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A new method for synthesis of allenes, including an optically active form, from aldehydes and alkenyl aryl sulfoxides with carbon–carbon bond-formation

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Abstract

Ligand exchange reaction of β-mesyloxy sulfoxides or β-acetoxy sulfoxides, which were derived from alkenyl aryl sulfoxides and aldehydes in two steps, with *n*-BuLi or EtMgBr at low temperature gave allenes in good yields. Optically active allenes were synthesized starting from optically active 2-phenylethenyl *p*-tolyl sulfoxides.

Allenes are quite important compounds in organic chemistry and a large number of studies have been reported on their chemistry and synthesis.[1] Some allenes have axial chirality and exist as an optically active form. Recently, asymmetric synthesis of allenes has received much attention.[2]

We previously reported[3] a method for synthesizing allenes **2** from sulfoxides **1** by the ligand exchange reaction of sulfoxides with *n*-BuLi.[4] In continuation of our study on the ligand exchange reaction of sulfoxides in organic synthesis, herein we report a new method for a synthesis of allenes **5**, including an optically active form, from alkenyl aryl sulfoxides **3** and aldehydes via mesylate or acetate **4** (Scheme 1).

According to the procedure reported by Marino,[5a] addition of the lithium carbanion of propenyl phenyl sulfoxide **6** (a mixture of geometrical isomers) to 3-phenylpropionaldehyde gave the adduct **7a** as a diastereomeric mixture in almost quantitative yield.[5] Mesylation of the adduct afforded the mesylate **7b** in good yield. Treatment of the mesylate **7** with alkylmetals was carried out in THF at −78°C with three alkylmetals as shown in Scheme 2. The elimination of both the mesyloxy and sulfinyl groups was realized to give the desired allene **8** in good yield. In the cases with *n*-BuLi and *t*-BuLi, the reactions were completed within 30 min; however, the reaction with EtMgBr required 1.5 h for completion.

Other examples of the synthesis of allenes from alkenyl aryl sulfoxides and aldehydes are summarized in Table 1. When R^1 and/or R^2 is an aromatic group, the mesylate (**4**: R=Ms) is quite unstable due to the formation of an allylic cation. In these cases we obtained the acetates (**4**: R=$COCH_3$) in high yields (entries 1–4). As shown in entry 1, the elimination reaction of the acetate with both *n*-BuLi and

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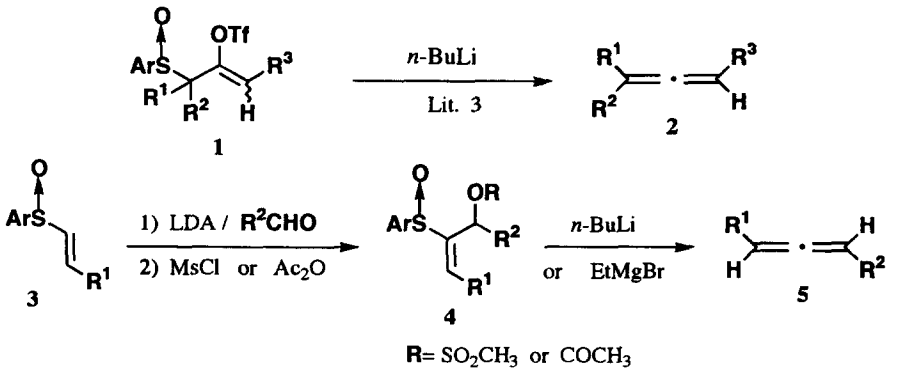
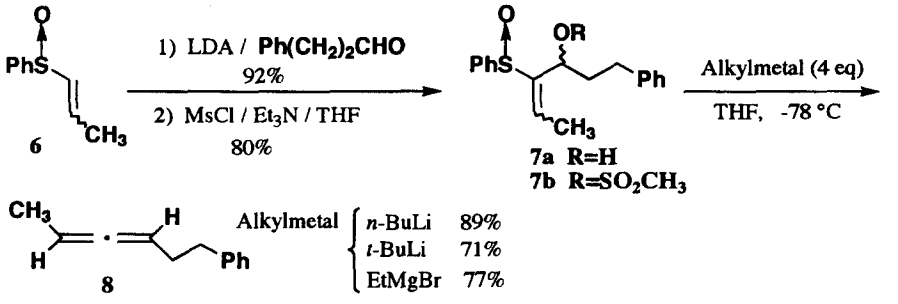


Scheme 1.



