ORGANIC
LETTERS

2009
Vol. 11, No. 18
4240−4243

Unusual Transposition of Allenic Framework in Intramolecular Cyclization of Acetal-Tethered (Allenylmethyl)silanes

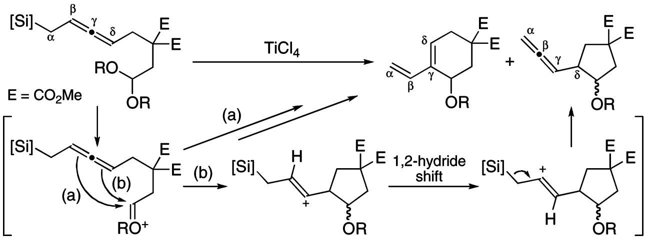
Masamichi Ogasawara,* Atsushi Okada, Hidetoshi Murakami, Susumu Watanabe, Yonghui Ge, and Tamotsu Takahashi*

Catalysis Research Center and Graduate School of Life Science, Hokkaido University, Kita-ku, Sapporo 001-0021, Japan

ogasawar@cat.hokudai.ac.jp; tamotsu@cat.hokudai.ac.jp

Received August 2, 2009

ABSTRACT



Treatment of acetal-tethered (allenylmethyl)silanes, which were obtained from the corresponding 3-bromo-5-silyl-1,3-pentadienes by a Pd-catalyzed reaction with an acetal-tethered malonate, with $TiCl_4$ gave not only vinylcyclohexene derivatives via a standard S_E2' pathway but also unusual allenylcyclopentane species via cyclization at the *δ*-position. Deuterium-labeling experiments revealed participation of a 1,2-hydride shift in a carbocation intermediate for the formation of the latter products.

Allenes are an important class of compounds and have gained increasing attraction as interesting building blocks in synthetic organic chemistry.[1,2] Substitution reactions of allenic substrates/reagents are often accompanied by concurrent reorganization/relocation of the carbon−carbon multiple bonds.[3] For example, reactions of allenylmetal reagents with an appropriate electrophile proceed in an S_E2' fashion to give the corresponding propargylic products (eq 1).[4] Substitution reactions of allenylmethyl halides afford conjugate dienes via an S_N2' pathway (eq 2).[5]

In this paper, we describe an unprecedented mode of allenic substitution reactions. Lewis acid promoted intramolecular electrophilic substitution/cyclization of an acetal-tethered (allenylmethyl)silane gives rise to an unusual

---

(1) (a) Taylor, D. R. *Chem. Rev.* **1967**, *67*, 317. (b) Pasto, D. J. *Tetrahedron* **1984**, *40*, 2805. (c) Rutledge, T. F. *Acetylenes and Allenes*; Reinhold: New York, 1969. (d) Patai, S., Ed. *The Chemistry of Ketenes, Allenes, and Related Compounds*; Wiley: Chichester, 1980. (e) Landor, S. R., Ed. *The Chemistry of the Allenes*; Academic Press: London, 1982. (f) Coppola, G. M.; Schuster, H. F. *Allenes in Organic Synthesis*; Wiley: New York, 1984. (g) Krause, N., Hashmi, A. S. K., Eds. *Modern Allene Chemistry*; Wiley-VCH: Weinheim, 2004.

(2) (a) Marshall, J. A. *Chem. Rev.* **1996**, *96*, 31. (b) Wang, K. K. *Chem. Rev.* **1996**, *96*, 207. (c) Yamamoto, Y.; Radhakrishnan, U. *Chem. Soc. Rev.* **1999**, *28*, 199. (d) Hashmi, A. S. K. *Angew. Chem., Int. Ed.* **2000**, *39*, 3590. (e) Zimmer, R.; Dinesh, C. U.; Nandanan, E.; Khan, F. A. *Chem. Rev.* **2000**, *100*, 3067. (f) Lu, X.; Zhang, C.; Xu, Z. *Acc. Chem. Res.* **2001**, *34*, 535. (g) Ma, S.; Li, L. *Synlett* **2001**, 1206. (h) Tius, M. A. *Acc. Chem. Res.* **2003**, *36*, 284. (i) Ma, S. *Acc. Chem. Res.* **2003**, *36*, 701. (j) Ma, S. *Eur. J. Org. Chem.* **2004**, 1175. (k) Brandsma, L.; Nedolya, N. A. *Synthesis* **2004**, 735.

