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Palladium-Catalyzed Coupling of Haloalkynes with Allyl Acetate: A Regio- and Stereoselective Synthesis of (*Z*)-β-Haloenol Acetates

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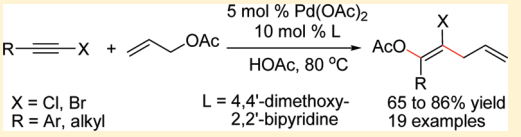
Supporting Information

ABSTRACT: A Pd-catalyzed coupling of haloalkynes with allyl acetate has been reported, providing a convenient method for the stereoselective synthesis of (*Z*)-β-haloenol acetates in good yields. The synthetic utility of this method is demonstrated by the formation of functionalized enol acetates via the Suzuki−Miyaura or Sonogashira coupling of the resulting (*Z*)-β-haloenol acetate products.

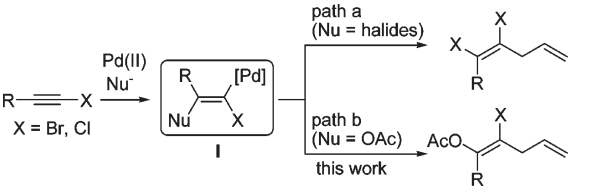


Haloalkenes are a fundamental and pivotal class of compounds that undergo numerous chemical transformations.[1−6] In this respect, the β-haloenol acetates encompass the reactivity of enol acetates and carbon−halide bonds, which renders them as one of the most important building blocks in organic synthesis. The versatile scopes of the applications include the transition-metal-catalyzed cross-coupling reactions, the halogen-metal exchange reactions,[7,8] the precursors for β-keto dianions,[9−11] and others. However, there are only a few methods that exist for the effective synthesis of stereodefined β-haloenol acetates.[12] In 1990, Barluenga[13] described a facile protocol for the synthesis of (*E*)-haloenol acetates via the electrophilic addition of terminal alkynes. More recently, Jiang and co-workers[14] discovered an elegant method for the stereoselective synthesis of (*Z*)-β-haloenol acetates based on the silver-catalyzed difunctionalization reaction of terminal alkynes.

We have recently[15] reported a regio- and stereoselective synthesis of (*Z*)-1,2-dihalo-1,4-dienes through the Pd-catalyzed coupling of alkynyl halides and allyl halides, with the alkenyl palladium intermediate **I** as the key intermediate (path a, Scheme 1). On the other hand, pioneered by Lu et al.,[16−23] the acetoxypalladation of acetylenes[24−30] is witnessing a great deal of interest because of the formation of carbon−carbon bond and carbon−oxygen bond in a rather efficient and atom-economic fashion. As such, we envisioned that the employment of allyl acetates as the capture reagents for the palladium intermediate **I** would eventually offer facile access to (*Z*)-β-haloenol acetates (path b, Scheme 1). Herein, we reported our recent work on Pd-catalyzed coupling of alkynyl halides with allyl acetate, in which the (*Z*)-β-haloenol acetates were synthesized in a highly regio- and stereoselective manner.

At the outset of this investigation, we examined the coupling reaction between phenylethynyl chloride (**1a**) and allyl acetate (**2a**) using 5 mol % of $PdCl_2$, 2.0 equiv of LiOAc, and 10 mol % of 2,2′-bipyridine (**L1**) (see Figure 1) as the ligand. Gratifyingly, the reaction gave the desired (*Z*)-β-haloenol acetate (*Z*)-**3aa** in 50% GC yield, after stirring for 8 h in HOAc at 80 °C. The regiochemistry of this reaction was determined by the NOE

Scheme 1. Two Nucleopalladation-Initiated Reactions of Haloalkynes



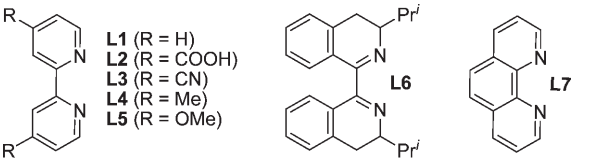


Figure 1. The Structure of Ligands.

measurements and further confirmed by X-ray diffraction analysis of (*Z*)-**3ka**. Inspired by this promising result, we further examined the reaction conditions, and the results are summarized in Table 1.

First, we tested a variety of palladium sources for this reaction using HOAc as the solvent. The employment of $Pd(OAc)_2$ resulted in the best yield, giving the (*Z*)-β-haloenol acetate product (*Z*)-**3aa** in 60% GC yield, while decreased yields were observed when other palladium catalysts such as $PdBr_2$, $Pd(MeCN)_2Cl_2$, and $Pd(PhCN)_2Cl_2$ were employed (entries 1−4, Table 1). A brief survey of the solvents revealed that HOAc was critical for this reaction, and the use of other solvents, such as CH_3CN or DMSO, failed to give the desired products (entries 6 and 7, Table 1). Interestingly, a significant increase of the yield was observed when the reaction was

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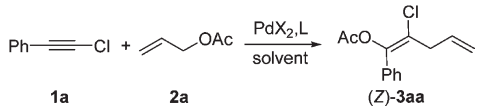
Table 1. Selected Results of Screening the Reaction Conditions[a]



