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A Highly Stereoselective Synthesis of *Z*-Disubstituted Olefin by *O*-Assisted Still-Wittig Rearrangement†

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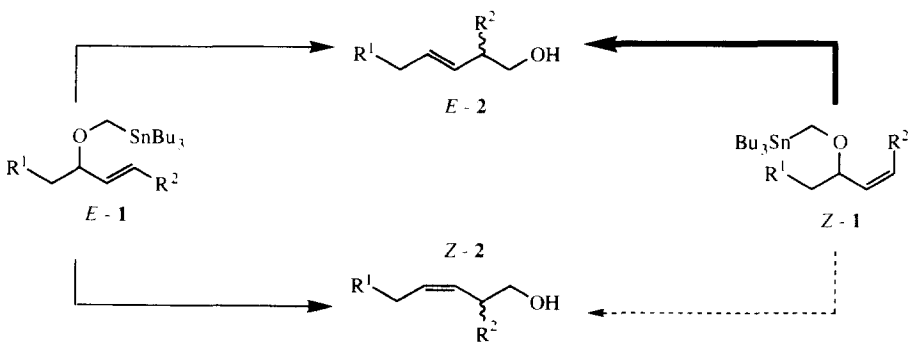
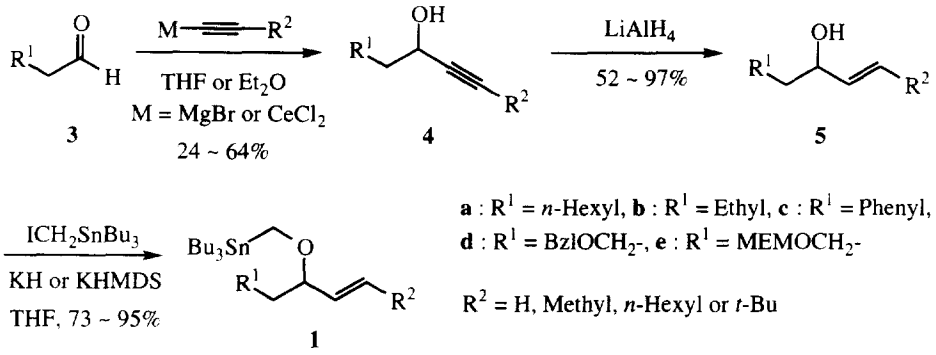
Abstract: In the Still-Wittig rearrangement, stannylated methyl (*E*)-allylic ethers having an aliphatic side chain (**1a-c**) exhibited the usual similar stereoselectivity, although the poor stereoselectivity was remarkably improved by the assistance of an alkoxy moiety on the alkenyl chain. A stannylated methyl (*Z*)-allylic ether bearing an alkoxy moiety on the alkenyl chain (**1e**) also showed a high *E* selectivity as previously reported.

[2, 3]-Sigmatropic rearrangement is one of important reactions for the stereoselective synthesis of olefins as well as [3, 3]-sigmatropic rearrangement, Wittig reaction, and other reactions. In the Wittig rearrangement,[1] disubstituted olefins with an *E* geometry can be obtained from allylic ether with an electron-withdrawing group which is able to stabilize the secondary anion regardless of its geometry. The *Z* stereoselection prepared from (*E*)-allylic ethers was controlled with the addition of Cp_2ZrCl_2 as an additive[2] in the ester enolate Wittig rearrangement. On the other hand, the Still-Wittig rearrangement,[3] which uses a stannylated methyl allylic ether as a substrate, also shows the high *E* selectivity by use of (*Z*)-allylic ether *Z* - **1**, although (*E*)-allylic ether *E* - **1** usually gives a homoallylic alcohol as a mixture of *Z* and *E* except for the preparation of trisubstituted olefins.[4] In order to expand the utility of this reaction, we report the first *Z*-selective synthesis of disubstituted olefins with the Still-Wittig rearrangement.



† Dedicated to Professor Takayuki Shioiri on the occasion of his 60th birthday.



Scheme 1

The substrates used for the reaction were prepared as follows: β-alkoxy aldehydes or other aldehydes were treated with metallated acetylide[5] to give a propargyl alcohol **4** in moderate yield. After reduction of alkyns with LiAlH4 to obtain *E* olefins, the allylic hydroxy group was deprotonated with KH or KHMDS and alkylated with iodomethyltributyltin[6] to afford the desired stannylated methyl allylic ether derivatives[7] (Scheme 1).

