ORGANIC LETTERS

1999
Vol. 1, No. 6
917−919

Stereoselective Allylation of Acetals through Intramolecular Transfer of an Allylsilane

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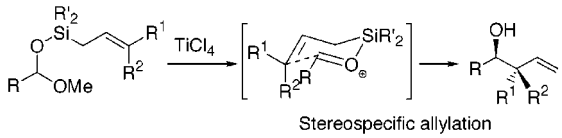
Received July 20, 1999

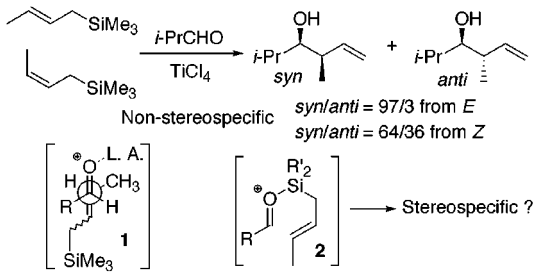
ABSTRACT



Through a cyclic transition state of tetravalent silicon intermediate, the reaction of allylsilyl acetal in the presence of $TiCl_4$ proceeded in a stereoselective manner. Highly diastereoselective allylation of lactols could be performed in two steps. On the other hand, Me_3SiOTf-mediated reaction of allylsilyl acetal provided homoallyl methyl ether without stereoselectivity.

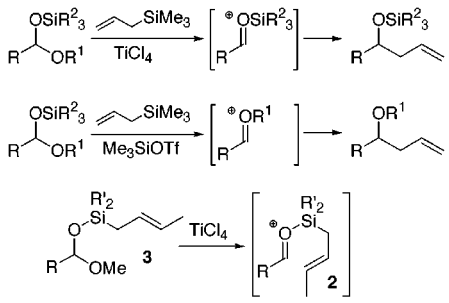
Lewis acid-mediated reaction of allylsilanes with aldehydes (Hosomi−Sakurai reaction) has been broadly used for the synthesis of homoallylic alcohols.[1] In the reaction of crotylsilane, although the reactions proceed with high regioselectivity, *syn*-homoallylic alcohols are obtained predominantly regardless of the geometry of crotylsilane (Scheme 1).[2] The stereochemical outcome of these reactions has been explained by reaction through an acyclic transition state such as **1**. On the other hand, some stereoselective allylations using allylic silanes via hypervalent silicate intermediates have been reported.[3] These reactions presumably proceed via a six-membered cyclic transition state. Then, if a silyl oxocarbenium ion species **2** possessing an allylsilane moiety on the oxygen can be prepared, what is observed regarding its stereochemical outcome? Herein we wish to report the stereoselective allylation reaction of alkyl allylsilyl mixed acetals through a tetravalent silicon intermediate.

Scheme 1



We have recently reported the reaction of alkyl silyl mixed acetal with allylsilane in the presence of Lewis acids (Scheme 2).[4,5] The use of $TiCl_4$ as a Lewis acid caused a replacement of the methoxy group by an allyl moiety exclusively via a silyl oxocarbenium intermediate. Then, it was anticipated that the use of an allyl-substituted silyl acetal **3** as the starting

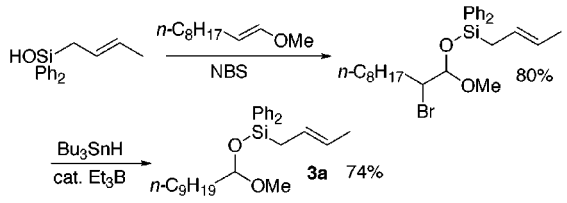
Scheme 2



10.1021/ol990840m CCC: $18.00 © 1999 American Chemical Society
Published on Web 08/31/1999

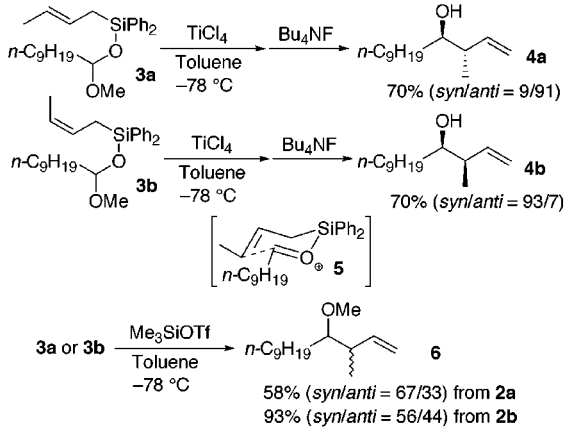
material would provide us the desired cationic intermediate **2** containing an allylsilane moiety. The acetals could be prepared in two steps by the reported procedure from silanol (Scheme 3).[6]

