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An operationally simple approach to (*E*)-α-halo vinyl sulfides and their applications for accessing stereodefined trisubstituted alkenes†

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An operationally simple and practical protocol for the synthesis of (*E*)-α-halo vinyl sulfides has been achieved *via* a highly regio- and stereoselective hydrohalogenation of alkynyl thioethers using lithium halides in HOAc or propionic acid at room temperature. It permits the formation of (*E*)-α-chloro and (*E*)-α-bromo vinyl sulfides in satisfactory yields with good to excellent stereoselectivities. Moreover, this work results in a new method for the assembly of stereodefined (*E*)- or (*Z*)-trisubstituted alkenes featuring the first coupling of the C–X bond of (*E*)-α-halo vinyl sulfides followed by a subsequent Ni-catalyzed coupling of the C–S bond with Grignard reagents.

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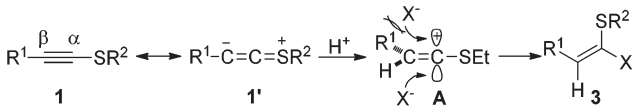
Introduction

The hydrohalogenation of the C–C triple bond is one of the most fundamental reactions in organic chemistry. However, this reaction usually does not proceed in a preparatively useful manner due to the formation of some regio- and stereoisomers that are difficult to separate or purify.[1] It is worth mentioning that the hydrohalogenation of acetylenes allows straightforward and convenient access to alkenyl halides, which are versatile building blocks in organic synthesis. As such, the exploration of the regio- and stereocontrolled acetylenic hydrohalogenation reaction is highly desirable. Along this line, some notable results have been achieved in the hydrohalogenation of terminal alkynes[2] or activated alkynes.[3]

In contrast, the hydrohalogenation of internal unsymmetric alkynes constitutes a formidable challenge.[4] Indeed, some promising examples came from the reaction of acetylenic tosylates,[5] ethers,[6] alkynyl selenides,[7] ynamides,[8] and haloalkynes.[9] Quite recently, we[10] described a Pd-catalyzed hydrochlorination or hydrobromination of alkynyl halides for the regio- and stereoselective synthesis of (*Z*)-1,2-dihaloalkenes. All these aforementioned methods indicated that the heteroatoms might play a crucial role in controlling the regioselectivity, presumably through polarization of the C–C triple bond, thus enabling the attack of halides to the relatively positively charged carbon. Following this concept, we envisaged that a *cis*-hydrohalogenation of alkynyl thioethers (Scheme 1) would be feasible because of two important facts: (1) the negative charge of the β-carbon of **1** could result in the regioselective protonation of β-carbon;[11] (2) the attack of halides from the less hindered side (with the H atom) of vinyl cation intermediate[5] **A** might lead to the *syn*-addition products stereoselectively.



Scheme 1 Proposed hydrohalogenation of alkynyl thioethers.

On the other hand, the stereodefined trisubstituted alkenes occur in a number of natural products and related compounds of biological and medicinal interest. Accordingly, the task of assembly of these motifs is a significant challenge in organic synthesis.[12] Of these, Pd-catalyzed stepwise cross-coupling of 1,1-dihaloalkenes **B** has been particularly effective at establishing stereodefined trisubstituted alkenes **E** (Scheme 2).[13] Clearly, the success of this methodology depends on the efficient construction of compound **C** *via* the mono-coupling of the *trans* C–X bond of the R^1 group in **B**. However, this *trans*-selective monosubstitution reaction does not always proceed well and sometimes suffers from the formation of large amounts of by-product **D**, which is quite difficult to separate in some cases.

To address the challenge, we envisioned that the utilization of stereodefined α-halo vinyl sulfides[14] **3** instead of

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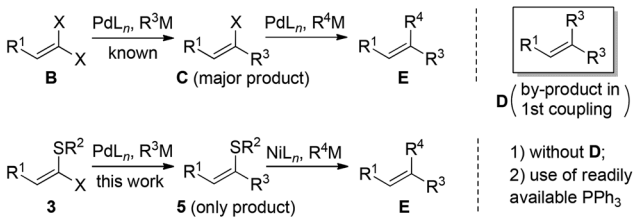


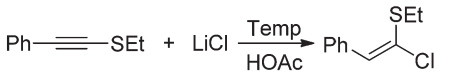
Scheme 2 Approaches to trisubstituted alkenes.

1,1-dihaloalkenes **B** would enable the exclusive formation of monosubstitution product **5** under mild conditions, due to the obviously different reactivity of C–X and C–S bonds. Thus, a subsequent coupling of the C–S bond can ultimately provide a new access to stereodefined trisubstituted olefins. As such, pursuing our interests in the functionalization of heteroatom-substituted alkynes,[10,15] we wish to report here an operationally simple and mild approach to (*E*)-α-halo vinyl sulfides by a highly regio- and stereoselective hydrohalogenation of alkynyl thioethers, as well as a new entry to stereodefined trisubstituted alkenes featuring the stepwise cross-coupling reactions of the C–X and C–S bonds of (*E*)-α-halo vinyl sulfides.

Results and discussion

At the outset, phenylethynyl thioether (**1a**) was treated with 3 equiv. of LiCl in HOAc[3a,7b,16] at 80 °C, and the hydrochlorination product **3a** was obtained in 82% yield as a 92 : 8 mixture of *E*/*Z* isomers. We found that the reaction temperature had a significant effect on the stereochemistry (Scheme 3). Running the reaction at room temperature for 24 h led to (*E*)-α-chloro vinyl sulfide **3a** as a single *E*-isomer in 88% yield, while no other regio- and stereoisomers were observed. Thus, further substrate screenings were carried out employing 3 equiv. of LiCl, room temperature, and HOAc as the solvent. Notably, the stereoselectivity of **3a** examined at 11%, 28% or 65% conversion was uniformly >98% *E*, implying that the stereochemistry is controlled by kinetic effects.

As shown in Table 1, the hydrohalogenation process exhibited good compatibility with a wide range of substituted aromatic rings in substrate **1**. Both electron-poor and electron-rich aromatic acetylenic thioethers successfully afforded (*E*)-α-chloro vinyl sulfides in good yields and excellent

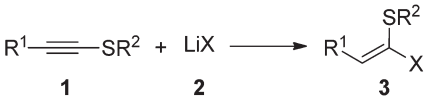


Entry	Temp/°C	Time/h	Yield/%[a]	*E*/*Z*[b]
1	110	3	76	57/43
2	80	4	82	92/8
3	25	24	88	>98/2

[a] Isolated yield. [b] Determined by GC.

Scheme 3 Temperature effect.

Table 1 Hydrohalogenation of alkynyl thioethers[a]



Entry	R^1/R^2	LiX	Yield[b] (%)
1	Ph/Et (**1a**)	LiCl (**2a**)	**3a** 88
2	Ph/Ph (**1b**)	LiCl (**2a**)	**3b** 75
3	4-F-C_6H_4/Et (**1c**)	LiCl (**2a**)	**3c** 91
4	4-Cl-C_6H_4/Et (**1d**)	LiCl (**2a**)	**3d** 83
5	4-Br-C_6H_4/Et (**1e**)	LiCl (**2a**)	**3e** 87
6	4-Me-C_6H_4/Et (**1f**)	LiCl (**2a**)	**3f** 85
7	4-*t*-Bu-C_6H_4/Et (**1g**)	LiCl (**2a**)	**3g** 87
8	4-OMe-C_6H_4/Et (**1h**)	LiCl (**2a**)	**3h** 79
9	3,4-$(OMe)_2$-C_6H_3/Et (**1i**)	LiCl (**2a**)	**3i** 75
10	4-NO_2-C_6H_4/Et (**1j**)	LiCl (**2a**)	**3j** 81
11	2-Naphthyl/Et (**1k**)	LiCl (**2a**)	**3k** 78
12	*n*-C_9H_{19}/Et (**1l**)	LiCl (**2a**)	**3l** 85 (92/8)[c,d]
13	TBDPSO$(CH_2)_2$/Et (**1m**)	LiCl (**2a**)	**3m** 84 (92/8)[c,d]
14	*n*-C_4H_9(Et)CH/Et (**1n**)	LiCl (**2a**)	**3n** 91 (94/6)[c,d]
15	TBDPSOCH_2(Me)CH/Et (**1o**)	LiCl (**2a**)	**3o** 94 (89/11)[c,d]
16	*n*-C_4H_9/Ph (**1p**)	LiCl (**2a**)	**3p** 92 (90/10)[c,d]
17	2-Thienyl (**1q**)	LiCl (**2a**)	**3q** 80
18	TES/Et (**1r**)	LiCl (**2a**)	NR
19	Ph/Et (**1a**)	LiBr (**2b**)	**3r** 78[e]
20	Ph/Ph (**1b**)	LiBr (**2b**)	**3s** 74[e]
21	4-Cl-C_6H_4/Et (**1d**)	LiBr (**2b**)	**3t** 75[e]
22	4-Me-C_6H_4/Et (**1f**)	LiBr (**2b**)	**3u** 80[e]
23	*n*-C_4H_9(Et)CH/Et (**1n**)	LiBr (**2b**)	**3v** 91 (91/9)[c,d]
24	TBDPSOCH_2(Me)CH/Et (**1o**)	LiBr (**2b**)	**3w** 86 (94/6)[c,d,f]
25	*n*-C_4H_9/Ph (**1p**)	LiBr (**2b**)	**3x** 90 (91/9)[c,d]
26	2-Thienyl (**1q**)	LiBr (**2b**)	**3y** 77
27	Ph/Et (**1a**)	LiI (**2c**)	Complex[g]

[a] Reaction conditions: **1** (0.5 mmol) and LiX (1.5 mmol) in 2 mL of HOAc at rt for 24 h. [b] Isolated yield. [c] The ratio of *E*/*Z* isomers. [d] The reaction was carried out in propionic acid. [e] 48 h. [f] 15 °C. [g] 70 °C.

stereoselectivities. For example, **1c** and **1d** led to products **3c** and **3d** in excellent yields (Table 1, entries 3 and 4). In contrast, under the standard conditions for 4 h, the aliphatic substrate **1l** delivered 86% yield of **3l** as a 4 : 1 mixture of *E*/*Z* isomers. Fortunately, we found that the use of less polar and acidic solvents could obviously slow down the hydrohalogenation reaction, thereby improving the stereoselectivity. As a result, the reaction performed in propionic acid at room temperature for 24 h provided **3l** in 85% yield with a high stereoselectivity (*E*/*Z* = 92/8) (Table 1, entry 12). Other acidic solvents proved to be less effective. Therefore, we decided to use propionic acid as the solvent for the reaction of aliphatic alkynyl thioethers. Pleasingly, the steric demanding substrates **1n** and **1o** offered excellent yields of hydrochlorination products **3n** and **3o** in good stereoselectivities under the modified conditions (Table 1, entries 14 and 15).

