Reaction of Ethyl (Trimethylgermyl)acetate with Carboxylic Acid Derivatives

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Summary: Reactions of the lithium enolate of ethyl (trimethylgermyl)acetate (**1**) or ethyl bis(trimethylgermyl)-acetate (**12**) with some carboxylic acid derivatives were examined. High yields of ethyl 3-oxoalkanoates (**10**) were obtained from the reaction of **1** with *S*-benzyl carbothioates (**6b,c,e**); however, mixtures of **10** and **12** were produced in about 1:1 ratios from the reaction with acyl chlorides (**2a–e**), 1-acylimidazoles (**3b,e**), and benzoyl chloride (**4**). Reaction of the lithium enolate of **12** with benzoyl chloride (**2e**) also gave **10e**.

(Trimethylgermyl)acetic acid esters react with aldehydes with the aid of lithium diisopropylamide (LDA) to give 2-alkenoic acid esters,[1] similarly to the Peterson reaction with (trimethylsilyl)acetate.[2] In this reaction, lithium trimethylgermyl oxide is eliminated from the initial adduct to give the final product. When acyl halides are employed in this reaction, three different reaction paths are conceivable because lithium trimethylgermyl oxide, trimethylgermyl halides, and lithium halides can be eliminated from the initial adduct to produce respectively different types of products: 3-halo-2-alkenoates, 3-oxoalkanoates, and 3-oxo-2-(trimethylgermyl)alkanoates.

Hartzell and Rathke previously reported that the reaction of the *tert*-butyl (trimethylsilyl)acetate lithium enolate with acetyl chloride gave a complicated mixture, but with 1-acylimidazoles it afforded 3-oxoalkanoates.[3] We examined the reaction of the ethyl (trimethylgermyl)acetate lithium enolate (**1′**) with acyl chlorides (**2**) and related carboxylic acid derivatives (**3–6**).

Results and Discussion

When ethyl (trimethylgermyl)acetate (**1**) was treated with an equimolar amount of LDA followed by acyl chlorides (**2a–c,e**) at −78 °C in tetrahydrofuran (THF), ethyl 3-oxoalkanoates (**10a–c,e**) and ethyl bis(trimethylgermyl)acetate (**12**) were obtained in about 1:1 ratios, but neither ethyl 3-chloro-2-alkenoate nor ethyl 3-oxo-2-(trimethylgermyl)alkanoates (**11**) were isolated (entries 1–5 in Table I). These results suggest that the reaction proceeds to initially form the 3-oxoalkanoic ester enolate (**9**) and chlorotrimethylgermane (**8**, X = Cl). The latter was apparently converted to **12** by reaction with enolate **1′** remaining in the reaction mixture (Scheme I). Compound **12** is not produced if the reaction proceeds by the elimination of lithium chloride to give **11**, which is hydrolyzed to **10** during the aqueous workup.[4] Because half of the

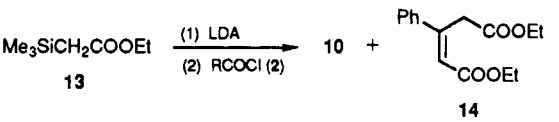
Table I. Reaction of Ethyl (Trimethylgermyl)acetate (1) with Carboxylic Acid Derivatives (2–6)[a]

entry no.	RCOX			amt, mol equiv	yield, %		ref for **10**
		R	X		**10**[b]	others	
1	**2a**	Me	Cl	1.2	12	19 (**12**)	
2	**2b**	*n*-Pr	Cl	1.2	35	52 (**12**)	5
3	**2c**	*t*-Bu	Cl	1.2	34	45 (**12**)	6
4	**2e**	Ph	Cl	1.2	58	50 (**12**)	
5	**2e**	Ph	Cl	1.2	54[c]	45[c] (**12**)	7
6	**2b**	*n*-Pr	Cl	2.2	74	69 (**12**)	
7	**2c**	*t*-Bu	Cl	2.2	64	85 (**12**)	
8	**2d**	PhCH=CH	Cl	2.2	92	72 (**12**)	8
9	**2e**	Ph	Cl	2.2	97	84 (**12**)	
10	**3b**	*n*-Pr	imid	1.2	43	52 (**12**)	
11	**3e**	Ph	imid	1.2	50	48 (**12**)	
12	**4**	Ph	CN	1.2	65	31 (**12**)	
13	**5**	Ph	OEt	1.2	57	9 (**12**)	
14	**6b**	*n*-Pr	SCH_2Ph	1.2	80	94 (*d*)	
15	**6c**	*t*-Bu	SCH_2Ph	1.2[e]	67	67 (*d*)	
16	**6e**	Ph	SCH_2Ph	1.2	92	84 (*d*)	
17	**6e**	Ph	SCH_2Ph	1.2	82	86 (**8**[f])	