1a 2a (Z)-3aa

entry	PdX_2	solvent	LiOAc (equiv)	ligand	yield (%)[b,c]
1	$PdCl_2$	HOAc	2.0	**L1**	50
2	$PdBr_2$	HOAc	2.0	**L1**	52
3	$Pd(MeCN)_2Cl_2$	HOAc	2.0	**L1**	55
4	$Pd(PhCN)_2Cl_2$	HOAc	2.0	**L1**	56
5	$Pd(OAc)_2$	HOAc	2.0	**L1**	60
6	$Pd(OAc)_2$	CH_3CN	2.0	**L1**	NR
7	$Pd(OAc)_2$	DMSO	2.0	**L1**	0
8	$Pd(OAc)_2$	HOAc	–	**L1**	73
9	$Pd(OAc)_2$	HOAc	–	**L2**	55
10	$Pd(OAc)_2$	HOAc	–	**L3**	45
11	$Pd(OAc)_2$	HOAc	–	**L4**	74
12	$Pd(OAc)_2$	HOAc	–	**L5**	89 (86)[c]
13	$Pd(OAc)_2$	HOAc	–	**L5**[d]	57
14	$Pd(OAc)_2$	HOAc	–	pyr	47
15	$Pd(OAc)_2$	HOAc	–	**L6**	18
16	$Pd(OAc)_2$	HOAc	–	**L7**	75

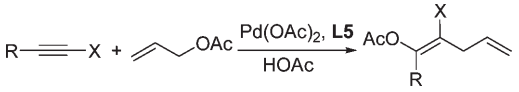
[a] Reaction conditions: **1a**, 0.5 mmol; **2a**, 0.75 mmol; ligand, 0.05 mmol; and Pd catalyst, 0.025 mmol, in 2.5 mL of solvent at 80 °C. [b] GC yield, with naphthalene as the internal standard. [c] Isolated yield. [d] 6 mol % of **L5** was used.

conducted without adding LiOAc, and the yield was increased to 73% (entry 8, Table 1).

We then focused on screening the ligands for this reaction. As clearly demonstrated in Table 1, the electronic nature of ligands plays an important role in the Pd-catalyzed coupling of alkynyl halides with allyl acetate. The utilization of electron-deficient ligands, such as 4,4′-dicarboxylic-2,2′-bipyridine (**L2**) and 4,4′-dicyano-2,2′-bipyridine (**L3**), led to a substantial decrease of the yields to 55% and 45%, respectively (entries 9 and 10, Table 1). In sharp contrast, when the electron-rich ligand 4,4′-dimethoxy-2,2′-bipyridine (**L5**), for example, was chosen as the ligand for this reaction, the desired product (*Z*)-**3aa** was obtained in a much higher yield (86%) (entry 12, Table 1). Notably, the 2/1 ligand/metal ratio turned out to be essential for achieving the high yield, and the use of 5 mol % of $Pd(OAc)_2$ and 6 mol % of ligand (**L5**) resulted in a dramatic decrease of the yield to 57% (entry 13, Table 1). Other ligands, such as pyridine, **L6**, and **L7**, led to no improvement of the yields (entries 14−16, Table 1). Furthermore, the reaction had to be performed at 80 °C, because at a lower temperature (60 °C), the conversions remained incomplete. Finally, we chose 5 mol % of $Pd(OAc)_2$ as the catalyst, 10 mol % of 4,4′-dimethoxy-2,2′-bipyridine (**L5**) as the ligand, and 80 °C for the optimal reaction conditions.

After establishing the optimized conditions, the scope and limitations of this reaction were then investigated in detail with other haloalkynes under the optimal conditions. As outlined in Table 2, the reaction was found to be widely applicable to various functionalized chloroalkynes, except triethylsilylethynyl chloride (**1t**) (entry 20, Table 2). Either electron-rich or electron-deficient chloroalkynes were smoothly converted into the (*Z*)-*β*-haloenol acetate products in good yields with excellent

Table 2. Scope and Limits of the Reaction[a]



1 2a (Z)-3

entry	1	R	X	3	yield (%)[b]
1	**1a**	Ph	Cl	(*Z*)-**3aa**	86
2	**1b**	*p*-F-C_6H_4	Cl	(*Z*)-**3ba**	76
3	**1c**	*p*-Cl-C_6H_4	Cl	(*Z*)-**3ca**	80
4	**1d**	*o*-Cl-C_6H_4	Cl	(*Z*)-**3da**	74
5	**1e**	*p*-Br-C_6H_4	Cl	(*Z*)-**3ea**	81
6	**1f**	*o*-Br-C_6H_4	Cl	(*Z*)-**3fa**	71
7	**1g**	*p*-Me-C_6H_4	Cl	(*Z*)-**3ga**	85
8	**1h**	*p*-OMe-C_6H_4	Cl	(*Z*)-**3ha**	70
9	**1i**	*m*-OMe-C_6H_4	Cl	(*Z*)-**3ia**	73
10	**1j**	*o*-OMe-C_6H_4	Cl	(*Z*)-**3ja**	65
11	**1k**	3,4-OMe_2-C_6H_3	Cl	(*Z*)-**3ka**	77
12	**1l**	2,4-Cl_2-C_6H_3	Cl	(*Z*)-**3la**	72
13	**1m**	4-*i*-Pr-C_6H_4	Cl	(*Z*)-**3ma**	71
14	**1n**	4-*t*-Bu-C_6H_4	Cl	(*Z*)-**3na**	80
15	**1o**	Ph	Br	(*Z*)-**3oa**	74
16	**1p**	*p*-Cl-C_6H_4	Br	(*Z*)-**3pa**	77
17	**1q**	$CH_3(CH_2)_4$	Cl	(*Z*)-**3qa**	75
18	**1r**	$TBSOCH_2CH_2$	Cl	(*Z*)-**3ra**	72
19	**1s**	$BnOCH_2CH_2$	Cl	(*Z*)-**3sa**	82
20	**1t**	$(CH_3CH_2)_3Si$	Cl	(*Z*)-**3ta**	0
21	**1u**	Ph	I	(*Z*)-**3ua**	0
22[c]	**1a**	Ph	Cl	(*Z*)-**3aa**	52
23[d]	**1a**	Ph	Cl	(*Z*)-**3aa**	trace