Scheme 3



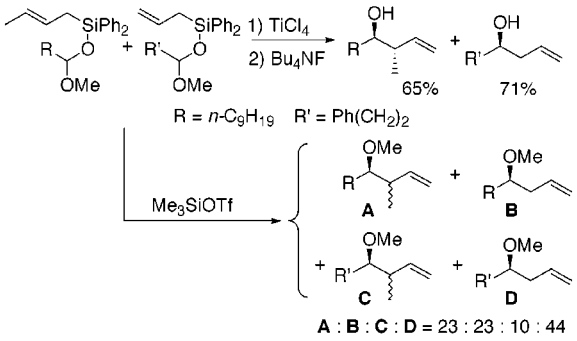
To a solution of (*E*)-crotylsilyl acetal **3a** in toluene was added $TiCl_4$ at −78 °C, and the mixture was stirred for 1.5 h. After the usual workup, treatment of the crude mixture with Bu_4NF provided *anti*-homoallylic alcohol **4a** selectively in 70% yield.[7] On the other hand, starting from (*Z*)-crotylsilyl acetal **3b**, *syn*-homoallylic **4b** alcohol was obtained with high selectivity under the same reaction conditions (Scheme 4).

Scheme 4



On the basis of these results, it is obvious that the reaction proceeds in a stereoselective manner through a six-membered cyclic transition state **5**. The intramolecular nature of the $TiCl_4$-promoted allylation process is clear from the following crossover experiment (Scheme 5). No crossover products

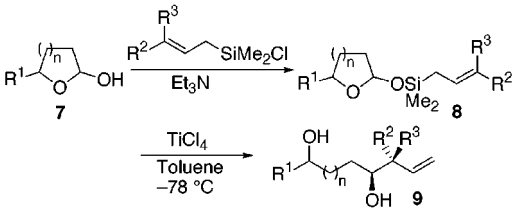
Scheme 5



were obtained. In contrast, the use of Me_3SiOTf instead of $TiCl_4$ as a Lewis acid provided methyl ethers **6** in good yield.[8] The stereoselectivities of **6** are low, and stereospecificity could not be observed. The crossover experiment in the presence of Me_3SiOTf as a Lewis acid provided four possible homoallylic methyl ethers. Thus, the allylation occurred intermolecularly to afford **6** without stereoselectivity through an acyclic transition state.

Preparative methods of the starting silyl acetals from silanols are quite limited. Thus, we then examined direct silylation of hemiacetals to develop an alternative, more facile route to silyl acetals. In fact, silylation of lactol **7** effectively provided the corresponding cyclic silyl acetal **8** in one step. Table 1 summarizes the results of silylation of lactols and

Table 1. Silylation and Allylation Reaction of Lactols



entry	n	R^1	R^2	R^3	yield of **8** (%)	yield of **9** (%)	syn/anti
1	1	H	n-C_6H_{13}	H	32 (**8a**)	69 (**9a**)	1/>99
2	2	H	n-C_6H_{13}	H	65 (**8b**)	61 (**9b**)	1/>99
3	1	CH_3	n-C_6H_{13}	H	67 (**8c**)	53 (**9c**)	1/>99
4	1	H	H	n-C_6H_{13}	33 (**8d**)	61 (**9d**)	>99/1
5	2	H	H	n-C_6H_{13}	76 (**8e**)	69 (**9e**)	>99/1
6	1	CH_3	H	n-C_6H_{13}	71 (**8f**)	50 (**9f**)	>99/1

allylation of the cyclic acetals **8** in the presence of $TiCl_4$.[9] The reaction of γ-lactol with chlorosilanes gave the corresponding silyl acetals **8a** and **8d** in low yields because of the competitive formation of 4-siloxyaldehydes derived from silylation of γ-hydroxyaldehyde (entries 1 and 4). High

(1) (a) Hosomi, A.; Sakurai, H. *Tetrahedron Lett.* **1976**, 1295. (b) Sakurai, H. *Pure Appl. Chem.* **1982**, *54*, 1. (c) Hosomi, A.; Sakurai, H. *J. Synth. Org. Chem. Jpn*, **1985**, *43*, 406. (d) Fleming, I.; Dunogues, J.; Smithers, R. *Org. React.* **1989**, *37*, 57. (e) Fleming, I.; Barbero, A.; Walter, D. *Chem. Rev.* **1997**, *97*, 2063. (f) Yamamoto, Y.; Asao, N. *Chem. Rev.* **1993**, *93*, 2207−2293.

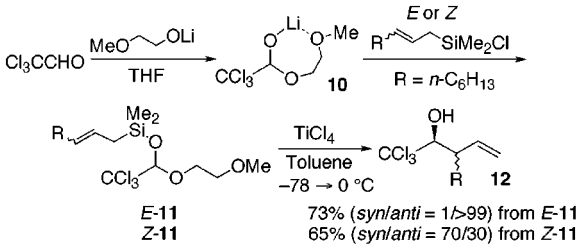
(2) Hayashi, T.; Kabeta, K. Hamachi, I.; Kumada, M. *Tetrahedron Lett.* **1983**, *24*, 2865.

