Stereoselective Synthesis of Allyl Vinyl Ethers from Silyl Enol Ethers

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Claisen rearrangement of allyl vinyl ethers is one of the most powerful tools for stereoselective carbon−carbon bond formation.[1] The stereoselective formation of the enol ether moiety is the key to diastereocontrol over the newly created chiral centers of the product. However, acyclic enol ether Claisen rearrangement shows no significant diastereoselectivity because of the lack of stereoselective synthesis of the enol ether moiety.[2] Allyl vinyl ethers are typically prepared by either mercury- or acid-catalyzed vinyl ether exchange with allylic alcohols or by Wittig-type alkenation reactions from carbonyl precursors.[3] However, the stereoselectivity in these reactions is usually low.[4] We report here the stereoselective synthesis of allyl vinyl ethers from silyl enol ethers through mixed iodo acetals.

Mixed iodo acetals were very easily prepared stereoselectively[5] by the addition of a solution of silyl enol ether in dichloromethane to a stirred heterogeneous mixture of *N*-iodosuccinimide (NIS) and a primary or secondary allylic alcohol in dichloromethane at −78 °C.[6,7] While (*Z*)-1-(*tert*-butyldimethylsiloxy)-1-decene (**1b**)[8] selectively gave *erythro*-1-(allyloxy)-1-(*tert*-butyldimethylsiloxy)-2-iodododecane (**2bD**) (*erythro*/*threo* = 99/1)[9] in 94% yield, (*E*)-silyl enol ether **1c**[8] selectively gave *threo*-1-(allyloxy)-1-siloxy-2-iodododecane (**2cD**) (*threo*/*erythro* = 96/4) in 77% yield upon treatment with (*E*)-2-hexen-1-ol and NIS. Even the tertiary allylic alcohol linalool gave **2aC** in 42% yield by this method. The results are summarized in Table 1. The results on the reaction of these iodo acetals with butyllithium in DME are also shown in Table 1.

The addition of butyllithium (2.4 equiv) to a solution of **2aA**, **2aB**, or **2aC** in DME at −78 °C gave allyl vinyl ether **3aA**, **3aB**, or **3aC** at a yield of 66%, 92%, or 60%, respectively.[10,11] Surprisingly, the *tert*-butyldimethylsiloxy group was selectively eliminated prior to the allyloxy group, and only a small amount of silyl enol ether **1a** was obtained (<9% yield).[12] Treatment of **2bD** (*erythro*/*threo* = 99/1) with butyllithium in DME at −78 °C gave allyl vinyl ether **3bD** (*E*/*Z* = 96/4, 76% yield) along with silyl enol ether (18%, **1c**/**1b** = 92/8). The addition of HMPA (4 equiv to *n*-BuLi) increased the yield of **3bD** at the expense of **1c**/**1b** (3%), although *E* stereoselectivity decreased slightly (*E*/*Z* = 90/10). Furthermore, treatment of **2cD** (*erythro*/*threo* = 4/96) with butyllithium in DME at −78 °C gave 1-(allyloxy)-1-decene (**3cD**) (*Z*/*E* = 86/14, 79% yield) in addition to 1-siloxy-1-decene (19%, **1c**/**1b** = 55/45). The addition of HMPA improved both the yield of **3cD** and its *Z* stereoselectivity. Thus, (*Z*)-1-(allyloxy)-1-decene (**3cD**) (*Z*/*E* = 96/4, 81% yield) was obtained selectively along with a small amount of **1c**/**1b** (9%, **1c**/**1b** = 84/16). Similar results were obtained from **2dE** and **2eE**. Trisubstituted allyl alkenyl ethers **3fE** and **3gE** were also prepared from **1f** and **1g**, respectively, in good yield.[13]

The solvent plays a critical role in the distribution of the products. A complete change in the course of the reactions was observed when hexane was used as a solvent in place of DME. For instance, treatment of *erythro* **2bD** with butyllithium in hexane at −78 °C gave 1-(*tert*-butyldimethylsiloxy)-1-decene **1c** as the sole product with high stereoselectivity (*E*/*Z* = >99/<1). A trace of allyl vinyl ether **3bD** (<5%) could be detected in the

