **1977**, *99*, 4836.

Table 3. Addition of Reagents 1−3 and 5 to Ethyl But-2-ynoate (11)



entry	reagent[a]	12:13[b]	yield (%)[c]
1	**1**	>99:<1	81
2	**3**	>99:<1	90
3	**2**	1.7:1	90[d]
4	**5**	1:3.9	17 (*E*), 69 (*Z*)

[a] 1.3 equiv of reagent was employed except for reagent **2**, for which 0.66 equiv was used. [b] Ratio determined by GLC analysis of an aliquot of the crude product. [c] Yield of isolated and purified product unless otherwise stated. [d] Isolated as a mixture of *E*/*Z* isomers.

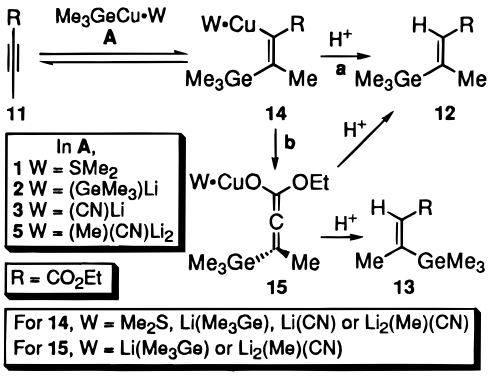
Reaction of the enone **7** with reagent **4** at −78 °C for 1 h, followed by addition of hexamethylphosphoramide (HMPA, 2.6 equiv) and warming of the reaction mixture to 0 °C, afforded the adduct **10** in mediocre yield (42%, Table 2, entry 1). Alternatively, when the higher order cuprate **5** (1.2 equiv) was allowed to react with **7** in the absence of an additive, the product **10** was produced in even lower yield (33%, entry 2). The use of Me_3SiCl (1.2 equiv) as a reaction facilitator[6a] was not effective (entry 3). On the other hand, reaction of **7** with reagent **5** in the presence of Me_3SiBr[8] produced the cyclohexanone **10** in good yield (66%, entry 4). These results indicate that neither HMPA nor Me_3SiCl is a useful additive in this transformation. However, Me_3SiBr serves as an effective facilitator for the production of the conjugate addition product **10**, increasing the yield from 33% to 66% under otherwise similar experimental conditions (compare entries 2 and 4).

The possibility of employing the (trimethylgermyl)copper(I) reagents for the stereocontrolled preparation of alkyl (*E*)- or (*Z*)-3-(trimethylgermyl)alk-2-enoates, via conjugate addition to alkyl alk-2-ynoates, was also examined briefly. The reactions of the initially chosen substrate, ethyl but-2-ynoate (**11**), with reagents **1**, **3**, **2**, and **5** are summarized in Table 3. Reaction of **11** with $Me_3GeCu{\cdot}Me_2S$ (**1**, 1.3 equiv) in THF at −78 °C, followed by a suitable workup procedure, afforded the single substance **12** (81%, entry 1). Similarly, when reagent **3** was allowed to react with **11**, the same product **12** was produced in 90% yield (entry 2). On the other hand, conjugate addition of $(Me_3Ge)_2CuLi$ (**2**) to **11** afforded a mixture of **12** and the corresponding geometric isomer **13** (ratio ∼1.7:1, respectively) in excellent yield (entry 3). Finally, treatment of **11** with reagent **5** under similar experimental conditions gave **12** and **13** in a ratio of about 1:3.9. Straightforward chromatographic separation of this mixture provided the isomeric products in yields of 17 and 69%, respectively.

The configurations of the diastereomeric α,β-unsaturated esters **12** and **13** were easily established by ^1H NMR spectroscopy. For example, in a nuclear Overhauser enhancement difference (NOED) experiment, irradiation at δ 5.95 (olefinic proton signal) in the ^1H NMR spectrum of **12** caused enhancement of the resonance due to the Me_3Ge function (δ 0.23). Similarly,

(8) Piers, E.; Oballa, R. M. *J. Org. Chem.* **1996**, *61*, 8439 and references therein.

