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Olefinic stereoselection in the [2,3]-Wittig rearrangement of α,β-disubstituted allylic ethers forming trisubstituted olefins

Katsuhiko Tomooka, Tatsuya Igarashi, Naoyuki Kishi and Takeshi Nakai *

Department of Chemical Technology, Tokyo Institute of Technology, Meguro-ku, Tokyo 152-8552, Japan

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Abstract

The *E/Z*-selectivities in the [2,3]-Wittig rearrangements of secondary β-(methyl or silyl)allylic ethers are shown to depend critically on the nature of groups on the carbanion terminus, thereby permitting elucidation of the structural requirements for attaining high *Z*-selectivity. © 1999 Elsevier Science Ltd. All rights reserved.

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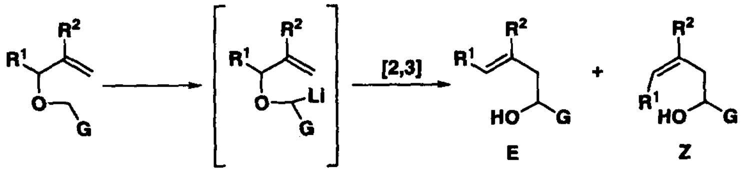
While the [2,3]-Wittig rearrangement of secondary allylic ethers generally exhibits a high *E*-selectivity over the newly created olefin bond, several exceptions to the *E*-selection attribute have been reported, in particular, with respect to α,β-disubstituted allylic ethers (Eq. 1).[1] The most notable is the Wittig–Still variant (G=H, R^1=alkyl, R^2=Me) which shows a remarkably high level (>95%) of *Z*-selection[2] and hence has found applications for *Z*-trisubstituted olefin synthesis.[1] Another notable exception is the rearrangement of the β-(silyl)allylic propargyl ether (G=C≡CSiMe$_3$, R^1=pentyl, R^2=SiMe$_3$) which provides 80% '*Z*'-selectivity,[3,4] while the allyl counterpart (G=CH=CH$_2$, R^1=methyl or pentyl) shows only 36–33% '*Z*'-selectivity.[4,5] While these high *Z*-selectivities have been interpreted as a result of the alleviation of the steric 1,2-repulsion between R^1 and R^2 in the transition states, these examples point out that the nature of G group must be considered as another key factor in dictating the level of *Z*-selectivity.[6] Thus, the question arises as to how the nature of the G group affects the *E/Z*-selectivity in the [2,3]-Wittig rearrangement in general or what the requisite structural factors are for attaining high *Z*-selectivity. Herein we wish to address this fundamental question based on the *E/Z*-selections observed in the [2,3]-rearrangements of two types of α,β-disubstituted allylic ethers with different G groups.



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* Corresponding author. Fax: +81-3-5734-2885; e-mail: takeshi@o.cc.titech.ac.jp

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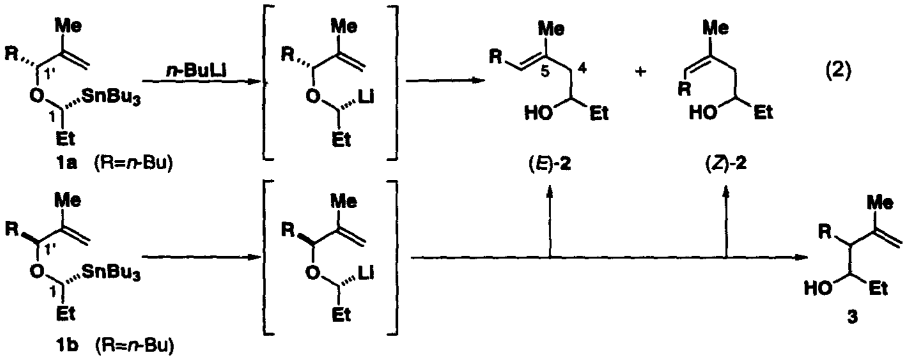
First, we examined the *E/Z*-selectivity in the Still-type rearrangement of the diastereomeric pair of the methallylic ether **1a** and **1b** where the transmetallation proceeds with complete retention of configuration and the Li-bearing terminus is configurationally stable[7] (Eqs. 2 and 3). Diastereo-defined substrates **1a** and **1b** were obtained by column-chromatographic separation and the relative configuration was assigned by ^{1}H NMR comparison with an authentic (1*R*, 1′*S*)-enantiomer of **1b** prepared via the reaction of the mesylate of (*R*)-α-hydroxypropylstannane with the potassium salt of (*R*)-2-methyl-2-hepten-3-ol.[7,8] Thus, **1a** was treated with *n*-BuLi in THF at −78°C to give the (*E*)-olefin **2** as a single isomer in 76% yield, whereas a similar rearrangement of **1b** was much slower to give rise to an isomeric mixture (*E*:*Z*=24:76) of **2** in 25% yield, along with 16% of the [1,2]-Wittig product **3**.[9]