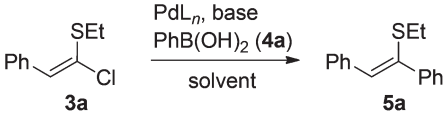
Next, the hydrobromination of acetylenic thioethers was also briefly investigated, and as expected, the reaction occurred smoothly to generate the desired products in satisfactory yields by the utilization of LiBr. For example, the reaction of **1a** and **1b** proceeded successfully to afford (*E*)-α-bromo vinyl sulfides **3r** and **3s** in good yields, albeit in a prolonged reaction time (48 h) (Table 1, entries 19 and 20). Likewise, aliphatic acetylenic thioethers such as **1n**, **1o**, and **1p** resulted in the

desired products in excellent yields and good stereoselectivities (Table 1, entries 23–25). We also tried to extend this reaction to the access of (*E*)-α-iodo vinyl sulfides; however, only low conversion was observed for the hydroiodination of **1a** at room temperature, while the reaction run at a higher temperature (70 °C) just gave a complex mixture (Table 1, entry 27). The regio- and stereochemistry of this transformation was determined by the ^{1}H NMR and ^{13}C NMR analysis of the products,[6b] and further confirmed by the X-ray diffraction analysis of **3s**.

As such, we have developed a highly regio- and stereoselective hydrohalogenation of acetylenic thioethers featuring the use of readily available lithium halides in weakly acidic solvents such as HOAc or propionic acid, in which (*E*)-α-halo vinyl sulfides were synthesized in high yields with good to excellent stereoselectivities. In comparison to the previous reports using the TMSX/MeOH reaction system,[6b] our protocol developed here avoids the use of moisture sensitive reagents, anhydrous methanol, and strict reaction conditions (−40 °C for TMSBr/MeOH). Therefore, it provides an operationally simple, highly efficient, and practical alternative to assemble (*E*)-α-halo vinyl sulfides.

Then, we turned our attention to the synthesis of stereodefined trisubstituted olefins from the (*E*)-α-halo vinyl sulfides thus obtained. Firstly, **3a** was treated with 1.3 equiv. of PhB(OH)$_2$ (**4a**), 5 mol% of Pd(OAc)$_2$, 20 mol% of PPh$_3$, and 1.5 equiv. of KF in THF at 40 °C for 12 h. As expected, the Suzuki[17] coupling of **3a** occurred exclusively at the C–X bond to furnish vinyl sulfide **5a** in 84% yield, albeit at a 3 : 1 *Z*/*E* mixture (Table 2, entry 1), and the double substitution product could not be observed by GC, GC-MS or NMR.

Table 2 Optimization of the Suzuki coupling of **3a**[a]



Entry	Ligand/ equiv.	Base	Solvent	Time (h)	Yield[b] (%)	*Z*/*E*[c]
1	PPh$_3$/0.2	KF	THF	12	84	75/25
2	PPh$_3$/0.2	K$_3$PO$_4$	THF	12	87	61/39
3	PPh$_3$/0.2	KOH	THF	12	82	91/9
4	PPh$_3$/0.2	K$_2$CO$_3$	THF	12	67	56/44
5	PPh$_3$/0.2	NaOEt	THF	12	76	95/5
6	PPh$_3$/0.2	CsF	THF	12	90	91/9
7	PPh$_3$/0.2	*t*-BuOK	THF	5	82	>98/2
8	PPh$_3$/0.2	Cs$_2$CO$_3$	THF	5	88	>98/2
9	PPh$_3$/0.2	Cs$_2$CO$_3$	Toluene	5	65	62/38
10	PPh$_3$/0.2	Cs$_2$CO$_3$	Dioxane	5	77	93/7
11	PPh$_3$/0.2	Cs$_2$CO$_3$	DMF	5	83	96/4
12[d]	PPh$_3$/0.2	Cs$_2$CO$_3$	THF	24	65	>98/2
13	/	Cs$_2$CO$_3$	THF	5	46	90/10
14	PPh$_3$/0.1	Cs$_2$CO$_3$	THF	5	91	>98/2
15	P(*o*-tol)$_3$/0.1	Cs$_2$CO$_3$	THF	5	78	88/12
16	P(2-furyl)$_3$/0.1	Cs$_2$CO$_3$	THF	5	85	95/5
17	PCy$_3$/0.1	Cs$_2$CO$_3$	THF	5	62	90/10
18	dppe/0.05	Cs$_2$CO$_3$	THF	5	87	68/32

[a] Reaction conditions: **3a** (0.5 mmol), **4a** (0.65 mmol), Pd(OAc)$_2$ (0.025 mmol), ligand (0–0.1 mmol), base (0.75 mmol), THF, 40 °C. [b] Isolated yield. [c] Determined by GC. [d] Room temperature.

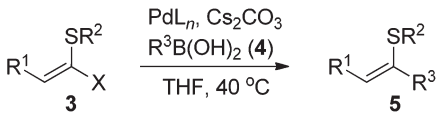
Further optimization demonstrated that the base plays a key role in this reaction. For example, the utilization of Cs$_2$CO$_3$ and *t*-BuOK provided high yields of **5a** in a single *Z*-isomer, while the reaction performed with K$_3$PO$_4$, KOH, CsF, or K$_2$CO$_3$ resulted in significantly decreased stereoselectivities (Table 2, entries 2–8). Experiments with other solvents such as toluene, dioxane, and DMF had no benefical consequences (Table 2, entries 9–11). Interestingly, PPh$_3$ proved to be the most effective ligand for this reaction, whereas other ligands such as P(*o*-tol)$_3$, P(2-furyl)$_3$, PCy$_3$, and dppe were found to be inferior ones (Table 2, entries 14–18). Finally, the optimized reaction conditions for the Suzuki coupling of **3** consisted of 5 mol% of Pd(OAc)$_2$, 10 mol% of PPh$_3$, 1.3 equiv. of R^{3}B(OH)$_2$, and 1.5 equiv. of Cs$_2$CO$_3$ in THF at 40 °C for 5 h, which produced the stereoisomerically pure **5a** in 91% isolated yield.

Having identified the optimal reaction conditions, we then investigated the scope of the Suzuki coupling of **3**. As shown in Table 3, the reaction was widely applicable for the coupling of various substituted α-halo vinyl sulfides, allowing facile access to polysubstituted vinylic sulfides in good yields. For instance, **3c** and **3h** produced the desired products **5c** and **5h** in 87% and 89% yield, respectively (Table 3, entries 3 and 9). In contrast, the substrate **3j**, with a strong electron-withdrawing substituent (NO$_2$), only led to traces of the desired product due to the dehydrochlorination process under the standard conditions (Table 3, entry 11). Pleasingly, the use of steric demanding substrate **3n** also resulted in **5l** in high yield (Table 3, entry 14). Meanwhile, α-bromo vinyl sulfides coupled successfully with **4a** to furnish the corresponding products in good yields (Table 3, entries 15–17).

Then, the scope of this reaction with respect to boronic acids was briefly examined. As an example, the alkenyl boronic acid **4b** was an effective substrate for this reaction (Table 3, entry 18). It should be noted that the steric hindrance has some effect on this Suzuki coupling reaction, and for instance, the reaction of 4-tolylboronic acid (**4c**), 3-tolylboronic acid (**4d**), and 2-tolylboronic acid (**4e**) formed the products **5n**, **5o**, and **5p** in respective yields of 93%, 86%, and 62% (Table 3, entries 19–21). Heteroaromatic boronic acids such as 2-thienylboronic acid (**4j**) and 2-furylboronic acid (**4k**) coupled smoothly with **3a** to afford the desired products in good yields (Table 3, entries 26 and 27). In addition, methylboronic acid (**4l**) turned out to be a competent coupling partner and provided **5w** in a reasonable yield (Table 3, entry 28), while BuB(OH)$_2$ (**4m**) was found to be almost unreactive even at an elevated temperature (70 °C). The stereochemistry of resultant vinyl sulfides **5** was determined by comparison with the literature data[18] as well as NOE measurements.