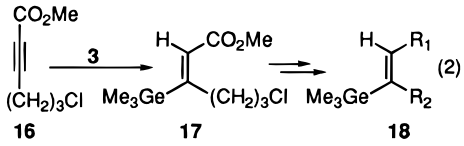
Scheme 1



irradiation of the signal (δ 6.28) due to the olefinic proton in **13** increased the intensity of the vinylic methyl group resonance (δ 2.01).

The results summarized in Table 3 require additional comments regarding the stereoselective formation of isomers **12** and **13**. A possible pathway rationalizing the production of these two isomers is depicted in Scheme 1. Thus, cis addition[9−11] of a (trimethylgermyl)-copper(I) reagent (general structure **A**) to the alkyne function of **11** produces an alkenylcopper intermediate of general structure **14**. Protonation of the latter intermediate (pathway **a**) produces the (*E*) isomer **12**. Alternatively, **14** could isomerize (path **b**) to the (postulated) allenoate species **15**. Although protonation of the latter intermediate could, in theory, produce either **12** or **13**, one would expect predominant protonation from the side opposite the bulky Me_3Ge group to generate **13** as the major product. It is highly likely that the conversions of **11** into **12** by use of the reagents $Me_3GeCu{\cdot}Me_2S$ (**1**) and $Me_3GeCu(CN)Li$ (**3**) (see entries 1 and 2 in Table 3) occur exclusively via pathway **a**. On the other hand, it is reasonable to conclude that both pathways **a** and **b** are operative when the cuprate **2** is used (Table 3, entry 3), whereas, when $Me_3Ge(Me)Cu(CN)Li_2$ (**5**) is employed, pathway **b** is followed exclusively (or at least predominantly) (Table 3, entry 4). Interestingly, the nature of W (see Scheme 1) seems to have a profound influence on the ease of formation of the allenoates **15** from the initially formed intermediates **14**.[12] Under identical experimental conditions reagents **1** and **3** appear to generate "stable" intermediates of general structure **14**, while the corresponding intermediates derived from reagents **2** and **5** readily undergo (partial) isomerization to the allenoates **15**.

Substances of general structure **18** (R^1 and R^2 = functionalized alkyl groups), which are potentially useful intermediates for synthesis, should be readily synthesized via the germylcupration chemistry described above. The stereocontrolled preparation of methyl (*E*)-6-chloro-3-trimethylgermylhex-2-enoate (**17**, 92% yield) via reaction of methyl 6-chlorohex-2-ynoate (**16**) with 1.3 equiv of reagent **3** illustrates the point (eq 2). Conversion of **17** and other structurally related substances into trifunctional reagents of general structure **18** in which R^1 and R^2 both possess reactive functional groups should be accomplished in a straightforward manner via functional group manipulations.



Conclusion

The novel (trimethylgermyl)cuprate reagents **2**−**5**, which are readily prepared, serve as good-to-excellent reagents for conjugate addition of the Me_3Ge group to cyclic enones. The reagents $Me_3GeCu{\cdot}Me_2S$ (**1**) and $Me_3GeCu(CN)Li$ (**3**) undergo stereocontrolled cis addition to the alkyne function of ethyl but-2-ynoate (**11**) at low temperature to produce, upon workup, ethyl (*E*)-2-(trimethylgermyl)but-2-enoate (**12**). Although the completely stereoselective conversion of **11** into ethyl (*Z*)-2-(trimethylgermyl)but-2-enoate (**13**) was not achieved, facile chromatographic separation of the mixture of geometric isomers produced by reaction of **11** with reagent **5** afforded the *Z* isomer **13** in a synthetically useful yield (∼70%). Finally, stereocontrolled germylcupration of functionalized alkyl alk-2-ynoates are also readily accomplished (e.g. **16** → **17**, eq 2).

Experimental Section

All solvents and reagents were purified using established procedures.[13] All glassware was dried at ∼140 °C in an oven or flame-dried prior to use, and all reactions were performed under an atmosphere of dry argon. The pH of the aqueous NH_4Cl-NH_4OH solution used was in the range 8−9. Flash chromatography[14] was performed using 230−400 mesh silica gel 60 from E. Merck. TLC grade flash chromatography was performed using Sigma type H silica gel (10−40 mm, no binder), following the technique described by Taber.[15]

Preparation of Lithium Bis(trimethylgermyl)cuprate (2). A cold (−10 °C) solution of Me_3GeLi[2] (1.40 mmol, 1 equiv) in dry THF (0.6 mL) was transferred via a cannula to a cold (−78 °C), stirred suspension of $CuBr{\cdot}Me_2S$ (144 mg, 0.70 mmol, 0.50 equiv) in dry THF (9 mL). The flask that initially contained the Me_3GeLi solution was rinsed with dry THF (2 × 1.2 mL), and the rinses were transferred via a cannula to the suspension of $CuBr{\cdot}Me_2S$. The suspension was stirred at −78 °C for 1 h to afford a clear golden solution of reagent **2**.