[a] Reaction conditions: **1**, 0.5 mmol; **2a**, 1.5 mmol; **L5**, 0.05 mmol; and $Pd(OAc)_2$, 0.025 mmol, in 2.5 mL of HOAc at 80 °C. [b] Isolated yield. [c] Allyl benzoate was used. [d] Allyl ethyl ether was used.

stereoselectivity. For example, the reaction of chloroalkynes **1b** and **1c** afforded the desired (*Z*)-*β*-haloenol acetates (*Z*)-**3ba** and (*Z*)-**3ca** in 76% and 80% yields, respectively (entries 2 and 3, Table 2). The reaction of substances possessing a substituent ortho to the C−C triple bond was effective as well, producing the (*Z*)-*β*-haloenol acetates in good yields (entries 4, 6, and 10, Table 2). Moreover, bromoalkynes **1o** and **1p** were converted into the (*Z*)-*β*-bromoenol acetates (*Z*)-**3oa** and (*Z*)-**3pa** in 74% and 77% yields, respectively (entries 15 and 16, Table 2). Aliphatic haloalkynes also participated well in this reaction. For example, the (*Z*)-*β*-haloenol acetate (*Z*)-**3qa** was generated from alkynyl chloride **1q** in 75% yield (entry 17, Table 2). In contrast, the reaction of phenylethynyl iodide (**1u**) only led to the decomposition of the starting materials, probably due to the worse stability of the C−I bond in the presence of palladium catalyst (entry 21, Table 2). Interestingly, allyl benzoate reacted smoothly with **1a** to give the (*Z*)-*β*-haloenol acetate (*Z*)-**3aa** in 52% yield, while only a trace of the desired product was obtained when allyl ethyl ether was used (entries 22 and 23, Table 2).

Then, we carried out the coupling reactions of **1a** with substituted allyl acetates, such as **2b**, **2c**, **2d**, and **2e** (Figure 2); however, the starting material **1a** was mostly intact in these cases, probably due to the sluggish carbopalladation of the alkenyl

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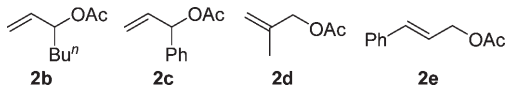
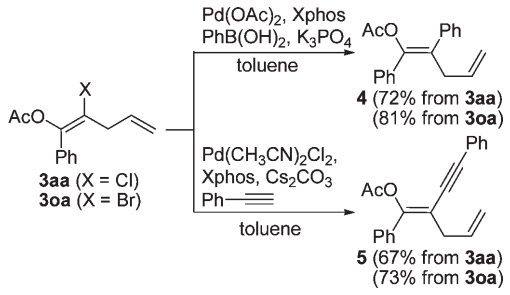
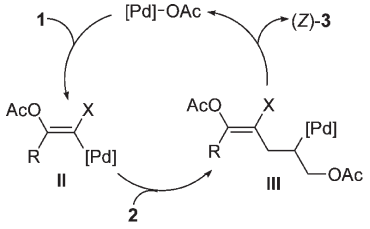


Figure 2. The structure of **2**.

Scheme 2. Pd-Catalyzed Cross-Coupling Reactions of (*Z*)-3



Scheme 3. Proposed Mechanism for Pd-Catalyzed Coupling of Haloalkynes with Allyl Acetate



palladium intermediate with the substituted allyl acetates (see the proposed mechanism).

To demonstrate the synthetic utility of this protocol, we further examined the resulting products in the transition-metal-catalyzed cross-coupling reactions (Scheme 2). For instance, (*Z*)-*β*-haloenol acetates (*Z*)-**3aa** and (*Z*)-**3oa** underwent the Suzuki−Miyaura coupling[31] with PhB(OH)$_2$ in the presence of Xphos[32,33] to produce the highly functionalized enol acetate **4** in 72% and 81% yields, respectively. The X-ray analysis of **4** clearly demonstrated the structure of the product. On the other hand, the Sonogashira coupling[34,35] of (*Z*)-**3aa** and (*Z*)-**3oa** occurred uneventfully as well, providing the enol acetate **5** in 67% and 73% yields, respectively. The generated enol acetate products may be amenable to further chemical transformations.[36−40]

In view of the previous reports on the acetoxypalladation reactions, we proposed a plausible mechanism in Scheme 3 to account for this reaction. The reaction was initiated by the trans-acetoxypalladation[16−23] of haloalkyne **1** to form the alkenyl palladium intermediate **II**. Then, the following carbopalladation reaction of alkenylpalladium intermediate **II** with allyl acetate resulted in an alkylpalladium complex **III**. Finally, the *β*-hetero-atom elimination in the presence of nitrogen-containing ligand furnished the (*Z*)-*β*-haloenol acetate product (*Z*)-**3** and closed the catalytic cycle (Scheme 3).