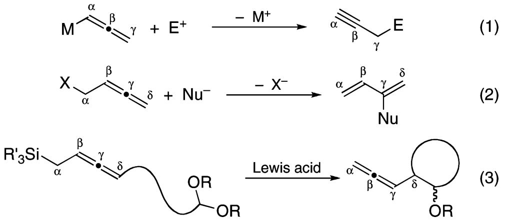
(3) (a) Landor, S. R. In *The Chemistry of the Allenes*; Landor, S. R., Ed.; Academic Press: London, 1982; p 235. (b) Zimmer, R.; Reissig, H.-U. In *Modern Allene Chemistry*; Krause, N., Hashmi, A. S. K., Eds.; Wiley-VCH: Weinheim, 2004; p 847.

(4) (a) Fleming, I.; Barbero, A.; Walter, D. *Chem. Rev.* **1997**, *97*, 2063. (b) Marshall, J. A. *Chem. Rev.* **2000**, *100*, 3163. (c) Marshall, J. A. In *Lewis Acids in Organic Synthesis*; Yamamoto, H., Ed.; Wiley-VCH: Weinheim, 2000; p 453. (d) Marshall, J. A.; Gung, B. W.; Grachan, M. L. In *Modern Allene Chemistry*; Krause, N., Hashmi, A. S. K., Eds.; Wiley-VCH: Weinheim, 2004; p 493. (e) Marshall, J. A. *J. Org. Chem.* **2007**, *72*, 8153.

(5) For recent examples, see: (a) Gharibian, H.; Palikyan, G.; Badanyan, S. H.; Paulsen, K.; Melikyan, G. G. *Helv. Chim. Acta* **2000**, *83*, 3291. (b) Shen, Q.; Hammond, G. B. *Org. Lett.* **2001**, *3*, 2213. (c) Brel, V. K.; Belsky, V. K.; Stash, A. I.; Zavodnik, V. E.; Stang, P. J. *Org. Biomol. Chem.* **2003**, *1*, 4220. (d) Brel, V. K. *Synthesis* **2007**, 2674.

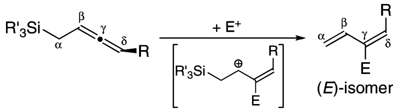
10.1021/ol901780d CCC: $40.75

transposition of the allenic substructure from the β,γ,δ-position to the adjacent α,β,γ-position upon elimination of the silyl group (eq 3). Scope and limitation of this novel allenic substitution reaction as well as results of mechanistic studies will be described in detail.



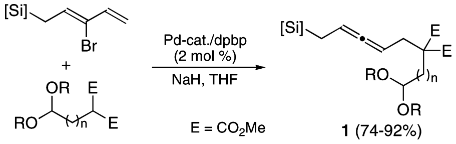
An intermolecular reaction of an (allenylmethyl)silane with an appropriate electrophile is generally regiospecific and takes place in an S_E2' fashion to give the corresponding 1,3-dien-2-yl products.[6] By the use of scalemic δ-monosubstituted (allenylmethyl)silanes, which are axially chiral, unique axial-to-central chirality transfer was realized with fair success.[7] In the reactions with δ-substituted (allenylmethyl)silanes, products were obtained as (*E*)-isomers predominantly,[6b,7] and the stereoselectivity was explained by steric repulsion between the δ-substituent and the incoming electrophile in a transition state (Scheme 1).

Scheme 1



Intramolecular variants of the electrophilic substitution reactions of (allenylmethyl)silanes were examined by assembling both an (allenylmethyl)silane and a proelectrophile moieties into a single molecule. A series of acetal-tethered (allenylmethyl)silanes **1** was prepared from the corresponding 3-bromo-5-silyl-1,3-pentadienes[8] by the Pd-catalyzed reaction according to our previous reports[7b,9] (Scheme 2).