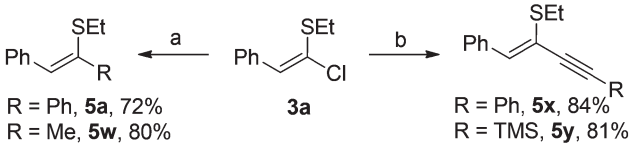
Moreover, the (*E*)-α-halo vinyl sulfides **3** exhibited versatile reactivity in other transition-metal-catalyzed cross-coupling reactions. For example, the Negishi coupling[19] of **3a** with either PhZnBr or MeZnBr successfully furnished the desired products **5a** or **5w** in good yields (unoptimized). Thus, it provided an effective alternative to assemble the vinyl sulfides **5**. Additionally, the Sonogashira coupling[20] of **3a** with

Table 3 Synthesis of vinyl sulfide **5** *via* the Suzuki coupling of **3**[a]



Entry	$R^1/R^2/X$ (**3**)	R^3 (**4**)	Yield[b] (%)
1	Ph/Et/Cl (**3a**)	Ph (**4a**)	91 (**5a**)
2	Ph/Ph/Cl (**3b**)	Ph (**4a**)	84 (**5b**)
3	4-F-C_6H_4/Et/Cl (**3c**)	Ph (**4a**)	87 (**5c**)
4	4-Cl-C_6H_4/Et/Cl (**3d**)	Ph (**4a**)	86 (**5d**)
6	4-Br-C_6H_4/Et/Cl (**3e**)	Ph (**4a**)	79 (**5e**)
7	4-Me-C_6H_4/Et/Cl (**3f**)	Ph (**4a**)	85 (**5f**)
8	4-*t*-Bu-C_6H_4/Et/Cl (**3g**)	Ph (**4a**)	90 (**5g**)
9	4-OMe-C_6H_4/Et/Cl (**3h**)	Ph (**4a**)	89 (**5h**)
10	3,4-$(OMe)_2$-C_6H_3/Et/Cl (**3i**)	Ph (**4a**)	94 (**5i**)
11	4-NO_2-C_6H_4/Et/Cl (**3j**)	Ph (**4a**)	Trace
12	2-Naphthyl/Et/Cl (**3k**)	Ph (**4a**)	82 (**5j**)
13	*n*-C_9H_{19}/Et/Cl (**3l**)	Ph (**4a**)	85 (**5k**)[c]
14	*n*-C_4H_9(Et)CH/Et/Cl (**3n**)	Ph (**4a**)	89 (**5l**)[c]
15	Ph/Et/Br (**3r**)	Ph (**4a**)	87 (**5a**)
16	4-Cl-C_6H_4/Et/Br (**3t**)	Ph (**4a**)	83 (**5d**)
17	4-Me-C_6H_4/Et/Br (**3u**)	Ph (**4a**)	87 (**5f**)
18	Ph/Et/Cl (**3a**)	(*E*)-Styryl (**4b**)	71 (**5m**)
19	Ph/Et/Cl (**3a**)	4-Me-C_6H_4 (**4c**)	93 (**5n**)
20	Ph/Et/Cl (**3a**)	3-Me-C_6H_4 (**4d**)	86 (**5o**)
21	Ph/Et/Cl (**3a**)	2-Me-C_6H_4 (**4e**)	62 (**5p**)
22	Ph/Et/Cl (**3a**)	4-OMe-C_6H_4 (**4f**)	89 (**5q**)
23	Ph/Et/Cl (**3a**)	3,4-$(OMe)_2$-C_6H_3 (**4g**)	86 (**5r**)
24	Ph/Et/Cl (**3a**)	4-F-C_6H_4 (**4h**)	80 (**5s**)
25	Ph/Et/Cl (**3a**)	2-Naphthyl (**4i**)	81 (**5t**)
26	Ph/Et/Cl (**3a**)	2-Thienyl (**4j**)	76 (**5u**)
27	Ph/Et/Cl (**3a**)	2-Furyl (**4k**)	75 (**5v**)
28	Ph/Et/Cl (**3a**)	Me (**4l**)	66 (**5w**)

[a] Reaction conditions: **3** (0.5 mmol), **4** (0.65 mmol), $Pd(OAc)_2$ (0.025 mmol), PPh_3 (0.05 mmol), Cs_2CO_3 (0.75 mmol), THF, 40 °C, 5 h. [b] Isolated yield. [c] *Z*/*E* > 95/5.

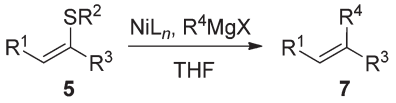


Scheme 4 Other cross-coupling reactions of **3a**.

phenylacetylene and trimethylsilylacetylene proceeded well to give **5x** and **5y** in high yields (Scheme 4).

Next, the elaboration of trisubstituted alkenes was investigated by the Ni-catalyzed coupling of the C–S bond with Grignard reagents[21] and the results are summarized in Table 4. For example, treating **5a** with 10 mol% of $Ni(PPh_3)_2Cl_2$ and 3 equiv. of MeMgCl (**6a**) in THF at room temperature resulted in the establishment of trisubstituted alkene **7a**[22] in 86% yield (Table 4, entry 1). Regarding the variation of the aromatic group of **5**, common functional groups were well tolerated (Table 4, entries 3–8). The reaction of **5n** (R^3 = 4-Me-C_6H_4) and **5o** (R^3 = 3-Me-C_6H_4) proceeded successfully to deliver **7i** and **7j** in respective yields of 89% and 75%, while the coupling of **5p** (R^3 = 2-Me-C_6H_4) almost did not take place even at a higher temperature of 50 °C, indicating that the coupling of the C–S bond was sensitive to steric hindrance (Table 4, entries 10–12).

Table 4 Synthesis of trisubstituted alkenes from **5**[a]



Entry	$R^1/R^2/R^3$	R^4MgX (**6**)	Yield[b] (%)
1	Ph/Et/Ph (**5a**)	MeMgCl (**6a**)	86 (**7a**)
2	Ph/Ph/Ph (**5b**)	MeMgCl (**6a**)	76 (**7a**)
3	4-F-C_6H_4/Et/Ph (**5c**)	MeMgCl (**6a**)	75 (**7b**)
4	4-Me-C_6H_4/Et/Ph (**5f**)	MeMgCl (**6a**)	80 (**7c**)
5	4-*t*-Bu-C_6H_4/Et/Ph (**5g**)	MeMgCl (**6a**)	81 (**7d**)
6	4-OMe-C_6H_4/Et/Ph (**5h**)	MeMgCl (**6a**)	80 (**7e**)
7	3,4-$(OMe)_2$-C_6H_3/Et/Ph (**5i**)	MeMgCl (**6a**)	84 (**7f**)
8	2-Naphthyl/Et/Ph (**5j**)	MeMgCl (**6a**)	78 (**7g**)
9	*n*-C_9H_{19}/Et/Ph (**5k**)	MeMgCl (**6a**)	71 (**7h**)
10	Ph/Et/4-Me-C_6H_4 (**5n**)	MeMgCl (**6a**)	89 (**7i**)
11	Ph/Et/3-Me-C_6H_4 (**5o**)	MeMgCl (**6a**)	75 (**7j**)
12[c]	Ph/Et/2-Me-C_6H_4 (**5p**)	MeMgCl (**6a**)	Trace
13	Ph/Et/4-OMe-C_6H_4 (**5q**)	MeMgCl (**6a**)	82 (**7k**)
14	Ph/Et/3,4-$(OMe)_2$-C_6H_3 (**5r**)	MeMgCl (**6a**)	80 (**7l**)
15	Ph/Et/2-Naphthyl (**5t**)	MeMgCl (**6a**)	87 (**7m**)
16	Ph/Et/Ph (**5a**)	EtMgBr (**6b**)	Trace
17[c]	*n*-C_9H_{19}/Et/Ph (**5k**)	4-MeO-C_6H_4MgBr (**6c**)	61 (**7n**)
18[c]	Ph/Et/Me (**5w**)	PhMgCl (**6d**)	71 (**7o**)
19[c]	Ph/Et/4-F-C_6H_4 (**5s**)	4-MeO-C_6H_4MgBr (**6c**)	65 (**7p**)
20[c]	Ph/Et/4-F-C_6H_4 (**5s**)	4-Me-C_6H_4MgBr (**6e**)	70 (**7q**)

[a] Reaction conditions: **5** (0.25 mmol), **6** (0.75 mmol), $Ni(PPh_3)_2Cl_2$ (0.025 mmol), THF, rt. [b] Isolated yield. [c] 50 °C.

As for other Grignard reagents, EtMgBr (**6b**), for instance, only afforded traces of the desired product because of the occurrence of the β-H elimination reaction (Table 4, entry 16). In contrast, 4-MeO-C_6H_4MgBr (**6c**) coupled smoothly with **5k** to give (*Z*)-trisubstituted alkene **7n** in a reasonable yield, while the coupling of PhMgCl (**6d**) with **5w** afforded 71% of (*Z*)-trisubstituted alkene **7o**[23] (Table 4, entries 17 and 18). Moreover, both 4-MeO-C_6H_4MgBr (**6c**) and 4-Me-C_6H_4MgBr (**6e**) reacted smoothly with **5s** to provide the desired products in good yields (Table 4, entries 19 and 20).

Therefore, we have realized a novel approach to stereodefined (*E*)- or (*Z*)-trisubstituted alkenes by the iterative cross-coupling of the C–X and C–S bonds of (*E*)-α-halo vinyl sulfides (**3**). It is worth mentioning that the selective coupling of the C–X bond of **3** is much more easy to be implemented than that of 1,1-dihaloalkenes **B**, due to the better reactivity of the C–X bond than the C–S bond towards the transition-metal-catalyzed cross-coupling reactions, thus enabling one to avoid the utilization of elaborate ligands and substrate-dependent reaction conditions. Although the one-pot tandem cross-coupling of the C–X and C–S bonds of **3** has not been achieved at the current stage, the two-step strategy developed here will still represent a promising approach to stereodefined (*E*)- or (*Z*)-trisubstituted alkenes.

Conclusions

In conclusion, we have developed an operationally simple and practical protocol for the access of (*E*)-α-halo vinyl sulfides by a highly regio- and stereoselective hydrohalogenation of alkynyl thioethers featuring the use of lithium halides in HOAc or propionic acid at room temperature. Both (*E*)-α-bromo and (*E*)-α-chloro vinyl sulfides could be synthesized in satisfactory yields with good to excellent stereoselectivities under mild conditions. In addition, a new method for the elaboration of stereodefined (*E*)- or (*Z*)-trisubstituted alkenes has been achieved through the stepwise cross-coupling reactions of the C–X and C–S bonds of (*E*)-α-halo vinyl sulfides.

Experimental section

General

$Pd(PPh_3)_4$, $Pd(OAc)_2$, $Pd(dba)_2$, and other reagents were obtained commercially and used without further purification. Column chromatography was performed using silica gel (300–400 mesh). The ^1H NMR and ^{13}C NMR spectra were recorded on 400 or 600 MHz NMR spectrometers. High-resolution mass spectra (HRMS) analyses were carried out using electron ionization–quadrupole or electrospray ionization–time-of-flight (ESI-TOF) mass spectrometry. Melting points were obtained on a melting point apparatus with open capillary tubes and are uncorrected.