In summary, we have developed a convenient and practical method for the regio- and stereoselective synthesis of (*Z*)-*β*-haloenol acetates via the palladium-catalyzed coupling of alkynyl halides with allyl acetate under mild conditions. The synthetic utility of the resulting (*Z*)-*β*-haloenol acetate products was well-demonstrated in the followed Pd-catalyzed cross-coupling reactions, such as Suzuki and Sonogashira coupling reactions. Further synthetic applications of this reaction are on the way.

EXPERIMENTAL SECTION

General. Unless otherwise noted, all reactions and manipulations were conducted under air atmosphere. Column chromatography was performed using silica gel (300−400 mesh). ^{1}H NMR and ^{13}C NMR spectra were recorded on a 400 MHz NMR spectrometers. Chemical shifts were reported in ppm downfield from tetramethylsilane with the solvent resonance as the internal standard. MS and microanalysis were performed in the state-authorized analytical center of Zhejiang Normal University.

General Procedure for the Pd-Catalyzed Coupling of Haloalkynes with Allyl Acetate. To a solution of **2a** (75 mg, 0.75 mmol), Pd(OAc)$_2$ (6.5 mg, 0.025 mmol), and 4,4′-dimethoxy-2,2′-bipyridine (9.2 mg, 0.05 mmol) in 2.0 mL of HOAc was added **1a** (69 mg, 0.50 mmol) at rt. After stirring for 8 h at 80 °C, the reaction mixture was quenched with water, extracted with dichloromethane, washed with saturated NaHCO$_3$ and brine, and dried over anhydrous Na$_2$SO$_4$. Column chromatography on silica (petroleum ether/ethyl acetate = 100/1) gave 101 mg (yield: 86%) of (*Z*)-**3aa** as a yellow oil. ^{1}H NMR (CDCl$_3$, 400 MHz): *δ* 2.21 (s, 3 H), 3.18 (d, *J* = 6.0 Hz, 2 H), 5.22 (dd, *J* = 10.0, 1.2 Hz, 1 H), 5.25 (dd, *J* = 16.0, 1.2 Hz, 1 H), 5.86−5.93 (m, 1 H), 7.36−7.42 (m, 5 H). ^{13}C NMR (CDCl$_3$, 100 MHz): *δ* 20.4, 38.3, 117.5, 123.7, 128.1 (2 C), 128.2 (2 C), 128.9, 132.8, 133.4, 143.6, 167.7. MS (EI, *m*/*z*): 236 (M$^+$, 2), 201 (18), 196 (22), 194 (100), 179 (13). Anal. Calcd for C$_{13}$H$_{13}$ClO$_2$. HRMS (ESI): calcd 236.0604, found 236.0605.

*(Z)-2-Chloro-1-(4-fluorophenyl)penta-1,4-dienyl Acetate [(Z)-**3ba**].* Yield: 76% as a yellow oil. ^{1}H NMR (CDCl$_3$, 400 MHz): *δ* 2.20 (s, 3 H), 3.13 (dd, *J* = 5.6, 1.6 Hz, 2 H), 5.22 (dd, *J* = 10.2, 1.6 Hz, 1 H), 5.24 (dd, *J* = 17.2, 1.6 Hz, 1 H), 5.84−5.89 (m, 1 H), 7.03−7.08 (m, 2 H), 7.38−7.41 (m, 2 H). ^{13}C NMR (CDCl$_3$, 100 MHz): *δ* 20.3, 38.2, 115.3 (d, *J* = 21.0 Hz, 2 C), 117.5, 123.8, 129.4, 130.2 (d, *J* = 8.0 Hz, 2 C), 132.6, 142.7, 162.7 (d, *J* = 240.0 Hz), 167.7. MS (EI, *m*/*z*): 219 (M$^+$ − ^{35}Cl, 22), 214 (30), 212 (100), 197 (11), 177 (48). Anal. Calcd for C$_{13}$H$_{12}$ClFO$_2$. HRMS (ESI): calcd 254.0510, found 254.0511.

*(Z)-2-Chloro-1-(4-chlorophenyl)penta-1,4-dienyl Acetate [(Z)-**3ca**].* Yield: 80% as a yellow oil. ^{1}H NMR (CDCl$_3$, 400 MHz): *δ* 2.20 (s, 3 H), 3.14 (d, *J* = 6.0 Hz, 2 H), 5.23 (dd, *J* = 17.2, 1.6 Hz, 1 H), 5.25 (dd, *J* = 10.8, 1.2 Hz, 1 H), 5.84−5.91 (m, 1 H), 7.33 (s, 4 H). ^{13}C NMR (CDCl$_3$, 100 MHz): *δ* 20.3, 38.2, 117.6, 124.2 (2 C), 128.4 (2 C), 129.5, 131.8, 132.5, 134.9, 142.6, 167.7; MS (EI, *m*/*z*): 237 (10), 235 (M$^+$ − ^{35}Cl, 24), 230 (58), 228 (100), 195 (20), 193 (70). Anal. Calcd for C$_{13}$H$_{12}$Cl$_2$O$_2$. HRMS (ESI): calcd 270.0214, found 270.0211.