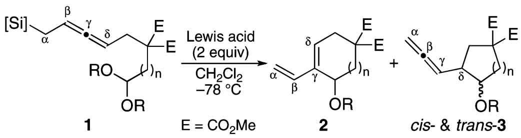
Scheme 2



1a: [Si] = $SiMe_3$, R = Me, n = 1
1b: [Si] = $SiEt_3$, R = Me, n = 1
1c: [Si] = Si^iPr_3, R = Me, n = 1
1d: [Si] = $SiMe_2Ph$, R = Me, n = 1
1e: [Si] = $SiMe_3$, R = Et, n = 1
1f: [Si] = $SiMe_3$, R = Me, n = 2
1g: [Si] = $SiMe_3$, R = Me, n = 0

Treatment of the acetal-tethered (allenylmethyl)silanes **1** with an appropriate Lewis acid (2 equiv to **1**) at −78 °C in dichloromethane promoted intramolecular electrophilic substitution (Table 1). With titanium(IV) chloride, ca. 90% of **1a** was consumed in 3 h. GC and NMR analyses revealed that the reaction mixture contained three major products (entry 1). One was a conjugated vinylcyclohexene **2a** (32% yield) derived by an intramolecular S_E2' pathway. The formation of **2a** was similar to the intermolecular process shown in Scheme 1; however, the internal olefin in **2a** (the $C_\gamma{=}C_\delta$ double bond) has a (*Z*)-configuration due to a geometric requirement of the cyclohexenyl skeleton in contrast to the (*E*)-configuration in intermolecular reaction products.[7b,9] The other two products from the intramolecular reaction were a diastereomeric pair of allenylcyclopentane derivatives, *cis*- and *trans*-**3a** (*cis*/*trans* = 33/67),[10] in 30% combined yield. Formation of **3a** was totally unpredictable, and apparently, it was a result of an unprecedented allene-to-allene rearrangement in the reaction. The allenic moiety

Table 1. Lewis Acid Promoted Intramolecular Cyclization of **1**[a]



entry	1	Lewis acid	conversion[b] (%)	yield (%) of **2**/**3**[c]	*cis*/*trans* in **3**[b]
1	**1a**	$TiCl_4$	90	32 (**2a**)/30 (**3a**)	33/67
2	**1a**	$AlCl_3$	<10	n.d.	
3	**1a**	$BF_3{\cdot}OEt_2$	15	15 (**2a**)/0	
4	**1a**	Me_3SiOTf	75	72 (**2a**)/0	
5	**1b**	$TiCl_4$	85	35 (**2a**)/23 (**3a**)	45/55
6	**1c**	$TiCl_4$	80	38 (**2a**)/14 (**3a**)	n.d.
7	**1d**	$TiCl_4$	80	28 (**2a**)/28 (**3a**)	8/92
8	**1e**	$TiCl_4$	90	56 (**2e**)/24 (**3e**)	31/69
9[d]	**1f**	$TiCl_4$	100	12 (**2f**)/trace	
10[e]	**1g**	$TiCl_4$	50	0/0	

[a] The reaction was carried out with **1** (0.10 mmol) and Lewis acid (0.20 mmol) in dichloromethane (5.0 mL) at −78 °C for 3 h. [b] Determined by ^1H NMR of the crude product. [c] Isolated yield by silica gel chromatography. [d] Formation of poorly characterized oligomeric products were detected. [e] The allene **4** was formed by elimination of acetal.

---

(6) (a) Montury, M.; Psaume, B.; Goré, J. *Tetrahedron Lett.* **1980**, *21*, 163. (b) Psaume, B.; Montury, M.; Goré, J. *Synth. Commun.* **1982**, *12*, 409. (c) Imai, T.; Nishida, S. *J. Org. Chem.* **1990**, *55*, 4849. (d) Hatakeyama, S.; Sugawara, K.; Kawamura, M.; Takano, S. *Tetrahedron Lett.* **1991**, *32*, 4509. (e) Hatakeyama, S.; Sugawara, K.; Takano, S. *Tetrahedron Lett.* **1991**, *32*, 4513. (f) Hatakeyama, S.; Sugawara, K.; Takano, S. *J. Chem. Soc., Chem. Commun.* **1991**, 1533. (g) Hatakeyama, S.; Kawamura, M.; Takano, S. *J. Am. Chem. Soc.* **1994**, *116*, 4081. (h) Hatakeyama, S.; Yoshida, M.; Esumi, T.; Iwabuchi, Y.; Irie, H.; Kawamoto, T.; Yamada, H.; Nishizawa, M. *Tetrahedron Lett.* **1997**, *38*, 7887. (i) Yu, C.-M.; Yoon, S.-K.; Lee, S.-J.; Lee, J.-Y.; Kim, S. S. *Chem. Commun.* **1998**, 2749. (j) Luo, M.; Matsui, A.; Esumi, T.; Iwabuchi, Y.; Hatakeyama, S. *Tetrahedron Lett.* **2000**, *41*, 4401. (k) Parsons, P. J.; Gold, H.; Semple, G.; Montagnon, T. *Synlett* **2000**, 1184. (l) Pacheco, M. C.; Gouverneur, V. *Org. Lett.* **2005**, *7*, 1267. (m) Berkheij, M.; Dijkink, J.; David, O. R. P.; Sonke, T.; IJzendoorn, D. R.; Blaauw, R. H.; van Maarseveen, J. H.; Schoemaker, H. E.; Hiemstra, H. *Eur. J. Org. Chem.* **2008**, 914.