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[1] Recent reviews: (a) Bartlett, P. A. *Tetrahedron* **1980**, *36*, 3. (b) Gajewski, J. J. *Hydrocarbon Thermal Isomerizations*; Academic Press: New York, 1981. (c) Lutz, R. P. *Chem. Rev.* **1984**, *84*, 205. (d) Hill, R. K. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic Press: New York, 1984; Vol. 3, p 503. (e) Murray, A. W. *Org. React. Mech.* **1986**, 429; **1987**, 457. (f) Moody, C. J. *Adv. Heterocycl. Chem.* **1987**, *42*, 203. (g) Ziegler, F. E. *Chem. Rev.* **1988**, *88*, 1423. (h) Kallmerten, J.; Wittman, M. D. *Stud. Nat. Prod. Chem.* **1989**, *3*, 233. (i) Blechert, S. *Synthesis* **1989**, 71. (j) Wipf, P. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Paquette, L. A., Eds.; Pergamon Press: New York, 1991; Vol. 5, Chapter 7.2, p 827.

[2] Sugihara, M.; Yanagisawa, M.; Nakai, T. *Synlett* **1995**, 447. Ziegler, F. E. *Acc. Chem. Res.* **1977**, *10*, 227.

[3] The Tebbe reagent has been used to prepare allyl vinyl ether. Kinney, W. A.; Coghlan, M. J.; Paquette, L. A. *J. Am. Chem. Soc.* **1985**, *107*, 7352.

[4] The selective preparation of (*Z*)-alkenyl ethers with a $RCHBr_2$−Zn−$TiCl_4$ system has been reported previously. Okazoe, T.; Takai, K.; Oshima, K.; Utimoto, K. *J. Org. Chem.* **1987**, *52*, 4410.

[5] Thiem, J.; Karl, H.; Schwentner, J. *Synthesis* **1978**, 696.

[6] For a related procedure, see: Stork, G.; Sher, P. M. *J. Am. Chem. Soc.* **1986**, *108*, 303.

[7] The use of (trimethylsiloxy)ethene in place of (*tert*-butyldimethylsiloxy)ethene gave an α-iodocarbonyl compound upon treatment with NIS in the presence of alcohols. Reaction of trimethylsilyl enol ethers with NCS has been reported to give α-chloro ketones. Hambly, G. F.; Chan, T. H. *Tetrahedron Lett.* **1986**, *27*, 2563.

[8] The stereoselective synthesis of silyl enol ethers has been studied extensively. Brownbridge, P. *Synthesis* **1983**, 1. Silyl enol ether **1a** was prepared according to the reported procedure. Jung, M. E.; Blum, R. B. *Tetrahedron Lett.* **1977**, 3791. (*Z*)-Isomer **1b** was generated from decanal with *t*-$BuMe_2SiOTf$ and triethylamine. Mander, L. N.; Sethi, S. P. *Tetrahedron Lett.* **1984**, *25*, 5953. (*E*)-Isomer **1c** was generated with *t*-$BuMe_2SiCl$ and DBU. Taniguchi, Y.; Inanaga, J.; Yamaguchi, M. *Bull. Chem. Soc. Jpn.* **1981**, *54*, 3229.

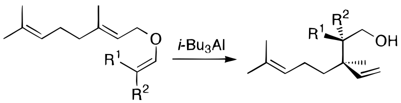
[9] For the nomenclature of *threo* and *erythro*, see: Noyori, R.; Nishida, H. *J. Am. Chem. Soc.* **1981**, *103*, 2106.

[10] A typical procedure is as follows. Butyllithium (1.6 *M* hexane solution, 1.5 mL, 2.4 mmol) was added to a solution of **2aA** (0.42 g, 1.0 mmol) in DME (6 mL) at −78 °C. After being stirred for 0.5 h, the resulting mixture was poured into saturated aqueous $NaHCO_3$ and extracted with hexane (10 mL × 2). The combined organic layers were dried over Na_2SO_4 and concentrated in vacuo. The residual oil was applied to an alumina (ICN alumina B activity III) column to give **3aA** (0.11 g) at a yield of 66% along with (*tert*-butyldimethylsiloxy)ethene (8%).

