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ARTICLE TYPE

A regio- and stereoselective entry to (*Z*)-β-halo alkenyl sulfides and their applications to the access of stereodefined trisubstituted alkenes

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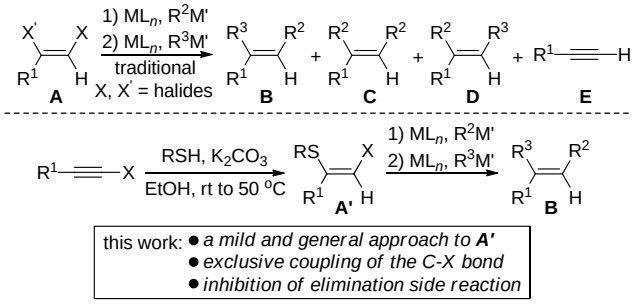
A mild and efficient preparation of (*Z*)-β-halo alkenyl sulfides via the K_2CO_3-promoted hydrothiolation of haloalkynes has been realized, producing (*Z*)-β-bromo and (*Z*)-β-chloro vinylic sulfides in high yields with excellent regio- and stereoselectivity. This approach covers a variety of substrates, including both aryl and alkyl haloalkynes. Meaningfully, it allows a facile access to stereodefined (*Z*)- or (*E*)-trisubstituted olefins featuring the iterative cross-coupling of carbon–halide and carbon–sulfur bonds of β-halo alkenyl sulfides.

Introduction

Alkenyl sulfides are key components in the synthesis of important building blocks, biologically active compounds, as well as novel materials.[1] Hydrothiolation of alkynes[2] proves to be a straightforward and atom-economic method toward vinylic sulfides. Up to date, a number of methods have been developed, including the base-mediated,[3] radical[4] and metal-catalyzed[5] approaches. Most of these developments focus on the addition of S─H bond to terminal alkynes, while less attention has been paid to the hydrothiolation of nonterminal acetylenes, presumably due to the challenge of controlling regio- and stereoselectivity in these cases. As such, to expand the scope and synthetic utility of this reaction, further exploration of hydrothiolation of internal alkynes is worthwhile.

A promising result came from Kataoka and co-workers,[6] where the regio- and stereoselective hydrothiolation of alkynylselenonium was achieved with catalytic amount of triethylamine. In 2007, Yorimitsu and Oshima reported an elegant Pd-catalyzed hydrothiolation of alkynylphosphines, leading to (*Z*)-1-phosphino-2-thio-1-alkenes in good yields.[7a] Later, the same group described the synthesis of (*Z*)-β-amino vinylic sulfides via a regio- and stereoselective radical addition of thiols to ynamides.[7b] Recently, Chen and Dou reported a very effective entry to (*Z*)-β-bromo alkenyl sulfides via a TBAF-mediated reaction between thiols and 1,1-dibromoalkenes,[8] which was proposed to proceed via the bromoalkyne intermediates generated in situ. Indeed, it represents the first example on the regio- and stereoselective hydrothiolation of haloalkynes. Despite the obvious success, there are some limitations in this protocol: (1) the reaction is not applicable for aryl 1,1-dibromoalkenes because alkynyl sulfides rather than alkenyl sulfides were obtained in this context,[9] (2) (*Z*)-β-chloro vinylic sulfides can neither be synthesized by this method; (3) the utilization of excessive TBAF results in poor functional-group compatibility. Therefore, the development of mild and general protocol for the access of (*Z*)-β-halo alkenyl sulfides remains to be explored.

On the other hand, trisubstituted alkenes are ubiquitous structural motifs in organic chemistry, and consequently, it is highly desirable to develop new and expeditious approaches to these compounds.[10] Along this line, transition-metal-catalyzed iterative cross-coupling strategy[11] has emerged as a powerful tool for constructing polysubstituted alkenes. However, the stepwise cross-coupling of 1,2-dihaloalkenes[12] has only met limited success, mainly because of the following facts: (1) only limited methods[13,14] are available for assembling stereocontrolled 1,2-dihaloalkenes **A**, especially thermodynamically unfavorable (*Z*)-isomers or mixed 1,2-dihaloalkenes (X ≠ X'); (2) problems are encountered in the selective mono-coupling of C─X bond. As a result, the desired product **B** is often messed with the double-substituted sideproduct **C**, regioisomer **D**, or elimination[12d,14e] byproduct **E** (Scheme 1). These undesired products can not only dramatically lower the reaction yield but also hamper the purification.



Scheme 1 The summary of this work.

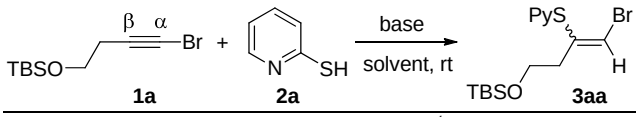
To tackle these challenges, we reasoned that replacement of a carbon─halide bond of **A** with carbon─sulfur bond, the less reactive and more stable one towards transition-metal-catalyzed reactions, might be able to realize the selective mono-coupling of

A' as well as inhibition of the elimination side reaction. As such, continuing on our interest in the functionalization of heteroatom-substituted alkynes,[14,15] we describe here an operationally simple and efficient method for the synthesis of (*Z*)-β-halo alkenyl sulfides via the regio- and stereoselective hydrothiolation of haloalkynes, ultimately resulting in a new entry to stereodefined (*Z*)- or (*E*)-trisubstituted alkenes featuring the iterative cross-coupling of C─X and C─S bonds of β-halo vinylic sulfides.

Results and discussion

To explore a mild and general access to (*Z*)-β-halo alkenyl sulfides, we decided to employ the silyl-substituted bromoalkyne **1a** as a model substrate for screening the reaction conditions. To our delight, promoted by 1.3 equiv of K_2CO_3, the hydrothiolation of **1a** with **2a** occurred smoothly in DMF to afford β-bromo alkenyl sulfide **3aa** in good yield with excellent regio- and stereoselectivity, while no α-regioisomer was observed (Table 1, entry 1). We believed that the induce effect of bromine atom may be responsible for the regioselective β-addition of thiols. Of the solvent, environmentally friendly EtOH worked the best and nonpolar solvents such as toluene and Et_2O only resulted in trace of **3aa** (Table 1, entries 1–10). Screening of the base revealed that the readily available K_2CO_3 was the most effective, and deprotection of the TBS group was not detected (Table 1, entries 5, 11 and 12). As such, the optimized reaction conditions for hydrothiolation of haloalkynes consisted of 1.3 equiv of K_2CO_3, EtOH as the solvent, and room temperature for 10 h, which provided **3aa** in 82% isolated yield (Table 1, entry 5).

Table 1 Optimization of the reaction conditions for hydrothiolation of haloalkynes[a]

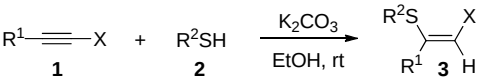


1a **2a** **3aa**

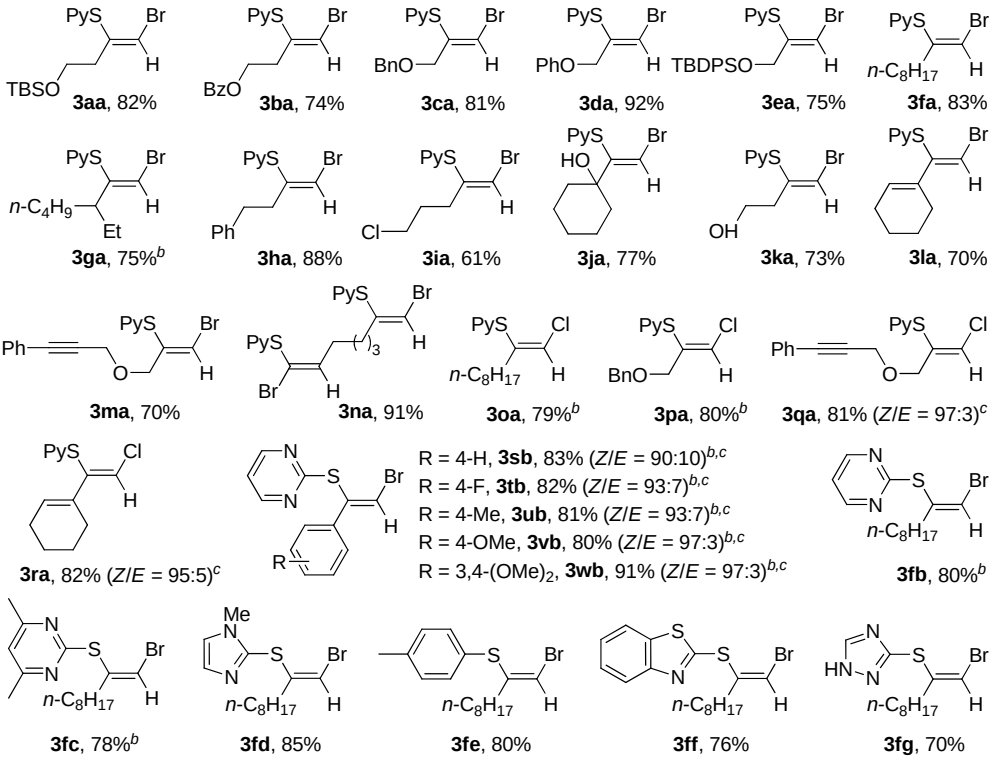
Entry	Base	Solvent	Yield (%)[b]	*Z*/*E*[c]
1	K_2CO_3	DMF	73	95/5
2	K_2CO_3	DMSO	83	96/4
3	K_2CO_3	NMP	68	97/3
4	K_2CO_3	CH_3CN	75	98/2
5	K_2CO_3	EtOH	82	>98/2
6	K_2CO_3	MeOH	80	>98/2
7	K_2CO_3	*i*-PrOH	61	>98/2
8	K_2CO_3	THF	52	>98/2
9	K_2CO_3	toluene	trace	/
10	K_2CO_3	Et_2O	trace	/
11	K_3PO_4	EtOH	68	>98/2
12	Cs_2CO_3	EtOH	59	>98/2
13	/	EtOH	trace	/

[a] Reaction conditions: **1a** (0.5 mmol), **2a** (0.6 mmol), base (0.65 mmol), rt, 10 h. [b] Combined isolated yield. [c] Determined by GC.

Table 2 Scope of hydrothiolation of alkynyl halides[a]



1 **2** **3**



[a] Reaction conditions: **1** (0.5 mmol), **2** (0.6 mmol), K_2CO_3 (0.65 mmol), EtOH, rt, 10 h. Unless otherwise noted, **3** were obtained with >98% *Z*-stereoselectivity. [b] Run at 50 °C. [c] Determined by GC.

Once the optimal reaction conditions were established, the scope and limitations of this reaction were then investigated. As

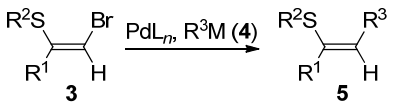
illustrated in Table 2, the hydrothiolation reaction was found to be quite effective over a wide range of alkynyl halides. Good yields were obtained with substrates possessing a number of conventional protecting groups, such as *tert*-butyldimethylsilyl (TBS), benzoyl (Bz), benzyl (Bn), and *tert*-butyldiphenylsilyl (TBDPS). For example, bromoalkyne **1f** led to the formation of **3fa** in 83% yield with excellent regio- and stereoselectivity (Table 2, **3fa**). The sterically demanding substrate **3g** also served as a viable substrate, although a high temperature of 50 °C was need for full conversion (Table 2, **3ga**). Moreover, functional groups such as halides, unprotected alcohols, alkenes, alkynes, aryl and heteroaryl groups were well tolerated (Table 2, **3ia**–**ma**). For instance, **2a** added to **1j** and **1k** in a highly regio- and stereoselective manner and furnished **3ja** and **3ka** in satisfactory yields (Table 2, **3ja** and **3ka**). Remarkably, the reaction of **1n** underwent smoothly to produce the double hydrothiolation product **3na** in an excellent yield (Table 2, **3na**).