(3) (a) Majetich, G.; Casares, A.; Chapman, D.; Behnke, M. *J. Org. Chem.* **1986**, *51*, 1745. (b) Kira, M.; Sato, K.; Sakurai, H. *J. Am. Chem. Soc.* **1988**, *110*, 4599. (c) Hosomi, A.; Kohra, S.; Ogata, K.; Yanagi, T.; Tominaga, Y. *J. Org. Chem.* **1990**, *55*, 2415. (d) Cerveau, G.; Chuit, C.; Corriu, R. J. P.; Reye, C. *J. Organomet. Chem.* **1987**, *328*, C17. (e) Matsumoto, K.; Oshima, K.; Utimoto, K. *J. Org. Chem.* **1994**, *59*, 7152. (f) Kobayashi, S.; Nishio, K. *J. Org. Chem.* **1994**, *59*, 6620.

(4) (a) Shinokubo, H.; Oshima, K.; Utimoto, K. *Chem. Lett.* **1995**, 461. (b) Maeda, K.; Shinokubo, H.; Oshima, K. *J. Org. Chem.* **1997**, *62*, 6429.

stereoselectivities are observed in the allylation reaction for all acetals examined.[10] Another access to silyl acetal is shown in Scheme 6. Treatment of lithium salt of 2-methoxyethanol

Scheme 6



with chloral followed by an addition of chlorosilane afforded the corresponding silyl acetal **11** in good yield. The reactions of these silyl acetals also proceeded in a stereoselective manner, although the stereoselectivity from *Z*-**11** was moderate (70/30).[11]

In summary, we have shown that the allylation reaction of allylsilyl mixed acetals in the presence of $TiCl_4$ occurred in a stereoselective manner. From (*E*)- or (*Z*)-crotylsilyl acetal, *anti*- or *syn*-homoallylic alcohol could be stereoselectively obtained, respectively. This stereochemical outcome clearly shows that the allylation reaction proceeds via a cyclic transition state. Excellent stereoselectivities were observed in the allylation reactions of lactol silyl ethers. Further efforts to extend the scope of this reaction are currently underway.

Acknowledgment. This work was supported by a Grant-in Aid for Scientific Research on Priority Area (No. 10208208) from the Ministry of Education, Science, Sports, and Culture, Japan.

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(5) Enantioselective syntheses of homoallylic ethers via alkyl silyl mixed acetal intermediate have been reported; see: Tietze, L. F.; Wulff, C.; Wegner, C.; Schuffenhauer, A.; Schiemann, K. *J. Am. Chem. Soc.* **1998**, *120*, 4276. Tietze, L. F.; Schiemann, K.; Wegner, C.; Wulff, C. *Chem. Eur. J.* **1998**, *4*, 1862. Tietze, L. F.; Schiemann, K.; Wegner, C.; Wulff, C. *Chem. Eur. J.* **1996**, *2*, 1164. Tietze, L. F.; Dölle, A.; Schiemann, K. *Angew. Chem., Int Ed. Engl.* **1992**, *31*, 1372. Tietze, L. F.; Schiemann, K.; Wegner, C. *J. Am. Chem. Soc.* **1995**, *117*, 5851. Mukaiyama, T.; Ohshima, M.; Miyoshi, N. *Chem. Lett.* **1987**, 1121.

(6) Shinokubo, H.; Oshima, K.; Utimoto, K. *Bull. Chem. Soc. Jpn.* **1997**, *70*, 2255.

(7) Before treatment with Bu_4NF, a hydroxydiphenylsilyl ether of allylic alcohol **4a** or **4b** was observed in the crude mixture.

(8) As to the switching effect of $TiCl_4$ to Me_3SiOTf, see ref 4b.

(9) Experimental procedure is as follows. To a solution of δ-lactol (0.56 g, 5.5 mmol) in ether and Et_3N (1.4 mL, 10.0 mmol) was added (*E*)-2-nonenyldimethylsilyl chloride (1.09 g, 5.0 mmol) in ether. A white precipitate was immediately formed, and the mixture was stirred for 4 h. After usual workup, purification by silica gel chromatography afforded starting silyl acetal **8b** in 65% yield. A toluene solution of $TiCl_4$ (1.0 mL, 1.0 M, 1.0 mmol) was added to **8b** (0.21 g, 0.75 mmol) in toluene (6 mL) at −78 °C. The reaction mixture was stirred for 1 h at this temperature. The mixture was quenched with saturated aqueous NH_4Cl, and the whole was extracted with ether. The combined organic extracts were concentrated in vacuo, and the residue was dissolved in methanol. To this was added two drops of concentrated HCl, and the mixture was stirred for 1 h. Extractive workup followed by purification by silica gel column chromatography afforded *anti*-6-hexyl-7-octene-1,5-diol (0.12 g, 0.52 mmol) in 61% yield.

(10) The preexisting stereogenic center of **8c** and **8f** seems to have no influence on the stereoselectivity of the reaction (entries 3 and 6). For instance, the isomeric ratio of **8c** (60/40) was maintained throughout the reaction and **9c** was obtained as a mixture of two *anti*-1,4-diols (60/40).

(11) The reason for the moderate selectivity in *Z*-isomer is not clear at this stage. A reviewer suggested a possible explanation as follows. The trichloromethyl group is quite large and its steric hindrance would make reaction through a cyclic transition state unfavorable in the case of the *Z* isomer.