Preparation of Lithium (Trimethylgermyl)cyanocuprate (3). A cold (−10 °C) solution of Me_3GeLi (1.52 mmol, 1 equiv) in dry THF (0.6 mL) was transferred via a cannula to a cold (−78 °C), stirred suspension of CuCN (136 mg, 1.52 mmol, 1 equiv) in dry THF (9 mL). The flask that initially contained the Me_3GeLi solution was rinsed with dry THF (2 × 1.2 mL), and the rinses were transferred via a cannula to the suspension of CuCN. The suspension was stirred at −78 °C for 1 h to afford a yellow, slightly opaque solution of reagent **3**.

Preparation of Dilithium Bis(trimethylgermyl)cyanocuprate (4). A cold (−10 °C) solution of Me_3GeLi (1.52 mmol, 1 equiv) in dry THF (0.6 mL) was transferred via a cannula to a cold (−78 °C), stirred suspension of CuCN (68 mg, 0.76

(9) Alexakis, A.; Normant, J. *J. Organomet. Chem.* **1975**, *96*, 471.
(10) Normant, J. F.; Bourgain, M. *Tetrahedron Lett.* **1971**, *27*, 2583.
(11) Normant, J. F.; Alexakis, A. *Synthesis* **1981**, 841.
(12) A similar intermediate has been proposed to rationalize the formation of alkyl (*Z*)-2-(trimethylstannyl)alk-2-enoates from reaction of $Me_3SnCu(SPh)Li$ with alkyl alk-2-ynoates: Piers, E.; Chong, J. M.; Morton, H. E. *Tetrahedron* **1989**, *45*, 363.
(13) Perrin, D. D.; Armarego, W. L. F. *Purification of Laboratory Chemicals*, 3rd ed.; Pergamon Press: New York, 1988.
(14) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.
(15) Taber, D. F. *J. Org. Chem.* **1982**, *47*, 1351.

mmol, 0.50 equiv) in dry THF (9 mL). The flask that initially contained the Me_3GeLi solution was rinsed with dry THF (2 × 1.2 mL), and the rinses were transferred via a cannula to the suspension of CuCN. The suspension was stirred at −78 °C for 1 h to afford a clear colorless solution of reagent **4**.

Preparation of Dilithium Methyl(trimethylgermyl)-cyanocuprate (5). To a cold (−10 °C) stirred solution of Me_3-GeLi (1.43 mmol, 1 equiv) in dry THF (0.6 mL) was added a solution of MeLi (1.37 M in Et_2O, 1.04 mL, 1.43 mmol, 1 equiv). The resultant solution was transferred via a cannula to a cold (−78 °C), stirred suspension of CuCN (128 mg, 1.43 mmol, 1 equiv) in dry THF (9 mL). The flask that initially contained the Me_3GeLi solution was rinsed with dry THF (2 × 1.2 mL), and the rinses were transferred via a cannula to the suspension of CuCN. The suspension was stirred at −78 °C for 1 h to afford a clear colorless solution of reagent **5**.