Pleasingly, the reaction between alkynyl chloride **1o** and **2a** occurred uneventfully forming (*Z*)-β-chloro olefinic sulfide **3oa** in 79% yield, albeit at elevated reaction temperature (50 °C) (Table 2, **3oa**). Likewise, chloroalkynes **1p**–**r**, possessing ether, alkene, or alkyne substituents, all led to the desired products in good yields and excellent stereoselectivity (Table 2, **3pa**–**ra**). Of note, this protocol represents a mild and effective protocol for the regio- and stereoselective synthesis of (*Z*)-β-chloro vinyl sulfides.[16]

Then, we turned our attention to extend this reaction to aryl bromoacetylenes, although it[8,9] was reported that acetylenic sulfides could be obtained by the treatment of aryl bromoalkynes with thiols. We envisioned that using soft thiol nucleophiles might favor the addition rather than substitution of ethynyl bromides. As such, 2-mercaptopyrimidine (**2b**) was employed as a thiol reagent, and as expected, the hydrothiolation product **3sb** was isolated in 83% yield by treating phenylethynyl bromide (**1s**) with **2b**, albeit in a somewhat lower stereoselectivity (*Z*/*E* = 90:10) as compared to that of alkyl counterparts. Furthermore, the reaction was applicable for other aryl bromoacetylenes, providing (*Z*)-β-bromo vinylic sulfides in good yields and high stereoselectivity (Table 2, **3sb**–**wb**). In particular, 4-fluorophenyl ethynylbromide (**1t**) coupled with **2b** to give 81% of **3tb** as a 93:7 mixture of *Z*/*E* isomers, while the reaction of 4-methoxyphenyl and 3,4-dimethoxyphenyl substrates **1v** and **1w** produced the desired (*Z*)-β-bromo vinylic sulfides **3vb** and **3wb** in similar stereoselectivity (*Z*/*E* = 97:3), indicating that the electronic effect of bromoalkynes has little influence on this reaction. Unfortunately, the hydrothiolation of aryl chloroalkynes only gave the corresponding products in synthetic useless stereoselectivity even after a number of efforts.

The scope of this reaction with respect to thiol nucleophiles proved to be satisfactory. Under the standard reaction conditions, not only **2b** but also the bulky thiol **2c** added to **1f** regio- and stereoselectively, providing **3fb** and **3fc** in good yields (Table 2, **3fb** and **3fc**). Other thiols bearing additional functionality underwent the hydrothiolation reaction smoothly to generate the expected products in good yields with excellent stereoselectivity (Table 2, **3fd**–**fg**). For example, the stereospecific addition of *p*-toluenethiol (**2e**) to **3f** furnished **3fe**[8] in 80% yield (Table 2, **3fe**). The regio- and stereochemistry of this reaction was determined by the NOE measurements, and further confirmed by comparison of the data of products **3fa** and **3fe**–**g** with the literature.[8]

Table 3 The selective mono-coupling of **3**[a]



3 **5**

Entry	**3**	R^1	R^2	R^3M/**4**	Yield (%)[b]
1	**3aa**	$TBSO(CH_2)_2$	2-pyridyl	$PhB(OH)_2$/**4a**	90/**5a**
2	**3da**	$PhOCH_2$	2-pyridyl	$PhB(OH)_2$/**4a**	70/**5b**
3	**3fa**	*n*-C_8H_{17}	2-pyridyl	$PhB(OH)_2$/**4a**	83/**5c**
4	**3ga**	*n*-$C_4H_9(CH)Et$	2-pyridyl	$PhB(OH)_2$/**4a**	79/**5d**
5	**3ha**	$Ph(CH_2)_2$	2-pyridyl	$PhB(OH)_2$/**4a**	76/**5e**
6	**3ia**	$Cl(CH_2)_3$	2-pyridyl	$PhB(OH)_2$/**4a**	67/**5f**
8	**3la**	2-cyclohexenyl	2-pyridyl	$PhB(OH)_2$/**4a**	72/**5g**
9	**3ma**	$PhC{\equiv}CCH_2OCH_2$	2-pyridyl	$PhB(OH)_2$/**4a**	75/**5h**
10	**3ub**	4-Me-C_6H_4	2-pyrimidyl	$PhB(OH)_2$/**4a**	76/**5i**[c]
11	**3vb**	4-MeO-C_6H_4	2-pyrimidyl	$PhB(OH)_2$/**4a**	70/**5j**[d]
12	**3wb**	3,4-$(OMe)_2$-C_6H_3	2-pyrimidyl	$PhB(OH)_2$/**4a**	75/**5k**
13	**3aa**	$TBSO(CH_2)_2$	2-pyridyl	4-Me-$C_6H_4B(OH)_2$/**4b**	85/**5l**
14	**3fa**	*n*-C_8H_{17}	2-pyridyl	4-Me-$C_6H_4B(OH)_2$/**4b**	80/**5m**
15	**3fa**	*n*-C_8H_{17}	2-pyridyl	3-Me-$C_6H_4B(OH)_2$/**4c**	75/**5n**
16	**3fa**	*n*-C_8H_{17}	2-pyridyl	2-Me-$C_6H_4B(OH)_2$/**4d**	84/**5o**
17	**3fa**	*n*-C_8H_{17}	2-pyridyl	4-MeO-$C_6H_4B(OH)_2$/**4e**	79/**5p**
18	**3fa**	*n*-C_8H_{17}	2-pyridyl	4-F-$C_6H_4B(OH)_2$/**4f**	82/**5q**
19	**3fa**	*n*-C_8H_{17}	2-pyridyl	4-CF_3-$C_6H_4B(OH)_2$/**4g**	85/**5r**
20	**3fa**	*n*-C_8H_{17}	2-pyridyl	2-naphthyl$B(OH)_2$/**4h**	68/**5s**
21	**3fa**	*n*-C_8H_{17}	2-pyridyl	2-thienyl$B(OH)_2$/**4i**	75/**5t**
22	**3fa**	*n*-C_8H_{17}	2-pyridyl	(*E*)-styryl$B(OH)_2$/**4j**	76/**5u**
23	**3fa**	*n*-C_8H_{17}	2-pyridyl	$MeB(OH)_2$/**4k**	trace
24	**3fa**	*n*-C_8H_{17}	2-pyridyl	MeMgCl/**4l**	84/**5v**[e]
25	**3fa**	*n*-C_8H_{17}	2-pyridyl	MeZnCl/**4m**	80/**5v**[e]

[a] Reaction conditions for the Suzuki coupling: **3** (0.5 mmol), **4** (0.65 mmol), $Pd(dba)_2$ (0.025 mmol), XPhos (0.05 mmol), K_2CO_3 (0.75 mmol), toluene, 50 °C, 10 h. [b] Isolated yield. [c] *Z*/*E* = 93:7. [d] *Z*/*E* = 95:5. [e] The reaction was run with 5 mol% of $Pd(PPh_3)_4$ in THF at rt for 8 h.

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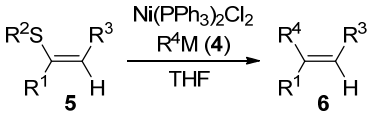
Next, the stepwise cross-coupling of (*Z*)-β-bromo alkenyl sulfides was investigated. Treatment of **3aa** with 5 mol% $Pd(dba)_2$, 10 mol% of PPh_3, 1.5 equiv of K_2CO_3, and 1.3 equiv of $PhB(OH)_2$ in THF at 80 °C for 10 h furnished the Suzuki[17] coupling product **5a** in 62% yield, and the C–S bond was completely intact under the reaction conditions. Utilizing toluene instead of THF as the solvent resulted in a better yield (80%). Finally, the evaluation of ligands revealed that Xphos[18] was the most effective ligand for this reaction, leading to **5a** in 90% yield (Table 3, entry 1). Therefore, running the reaction with 5 mol% of $Pd(dba)_2$, 10 mol% of Xphos, 1.5 equiv of K_2CO_3, and 1.3 equiv of $PhB(OH)_2$ in toluene at 80 °C appeared to the optimized reaction conditions for the Suzuki coupling of **3**.

As demonstrated in Table 3, in general, the Suzuki coupling of (*Z*)-β-bromo alkenyl sulfides **3** proceeded smoothly and provided olefinic sulfides **5** in high yields. Various functional groups like OTBS, OPh, F, Cl, Me, OMe, C–C double and triple bonds were well tolerated under the reaction conditions. (*Z*)-β-Bromo vinylic sulfide **3fa** gave rise to **5c** in 83% yield, while the reaction of **3ga** produced **5d** in 79% yield (Table 3, entries 3 and 4), implying the steric hindrance of **3** has no significant correlation with the yield.

On the other hand, the scope of this reaction with regard to boronic acids was investigated. In this respect, 4-, 3-, and 2-tolylboronic acids **4b**–**d** reacted with **3fa** to give the desired products in respective yields of 80%, 75%, and 84%, which indicated that the Suzuki coupling of **3** is not sensitive to steric hindrance of boronic acids (Table 3, entries 14–16). Introducing either electron-donating or electron-withdrawing groups into the benzene ring of **4** did not significantly affect the reaction yield, as demonstrated by the coupling of boronic acids **4e**–**g** (Table 3, entries 17–19). The reaction of heteroaryl boronic acid **4i** took place as well, forming the expected product **5t** in 75% yield (Table 3, entry 21). Additionally, the attempts to install a methyl group into **5** with the use of $MeB(OH)_2$ (**4k**) failed; fortunately, the utilization of Kumada coupling[19] with MeMgCl (**4l**) or Negishi coupling[20] with MeZnCl (**4m**) came to rescue, providing the methylation product **5v** in high yields (Table 3, entries 22–25). The stereochemistry of alkenyl sulfides **5** was identified by NOE measurements, and further confirmed by an X-ray diffraction analysis of **5i** (see ESI‡).