(7) (a) Mentink, G.; van Maarseveen, J. H.; Hiemstra, H. *Org. Lett.* **2002**, *4*, 3497. (b) Ogasawara, M.; Ueyama, K.; Nagano, T.; Mizuhata, Y.; Hayashi, T. *Org. Lett.* **2003**, *5*, 217.

(8) Roux, M.; Santelli, M.; Parrain, J.-L. *Org. Lett.* **2000**, *2*, 1701.

(9) (a) Ogasawara, M.; Ikeda, H.; Hayashi, T. *Angew. Chem., Int. Ed.* **2000**, *39*, 1042. (b) Ogasawara, M.; Ikeda, H.; Nagano, T.; Hayashi, T. *Org. Lett.* **2001**, *3*, 2615. (c) Ogasawara, M.; Ikeda, H.; Nagano, T.; Hayashi, T. *J. Am. Chem. Soc.* **2001**, *123*, 2089. (d) Ogasawara, M.; Ge, Y.; Uetake, K.; Fan, L.; Takahashi, T. *J. Org. Chem.* **2005**, *70*, 3871. (e) Ogasawara, M.; Nagano, T.; Hayashi, T. *J. Org. Chem.* **2005**, *70*, 5764.

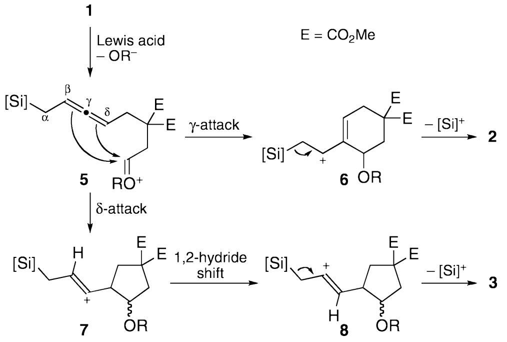
in **3a** consisted of the α,*β*,*γ*-carbons of the substrate **1a**, while the C═C═C framework comprised the *β*,*γ*,*δ*-carbons in **1a**.

The reaction was sensitive to choices of Lewis acid promoters. A reaction of **1a** with $AlCl_3$ was sluggish, and its conversion was less than 10% in 3 h (entry 2). $BF_3{\cdot}OEt_2$ and Me_3SiOTf promoters afforded **2a** exclusively, and no **3a** was detected (entries 3 and 4).

With a bulkier silyl group in **1**, the six-membered product **2a** became more dominant over the five-membered **3a** in the reaction. The TES-substituted substrate **1b** gave **2a** and **3a** in 35% and 23% yields, respectively (entry 5). The TIPS analogue **1c** afforded a mixture of **2a** (38%) and **3a** (14%; entry 6). In the same way, the diethyl acetal derivative **1e** reacted with $TiCl_4$ to give the vinylcyclohexene **2e** (56%) and the allenylcyclopentane **3e** (24%), respectively (entry 8).

Formation of the unusual product **3** was unique to the five-membered carbocycles. The (allenylmethyl)silane **1f**, which possesses an additional CH_2 moiety in the acetal tether, mainly produced poorly characterized oligomeric products together with vinylcycloheptene **2f** in 12% (entry 9). A reaction of **1g**, that is with a shorter acetal tether, facilitated elimination of the acetal group to give $Me_3SiCH_2CH{=}C{=}CHCH_2CH(CO_2Me)_2$ (**4**) in 34% yield, and no cyclized products were detected (entry 10).

