

## The First General Method for Z-Selective Olefination of Acylsilanes via Ynolate Anions Providing Multisubstituted Alkenes

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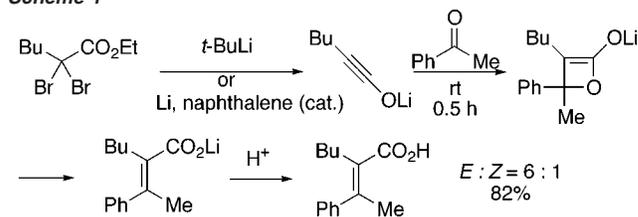
Silylalkenes (vinylsilanes) have frequently been used as a powerful synthetic tool in synthetic organic chemistry,<sup>1</sup> since their silyl groups can potentially be converted into other substituents<sup>2</sup> while also affording unique electronic effects such as  $\alpha$ -anion stabilization and  $\beta$ -cation stabilization.<sup>3</sup> Although olefination of acylsilanes<sup>4</sup> is expected to become a useful method for the preparation of silylalkenes, there have been few reports on this process because conventional reagents, such as phosphorus ylides, have low reactivity toward acylsilanes and afford poor selectivity.<sup>5</sup> Stereoselective synthesis of tri- and tetrasubstituted alkenes is indeed a continuing issue in synthetic organic chemistry,<sup>6</sup> since these types of alkenes not only serve as synthetic intermediates but are also important units in medicinal chemistry and material science.<sup>7</sup> Herein, we describe the first general and efficient method for highly Z-selective olefination of acylsilanes via ynolates leading to  $\beta$ -silyl- $\alpha,\beta$ -unsaturated esters in high yields.

Since developing a novel synthetic method of ynolate anions,<sup>8</sup> we have continued our investigation of ynolate chemistry.<sup>9</sup> In the course of this study, we found that ynolate anions react with ketones at room temperature to afford  $\alpha,\beta$ -unsaturated carboxylic acids with good to moderate stereoselectivities (Scheme 1).<sup>10</sup>

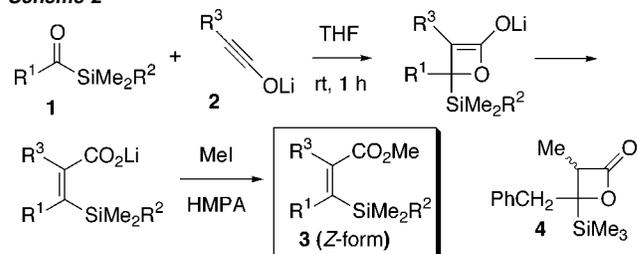
We therefore screened a variety of carbonyl compounds as substrates for the olefination via ynolates and found that acylsilanes show remarkably high efficiency in the olefination. To a THF solution of the ynolate anion (**2**, R<sup>3</sup> = Me), generated from the  $\alpha,\alpha$ -dibromoester with *t*-BuLi or lithium naphthalene, was added acylsilane (**1**, R<sup>1</sup> = PhCH<sub>2</sub>, R<sup>2</sup> = Me) at ambient temperature. After 1.5 h, the starting ketone disappeared, and iodomethane was added for esterification of the expected carboxylate. Finally, we isolated the desired  $\beta$ -silyl- $\alpha,\beta$ -unsaturated ester (**3**) in quantitative yield with excellent Z-selectivity (Scheme 2).

To establish the generality of this olefination, we examined reactions using a variety of acylsilanes and ynolates. As shown in Table 1, the desired  $\beta$ -silyl- $\alpha,\beta$ -unsaturated esters were obtained in high yields with perfect Z-selectivities.<sup>11</sup> *tert*-Butyldimethylacylsilanes also afforded the desired esters (entries 9, 13, 14, and 15). Functionalized alkylacylsilanes and benzoylsilane also gave the desired esters with no geometric isomers (entries 11–16). A TMS-substituted ynolate anion produced  $\alpha,\beta$ -disilyl- $\alpha,\beta$ -unsaturated ester, which could be the synthetic equivalents of di-, tri-, and tetrasubstituted alkenes (entry 10). Although Sonderegger has reported high selectivity in Wittig reaction<sup>5b,c</sup> and in Peterson olefination<sup>5d</sup> of acylsilanes giving *disubstituted* silylalkenes, there

### Scheme 1



### Scheme 2



**Table 1.** Olefination of Acylsilanes via Ynolate Anions<sup>a</sup>

Ent ry	R <sup>1</sup>	R <sup>2</sup>	R <sup>3</sup>	<b>3</b>	Z : E	Yield (%)
1	Me	Me	Me	<b>3a</b>	>99 : 1	80
2	Me	Me	Bu	<b>3b</b>	>99 : 1	94
3 <sup>b</sup>	Me	Me	Bu	<b>3b</b>	>99 : 1	91
4	Me	Me	Ph	<b>3c</b>	>99 : 1	89
5	PhCH <sub>2</sub>	Me	Me	<b>3d</b>	>99 : 1	98
6	PhCH <sub>2</sub>	Me	Bu	<b>3e</b>	>99 : 1	87
7	PhCH <sub>2</sub>	Me	iPr	<b>3f</b>	>99 : 1	87
8	PhCH <sub>2</sub>	Me	Ph	<b>3g</b>	>99 : 1	82
9	PhCH <sub>2</sub>	tBu	Me	<b>3h</b>	>99 : 1	92
10	PhCH <sub>2</sub>	Me	TMS	<b>3i</b>	>99 : 1	86
11	CH <sub>2</sub> =CHCH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub>	Me	Me	<b>3j</b>	>99 : 1	84
12	CH <sub>2</sub> =CHCH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub>	Me	Ph	<b>3k</b>	>99 : 1	99
13	CH <sub>2</sub> =CHCH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub>	tBu	Me	<b>3l</b>	>99 : 1	99
14		tBu	Me	<b>3m</b>	>99 : 1	75
15	MEMOCH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub>	tBu	Me	<b>3n</b>	>99 : 1	74
16	Ph	Me	Me	<b>3o</b>	>99 : 1	87