Table 4 Synthesis of trisubstituted alkenes via the Ni-catalyzed C–S bond coupling[a]



Entry	5	R^1	R^2	R^3	R^4M/4	Yield (%)[b]
1	**5a**	$TBSO(CH_2)_2$	2-pyridyl	Ph	MeMgCl/**4l**	80/**6a**
2	**5c**	*n*-C_8H_{17}	2-pyridyl	Ph	MeMgCl/**4l**	88/**6b**
3	**5d**	*n*-$C_4H_9(CH)Et$	2-pyridyl	Ph	MeMgCl/**4l**	trace
4	**5e**	$Ph(CH_2)_2$	2-pyridyl	Ph	MeMgCl/**4l**	72/**6c**
5	**5g**	2-cyclohexenyl	2-pyridyl	Ph	MeMgCl/**4l**	79/**6d**
6	**5i**	4-Me-C_6H_4	2-pyrimidyl	Ph	MeMgCl/**4l**	85/**6e**[c]
7	**5j**	4-MeO-C_6H_4	2-pyrimidyl	Ph	MeMgCl/**4l**	81/**6f**
8	**5l**	$TBSO(CH_2)_2$	2-pyridyl	4-Me-C_6H_4	MeMgCl/**4l**	78/**6g**
9	**5m**	*n*-C_8H_{17}	2-pyridyl	4-Me-C_6H_4	MeMgCl/**4l**	76/**6h**
10	**5n**	*n*-C_8H_{17}	2-pyridyl	3-Me-C_6H_4	MeMgCl/**4l**	72/**6i**
11	**5o**	*n*-C_8H_{17}	2-pyridyl	2-Me-C_6H_4	MeMgCl/**4l**	77/**6j**
12	**5p**	*n*-C_8H_{17}	2-pyridyl	4-MeO-C_6H_4	MeMgCl/**4l**	77/**6k**
13	**5q**	*n*-C_8H_{17}	2-pyridyl	4-F-C_6H_4	MeMgCl/**4l**	86/**6l**[c]
14	**5r**	*n*-C_8H_{17}	2-pyridyl	4-CF_3-C_6H_4	MeMgCl/**4l**	68/**6m**
15	**5s**	*n*-C_8H_{17}	2-pyridyl	2-naphthyl	MeMgCl/**4l**	81/**6n**
16	**5t**	*n*-C_8H_{17}	2-pyridyl	2-thienyl	MeMgCl/**4l**	66/**6o**[d]
17	**5u**	*n*-C_8H_{17}	2-pyridyl	(*E*)-styryl	MeMgCl/**4l**	80/**6p**
18	**5c**	*n*-C_8H_{17}	2-pyridyl	Ph	EtMgCl/**4n**	trace
19	**5c**	*n*-C_8H_{17}	2-pyridyl	Ph	PhMgCl/**4o**	69/**6q**[e]
20	**5c**	*n*-C_8H_{17}	2-pyridyl	Ph	4-Me-C_6H_4MgCl/**4p**	75/**6r**[f]
21	**5c**	*n*-C_8H_{17}	2-pyridyl	Ph	4-MeO-C_6H_4MgCl/**4q**	67/**6s**
22	**5c**	*n*-C_8H_{17}	2-pyridyl	Ph	CH_2=$CHCH_2$MgBr/**4r**	67/**6t**

[a] Reaction conditions: **5** (0.25 mmol), **4** (0.50 mmol), $Ni(PPh_3)_2Cl_2$ (0.025 mmol), THF, rt, 10 h. [b] Isolated yield. [c] *E*/*Z* = 93:7. [d] *E*/*Z* = 95:5. [e] *Z*/*E* = 97:3.[f] *Z*/*E* = 91:9.

Finally, the elaboration of stereodefined trisubstituted alkenes was achieved by the Ni-catalyzed coupling of C–S bond[21] with Grignard reagents. In the presence of 10 mol% of $Ni(PPh_3)_2Cl_2$, **5a** underwent the coupling with **4l** to generate the (*E*)-trisubstituted alkene **6a** in 80% yield (Table 4, entry 1). We found that the steric hindrance of R^1 group has a significant effect on the reaction. For example, the reaction of **5c** resulted in **6b**[11e] in 88% yield, while the bulky substrate **5d** was almost unreactive (Table 4, entries 2 and 3). In contrast, **5m**–**o** were converted into the corresponding products in comparable yields, which

demonstrated the steric hindrance of R^3 has little influence on the coupling reaction (Table 4, entries 9–11). Gratifyingly, the stereodefined 1,3-diene products could be assembled by this protocol, as shown by the production of **6d** and **6p** (Table 4, entries 5 and 17). It should be noted that **5b** and **5h** were not amenable to this reaction, owing to the cleavage of allylic or propagylic C–O bond under the reaction conditions.

Furthermore, the Grignard reagents were varied with **5c** acting as the coupling partner. As a result, the utilization of EtMgCl (**4n**) instead of **4l** only produced trace of the desired product because of the occurrence of β-H elimination process (Table 4, entry 18). On the contrary, aryl Grignard reagents were found to be effective coupling partners, for instance, the reaction of **5c** with PhMgCl (**4o**) provided (*Z*)-trisubstituted alkene **6q** in good yield with excellent stereoselectivity (Table 4, entry 19). In addition, CH_2=$CHCH_2MgBr$ (**4r**) also resulted in a reasonable yield of **6t** under the standard conditions (Table 4, entry 22).

Conclusions

In conclusion, we have developed an operationally simple and efficient protocol for the synthesis of (*Z*)-β-halo alkenyl sulfides via the K_2CO_3-promoted hydrothiolation of acetylenic halides under the mild reaction conditions, providing (*Z*)-β-bromo and (*Z*)-β-chloro alkenyl sulfides in high yields with good to excellent stereoselectivity. Both aryl and alkyl haloalkynes are effective substrates for this reaction. It constitutes a new advance in the development of regiocontrolled hydrothiolation of nonterminal alkynes. Notably, a new effective entry to stereodefined (*Z*)- or (*E*)-trisubstituted olefins featuring the iterative cross-coupling the C–X and C–S bonds of β-halo alkenyl sulfides has also been realized in this report.

Experimental section

General

Unless otherwise noted, materials obtained from commercial suppliers were used without further purification. ^1H and ^{13}C NMR spectra were measured on a 400 or 600 MHz NMR spectrometers using $CDCl_3$ as the solvent with tetramethylsilane (TMS) as the internal standard. Chemical shifts were given in δ relative to TMS, and the coupling constants were given in Hz. Column chromatography was performed using silica gel (300–400 mesh). High-resolution mass spectra (HRMS) analyses were carried out using a TOF MS instrument with EI or ESI source.

General procedure for K_2CO_3-promoted hydrothiolation of haloalkynes

To a mixture of 2-mercaptopyridine (**2a**) (66.6 mg, 0.6 mmol) and K_2CO_3 (89.7 mg, 0.65 mmol) in 2 mL of EtOH was added bromoalkyne **1a** (186.6 mg, 0.5 mmol). After stirring at room temperature for 10 h, the reaction mixture was quenched with water, extracted with EtOAc, dried over Na_2SO_4 and concentrated. Column chromatography on silica gel (petroleum ether/EtOAc = 20:1) gave **3aa** as a yellow oil (152.9 mg, 82% yield); ^1H NMR ($CDCl_3$, 400 MHz): δ 0.00 (s, 6H), 0.85 (s, 9H), 2.63 (t, J = 6.0 Hz, 2H), 3.72 (t, J = 6.1 Hz, 2H), 6.73 (s, 1H), 7.04–7.11 (m, 1H), 7.27 (d, J = 8.0 Hz, 1H), 7.56 (td, J = 7.8, 1.8 Hz, 1H), 8.47 (dd, J = 4.7, 0.8 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ –5.4, 18.2, 25.8, 40.7, 60.6, 113.4, 120.6, 123.5, 135.9, 136.9, 149.9, 156.9; MS (EI, *m*/*z*): 375 (2), 373 (M^+, 3), 294 (M^+–^{79}Br, 38), 163 (13); HRMS (EI) calcd for $C_{15}H_{24}BrNOSSi$ (M^+) 373.0531, found 373.0535.

Compound 3ba. 134.3 mg, 74% yield, colorless oil; ^1H NMR ($CDCl_3$, 600 MHz): δ 2.94 (t, J = 6.2 Hz, 2H), 4.48 (t, J = 6.2 Hz, 2H), 6.82 (s, 1H), 7.08–7.15 (m, 1H), 7.32 (d, J = 7.9 Hz, 1H), 7.46 (t, J = 7.7 Hz, 2H), 7.58 (qd, J = 7.7, 1.3 Hz, 2H), 8.02 (d, J = 8.2 Hz, 2 H), 8.51 (d, J = 4.2 Hz, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 36.7, 62.3, 113.6, 120.9, 123.7, 128.4, 129.5, 130.0, 133.0, 135.7, 136.8, 150.2, 156.3, 166.3; HRMS (ESI) calcd for $C_{16}H_{15}BrNO_2S$ $(M+H)^+$ 364.0007, found 364.0006.

Compound 3ca. 135.7 mg, 81% yield, yellow oil; ^1H NMR ($CDCl_3$, 400 MHz): δ 4.24 (s, 2H), 4.52 (s, 2H), 7.03–7.10 (m, 2H), 7.24–7.37 (m, 6H), 7.54 (td, J = 7.8, 1.7 Hz, 1H), 8.45 (d, J = 4.2 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 72.0, 72.3, 114.7, 120.8, 123.3, 127.6, 127.7, 128.3, 135.7, 136.7, 137.5, 149.9, 156.3; HRMS (ESI) calcd for $C_{15}H_{15}BrNOS$ $(M+H)^+$ 336.0058, found 336.0065.

Compound 3da. 147.7 mg, 92% yield, yellow oil; ^1H NMR ($CDCl_3$, 600 MHz): δ 4.80 (d, J = 1.5 Hz, 2H), 6.97 (d, J = 8.0 Hz, 2H), 7.00 (t, J = 7.4 Hz, 1H), 7.06–7.12 (m, 1H), 7.17 (t, J = 1.4 Hz, 1H), 7.30 (t, J = 8.0 Hz, 2H), 7.33 (d, J = 8.0 Hz, 1H), 7.54–7.60 (m, 1H), 8.49 (d, J = 4.8 Hz, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 70.1, 114.7, 115.5, 120.8, 121.3, 123.1, 129.4, 133.9, 136.8, 149.8, 155.9, 157.7; HRMS (ESI) calcd for $C_{14}H_{13}BrNOS$ $(M+H)^+$ 321.9901, found 321.9907.

Compound 3ea. 181.1 mg, 75% yield, white solid, mp 89–91 °C; ^1H NMR ($CDCl_3$, 400 MHz): δ 1.08 (s, 9H), 4.37 (d, J = 1.6 Hz, 2H), 6.98–7.08 (m, 2H), 7.27 (t, J = 1.5 Hz, 1H), 7.34–7.50 (m, 7H), 7.65 (dd, J = 6.5, 1.3 Hz, 4H), 8.37 (d, J = 3.6 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 19.2, 26.7, 66.8, 115.0, 120.4, 122.0, 127.7, 129.8, 132.7, 134.8, 135.4, 136.7, 149.8, 156.7; HRMS (ESI) calcd for $C_{24}H_{27}BrNOSSi$ $(M+H)^+$ 484.0766, found 484.0767.

Compound 3fa.[8] 135.7 mg, 83% yield, yellow oil; ^1H NMR (400 MHz, $CDCl_3$): δ 0.85 (t, J = 6.9 Hz, 3H), 1.16–1.28 (m, 10H), 1.43–1.53 (m, 2H), 2.41 (t, J = 7.4 Hz, 2H), 6.63 (s, 1H), 7.03–7.10 (m, 1H), 7.25 (d, J = 8.0 Hz, 1H), 7.55 (td, J = 7.9, 1.8 Hz, 1H), 8.47 (dd, J = 4.8, 0.9 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.0, 22.6, 28.1, 28.7, 29.1, 29.1, 31.7, 37.4, 110.7, 120.7, 123.8, 136.7, 139.9, 150.0, 156.8.

Compound 3ga. 117.4 mg, 75% yield, yellow oil; ^1H NMR ($CDCl_3$, 600 MHz): δ 0.81–0.94 (m, 6H), 1.18–1.29 (m, 4H), 1.42–1.58 (m, 4H), 2.31–2.38 (m, 1H), 6.80 (s, 1H), 7.00–7.06 (m, 1H), 7.20 (d, J = 8.1 Hz, 1H), 7.53 (td, J = 8.0, 1.6 Hz, 1H), 8.43 (d, J = 4.2 Hz, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 11.6, 13.9, 22.5, 26.0, 29.3, 32.5, 50.7, 114.6, 120.0, 122.3, 136.4, 142.3, 149.5, 157.4; MS (EI, *m*/*z*): 315 (4), 313 (M^+, 5), 234 (M^+–^{79}Br, 53), 177 (5); HRMS (EI) calcd for $C_{14}H_{20}BrNS$ (M^+) 313.0500, found 313.0502.

