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Stereoselective One-pot 1,4-Elimination and the [1,2]-Wittig Rearrangement of (*E*)-δ-(Arylmethoxy or 3-Silyl-2-propynyloxy)-substituted Allylic Sulfones

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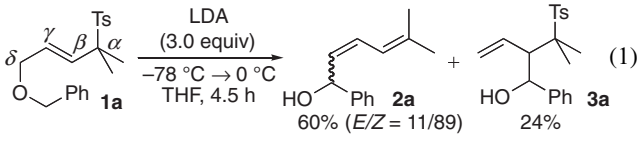
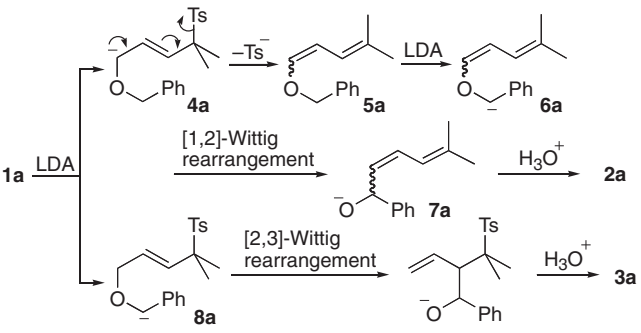
The successive treatment of (*E*)-δ-(arylmethoxy)-substituted allylic sulfones with *t*-BuOK and LDA afforded the corresponding (*Z*)-2,4-dienyl alcohols with high stereoselectivities via 1,4-elimination and the [1,2]-Wittig rearrangement. The predominant formation of (*Z*)-isomers, due to "*syn*-effect" in the elimination step, was further successfully applied to (*E*)-δ-(3-silyl-2-propynyloxy)-substituted allylic sulfones.

Stereoselective preparation of olefins is one of the most important problems in organic chemistry. In the course of studies on the preparation of allylic sulfones,[1] we investigated the stereochemistry of isomerization of α-unsubstituted (*E*)-vinylic sulfones to the corresponding allylic sulfones in the presence of a base and found that the sterically unfavorable (*Z*)-allylic sulfones were predominantly formed.[2] This experimental fact was rationalized by a "*syn*-effect,"[3] which is primarily caused by $\sigma \rightarrow \pi^*$ interaction and/or 6π-electron homoaromaticity.[2,4] In related studies on the "*syn*-effect," we revealed that it works also in various kinds of isomerization reactions and elimination reactions utilizing a base.[4,5] In particular, oxygen-substituted substrates always realized high *Z*-selectivities. During the course of the investigation of the 1,4-eliminative ring opening reaction of a benzyloxy-substituted (*E*)-vinyloxirane with LDA, the [1,2]-Wittig rearrangement[6] was found to proceed following the initial 1,4-eliminative ring opening reaction to give an (*E*,*Z*)-2,4-dienyl 1,6-diol in a highly stereoselective manner.[5g] This shows that the highest *Z*-selectivity based on the "*syn*-effect" observed for the oxygen-substituted substrates could be utilized for the successive stereoselective C–C bond formation. Herein we describe a one-pot 1,4-elimination of allylic sulfones and the subsequent [1,2]-Wittig rearrangement of (*E*)-δ-(arylmethoxy)-substituted allylic sulfones to give the corresponding (*Z*)-dienyl alcohols stereoselectively.

As described above, the "*syn*-effect" of 1,4-elimination of allylic sulfones by the treatment with a base was investigated and a δ-(benzyloxy)allylic sulfone was found to afford the corresponding (*Z*)-vinyl ether stereoselectively.[5a] If the δ-(benzyloxy)allylic sulfone was treated with excess amounts of a base, the successive 1,4-elimination and the [1,2]-Wittig rearrangement was also anticipated to proceed. When (*E*)-δ-(benzyloxy)allylic sulfone **1a** was treated with 3.0 equiv of LDA, the desired successive reaction product **2a** was obtained in 60% yield. Stereoselectivity of the double bond in **2a** was high as expected (*E*/*Z* = 11/89). However, a by-product **3a** was also produced (eq 1). As shown in Scheme 1, the 1,4-elimination via



(1)

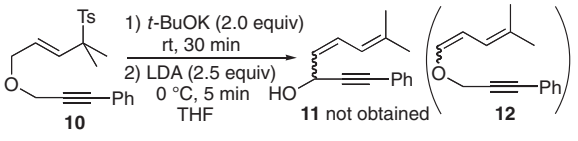


Scheme 1.