[a] The reactions were carried out at −78 °C in entries 1–12 and 0 °C in entries 13–17 for 1 h in THF. [b] Mixture of keto and enol forms. [c] *tert*-Butyl ester. [d] Phenylmethanethiol. [e] 20% DMPU in THF was used. [f] X = SCH_2Ph.

1′ used was consumed by the rapid reaction with **8** (X = Cl), completion of the reaction required 2 equiv of **1′**. Indeed, the use of 2 equiv brought a high yield of **10** and **12** (entries 6–9).

Comparative reactions of the lithium enolate of ethyl (trimethylsilyl)acetate[5] (**13**) with **2b** and **2e** also afforded **10b** (46%) and **10e** (42%). Diethyl (*E*)-3-phenyl-2-pentenedioate (**14**, 14%) was isolated from the reaction with **2e**. This compound is presumably produced by the Peterson reaction of **10e** with **13**.



As Rathke reported, the reactions of *tert*-butyl (trimethylsilyl)acetate lithium enolate with an equimolar amount of 1-acylimidazoles (**3b,e**) gave 74–78% yields of **10b,e** (*t*-Bu ester).[3] However, treatment of **1** with **3b,e** also afforded mixtures of **10b,e** and **12** in about a 1:1 ratio. This suggests that 1-(trimethylgermyl)imidazole (**8**, X = 1-imidazolyl) eliminated also reacts with **1′** to give **12**. Benzoyl cyanide (**4**) and ethyl benzoate (**5**) also reacted with **1′** to give mixtures of **10e** and **12** in moderate yields (entries 12 and 13). The reaction of **5** was slow, and the starting materials remained in the reaction mixture. No reaction of **1′** with *N,N*-dimethylbenzamide was observed.

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(2) For reviews of the Peterson reaction, see: (a) Ager, D. J. *Synthesis* **1984**, 384. (b) Weber, W. P. *Silicon Reagents for Organic Synthesis*; Springer-Verlag: West Berlin, 1983. (c) Colvin, E. W. *Silicon in Organic Synthesis*; Butterworths: London, 1981.

(3) Hartzell, S. L.; Rathke, M. W. *Tetrahedron Lett.* **1976**, 2757.

(4) A reviewer suggested an alternative mechanism for the formation of **10** and **12** as follows: **11** or 3-((trimethylgermyl)oxy)-2-alkenoate (*O*-germyl tautomer of **11**) is initially produced by the elimination of LiCl from **7**, and then it was reacted with **1′** to give **10** and **12**. However, no reaction was observed at −78 °C in a mixture of **1′** and ethyl 3-phenyl-3-((trimethylgermyl)oxy)-2-propenoate, which was prepared by germylation of **10e**. Ethyl 3-phenyl-3-((trimethylgermyl)oxy)-2-propenoate: ^{1}H NMR (C_6D_6) δ 0.32 (s, 9 H, $GeMe_3$), 1.10 (t, *J* = 7.0 Hz, 3 H, CH_3), 4.10 (q, *J* = 7.0 Hz, 2 H, CH_2), 5.90 (s, 1 H, =CH), 7.09–7.20 (m, 3 H, Ph) 7.95–8.05 (m, 2 H, Ph).

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(6) Wierenga, W.; Skulnick, H. I. *J. Org. Chem.* **1979**, *44*, 310.