[11] The conversion of halo ether or halo acetal to alkene or alkenyl ether with *n*-BuLi or *t*-BuLi has been reported in the total synthesis of natural products. Wender, P. A.; Keenan, R. M.; Lee, H. Y. *J. Am. Chem. Soc.* **1987**, *109*, 4390. Ireland, R. E.; Häbich, D.; Norbech, D. W. *J. Am. Chem. Soc.* **1985**, *107*, 3271.

[12] It is not clear why the siloxy group was eliminated prior to the allyloxy group. Selective elimination of the siloxy group may have occurred because silanol has a higher acidity than alcohols. Bassindale, A. R.; Taylor, P. G. In *The Chemistry of Organic Silicon Compounds;* Patai, S., Rappoport, Z., Eds.; John Wiley & Sons, Ltd.: New York, 1989; Part 1, Chapter 12, pp 809−838.

[13] We applied this new approach to the diastereoselective formation of adjacent quaternary carbon atoms. The organoaluminium-promoted Claisen rearrangement[14] of these ethers has been examined. For instance, treatment of a solution of **3fE** or **3gE** in dichloromethane with *i*-Bu_3Al at 25 °C gave the corresponding 4-alken-1-ol with contiguous quaternary carbon centers.[15]



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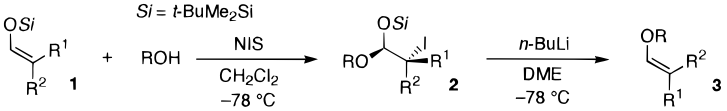
3fE: R^1 = Me R^2 = Et (*E*/*Z* = 94/6) 60% *erythro*/*threo* = 7/93
3gE: R^1 = Et R^2 = Me (*E*/*Z* = 8/92) 72% *erythro*/*threo* = 90/10

[14] Takai, K.; Mori, I.; Oshima, K.; Nozaki, H. *Bull. Chem. Soc. Jpn.* **1984**, *57* 446. Nonoshita, K.; Banno, H.; Maruoka, K; Yamamoto, H. *J. Am. Chem, Soc.* **1990**, *112*, 316. Maruoka, K.; Saito, S.; Yamamoto, H. *J. Am. Chem. Soc.* **1995**, *117*, 1165.

[15] Gilbert, J. C.; Kelley, T. A. *Tetrahedron* **1988**, *44*, 7587.

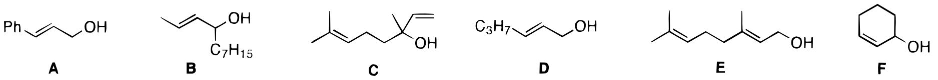
[16] The yield of the product could not be determined because of its volatility.

Table 1. Preparation and Reaction of Mixed Iodo Acetals

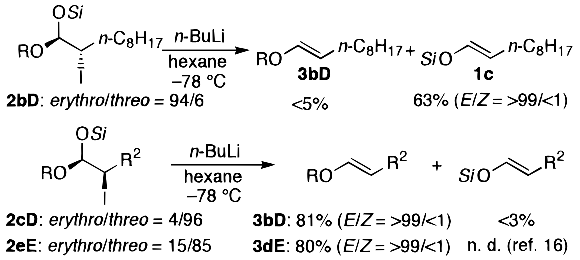


silyl enol ether **1**				acetal **2**			alkenyl ether **3**		
	R^1	R^2	allylic alcohol (ROH)		yield (%)	*erythro*/*threo*		yield (%)	*E*/*Z*
1a	H	H	A	**2aA**	92		**3aA**	66	
1a	H	H	B	**2aB**	66		**3aB**	92	
1a	H	H	C	**2aC**	42		**3aC**	60	
1b	n-C_8H_{17}	H	D	**2bD**	94	99/1	**3bD**	76	96/4
1c	H	n-C_8H_{17}	D	**2cD**	77	4/96	**3cD**	81[a]	4/96
1d	CH_3	H	E	**2dE**	89	99/1	**3dE**	86	92/8
1e	H	CH_3	E	**2eE**	69	15/85	**3eE**	77[a]	24/76
1b	n-C_8H_{17}	H	B	**2bB**	65	99/1	**3bB**	76	91/9
1b	n-C_8H_{17}	H	F	**2bF**	91	99/1	**3bF**	74	91/9
1f	C_2H_5	CH_3	E	**2fE**	79	98/2	**3fE**	94	94/6
1g	CH_3	C_2H_5	E	**2gE**	79	4/96	**3gE**	88	8/92

[a] HMPA (4 equiv to n-BuLi) was used as a cosolvent. See text.



