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Nickel-Catalyzed Regioselective Cleavage of C_{sp^2}–S Bonds: Method for the Synthesis of Tri- and Tetrasubstituted Alkenes

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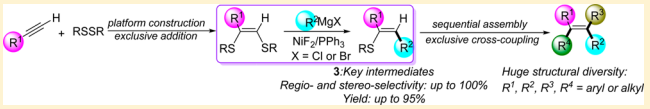
Supporting Information

ABSTRACT: We describe here an efficient route for the synthesis of (*Z*)-vinylic sulfides **3** via the highly regio- and stereoselective coupling of (*Z*)-1,2-bis(aryl(alkyl)thio)alkenes and Grignard reagents over a Ni catalyst under mild conditions. (*Z*)-Vinylic sulfides **3** are important intermediates in the synthesis of tri- and tetrasubstituted alkenes that are important construction blocks for drugs and natural products. The directing organosulfur groups (SR) can be converted to diaryl(alkyl) disulfides (RSSR) using H_2O_2 as oxidant, hence avoiding the waste of sulfur resources. The protocol provides a general method that is highly regio- and stereoselective for the synthesis of a diversity of tri- and tetrasubstituted alkenes.



INTRODUCTION

Since olefins can be readily obtained from ketone transformation,[1] they are widely used as building blocks for the synthesis of pharmaceuticals[2] and natural products[3] such as (*Z*)-tamoxifen[4a] and Nileprost analogues.[4b] There are four identical positions in an alkene molecule, each of which can be replaced by a different substituent, meaning that the structural diversity of alkene derivatives can be intrinsically extraordinary.[5] However, due to the lack of general methods for programmed synthesis of tri- and tetrasubstituted alkenes,[6] the potential of huge structural diversity has not been fully exploited. For the preparation of tri- and tetrasubstituted alkenes, carbometalation of alkynes (Scheme 1a) is generally accepted as the most widely used method,[7] despite the problems of poor stereoselectivity[7a,b] and the lack of structural flexibility.[7d] In comparison to the carbometalation approach, the sequential assembly strategy using configuration-fixed heteroatoms (E)[8a] or halogen-substituted[8b] alkenes as platforms has the advantages of high regioselectivity and structural flexibility. However, there are only two pioneering works,[8] and the studies were on aryl substituents using hard-won reagents as starting materials (Scheme 1b). Thus, it is highly desirable to develop a general method for the synthesis of tri- and tetrasubstituted alkenes.

Over the last decade, in the area of transition-metal-catalyzed cross-coupling reactions, C–E (S, Se, or Te) bond cleaving reactions have attracted considerable attention, as they provide a good way to form new C–C bonds with retention of configuration.[9] In the case of C–E bond cleaving reactions, both stoichiometric[10] and catalytic reactions catalyzed by Pd,[11] Ni,[12] or other metal[13] catalysts have been established by using organochalcogen compounds as substrates which are easy to construct.[14] The most widely used organochalcogen compounds for synthesis of multiply substituted alkenes are vinylic chalcogenides.[9a−e] However, until now, most of the synthetic applications have focused on vinylic monochalcogenides[9] and there have been few studies on vinylic dichalcogenides.[15] This is because, when vinylic dichalcogenides were treated with nucleophilic reagents, it was hard to control the cleavage of two C–E bonds regioselectively. In our previous work, we reported simple routes for the synthesis of (*Z*)-vinylic disulfides[16a] and (*Z*)-vinylic selenosulfides (tellurosulfides)[16b] via highly regio- and stereoselective reactions of terminal alkynes and diaryl(alkyl) disulfides (diselenides and ditellurides) catalyzed by cesium hydroxide under mild conditions. Due to the difference in the activities of C_{sp^2}–S and C_{sp^2}–Se (Te) bonds, (*Z*)-vinylic selenosulfides (tellurosulfides) can be used as effective platform molecules for the stereoselective synthesis of tri- and tetrasubstituted alkenes.[17] However, purification is a problem because the stereoisomers of (*Z*)-vinylic selenosulfides (tellurosulfides) are similar in polarity.[18]

During our attempt to develop a better way to synthesize trisubstituted alkenes by using (*Z*)-1,2-bis(aryl(alkyl)thio)-alkenes as platforms, we observed that the coupling of (*Z*)-1,2-bis(aryl(alkyl)thio)alkenes with Grignard reagents occurs only on $C^1_{sp^2}$–S bonds of (*Z*)-1,2-aryl(alkyl)thio alkenes, forming (*Z*)-1-aryl(alkyl)-2-(aryl(alkyl)thio)alkenes **3** exclusively in the presence of Ni catalysts (Scheme 1c, key step). According to previous works, (*Z*)-vinylic sulfides **3** are important intermediates in the stereoselective synthesis of tri- and tetrasubstituted alkenes via the arylation (alkylation) of C–S[19] and C–H[20] bonds. To our knowledge, highly regioselective coupling of (*Z*)-1,2-bis(aryl(alkyl)thio)alkenes with Grignard reagents has never been reported before. Herein, we report for the first time the synthesis of (*Z*)-vinylic sulfides **3** via the highly regioselective coupling of (*Z*)-1,2-bis(aryl(alkyl)thio)alkenes with Grignard reagents catalyzed by Ni catalysts and their application in the preparation of tri- and tetrasubstituted alkenes.