*(Z)-2-Chloro-1-(2-chlorophenyl)penta-1,4-dienyl Acetate [(Z)-**3da**].* Yield: 74% as a yellow oil. ^{1}H NMR (CDCl$_3$, 400 MHz): *δ* 2.17 (s, 3 H), 2.96 (d, *J* = 6.0 Hz, 2 H), 5.13 (dd, *J* = 11.2, 1.2 Hz, 1 H), 5.15 (dd, *J* = 17.2, 1.2 Hz, 1 H), 5.75−5.79 (m, 1 H), 7.25−7.33 (m, 2 H), 7.41−7.49 (m, 1 H), 7.50−7.51 (m, 1 H). ^{13}C NMR (CDCl$_3$, 100 MHz): *δ* 20.6, 38.4, 118.0, 126.1, 126.7, 129.8, 130.8, 132.3, 132.5, 132.6, 134.1, 140.9, 168.1. MS (EI, *m*/*z*): 237 (8), 235 (M$^+$ − ^{35}Cl, 24), 230 (62), 228 (100), 195 (23), 193 (75). Anal. Calcd for C$_{13}$H$_{12}$Cl$_2$O$_2$. HRMS (ESI): calcd 270.0214, found 270.0217.

*(Z)-2-Chloro-1-(4-bromophenyl)penta-1,4-dienyl Acetate [(Z)-**3ea**].* Yield: 81% as a yellow oil. ^{1}H NMR (CDCl$_3$, 400 MHz): *δ* 2.20 (s, 3 H), 3.14 (dt, *J* = 6.0, 1.2 Hz, 2 H), 5.21 (dd, *J* = 10.0, 1.6 Hz, 1 H), 5.24 (dd, *J* = 17.2, 1.6 Hz, 1 H), 5.84−5.91 (m, 1 H), 7.27−7.29 (m, 2 H), 7.50 (dd, *J* = 6.8, 2.0 Hz, 2 H). ^{13}C NMR (CDCl$_3$, 100 MHz): *δ* 20.3, 38.2, 117.6, 123.2, 124.3, 129.8 (2 C), 131.4 (2 C), 132.3, 132.5, 142.7, 167.7. MS (EI, *m*/*z*): 281 (13), 279 (M$^+$ − ^{35}Cl, 13), 276 (20), 274

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(100), 272 (72). Anal. Calcd for $C_{13}H_{12}BrClO_2$. HRMS (ESI): calcd 313.9709, found 313.9713.

*(Z)-2-Chloro-1-(2-bromophenyl)penta-1,4-dienyl Acetate [(Z)-**3fa**].* Yield: 71% as a yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.18 (s, 3 H), 2.94 (d, J = 6.0 Hz, 2 H), 5.15 (dd, J = 16.8, 6.0 Hz, 2 H), 5.73−5.83 (m, 1 H), 7.21−7.26 (m, 1 H), 7.30−7.34 (m, 1 H), 7.49−7.51 (m, 1 H), 7.60−7.62 (m, 1 H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 20.6, 38.4, 118.0, 123.8, 126.0, 127.3, 130.9, 132.5, 132.8, 133.0, 134.3, 142.2, 168.0. MS (EI, m/z): 281 (14), 279 ($M^+ - {}^{35}Cl$, 14), 276 (20), 274 (79), 272 (60). Anal. Calcd for $C_{13}H_{12}BrClO_2$. HRMS (ESI): calcd 313.9709, found 313.9702.

*(Z)-2-Chloro-1-p-tolylpenta-1,4-dienyl Acetate [(Z)-**3ga**].* Yield: 85% as a yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.21 (s, 3 H), 2.35 (s, 3 H), 3.20 (dd, J = 5.6, 1.2 Hz, 2 H), 5.23 (dd, J = 10.4, 1.2 Hz, 1 H), 5.26 (dd, J = 18.4, 1.2 Hz, 1 H), 5.87−5.94 (m, 1 H), 7.19 (d, J = 8.0 Hz, 2 H), 7.32 (d, J = 8.0 Hz, 2 H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 20.4, 21.1, 38.3, 117.4, 123.2, 128.0 (2 C), 128.9 (2 C), 130.5, 133.0, 139.0, 143.7, 167.8. MS (EI, m/z): 210 (25), 208 (100), 193 (28), 173 (29), 157 (11). Anal. Calcd for $C_{14}H_{15}ClO_2$. HRMS (ESI): calcd 250.0761, found 250.0768.

*(Z)-2-Chloro-1-(4-methoxyphenyl)penta-1,4-dienyl Acetate [(Z)-**3ha**].* Yield: 70% as a yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.20 (s, 3 H), 3.16 (dd, J = 6.0, 1.6 Hz, 2 H), 3.81 (s, 3 H), 5.20 (dd, J = 10.0, 1.2 Hz, 1 H), 5.24 (dd, J = 17.6, 1.6 Hz, 1 H), 5.85−5.90 (m, 1 H), 6.88 (dd, J = 6.8, 2.0 Hz, 2 H), 7.33 (dd, J = 6.8, 2.0 Hz, 2 H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 20.4, 38.3, 55.0, 113.5 (2 C), 117.3, 122.7, 125.7, 129.6 (2 C), 133.0, 143.5, 159.9, 167.8. MS (EI, m/z): 268 (4), 266 (M^+, 12), 226 (32), 224 (100), 189 (52). Anal. Calcd for $C_{14}H_{15}ClO_3$. HRMS: calcd 266.0710, found 266.0711.