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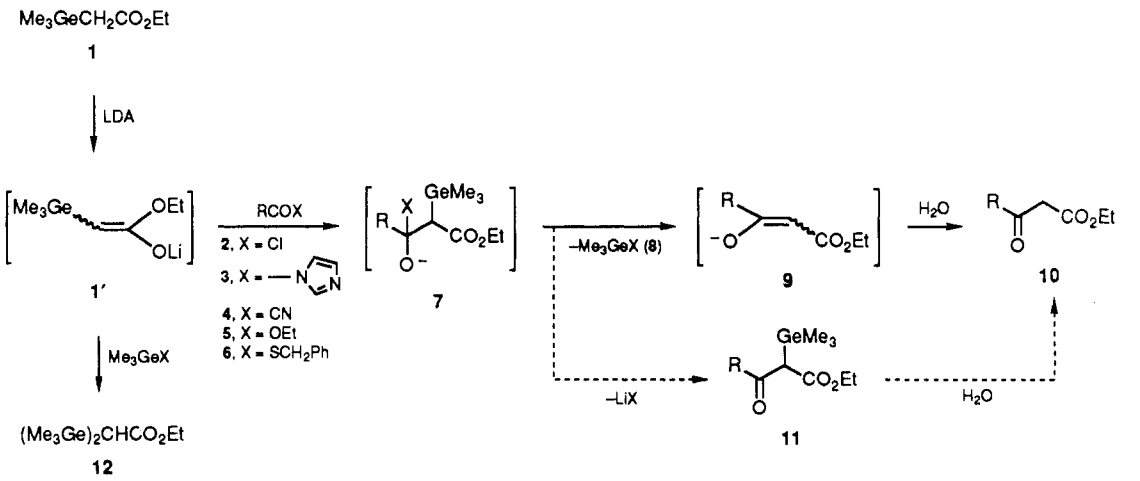
(8) (a) English, J.; Lapides, L. J. *J. Am. Chem. Soc.* **1943**, *65*, 2466. (b) Bodalski, R.; Pietrusiewicz, K. M.; Monkiewicz, J.; Koszuk, J. *Tetrahedron Lett.* **1980**, *21*, 2287.

(9) Kluger, R.; Brandl, M. *J. Org. Chem.* **1986**, *51*, 3964.

0276-7333/90/2309-1325$02.50/0

Scheme I



Successful results were obtained in the reaction of *S*-benzyl carbothioates (**6b,c,e**) with 1′ (entries 14–17). In this reaction, the use of an equimolar amount of 1′ is allowable because 1′ was not consumed by the reaction with phenylmethyl trimethylgermyl sulfide (**8**, X = SCH_2Ph) that was eliminated. Indeed, fractional distillation of the reaction mixture gave 86% of **8** (X = SCH_2Ph, entry 17), though it was hydrolyzed on a silica gel column to phenylmethanethiol (entries 14–16).

Thus, the reaction of 1′ with the carboxylic acid derivatives **2–6** proceeded exclusively by the elimination of **8**, and the elimination of lithium trimethylgermyl oxide or LiX did not occur. When **12** was applied in a similar reaction with **2e**, **10e** was obtained as the main product accompanied by small amounts of ethyl tris(trimethylgermyl)acetate and ethyl (*E*)-3-phenyl-2-(trimethylgermyl)-2-propenoate.[1a]

Experimental Section

All reactions were carried out under a nitrogen atmosphere. Tetrahydrofuran (THF) was distilled from sodium benzophenone ketyl prior to use. 1,3-Dimethyl-3,4,5,6-tetrahydro-2(1*H*)-pyrimidinone (DMPU) was distilled from calcium hydride. ^1H NMR spectra were recorded on a JEOL JNM-PMX 60, JNM-MH 100, or JNM-GSX-400 spectrometer using Me_4Si as internal standard. IR spectra were recorded on a JASCO IRA-2 spectrometer. Gas chromatographic analyses were carried out on a Gasukuro Kogyo Model 370 chromatograph with FID detector using a 2-m, 3% Silicone SE-30 column. All boiling points are uncorrected.