1a (R=*n*-Bu)

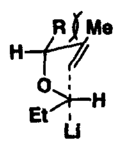
(*E*)-**2**

(*Z*)-**2**

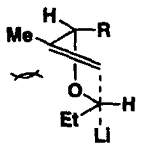
1b (R=*n*-Bu)

3

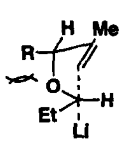
These outcomes reveal that the introduction of ethyl as the G group to the original Still system (G=H) no longer affords high Z-selectivity. This rather surprising observation suggests that a steric factor offered by the Et group predominates over the steric 1,2-repulsion between Me and R. Between the two transition states T_1(*exo*) and T_2 (*endo*) available for **1a**,[10] the former, despite the presence of the 1,2-repulsion, might be sterically much more favorable because the latter suffers a 1,3-repulsion between Et and Me. For the other diastereomer **1b**, on the other hand, while both T_3(*exo*) and T_4(*endo*) are sterically disfavored, the former being free of the 1,2-repulsion is more favorable, thus leading to the *Z*-selection. Thus, it is safe to say that the present rearrangement proceeds preferentially through the *exo*-transition states, either in the presence or absence of the 1,2-repulsion. That means that the *exo*-preference possessed inherently by the Et group prevails as a stereo-directing factor over the 1,2-repulsion. In other words, if the *exo/endo* complication is absent, the 1,2-steric repulsion would become the sole stereo-directing factor, thus leading to high Z-selectivity. That is exactly the case of the original Still variant (G=H).



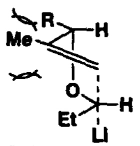
T_1 (*exo*) ⟶ *E*



T_2 (*endo*) ⟶ *Z*



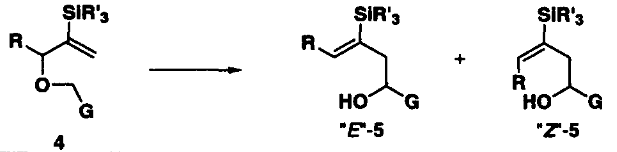
T_3 (*exo*) ⟶ *Z*



T_4 (*endo*) ⟶ *E*

Next, our attention was focused on *E/Z*-selection in the rearrangements of secondary β-(silyl)allylic ethers **4** where the Li-bearing terminus is configurationally labile (Eq. 4). The '*E/Z*'-selectivities thus observed are summarized in Table 1, along with the literature data for comparison. The most revealing is that the use of silylethynyl as the G group provides a significantly higher Z-selectivity than those of the vinylic ones (entry 2 vs. 8). Rather interestingly, the bulkiness of the β-silyl groups has little effect (entries 5–7). A remarkably high 'Z'-selectivity was attained when G was a silylethynyl and R was a bulky alkyl (entries 8 and 9). These trends are explicable by considering that the silylethynyl group is known as one of the few G groups that possess *endo*-preference in the transition states, whereas the vinylic

Table 1
The [2,3]-Wittig rearrangement of β-(silyl)allylic ethers[a]



(4)