Compound 3ha. 140.4 mg, 88% yield, yellow oil; ^1H NMR ($CDCl_3$, 400 MHz): δ 2.71–2.79 (m, 2H), 2,80–2.87 (m, 2H), 6.58 (s, 1H), 7.07 (d, J = 8.0 Hz, 2H), 7.09–7.14 (m, 1H), 7.15–7.21 (m, 1H), 7.21–7.28 (m, 2H), 7.30 (d, J = 8.0 Hz, 1H), 7.59 (td, J = 7.8, 1.6 Hz, 1H), 8.52 (d, J = 4.1 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 34.6, 39.2, 111.4, 120.9, 124.1, 126.1, 128.3, 136.8, 138.8, 140.5, 150.0, 156.4; MS (EI, *m*/*z*): 321 (6),

319 (M^+, 6), 241 (11), 240 (M^+–^{79}Br, 59), 162 (3); HRMS (EI) calcd for $C_{15}H_{14}BrNS$ (M^+) 319.0030, found 319.0038.

Compound 3ia. 88.8 mg, 61% yield, yellow oil; ^{1}H NMR ($CDCl_3$, 600 MHz): δ 1.82–1.90 (m, 2H), 2.54 (t, J = 7.1 Hz, 2H), 3.40 (t, J = 6.3 Hz, 2H), 6.63 (s, 1H), 6.98–7.04 (m, 1H), 7.19 (d, J = 7.4 Hz, 1H), 7.49 (td, J = 7.8, 1.8 Hz, 1H), 8.39 (d, J = 4.8 Hz, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 30.4, 34.0, 43.6, 111.9, 120.9, 124.0, 136.9, 138.0, 150.0, 156.0; MS (EI, *m*/*z*): 293 (6), 291 (M^+, 7), 214 (37), 212 (M^+–^{79}Br, 100), 148 (20); HRMS (EI) calcd for $C_{10}H_{11}BrClNS$ (M^+) 290.9484, found 290.9479.

Compound 3ja. 120.5 mg, 77% yield, white solid, mp 114–116 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.18–1.30 (m, 1H), 1.46–1.61 (m, 3H), 1.62–1.78 (m, 4H), 1.79–1.88 (m, 2H), 5.29 (br, 1H), 6.97–7.05 (m, 1H), 7.26–7.33 (m, 2H), 7.52 (td, J = 7.8, 1.7 Hz, 1H), 8.31 (d, J = 4.5 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 22.0, 25.4, 36.9, 74.9, 120.3, 120.8, 122.4, 136.8, 144.9, 149.1, 158.2; HRMS (ESI) calcd for $C_{13}H_{17}BrNOS$ $(M+H)^+$ 314.0214, found 314.0204.

Compound 3ka. 94.5 mg, 73% yield, yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.63 (t, J = 4.9 Hz, 2H), 3.78–3.86 (m, 2H), 4.50 (br, 1H), 6.93 (s, 1H), 7.03–7.09 (m, 1H), 7.35 (d, J = 8.0 Hz, 1H), 7.57 (td, J = 8.0, 1.8 Hz, 1H), 8.34 (d, J = 4.9 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 42.9, 58.6, 117.8, 120.7, 124.0, 135.6, 137.0, 149.6, 157.6; MS (EI, *m*/*z*): 261 (3), 259 (M^+, 4), 180 (M^+–^{79}Br, 100), 163 (20); HRMS (EI) calcd for $C_9H_{10}BrNOS$ (M^+) 258.9666, found 258.9670.

Compound 3la. 103.3 mg, 70% yield, yellow oil; ^{1}H NMR ($CDCl_3$, 600 MHz): δ 1.46–1.55 (m, 2H), 1.56–1.64 (m, 2H), 2.00–2.07 (m, 2H), 2.18–2.26 (m, 2H), 6.39 (t, J = 4.0 Hz, 1H), 6.93 (s, 1H), 6.99–7.08 (m, 2H), 7.51 (td, J = 7.9, 1.8 Hz, 1H), 8.43 (d, J = 4.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 21.7, 22.5, 25.8, 27.0, 113.1, 120.0, 122.1, 130.9, 134.8, 136.5, 140.8, 149.4, 158.4; MS (EI, *m*/*z*): 297 (5), 295 (M^+, 7), 217 (18), 216 (M^+–^{79}Br, 100), 214 (5); HRMS (EI) calcd for $C_{13}H_{14}BrNS$ (M^+) 295.0030, found 295.0031.

Compound 3ma. 125.7 mg, 70% yield, yellow oil; ^{1}H NMR ($CDCl_3$, 600 MHz): δ 4.38 (s, 2H), 4.41 (s, 2H), 7.03–7.09 (m, 1H), 7.12 (s, 1H), 7.26–7.38 (m, 4H), 7.41 (d, J = 6.5 Hz, 2H), 7.54 (td, J = 7.8, 1.3 Hz, 1H), 8.46 (d, J = 4.2 Hz, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 58.1, 71.3, 84.3, 86.7, 115.3, 120.7, 122.2, 123.4, 128.2, 128.5, 131.6, 135.2, 136.8, 149.9, 156.1; HRMS (ESI) calcd for $C_{17}H_{15}BrNOS$ $(M+H)^+$ 360.0058, found 360.0058.

Compound 3na. 220.2 mg, 91% yield, white solid, mp 124–126 °C; ^{1}H NMR ($CDCl_3$, 600 MHz): δ 1.38–1.46 (m, 4H), 2.37 (t, J = 6.1 Hz, 4H), 6.58 (s, 2H), 7.03–7.12 (m, 2H), 7.23 (d, J = 8.0 Hz, 2H), 7.56 (td, J = 7.8, 1.8 Hz, 2H), 8.46 (d, J = 4.0 Hz, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 27.1, 36.8, 110.9, 120.7, 123.8, 136.7, 139.3, 149.9, 156.4; HRMS (ESI) calcd for $C_{18}H_{19}Br_2N_2S_2$ $(M+H)^+$ 484.9356, found 484.9354.

Compound 3oa. 111.8 mg, 79% yield, yellow oil; ^{1}H NMR ($CDCl_3$, 600 MHz): δ 0.86 (t, J = 7.0 Hz, 3H), 1.16–1.30 (m, 10H), 1.43–1.57 (m, 2H), 2,40 (t, J = 5.8 Hz, 2H), 6.43–6.50 (m, 1H), 7.01–7.13 (m, 1H), 7.23 (d, J = 7.9 Hz, 1H), 7.51–7.60 (m, 1H), 8.47 (d, J = 4.6 Hz, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 14.0, 22.5, 28.0, 28.7, 29.0, 29.1, 31.7, 36.1, 120.5, 121.5, 123.4, 136.3, 136.6, 149.9, 156.8; HRMS (ESI) calcd for $C_{15}H_{23}ClNS$ $(M+H)^+$ 284.1240, found 284.1242.

Compound 3pa. 116.4 mg, 80% yield, yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 4.26 (d, J = 1.3 Hz, 2H), 4.53 (s, 2H), 6.87 (t, J = 1.3 Hz, 1H), 7.04–7.10 (m, 1H), 7.23–7.40 (m, 6H), 7.55 (td, J = 7.8, 1.9 Hz, 1H), 8.45 (d, J = 4.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 71.2, 72.3, 120.7, 123.2, 125.4, 127.7, 127.7, 128.4, 132.2, 136.7, 137.5, 149.9, 156.4; HRMS (ESI) calcd for $C_{15}H_{15}ClNOS$ $(M+H)^+$ 292.0563, found 292.0560.

Compound 3qa. 127.6 mg, 81% yield, yellow oil, *Z*/*E* = 97:3; ^{1}H NMR ($CDCl_3$, 600 MHz): δ 4.41 (s, 2H), 4.42 (s, 2H), 6.93 (s, 1H), 7.03–7.09 (m, 1H), 7.29–7.38 (m, 4H), 7.42 (dd, J = 7.8, 1.6 Hz, 2H), 7.55 (td, J = 7.8, 1.8 Hz, 1H), 8.47 (d, J = 4.5 Hz, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 58.1, 70.6, 84.3, 86.8, 120.7, 122.3, 123.3, 125.9, 128.2, 128.5, 131.7, 131.8, 136.8, 150.0, 156.3; HRMS (ESI) calcd for $C_{17}H_{15}ClNOS$ $(M+H)^+$ 316.0563, found 316.0564.

Compound 3ra. 102.9 mg, 82% yield, yellow oil, *Z*/*E* = 95:5; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.45–1.54 (m, 2H), 1.55–1.65 (m, 2H), 2.00–2.09 (m, 2H), 2.15–2.24 (m, 2H), 6.36 (t, J = 4.1 Hz, 1H), 6.71 (s, 1H), 6.95–7.04 (m, 2H), 7.48 (td, J = 7.9, 1.9 Hz, 1H), 8.39 (dd, J = 4.8, 0.9 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.7, 22.4, 25.8, 26.8, 119.9, 121.7, 123.0, 130.6, 133.7, 136.4, 137.4, 149.4, 158.5; MS (EI, *m*/*z*): 255 (1), 253 (4), 251 (M^+, 6), 216 (M^+–^{35}Cl, 100), 173 (19); HRMS (EI) calcd for $C_{13}H_{14}ClNS$ (M^+) 251.0535, found 251.0538.

Compound 3sb. 121.2 mg, 83% yield, yellow oil, *Z*/*E* = 90:10; ^{1}H NMR ($CDCl_3$, 600 MHz): δ 6.93 (t, J = 4.8 Hz, 1H), 7.15 (s, 1H), 7.27–7.31 (m, 3H), 7.58–7.63 (m, 2H), 8.42 (d, J = 4.8 Hz, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 115.6, 117.2, 127.3, 128.3, 128.4, 138.4, 138.9, 157.4, 170.0; MS (EI, *m*/*z*): 294 (11), 292 (M^+, 13), 215 (16), 213 (100), 212 (2); HRMS (EI) calcd for $C_{12}H_9BrN_2S$ (M^+) 291.9670, found 291.9673.

Compound 3tb. 127.1 mg, 82% yield, yellow oil, *Z*/*E* = 93:7, mp 64–66 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 6.90–6.99 (m, 3H), 7.06 (s, 1H), 7.52–7.58 (m, 2H), 8.40 (d, J = 4.8 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 115.2 (d, J = 21.5 Hz), 117.2, 129.1 (d, J = 8.2 Hz), 135.1 (d, J = 3.1 Hz), 137.4, 144.6, 157.5, 162.6 (d, J = 247 Hz), 169.8; MS (EI, *m*/*z*): 311 (8), 310 (M^+, 9), 233 (15), 231 (100), 199 (2); HRMS (EI) calcd for $C_{12}H_8BrFN_2S$ (M^+) 309.9576, found 309.9581.

Compound 3ub. 123.9 mg, 81% yield, yellow oil, *Z*/*E* = 93:7, mp 79–81 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.30 (s, 3H), 6.91 (t, J = 4.9 Hz, 1H), 7.08 (s, 1H), 7.10 (s, 2H), 7.49 (d, J = 8.2 Hz, 2H), 8.41 (d, J = 4.8 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.1, 114.9, 117.1, 127.2, 129.0, 136.1, 138.2, 138.4, 157.4, 170.2; MS (EI, *m*/*z*): 308 (4), 306 (M^+, 4), 227 (69), 226 (3), 147 (21); HRMS (EI) calcd for $C_{13}H_{11}BrN_2S$ (M^+) 305.9826, found 305.9828.

Compound 3vb. 128.8 mg, 80% yield, yellow oil, *Z*/*E* = 97:3, mp 90–92 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 3.75 (s, 3H), 6.74–6.81 (m, 2H), 6.90 (t, J = 4.8 Hz, 1H), 7.02 (s, 1H), 7.46–7.53 (m, 2H), 8.39 (d, J = 4.8 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 55.1, 113.6, 113.8, 117.1, 128.6, 131.3, 137.7, 157.4, 159.7, 170.1; MS (EI, *m*/*z*): 323 (11), 322 (M^+, 10), 243 (100), 242 (8), 212 (9); HRMS (EI) calcd for $C_{13}H_{11}BrN_2OS$ (M^+) 321.9775, found 321.9769.