Reaction of Ethyl (Trimethylgermyl)acetate (1)[1a] with Acyl Chlorides (2a–e), 1-Acylimidazoles[10] (3b,e), and Benzoyl Cyanide (4). General Procedure. *n*-BuLi (1.5 M in hexane, 0.8 mL, 1.2 mmol or 1.4 mL, 2.2 mmol) was added to a solution of diisopropylamine (121 mg, 1.2 mmol or 223 mg, 2.2 mmol) in THF (4 mL) at 0 °C with continuous stirring for 15 min. The resulting LDA solution was cooled to −78 °C, and a solution of **1** (246 mg, 1.2 mmol or 451 mg, 2.2 mmol) in THF (3 mL) was added dropwise. After 0.5 h, a solution of **2a–e**, **3b,e**, or **4** (1.0 mmol) in THF (3 mL) was added and stirring was continued for 1 h at the same temperature. Saturated aqueous NH_4Cl was added to the mixture. The organic layer was separated, and the aqueous layer was extracted with ether. The combined extracts were washed with water and saturated aqueous NaCl, dried over anhydrous $MgSO_4$, and concentrated under reduced pressure. The residue was chromatographed on a silica gel column (hexane/AcOEt) to give ethyl 3-oxoalkanoates (**10**) and ethyl bis(trimethylgermyl)acetate (**12**). The results are summarized in Table I.

Reaction of Ethyl (Trimethylsilyl)acetate (13)[5] with 2b,e. By the general procedure described above, **13** (192 mg, 1.2 mmol), diisopropylamine (121 mg, 1.2 mmol), *n*-BuLi (0.8 mL, 1.2 mmol), and **2b,e** (1.0 mmol) were treated. The reaction mixture was chromatographed on a silica gel column (hexane/AcOEt) to give **10b** (72 mg, 46%) or **10e** (80 mg, 42%) and diethyl (*E*)-3-phenyl-2-pentenedioate (**14**, 38 mg, 14%): bp 145 °C (13 mmHg, oven temperature of Büchi Kugelrohr distillation apparatus); IR (film) 1730, 1705, 1630, 1160 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.19 (t, J = 7.1 Hz, 3 H, CH_3), 1.31 (t, J = 7.1 Hz, 3 H, CH_3), 4.13 (q, J = 7.1 Hz, 2 H, OCH_2), 4.17 (s, 2 H, CH_2CO), 4.23 (q, J = 7.1 Hz, 2 H, OCH_2), 6.28 (s, 1 H, =CH), 7.36–7.37 (m, 3 H, Ph), 7.42–7.49 (m, 2 H, Ph). An NOE enhancement (6.6%) at 7.42–7.49 ppm was observed under irradiation at 6.28 ppm. Anal. Calcd for $C_{15}H_{18}O_4$: C, 68.69; H, 6.92. Found: C, 68.42; H, 6.95.

Reaction of 1 with *S*-Benzyl Carbothioates[11] (6b,c and e). A solution of **1** (246 mg, 1.2 mmol) in THF or 20% DMPU in THF (3 mL) was added at −78 °C to a solution of LDA prepared from *n*-BuLi (0.8 mL, 1.2 mmol) and diisopropylamine (121 mg, 1.2 mmol) in THF or 20% DMPU in THF (4 mL). After 0.5 h of stirring, a solution of **6** (1.0 mmol) in THF or 20% DMPU in THF (3 mL) was added at the same temperature; then the mixture was stirred for 1 h at 0 °C. Saturated aqueous NH_4Cl was added, and the mixture was extracted with ether. The extract was chromatographed on a silica gel column (hexane/AcOEt) to give **10b,c,e** and phenylmethanethiol. The results are summarized in Table I.

Fractional distillation of the extract from **1** with **6e** gave phenylmethyl trimethylgermyl sulfide (**8**, X = SCH_2Ph): bp 115 °C (15 mmHg, Kugelrohr); IR (film) 830, 700, 600, 565 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.43 (s, 9 H, $GeMe_3$), 3.74 (s, 2 H, CH_2), 7.02–7.54 (m, 5 H, Ph). Anal. Calcd for $C_{10}H_{16}GeS$: C, 49.86; H, 6.69. Found: C, 50.03; H, 6.61.

Reaction of Ethyl Bis(trimethylgermyl)acetate (12)[1a] with 2e. According to the general procedure, **12** (707 mg, 2.2 mmol), *n*-BuLi (1.4 mL, 2.2 mmol), diisopropylamine (223 mg, 2.2 mmol), and **2e** (141 mg, 1.0 mmol) were treated at −78 °C for 1 h. Silica gel column chromatography (hexane/AcOEt) of the extracts gave **10e** (158 mg, 82%), ethyl tris(trimethylgermyl)acetate[1a] (24 mg, 2%), and a mixture of **12** (GLC yield 49%) and ethyl (*E*)-3-phenyl-2-(trimethylgermyl)-2-propenoate[1a] (GLC yield 7%).

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