Efficient two-step synthesis of 3-halo-3-enals or 2-halo-2-alkenyl ketones from propargylic bromides *via* a unique cationic 1,2-aryl or proton shift in electrophilic addition reaction of 2,3-allenols with X^+†

Chunling Fu,[a] Jing Li[b] and Shengming Ma*[ab]

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The reaction of readily available 1-substituted 2,3-allenols with Br_2, NBS, or I_2 afforded the not-easily-available but synthetically useful 3-halo-3-alkenals or 2-halo-2-alkenyl ketones in good yields *via* a sequential electrophilic interaction of X^+ with the allene moiety , a 1,2-aryl or proton shift, and a H^+-elimination process; the structures of the products were established by X-ray diffraction study.

Although allenes had been considered as highly unstable for a long period of time, recent observation of nice reactivities and selectivities of allenes in organic synthesis has made their chemistry a hot research area.[1–3] However, the electrophilic addition of allenes has not been well developed, mainly due to the fact that the control of regio- and stereoselectivity is not easy.[4] In this paper, we wish to report the electrophilic interaction of 1-substituted 2,3-allenols, which are easily available from a one-step high-yielding reaction of propargylic bromides, aldehydes, and $SnCl_2$,[5] with X^+ leading to the formation of otherwise not easily available 3-halo-3-enals or 2-halo-2-alkenyl ketones due to the great tendency of the C=C bond to migrate from the β,γ-position to the more stable α,β-position.[6]

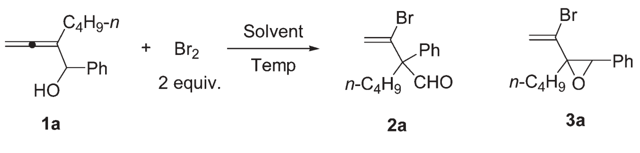
We have observed that introducing a sulfinyl, organosulfur, or organoselenium functionality can control the regio- and stereochemistry of the halohydroxylation of allenes.[7,8] It has also been reported that the Pd-catalyzed cyclization of 2,3-allenols will form vinylic epoxides[9] or dihydrofurans[10] highly selectively depending on the nature of the catalyst and the halides used. With our recent observation that 2,3-allenoates could be cyclized directly to afford butenolides,[11] we started to explore the chemistry of mixing 1-phenyl-2-butyl-2,3-butadienol (**1a**) with Br_2 to prepare vinylic epoxide **3a** directly in one step.[12]

The results in THF, toluene, or benzene were quite complicated (entries 1–3, Table 1). However, when the reaction was conducted in CH_3CN, instead of the expected vinylic epoxide **3a**, a β-bromo-β,γ-unsaturated enal with a structure shown as **2a** was formed in 35% yield unexpectedly (entry 4, Table 1)! By screening the most commonly used solvents, it was found that the same reaction in CCl_4 or CH_2Cl_2 afforded **2a** in 67% and 60% yields, respectively (entries 5 and 6, Table 1). Better results were achieved by running the reaction in aqueous MeCN (MeCN : H_2O = 15 : 1) at rt (entry 9, Table 1). Epoxide **3a** was formed in < 5% yield, if any. The ratios of MeCN/H_2O are also important for a higher yield of **2a** (compare entries 7–11, Table 1).

With the optimized reaction conditions in hand, we studied the scope of this reaction with the typical results summarized in Table 2. It can be concluded that 2,3-allenols with differently substituted phenyl groups at the 1-position can be used to prepare the 3-halo-3-enals in good yields. By introducing the allyl group into the 2-position of the 2,3-allenols, halogenation of the allylic C=C double bond was not observed, indicating the higher reactivity of the allene functionality. For the synthesis of bromides, both Br_2 and NBS can be applied, however, the yields with NBS are usually much higher than those with Br_2 (compare entries 2/3, 7/8, 10/11 and 12/13, Table 2). The corresponding reaction with I_2 can also occur smoothly to afford 3-iodo-3-enals **2j** or **2k** in good to high yields (entries 14 and 15, Table 2). The structures of the products were determined unambiguously by the X-ray diffraction study of **2j** (Fig. 1).[13]