Compound 3wb. 160.2 mg, 91% yield, yellow oil, *Z*/*E* = 97:3, mp 104–106 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 3.79 (d, J = 2.6 Hz, 6H), 6.71 (d, J = 8.4 Hz, 1H), 6.88 (t, J = 4.8 Hz, 1H), 7.00

(s, 1H), 7.07 (d, J = 2.1 Hz, 1H), 7.13 (dd, J = 8.4, 2.1 Hz, 1H), 8.37 (d, J = 4.9 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 55.6, 55.7, 110.3, 110.5, 113.6, 117.1, 120.1, 131.6, 138.0, 148.4, 149.1, 157.3, 170.0; HRMS (ESI) calcd for $C_{14}H_{14}BrN_2O_2S$ $(M+H)^+$ 352.9959, found 352.9955.

Compound 3fb. 131.2 mg, 80% yield, yellow solid, mp 40–41 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.84 (t, J = 6.8 Hz, 3H), 1.19–1.28 (m, 10H), 1.49–1.58 (m, 2H), 2.57 (t, J = 7.5 Hz, 2H), 6.73 (s, 1H), 6.99 (t, J = 4.8 Hz, 1H), 8.51 (d, J = 4.9 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.0, 22.5, 28.0, 28.8, 29.0, 29.1, 31.7, 37.8, 113.5, 117.0, 138.5, 157.5, 170.7; MS (EI, *m*/*z*): 329 (3), 328 (M^+, 3), 249 (M^+–^{79}Br, 100), 150 (33), 149 (6); HRMS (EI) calcd for $C_{14}H_{21}BrN_2S$ (M^+) 328.0609, found 328.0608.

Compound 3fc. 138.8 mg, 78% yield, yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.84 (t, J = 6.9 Hz, 3H), 1.19–1.29 (m, 10H), 1.47–1.56 (m, 2H), 2.37 (s, 6H), 2.61 (t, J = 7.5 Hz, 2H), 6.61 (s, 1H), 6.71 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.0, 22.5, 23.8, 28.1, 28.8, 29.1, 29.2, 31.7, 37.4, 111.6, 116.2, 139.1, 167.3, 169.3; HRMS (ESI) calcd for $C_{16}H_{26}BrN_2S$ $(M+H)^+$ 357.1000, found 357.1004.

Compound 3fd. 140.3 mg, 85% yield, yellow oil; ^{1}H NMR ($CDCl_3$, 600 MHz): δ 0.83 (t, J = 7.2 Hz, 3H), 1.08–1.26 (m, 10H), 1.33–1.39 (m, 2H), 1.93 (t, J = 7.6 Hz, 2H), 3.66 (s, 3H), 6.19 (s, 1H), 7.05 (s, 1H), 7.10 (s, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 14.0, 22.4, 27.6, 28.5, 28.9, 28.9, 31.6, 33.8, 36.0, 102.3, 123.7, 129.9, 136.1, 141.1; MS (EI, *m*/*z*): 331 (1), 330 (M^+, 1), 249 (2), 151 (3), 114 (100); HRMS (EI) calcd for $C_{14}H_{23}BrN_2S$ (M^+) 330.0765, found 330.0767.

Compound 3fe.[8] 136.0 mg, 80% yield, yellow oil; ^{1}H NMR ($CDCl_3$, 600 MHz): δ 0.91 (t, J = 7.2 Hz, 3H), 1.13–1.34 (m, 10H), 1.36–1.44 (m, 2H), 2.11 (t, J = 7.4 Hz, 2H), 2.36 (s, 3H), 6.24 (s, 1H), 7.17 (d, J = 7.9 Hz, 2H), 7.37 (d, J = 8.1 Hz, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 14.1, 21.1, 22.6, 28.1, 28.6, 29.0, 29.1, 31.7, 35.8, 102.2, 128.0, 129.7, 133.7, 138.2, 142.9.

Compound 3ff.[8] 145.5 mg, 76% yield, yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.86 (t, J = 6.9 Hz, 3H), 1.19–1.29 (m, 10H), 1.51–1.59 (m, 2H), 2.54 (t, J = 7.5 Hz, 2H), 6.74 (s, 1H), 7.35 (t, J = 7.6 Hz, 1H), 7.45 (t, J = 7.7 Hz, 1H), 7.78 (d, J = 8.0 Hz,1H), 7.96 (d, J = 8.1 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.0, 22.5, 28.1, 28.6, 29.0, 29.1, 31.7, 37.7, 112.9, 120.9, 122.3, 124.9, 126.2, 136.1, 139.2, 153.5, 163.0.

Compound 3fg.[8] 111.0 mg, 70% yield, yellow oil; ^{1}H NMR ($CDCl_3$, 600 MHz): δ 0.85 (t, J = 5.6 Hz, 3H), 1.14–1.28 (m, 10H), 1.42–1.52 (m, 2H), 2.23 (t, J = 6.5 Hz, 2H), 6.36 (s, 1H), 8.44 (s, 1H), 12.42 (br, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 14.0, 22.5, 27.8, 28.6, 29.0, 29.1, 31.7, 36.6, 106.0, 139.3, 146.4, 153.5.

General procedure for the Suzuki coupling of 3

To a mixture of $PhB(OH)_2$ (97.3 mg 0.65 mmol), $Pd(dba)_2$ (14.3 mg, 0.025 mmol), XPhos (23.8 mg, 0.05 mmol), and K_2CO_3 (103.5 mg, 0.75 mmol) in 2 mL of toluene was added **3aa** (186.5 mg, 0.5 mmol) under nitrogen atmosphere. The resulting mixture was stirred at 80 °C overnight (around 10 h), then quenched with water, extracted with EtOAc, dried over Na_2SO_4 and concentrated. Column chromatography on silica gel (petroleum ether/EtOAc = 15:1) gave **5a** as a colorless oil (167.0 mg, 90% yield); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.05 (s, 6H), 0.90 (s, 9H), 2.71 (t, J = 6.2 Hz, 2H), 3.88 (t, J = 6.3 Hz, 2H), 6.96–7.03 (m, 1H), 7.08 (s, 1H), 7.19–7.33 (m, 4H), 7.49 (td, J = 7.9, 1.8 Hz, 1H), 7.56 (d, J = 7.5 Hz, 2H), 8.45 (d, J = 4.3 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ –5.4, 18.2, 25.8, 42.7, 61.5, 120.0, 122.6, 127.5, 127.9, 129.0, 129.1, 136.2, 136.5, 138.2, 149.7, 158.8; MS (EI, *m*/*z*): 371 (M^+, 6), 256 (3), 240 (2), 226 (60); HRMS (EI) calcd for $C_{21}H_{29}NOSSi$ (M^+) 371.1739, found 371.1742.

Compound 5b. 111.7 mg, 70% yield, yellow oil, mp 113–115 °C; ^{1}H NMR ($CDCl_3$, 600 MHz): δ 4.87 (d, J = 1.5 Hz, 2H), 6.98–7.03 (m, 1H), 7.04–7.09 (m, 3H), 7.28–7.37 (m, 6H), 7.47 (s, 1H), 7.55 (td, J = 7.8, 1.9 Hz, 1H), 7.65 (d, J = 7.4 Hz, 2H), 8.55 (ddd, J = 4.9, 1.8, 0.8 Hz, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 71.4, 115.0, 120.3, 121.1, 122.3, 126.6, 128.0, 128.2, 129.4, 129.4, 135.4, 136.8, 137.2, 149.9, 158.2, 158.3; HRMS (ESI) calcd for $C_{20}H_{18}NOS$ $(M+H)^+$ 320.1109, found 320.1110.

Compound 5c. 134.9 mg, 83% yield, yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.88 (t, J = 6.6 Hz, 3H), 1,15–1.27 (m, 10H), 1.56–1.70 (m, 2H), 2.49 (t, J = 7.5 Hz, 2H), 6.96–7.04 (m, 2H), 7.17–7.25 (m, 2H), 7.29 (dd, J = 13.9, 6.3 Hz, 2H), 7.50 (td, J = 7.8, 1.7 Hz, 1H), 7.55 (d, J = 7.5 Hz, 2H), 8.46 (d, J = 4.7 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.1, 22.6, 28.8, 28.9, 29.2, 29.3, 31.8, 39.5, 120.0, 122.7, 127.4, 127.9, 129.2, 133.3, 135.8, 136.4, 136.4, 149.9, 158.9; MS (EI, *m*/*z*): 325 (M^+, 2), 248 (8), 226 (67), 212 (33), ; HRMS (EI) calcd for $C_{21}H_{27}NS$ (M^+) 325.1864, found 325.1854.

Compound 5d. 122.8 mg, 79% yield, yellow oil; ^{1}H NMR ($CDCl_3$, 600 MHz): δ 0.90 (t, J = 7.0 Hz, 3H), 0.95 (t, J = 7.4 Hz, 3H), 1.28–1.37 (m, 4H), 1.54–1.72 (m, 4H), 2.32–2.40 (m, 1H), 6.92–6.97 (m, 1H), 6.99 (s, 1H), 7.14–7.20 (m, 2H), 7.24 (t, J = 7.5 Hz, 2H), 7.37–7.41 (m, 1H), 7.62 (d, J = 7.6 Hz, 2H), 8.40 (ddd, J = 4.9, 1.8, 0.8 Hz, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 11.7, 14.0, 22.8, 26.4, 29.5, 32.9, 51.6, 119.6, 122.0, 127.4, 127.9, 129.1, 135.9, 136.0, 136.2, 136.3, 149.2, 159.2; MS (EI, *m*/*z*): 311 (M^+, 4), 282 (48), 234 (24), 112 (100); HRMS (EI) calcd for $C_{20}H_{25}NS$ (M^+) 311.1708, found 311.1706.

Compound 5e. 120.5 mg, 76% yield, yellow oil; ^{1}H NMR ($CDCl_3$, 600 MHz): δ 2.85 (t, J = 8.0 Hz, 2H), 3.02 (t, J = 7.0 Hz, 2H), 6.95 (s, 1H), 7.04–7.10 (m, 1H), 7.17–7.25 (m, 3H), 7.26–7.36 (m, 6H), 7.50–7.60 (m, 3H), 8.53 (dd, J = 4.9, 0.8 Hz, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 35.1, 41.3, 120.1, 122.9, 125.9, 127.5, 127.9, 128.2, 128.5, 129.1, 131.9, 136.2, 136.6, 136.7, 141.2, 149.8, 158.6; MS (EI, *m*/*z*): 317 (M^+, 3), 240 (3), 226 (100), 149 (5); HRMS (EI) calcd for $C_{21}H_{19}NS$ (M^+) 317.1238, found 317.1242.

Compound 5f. 96.8 mg, 67% yield, yellow oil; ^{1}H NMR ($CDCl_3$, 600 MHz): δ 2.08–2.17 (m, 2H), 2,71 (t, J = 7.2 Hz, 2H), 3.59 (t, J = 6.4 Hz, 2H), 7.04–7.09 (m, 1H), 7.10 (s, 1H), 7.23–7.30 (m, 2H), 7.33 (t, J = 7.4 Hz, 2H), 7.52–7.60 (m, 3H), 8.49 (dd, J = 4.9, 1.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 31.1, 36.2, 44.0, 120.3, 123.0, 127.7, 128.0, 129.2, 131.0, 135.9, 136.8, 137.2, 149.7, 158.1; MS (EI, *m*/*z*): 291 (1), 289 (M^+, 2), 254 (1), 226 (23), 212 (12); HRMS (EI) calcd for $C_{16}H_{16}ClNS$ (M^+) 289.0692, found 289.0697.

