New [3 + 4] Annulation. Reactions of (β-(Trimethylsilyl)acryloyl)silanes with the Lithium Enolates of α,β-Unsaturated Methyl Ketones

Kei Takeda,* Mika Takeda, Akemi Nakajima, and Eiichi Yoshii*

Faculty of Pharmaceutical Sciences
Toyama Medical and Pharmaceutical University
2630 Sugitani, Toyama 930-01, Japan

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We have recently reported a new [3 + 2] annulation reaction, which involves the reaction of (β-(phenylthio)acryloyl)silane and lithium enolates of 2-alkanones (generated with LDA) to afford 1-alkyl-2-(phenylthio)-4-(silyloxy)-3-penten-1-ol.[1] We now describe the discovery of an efficient [3 + 4] annulation reaction,[2] which has been achieved by using (*E*)-(β-(trimethylsilyl)acryloyl)-*tert*-butyldimethylsilane (**1**)[3] in combination with α,β-unsaturated methyl ketone enolates **2** as the four-carbon components, affording novel, highly functionalized cycloheptenones **3** in a straightforward manner (Scheme 1).

We first investigated the reaction of (*E*)-**1** with acyclic α,β-unsaturated methyl ketones under the same conditions as employed in the aforementioned [3 + 2] annulation. Thus, the lithium enolate of 3-hepten-2-one (generated with LDA in THF at −80 °C) was added to a THF solution of (*E*)-**1** at −80 °C, and the mixture (0.02 M) was allowed to warm to −30 °C over a period of 1 h to afford *cis*-6-propyl-5-(trimethylsilyl)-3-cycloheptenone (**3a**) as the only detectable stereoisomer[4] and in 73% yield after silica gel chromatography (Table 1, entry 1).

Additional examples using acyclic enone enolates **2b−d** are given in entries 2−4. The same [3 + 4] annulation reaction was also realized with five- and six-membered cycloalkenyl methyl ketone enolates **2e,f**, affording cis-fused bicyclic cycloheptenones **3e,f** in good yields (entries 5 and 6).[4] Lastly, it is remarkable that 2′-bromoacetophenone enolate **2g** undergoes the same cycloaddition to give benzocycloheptenone **3g** albeit in a reduced yield (entry 7), showing that a benzenoid unsaturation can also participate in our [3 + 4] cycloaddition reaction.

In sharp contrast to the case of (*E*)-**1**, the reaction of (*Z*)-**1** with **2a−d** under the same reaction conditions proved quite sluggish and afforded 5,6-trans isomers **4a−c** in poor yields (11−31%),[4] along with substantial recovery of the starting acylsilane (*Z*)-**1** (Table 2). Moreover, it should be noted that no reaction was observed with 2′-bromoacetophenone enolate **2g**.

The observed difference in stereochemical outcomes depending on the *E*/*Z* geometry of **1** provides a key to proposing the reaction mechanism. Of the conceivable pathways from the 1,2-adduct **5** (Scheme 2), which is isolable,[5a] a tandem Brook rearrangement[6,7]/Michael addition route (**5** → **6**, **7** → **9**) is unlikely, since it is difficult to explain the stereospecific formation of the less stable 5,6-cis isomer from (*E*)-**1** and also the successful cycloaddition with 2′-bromoacetophenone enolate