Typical Procedure for the Synthesis of 3-(Trimethylgermyl)cyclohexanone (8). To a cold (−78 °C), stirred solution of $Me_3GeCu(CN)Li$ (**3**; 1.52 mmol, 1.30 equiv) in dry THF (12.1 mL) was added a solution of cyclohex-2-en-1-one (**6**; 113 mg, 1.17 mmol, 1 equiv) in dry THF (2.5 mL). The clear colorless solution was stirred at −78 °C for 0.5 h and then was poured into stirred aqueous NH_4Cl-NH_4OH (20 mL). Et_2O (40 mL) was added, and the heterogeneous mixture was stirred vigorously, open to the atmosphere, until the aqueous layer was deep blue. The layers were separated, and the aqueous portion was extracted with Et_2O (2 × 10 mL). The combined organic extracts were washed with water (2 × 10 mL) and brine (10 mL) and then were dried ($MgSO_4$) and concentrated. Flash chromatography (10 g of silica gel, 17:3 petroleum ether−Et_2O) and distillation (150−160 °C/12 Torr) afforded 227 mg (90%) of **8** as a clear colorless oil. IR (neat): 1713, 1228, 823, 600 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 2.41−2.24 (m, 3 H), 2.20−2.10 (m, 2 H), 1.86−1.78 (m, 1 H), 1.71 (ddddd, 1 H, J = 12.8, 12.8, 12.8, 5.0, and 3.8 Hz), 1.46 (dddd, 1 H, J = 12.8, 12.8, 12.8, and 3.6 Hz), 1.30 (dddd, 1 H, J = 13.6, 12.8, 3.4, and 3.4 Hz), 0.10 (s, 9 H). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 212.5, 43.6, 41.9, 29.7, 28.6, 27.0, −4.5. Exact mass: calcd for $C_9H_{18}{}^{74}GeO$, 216.0569; found (HRMS), 216.0565. Anal. Calcd for $C_9H_{18}GeO$: C, 50.32; H, 8.45. Found: C, 50.30; H, 8.30.

Addition of (Trimethylgermyl)lithium to Cyclohex-2-en-1-one (6). Synthesis of 1-(Trimethylgermyl)cyclohex-2-en-1-ol (9). A cold (−10 °C) solution of Me_3GeLi (2.07 mmol, 1.30 equiv) in dry THF (0.9 mL) was transferred via a cannula to cold (−78 °C), stirred dry THF (16 mL). The flask that initially contained the Me_3GeLi solution was rinsed with dry THF (2 × 1 mL), and the rinses were transferred via a cannula to the cold (−78 °C) reaction flask. After the solution had been stirred for 5 min, a solution of cyclohex-2-en-1-one (**6**; 153 mg, 1.59 mmol, 1 equiv) in dry THF (2 mL) was added via a cannula. The reaction mixture was stirred at −78 °C for 5 min and then was poured into stirred aqueous NH_4Cl-NH_4-OH (20 mL). Et_2O (30 mL) was added to the mixture, the layers were separated, and the aqueous portion was extracted with ethyl acetate (2 × 10 mL). The combined organic extracts were washed with water (2 × 10 mL) and brine (10 mL) and then were dried ($MgSO_4$) and concentrated. Flash chromatography (35 g of TLC grade silica gel, 49:1 $CH_2Cl_2-Et_2O$) of the crude oil afforded initially 69 mg (20%) of 3-(trimethylgermyl)cyclohexanone (**8**). The second compound to be eluted was distilled (130−140 °C/9 Torr) to afford 202 mg (59%) of 1-(trimethylgermyl)cyclohex-2-en-1-ol (**9**) as a clear colorless oil. IR (neat): 3435, 3016, 2932, 1234 823, 737, 602 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 5.75 (ddd, 1H, J = 9.8, 3.8, and 3.0 Hz), 5.69 (ddd, 1H, J = 9.8, 1.4, and 1.4 Hz), 2.08−1.98 (m, 1H), 1.94−1.72 (m, 3H), 1.68−1.50 (m, 2H), 1.27 (s, 1H, exchanges with D_2O), 0.17 (s, 9H). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 131.4, 128.4, 67.7, 34.0, 25.0, 18.3, −4.6. Exact mass: calcd for $C_9H_{18}{}^{74}GeO$, 216.0569; found (HRMS), 216.0565. Anal. Calcd for $C_9H_{18}GeO$: C, 50.32; H, 8.45. Found: C, 50.36; H, 8.52.

