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Unexpected S_N2'-type addition–elimination reactions of 1-aryl-2,3-allenols with LiX. Synthesis and synthetic application of 1-aryl-3-halo-1,3-dienes

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Abstract—1-Aryl-3-halo-1,3-dienes were prepared from the sequential addition–elimination reaction of 1-aryl-2,3-allenols with LiX (X = Br, Cl) in HOAc in moderate to good yields. Here the aromatic substituent is crucial to this interesting transformation since no reaction was observed with 1-alkyl or perfluoroalkyl-2,3-allenols. The 1-aryl-3-halo-1,3-dienes prepared can be used as useful partners in Diels–Alder reactions with dienophiles leading to polycyclic quinone derivatives. © 2002 Elsevier Science Ltd. All rights reserved.

1,3-Dienes are important intermediates in organic synthesis,[1] especially as a partner in Diels–Alder reactions.[2] Recently, during our study of allene chemistry,[3] we observed that the Pd(0)-catalyzed coupling-cyclization of organic halides and 2,3-allenols afforded vinylic oxiranes[4] or 2,5-dihydrofurans,[5] whilst the Pd(0)-catalyzed reaction of 2,3-allenols with aryl halides in the presence of amines afforded α- or γ-aminoalcohols regioselectively and stereoselectively,[6] showing the synthetic potential of 2,3-allenols.[7–9] A recent study of Pd-catalyzed synthesis of (*Z*,*E*)-2-bromo-1,3-dienes from α-allenic acetates by Bäckvall et al.[10] prompted us to report an unexpected reaction of 1-aryl-2,3-allenols with lithium halides affording 1-aryl-3-halo-1,3-dienes.

Recently, Bäckvall et al. reported a palladium-catalyzed reaction of 4,5-allenols with LiBr in the presence of benzoquinone to afford vinylic tetrahydrofuran derivatives.[11] Based on this result we reasoned that the corresponding reaction of 2,3-allenols with lithium halides would produce 3-bromo-2,5-dihydrofurans. However, when a mixture of 1-phenyl-2,3-butadienol **1a**, LiBr (5 equiv.) and benzoquinone (2.5 equiv.) was treated with 5 mol% of $Pd(OAc)_2$ in HOAc, the reaction afforded an unexpected product whose structure upon X-ray diffraction analysis was determined to be that of **2a** (Fig. 1). Using 5 mol% of $PdCl_2(CH_3CN)_2$ or $PdCl_2(PPh_3)_2$, the same product **2a** was formed, respectively. Surprisingly, it is interesting to note that this reaction can occur to afford **2a** even *in the absence of* any Pd catalyst. Here, it is obvious that the reaction proceeded via the intermediacy of 1-phenyl-3-bromo-1(*E*),3-butadiene **3a**.

With these results in hand, we studied the reaction in the absence of a dienophile in order to isolate the synthetically useful 2-halo-1,3-butadiene derivatives. When we ran this reaction with LiBr in a mixture of HOAc and CH_3CN (1:19), the reaction was complicated. Heating the mixture of $LiBr·H_2O$ with **1a** in HOAc at 50°C afforded 1-phenyl-3-bromo-1,3-butadiene **3a** in 70% yield. The yield can be further improved to 76% when the reaction was carried out in the presence of 20 mol% of hydroquinone (Scheme 1).

Thus, by applying these standard reaction conditions, the reactions of differently substituted 1-aryl-2,3-allenols with LiX in the presence of 20 mol% hydroquinone in HOAc afforded 1,3-butadienes. Some typical results are summarized in Table 1.

From the results in Table 1, it is obvious that the yields for the formation of 3-halo-1-aryl-1,3-butadienes are from moderate to good. The reaction was complete within a few hours. Both bromides and chlorides can be prepared. LiX monohydrate and anhydrous LiX did not show obvious differences in terms of yields of the products.

Keywords: allenes; alcohols; substitution; dienes.