Compound 5g. 105.5 mg, 72% yield, yellow oil; ^{1}H NMR ($CDCl_3$, 600 MHz): δ 1.55–1.63 (m, 2H), 1.68–1.76 (m, 2H), 2.11–2.17 (m, 2H), 2.40–2.47 (m, 2H), 6.56 (t, J = 3.8 Hz, 1H), 6.95–7.01 (m, 1H), 7.08 (d, J = 8.1 Hz, 1H), 7.18–7.26 (m, 2H), 7.30 (t, J = 7.6 Hz, 2H), 7.42–7.49 (m, 1H), 7.62 (d, J = 7.6 Hz, 2H), 8.42 (d, J = 4.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 22.0, 22.9, 26.0, 27.3, 119.5, 121.4, 127.5, 127.9, 128.3, 128.9,

129.6, 129.9, 133.8, 136.4, 136.6, 149.2, 160.6; MS (EI, *m*/*z*): 293 (M^+, 8), 260 (25), 216 (82), 112 (100); HRMS (EI) calcd for $C_{19}H_{19}NS$ (M^+) 293.1238, found 293.1236.

Compound 5h. 133.9 mg, 75% yield, yellow oil; ^{1}H NMR ($CDCl_3$, 600 MHz): δ 4.48 (d, J = 1.3 Hz, 2H), 4.51 (s, 2H), 7.02 (ddd, J = 7.4, 4.9, 0.9 Hz, 1H), 7.28–7.37 (m, 7H), 7.41–7.46 (m, 3H), 7.50 (td, J = 7.8, 1.9 Hz, 1H), 7.66 (d, J = 7.3 Hz, 2H), 8.47 (ddd, J = 4.8, 1.8, 0.8 Hz, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 58.1, 73.1, 84.8, 86.5, 120.2, 122.5, 127.8, 128.0, 128.1, 128.2, 128.4, 129.4, 131.7, 135.5, 136.6, 137.3, 149.9, 158.2; HRMS (ESI) calcd for $C_{23}H_{20}NOS$ $(M+H)^+$ 358.1266, found 358.1263.

Compound 5i. 115.5 mg, 76% yield, white solid, *Z*/*E* = 93:7, mp 136–138 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.35 (s, 3H), 6.87 (t, J = 4.8 Hz, 1H), 7.14 (d, J = 8.1 Hz, 2H), 7.23–7.29 (m, 1H), 7.30–7.40 (m, 3H), 7.64–7.72 (m, 4H), 8.40 (d, J = 4.8 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.1, 116.9, 127.2, 127.9, 128.0, 128.9, 129.5, 131.1, 136.6, 137.1, 137.7, 138.8, 157.4, 171.6; MS (EI, *m*/*z*): 304 (M^+, 8), 225 (3), 213 (14), 193 (18); HRMS (EI) calcd for $C_{19}H_{16}N_2S$ (M^+) 304.1034, found 304.1033.

Crystal data for **5i** ($C_{19}H_{16}N_2S$, 304.66): triclinic, space group P1, a = 11.0704(14) Å, b = 22.732(3) Å, c = 17.8836(17) Å, U = 13.0490(17) Å^3, Z = 1, T = 296(2) K, absorption coefficient 0.201 mm^{-1}, reflections collected 27224, independent reflections 13018 [R(int) = 0.0826], refinement by full-matrix least-squares on F^2, data/restraints/parameters 13018/1/793, goodness-of-fit on F^2 = 0.913, final R indices [I>2σ(I)] R_1 = 0.0785, wR_2 = 0.1706, R indices (all data) R_1 = 0.2186, wR_2 = 0.2387, largest diff peak and hole 0.806 and –0.282 e.Å^{-3}. Crystallographic data for the structure **5i** have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC 981003.

Compound 5j. 112.0 mg, 70% yield, yellow solid, *Z*/*E* = 95:5, mp 107–109 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 3.80 (s, 3H), 6.82–6.90 (m, 3H), 7.22–7.28 (m, 1H), 7.29–7.36 (m, 3H), 7.66 (d, J = 7.6 Hz, 2H), 7.72 (d, J = 8.8 Hz, 2H), 8.40 (d, J = 4.9 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 55.2, 113.5, 116.9, 127.7, 128.0, 128.6, 129.4, 130.7, 134.1, 136.2, 136.7, 157.4, 159.4, 171.6; MS (EI, *m*/*z*): 321 (3), 320 (M^+, 2), 289 (8), 241 (18), 240 (100); HRMS (EI) calcd for $C_{19}H_{16}N_2OS$ (M^+) 320.0983, found 320.0989.

Compound 5k. 131.3 mg, 75% yield, yellow solid, mp 141–143 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 3.86 (d, J = 6.5 Hz, 6H), 6.81 (d, J = 8.4 Hz, 1H), 6.87 (t, J = 4.8 Hz, 1H), 7.20–7.27 (m, 1H), 7.28–7.35 (m, 4H), 7.37 (dd, J = 8.4, 2.1 Hz, 1H), 7.66 (d, J = 7.5 Hz, 2H), 8.39 (d, J = 4.8 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 55.7, 55.8, 110.4, 110.6, 116.9, 120.0, 127.7, 128.0, 129.3, 131.0, 134.3, 136.1, 136.6, 148.4, 148.8, 157.3, 171.4; HRMS (ESI) calcd for $C_{20}H_{19}N_2O_2S$ $(M+H)^+$ 351.1167, found 351.1170.

Compound 5l. 163.6 mg, 85% yield, yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.03 (s, 6H), 0.88 (s, 9H), 2.32 (s, 3H), 2.69 (t, J = 6.3 Hz, 2H), 3.86 (t, J = 6.3 Hz, 2H), 7.00–7.07 (m, 2H), 7.10 (d, J = 8.0 Hz, 2H), 7.23–7.29 (m, 1H), 7.45 (d, J = 8.0 Hz, 2H), 7.52 (td, J = 7.9, 1.7 Hz, 1H), 8.46 (d, J = 4.2 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ –5.3, 18.3, 21.2, 25.9, 42.9, 61.5, 120.0, 122.6, 127.7, 128.7, 129.1, 133.3, 136.9, 137.6, 138.7, 149.4, 159.0; MS (EI, *m*/*z*): 385 (M^+, 1), 254 (7), 240 (89), 148 (3); HRMS (EI) calcd for $C_{22}H_{31}NOSSi$ (M^+) 385.1896, found 385.1892.

Compound 5m. 135.6 mg, 80% yield, yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.89 (t, J = 6.9 Hz, 3H), 1.22–1.34 (m, 10H), 1.59–1.69 (m, 2H), 2.32 (s, 3H), 2.50 (t, J = 7.3 Hz, 2H), 6.97–7.05 (m, 2H), 7.11 (d, J = 8.0 Hz, 2H), 7.22 (d, J = 8.0 Hz, 1H), 7.44–7.54 (m, 3H), 8.47 (dd, J = 4.9, 1.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.0, 21.2, 22.6, 28.8, 28.9, 29.1, 29.3, 31.8, 39.5, 119.8, 122.5, 128.6, 129.1, 132.1, 133.5, 136.0, 136.4, 137.3, 149.7, 159.1; MS (EI, *m*/*z*): 339 (M^+, 3), 248 (10), 240 (85), 226 (30); HRMS (EI) calcd for $C_{22}H_{29}NS$ (M^+) 339.2021, found 339.2028.

Compound 5n. 127.1 mg, 75% yield, yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.90 (t, J = 6.6 Hz, 3H), 1.23–1.34 (m, 10H), 1.61–1.67 (m, 2H), 2.32 (s, 3H), 2.50 (t, J = 7.5 Hz, 2H), 6.94–7.10 (m, 3H), 7.15–7.25 (m, 2H), 7.35 (s, 1H), 7.40 (d, J = 7.7 Hz, 1H), 7.49 (td, J = 7.8, 1.7 Hz, 1H), 8.46 (d, J = 4.2 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.0, 21.3, 22.6, 28.8, 28.9, 29.1, 29.3, 31.8, 39.4, 119.9, 122.7, 126.1, 127.8, 128.2, 129.9, 133.0, 135.8, 136.2, 136.4, 137.3, 149.7, 158.9; MS (EI, *m*/*z*): 339 (M^+, 3), 248 (22), 226 (43), 111 (100); HRMS (EI) calcd for $C_{22}H_{29}NS$ (M^+) 339.2021, found 339.2019.

Compound 5o. 142.4 mg, 84% yield, yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.89 (t, J = 6.6 Hz, 3H), 1.20–1.34 (m, 10H), 1.60–1.70 (m, 2H), 2.31 (s, 3H), 2.54 (t, J = 7.3 Hz, 2H), 6.98–7.04 (m, 2H), 7.08–7.18 (m, 3H), 7.20 (d, J = 8.0 Hz, 1H), 7.39 (d, J = 7.2 Hz, 1H), 7.50 (td, J = 7.8, 1.9 Hz, 1H), 8.47 (dd, J = 4.9, 1.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.1, 20.0, 22.6, 28.6, 28.9, 29.2, 29.3, 31.8, 38.3, 119.8, 123.0, 125.2, 127.5, 129.1, 129.5, 134.6, 134.9, 136.1, 136.1, 136.2, 149.8, 159.2; MS (EI, *m*/*z*): 339 (M^+, 4), 248 (23), 240 (100), 226 (38); HRMS (EI) calcd for $C_{22}H_{29}NS$ (M^+) 339.2021, found 339.2023.

Compound **5p.** 140.2 mg, 79% yield, yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.88 (t, J = 6.8 Hz, 3H), 1.22–1.30 (m, 10H), 1.57–1.67 (m, 2H), 2.47 (t, J = 7.3 Hz, 2H), 3.78 (s, 3H), 6.78–6.88 (m, 2H), 6.95 (s, 1H), 7.00 (ddd, J = 7.4, 4.9, 0.9 Hz, 1H), 7.21 (d, J = 8.0 Hz, 1H), 7.49 (td, J = 7.8, 1.9 Hz, 1H), 7.55 (d, J = 8.7 Hz, 2H), 8.43–8.48 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.0, 22.6, 28.8, 28.9, 29.1, 29.3, 31.8, 39.7, 55.1, 113.3, 119.8, 122.3, 128.9, 130.5, 130.7, 135.8, 136.5, 149.7, 158.9, 159.2; MS (EI, *m*/*z*): 355 (M^+, 2), 256 (30), 248 (2), 160 (100); HRMS (EI) calcd for $C_{22}H_{29}NOS$ (M^+) 355.1970, found 355.1971.

Compound 5q. 140.6 mg, 82% yield, yellow oil; ^{1}H NMR ($CDCl_3$, 600 MHz): δ 0.90 (t, J = 7.1 Hz, 3H), 1.22–1.36 (m, 10H), 1.60–1.67 (m, 2H), 2.50 (t, J = 7.4 Hz, 2H), 6.94–7.03 (m, 3H), 7.04 (ddd, J = 7.3, 4.9, 0.8 Hz, 1H), 7.23 (d, J = 8.0 Hz, 1H), 7.52 (td, J = 7.8, 1.9 Hz, 1H), 7.52–7.58 (m, 2H), 8.45–8.50 (m, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 14.0, 22.6, 28.7, 28.9, 29.1, 29.3, 31.8, 39.5, 114.8 (d, J = 21.5 Hz), 120.0, 122.7, 130.8 (d, J = 8.2 Hz), 132.4 (d, J = 3.2 Hz), 133.2, 134.5, 136.4, 149.9, 158.6, 161.9 (d, J = 246.1 Hz); MS (EI, *m*/*z*): 343 (M^+, 2), 244 (13), 230 (5), 152 (4); HRMS (EI) calcd for $C_{21}H_{26}FNS$ (M^+) 343.1770, found 343.1769.