A rationale for this interesting transformation is shown in Scheme 1. The interaction of "X^+" with the internal C=C bond of the allene moiety would form intermediate **4**, which would undergo a 1,2-shift of the Ar group (R^2 = Ar) to open the three-membered ring forming the cationic homoallylic alcohol

Table 1 Reaction of 1-phenyl-2-(*n*-butyl)-2,3-butadien-1-ol (**1a**) with Br_2 under different conditions



Entry	Solvent	Temp (°C)	*t* (h)	Yield[a] of **2a** (%)
1	THF	33	19	[b]
2	Toluene	33	19	[b]
3	Benzene	25	1	[b]
4	CH_3CN	25	24	35
5	CH_2Cl_2	32	2	60
6	CCl_4	32	2	63
7	CH_3CN/H_2O = 4 : 1	32	1	68
8	CH_3CN/H_2O = 8 : 1	32	2	65
9	CH_3CN/H_2O = 15 : 1	25	0.5	77
10	CH_3CN/H_2O = 60 : 1	30	1	60
11	CH_3CN/H_2O = 15 : 1	−30	1	50

[a] Isolated yield. [b] The reaction was complicated.

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[a] *Laboratory of Molecular Recognition and Synthesis, Department of Chemistry, Zhejiang University, Hangzhou, 310027, Zhejiang, P. R. China*
[b] *State Key Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 354 Fenglin Lu, Shanghai, 200032, P. R. China. E-mail: masm@mail.sioc.ac.cn*

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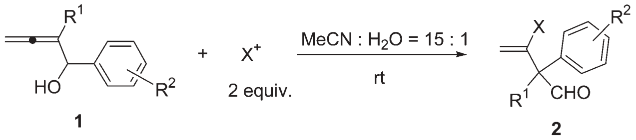
Table 2 Reaction of 2,3-allenols with X^{+a}



Entry	R^1	R^2	X_2	t (h)	Yield (%)[b]
1	n-C_4H_9	H	Br_2	0.5	77 (**2a**)
2	n-C_4H_9	p-CH_3	Br_2	0.5	73 (**2b**)
3	n-C_4H_9	p-CH_3	NBS[d,e]	2	93 (**2b**)
4	n-C_4H_9	p-OCH_3	Br_2	1.5	73 (**2c**)
5	n-C_4H_9	m, p-OCH_2O	Br_2	0.5	78 (**2d**)
6	allyl	p-OCH_3	Br_2[c,d]	1.5	57 (**2e**)
7	allyl	p-CH_3	Br_2[c,d]	1	52 (**2f**)
8	allyl	p-CH_3	NBS[d,e]	1	71 (**2f**)
9	C_2H_5	p-CH_3	Br_2	1.5	71 (**2g**)
10	C_2H_5	p-OCH_3	Br_2[d,e]	1	80 (**2h**)
11	C_2H_5	p-OCH_3	NBS[d,e]	0.7	88 (**2h**)
12	C_2H_5	m, p-OCH_2O	Br_2	1.5	64 (**2i**)
13	C_2H_5	m, p-OCH_2O	NBS[d,e]	0.5	84 (**2i**)
14	n-C_4H_9	m, p-OCH_2O	I_2	1	80 (**2j**)
15	C_2H_5	m, p-OCH_2O	I_2	0.5	69 (**2k**)

[a] The reaction was conducted using 0.3–0.5 mmol of 2,3-allenols and Br_2, NBS, or I_2 (2 equiv. unless otherwise stated) in MeCN (4 mL) and H_2O (0.27 mL). [b] Isolated yield. [c] 1.2 equiv. of Br_2 were used. [d] The reaction was conducted at 0 °C. [e] 1.2 equiv. of NBS were used.