General procedure for hydrohalogenation of alkynyl thioethers

To a solution of **1a** (81 mg, 0.5 mmol) in 2 mL of acetic acid was added LiCl (64 mg, 1.5 mmol). After stirring at room temperature for 24 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 gel (petroleum ether/EtOAc = 100/1) gave 87 mg (88%) of **3a** as a colorless oil. ^1H NMR ($CDCl_3$, 400 MHz) δ 1.32 (t, J = 7.4 Hz, 3H), 2.97 (q, J = 7.4 Hz, 2H), 7.04 (s, 1H), 7.29–7.31 (m, 1H), 7.37 (t, J = 7.2 Hz, 2H), 7.55 (d, J = 7.6 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.7, 28.2, 127.8, 128.2, 129.2, 129.2, 134.5, 134.9; MS (EI, *m*/*z*) 200 (22), 198 (M^+, 65), 171 (10), 169 (26), 134 (100); HRMS (EI) calcd for $C_{10}H_{11}ClS$ (M^+) 198.0270, found 198.0275.

Compound 3b. 75% yield (92 mg), colorless oil; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.25 (s, 1H), 7.30–7.41 (m, 6H), 7.45 (d, J = 8.0 Hz, 2H), 7.62 (d, J = 7.6 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 127.6, 127.7, 128.4, 128.5, 129.1, 129.2, 130.5, 132.7, 134.6, 137.6; MS (EI, *m*/*z*) 248 (9), 246 (M^+, 32), 219 (13), 217 (40), 182 (75); HRMS (EI) calcd for $C_{14}H_{11}ClS$ (M^+) 246.0270, found 246.0268.

Compound 3c. 91% yield (98 mg), colorless oil; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.30 (t, J = 7.4 Hz, 3H), 2.96 (q, J = 7.4 Hz, 2H), 6.98 (s, 1H), 7.02–7.07 (m, 2H), 7.51–7.55 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.7, 28.2, 115.2 (d, J = 21.5 Hz), 129.3 (d, J = 2.4 Hz), 131.0 (d, J = 8.0 Hz), 131.1 (d, J = 3.4 Hz), 133.4, 162.1 (d, J = 247.2 Hz); MS (EI, *m*/*z*) 218 (4), 216 (M^+, 12), 189 (3), 187 (8), 152 (100); HRMS (EI) calcd for $C_{10}H_{10}ClFS$ (M^+) 216.0176, found 216.0177.

Compound 3d. 83% yield (96 mg), colorless oil; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.30 (t, J = 7.2 Hz, 3H), 2.97 (q, J = 7.6 Hz, 2H), 6.96 (s, 1H), 7.32 (d, J = 8.4 Hz, 2H), 7.48 (d, J = 8.4 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.6, 28.1, 128.3, 130.3, 130.3, 132.9, 133.2, 133.4; MS (EI, *m*/*z*) 236 (4), 234 (32), 232 (M^+, 52), 199 (3), 197 (9); HRMS (EI) calcd for $C_{10}H_{10}Cl_2S$ (M^+) 231.9880, found 231.9877.

Compound 3e. 87% yield (120 mg), colorless oil; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.29 (t, J = 7.4 Hz, 3H), 2.95 (q, J = 7.4 Hz, 2H), 6.92 (s, 1H), 7.40 (d, J = 8.4 Hz, 2H), 7.47 (d, J = 8.4 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.7, 28.3, 121.7, 130.7, 131.4, 131.4, 133.1, 133.8; HRMS (ESI) calcd for $C_{10}H_{10}BrClS$ (M^+) 275.9375, found 275.9370.

Compound 3f. 85% yield (90 mg), colorless oil; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.31 (t, J = 7.4 Hz, 3H), 2.37 (s, 3H), 2.97 (q, J = 7.4 Hz, 2H), 7.02 (s, 1H), 7.18 (d, J = 8.0 Hz, 2H), 7.46 (d, J = 8.0 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.7, 21.3, 28.2, 128.5, 128.9, 129.1, 132.2, 134.7, 137.9; MS (EI, *m*/*z*) 214 (35), 212 (M^+, 100), 185 (11), 183 (31), 148 (88); HRMS (EI) calcd for $C_{11}H_{13}ClS$ (M^+) 212.0426, found 212.0428.

Compound 3g. 87% yield (110 mg), colorless oil; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.32–1.37 (m, 12H), 3.00 (q, J = 7.4 Hz, 2H), 7.04 (s, 1H), 7.42 (d, J = 8.4 Hz, 2H), 7.55 (d, J = 8.4 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.6, 28.1, 31.2, 34.6, 125.1, 128.4, 128.9, 132.0, 134.4, 150.9; MS (EI, *m*/*z*) 256 (15), 254 (M^+, 48), 239 (11), 227 (7), 225 (20); HRMS (EI) calcd for $C_{14}H_{19}ClS$ (M^+) 254.0896, found 254.0910.

Compound 3h. 79% yield (90 mg), colorless oil; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.31 (t, J = 7.4 Hz, 3H), 2.95 (t, J = 7.4 Hz, 2H), 3.83 (s, 3H), 6.89 (d, J = 8.8 Hz, 2H), 6.98 (s, 1H), 7.53 (d, J = 8.8 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.6, 28.2, 55.3, 113.6, 127.1, 127.6, 130.6, 134.5, 159.2; MS (EI, *m*/*z*) 230 (27), 228 (M^+, 100), 195 (13), 193 (38), 179 (73); HRMS (EI) calcd for $C_{11}H_{13}ClOS$ (M^+) 228.0376, found 228.0376.

Compound 3i. 75% yield (97 mg), colorless oil; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.31 (t, J = 7.4 Hz, 3H), 2.96 (q, J = 7.4 Hz, 2H), 3.90 (s, 3H), 3.90 (s, 3H), 6.84 (d, J = 8.4 Hz, 1H), 6.96 (s, 1H), 7.05–7.08 (m, 1H), 7.30 (d, J = 2.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.7, 28.2, 55.9, 55.9, 110.7, 112.0, 122.6, 127.2, 127.8, 134.6, 148.4, 148.8; MS (EI, *m*/*z*) 260 (23), 258 (M^+, 75), 231 (30), 229 (87), 194 (100); HRMS (EI) calcd for $C_{12}H_{15}ClO_2S$ (M^+) 258.0481, found 258.0480.

Compound 3j. 81% yield (98 mg), yellow oil; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.32 (t, J = 7.4 Hz, 3H), 3.02 (q, J = 7.4 Hz, 2H), 7.00 (s, 1H), 7.67–7.70 (m, 2H), 8.18–8.20 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.8, 28.5, 123.5, 129.7, 131.2, 134.5, 141.3, 146.5; MS (EI, *m*/*z*) 245 (2), 243 (M^+, 6), 168 (13), 166 (41), 130 (100); HRMS (EI) calcd for $C_{10}H_{10}ClNO_2S$ (M^+) 243.0121, found 243.0119.

Compound 3k. 78% yield (97 mg), colorless oil; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.36 (t, J = 7.4 Hz, 3H), 3.02 (q, J = 7.4 Hz, 2H), 7.22 (s, 1H), 7.50–7.53 (m, 2H), 7.75–7.77 (m, 1H), 7.83–7.88 (m, 3H), 7.99 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.7, 28.3, 126.3, 126.4, 126.7, 127.6, 127.7, 128.3, 128.8, 129.8,

132.4, 132.7, 133.1, 134.5; MS (EI, *m*/*z*) 250 (3), 248 (M^+, 12), 221 (8), 219 (25), 184 (37); HRMS (EI) calcd for $C_{14}H_{13}ClS$ (M^+) 248.0426, found 248.0422.

Compound 3l. 85% yield (105 mg), colorless oil, *E*/*Z* = 92/8; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 0.88 (t, *J* = 6.8 Hz, 3H), 1.23–1.43 (m, 17H), 2.25 (dd, *J* = 14.6, 7.4 Hz, 2H), 2.82 (q, *J* = 7.3 Hz, 2H), 6.08 (t, *J* = 7.6 Hz, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 14.1, 14.6, 22.7, 27.1, 29.0, 29.1, 29.3, 29.4, 29.6, 30.6, 31.9, 126.7, 138.4; MS (EI, *m*/*z*) 250 (5), 248 (M^+, 12), 221 (6), 219 (18); HRMS (EI) calcd for $C_{13}H_{25}ClS$ (M^+) 248.1365, found 248.1357.

Compound 3m. 84% yield (170 mg), colorless oil, *E*/*Z* = 92/8; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 1.10 (s, 9H), 1.25 (t, *J* = 7.3 Hz, 3H), 2.57 (dd, *J* = 13.9, 6.5 Hz, 2H), 2.83 (q, *J* = 7.3 Hz, 2H), 3.74 (dt, *J* = 12.9, 6.5 Hz, 2H), 6.18 (t, *J* = 7.5 Hz, 1H), 7.36–7.55 (m, 6H), 7.60–7.82 (m, 4H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 14.6, 19.2, 26.8, 27.2, 34.0, 62.7, 127.7, 128.6, 129.7, 133.7, 134.7, 135.6; HRMS (ESI) calcd for $C_{22}H_{29}ClOSSi$ (M^+) 404.1397, found 404.1396.

Compound 3n. 91% yield (100 mg), colorless oil, *E*/*Z* = 94/6; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.87 (q, *J* = 7.3 Hz, 6H), 1.15–1.55 (m, 11H), 2.46–2.61 (m, 1H), 2.82 (q, *J* = 7.3 Hz, 2H), 5.79 (d, *J* = 10.2 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 11.8, 14.0, 14.7, 22.8, 27.2, 28.2, 29.5, 34.7, 42.6, 126.6, 142.8; MS (EI, *m*/*z*) 222 (3), 220 (M^+, 8), 171 (10), 169 (26), 134 (100); HRMS (EI) calcd for $C_{11}H_{21}ClS$ (M^+) 220.1052, found 220.1055.