4a stereoselectively gave (*Z*)-vinyl ether **5a** originating from the "*syn*-effect," which was further deprotonated at the benzylic position followed by the [1,2]-Wittig rearrangement to give **2a**. On the other hand, when deprotonation at the benzylic position initially occurred, the benzylic anion **8a** might afford **3a** by the [2,3]-Wittig rearrangement.

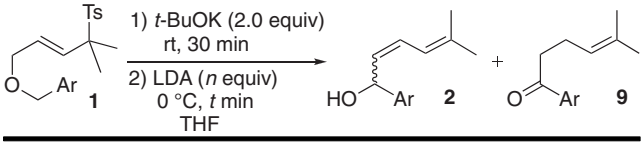
In order to suppress the generation of **8a**, a weaker base *t*-BuOK was first used for generation of **4a** selectively to complete the 1,4-elimination, followed by addition of LDA for further the [1,2]-Wittig transformation via **6a**. In this way, only the desired reaction proceeded to give **2a** with high *Z*-selectivity (Table 1).[7] When 3.5 equiv of LDA was used, a by-product **9a** was also obtained (Entry 1), which might be produced via deprotonation of the rearranged intermediate **7a** and subsequent isomerization (Scheme 2).[8] By decreasing the amount of LDA and shortening the reaction time for the [1,2]-Wittig rearrangement, the production of the by-product **9a** was rather inhibited and the stereoselectivity was further improved (Entries 2–4). By treating with 2.5 equiv of LDA for 5 min, **2a** was obtained with excellent stereoselectivity in high yield (Entry 3). Several other δ-(arylmethoxy)allylic sulfones **1b**–**1d** were subjected to the present one-pot 1,4-elimination reaction and the [1,2]-Wittig rearrangement, and the corresponding (*Z*)-dienyl alcohols **2b**–**2d** were stereoselectively obtained (Entries 5–7).

Next, propargylic ethers instead of benzylic ethers **1**, were investigated in the one-pot transformation. When (*E*)-3-phenyl-2-propynyl ether **10** was treated with *t*-BuOK, 1,4-elimination to **12** was monitored by TLC. After the addition of LDA, the reaction became messy and desired rearranged product **11** was not obtained (eq 2).[9]



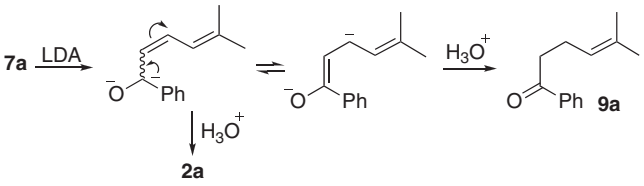
(2)

Table 1. One-pot 1,4-elimination and the [1,2]-Wittig rearrangement of **1**



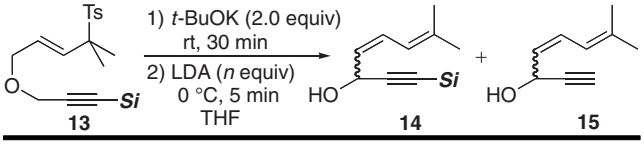
Entry	Ar		1	*n*/equiv	*t*/min	Yield of **2**/%	*E*/*Z*[a]	Yield of **9**/%
1	Ph		**a**	3.5	80	69	5/95	4
2				3.0	15	65	2/98	4
3				2.5	5	89[b]	1/99	1
4				2.0	1	80[b]	2/98	—
5	4-$CH_3C_6H_4$		**b**	2.5	5	89	2/98	—
6	4-$CH_3OC_6H_4$		**c**	2.5	5	85[c]	3/97	2
7	2-Nap		**d**	2.5	5	89[c]	2/98	1

[a]The ratios were determined by 400 MHz ^{1}H NMR spectra. [b]Vinyl ether **5a** was obtained in 7% (Entry 3) and 10% (Entry 4) yields, respectively. [c]Vinyl ethers **5c** and **5d** were obtained in 7% (Entry 6) and 6% (Entry 7) yields, respectively.



Scheme 2.