Scheme 2.

t-BuLi gave only a complex mixture. Fortunately, the elimination was successful with EtMgBr to give the desired allene in 88% yield. Entry 4 shows that in the case that both R^1 and R^2 are an alkyl group, much better yields were obtained with the mesylate than with the acetate (compare the results in entry 4 and that in Scheme 2). Entry 6 shows the synthesis of 3-(2-naphthyl)-1,2-propadiene. The addition of the carbanion of phenyl vinyl sulfoxide with β-naphthaldehyde gave a moderate yield of the adduct; however, the elimination of the acetate with EtMgBr gave a quantitative yield.

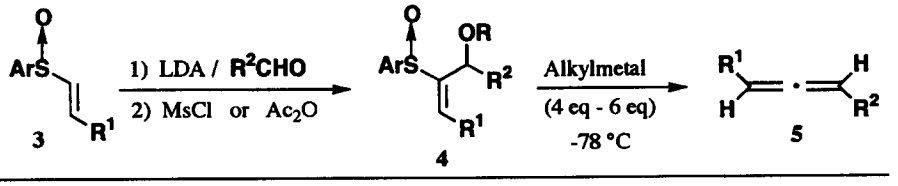
Next, we investigated the asymmetric synthesis of allenes starting from the optically active 2-phenylethenyl *p*-tolyl sulfoxide[6] **9** with β-naphthaldehyde and 3-phenylpropionaldehyde (Scheme 3).

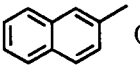
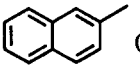
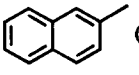
Addition of the lithium carbanion of **9** to β-naphthaldehyde at −100°C gave a mixture of two diastereomers, which were separated by silica gel column chromatography (**10a**, 53%; **11a**, 43%). The newly created chiral centers were assigned as *R* and *S*, respectively, as shown in Scheme 3, by comparison of the data with those of Marino's report.[5a]

Acetylation of the adducts **10a** and **11a** gave the acetates **12a** ($[\alpha]_D$ +121) and **13a** ($[\alpha]_D$ +1.5), respectively, in almost quantitative yields. The elimination of the acetate **12a** in THF with EtMgBr was found to be rather sluggish; however, use of 10 equivalents of EtMgBr at −25°C for 20 min gave the desired allene (*R*)-**14a**[7] ($[\alpha]_D$ −531) in 92% yield as colorless crystals. The enantiomeric excess was calculated to be 68% by HPLC using a chiral column (Daicel, Chiralpak AD, hexane:*i*-PrOH=9:1). Recrystallization of the product with AcOEt–hexane gave the allene having much higher optical purity (mp 85.5–87°C; $[\alpha]_D$ −668 (c 0.55, $CHCl_3$), 95% ee by HPLC). Similar treatment of **13a** in THF at −25°C with 4 equivalents of EtMgBr for 10 min gave the optically active allene (*S*)-**15a** ($[\alpha]_D$ +515; 74% ee) as colorless crystals in 73% yield.