Scheme 1

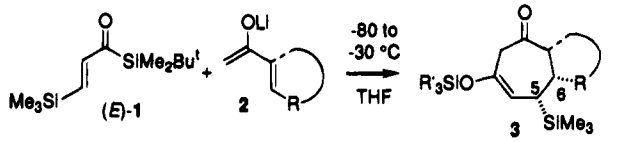


Table 1. [3 + 4] Annulation of (*E*)-**1** with Ketone Enolates

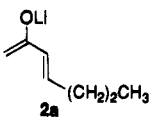
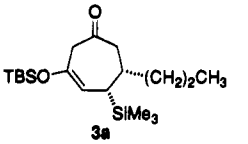
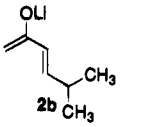
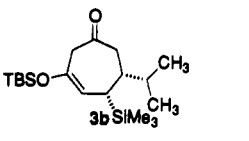
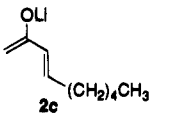
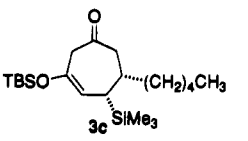
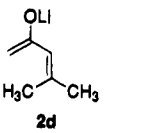
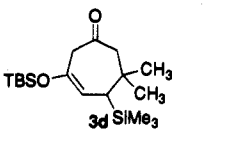
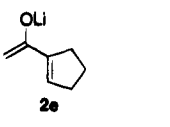
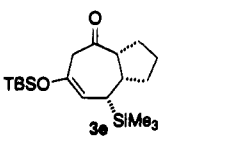
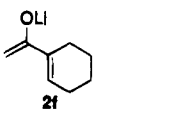
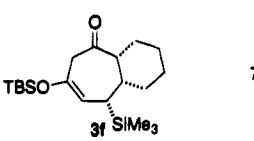
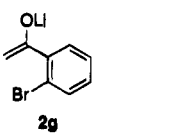
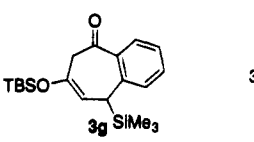
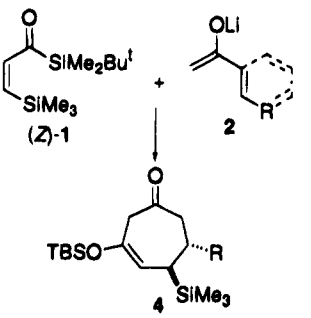
entry	ketone enolate	product	yield
1			73%
2			84%
3			84%
4			65%
5			73%
6			73%
7			30%

Table 2. [3 + 4] Annulation of (*Z*)-**1**



enolate[a]	product	% yield (recoverty of (*Z*)-1)
2a	4a	31 (56)
2b	4b	11 (59)
2c	4c	29 (44)
2d	4d	18 (31)
2g	4g	0 (77)

[a] See Table 1.

(1) Takeda, K.; Fujisawa, M.; Makino, T.; Yoshii, E.; Yamaguchi, K. *J. Am. Chem. Soc.* **1993**, *115*, 9351−9352.

(2) For a review on [3 + 4] cycloadditions, see: Hosomi, A.; Tominaga, Y. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, 1991; Vol. 5, pp 593−615. See also: (a) Trost, B. M.; Yamazaki, S. *Chem. Lett.* **1994**, 2245−2248 and references cited therein. (b) Hudlicky, T.; Fleming, A.; Radesca, L. *J. Am. Chem. Soc.* **1989**, *111*, 6691−6707 and references cited therein.

(3) Reich, H. J.; Kelly, M. J.; Olson, R. E.; Holtan, R. C. *Tetrahedron* **1983**, *39*, 949−960.

(4) All the cycloheptenones except **3f** were obtained as oils. The relative stereochemistries for **3a−c** (cis) and **4a−c** (trans) were assigned on the basis of $J_{5,6}$ (**3a−c** = 3.8−4.5 Hz; **4a−c** = 6.4−7.9 Hz) and NOESY experiments. The stereostructure of **3f** was determined by X-ray analysis, and the same all-cis stereochemistry of **3e** was derived from a NOESY experiment.

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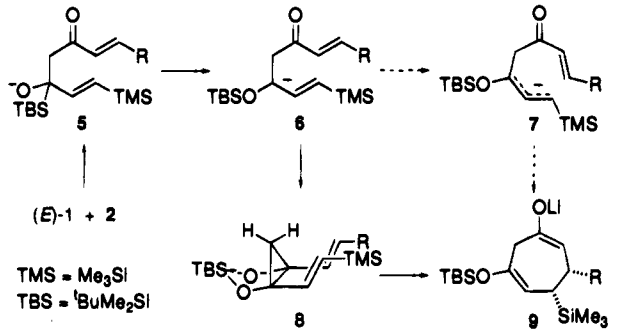
Scheme 2



2g. We propose an alternative pathway that involves the intermediacy of 1,2-divinylcyclopropanediolates **8**[5b,c] generated by way of a Brook rearrangement/cyclopropanation sequence in a concerted manner (**5** → **6** → **8**). The intermediate **8** is expected to rapidly undergo a stereospecific oxyanion-accelerated Cope rearrangement[8-10] under the reaction conditions to produce the cycloheptenone enolate **9** having the correct stereochemistry.[11]

In summary, we have developed a new [3 + 4] annulation, which involves the reaction of (*E*)-(β-(trimethylsilyl)acryloyl)-silane **1** with the lithium enolate of α,β-unsaturated methyl ketones and provides an easy access to *cis*-6-alkyl- and 6,7-cyclo-5-(trimethylsilyl)-2-(silyloxy)-3-cycloheptenones (**3**). Efforts toward further manipulation of the functionalities of **3** to expand the scope of the [3 + 4] annulation methodology are in progress in this laboratory.

