

## Carbon–Carbon Bond Formation at the $\gamma$ -Position of Dienolates via the Germanium Masked Dienolates

Yoshinori Yamamoto,\* Satoshi Hatsuya, and Jun-ichi Yamada

Department of Chemistry, Faculty of Science, Tohoku University, Sendai 980, Japan

Trapping of the lithium dienolate (1), derived from 3-methyl-2-butenolate, with  $\text{Me}_3\text{GeX}$  (X = Br or Cl) gives the  $\alpha$ -germylated derivative (2), which reacts with various electrophiles at the  $\gamma$ -position.

Carbon–carbon bond formation at the  $\gamma$ -position of dienolates has been a long standing problem in organic chemistry. It is generally accepted that dienolates, derived from enoates, undergo selective alkylation at the  $\alpha$ -position under kinetic control in preference to the  $\gamma$ -position.<sup>1</sup> We report that use of

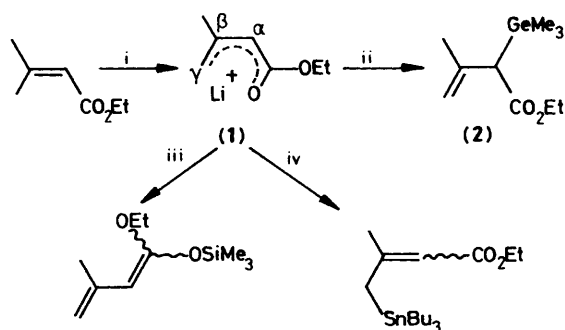
the germanium masked dienolates solves some of the inherent problems associated with dienolate chemistry.

The lithium dienolate (1), generated from the corresponding enoate and lithium diethylamide (LDA), was trapped with  $\text{Me}_3\text{GeX}$  (X = Br or Cl). Interestingly, the  $\alpha$ -germylated ester

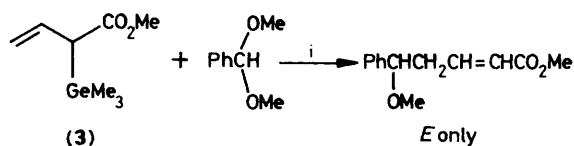
**Table 1.** C–C bond formation at the  $\gamma$ -position via the germanium masked dienolate (2).<sup>a</sup>

Entry	Electrophile	Reaction conditions	Product ( <i>E</i> : <i>Z</i> )	Isolated % yield
1	$\text{PhCH}(\text{OMe})_2$	$\text{TiCl}_4$ , $-78$ to $-40$ °C	$\text{PhC}(\text{OMe})\text{HCH}_2\text{C}(\text{Me})=\text{CHCO}_2\text{Et}$ (9.5:1)	87
2	$n\text{-C}_7\text{H}_{15}\text{CH}(\text{OMe})_2$	$\text{TiCl}_4$ , $-78$ to $-35$ °C	$n\text{-C}_7\text{H}_{15}\text{CH}(\text{OMe})\text{CH}_2\text{C}(\text{Me})=\text{CHCO}_2\text{Et}$ (5:1)	78
3	$\text{PhCH}=\text{CHCH}(\text{OMe})_2$	$\text{TiCl}_4$ , $-78$ to $-40$ °C	$\text{PhCH}=\text{CHC}(\text{OMe})\text{HCH}_2\text{C}(\text{Me})=\text{CHCO}_2\text{Et}$ (12:1)	89
4	$\text{PhCH}=\text{CHCH}(\text{OMe})_2$	$\text{CF}_3\text{SO}_3\text{SiMe}_3$ , $-78$ to $-40$ °C	$\text{PhCH}=\text{CHC}(\text{OMe})\text{HCH}_2\text{C}(\text{Me})=\text{CHCO}_2\text{Et}$ (4.5:1)	91
5	$\text{Me}_2\text{C}(\text{OMe})_2$	$\text{TiCl}_4$ , $-78$ to $-35$ °C	$\text{Me}_2\text{C}(\text{OMe})\text{CH}_2\text{C}(\text{Me})=\text{CHCO}_2\text{Et}$ (3:1)	77
6	$\text{PhCHO}$	$\text{TiCl}_4$ , $-78$ °C	$\text{PhCH}(\text{OH})\text{CH}_2\text{C}(\text{Me})=\text{CHCO}_2\text{Et}$ (4.5:1)	37
7	$\text{PhC}(\text{Me})\text{HBr}$	$\text{ZnBr}_2$ , $-78$ to $0$ °C	$\text{PhCH}(\text{Me})\text{CH}_2\text{C}(\text{Me})=\text{CHCO}_2\text{Et}$ (1.3:1)	45
8	$\text{MeOCH}_2\text{Cl}$	$\text{TiCl}_4$ , $-78$ to $-10$ °C	$\text{MeOCH}_2\text{CH}_2\text{C}(\text{Me})=\text{CHCO}_2\text{Et}$ (3.5:1)	38
9	$\text{PhCH}=\text{CHCH}_2\text{Br}$	$\text{TMSCl}$ , $25$ °C, 10 Kbar	$\text{PhCH}=\text{CHCH}_2\text{CH}_2\text{C}(\text{Me})=\text{CHCO}_2\text{Et}$ (1.2:1)	91 <sup>b</sup>
10	$\text{Me}_2\text{C}=\text{CHCH}_2\text{Br}$	$\text{TMSCl}$ , $25$ °C, 10 Kbar	$\text{Me}_2\text{C}=\text{CHCH}_2\text{CH}_2\text{C}(\text{Me})=\text{CHCO}_2\text{Et}$ (1.2:1)	38 <sup>b</sup>

<sup>a</sup> To a  $\text{CH}_2\text{Cl}_2$  solution of an electrophile (0.5 mmol) and (2) (1.2 equiv.) was added a Lewis acid (1 equiv.) at  $-78$  °C, and the reaction was quenched at the temperature written in the Table. The *E*:*Z* ratio was determined by  $^1\text{H}$  n.m.r. analysis. <sup>b</sup> Small amounts (5–10%) of the  $\alpha$ -isomers were formed along with the  $\gamma$ -isomers.