<sup>a</sup> The ynolates were prepared by lithium–halogen exchange with *tert*-butyllithium, otherwise noted. <sup>b</sup> The ynolate was prepared by the method of reductive lithiation with lithium metal and catalytic naphthalene (see Supporting Information).

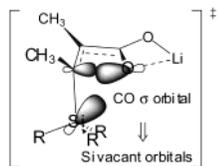
have been no reports on the highly stereoselective synthesis of trisubstituted silylalkenes. An attempted Horner–Emmons reaction with acylsilane (**1**) resulted in a complex mixture. Peterson olefination of acetyl trimethylsilane was reported to give a 3:1 mixture of trisubstituted silylalkenes.<sup>5d</sup> Therefore ynolate anions are superior to the conventional reagents for olefination of acylsilanes to afford  $\beta$ -silyl- $\alpha,\beta$ -unsaturated esters.

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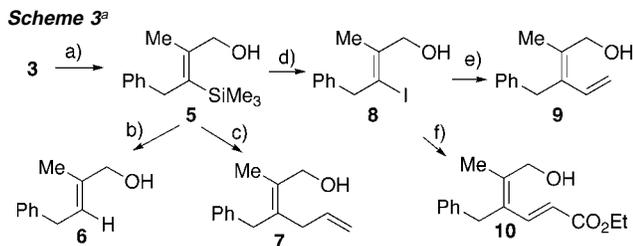
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**Figure 1.** An orbital interaction of inward TS in the ring opening of a  $\beta$ -lactone enolate.



<sup>a</sup> Reagents: (a) DIBAH, 88%; (b) TsOH, 60%; (c) CuI, LiOrBu, allyl bromide then TBAF, 89%; (d) I<sub>2</sub>, CF<sub>3</sub>CO<sub>2</sub>Ag, 47% (*Z*:*E* = 96:4) (16% recovery of the starting material); (e) tributylvinyltin, (CH<sub>3</sub>CN)<sub>2</sub>PdCl<sub>2</sub>, 79%; (f) ethyl acrylate, (Ph<sub>3</sub>P)<sub>2</sub>PdCl<sub>2</sub>, Et<sub>3</sub>N, 60%

To probe the reaction path, we attempted to trap the intermediate  $\beta$ -lactone enolate. The reaction of the acylsilane (**1**, R<sup>1</sup> = PhCH<sub>2</sub>, R<sup>2</sup> = Me) with the ynoate (**2**, R<sup>3</sup> = Me) at  $-78$  °C produced  $\beta$ -lactone (**4**) in good yield (IR, 1811 cm<sup>-1</sup>)<sup>12</sup> thus revealing that the  $\beta$ -lactone enolates are the intermediates in this olefination.

The stereochemistry would be controlled in the electrocyclic ring-opening step<sup>10f</sup> of the  $\beta$ -lactone enolate (Figure 1). When *tert*-butyl methyl ketone was employed for comparison sake, the *Z*:*E* selectivity was only 4:1.<sup>13</sup> The marked difference in the selectivities could be explained by the stereoelectronic effect of silicon. With the aid of B3LYP/6-31G\* calculations (R = H in Figure 1), the transition state in the ring opening with inward rotation of the silanyl group was found to be more stable in Gibbs energy than the outward one by 17.5 kJ/mol. A localized molecular orbital analysis of the TS of the inward ring opening can account for the torquoselectivity as the interaction between a breaking C–O  $\sigma$  orbital and Si vacant orbitals (i.e. 3d or 4sp orbitals, Figure 1).<sup>14</sup>

The silyl group of the silylalkenes can be transformed to other functionalities (Scheme 3). After reduction of the ester, the resulting silylalkene (**5**) was desilylated to give the *E*-alkene (**6**). The silylalkene (**5**) was also coupled with allyl bromide<sup>2c</sup> to provide the skipped diene (**7**). The conversion of silyl group into the iodide<sup>2d</sup> was employed to afford the corresponding *Z*-iodoalkene (**8**), which underwent a Heck reaction with ethyl acrylate and a Stille coupling with vinyl tin to provide the dienes **9** and **10**, respectively. Thus, the efficient stereoselective synthesis of tetrasubstituted alkenes was achieved.

In conclusion, we have developed a stereoselective olefination of acylsilanes via ynoate anions to produce (*Z*)- $\beta$ -silyl- $\alpha,\beta$ -unsaturated esters, which leads to tri- and tetrasubstituted alkenes. This process is the first general method for producing tetrasubstituted alkenes by olefination of acylsilanes. Finally, it demonstrates the synthetic utility of the multifunctional carbanions of ynoate anions.

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**Supporting Information Available:** Experimental and computational procedures and spectral data of selected compounds (PDF). This material is available free of charge via the Internet at <http://pubs.acs.org>.

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