Entry	Substrate 4			Base	"E"/"Z"[b]	%yield
1[c]	G=CH=CH$_2$,	R=Me,	R'=Me	LDCA[d]	64 : 36	62
2[e]		R=*n*-C$_5$H$_{11}$		*n*-BuLi	67 : 33	78
3	G=C(Me)=CH$_2$,	R=Me,	R'=Me	LDCA[d]	59 : 41	87
4[c]				*n*-BuLi	95 : 5	35
5	G=C≡CSiMe$_3$,	R= Me,	R'=Me	*n*-BuLi	46 : 54	98
6			R'=Et		44 : 56	99
7			R'=Ph		52 : 48	98
8	G=C≡CSiMe$_3$,	R=*n*-C$_5$H$_{11}$,	R'=Me	*n*-BuLi	22 : 78 (20 : 80)[e]	98
9	G=C≡CSiMe$_3$,	R=*i*-Pr,	R'=Me	*n*-BuLi	1 : 99[f]	87
10[g]	G=H (SuBu$_3$),	R=Me,	R'=Me	*n*-BuLi	1 : 99[f]	99

[a] The reactions were carried out in THF at -78 °C. [b] The geometry was assigned by ^{1}H NMR spectra on the basis of the empirical rule for the olefinic protons' peaks (refs. 5 and 11), and the ratio was determined by ^{1}H NMR and/or GLC. [c] Cited from ref. 5. [d] Lithium dicyclohexylamide. [e] Cited from ref. 3. [f] The " Z" geometry of the major product was confirmed by its conversion to the corresponding *Z*-disubstituted olefin via protiodesilylation (refs. 5 and 11b). [f] Performed using Still's transmetallation method.

groups have *exo*-preference.[1,12] Thus, it appears likely that the relatively high *Z*-selectivity observed with G=C≡CSiR$_3$ reflects the special situation where the *endo*-TS corresponding to **T$_2$** (free of 1,2-repulsion) prevails overwhelmingly over the other *endo*-TS corresponding to **T$_4$** (suffering 1,2-repulsion). Thus, it is safe to conclude that a high *Z*-selectivity can be attained only when one employs G=H (where the *endo*/*exo* complication is absent) or such G group as silylethynyl that possesses a large *endo*-preference in the transition states. In other words, the *E*/*Z*-selectivity of the [2,3]-Wittig rearrangement in general is determined by the balance between the magnitude of the 1,2-repulsion between R^1 and R^2 and the *exo*/*endo*-preference of G-group used. The more *endo*-preference, the more *Z*-selectivity.

In summary, we have demonstrated that the *E*/*Z*-selectivity in the [2,3]-Wittig rearrangements of α,β-disubstituted allylic ethers depends critically upon the nature of G groups. Moreover, we have clarified not only the mechanistic origin of the high *Z*-selectivity reported for the Wittig–Still variant (G=H) and G=C≡CSiMe$_3$, but also the requirements for attaining high *Z*-selectivity. Further work is in progress to develop other *Z*-selective [2,3]-Wittig variants.

Acknowledgements

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4. Throughout this paper, the descriptor '*Z*' is used for (*E*)-silylolefin products (where R^1 and R^2=SiR_3 are *trans*) for the sake of consistency. Thus, note that '*E*' corresponds to *Z* (by the usual convention).
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6. For other *Z*-selective variants with different G groups, consult Ref. 1.
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8. The two substrates are unequivocally distinguishable by ^{1}H NMR spectra: e.g., δ (ppm, $CDCl_3$) for 1-H, 3.69 (dd, J=5.8, 7.4 Hz) for **1a** and 3.47 (dd, J=6.4, 7.4 Hz) for **1b**.
9. The product geometry was assigned by ^{13}C NMR spectra on the basis of the 'γ-effect' on allylic carbons (cf. Ref. 2). The most distinguishable are the peaks (ppm) due to 5-Me and C4: 16.1 and 47.6 for (*E*)-**2** and 23.8 and 39.7 for (*Z*)-**2**. Byproduct **3**: ^{1}H NMR, δ 0.88 (t, J=7.2 Hz, 3H), 0.98 (t, 7.4 Hz, 3H), 1.10–1.42 (m, 8H), 1.59 (br. s, 1H), 1.68 (s, 3H), 2.04 (ddd, J=4.4, 8.5, 10.5 Hz, 1H), 3.34–3.42 (m, 1H), 4.81–4.84 (m, 1H), 4.95–4.98 (m, 1H).
10. Note that the [2,3]-Wittig rearrangement is well-established to proceed with complete inversion of configuration at the Li-bearing terminus (Ref. 7a).
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