Compound 3o. 94% yield (196 mg), colorless oil, *E*/*Z* = 89/11; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.99–1.10 (m, 12H), 1.23–1.28 (m, 3H), 2.77–2.88 (m, 2H), 2.92–3.08 (m, 1H), 3.57 (dd, *J* = 15.1, 5.9 Hz, 2H), 5.98 (d, *J* = 9.7 Hz, 1H), 7.35–7.52 (m, 6H), 7.69 (d, *J* = 7.0 Hz, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.6, 16.7, 19.3, 26.9, 27.2, 38.4, 67.8, 127.7, 129.6, 133.7, 135.6, 135.7, 140.9; HRMS (ESI) calcd for $C_{23}H_{31}ClOSSi$ (M^+) 418.1553, found 418.1560.

Compound 3p.[6b] 92% yield (104 mg), colorless oil, *E*/*Z* = 90/10; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 0.93–1.01 (m, 3H), 1.36–1.52 (m, 4H), 2.42 (dd, *J* = 14.8, 7.5 Hz, 2H), 6.30–6.38 (m, 1H), 7.28–7.32 (m, 1H), 7.34–7.47 (m, 4H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 13.9, 22.3, 30.8, 31.1, 125.3, 127.1, 129.1, 129.6, 133.3, 141.4; MS (EI, *m*/*z*) 228 (7), 226 (M^+, 20), 191 (12), 183 (23), 181 (72). ^{1}H NMR and ^{13}C NMR spectra data are in good agreement with those obtained by Jin's method.[6b]

Compound 3q. 80% yield (82 mg), colorless oil; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.35 (t, *J* = 7.6 Hz, 3H), 2.99 (q, *J* = 7.4 Hz, 2H), 6.98–7.03 (m, 1H), 7.13–7.16 (m, 1H), 7.23 (s, 1H), 7.31–7.35 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.6, 28.5, 126.1, 126.3, 127.0, 129.8, 129.9, 138.1; HRMS (EI) calcd for $C_8H_9ClS_2$ (M^+) 203.9834, found 203.9839.

Compound 3r. 78% yield (94 mg), colorless oil; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.30 (t, *J* = 7.4 Hz, 3H), 2.94 (q, *J* = 7.4 Hz, 2H), 7.30–7.38 (m, 4H), 7.57 (d, *J* = 7.6 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.5, 30.4, 119.6, 128.0, 128.2, 129.2, 135.8, 139.4; MS (EI, *m*/*z*) 244 (12), 242 (M^+, 11), 215 (43), 213 (45); HRMS (EI) calcd for $C_{10}H_{11}BrS$ (M^+) 241.9765, found 241.9767.

Compound 3s. 74% yield (107 mg), white solid, mp 117–118 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.33–7.46 (m, 8H), 7.55 (s, 1H), 7.64 (d, *J* = 7.2 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 116.3, 127.7, 128.5, 128.6, 129.0, 129.3, 130.2, 133.8, 135.5, 142.3; MS (EI, *m*/*z*) 292 (8), 290 (M^+, 10), 221 (7), 210 (41), 178 (100), 121 (52); HRMS (EI) calcd for $C_{14}H_{11}BrS$ (M^+) 289.9765, found 289.9760. Crystal data for **3s** ($C_{14}H_{11}BrS$, 291.20) orthorhombic, space group *P*2(1)2(1)2(1), *a* = 6.0206(4) Å, *b* = 10.2488(7) Å, *c* = 20.3688(13) Å, volume = 1256.83(14) Å^3, *Z* = 4, specimen 0.403 × 0.204 × 0.057 mm^3, *T* = 296(2) K, SIEMENS P4 diffractometer, absorption coefficient 3.405 mm^{-1}, reflections collected 8909, independent reflections 2206 [*R*(int) = 0.0350], refinement by full-matrix least-squares on F^2, data/restraints/parameters 2206/0/145, goodness-of-fit on F^2 = 1.059, final *R* indices [$I > 2\sigma(I)$] R_1 = 0.0353, wR_2 = 0.0740, *R* indices (all data) R_1 = 0.0682, wR_2 = 0.0815, largest diff peak and hole 0.573 and −0.371 e Å^{-3}. CCDC 902936 (**3s**) contains the supplementary crystallographic data for this paper.

Compound 3t. 75% yield (104 mg), colorless oil; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.30 (t, *J* = 7.4 Hz, 3H), 2.94 (q, *J* = 7.4 Hz, 2H), 7.25 (s, 1H), 7.32 (d, *J* = 8.4 Hz, 2H), 7.51 (d, *J* = 8.4 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.6, 30.5, 120.3, 128.4, 130.4, 133.6, 134.2, 138.0; MS (EI, *m*/*z*) 280 (11), 278 (40), 276 (M^+, 54), 214 (60), 212 (63); HRMS (EI) calcd for $C_{10}H_{10}BrClS$, (M^+) 275.9375, found 275.9379.

Compound 3u. 80% yield (106 mg), colorless oil; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.31 (t, *J* = 7.4 Hz, 3H), 2.36 (s, 3H), 2.94 (q, *J* = 7.4 Hz, 2H), 7.18 (d, *J* = 8.0 Hz, 2H), 7.30 (s, 1H), 7.48 (d, *J* = 8.0 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.5, 21.4, 30.4, 118.5, 129.0, 129.1, 133.0, 138.0, 139.6; MS (EI, *m*/*z*) 258 (36), 256 (M^+, 34), 229 (7), 227 (8), 188 (70); HRMS (EI) calcd for $C_{11}H_{13}BrS$ (M^+) 255.9921, found 255.9920.

Compound 3v. 91% yield (120 mg), colorless oil, *E*/*Z* = 91/9; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.85–0.90 (m, 6H), 1.05–1.54 (m, 11H), 2.52–2.59 (m, 1H), 2.80 (q, *J* = 7.3 Hz, 2H), 6.06 (d, *J* = 10.2 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 11.9, 14.1, 14.6, 22.8, 28.0, 28.9, 29.5, 34.6, 43.8, 116.0, 147.9; MS (EI, *m*/*z*) 266 (9), 264 (M^+, 10), 237 (11), 235 (12), 208 (10), 206 (10); HRMS (EI) calcd for $C_{11}H_{21}BrS$ (M^+) 264.0547, found 264.0546.

Compound 3w. 86% yield (199 mg), colorless oil, *E*/*Z* = 94/6; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.0 (d, *J* = 6.8 Hz, 3H), 1.14 (s, 9H), 1.28 (t, *J* = 7.4 Hz, 3H), 2.83 (q, *J* = 7.4 Hz, 2H), 3.01–3.20 (m, 1H), 3.58–3.61 (m, 2H), 6.31 (d, *J* = 9.6 Hz, 1H), 7.43–7.49 (m, 6H), 7.73–7.76 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.6, 16.6, 19.4, 26.9, 28.9, 39.5, 67.6, 117.0, 127.8, 129.7, 133.7, 135.7, 146.0; HRMS (ESI) calcd for $C_{23}H_{31}BrOSSi$ (M^+) 462.1048, found 462.1051.

Compound 3x.[6b] 90% yield (122 mg), colorless oil, *E*/*Z* = 91/9; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 0.96–1.10 (m, 3H), 1.40–1.50 (m, 4H), 2.39–2.42 (m, 2H), 6.62–6.64 (m, 1H), 7.31–7.33 (m, 1H), 7.37–7.41 (m, 4H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 13.9, 22.3, 30.9, 31.9, 113.3, 127.1, 129.1, 129.4, 134.1, 146.4. ^{1}H NMR and ^{13}C NMR spectra data are in good agreement with those obtained by Jin's method.[6b]

Compound 3y. 77% yield (95 mg), colorless oil; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 1.31 (t, *J* = 7.4 Hz, 3H), 2.94 (q, *J* = 7.4 Hz, 2H), 6.97 (dd, *J* = 5.0, 3.7 Hz, 1H), 7.13 (d, *J* = 3.4 Hz, 1H), 7.32

(d, J = 5.0 Hz, 1H), 7.45 (s, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 14.5, 30.3, 115.5, 126.2, 127.3, 130.3, 134.3, 139.0; HRMS (EI) calcd for $C_8H_9BrS_2$ (M^+) 247.9329, found 247.9336.

General procedure for the Suzuki coupling of 3

To a mixture of **4a** (79 mg, 0.65 mmol), $Pd(OAc)_2$ (5.6 mg, 0.025 mmol), Cs_2CO_3 (244 mg, 0.75 mmol), and PPh_3 (13.1 mg, 0.05 mmol) in 2 mL of THF was added **3a** (99 mg, 0.5 mmol) under a nitrogen atmosphere. After stirring at 40 °C for 5 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 gel (petroleum ether/EtOAc = 50/1) gave 109 mg (91%) of **5a** as a colorless oil. **5a** could also be prepared from **3r** in 87% yield (104 mg). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.13 (t, J = 7.4 Hz, 3H), 2.49 (q, J = 7.4 Hz, 2H), 6.87 (s, 1H), 7.28–7.37 (m, 1H), 7.39–7.46 (m, 5H), 7.65 (d, J = 9.2 Hz, 2H), 7.76 (d, J = 8.0 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.9, 26.9, 127.1, 127.8, 128.0, 128.2, 128.3, 129.6, 132.1, 137.1, 137.6, 141.1; MS (EI, m/z) 240 (M^+, 96), 211 (100), 178 (66), 164 (11); HRMS (EI) calcd for $C_{16}H_{16}S$ (M^+) 240.0973, found 240.0976.

Compound 5b.[18] 84% yield (121 mg), colorless oil; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.08–7.11 (m, 1H), 7.15–7.22 (m, 2H), 7.25–7.40 (m, 7H), 7.45 (dd, J = 10.5, 4.7 Hz, 2H), 7.71–7.78 (m, 2H), 7.84 (d, J = 7.5 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 125.9, 127.9, 128.0, 128.1, 128.3, 128.3, 128.8, 129.2, 129.6, 134.8, 135.3, 135.8, 136.8, 141.0.