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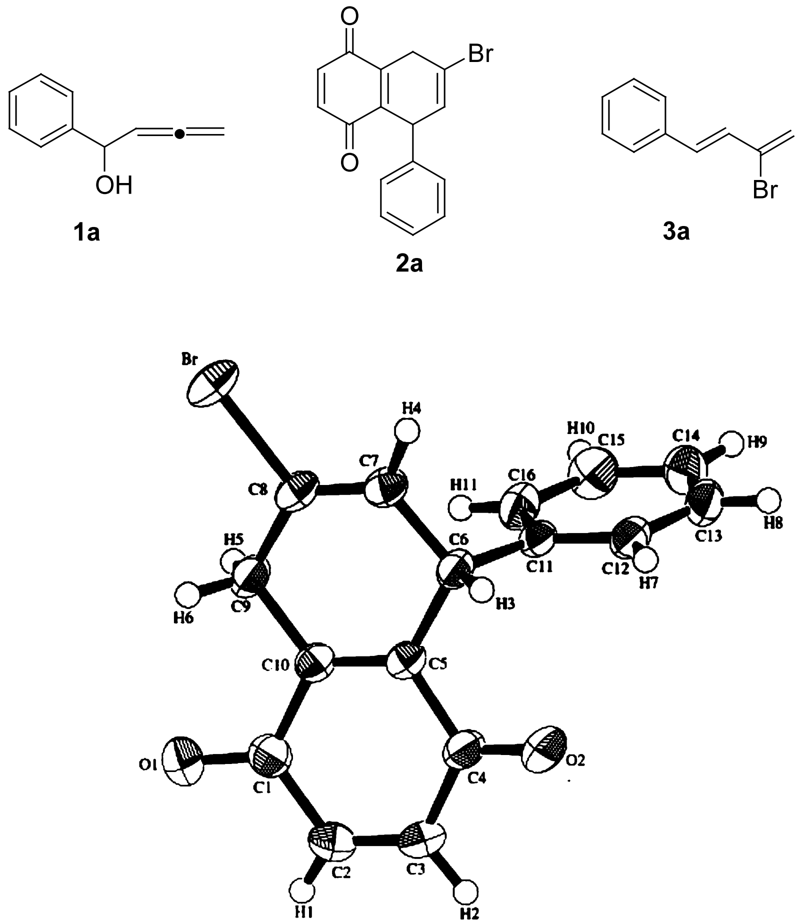
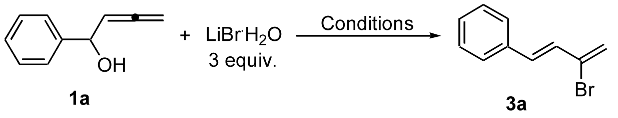


Figure 1. Structures **1a**, **2a** and **3a** and the ORTEP representation of **2a**.



AcOH/CH$_3$CN(1: 19)	reflux	10 h	complicated
AcOH	50°C	1 h	70 %
AcOH, HQ (20 mol%)	50°C	40 min.	76 %

Scheme 1.

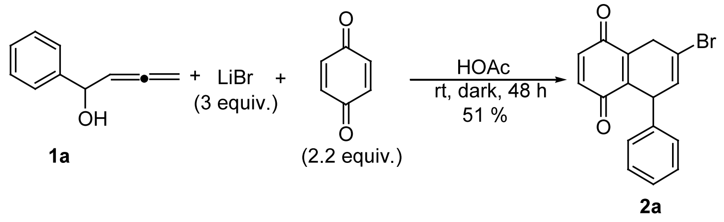
With 2-(*n*-butyl)-1-phenyl-2,3-butadienol **1e**, the reaction afforded *E*/*Z* mixtures of 3-halo-1-phenyl-2-(*n*-butyl)-1,3-butadienes (Scheme 2). The stereochemistry was determined by the ^{1}H–^{1}H NOESY spectra of **3j**.

This reaction can also be extended to the tertiary alcohol **1f** to afford the corresponding products in good yields (Scheme 3).

However, it is interesting to observe that the corresponding reaction of 1-alkyl or perfluoroalkyl-substituted allenols **1g** and **1h** did not yield the expected products (Scheme 4).

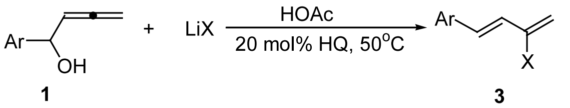
The reaction is believed to proceed through an S_N2'-type addition–elimination process.[12] In HOAc, the phenyl group may stabilize the corresponding carbocationic intermediate formed by the interaction of HOAc with the hydroxy group of 1-phenyl-2,3-allenols.

The dienes prepared can be used for the synthesis of polycyclic quinones via Diels–Alder oxidation reactions. 1,4-Naphthoquinones are a class of compounds with biological activities such as antiinflammatory, antitumor, antiparasitic and antimicrobial action.[13] Thus, we used benzoquinone as the dienophile to optimize the reaction conditions for the one-pot addition–elimination-Diels–Alder process. The reaction afforded the Diels–Alder adduct **2a** in 51% yield at rt in the dark (Eq. (1)). Using these standard reaction conditions, the