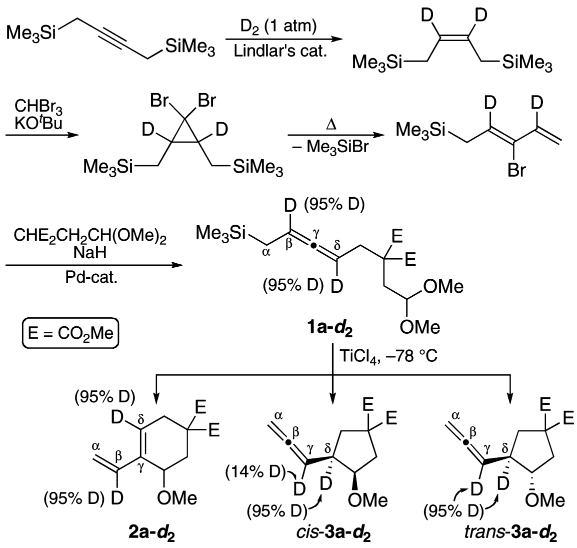
Scheme 3



A plausible mechanism of the intramolecular cyclization of **1** is shown in Scheme 3. A cationic intermediate **5**, which is generated in situ by Lewis acid promoted abstraction of OR$^-$ from **1**, reacts in two separate pathways. The electrophilic oxonium moiety in **5** reacts primarily at the *γ*-carbon of the (allenylmethyl)silane unit as reported in the intermolecular reactions.[6] Following elimination of the silyl group from the *β*-silyl carbocation, intermediate **6** furnishes the vinylcyclohexene **2**. On the other hand, a nucleophilic attack of the *δ*-carbon to the oxonium cation is competeing with the *γ*-attack in certain cases. An initially formed vinyl cation **7** is transformed to **8** via an 1,2-hydride shift. Presumably, stabilization of a positive charge in **8** by the *β*-silicon effect is the main driving force to facilitate the hydride shift. Subsequent elimination of the silyl group from **8** affords the allenylcyclopentanes **3**. The selectivity between **2** and **3** in the cyclization of **1** should be determined by nature of the oxonium intermediate **5**, which exists as an ion pair with an anionic adduct between RO$^-$ and a Lewis acid. Since pairing affinity between **5** and the anion depends on the Lewis acid moiety in the anion, nature/reactivity of **5** also depends on the Lewis acid. This can be attributed to the Lewis acid-dependent selectivity in the present reaction.[11]

A key step in the pathway to the unusual products **3** is the 1,2-hydride shift in **7**. The validity of the proposed reaction mechanism was justified by a deuterium-labeling experiment. A partially deuterated (allenylmethyl)silane **1a-d_2** (95% deuterium incorporation) was prepared as shown in Scheme 4. Treatment of **1a-d_2** with $TiCl_4$ as in entry 1 in Table 1 provided a mixture of **2a-d_2** and **3a-d_2** with the same yields and the same distribution within experimental errors. The ^{1}H- and ^{2}D-NMR spectra of the products revealed that the deuterium atoms were retained on the *β*- and *δ*-carbons in **2a-d_2**. On the other hand, the deuterium atoms were incorporated on the *γ*- and *δ*-carbons in *cis*- and *trans*-**3a-d_2** as expected from the mechanism in Scheme 3. No other extra deuteration was detected in all three products. These results clearly support involvement of the 1,2-hydride shift process in the formation of **3**.

Scheme 4



It was found that, however, the D-content at the *γ*-carbon in *cis*-**3a-d_2** was significantly diminished to 14%. Despite our best efforts,[12] proton sources of the D-content reduction in *cis*-**3a-d_2** could not be identified. The lower D-content

---

(10) The configurations of the *cis*- and *trans*-**3** were determined by ^{1}H NMR NOE experiments.

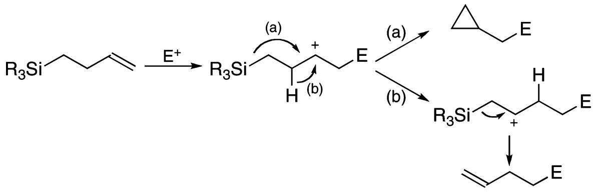
(11) Santelli, M.; Pons, J.-M. *Lewis Acids and Selectivity in Organic Synthesis*; CRC Press: New York, 1996; p 185 and references cited therein.