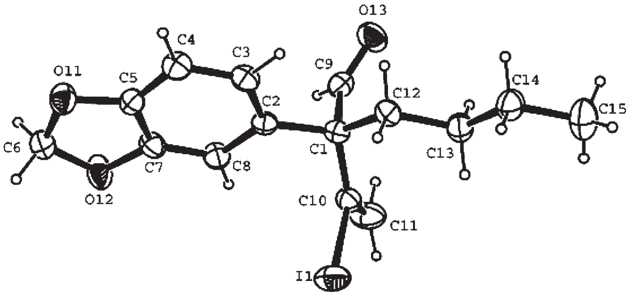
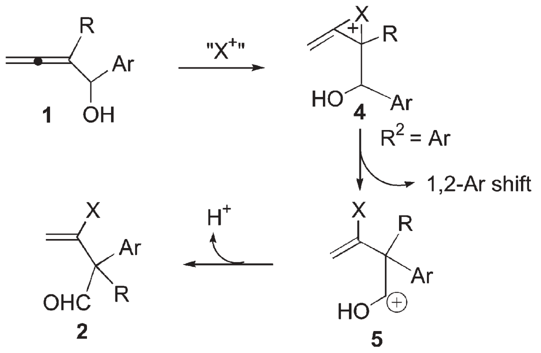
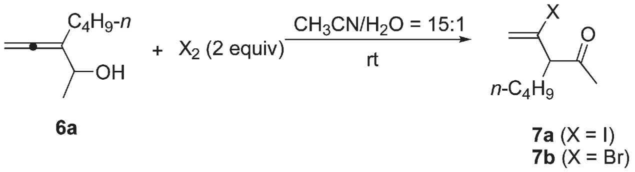


Fig. 1 Drawing of **2j**. Only one of the two independent molecules in the asymmetric unit is shown.



Scheme 1

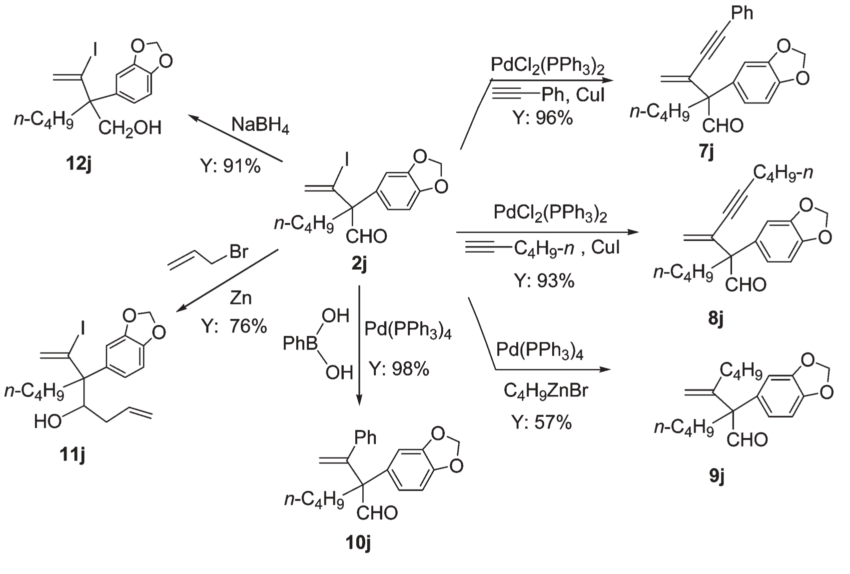


Scheme 2

intermediate **5**.[14] Release of H^+ from **5** would form the final 3-halo-3-enals **2**.

However, the corresponding reaction of 3-(n-butyl)penta-3,4-dien-2-ol (**6a**) with X_2 afforded the 1,2-H shift products **7a** and **7b** highly selectively (Scheme 2). The migration of the C=C bond in **7a** and **7b** was not observed.

3-Halo-3-enals are very useful building blocks in organic synthesis due to the presence of the C–X bond, the C=C bond and the C=O bond. The synthetic potential of this methodology was demonstrated by the reactions of **2j** as shown in Scheme 3. With the coupling protocols of the C–I bond in **2j**,[15] 1-alkynyl, aryl, alkyl groups can be introduced into the 3-position; the aldehyde functionality in **2j** can be easily reduced with $NaBH_4$ or react with organometallic reagents to afford corresponding alcohols **11j** and **12j** (Scheme 3).[16]



Scheme 3

In conclusion, we have developed a sequential electrophilic addition and 1,2-aryl or proton shift reaction of X^+ (X = Br or I) with 1-substituted-2,3-allenols forming 3-halo-3-enals or 2-halo-2-alkenyl ketones efficiently. Due to the easy availability of the starting compounds[5] and the not-readily-available nature as well as synthetic potential of these compounds, this method will be very useful in organic synthesis. Further studies including the scope and synthetic application of this reaction are being carried out in our laboratory.

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