Compound 5c. 87% yield (112 mg), colorless oil; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.10 (t, J = 7.4 Hz, 3H), 2.46 (q, J = 7.4 Hz, 2H), 6.79 (s, 1H), 7.06–7.11 (m, 2H), 7.35–7.40 (m, 1H), 7.41–7.43 (m, 2H), 7.60–7.62 (m, 2H), 7.70–7.74 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 15.0, 26.9, 115.0 (d, J = 21.2 Hz), 127.9, 128.3, 128.4, 131.0, 131.3 (d, J = 7.9 Hz), 133.2 (d, J = 3.3 Hz), 137.3, 141.0, 161.7 (d, J = 245.9 Hz); MS (EI, m/z) 258 (M^+, 100), 229 (54), 196 (30), 183 (8); HRMS (EI) calcd for $C_{16}H_{15}FS$ (M^+) 258.0878, found 258.0883.

Compound 5d. It was prepared from **3d** and **3s** in respective yields of 86% (118 mg) and 83% (114 mg) as a colorless oil; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.12 (t, J = 7.4 Hz, 3H), 2.48 (q, J = 7.4 Hz, 2H), 6.79 (s, 1H), 7.36–7.39 (m, 3H), 7.44 (t, J = 6.8 Hz, 2H), 7.63 (d, J = 7.6 Hz, 2H), 7.70 (d, J = 8.4 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 15.0, 27.0, 128.0, 128.1, 128.2, 128.4, 130.7, 130.9, 132.6, 135.5, 138.5, 140.9; MS (EI, m/z) 276 (2), 274 (M^+, 7), 247 (48), 245 (100), 210 (11); HRMS (EI) calcd for $C_{16}H_{15}ClS$ (M^+) 274.0583, found 274.0583.

Compound 5e. 79% yield (126 mg), colorless oil; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.10 (t, J = 7.4 Hz, 3H), 2.46 (q, J = 7.4 Hz, 2H), 6.75 (s, 1H), 7.36–7.40 (m, 1H), 7.41–7.42 (m, 2H), 7.50–7.53 (m, 2H), 7.59–7.63 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 15.0, 27.0, 120.9, 128.1, 128.3, 128.5, 130.8, 131.1, 131.2, 136.0, 138.7, 140.9; MS (EI, m/z) 320 (1), 318 (M^+, 1), 291 (8), 289 (11), 210 (100); HRMS (EI) calcd for $C_{16}H_{15}BrS$ (M^+) 318.0078, found 318.0072.

Compound 5f. It was prepared from **3f** and **3t** in respective yields of 85% (108 mg) and 87% (110 mg) as a colorless oil; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.13 (t, J = 7.4 Hz, 3H), 2.42 (s, 3H), 2.49 (q, J = 7.4 Hz, 2H), 6.86 (s, 1H), 7.23–7.25 (m, 2H), 7.36–7.38 (m, 1H), 7.41–7.45 (m, 2H), 7.64–7.69 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 15.0, 21.4, 26.9, 127.7, 128.3, 128.4, 128.8, 129.6, 132.3, 134.4, 136.6, 137.0, 141.3; MS (EI, m/z) 254 (M^+, 100), 225 (63), 210 (58), 192 (14), 178 (12); HRMS (EI) calcd for $C_{17}H_{18}S$ (M^+) 254.1129, found 254.1127.

Compound 5g. 90% yield (133 mg), colorless oil; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.13 (t, J = 7.4 Hz, 3H), 1.38 (s, 9H), 2.48 (q, J = 7.4 Hz, 2H), 6.84 (s, 1H), 7.35–7.37 (m, 1H), 7.40–7.46 (m, 4H), 7.62–7.65 (m, 2H), 7.74 (d, J = 8.4 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 15.0, 27.0, 31.3, 34.7, 125.0, 127.7, 128.3, 128.3, 128.4, 129.4, 132.2, 134.3, 141.4, 150.2; MS (EI, m/z) 296 (M^+, 74), 281 (86), 239 (40); HRMS (EI) calcd for $C_{20}H_{24}S$ (M^+) 296.1599, found 296.1592.

Compound 5h. 89% yield (120 mg), colorless oil; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.15 (t, J = 7.4 Hz, 3H), 2.50 (q, J = 7.4 Hz, 2H), 3.87 (s, 3H), 6.85 (s, 1H), 6.98 (d, J = 8.8 Hz, 2H), 7.36–7.40 (m, 1H), 7.41–7.45 (m, 2H), 7.65–7.67 (m, 2H), 7.78 (d, J = 8.4 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.9, 26.8, 55.1, 113.3, 127.5, 128.1, 128.2, 129.8, 130.9, 131.9, 135.0, 141.3, 158.6; MS (EI, m/z) 270 (M^+, 100), 241 (56), 226 (34), 210 (15); HRMS (EI) calcd for $C_{17}H_{18}OS$ (M^+) 270.1078, found 270.1083.

Compound 5i. 94% yield (141 mg), colorless oil; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.12 (t, J = 7.4 Hz, 3H), 2.47 (q, J = 7.4 Hz, 2H), 3.91 (s, 3H), 3.95 (s, 3H), 6.79 (s, 1H), 6.89 (d, J = 8.4 Hz, 1H), 7.25–7.34 (m, 2H), 7.39 (t, J = 7.2 Hz, 2H), 7.56–7.63 (m, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 15.1, 27.0, 55.9, 55.9, 110.7, 112.6, 123.1, 127.7, 128.3, 128.4, 130.2, 132.2, 135.3, 141.4, 148.3, 148.3; MS (EI, m/z) 300 (M^+, 70), 271 (66), 240 (100), 225 (44); HRMS (EI) calcd for $C_{18}H_{20}O_2S$ (M^+) 300.1184, found 300.1186.

Compound 5j. 82% yield (119 mg), colorless oil; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.19 (t, J = 7.4 Hz, 3H), 2.56 (q, J = 7.4 Hz, 2H), 7.07 (s, 1H), 7.42–7.55 (m, 5H), 7.73–7.75 (m, 2H), 7.90–7.95 (m, 3H), 8.02 (d, J = 8.8 Hz, 1H), 8.22 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 15.1, 27.1, 126.1, 126.2, 127.5, 127.7, 127.7, 128.0, 128.3, 128.4, 128.5, 129.0, 132.3, 132.6, 133.4, 134.8, 138.2, 141.3; HRMS (ESI) calcd for $C_{20}H_{18}S$ (M^+) 290.1129, found 290.1134.

Compound 5k. 85% yield (122 mg), colorless oil, Z/E > 95/5; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.93 (t, J = 6.7 Hz, 3H), 1.10 (t, J = 7.3 Hz, 3H), 1.29–1.43 (m, 14H), 2.41 (q, J = 7.3 Hz, 2H), 2.49 (q, J = 7.2 Hz, 2H), 6.04 (t, J = 7.2 Hz, 1H), 7.29 (t, J = 7.4 Hz, 1H), 7.36 (dd, J = 10.2, 4.6 Hz, 2H), 7.51–7.59 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.2, 15.1, 22.7, 26.1, 29.0, 29.4, 29.5, 29.6, 29.7, 30.6, 32.0, 127.3, 127.9, 128.2, 135.4, 136.4, 140.7; HRMS (ESI) calcd for $C_{19}H_{30}S$ (M^+) 290.2068, found 290.2072.

Compound 5l. 89% yield (123 mg), colorless oil, E/Z > 95/5; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.86–0.95 (m, 6H), 1.06 (t, J = 7.3 Hz, 3H), 1.23–1.41 (m, 6H), 1.44–1.56 (m, 2H), 2.36 (q, J = 7.3 Hz, 2H), 2.75–2.95 (m, 1H), 5.72 (d, J = 9.8 Hz, 1H), 7.24–7.31 (m, 1H), 7.35 (t, J = 7.4 Hz, 2H), 7.48–7.60 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 12.0, 14.1, 15.2, 22.9, 26.0, 28.7, 29.7, 35.2, 41.8, 127.3, 127.9, 128.2, 135.5, 140.7, 141.7; HRMS (ESI) calcd for $C_{17}H_{26}S$ (M^+) 262.1755, found 262.1750.

Compound 5m. 71% yield (94 mg), colorless oil; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 1.24 (t, J = 7.6 Hz, 3H), 2.76 (q, J = 7.6 Hz, 2H), 7.02 (d, J = 15.5 Hz, 1H), 7.07 (s, 1H), 7.25 (d, J = 15.5 Hz, 1H), 7.31–7.36 (m, 2H), 7.39–7.48 (m, 4H), 7.56 (d, J = 7.8 Hz, 2H), 7.88 (d, J = 7.8 Hz, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 14.8, 27.9, 126.7, 127.6, 127.7, 128.0, 128.7, 129.9, 131.4, 131.6, 133.8, 136.5, 136.7, 137.0; HRMS (ESI) calcd for $C_{18}H_{18}S$ (M^+) 266.1129, found 266.1125.

Compound 5n. 93% yield (118 mg), colorless oil; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.16 (t, J = 7.4 Hz, 3H), 2.43–2.56 (m, 5H), 6.88 (s, 1H), 7.21–7.37 (m, 3H), 7.45 (t, J = 7.7 Hz, 2H), 7.58 (d, J = 8.0 Hz, 2H), 7.80 (d, J = 7.6 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 15.1, 21.3, 27.0, 127.1, 128.1, 128.2, 129.2, 129.7, 131.6, 137.3, 137.6, 137.7, 138.3; MS (EI, m/z) 255 (30), 254 (M^+, 100), 226 (25), 225 (98), 193 (26); HRMS (EI) calcd for $C_{17}H_{18}S$ (M^+) 254.1129, found 254.1126.

Compound 5o. 86% yield (109 mg), colorless oil; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.33 (t, J = 7.4 Hz, 3H), 2.45–2.50 (m, 5H), 6.85 (s, 1H), 7.19 (d, J = 7.3 Hz, 1H), 7.29–7.32 (m, 2H), 7.40–7.46 (m, 4H), 7.76 (d, J = 7.4 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 15.0, 21.5, 27.0, 125.5, 127.1, 128.1, 128.3, 128.7, 129.0, 129.7, 131.9, 137.2, 137.7, 138.0, 141.1; MS (EI, m/z) 255 (3), 254 (M^+, 21), 226 (4), 225 (31), 193 (6); HRMS (EI) calcd for $C_{17}H_{18}S$ (M^+) 254.1129, found 254.1122.