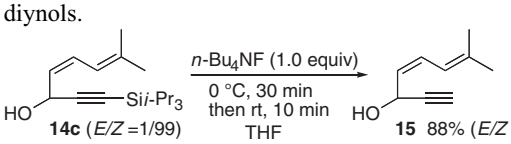
Table 2. One-pot 1,4-elimination and the [1,2]-Wittig rearrangement of *δ*-(3-silyl-2-propynyloxy)allylic sulfones **13**



Entry	*Si*	**13**	*n*/equiv	Products	Yield/%	*E*/*Z*[a]
1	Me_3Si	**a**	2.5	**15**	45	12/88
2	*t*-$BuPh_2Si$	**b**	2.5	**14b**	29	3/97
3[b]	*i*-Pr_3Si	**c**	2.5	**14c**	70[c]	1/99
4[b]			2.2	**14c**	74[c]	1/99

[a]The ratios were determined by 400 MHz ^{1}H NMR spectra. [b]On step 1, **13c** was treated with *t*-BuOK at 0 °C for 20 min. [c]A by-product, 7-methyl-1-(triisopropylsilyl)-6-octen-1-yn-3-one, produced via deprotonation of the rearranged intermediate followed by isomerization, was obtained in 14% (Entry 3) and 15% (Entry 4) yields, respectively.

When (*E*)-*δ*-(3-silyl-2-propynyloxy)allylic sulfones **13** were used as substrates, the desired [1,2]-Wittig rearrangement was found to proceed (Table 2). In the case of trimethylsilyl-substituted substrate **13a**, the rearranged desilylated product **15** was obtained (Entry 1). In order to prevent the desilylation, bulky silyl groups were introduced (Entries 2–4). *γ*-(Triisopropylsilyl)propargylic ether was a substrate of choice to give the desired product **14c** with excellent *Z*-selectivity (Entries 3 and 4). The desilylation of **14c** was readily carried out by treating with tetrabutylammonium fluoride to afford **15** (eq 3),[10] which could not be prepared by the conventional Lindlar reduction of diynols.



(3)

As described above, the one-pot transformation of (*E*)-*δ*-(arylmethoxy)- or (3-silyl-2-propynyloxy)-substituted allylic sulfones into (*Z*)-2,4-dienyl alcohols via 1,4-elimination and the [1,2]-Wittig rearrangement were developed,[11] which demonstrates a smart application of the "*syn*-effect" to stereoselective C–C bond formation.

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8 The formation of **9a** was not observed by the treatment of **2a** with LDA (2.5 equiv) in THF at 0 °C for 80 min. However, after 1 d at rt, **9a** was confirmed to be produced in ca. 4% yield based on the analysis of a ^{1}H NMR spectrum of the crude products. Furthermore, isomerization was also observed (*E*/*Z* of **2a**; from 5/95 to 14/86).
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11 A representative procedure for the one-pot 1,4-elimination and the [1,2]-Wittig rearrangement of **1a** (Table 1, Entry 3): To a suspension of *t*-BuOK (125 mg, 1.12 mmol) in THF (1.1 mL), a THF (4.5 mL) solution of **1a** (193 mg, 0.56 mmol) was added under a N_2 atmosphere and the mixture was stirred for 30 min at rt. After the mixture was cooled to 0 °C, LDA·THF (0.934 mL, 1.40 mmol, 1.5 M in cyclohexane) was added and the reaction mixture was stirred for 5 min at 0 °C. The reaction was quenched by the addition of saturated aqueous solution of NH_4Cl, and the organic substances were extracted with AcOEt. The combined organic extracts were washed with water and brine, dried over Na_2SO_4, and condensed in vacuo. The residue was separated by flash column chromatography (SiO_2, hexane/AcOEt = 30/1–15/1, v/v) to give **2a** (94 mg, 89%, *E*/*Z* = 1/99) and a mixture of **5a** (7%) and **9a** (1%) (total 8 mg). ^{1}H NMR (400 MHz, $CDCl_3$): (*Z*)-**2a**; δ 1.78 (3H, s), 1.85 (3H, s), 1.87 (1H, br s), 5.50 (1H, dd, J = 10.7, 8.8 Hz), 5.71 (1H, d, J = 8.8 Hz), 6.26 (1H, d, J = 11.7 Hz), 6.34 (1H, dd, J = 11.7, 10.7 Hz), 7.24–7.42 (5H, m). (*E*)-**2a**; δ 1.78 (6H, s), 1.91 (1H, br s), 5.26 (1H, d, J = 7.0 Hz), 5.73 (1H, dd, J = 15.0, 7.0 Hz), 5.83 (1H, d, J = 11.0 Hz), 6.53 (1H, dd, J = 15.0, 11.0 Hz), 7.24–7.42 (5H, m).