Scheme 1



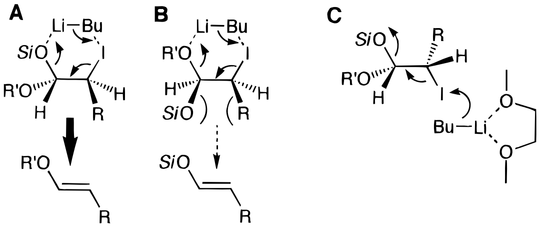
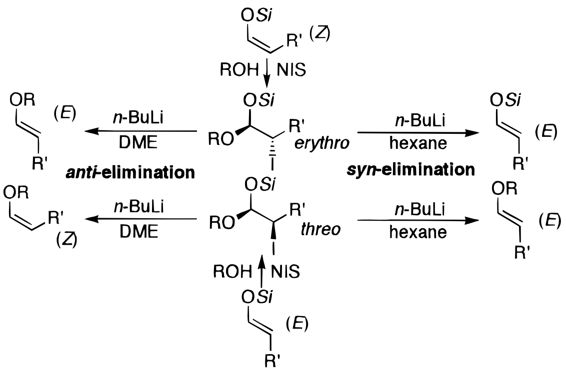


Figure 1.

Scheme 2



reaction mixture. Thus, (*Z*)-1-(*tert*-butyldimethylsiloxy)-1-decene (**1b**) could be converted exclusively into the (*E*)-isomer **1c** through 1-(allyloxy)-1-(*tert*-butyldimethylsiloxy)-2-iododecane (**2bD**). On the other hand, *threo* **2cD** afforded (*E*)-1-(allyloxy)-1-decene (**3bD**) exclusively without contamination by siloxy-1-decene **1c** upon treatment with n-BuLi in hexane. Therefore, both (*E*)-**3bD** and (*Z*)-**3cD** could be prepared selectively by changing solvents from the same mixed iodo acetal **2cD** (Scheme 1).

We are tempted to assume the following reaction mechanism. In hexane, the reaction might proceed via the syn periplanar transition state of an E2 reaction (Figure 1, **A** or **B**, **2cD**: R = n-C_8H_{17}, R′ = n-PrCH=CH-CH_2). Coordination of the siloxy group to lithium triggers the attack of iodine by the butyl anion. Severe steric repulsion between the siloxy group and the alkyl group makes transition state B less favorable. Thus, treatment of *threo* **2cD** with butyllithium gives (*E*)-1-(allyloxy)-1-alkene **3bD** selectively through transition state **A**. Using the same argument, *erythro* **2bD** exclusively gives (*E*)-1-(siloxy)-1-alkene **1c**. On the other hand, in DME, 1-(allyloxy)-1-siloxy-2-iodo species **2bD** and **2cD** could undergo the stereoselective anti elimination of the siloxy and iodine moieties (Figure 1, **C**). In polar solvents such as DME and DME−HMPA, lithium is surrounded by solvents and cannot be coordinated by the siloxy or allyloxy group, as shown in **A** and **B**.

In conclusion, (1) in DME, stereospecific *anti*-elimination of the siloxy and iodine moieties proceeded. Thus, employment of *erythro* mixed acetal led to the formation of (*E*)-alkenyl ether. Conversely, reaction of *threo* isomer gave the (*Z*)-alkenyl ether. (2) In hexane, *syn*-elimination took place preferentially. Elimination of the elements of alcohol proceeded to give (*E*)-silyl enol ether from *erythro* mixed acetal, while reaction of *threo* isomer afforded only the (*E*)-alkenyl ether (Scheme 2).

Supporting Information Available: Characterization data (4 pages).

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