Compound 5r. 167.0 mg, 85% yield, yellow oil; ^{1}H NMR ($CDCl_3$, 600 MHz): δ 0.90 (t, J = 7.0 Hz, 3H), 1.24–1.35 (m, 10H), 1.62–1.70 (m, 2H), 2.54 (t, J = 7.4 Hz, 2H), 7.00 (s, 1H), 7.04–7.09 (m, 1H), 7.26 (d, J = 8.0 Hz, 1H), 7.51–7.58 (m, 3H), 7.65 (d, J = 8.2 Hz, 2H), 8.50 (dd, J = 4.8, 0.9 Hz, 1H); ^{13}C

NMR ($CDCl_3$, 150 MHz): δ 14.1, 22.6, 28.7, 28.9, 29.2, 29.3, 31.8, 39.4, 120.4, 123.3, 124.2(q, J = 270.3 Hz), 124.9 (q, J = 3.7 Hz), 129.1, 129.4, 133.7, 136.6, 140.1, 150.1, 158.1; MS (EI, m/z): 393 (M^+, 1), 294 (11), 280 (8), 248 (8); HRMS (EI) calcd for $C_{22}H_{26}F_3NS$ (M^+) 393.1738, found 393.1738.

Compound 5s. 127.5 mg, 68% yield, yellow oil; ^{1}H NMR ($CDCl_3$, 600 MHz): δ 0.78 (t, J = 7.1 Hz, 3H), 1.13–1.25 (m, 10H), 1.53–1.61 (m, 2H), 2.44 (t, J = 7.3 Hz, 2H), 6.88 (ddd, J = 7.4, 4.9, 1.0 Hz, 1H), 7.04 (s, 1H), 7.14 (d, J = 8.0 Hz, 1H), 7.28–7.34 (m, 2H), 7.35–7.40 (m, 1H), 7.60–7.70 (m, 4H), 7.86 (s, 1H), 8.36 (ddd, J = 4.9, 1.8, 0.7 Hz, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 14.0, 22.6, 28.8, 28.9, 29.2, 29.3, 31.8, 39.6, 120.0, 122.9, 125.9, 126.0, 127.0, 127.3, 127.4, 128.1, 128.5, 132.6, 133.0, 133.7, 133.9, 135.7, 136.5, 149.7, 158.8; MS (EI, m/z): 375 (M^+, 5), 276 (13), 262 (3), 181 (100); HRMS (EI) calcd for $C_{25}H_{29}NS$ (M^+) 375.2021, found 375.2017.

Compound 5t. 124.1 mg, 75% yield, yellow oil; ^{1}H NMR ($CDCl_3$, 600 MHz): δ 0.90 (t, J = 7.0 Hz, 3H), 1.23–1.34 (m, 10H), 1.59–1.70 (m, 2H), 2.49 (t, J = 7.4 Hz, 2H), 6.96–7.00 (m, 1H), 7.00–7.05 (m, 1H), 7.16–7.27 (m, 4H), 7.51 (td, J = 7.8, 1.8 Hz, 1H), 8.48 (d, J = 4.7 Hz, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 14.0, 22.6, 28.8, 29.0, 29.2, 29.3, 31.8, 39.7, 120.0, 121.7, 125.9, 127.2, 129.7, 129.9, 130.9, 136.6, 139.5, 149.9, 158.8; HRMS (ESI) calcd for $C_{19}H_{26}NS_2$ $(M+H)^+$ 332.1507, found 332.1512.

Compound 5u. 133.4 mg, 76% yield, yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.89 (t, J = 6.8 Hz, 3H), 1.24–1.34 (m, 10H), 1.55–1.63 (m, 2H), 2.46 (t, J = 7.5 Hz, 2H), 6.69 (d, J = 15.7 Hz, 1H), 6.77 (d, J = 10.5 Hz, 1H), 6.98–7.05 (m, 1H), 7.16–7.45 (m, 7H), 7.51 (td, J = 7.9, 1.8 Hz, 1H), 8.47 (dd, J = 4.8, 0.9 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.0, 22.6, 28.7, 29.0, 29.1, 29.3, 31.8, 38.8, 119.8, 121.9, 125.9, 126.6, 127.8, 128.5, 134.1, 134.4, 136.5, 137.1, 137.2, 149.8, 159.5; HRMS (ESI) calcd for $C_{23}H_{30}NS$ $(M+H)^+$ 352.2099, found 352.2091.

Compound 5v. It was prepared from **3fa** and 1.3 equiv of MeMgCl with 5 mol% of $Pd(PPh_3)_4$ in THF at rt for 8 h, 110.5 mg, 84% yield, colorless oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.86 (t, J = 6.8 Hz, 3H), 1.18–1.29 (m, 10H), 1.44–1.57 (m, 2H), 1.86 (d, J = 6.7 Hz, 3H), 2.31 (t, J = 7.5 Hz, 2H), 6.14 (q, J = 6.6 Hz, 1H), 6.95–7.01 (m, 1H), 7.12 (d, J = 8.0 Hz, 1H), 7.49 (td, J = 7.7, 1.8 Hz, 1H), 8.43 (d, J = 3.9 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.1, 15.8, 22.6, 28.5, 28.9, 29.2, 29.3, 31.8, 38.7, 119.4, 121.3, 132.4, 133.8, 136.3, 149.7, 159.7; MS (EI, m/z): 263 (M^+, 1), 248 (68), 150 (62), 137 (2); HRMS (EI) calcd for $C_{16}H_{25}NS$ (M^+) 263.1708, found 263.1703.

General procedure for the Ni-catalyzed coupling of 5

To a mixture of $Ni(PPh_3)_2Cl_2$ (16.4 mg, 0.025 mmol) and **5a** (92.3 mg, 0.25 mmol) in 1 mL of THF was added 3.0 M MeMgCl solution in THF (0.17 mL, 0.5 mmol) under nitrogen atmosphere. After stirring at room temperature for 10 h, the reaction mixture was quenched with water, extracted with EtOAc, dried over Na_2SO_4 and concentrated. Column chromatography on silica gel (petroleum ether) gave **6a** as a colorless oil (55.2 mg, 80% yield); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.13 (s, 6H), 0.96 (s, 9H), 1.93 (d, J = 1.2 Hz, 3H), 2.44 (t, J = 6.8 Hz, 2H), 3.84 (t, J = 6.9 Hz, 2H), 6.36 (s, 1H), 7.22 (t, J = 7.2 Hz, 1H), 7.28 (t, J = 7.1 Hz, 2H), 7.36 (t, J = 7.6 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ –5.3, 1.0, 18.2, 25.9, 44.0, 62.2, 125.9, 126.7, 128.0, 128.8, 136.0, 138.4; MS (EI, m/z): 276 (M^+, 3), 219 (100), 161 (3), 145 (27); HRMS (EI) calcd for $C_{17}H_{28}OSi$ (M^+) 276.1909, found 276.1915.

Compound 6b.[11e] 50.6 mg, 88% yield, colorless oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.91 (t, J = 6.6 Hz, 3H), 1.25–1.35 (m, 10H), 1.49–1.58 (m, 2H), 1.87 (d, J = 1.0 Hz, 3H), 2.18 (t, J = 7.5 Hz, 2H), 6.29 (s, 1H), 7.20 (d, J = 7.2 Hz, 1H), 7.26 (d, J = 7.3 Hz, 2H), 7.33 (t, J = 7.5 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.1, 17.7, 22.7, 28.0, 29.3, 29.3, 29.5, 31.9, 40.8, 124.6, 125.7, 128.0, 128.8, 138.7, 139.4.

Compound 6c.[22] 40.0 mg, 72% yield, colorless oil; ^{1}H NMR ($CDCl_3$, 600 MHz): δ 1.99 (d, J = 1.1 Hz, 3H), 2.56 (t, J = 9.0 Hz, 2H), 2.92 (t, J = 7.9 Hz, 2H), 6.35 (s, 1H), 7.23–7.33 (m, 6H), 7.34–7.42 (m, 4H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 17.9, 34.7, 42.6, 125.4, 125.8, 125.9, 128.0, 128.3, 128.4, 128.8, 138.2, 138.5, 142.0.

Compound 6d.[23] 39.1 mg, 79% yield, yellow solid, mp 44–46°C; ^{1}H NMR ($CDCl_3$, 600 MHz): δ 1.64–1.71 (m, 2H), 1.75–1.82 (m, 2H), 2.04 (s, 3H), 2.23–2.29 (m, 2H), 2.35–2.42 (m, 2H), 6.07 (t, J = 4.1 Hz, 1H), 6.62 (s, 1H), 7.24 (t, J = 7.3 Hz, 1H), 7.30 (d, J = 7.3 Hz, 2H), 7.37 (t, J = 7.7 Hz, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 15.1, 22.3, 23.1, 26.0, 26.2, 123.8, 125.2, 125.9, 127.9, 129.3, 137.9, 137.9, 139.0.

Compound 6e.[11n] 44.2 mg, 85% yield, white solid, E/Z = 93:7, mp 76–78 °C; ^{1}H NMR ($CDCl_3$, 600 MHz): δ 2.32 (d, J = 1.2 Hz, 3H), 2.42 (s, 3H), 6.87 (s, 1H), 7.23 (d, J = 8.0 Hz, 2H), 7.26–7.29 (m, 1H), 7.39–7.45 (m, 4H), 7.48 (d, J = 8.1 Hz, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 17.4, 21.1, 125.8, 126.3, 126.9, 128.1, 129.0, 129.1, 136.9, 137.2, 138.5, 141.0.

Compound **6f.**[11n] 45.4 mg, 81% yield, white solid, E/Z = 98:2, mp 103–105 °C; ^{1}H NMR ($CDCl_3$, 600 MHz): δ 2.26 (d, J = 1.1 Hz, 3H), 3.84 (s, 3H), 6.79 (s, 1H), 6.89–6.94 (m, 2H), 7.21–7.25 (m, 1H), 7.34–7.40 (m, 4H), 7.46–7.51 (m, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 17.4, 55.3, 113.7, 126.2, 126.2, 127.0, 128.1, 129.1, 136.4, 136.8, 138.5, 158.9.

Compound 6g. 56.6 mg, 78% yield, yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.12 (s, 6H), 0.94 (s, 9H), 1.91 (d, J = 1.3 Hz, 3H), 2.37 (s, 3H), 2.41 (t, J = 6.9 Hz, 2H), 3.82 (t, J = 6.9 Hz, 2H), 6.30 (s, 1H), 7.16 (s, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ –5.3, 1.0, 18.2, 21.1, 25.9, 44.0, 62.3, 126.5, 128.7, 135.3, 135.4, 135.6; MS (EI, m/z): 290 (M^+, 8), 233 (100), 203 (18), 175 (3); HRMS (EI) calcd for $C_{18}H_{30}OSi$ (M^+) 290.2066, found 290.2067.

Compound 6h. 46.4 mg, 76% yield, yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.93 (t, J = 6.8 Hz, 3H), 1.28–1.38 (m, 10H), 1.50–1.56 (m, 2H), 1.88 (d, J = 1.2 Hz, 3H), 2.19 (t, J = 7.0 Hz, 2H), 2.37 (s, 3H), 6.27 (s, 1H), 7.11–7.21 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.1, 17.7, 21.1, 22.7, 28.0, 29.3, 29.4, 29.6, 31.9, 40.8, 124.5, 128.7, 128.7, 135.2, 135.8, 138.7; MS (EI, m/z): 244 (M^+, 16), 145 (100), 131 (20), 130 (14); HRMS (EI) calcd for $C_{18}H_{28}$ (M^+) 244.2191, found 244.2187.