Compound 5p. 62% yield (79 mg), colorless oil; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 1.11 (t, J = 7.4 Hz, 3H), 2.31 (q, J = 7.4 Hz, 2H), 2.48 (s, 3H), 6.50 (s, 1H), 7.22–7.35 (m, 5H), 7.43 (t, J = 7.7 Hz, 2H), 7.69 (d, J = 7.7 Hz, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 14.8, 19.8, 26.4, 125.6, 126.8, 127.7, 128.1, 128.6, 129.3, 129.6, 130.2, 136.3, 137.0, 137.7, 140.2; MS (EI, m/z) 255 (14), 254 (M^+, 100), 226 (17), 225 (100), 193 (14); HRMS (EI) calcd for $C_{17}H_{18}S$ (M^+) 254.1129, found 254.1129.

Compound 5q. 89% yield (120 mg), colorless oil; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.14 (t, J = 7.2 Hz, 3H), 2.50 (dd, J = 14.4, 7.2 Hz, 2H), 3.88 (s, 3H), 6.83 (s, 1H), 6.98 (d, J = 8.3 Hz, 2H), 7.30 (t, J = 7.0 Hz, 1H), 7.43 (t, J = 7.3 Hz, 2H), 7.60 (d, J = 8.3 Hz, 2H), 7.78 (d, J = 7.5 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 15.1, 27.0, 55.4, 113.8, 127.0, 128.1, 129.5, 129.6, 131.2, 133.6, 137.2, 137.4, 159.5; HRMS (ESI) calcd for $C_{17}H_{18}OS$ (M^+) 270.1078, found 270.1079.

Compound 5r. 86% yield (129 mg), colorless oil; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.11 (t, J = 7.4 Hz, 3H), 2.48 (q, J = 7.4 Hz, 2H), 3.90–395 (m, 6H), 6.81 (s, 1H), 6.89 (d, J = 8.3 Hz, 1H), 7.15–7.40 (m, 5H), 7.73 (d, J = 8.3 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 15.1, 27.0, 55.9, 56.0, 110.8, 111.4, 120.7, 127.0, 128.0, 129.6, 131.2, 134.0, 137.2, 137.3, 148.7, 148.9; HRMS (ESI) calcd for $C_{18}H_{20}O_2S$ (M^+) 300.1184, found 300.1188.

Compound 5s. 80% yield (103 mg), colorless oil; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 1.15 (t, J = 7.4 Hz, 3H), 2.49 (q, J = 7.3 Hz, 2H), 6.85 (s, 1H), 7.15 (t, J = 8.6 Hz, 2H), 7.33 (t, J = 7.3 Hz, 1H), 7.45 (t, J = 7.7 Hz, 2H), 7.64 (dd, J = 8.3, 5.6 Hz, 2H), 7.79 (d, J = 7.8 Hz, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 15.0, 27.0, 115.3 (d, J = 21.2 Hz), 127.3, 128.1, 129.7, 129.9 (d, J = 7.9 Hz), 132.4, 136.5, 137.0, 137.3 (d, J = 3.0 Hz), 162.5 (d, J = 246.0 Hz); MS (EI, m/z) 259 (11), 258 (M^+, 61), 230 (15), 229 (76), 228 (14); HRMS (EI) calcd for $C_{16}H_{15}FS$ (M^+) 258.0878, found 258.0878.

Compound 5t. 81% yield (117 mg), colorless oil; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.12 (t, J = 7.3 Hz, 3H), 2.49 (q, J = 7.3 Hz, 2H), 6.99 (s, 1H), 7.26–7.56 (m, 6H), 7.79–7.96 (m, 5H), 8.08 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 15.1, 27.1, 126.2, 126.4, 126.5, 127.1, 127.3, 127.7, 128.0, 128.1, 128.2, 129.7, 132.7, 133.0, 133.4, 137.2, 137.6, 138.7; HRMS (ESI) calcd for $C_{20}H_{18}S$, (M^+) 290.1129, found 290.1134.

Compound 5u. 76% yield (93 mg), colorless oil; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 1.30 (t, J = 7.4 Hz, 3H), 2.78 (q, J = 7.3 Hz, 2H), 7.11–7.18 (m, 1H), 7.26 (s, 1H), 7.37–7.40 (m, 2H), 7.43–7.54 (m, 3H), 7.91 (d, J = 7.4 Hz, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 14.8, 27.9, 125.4, 125.4, 127.3, 127.4, 128.0, 129.0, 129.6, 132.1, 136.5, 146.3; MS (EI, m/z) 247 (3), 246 (M^+, 26), 217 (25), 185 (39); HRMS (EI) calcd for $C_{14}H_{14}S_2$ (M^+) 246.0537, found 246.0539.

Compound 5v. 75% yield (86 mg), yellow oil; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 1.23 (t, J = 7.6 Hz, 3H), 2.75 (q, J = 7.6 Hz, 2H), 6.52 (d, J = 1.7 Hz, 1H), 6.77 (d, J = 5.2 Hz, 1H), 7.34 (t, J = 7.4 Hz, 1H), 7.42–7.47 (m, 3H), 7.51 (s, 1H), 7.91 (d, J = 7.8 Hz, 2H); ^{13}C NMR ($CDCl_3$, 151 MHz) δ 14.7, 28.2, 109.4, 111.6, 124.0, 127.6, 128.0, 129.8, 131.2, 136.3, 142.5, 154.5; HRMS (EI) calcd for $C_{14}H_{14}OS$ (M^+) 230.0765, found 230.0758.

Compound 5w. 66% yield (59 mg), colorless oil; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.30 (t, J = 7.4 Hz, 3H), 2.27 (s, 3H), 2.85 (q, J = 7.4 Hz, 2H), 6.52 (s, 1H), 7.23 (t, J = 7.2 Hz, 1H), 7.37 (t, J = 7.5 Hz, 2H), 7.55 (d, J = 7.8 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 15.1, 24.7, 25.2, 126.4, 127.3, 128.0, 129.1, 132.7, 137.2; MS (EI, m/z) 179 (1), 178 (M^+, 11), 150 (5), 149 (15), 117 (22); HRMS (EI) calcd for $C_{11}H_{14}S$ (M^+) 178.0816, found 178.0818.

General procedure for the Negishi coupling of 3a

To a solution of **3a** (99 mg, 0.5 mmol) and $Pd(PPh_3)_4$ (29 mg, 0.025 mmol) in anhydrous THF (1 mL) and NMP (1 mL) was added PhZnBr (0.75 mmol) at room temperature. After stirring at 50 °C for 3 h, the reaction mixture was quenched with water, extracted with EtOAc, washed with brine, dried over Na_2SO_4 and concentrated. Column chromatography on silica gel (petroleum ether/EtOAc = 50/1) gave 86 mg (72%) of **5a** as a colorless oil. The spectra data are in good agreement with those obtained above.

General procedure for the Sonogashira coupling of 3a

To a mixture of **3a** (99 mg, 0.5 mmol), $PdCl_2$ (4.4 mg, 0.025 mmol), CuI (9.5 mg, 0.05 mmol), PPh_3 (13.1 mg, 0.05 mmol), and Cs_2CO_3 (326 mg, 1.0 mmol) in 2 mL of THF was added phenylacetylene (102 mg, 1.0 mmol). After stirring at room temperature for 8 h, the reaction mixture was quenched with water, extracted with EtOAc, washed with brine, dried over Na_2SO_4 and concentrated. Column chromatography on silica gel (petroleum ether/EtOAc = 50/1) gave 111 mg (84%) of **5x** as a colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.47 (t, J = 7.4 Hz, 3H), 3.18 (q, J = 7.4 Hz, 2H), 7.15 (s, 1H), 7.33–7.35 (m, 1H), 7.41–7.47 (m, 5H), 7.57–7.60 (m, 2H), 7.71 (d, J = 8.0 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 15.5, 27.8, 87.3, 92.1, 119.1, 123.0, 127.7, 128.3, 128.5, 128.6,

129.7, 131.6, 134.8, 136.2; MS (EI, *m*/*z*): 264 (M^+, 12), 235 (15), 215 (86), 202 (40), 189 (100); HRMS (EI) calcd for $C_{18}H_{16}S$ (M^+) 264.0973, found 264.0976.

Compound 5y. 81% yield (105 mg), colorless oil; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.28 (s, 9H), 1.35 (t, J = 7.4 Hz, 3H), 3.02 (q, J = 7.4 Hz, 2H), 7.01 (s, 1H), 7.18–7.30 (m, 1H), 7.37 (t, J = 7.8 Hz, 2H), 7.52–7.62 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ −0.1, 15.5, 27.7, 97.3, 101.8, 119.0, 127.6, 128.2, 129.6, 135.1, 136.0; HRMS (ESI) calcd for $C_{15}H_{20}SSi$ (M^+), 260.1055, found 260.1048.

General procedure for the synthesis of 7

To a mixture of **5a** (60 mg, 0.25 mmol) and $Ni(PPh_3)_2Cl_2$ (16.3 mg, 0.025 mmol) in 2 mL of THF was added the **6a** (0.75 mmol) under a nitrogen atmosphere. After stirring for 12 h at room temperature, the reaction mixture was quenched with water, extracted with EtOAc, washed with brine, dried over Na_2SO_4 and concentrated. Column chromatography on silica gel (petroleum ether/Et_2O = 100/1) gave 42 mg (86%) of **7a**[22] as a white solid, mp 81–82 °C. It was also prepared from **5b** in 76% yield (37 mg) as a white solid; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.35 (s, 3H), 6.91 (s, 1H), 7.31–7.37 (m, 2H), 7.42–7.45 (m, 6H), 7.58–7.60 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 17.5, 126.0, 126.5, 127.2, 127.8, 128.2, 128.4, 129.2, 137.5, 138.4, 144.0.