(12) No deuterium introduction was detected in the reactions of **1a** using a deuterated solvent (CD_2Cl_2) and/or a deuterated quencher (a mixture of CD_3OD and D_2O). A partially deuterated **1a**, which is with a deuterated acetal pendant $-CH(OCD_3)_2$, afforded the products which were deuterated only in the $-OCD_3$ substituents.

postulates participation of an intermolecular process,[13] which is competing with the intramolecular pathway, in the formation of *cis*-**3a**-$\boldsymbol{d_2}$.

Silicon atoms promote the formation of a positive charge at the β-position, which is known as the β-silicon effect.[14] High reactivity of carbon−carbon double bonds in allylsilane derivatives toward electrophiles could be ascribed to the effect. Silicon atoms are also capable of stabilizing a cation at the γ-position in the same way (the γ-silicon effect), but the γ-silicon effect is much weaker than the β-counterpart.[15] Thus, synthetic applications of the γ-silicon effect have been rather limited. It was reported that homoallylsilanes (3-butenylsilanes) reacted with an electrophile at the δ-positions to generate the corresponding γ-cation intermediates, which were transformed to final products either by desilylative cyclopropanation (path (a) in Scheme 5)[16] or by the 1,2-hydride shift/silicon elimination sequence (path (b)).[16a,17]

Scheme 5



An (allenylmethyl)silane possesses both an allylsilane and a homoallylsilane substructure within a single molecule. Whereas the β-silicon effect is dominant over the γ-effect, reactions of (allenylmethyl)silanes with an electrophile generally takes place in the same way as those of allylsilanes. Thus, a usual intermolecular reaction of an (allenylmethyl)-silane with an electrophile takes place at the allenic central *sp*-carbon (the γ-carbon).[6] In the cases of **1a**−**e**, however, reactions at the less nucleophilic δ-carbons were competing with those at the γ-carbons due to constrained steric requirements of the intramolecular process. As a consequence, the (allenylmethyl)silanes showed the reaction mode analogous to that of homoallylsilanes to give the unusual allenic rearrangement products **3**.

In summary, we have found out an unprecedented mode of an allenic substitution reaction. The unusual transposition of allenic frameworks was concomitant with the intramolecular electrophilic substitution/cyclization of the acetal-tethered (allenylmethyl)silanes. To the best of our knowledge, this is the first demonstration that (allenylmethyl)silanes show homoallylsilane-like ractivity in electrophilic substitutions.

Acknowledgment. A part of this work was supported by a Grant-in-Aid for Scientific Research on Priority Areas “Advanced Molecular Transformations of Carbon Resources” from the Ministry of Education, Culture, Sports, Science and Technology, Japan.

Supporting Information Available: Detailed experimental procedures and compound characterization data. This material is available free of charge via the Internet at http://pubs.acs.org.

OL901780D

---

[13] As a possible intermolecular process for the loss of D-content in *cis*-**3a**-$\boldsymbol{d_2}$, the following route is postulated: initial deprotonation of the intermediate *cis*-**7**-$\boldsymbol{d_2}$ gives the corresponding propargylsilane, which undergoes successive protodesilylation to afford *cis*-**3a**-$\boldsymbol{d_2}$. Whereas the reaction mixture must be protic due to inevitable partial hydrolysis of $TiCl_4$, this route gives *cis*-**3a**-$\boldsymbol{d_2}$ of the lower D-content at the γ-carbon. Nevertheless, the difference between *cis*- and *trans*-**3a**-$\boldsymbol{d_2}$ in the D-contents at the γ-positions cannot be rationalized by this process.

[14] (a) Weber, W. P. *Silicon Reagents for Organic Synthesis*; Springer-Verlag: Berlin, Heidelberg, 1983. (b) Colvin, E. W. *Silicon Reagents in Organic Synthesis*; Academic Press: London, 1988. (c) Fleming, I. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Paquette, L. A., Eds; Pergamon Press: Oxford, 1991; Vol. 2, p 563. (d) Fleming, I.; Dunoguès, J.; Smithers, R. *Org. React.* **1989**, *37*, 57.

[15] Sakurai, H.; Hosomi, A.; Kumada, M. *J. Org. Chem.* **1969**, *34*, 1764.

[16] (a) Sakurai, H.; Imai, T.; Hosomi, A. *Tetrahedron Lett.* **1977**, *18*, 4045. (b) Hatanaka, Y.; Kuwajima, I. *Tetrahedron Lett.* **1986**, *27*, 719.

[17] Masuya, K.; Tanino, K.; Kuwajima, I. *Synlett* **1999**, 647.