*(Z)-2-Chloro-1-(3-methoxyphenyl)penta-1,4-dienyl Acetate [(Z)-**3ia**].* Yield: 73% as a yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.21 (s, 3 H), 3.20 (d, J = 5.6 Hz, 2 H), 3.79 (s, 3 H), 5.23 (d, J = 11.2 Hz, 1 H), 5.26 (d, J = 17.2 Hz, 1 H), 5.87−5.94 (m, 1 H), 6.89−7.00 (m, 3 H), 7.28−7.30 (m, 1 H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 20.6, 38.6, 55.3, 113.8, 114.9, 117.7, 120.8, 124.0, 129.5, 133.1, 134.8, 143.7, 159.4, 168.0. MS (EI, m/z): 266 (M^+, 1), 231 (9), 226 (16), 224 (48), 209 (100). Anal. Calcd for $C_{14}H_{15}ClO_3$. HRMS: calcd 266.0710, found 266.0711.

*(Z)-2-Chloro-1-(2-methoxyphenyl)penta-1,4-dienyl Acetate [(Z)-**3ja**].* Yield: 65% as a yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.15 (s, 3 H), 2.98 (d, J = 6.0 Hz, 2 H), 3.84 (s, 3 H), 5.13 (d, J = 16.0 Hz, 1 H), 5.15 (d, J = 10.0 Hz, 1 H), 5.75−5.83 (m, 1 H), 6.90−6.96 (m, 3 H), 7.33−7.37 (m, 1 H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 20.7, 38.6, 55.6, 111.0, 117.6, 120.3, 122.2, 124.8, 130.9, 131.6, 133.3, 140.5, 157.2, 168.0. MS (EI, m/z): 266 (M^+, 4), 233 (2), 231 (16), 226 (31), 224 (100). Anal. Calcd for $C_{14}H_{15}ClO_3$. HRMS: calcd 266.0710, found 266.0707.

*(Z)-2-Chloro-1-(3,4-dimethoxyphenyl)penta-1,4-dienyl Acetate [(Z)-**3ka**].* Yield: 77% as a colorless solid. Mp: 74−76 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.19 (s, 3 H), 3.16 (dd, J = 7.2, 3.2 Hz, 2 H), 3.84 (s, 3 H), 3.87 (s, 3 H), 5.20 (dd, J = 10.4, 1.6 Hz, 1 H), 5.25 (dd, J = 17.6, 1.2 Hz, 1 H), 5.86−5.90 (m, 1 H), 6.83 (d, J = 8.0 Hz, 1 H), 6.90 (d, J = 2.0 Hz, 1 H), 6.95−6.98 (m, 1 H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 20.7, 38.7, 55.9 (2 C), 110.7, 111.3, 117.6, 121.3, 123.1, 126.1, 133.3, 143.8, 148.6, 149.7, 168.2. MS (EI, m/z): 298 (10), 296 (M^+, 30), 256 (30), 254 (100), 239 (83). Anal. Calcd for $C_{15}H_{17}ClO_4$. HRMS: calcd 296.0815, found 296.0816.

Crystal data for (Z)-**3ka** ($C_{15}H_{17}ClO_4$, 296.08): triclinic, space group $P\bar{1}$, a = 8.9785(9) Å, b = 11.6414(12) Å, c = 14.8917(17) Å, U = 1486.9(3) Å^3, Z = 4, specimen 0.254 × 0.102 × 0.045 mm^3, T = 296(2) K, SIEMENS P4 diffractometer, absorption coefficient 0.267 mm^{-1}, reflections collected 23 798, independent reflections 6784 [R(int) = 0.0337], refinement by full-matrix least-squares on F^2, data/restraints/parameters 6784/0/367, goodness-of-fit on F^2 = 1.029, final R indices [$I > 2\sigma(I)$] R1 = 0.0446, wR2 = 0.1188, R indices (all data) R1 = 0.0797, wR2 = 0.1373, largest diff peak and hole 0.225 and −0.266 e Å^{-3}. Crystallographic data for the structure (Z)-**3ka** have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-823487.

*(Z)-2-Chloro-1-(2,4-dichlorophenyl)penta-1,4-dienyl Acetate [(Z)-**3la**].* Yield: 72% as a yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.17 (s, 3 H), 2.94 (d, J = 6.0 Hz, 2 H), 5.12 (dd, J = 11.6, 1.2 Hz, 1 H), 5.14 (dd, J = 15.6, 1.6 Hz, 1 H), 5.78−5.80 (m, 1 H), 7.24−7.27 (m, 1 H), 7.43 (dd, J = 8.4, 1.6 Hz, 2 H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 20.5, 38.3, 118.1, 126.6, 127.1, 129.7, 130.8, 132.3, 133.3, 135.0, 136.2, 139.9, 168.0. MS (EI, m/z): 273 (3), 271 (16), 269 ($M^+ - {}^{35}Cl$, 26), 266 (31), 264 (96), 262 (100). Anal. Calcd for $C_{13}H_{11}Cl_3O_2$. HRMS (ESI): calcd 303.9825, found 303.9833.

*(Z)-2-Chloro-1-(4-isopropylphenyl)penta-1,4-dienyl Acetate [(Z)-**3ma**].* Yield: 71% as a yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.22 (d, J = 8.8 Hz, 3 H), 1.25 (d, J = 6.0 Hz, 3 H), 2.18 (s, 3 H), 2.88−2.92 (m, 1 H), 3.18 (dd, J = 5.6, 1.2 Hz, 2 H), 5.21 (dd, J = 12.0, 1.6 Hz, 1 H), 5.25 (dd, J = 17.6, 1.6 Hz, 1 H), 5.86−5.93 (m, 1 H), 7.21 (d, J = 8.4 Hz, 2 H), 7.31 (d, J = 8.0 Hz, 2 H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 20.7, 23.8 (2 C), 34.0, 38.6, 117.7, 123.5, 126.5 (2 C), 128.3 (2 C), 130.0, 133.3, 144.0, 150.0, 168.1. MS (EI, m/z): 280 (1), 278 (M^+, 3), 238 (32), 236 (100), 193 (62). Anal. Calcd for $C_{16}H_{19}ClO_2$. HRMS: calcd 278.1074, found 278.1073.