Typical Procedure for the Synthesis of 3,5,5-Trimethyl-3-(trimethylgermyl)cyclohexanone (10) from Isophorone (7). To a cold (−78 °C), stirred solution of $Me_3Ge(Me)Cu(CN)Li_2$ (**5**; 1.51 mmol, 1.30 equiv) in dry THF (13.1 mL) was added Me_3SiBr (0.70 g, 4.6 mmol, 4.0 equiv) via a cannula. After the mixture had been stirred for 5 min, a solution of isophorone (**7**; 160 mg, 1.16 mmol, 1 equiv) in dry THF (2 mL) was added via a cannula. The red-brown mixture was stirred at −78 °C for 1 h and then was warmed to −15 °C over a 2 h period. The mixture was poured into stirred aqueous NH_4Cl-NH_4OH (20 mL), and Et_2O (40 mL) was added to the mixture. The heterogeneous mixture was stirred vigorously, open to the atmosphere, until the aqueous layer was deep blue. The layers were separated, and the aqueous portion was extracted with Et_2O (2 × 10 mL). The combined organic extracts were washed with water (2 × 10 mL) and brine (10 mL) and then were dried ($MgSO_4$) and concentrated. The crude oil was dissolved in THF (15 mL), and 1 M hydrochloric acid (6 drops) was added. The mixture was stirred at room temperature for 1 h, and Et_2O (15 mL) was added. The solution was dried ($MgSO_4$) and concentrated. Flash chromatography (25 g of TLC grade silica gel, 4:1 petroleum ether−Et_2O) and distillation (86−96 °C/0.05 Torr) afforded 198 mg (66%) of **10** as a colorless oil. IR (neat): 1713, 1273, 1238, 823, 597 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 2.35 (d, 1H, J = 13.0 Hz), 2.23 (d, 1H, J = 13.0 Hz), 2.10 (ddd, 1H, J = 13.0, 2.0, and 2.0 Hz), 2.00 (ddd, 1H, 13.0, 2.0, and 2.0 Hz), 1.74 (d, 1H, J = 13.0 Hz), 1.46 (ddd, 1H, J = 13.0, 2.0, and 2.0 Hz), 1.13 (s, 3H), 1.05 (s, 3H), 1.02 (s, 3H), 0.10 (s, 9H). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 213.0, 54.4, 47.8, 44.9, 39.1, 34.2, 29.1, 28.4, 22.7, −5.6. Exact mass: calcd for $C_{12}H_{24}{}^{74}GeO$, 258.1039; found (HRMS), 258.1032. Anal. Calcd for $C_{12}H_{24}GeO$: C, 56.10; H, 9.42. Found: C, 56.48; H, 9.47.

Typical Procedure for the Synthesis of Ethyl (*E*)-3-(Trimethylgermyl)but-2-enoate (12) from Ethyl But-2-ynoate (11). To a cold (−78 °C), stirred solution of Me_3GeCu-(CN)Li (**3**; 1.11 mmol, 1.30 equiv) in dry THF (10 mL) was added a solution of ethyl but-2-ynoate (**11**; 97 mg, 0.86 mmol, 1 equiv) in dry THF (1.5 mL) via a cannula. The light orange mixture was stirred at −78 °C for 20 min; then acetic acid (0.20 g, 3.3 mmol, 3.9 equiv) was added via a syringe. The thick mixture was stirred for an additional 5 min and then was poured into stirred aqueous NH_4Cl-NH_4OH (20 mL). Et_2O (25 mL) was added to the mixture. The layers were separated, and the aqueous portion was extracted with Et_2O (2 × 10 mL). The combined organic extracts were washed with water (2 × 10 mL) and brine (2 × 10 mL) and then were dried ($MgSO_4$) and concentrated. Flash chromatography (10 g of TLC grade silica gel, 32:1 petroleum ether−Et_2O) and distillation (110−120 °C/11 Torr) provided 180 mg (90%) of **12** as a colorless oil. IR (neat): 1718, 1614, 1367, 1340, 1239, 1181, 1117, 1040, 826, 603 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 5.95 (q, 1H, J = 1.8 Hz), 4.14 (q, 2H, J = 7.2 Hz), 2.26 (d, 3H, J = 1.8 Hz), 1.27 (t, 3H, J = 7.2 Hz), 0.23 (s, 9H). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 165.3, 165.2, 124.8, 59.5, 18.2, 14.3, −3.0. Anal. Calcd for $C_9H_{18}GeO_2$: C, 46.83; H, 7.86. Found: C, 47.10; H, 7.70.