Supplementary Material Available: General procedures for the annulation reaction, characterization data for **3a**–**g** and **4a**–**c**, and X-ray crystallographic data and an ORTEP drawing for **3f** (7 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, can be ordered from the ACS, and can be downloaded from the Internet; see any current masthead page for ordering information and Internet access instructions.

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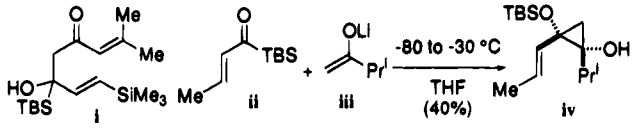
(5) (a) On quenching the reaction of (*E*)-**1** and **2d** after 30 min at −80 °C, the 1,2-adduct (i) was isolated in 47% yield along with the annulation product **3d** (30%) and (*E*)-**1** (18%). (b) An attempt to isolate the proposed cyclopropane intermediate **8** by treatment of i with LDA at −80 °C was unsuccessful, only **3d** (25%) and i (67%) being obtained after 5 min. (c) The closely related *cis*-cyclopropanediol iv has been isolated by us in the reaction of crotonoylsilane ii with a saturated methyl ketone enolate (iii). Takeda, K.; Nakatani, J.; Nakamura, H.; Sako, K.; Yoshii, E.; Yamaguchi, K. *Synlett* **1993**, 841–843.



(6) For a review of the Brook rearrangement, see: Brook, A. G.; Bassindale, A. R. In *Rearrangements in Ground and Excited States*; de Mayo, P., Ed.; Academic Press: New York, 1980; pp 149–221.

(7) (a) Reich, H. J.; Holtan, R. C.; Bolm, C. *J. Am. Chem. Soc.* **1990**, *112*, 5609–5617 and references cited therein. (b) Enda, J.; Kuwajima, I. *J. Am. Chem. Soc.* **1985**, *107*, 5495–5501 and references cited therein. (c) Koreeda, M.; Koo, S. *Tetrahedron Lett.* **1990**, *31*, 831–834. (d) Nakajima, T.; Segi, M.; Sugimoto, F.; Hioki, R.; Yokota, S.; Miyashita, K. *Tetrahedron* **1993**, *49*, 8343–8358.

(8) (a) Wilson, S. R. *Org. React. (N.Y.)* **1993**, *43*, 93–250. For related oxyanion-accelerated vinylcyclopropane rearrangements, see: (b) Bronson, J. J.; Danheiser, R. L.; In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, 1991; Vol. 5, pp 999–1036.

(9) For reviews on rearrangement of divinylcyclopropanes, see: (a) Hudlicky, T.; Fan, R.; Reed, J. W.; Gadamasetti, K. G. *Org. React. (N.Y.)* **1992**, *41*, 1–133. (b) Piers, E. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, 1991; Vol. 5, pp 971–998. (c) Hill, R. K. *Ibid.* Vol. 5, pp 785–826. For thermal Cope rearrangement of *cis*-1-aryl-2-vinylcyclopropanes, see: (d) Marvell, E. N.; Lin, C. *J. Am. Chem. Soc.* **1978**, *100*, 877–883.

(10) For a tandem cyclopropanation/Cope rearrangement, see: (a) Wulff, W. D.; Yang, D. C.; Murray, C. K. *J. Am. Chem. Soc.* **1989**, *110*, 2653–2655. (b) Hudlicky, T.; Nguyen, P. V. *J. Org. Chem.* **1992**, *57*, 1933–1935. (c) Davies, H. M. L.; Clark, T. J.; Kimmer, G. F. *J. Org. Chem.* **1991**, *56*, 6440–6447. (d) Davies, H. M. L.; Clark, T. J.; Smith, H. D. *J. Org. Chem.* **1991**, *56*, 3817–3824. (e) Cantrell, W. R., Jr.; Davies, H. M. L. *J. Org. Chem.* **1991**, *56*, 723–727. (f) Davies, H. M. L.; McAfee, M. J. *J. Org. Chem.* **1989**, *54*, 930–936.

(11) The significantly slow reaction of (*Z*)-**1** may be explainable by slow formation of the 1,2-adduct v. In fact, the reaction of (*Z*)-**1** with **2d** at −80 °C for 30 min resulted in recovery of the starting acylsilane (*Z*)-**1** in 67% yield.