Compound 7b.[24] 75% yield (40 mg), white solid, mp 85–86 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.29 (d, J = 1.2 Hz, 3H), 6.82 (s, 1H), 7.10 (t, J = 8.8 Hz, 2H), 7.33–7.43 (m, 5H), 7.56 (d, J = 9.2 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 17.5, 115.1 (d, J = 21.1 Hz), 126.0, 126.6, 127.3, 128.4, 130.7 (d, J = 7.8 Hz), 134.4 (d, J = 3.4 Hz), 137.4, 143.8, 161.4 (d, J = 244.5 Hz).

Compound 7c.[25] 80% yield (42 mg), white solid, mp 48–50 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.32 (d, J = 1.2 Hz, 3H), 2.40 (s, 3H), 6.85 (s, 1H), 7.22 (d, J = 8.0 Hz, 2H), 7.30–7.33 (m, 3H), 7.40 (t, J = 7.2 Hz, 2H), 7.54–7.57 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 17.5, 21.2, 126.0, 127.1, 127.7, 128.3, 128.9, 129.1, 135.5, 136.2, 136.7, 144.2.

Compound 7d. 81% yield (51 mg), white solid, mp 73–74 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.45 (s, 9H), 2.40 (s, 3H), 6.92 (s, 1H), 7.41–7.51 (m, 7H), 7.62 (t, J = 7.6 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 17.6, 31.5, 34.6, 125.2, 126.1, 127.1, 127.7, 128.4, 129.0, 135.6, 136.9, 144.3, 149.5; MS (EI, *m*/*z*) 250 (M^+, 39), 235 (100), 193 (11), 178 (18), 115 (30); HRMS (EI) calcd for $C_{19}H_{22}$ (M^+) 250.1722, found 250.1718.

Compound 7e.[26] 80% yield (45 mg), white solid, mp 85–86 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.29 (s, 3H), 3.85 (s, 3H), 6.79 (s, 1H), 6.93 (d, J = 8.4 Hz, 2H), 7.26–7.40 (m, 5H), 7.53 (d, J = 7.6 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 17.5, 55.3, 113.6, 126.0, 127.0, 127.3, 128.3, 130.4, 131.0, 135.9, 144.2, 158.2.

Compound 7f. 84% yield (53 mg), white solid, mp 153–154 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.32 (s, 3H), 3.92 (s, 6H), 6.80 (s, 1H), 6.91–6.96 (m, 3H), 7.36–7.38 (m, 3H), 7.53 (d, J = 7.2 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 17.6, 55.9, 55.9, 111.0, 112.5, 121.7, 126.0, 127.0, 127.5, 128.3, 131.3, 136.3, 144.1, 147.8, 148.6; MS (EI, *m*/*z*) 254 (M^+, 78), 224 (17), 179 (100), 165 (74), 152 (51); HRMS (EI) calcd for $C_{17}H_{18}O_2$ (M^+) 254.1307, found 254.1305.

Compound 7g. 78% yield (48 mg), white solid, mp 112–113 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.41 (s, 3H), 7.04 (s, 1H), 7.35–7.37 (m, 1H), 7.44 (t, J = 7.6 Hz, 2H), 7.51–7.56 (m, 3H), 7.62 (d, J = 7.2 Hz, 2H), 7.87–7.89 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 17.7, 125.8, 126.1, 126.1, 126.1, 127.3, 127.7, 127.8, 127.8, 128.0, 128.4, 128.4, 132.2, 133.4, 135.9, 137.9, 144.0; MS (EI, *m*/*z*) 244 (M^+, 14), 229 (18), 215 (31), 165 (100); HRMS (EI) calcd for $C_{19}H_{16}$ (M^+) 244.1252, found 244.1258.

Compound 7h. 71% yield (43 mg), yellow oil; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 0.91 (t, J = 7.0 Hz, 3H), 1.21–1.47 (m, 14H), 2.05 (s, 3H), 2.19–2.23 (m, 2H), 5.79–5.82 (m, 1H), 7.24 (d, J = 7.3 Hz, 1H), 7.31–7.34 (m, 2H), 7.40–7.41 (m, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 14.1, 15.8, 22.7, 28.8, 29.3, 29.4, 29.6, 29.6, 29.6, 31.9, 125.6, 126.4, 128.1, 128.9, 134.5, 144.1; MS (EI, *m*/*z*) 245 (2), 244 (M^+, 8), 132 (13), 131 (100), 130 (8), 129 (15), 118 (93); HRMS (EI) calcd for $C_{18}H_{28}$ (M^+) 244.2191, found 244.2198.

Compound 7i.[26] 89% yield (46 mg), white solid, mp 72–73 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.25 (d, J = 1.3 Hz, 3H), 2.35 (s, 3H), 6.81 (d, J = 1.0 Hz, 1H), 7.16 (d, J = 8.0 Hz, 2H), 7.20–7.23 (m, 1H), 7.34 (d, J = 4.6 Hz, 4H), 7.41 (d, J = 8.2 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 17.5, 21.2, 126.0, 126.4, 127.0, 128.2, 129.1, 129.2, 137.0, 137.3, 138.6, 141.2.

Compound 7j. 75% yield (39 mg), white solid, mp 65–67 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.29 (s, 3H), 2.41 (s, 3H), 6.84 (s, 1H), 7.10–7.14 (m, 1H), 7.26–7.33 (m, 2H), 7.35–7.40 (M, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 17.6, 21.6, 123.2, 126.4, 126.8, 127.5, 127.9, 128.1, 128.2, 129.2, 137.6, 137.9, 138.4, 144.0; HRMS (ESI) calcd for $C_{16}H_{16}$ (M^+) 208.1252, found 208.1255.

Compound 7k.[27] 82% yield (46 mg), white solid, mp 95–96 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.28 (s, 3H), 3.85 (s, 3H), 6.80 (s, 1H), 6.88–6.98 (m, 2H), 7.21–7.30 (m, 1H), 7.35–7.42 (m, 4H), 7.44–7.52 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 17.5, 55.4, 113.7, 126.2, 126.3, 127.1, 128.2, 129.1, 136.4, 136.8, 138.6, 159.0.

Compound 7l. 80% yield (51 mg), yellow solid, mp 134–136 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.28 (s, 3H), 3.92 (s, 3H), 3.96 (s, 3H), 6.81 (s, 1H), 6.89 (d, J = 8.0 Hz, 1H), 7.09–7.11 (m, 2H), 7.26–7.27 (m, 1H), 7.37–7.39 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 17.6, 55.9, 56.0, 109.4, 111.0, 118.4, 126.4, 126.6, 128.2, 129.1, 136.9, 137.1, 138.5, 148.5, 148.7; MS (EI, *m*/*z*) 254 (M^+, 100), 224 (57), 179 (61), 165 (47), 152 (39); HRMS (EI) calcd for $C_{17}H_{18}O_2$ (M^+) 254.1307, found 254.1310.

Compound 7m.[26] 87% yield (53 mg), white solid, mp 146–148 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.42 (d, J = 1.2 Hz, 3H), 7.04 (s, 1H), 7.23–7.35 (m, 1H), 7.42–7.51 (m, 6H), 7.73–7.76 (m, 1H), 7.85–7.90 (m, 3H), 7.97 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 17.5, 124.4, 124.7, 125.8, 126.2, 126.6, 127.6, 127.8, 128.2, 128.2, 128.3, 129.3, 132.7, 133.5, 137.2, 138.4, 141.1.

Compound 7n. 61% yield (51 mg), yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.90 (t, J = 7.1 Hz, 3H), 1.24–1.36 (m, 14H), 2.14 (q, J = 7.3 Hz, 2H), 3.88 (s, 3H), 6.05 (t, J = 7.4 Hz, 1H),

6.92 (d, J = 8.3 Hz, 2H), 7.11 (d, J = 8.3 Hz, 2H), 7.21–7.28 (m, 5H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 14.1, 22.7, 29.3, 29.3, 29.5, 29.6, 29.8, 30.0, 31.9, 55.2, 113.5, 126.7, 127.3, 128.0, 130.2, 131.1, 132.7, 141.0, 143.4, 158.5; HRMS (ESI) calcd for $C_{24}H_{32}O$ (M^+) 336.2453, found 336.2459.

Compound 7o.[23] 71% yield (34 mg), white solid, mp 48–49 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.25 (s, 3H), 6.51 (s, 1H), 6.98 (d, J = 7.2 Hz, 2H), 7.09–7.15 (m, 3H), 7.22 (d, J = 7.6 Hz, 2H), 7.28–7.33 (m, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 27.2, 126.1, 126.6, 126.9, 127.9, 128.2, 128.5, 129.0, 137.6, 138.8, 142.1.

Compound 7p. 65% yield (49 mg), white solid, mp 211–213 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 3.89 (s, 3H), 6.91–6.97 (m, 3H), 7.06 (t, J = 8.7 Hz, 2H), 7.14–7.23 (m, 7H), 7.35–7.38 (m, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 55.2, 114.2, 115.1 (d, J = 21.5 Hz), 126.7, 127.7, 128.1, 129.4 (d, J = 8.2 Hz), 129.5, 131.7, 132.4, 137.6, 140.0 (d, J = 2.8 Hz), 141.3, 159.2, 162.5 (d, J = 245.8 Hz); MS (EI, m/z) 305 (22), 304 (M^+, 100), 203 (16), 273 (10), 271 (12), 257 (12); HRMS (EI) calcd for $C_{21}H_{17}FO$ (M^+) 304.1263, found 304.1266.

Compound 7q. 70% yield (50 mg), white solid, mp 190–192 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 2.47 (s, 3H), 6.97 (s, 1H), 7.04–7.10 (m, 2H), 7.13–7.25 (m, 9H), 7.36–7.41 (m, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 21.4, 115.0, 115.2, 126.8, 127.8, 128.1, 129.4 (d, J = 7.8 Hz), 129.5, 129.6, 130.3, 137.2, 137.4 (d, J = 27.2 Hz), 140.0 (d, J = 3.2 Hz), 141.7, 162.5 (d, J = 245.3 Hz); MS (EI, m/z) 289 (22), 288 (M^+, 100), 287 (14), 273 (34), 272 (16); HRMS (EI) calcd for $C_{21}H_{17}F$ (M^+) 288.1314, found 288.1316.

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