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A facile and stereoselective synthetic method for allylic 1,3-dienyl ethers

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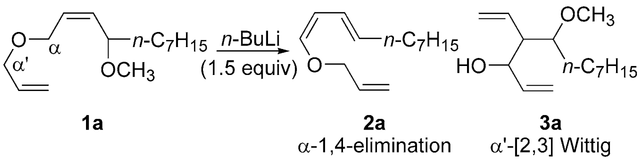
Abstract—The 1,4-elimination reaction of 1-allyloxy-4-methoxy-(2*Z*)-alkenes with *n*-butyllithium is shown to proceed in a marked preference to the [2,3] Wittig rearrangement to afford the allylic (1*Z*,3*E*)-dienyl ethers in high stereoselectivities. The synthetic utility of this method is demonstrated by the Claisen rearrangement of the dienyl ethers thus obtained.

The Claisen rearrangement is one of the most important transformations in organic synthesis, since it can readily create a new C–C bond with a high degree of stereocontrol.[1] Among several Claisen variants developed so far, the original Claisen rearrangement of allylic enol (or dienol) ethers has found relatively limited use due to the difficulty with the stereoselective preparations of the substrates thereof. Very recently, we have reported an efficient and stereoselective synthetic method of 1,3-dienyl silyl ethers via the 1,4-elimination of 1-siloxy-4-methoxy-(2*Z*)-alkenes with *n*-butyllithium.[2–4] With the method in hand, we have now explored the feasibility of the similar 1,4-elimination of the 1-allyloxy derivatives, which would afford the corresponding allyl 1,3-dienyl ethers, useful substrates for the Claisen and tandem Claisen–Cope rearrangement, while the 1-allyloxy substrates (as bis-allylic ethers) might also undergo the [2,3] Wittig rearrangement[5] (vide infra) which suppresses the desired 1,4-elimination. We now wish to report that a simple treatment of 1-allyloxy-4-methoxy-(2*Z*)-alkenes (**1**) with *n*-butyllithium affords the allylic 1,3-dienyl ethers (**2**) in a high (1*Z*,3*E*)-stereoselectivity without appreciable occurrence of the [2,3] Wittig rearrangement concerned.

First, we carried out the reaction of 1-allyloxy-4-methoxy-(2*Z*)-undecene (**1a**)[6] with *n*-butyllithium (1.5 equiv) in ether. Fortunately, the 1,4-elimination product, 1-allyloxy-1,3-undecadiene (**2a**) was obtained in a 77% yield with a high (1*Z*,3*E*)-stereoselectivity.[7] The stereochemistry was determined by the ^{1}H NMR assay ($J_{1H,2H} = 6.2$ Hz and $J_{3H,4H} = 15.2$ Hz). Interestingly, the formation of the α′-[2,3] Wittig product **3a** was almost completely inhibited (5%).[8] In contrast, a similar reaction, when carried out in THF at −78 °C, provided the α′-[2,3] Wittig product **3a** in a 40% yield (as an almost single diastereomer) along with a 22% recovery of **1a**.[9] Any appreciable amount of the α-1,4-elimination product **2a** was not detected (Scheme 1).

Of mechanistic interest is that the α-1,4-elimination overwhelmingly prevails the α′-[2,3] Wittig rearrangement *in ether* (not in THF). This observation strongly suggests that the 1,4-elimination in ether does not involve any lithiation process, since the [2,3] Wittig rearrangement of bis-allylic ethers is known to proceed via lithiation preferentially on the *less* substituted allylic



	2a	3a
Et$_2$O, –40 °C, 3 h	77 %	5 %[a]
THF, –78 °C, 12 h[b]	0 %	40 %

Scheme 1. α-1,4-Elimination reaction of 1-allyloxy-4-methoxy-(2*Z*)-undecene (**1a**) with *n*-butyllithium: [a] The yield was determined by ^{1}H NMR assay using 1,4-bis(trifluoromethyl)benzene as an internal standard. [b] The starting material **1a** was recovered in 22%.

Keywords: Allylic 1,3-dienyl ethers; 1,4-Elimination; Wittig rearrangement; Claisen rearrangement; Cope rearrangement.

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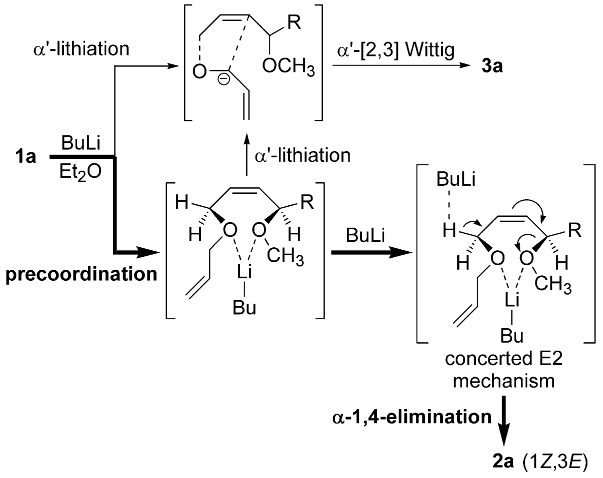


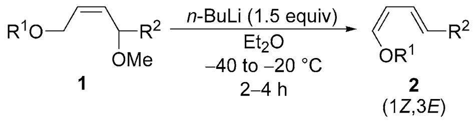
Scheme 2. The E2 elimination mechanism of α-1,4-elimination reaction.

moiety (α′-position at this case) as actually observed in THF.[10] Thus, it appears likely that 1,4-elimination in ether proceeds via an initial precoordination of the two alkoxy-oxygens to *n*-butyllithium followed by a concerted E2-like mechanism to result in the selective formation of the (1*Z*,3*E*)-dienyl ether as depicted in Scheme 2. The reaction of **1a** carried out in THF might suppress the precoordination since a stronger coordination occurs between THF–*n*-butyllithium than **1a**–*n*-butyllithium. In this case, the α′-lithiation occurs to provide the α′-[2,3] Wittig product **3a**.