*(Z)-2-Chloro-1-(4-tert-butylphenyl)penta-1,4-dienyl Acetate [(Z)-**3na**].* Yield: 80% as a yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.34 (s, 9 H), 2.21 (s, 3 H), 3.22 (dt, J = 6.0, 1.6 Hz, 2 H), 5.24 (dd, J = 10.6, 1.6 Hz, 1 H), 5.28 (dd, J = 17.2, 1.6 Hz, 1 H), 5.88−5.93 (m, 1 H), 7.34−7.41 (m, 4H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 20.7, 31.2 (2 C), 34.8, 38.6, 117.7, 123.5, 125.4 (2 C), 128.1 (2 C), 130.7, 133.3, 144.0, 152.3, 168.1. MS (EI, m/z): 294 (1), 292 (M^+, 3), 257 (14), 252 (32), 250 (100), 235 (70). Anal. Calcd for $C_{17}H_{21}ClO_2$. HRMS: calcd 292.1230, found 292.1231.

*(Z)-2-Bromo-1-phenylpenta-1,4-dienyl Acetate [(Z)-**3oa**].* Yield: 74% as a yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.20 (s, 3 H), 3.28 (dd, J = 5.6, 4.4 Hz, 2 H), 5.22 (dd, J = 10.0, 1.6 Hz, 1 H), 5.26 (dd, J = 17.2, 1.2 Hz, 1 H), 5.85−5.92 (m, 1 H), 7.35−7.43 (m, 5 H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 20.5, 39.8, 115.9, 117.4, 128.1 (2 C), 128.2 (2 C), 128.3, 128.9, 133.4, 145.5, 167.7. MS (EI, m/z): 240 (32), 238 (34), 202 (13), 201 (100), 159 (31). Anal. Calcd for $C_{13}H_{13}BrO_2$. HRMS (ESI): calcd 280.0099, found 280.0102.

*(Z)-2-Bromo-1-(4-chlorophenyl)penta-1,4-dienyl Acetate [(Z)-**3pa**].* Yield: 77% as a yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.24 (s, 3 H), 3.25 (dd, J = 4.0, 1.2 Hz, 2H), 5.23 (dd, J = 11.2, 1.2 Hz, 1 H), 5.26 (dd, J = 16.0, 1.6 Hz, 1 H), 5.82−5.90 (m, 1 H), 7.34 (s, 4 H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 20.5, 39.8, 116.3, 117.6, 128.5 (2 C), 129.4 (2 C), 131.8, 133.1, 135.0, 144.4, 167.7. MS (EI, m/z): 276 (11), 274 (50), 272 (40), 195 (5), 193 (16). Anal. Calcd for $C_{13}H_{12}BrClO_2$. HRMS (ESI): calcd 313.9709, found 313.9707.

*(Z)-2-Chloro-1-pentyl-penta-1,4-dienyl Acetate [(Z)-**3qa**].* Yield: 75% as a colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.88 (t, J = 6.8 Hz, 3 H), 1.25−1.34 (m, 4 H), 1.41−1.48 (m, 2 H), 2.20 (s, 3 H), 2.29 (t, J = 7.6 Hz, 2 H), 3.13 (d, J = 6.0 Hz, 2 H), 5.14 (dd, J = 10.2, 1.6 Hz, 1 H), 5.20 (dd, J = 17.2, 1.6 Hz, 1 H), 5.74−5.85 (m, 1 H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 13.7, 20.3, 22.1, 26.2, 30.2, 31.0, 37.7, 117.0, 120.2, 132.6, 145.3, 167.8. MS (EI, m/z): 195 ($M^+ - {}^{35}Cl$, 22), 190 (30), 188 (100), 161 (3), 159 (7). Anal. Calcd for $C_{12}H_{19}ClO_2$. HRMS (ESI): calcd 230.1074, found 230.1068.

*(Z)-4-Chloro-1-tert-butyldimethylsilyloxy-hepta-3,6-dien-3-yl Acetate [(Z)-**3ra**].* Yield: 72% as a colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.04 (s, 6 H), 0.88 (s, 9 H), 2.19 (s, 3 H), 2.52 (t, J = 6.4 Hz, 2 H), 3.15 (d, J = 6.0 Hz, 2 H), 3.70 (t, J = 6.6 Hz, 2 H), 5.14 (dd, J = 10.0, 1.2 Hz, 1 H), 5.21 (dd, J = 17.2, 1.6 Hz, 1 H), 5.78−5.85 (m, 1 H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ −5.7, 18.0, 20.3, 25.6, 34.1, 37.7, 59.7, 117.1, 122.1, 132.6, 142.4, 167.8. MS (EI, m/z): 263 (14), 261 ($M^+ - Bu^t$, 40),

221 (34), 219 (100), 189 (67). Anal. Calcd for $C_{15}H_{27}ClO_3Si$. HRMS (ESI): calcd 318.1418, found 318.1414.