Synthesis of Ethyl (*Z*)-3-(Trimethylgermyl)but-2-enoate (13) from Ethyl But-2-ynoate (11) Using Reagent 5. To a cold (−78 °C), stirred solution of $Me_3Ge(Me)Cu(CN)Li_2$ (**5**; 1.11 mmol, 1.30 equiv) in dry THF (10 mL) was added a solution of ethyl but-2-ynoate (**11**; 96 mg, 0.86 mmol, 1 equiv) in dry THF (1.5 mL) via a cannula. The mixture was stirred at −78 °C for 30 min; then acetic acid (0.13 g, 2.2 mmol, 2.6 equiv) was added via a syringe. The heterogeneous mixture was stirred for an additional 5 min and then was poured into stirred aqueous NH_4Cl-NH_4OH (15 mL). Et_2O (20 mL) was added to the mixture. The heterogeneous mixture was stirred vigorously, open to the atmosphere, until the aqueous layer was deep blue. The layers were separated, and the aqueous

portion was extracted with Et_2O (2 × 10 mL). The combined organic extracts were washed with water (2 × 10 mL) and brine (2 × 10 mL) and then were dried ($MgSO_4$) and concentrated. Flash chromatography (20 g of TLC grade silica gel, 49:1 petroleum ether−Et_2O) and distillation (100−110 °C/10 Torr) of the initially eluted compound furnished 137 mg (69%) of ethyl (*Z*)-3-(trimethylgermyl)but-2-enoate (**13**) as a clear colorless oil. IR (neat): 1718, 1610, 1326, 1196, 1046, 832 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 6.28 (q, 1H, J = 1.6 Hz), 4.13 (q, 2H, J = 7.2 Hz), 2.01 (d, 3H, J = 1.6 Hz), 1.26 (t, 3H, J = 7.2 Hz), 0.29 (s, 9H). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 166.5, 166.0, 128.4, 59.8, 26.2, 14.3, −0.8. Anal. Calcd for $C_9H_{18}GeO_2$: C, 46.83; H, 7.86. Found: C, 46.94; H, 7.87.

The second compound to be eluted during the above chromatographic separation was ethyl (*E*)-3-(trimethylgermyl)but-2-enoate (**12**, 33 mg, 17%).

Synthesis of Methyl (*E*)-6-Chloro-3-(trimethylgermyl)-hex-2-enoate (17). To a cold (−78 °C), stirred solution of $Me_3GeCu(CN)Li$ (**3**; 1.24 mmol, 1.30 equiv) in dry THF (11 mL) was added a solution of methyl 6-chlorohex-2-ynoate (**16**)[16] (154 mg, 0.96 mmol, 1 equiv) in dry THF (1.5 mL) via a cannula. The reaction mixture was stirred at −78 °C for 30 min; then acetic acid (90 mg, 1.5 mmol, 1.6 equiv) was added via a syringe. The mixture was stirred for an additional 5 min and then was poured into stirred aqueous NH_4Cl-NH_4OH (15 mL). Et_2O (20 mL) was added to the mixture, the layers were separated, and the aqueous portion was extracted with Et_2O (2 × 10 mL). The combined organic extracts were washed with water (2 × 10 mL) and brine (10 mL) and then were dried ($MgSO_4$) and concentrated. Flash chromatography (20 g TLC grade silica gel, 24:1 petroleum ether-Et_2O) gave 248 mg (92%) of **17** as a clear colorless oil. IR (neat): 1718, 1607, 1434, 1347, 1181, 1156, 828, 603 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 6.02 (s, 1H), 3.70 (s, 3H), 3.56 (t, 2H, J = 6.6 Hz), 2.86 (t, 2H, J = 8.0 Hz), 1.86 (tt, 2H, J = 8.0 and 6.6 Hz), 0.29 (s, 9H). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 168.7, 165.0, 125.5, 50.9, 44.9, 32.1, 29.9, −2.1. Anal. Calcd for $C_{10}H_{19}ClGeO_2$: C, 43.00; H, 6.86. Found: C, 42.98; H, 6.68.

(16) Piers, E.; Friesen, R. W.; Rettig, S. J. *Can. J. Chem.* **1992**, *70*, 1385.

Acknowledgment. We thank the NSERC of Canada for financial support, as well as the NSERC of Canada and Fonds FCAR (Québec) for Postgraduate Scholarships (to R.L.).

OM980537+