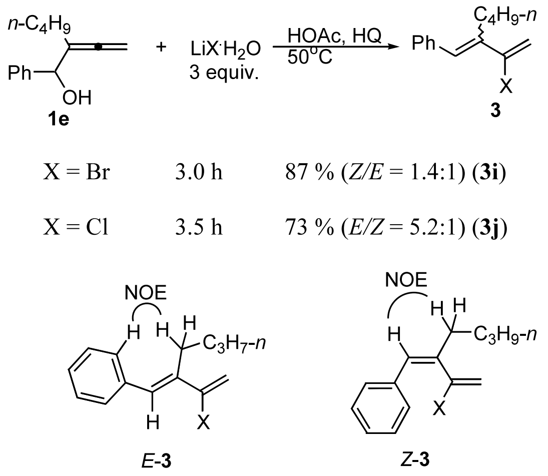


(1)

Table 1. Synthesis of 1-phenyl-3-halo-1,3-butadiene via the reaction of 1-phenyl-2,3-allenols with LiX in HOAc



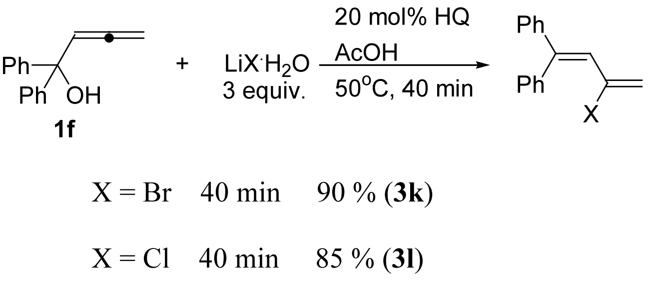
Entry	**1** (Ar)	LiX	Time (h)	Yield of **3** (%)
1	Ph (**1a**)	LiBr·H_2O	40 min	76 (**3a**)
2	Ph (**1a**)	LiCl	2	60 (**3b**)
3	p-$CH_3OC_6H_4$ (**1b**)	LiBr	2	33 (**3c**)
4	p-$CH_3OC_6H_4$ (**1b**)	LiCl	2	53 (**3d**)
5	o-ClC_6H_4 (**1c**)	LiBr·H_2O	1.5	82 (**3e**)
6	o-ClC_6H_4 (**1c**)	LiCl	1.5	60 (**3f**)
7	Naphthyl (**1d**)	LiBr·H_2O	0.5	81 (**3g**)
8	Naphthyl (**1d**)	LiCl·H_2O	0.5	88 (**3h**)



X = Br 3.0 h 87 % (Z/E = 1.4:1) (**3i**)

X = Cl 3.5 h 73 % (E/Z = 5.2:1) (**3j**)

Scheme 2.



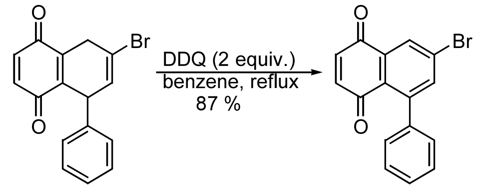
X = Br 40 min 90 % (**3k**)

X = Cl 40 min 85 % (**3l**)

Scheme 3.

reaction of **1a**, LiBr and naphthoquinone afforded **2b** in 72% yield (Scheme 5).

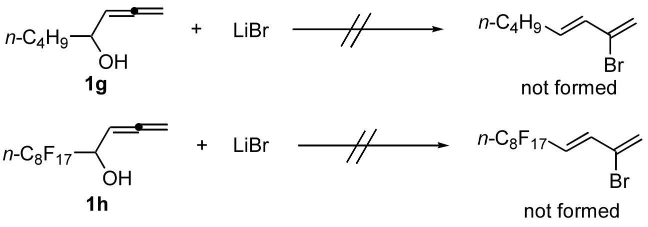
Upon treatment with DDQ, **2a** was oxidized to afford the naphthoquinone derivative **2a′** in 87% yield (Eq. (2)).



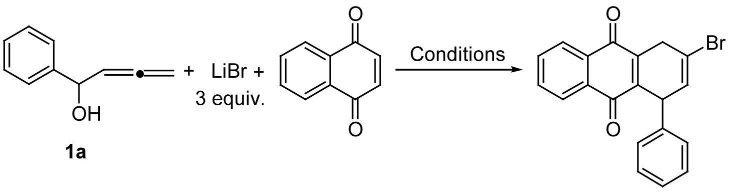
(2)

2a **2a′**

In conclusion, we have observed an interesting S_N2'-type addition–elimination reaction of 1-phenyl-2,3-allenols with LiX (X = Br, Cl). The 2-halo-1,3-dienes prepared show good reactivities towards quinones. Further studies on the scope and synthetic potentials of this reaction are being carried out in our laboratory.



Scheme 4.



2b

Conditions	Yield(%)
AcOH, 40°C, 42 h	53
AcOH, dark, rt, 48 h	72

Scheme 5.

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