The results of the Still-Wittig rearrangement are shown in the Table. In the rearrangement of **1** bearing an alkyl or aromatic group at R^1 under the conditions listed, the *Z*-selectivity was very low (entry 3 - 5). These results are similar to previous results reported by Still and Midland groups[3] (entry 1, 2). The substitution of a benzyloxy group for the alkyl group at R^1, however, remarkably improved the stereoselectivity but the yield was very low (entry 6). This phenomenon was also observed in the ester enolate Wittig rearrangement by Katsuki *et al.*.[2b] The improvement of yield in this reaction was accomplished by the treatment of **1d** (R^2=H) with *n*-BuLi in DME, giving the corresponding homoallylic alcohol in 76% yield (entry 7). The *Z* geometry of the resulting olefin was supported with the coupling constant of the olefinic proton (J = 11Hz) characterized by NMR spectroscopy and transformation to *E* olefin with photoisomerization reaction.[8] The stereoselectivity was less affected by the solvent and R^2 (entry 7 - 11). However, DME usually gave better yields than THF in this reaction. Therefore, DME was considered to stabilize the oxymethyllithium generated by the tin lithium exchange reaction.[9] The (*Z*)-allylic ether, which was obtained from reduction of **4e** (R^2 = *n*-Hexyl) with Lindar catalyst, was treated with *n*-BuLi in DME to indicate the high *E* -stereoselection (entry 12) as mentioned above.

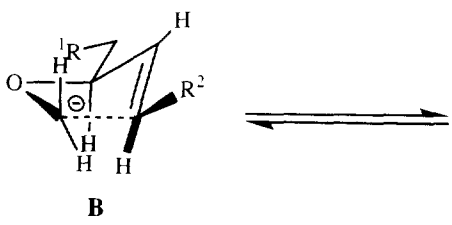
The stereoselectivity of (*E*)-allylic ether in the Still-Wittig rearrangement is explained by the fact that the transition state **A** having a pseudoaxial orientation of substituent predominates over transition state **B** (Scheme 2), and alkenic stereoselection is usually understood from conformational control in the very early transition state.[3] In this case, the coordination of the benzyloxy's oxygen atom to lithium ion, which contributes to stabilize the oxymethyl ion, is considered to further promote the generally unfavorable pseudoaxial orientation of the alkoxy substituent in the transition state (Fig. 1), resulting in the formation of (*Z*)-homoallylic alcohol.

In conclusion, a stannylated (*E*)-allyl ether bearing an alkoxy moiety on the alkenyl chain would exhibit a high *Z* selectivity and this method would be very useful for the synthesis of disubstituted olefins. Thus, it is feasible for stannylated (*Z*)- and (*E*)-allylic ethers bearing an oxygen functionality on the alkenyl side chain, that

Table. Still - Wittig rearragement of tributylstannylmethyl allylic ether bearing an alkoxy function on the side chain

Entry	R^1	R^2	Conditions	Yields(%)	*Z* : *E*
1[1)]	*n* - Hex	H	*n* - BuLi, THF, -78°C, 30min.	>95	60 : 40
2[1)]	*n* - Hex	Me	*n* - BuLi, THF, -78°C, 30min.	96	65 : 35
3	Et	*n* - Hex	*n* - BuLi, THF, -78°C, 60min.	51	53 : 47
4	Et	*n* - Hex	*n* - BuLi, DME, -60°C, 60min.	84	57 : 43
5	Ph	*n* - Hex	*n* - BuLi, THF, -78°C, 30min.	77	40 : 60
6	$BzlOCH_2$	H	*n* - BuLi, THF, -78°C, 30min.	<20	100 : 0
7	$BzlOCH_2$	H	*n* - BuLi, DME, -60°C, 180min.	76	100 : 0
8	$BzlOCH_2$	Me	*n* - BuLi, DME, -60°C, 25min.	84	100 : 0
9	$BzlOCH_2$	*n* - Hex	*n* - BuLi, THF, -78°C, 60min.	72	100 : 0
10	$BzlOCH_2$	*n* - Hex	*n* - BuLi, DME, -60°C, 25min.	76	100 : 0
11	$BzlOCH_2$	*t*-Bu	*n* - BuLi, DME, -60°C, 25min.	56	90 :10
12	$MEMOCH_2$	*n* - Hex	*n* - BuLi, THF, -78°C, 60min.	71	95 : 5
13[2)]	$MEMOCH_2$	*n* - Hex	*n* - BuLi, THF, -78°C, 25min.	14	13 : 87

1) Still, W.C.; Mitra, A. *J. Am. Chem. Soc.*, **1978**, *100*, 1927. 2) This reaction was carried out with *Z* - olefin as a substrate.



Scheme 2

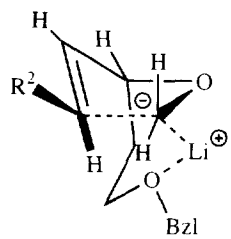


Fig. 1

were prepared from same propargyl alcohol derivative, to be converted to (*E*)- and (*Z*)-homoallylic alcohol, respectively, *via* the Still-Wittig rearrangement.

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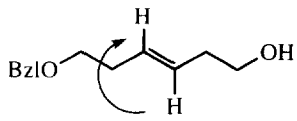
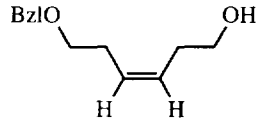
7) All new compounds had IR, NMR, and MS data consistent with the structure.

8) The irradiation (high pressure Hg lamp) of **2a** (R^2 = *n*-Hexyl) in the presence of PhSSPh in n-hexane at rt afforded a mixture of (*E*)- and (*Z*)- **2a** in the ratio of 9:1 in 95% yield.



J = 15Hz



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