Compound 6i. 43.9 mg, 72% yield, yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.95 (t, J = 6.8 Hz, 3H), 1.30–1.42 (m, 10H), 1.50–1.59 (m, 2H), 1.90 (d, J = 1.2 Hz, 3H), 2.21 (t, J = 7.0 Hz, 2H), 2.39 (s, 3H), 6.29 (s, 1H), 7.04 (d, J = 7.4 Hz, 1H), 7.08–7.14 (m, 2H), 7.21–7.29 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.1, 17.7, 21.4, 22.7, 28.0, 29.3, 29.6, 31.9, 40.8, 124.7, 125.9, 126.5, 127.9, 129.6, 137.4, 138.7, 139.2; MS (EI, m/z): 244 (M^+, 16), 145 (100), 131 (48), 130 (20); HRMS (EI) calcd

for $C_{18}H_{28}(M^+)$ 244.2191, found 244.2193.

Compound 6j. 47.0 mg, 77% yield, yellow oil; ^{1}H NMR ($CDCl_3$, 600 MHz): δ 0.90 (t, J = 7.0 Hz, 3H), 1.25–1.35 (m, 10H), 1.49–1.56 (m, 2H), 1.68 (d, J = 1.2 Hz, 3H), 2.19 (t, J = 7.5 Hz, 2H), 2.24 (s, 3H), 6.22 (s, 1H), 7.10–7.20 (m, 4H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 14.1, 17.4, 19.9, 22.7, 28.0, 29.3, 29.4, 29.5, 31.9, 39.9, 123.7, 125.2, 126.1, 129.4, 129.6, 136.3, 138.0, 138.9; MS (EI, *m*/*z*): 244 (M^+, 6), 145 (100), 131 (59), 130 (42); HRMS (EI) calcd for $C_{18}H_{28}$ (M^+) 244.2191, found 244.2188.

Compound 6k. 50.1 mg, 77% yield, yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.90 (t, J = 6.9 Hz, 3H), 1.25–1.35 (m, 10H), 1.44–1.52 (m, 2H), 1.85 (d, J = 1.2 Hz, 3H), 2.15 (t, J = 7.2 Hz, 2H), 3.82 (s, 3H), 6.21 (s, 1H), 6.87 (d, J = 8.8 Hz, 2H), 7.18 (d, J = 8.6 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.1, 17.7, 22.7, 28.1, 29.3, 29.3, 29.5, 31.9, 40.8, 55.2, 113.4, 124.0, 129.9, 131.4, 137.9, 157.6; MS (EI, *m*/*z*): 260 (M^+, 12), 161 (100), 147 (8), 146 (8); HRMS (EI) calcd for $C_{18}H_{28}O$ (M^+) 260.2140, found 260.2138.

Compound 6l. 53.3 mg, 86% yield, yellow oil, *E*/*Z* = 93:7; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.93 (t, J = 6.8 Hz, 3H), 1.28–1.38 (m, 10H), 1.50–1.58 (m, 2H), 1.85 (d, J = 1.0 Hz, 3H), 2.19 (t, J = 7.2 Hz, 2H), 6.25 (s, 1H), 6.98–7.07 (m, 2H), 7.17–7.25 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.1, 17.6, 22.7, 28.0, 29.3, 29.4, 29.6, 31.9, 40.6, 114.8 (d, J = 21.0 Hz), 123.5, 130.2 (d, J = 7.6 Hz), 134.7 (d, J = 3.2 Hz), 139.3, 161.0 (d, J = 243.3 Hz); MS (EI, *m*/*z*): 248 (M^+, 16), 149 (100), 135 (33); HRMS (EI) calcd for $C_{17}H_{25}F$ (M^+) 248.1940, found 248.1941.

Compound 6m. 50.7 mg, 68% yield, yellow oil; ^{1}H NMR ($CDCl_3$, 600 MHz): δ 0.90 (t, J = 7.0 Hz, 3H), 1.24–1.36 (m, 10H), 1.49–1.58 (m, 2H), 1.86 (d, J = 1.2 Hz, 3H), 2.19 (t, J = 7.4 Hz, 2H), 6.28 (s, 1H), 7.33 (d, J = 8.2 Hz, 2H), 7.56 (d, J = 8.2 Hz, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 14.1, 17.8, 22.7, 27.9, 29.3, 29.3, 29.5, 31.9, 40.8, 123.6, 124.4 (q, J = 269.7 Hz), 124.9 (q, J = 3.8 Hz), 127.4 (q, J = 32.0 Hz), 129.0, 142.0, 142.3; MS (EI, *m*/*z*): 298 (M^+, 13), 199 (97), 186 (100), 153 (3); HRMS (EI) calcd for $C_{18}H_{25}F_3$ (M^+) 298.1908, found 298.1917.

Compound 6n. 56.7 mg, 81% yield, yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.99 (t, J = 6.7 Hz, 3H), 1.34–1.45 (m, 10H), 1.58–1.65 (m, 2H), 2.01 (d, J = 1.1 Hz, 3H), 2.29 (t, J = 7.5 Hz, 2H), 6.50 (s, 1H), 7.42–7.54 (m, 3H), 7.75 (s, 1H), 7.81–7.89 (m, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.1, 17.9, 22.7, 28.1, 29.3, 29.4, 29.6, 31.9, 40.8, 124.7, 125.3, 125.8, 127.1, 127.4, 127.5, 127.6, 127.7, 131.8, 133.4, 136.3, 140.0; MS (EI, *m*/*z*): 280 (M^+, 26), 181 (100), 167 (26); HRMS (EI) calcd for $C_{21}H_{28}$ (M^+) 280.2191, found 280.2188.

Compound 6o. 38.9 mg, 66% yield, yellow oil, *E*/*Z* = 95:5; ^{1}H NMR ($CDCl_3$, 600 MHz): δ 0.92 (t, J = 6.8 Hz, 3H), 1.26–1.36 (m, 10H), 1.48–1.55 (m, 2H), 2.00 (s, 3H), 2.20 (t, J = 7.6 Hz, 2H), 6.43 (s, 1H), 6.94 (d, J = 3.2 Hz, 1H), 7.03 (t, J = 3.7 Hz, 1H), 7.22 (d, J = 5.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 14.1, 18.5, 22.7, 28.1, 29.3, 29.5, 29.7, 31.9, 41.0, 118.0, 123.7, 125.7, 126.7, 138.6, 141.8; MS (EI, *m*/*z*): 236 (M^+, 5), 138 (14), 137 (100), 123 (8); HRMS (EI) calcd for $C_{15}H_{24}S$ (M^+) 236.1599, found 236.1606.

Compound 6p. 51.2 mg, 80% yield, yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.93 (t, J = 7.0 Hz, 3H), 1.21–1.39 (m, 10H), 1.46–1.56 (m, 2H), 1.88 (s, 3H), 2.15 (t, J = 7.4 Hz, 2H), 6.05 (d, J = 10.9 Hz, 1H), 6.49 (d, J = 15.6 Hz, 1H), 7.00–7.11 (m, 1H), 7.22 (t, J = 7.3 Hz, 1H), 7.34 (t, J = 7.6 Hz, 2H), 7.44 (d, J = 7.6 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.1, 16.8, 22.7, 27.9, 29.3, 29.4, 29.5, 31.9, 40.1, 124.9, 125.7, 126.0, 126.8, 128.5, 129.7, 138.1, 140.6; MS (EI, *m*/*z*): 257 (10), 256 (M^+, 25), 157 (62), 143 (74), 129 (100); HRMS (EI) calcd for $C_{19}H_{28}$ (M^+) 256.2191, found 256.2197.

Compound 6q. 50.4 mg, 69% yield, colorless oil, *Z*/*E* = 97:3; ^{1}H NMR ($CDCl_3$, 600 MHz): δ 0.91 (t, J = 7.0 Hz, 3H), 1.27–1.39 (m, 10H), 1.41–1.46 (m, 2H), 2.52 (t, J = 7.3 Hz, 2H), 6.47 (s, 1H), 6.95 (d, J = 7.1 Hz, 2H), 7.04–7.14 (m, 3H), 7.16–7.21 (m, 2H), 7.26–7.31 (m, 1H), 7.33 (t, J = 7.2 Hz, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 14.1, 22.7, 27.9, 29.2, 29.3, 29.4, 31.9, 40.7, 126.0, 126.0, 126.8, 127.8, 128.4, 128.5, 128.9, 137.5, 141.4, 143.6; MS (EI, *m*/*z*): 292 (M^+, 8), 193 (87), 179 (88), 115 (100); HRMS (EI) calcd for $C_{22}H_{28}$ (M^+) 292.2191, found 292.2188.

Compound 6r. 57.4 mg, 75% yield, colorless oil, *Z*/*E* = 91:9; ^{1}H NMR ($CDCl_3$, 600 MHz): δ 0.87 (t, J = 6.8 Hz, 3H), 1.24–1.31 (m, 10H), 1.35–1.40 (m, 2H), 2.34 (s, 3H), 2.46 (t, J = 7.1 Hz, 2H), 6.40 (s, 1H), 6.93 (d, J = 7.3 Hz, 2H), 7.04 (t, J = 5.9 Hz, 3H), 7.09 (t, J = 8.0 Hz, 4H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 14.1, 21.2, 22.6, 28.0, 29.2, 29.3, 29.4, 31.9, 40.8, 125.8, 125.9, 127.8, 128.4, 128.9, 129.1, 136.3, 137.8, 138.3, 143.6; HRMS (ESI) calcd for $C_{23}H_{31}$ $(M+H)^+$ 307.2426, found 307.2425.

Compound 6s. 53.9 mg, 67% yield, colorless oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.91 (t, J = 6.7 Hz, 3H), 1.27–1.39 (m, 10H), 1.40–1.49 (m, 2H), 2.49 (t, J = 7.3 Hz, 2H), 3.82 (s, 3H), 6.43 (s, 1H), 6.84 (d, J = 8.6 Hz, 2H), 6.97 (d, J = 6.9 Hz, 2H), 7.03–7.14 (m, 5H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.0, 22.6, 28.1, 29.2, 29.3, 29.4, 31.9, 40.7, 55.2, 114.0, 125.9, 126.0, 127.8, 129.0, 129.7, 133.7, 138.0, 143.2, 158.7; MS (EI, *m*/*z*): 322 (M^+, 2), 209 (12), 178 (43), 133 (100). HRMS (EI) calcd for $C_{23}H_{30}O$ (M^+) 322.2297, found 322.2295.

Compound 6t. 42.9 mg, 67% yield, colorless oil; ^{1}H NMR ($CDCl_3$, 600 MHz): δ 0.92 (t, J = 6.9 Hz, 3H), 1.26–1.36 (m, 10H), 1.50–1.56 (m, 2H), 2.19 (t, J = 7.5 Hz, 2H), 3.01 (d, J = 6.1 Hz, 2H), 5.10–5.16 (m, 2H), 5.86–5.95 (m, 1H), 6.41 (s, 1H), 7.23 (t, J = 7.3 Hz, 1H), 7.27 (t, J = 8.0 Hz, 2H), 7.34 (t, J = 7.6 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.1, 22.7, 28.0, 29.3, 29.4, 29.5, 31.9, 35.4, 37.2, 115.9, 126.0, 126.0, 128.0, 128.5, 136.3, 138.2, 140.7; MS (EI, *m*/*z*): 257 (1), 256 (M^+, 3), 199 (42), 179 (13), 158 (2). HRMS (EI) calcd for $C_{19}H_{28}$ (M^+) 256.2191, found 256.2195.

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Notes and references

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