Next, the adducts of **9** with 3-phenylpropionaldehyde (**10b** and **11b**) were acetylated to give the acetates **12b** ($[\alpha]_D$ +68) and **13b** ($[\alpha]_D$ +51). Treatment of **12b** with 14 equivalents of EtMgBr at −30°C

Table 1
Synthesis of allenes 5 from alkenyl sulfoxides 3 and aldehydes through the ligand exchange reaction of sulfoxides



Entry	3		R²CHO		4		Alkylmetal	5
	Ar	R¹	R² (Yield / %)[a]		R (Yield / %)[b]			Yield / %[c]
1	Ph	Ph	$PhCH_2CH_2$	(87)	Ac	(96)	*n*-BuLi	——[d]
							t-BuLi	——[d]
							EtMgBr	88
2	Ph	Ph		(99)	Ac	(92)	EtMgBr[e]	92
3	Ph	CH_3		(77)	Ac	(94)	EtMgBr[f]	77
4	Ph	CH_3	$PhCH_2CH_2$	(92)	Ac	(86)	EtMgBr	42
5	*p*-Tol	$CH_3(CH_2)_3$	$PhCH_2CH_2$	(82)	Ms	(82)	*n*-BuLi	90
							EtMgBr	77
6	Ph	H		(53)	Ac	(95)	EtMgBr	99

a) The yield of the reaction of 3 with the aldehyde. b) The yield for the acetylation or mesylation. c) Isolated purified yield after silica gel column chromatography. d) A complex mixture was obtained. e) at -25 °C, 20 min. f) at -100 °C, 2 h.

for 1 h gave the allene (*R*)-**14b** ($[\alpha]_D$ –63; 21% ee, by Daicel Chiralcel OD) in 93% yield as an oil. Similar treatment of **13b** with 6 equivalents of EtMgBr at –30°C for 1 h gave allene (*S*)-**15b** ($[\alpha]_D$ +101.5; 61% ee) in 94% yield. The reason why the optical yield of **14b** is so low is obscure at present.

By comparison of the absolute configurations of **12** and **13** with those of **14** and **15**, the elimination was thought to proceed mainly via the *anti*-conformation as shown in Scheme 3.

We are continuing to study the scope and limitations of this method and to improve the optical yield of the elimination step.

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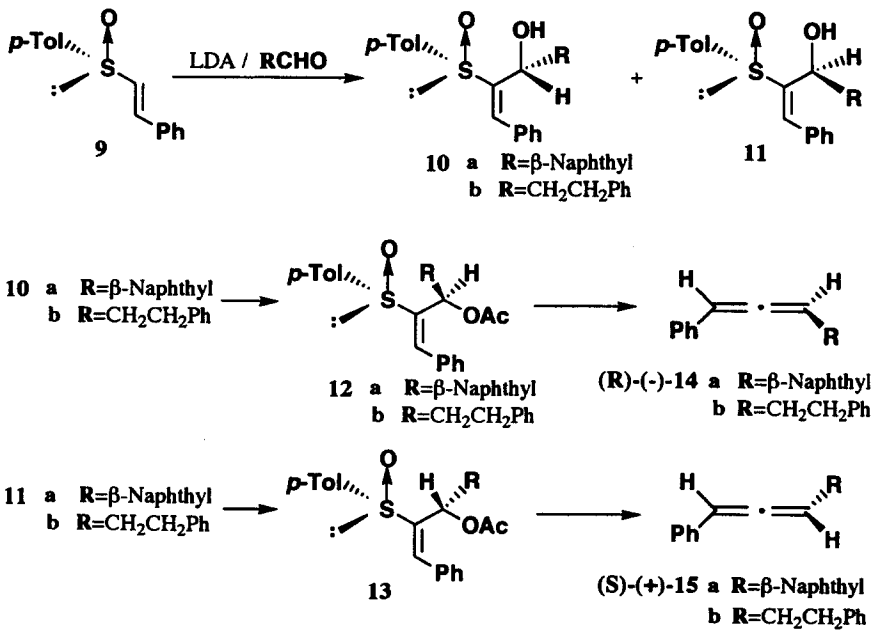

Scheme 3.

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7. The absolute configuration was determined by the sign of optical rotation: see Ref. 1c, pp. 31–32.