**Scheme 1.** Reagents: i, LDA, THF; ii,  $\text{Me}_3\text{GeX}$ ; iii,  $\text{Me}_3\text{SiCl}$ ; iv,  $\text{Bu}_3\text{SnCl}$ .



**Scheme 2.** Reagents and conditions: i,  $\text{TiCl}_4$ ,  $-78$  to  $-40^\circ\text{C}$ , 82%.

(2) was obtained in 87% isolated yield [b.p.  $100^\circ\text{C}/5$  mmHg (Kugelrohr)].<sup>†</sup> This  $\alpha$ -regioselectivity is in a striking contrast to the  $\gamma$ -regioselectivity shown with  $\text{Bu}_3\text{SnX}^2$  and to the O-silylation shown with  $\text{Me}_3\text{SiX}^3$  (Scheme 1). The  $\gamma$ -stannylation is presumably due to the thermodynamic stability of the product and the  $\alpha$ -germylation is a reflection of kinetic control {the C–Ge bond is stronger than the C–Sn bond [ $D(\text{Ge–Et}) = 237 \text{ kJ mol}^{-1}$ ,  $D(\text{Sn–Et}) = 193 \text{ kJ mol}^{-1}$ ]}.<sup>4</sup> The strong affinity of Si for oxygen produces the O-silylated derivative. The  $\alpha$ -germylation (3) was also observed for the dienolate derived from methyl crotonate, so it may be concluded that the kinetic C-metallation is realized with  $\text{Me}_3\text{GeX}$ .

Next we examined the C–C bond formation *via* the germanium masked dienolate (2) (Table 1). Acetals reacted regioselectively at the  $\gamma$ -position in high yields (entries 1–5). The stereochemistries of enoates were predominantly *E*. It is noteworthy that the  $\alpha,\beta$ -unsaturated acetal undergoes regioselective head-to-tail coupling with (2) (entries 3 and 4).<sup>5</sup> Aldehydes and reactive halides also gave the  $\gamma$ -alkylation products in moderate to allowable yields (entries 6–8). The reaction of allylic halides in the presence of ordinary Lewis acids ( $\text{TiCl}_4$ ,  $\text{BF}_3$ ,  $\text{AlCl}_3$ ,  $\text{ZnX}_2$ , etc.) resulted in the produc-

tion of complex mixtures. However, use of  $\text{Me}_3\text{SiCl}(\text{TMSCl})$  at 10 kbar solved this problem;<sup>6</sup> the head-to-tail coupling takes place either in high yield (entry 9) or in allowable yield (entry 10).<sup>‡</sup>

The  $\gamma$ -regioselectivity was also observed for (3) (Scheme 2); although (3) contained small amounts of the  $\gamma$ -germylated isomer, this regioisomer did not react with electrophiles and was recovered without change.

The present development shows two important aspects of organogermanium compounds in organic synthesis; (i) the kinetically controlled C-metallation is achieved, which is difficult with other metals; (ii) the  $\alpha$ -alkoxycarbonyl substituted allylic germanium compounds react smoothly with electrophiles in contrast to the corresponding silyl derivatives.<sup>7</sup>

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<sup>†</sup> Selected spectroscopic data for (2):  $^1\text{H}$  n.m.r. (90 MHz,  $\text{CCl}_4$ )  $\delta$  0.24 (9H, s,  $\text{GeMe}_3$ ), 1.24 (3H, t,  $J$  7.5 Hz,  $\text{OCH}_2\text{CH}_3$ ), 1.79 (3H, s,  $=\text{CCH}_3$ ), 2.87 (1H, s,  $\text{GeCH}$ ), 4.03 (2H, q,  $J$  7.5 Hz,  $\text{OCH}_2-$ ), 4.67 and 4.75 (2H,  $\text{H}_2\text{C}^-$ ).

For (3):  $^1\text{H}$  n.m.r. (90 MHz,  $\text{CCl}_4$ )  $\delta$  0.21 (9H, s,  $\text{GeMe}_3$ ), 2.89 (1H, d,  $J$  10.0 Hz,  $\text{GeCH}$ ), 3.60 (3H, s, OMe), 4.74 (1H, m), 4.90 (s, 1H), 6.0 (1H, m) (these last three protons are assigned as olefinic protons).

<sup>‡</sup> The  $\alpha$ -germylated ester (2) was recovered in the  $\gamma$ -germylated form after the reaction ceased. The coupling took place at the  $\alpha$ -position of allylic halides exclusively. A minor isomer (~5%) presumably arose from the isomerized  $\gamma$ -germylated ester. In entry 6, benzaldehyde was recovered.