*(Z)-4-Chloro-1-phenoxyhepta-3,6-dien-3-yl Acetate [(Z)-**3sa**].* Yield: 82% as a colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.17 (s, 3 H), 2.64 (t, J = 6.4 Hz, 2 H), 3.17 (t, J = 6.0 Hz, 2 H), 3.58 (t, J = 6.4 Hz, 2 H), 4.52 (s, 2 H), 5.13 (dd, J = 10.4, 1.6 Hz, 1 H), 5.21 (dd, J = 17.2, 1.6 Hz, 1 H), 5.78−5.82 (m, 1 H), 7.30−7.37 (m, 5 H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 20.6, 31.5, 38.1, 66.9, 73.1, 117.4, 122.4, 127.6 (2 C), 127.7, 128.4 (2 C), 132.8, 138.1, 142.6, 168.1. MS (EI, m/z): 294 (M^+, 1) 259 (8), 252 (12), 234 (10), 163 (32), 161 (94). Anal. Calcd for $C_{16}H_{19}ClO_3$. HRMS: calcd 294.1023, found 294.1022.

*Compound **4**.* To a mixture of $PhB(OH)_2$ (92 mg, 1.5 mmol), $Pd(OAc)_2$ (5.6 mg, 0.025 mmol), K_3PO_4 (1.5 mmol), and Xphos (23.8 mg, 0.05 mmol) in 1 mL of toluene was added a solution of (*Z*)-**3aa** (119 mg, 0.5 mmol) in 1 mL of toluene under nitrogen. After stirring at 110 °C for 10 h, the reaction mixture was quenched with water, extracted with ethyl acetate, washed with brine, dried over Na_2SO_4, and concentrated. Column chromatography on silica (petroleum ether/ethyl acetate = 70/1) gave 100 mg (yield: 72%) of **4** as a yellow solid. The β-haloenol acetate (*Z*)-**3oa** was subjected to the same procedure to yield compound **4** in 81% yield. Mp: 69−71 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.87 (s, 3 H), 3.25 (dt, J = 4.8, 1.2 Hz, 2 H), 5.04 (dd, J = 10.4, 1.6 Hz, 1 H), 5.12 (dd, J = 17.2, 1.6 Hz, 1 H), 5.75−5.79 (m, 1 H), 7.32−7.40 (m, 8 H), 7.52−7.55 (m, 2 H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 20.8, 37.6, 116.7, 127.2, 128.1 (2 C), 128.2 (2 C), 128.3 (2 C), 128.5 (2 C), 128.6 (2 C), 135.2, 135.5, 138.7, 143.7, 169.7. MS (EI, m/z): 278 (M^+, 3), 237 (100), 236 (32), 195 (62), 194 (15). Anal. Calcd for $C_{19}H_{18}O_2$. HRMS: calcd 278.1307, found 278.1310.

Crystal data for **4** ($C_{19}H_{18}O_2$, 278.35): orthorhombic, space group $P2(1)2(1)2(1)$, a = 9.4980(5) Å, b = 16.8744(8) Å, c = 19.4763(10)Å, U = 3121.5(3) Å^3, Z = 8, specimen 0.431 × 0.282 × 0.153 mm^3, T = 296(2) K, SIEMENS P4 diffractometer, absorption coefficient 0.076 mm^{-1}, reflections collected 42 922, independent reflections 5503 [R(int) = 0.0416], refinement by Full-matrix least-squares on F^2, data/restraints/parameters 5503/2/381, goodness-of-fit on F^2 = 1.057, final R indices [$I > 2\sigma(I)$] R1 = 0.0426, wR2 = 0.1107, R indices (all data) R1 = 0.0499, wR2 = 0.1159, largest diff peak and hole 0.185 and −0.146 e Å^{-3}. Crystallographic data for the compound **4** have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-816364.

*Compound **5**.* To a mixture of (*Z*)-**3aa** (119 mg, 0.50 mmol), $Pd(CH_3CN)_2Cl_2$ (6.5 mg, 0.025 mmol), Cs_2CO_3 (2 equiv), and Xphos (23.8 mg, 0.05 mmol) in 1 mL of toluene was added a solution of phenylacetylene (110 μL, 1 mmol) in 1 mL of dry toluene under nitrogen. After stirring at 110 °C for 10 h, the reaction mixture was quenched with water, extracted with ethyl acetate, washed with saturated brine, and dried over Na_2SO_4. Column chromatography on silica (petroleum ether/ethyl acetate = 70/1) gave 102 mg (yield: 67%) of **5** as a yellow oil. The β-haloenol acetate (*Z*)-**3oa** was subjected to the same procedure at 80 °C to generate compound **5** in 73% yield. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.26 (s, 3 H), 3.12 (d, J = 6.0 Hz, 2 H), 5.19 (dd, J = 10.4, 1.2 Hz, 1 H), 5.27 (dd, J = 16.8, 1.2 Hz, 1 H), 5.98−6.05 (m, 1 H), 7.32−7.46 (m, 10 H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 20.9, 35.8, 86.3, 95.8, 112.0, 116.8, 123.2, 128.2 (2 C), 128.3 (3 C), 128.4 (2 C), 129.1, 131.5 (2 C), 134.1, 134.7, 151.7, 168.7. MS (EI, m/z): 302 (M^+, 4), 261 (16), 260 (14), 219 (3), 201 (3). Anal. Calcd for $C_{21}H_{18}O_2$. HRMS: calcd 302.1307, found 302.1313.

■ ASSOCIATED CONTENT

Supporting Information. Spectroscopic data of the products and crystallographic data of (*Z*)-**3ka** and compound **4**. This material is available free of charge via the Internet at http://pubs.acs.org.

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