To define the scope and limitation of the present method, we prepared a series of 1,4-dialkoxy-(2*Z*)-alkenes **1b**–**1f**[11] and carried out their reactions with *n*-butyllithium in ether. As shown in Table 1, various types of allylic 1,3-dienyl ethers **2b**–**2e** were obtained in good yields with high (1*Z*,3*E*)-stereoselectivities. Our method is also useful for the preparation of benzyl 1,3-dienyl ether **2f** (entry 5).[12] In all cases, an appreciable amount of any Wittig products were not formed.

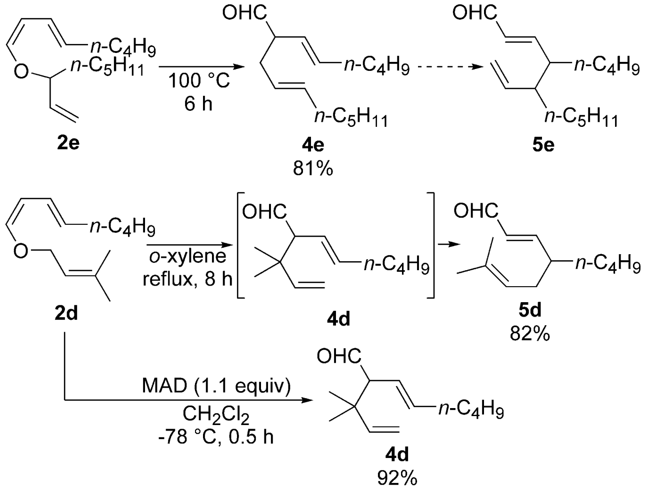
Finally, the Claisen rearrangement of allylic 1,3-dienyl ethers **2** thus obtained was performed (Scheme 3). The thermolysis (neat, 100 °C) of **2e** gave the (4*E*,1′*E*)-β,γ-unsaturated aldehyde **4e** in a 81% yield without occurrence of the subsequent Cope rearrangement **4e** leading to **5e**. Interestingly, the thermolysis of **2d** (refluxing in *o*-xylene) afforded the tandem Claisen–Cope[13] product **5d** in a 82% yield, whereas the treatment of **2d** with methylaluminium bis(2,6-di-*tert*-butyl-4-methylphenoxide) (MAD) allowed for the isolation of the Claisen product **4d** in a 92% yield.

Table 1. 1,4-Elimination reaction of various types of 1-alkoxy-4-methoxy-(2*Z*)-alkene **1**



Entry	R^1	R^2		Yield[a] (%)
1	(*E*)-$CH_2CH{=}CHCH_3$	*n*-C_7H_{15}	**b**	90
2	$-CH_2C(CH_3){=}CH_2$	*n*-C_7H_{15}	**c**	74
3	$-CH_2CH{=}CH(CH_3)_2$	*n*-C_4H_9	**d**	91
4	$-CH($*n*$-C_5H_{11})CH{=}CH_2$	*n*-C_4H_9	**e**	84
5	$-CH_2Ph$	*n*-C_4H_9	**f**	84

[a] Isolated yield.



Scheme 3. Application of allylic 1,3-dienyl ethers for Claisen or Claisen–Cope tandem rearrangements.

In summary, we have shown that the 1,4-elimination reaction of 1-allyloxy-4-methoxy-(2*Z*)-alkenes with *n*-butyllithium is shown to proceed smoothly in ether to afford various types of allylic 1,3-dienyl ethers in high (1*Z*,3*E*)-stereoselectivities. Thus, this method is widely applicable for the preparations of different types of the Claisen and tandem Claisen–Cope substrates.

Acknowledgments

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2006.08.100.

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6. Prepared from 3-(1-ethoxyethoxy)prop-1-yne in five steps (85% overall yield): (i) n-BuLi, THF, n-$C_7H_{15}CHO$, −78 °C to rt. (ii) NaH, MeI, THF, 0 °C to rt. (iii) H_2 (1 atm), Lindlar-cat., quinoline, EtOAc, rt. (iv) p-TsOH, MeOH, rt. (v) Bu_4NBr, allyl bromide, benzene, 50% aq NaOH, rt. Details: see Supplementary data.
7. Use of *sec*- or *tert*-butyllithium instead of *n*-butyllithium resulted in lower yields due to de-allylation of **1a**.
8. A similar reaction of 1-allyloxy-4-methoxy-(2*E*)-undecene [(*E*)-**1a**] in ether was found to give a geometric mixture of **2a** in a 31% yield [(1*Z*,3*E*)/(1*Z*,3*Z*) = 6:4] and a complicated diastereomixture of **3a** in a 10% yield with the recovery of the starting material in 37% yield.
9. Use of TMEDA–Et_2O instead of THF gave almost the same result.
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11. Compound **1b**–**1d** and **1f** were prepared by the same procedure depicted in Ref. 6. **1e** was prepared from oct-1-en-3-ol in four steps (66% overall yield). (i) $Bu_4N{\cdot}HSO_4$, propargyl bromide, benzene, 50% aq NaOH, rt. (ii) n-BuLi, THF, n-C_4H_9CHO, −78 °C to rt. (ii) NaH, MeI, THF, 0 °C to rt. (iii) H_2 (1 atm), Lindlar-cat., quinoline, EtOAc, rt. Details: see Supplementary data.
12. Examples of 1,4-elimination reaction of γ-benzylicoxy-α,β-unsaturated acetals have been reported: see Ref. 3b and c.
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