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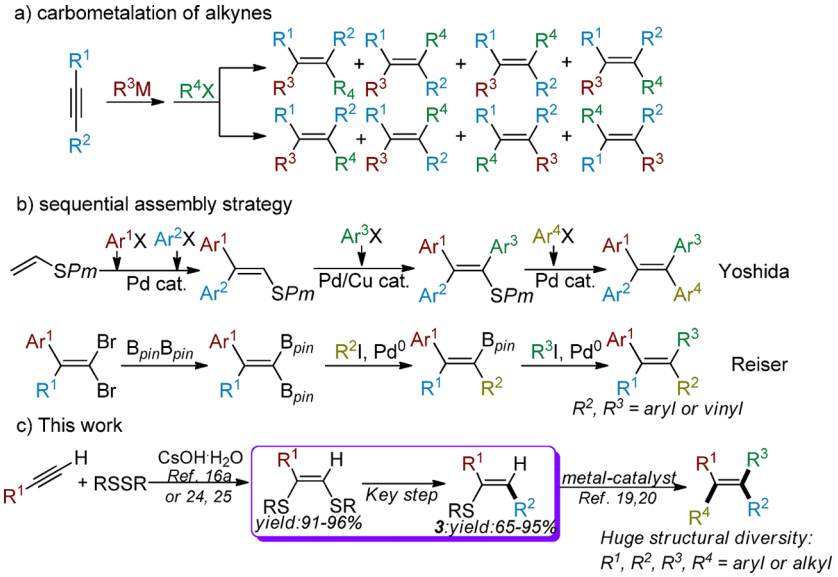
Scheme 1. General Methods for Synthesis of Tri- and Tetrasubstituted Alkenes



RESULTS AND DISCUSSION

We initiated our studies with the coupling of (*Z*)-1,2-bis(phenylthio)styrene (**1a**) and methylmagnesium chloride (**2a**) in the presence of $NiCl_2$ (1.0 equiv) and PPh_3 (1.0 equiv) under a nitrogen atmosphere at room temperature for 10 h. The desired product **3a** was obtained in 46% yield, and there was no detection of **4a** or the regioisomer of **3a** by ^1H NMR analysis of the crude products (Table 1, entry 1).

After a systematic study on the influence of catalysts and ligands on the reaction, we found that NiF_2 is the best catalyst and PPh_3 is the best ligand. Together they afford the desired product in 88% yield (Table 1, entry 8). Then we examined the minimum amount of NiF_2 and PPh_3 required to promote the reaction (Table 1, entries 11−18), and the results show that the use of 0.05 equiv of NiF_2 and 0.05 equiv of PPh_3 is good enough to effectively promote the reaction, giving the corresponding product in 94% yield in 25 h (Table 1, entry 16). We also explored solvents such as toluene, DCM, and THF (Table 1, entries 16, 20, and 21) and found that THF is the most suitable. It is noted that, when the temperature was raised to 50 °C, there was reduction of the product yield to 80%, and generation of byproduct. Finally, we examined the influence of the amount of methylmagnesium chloride (**2a**) on the cross-coupling reaction and found that 1.25 equiv of methylmagnesium chloride (**2a**) is enough to promote the reaction efficiently (Table 1, entries 22 and 23). In addition, after H_2O_2 oxidation, diphenyl disulfide is obtained as the major byproduct with a yield of 72%. When an excess amount of methylmagnesium chloride (**2a**) was used, several other byproducts such as biphenyl, toluene, and diphenyl disulfide were detected. Thus, the optimized reaction conditions are 0.05 equiv of NiF_2, 0.05 equiv of PPh_3, 1.0 equiv of **1a**, and 1.25 equiv of **2a** in THF at room temperature under nitrogen for 25 h.

The scope of the coupling reaction was investigated under the optimized conditions. A variety of (*Z*)-vinylic disulfides could efficiently undergo cross-coupling to afford the desired products in good to excellent yields (Table 2). Electron-donating and electron-withdrawing functional groups at the meta and para positions of the phenyl ring of aromatic ethylene affect the cross-coupling only slightly, affording the corresponding products in good to excellent yields (**3a**−**g**, 83−93%). The cross-coupling of 1,2-bis(phenylthio)-4-(*tert*-butyl)styrene with methylmagnesium chloride proceeds well with good yield (**3d**, 93%), suggesting that the steric effect of the substituted group present in the aromatic rings of aromatic ethylene on the reaction is insignificant. The cross-coupling is also suitable for (*Z*)-1,2-bis(phenylthio)thiophene alkene and (*Z*)-1,2-bis(phenylthio)-pentene, affording the corresponding products **3h**,**i** in 83% and 94% yields, respectively. In addition, substitution by electron-donating and electron-withdrawing functional groups at the phenyl ring bonded to the sulfur atom only slightly affects the cross-coupling reaction (**3j**−**q**, 82−95%). Good yields were also obtained when (*Z*)-vinylic disulfides were treated with ethylmagnesium chloride under the optimal conditions (**3r**,**s**, 93% and 88%, respectively). The structure of product **3i** was determined by examining its NOESY H−H and COSY H−H interactions (Supporting Information), and the results show that the cross-coupling of (*Z*)-1,2-bis(aryl(alkyl)thio)alkenes with Grignard reagents occurs stereoselectively to give exclusively *Z* isomers.

Unfortunately, poor yields were obtained when (*Z*)-vinylic disulfides were treated with other Grignard reagents (except for methylmagnesium chloride and ethylmagnesium chloride) under the above conditions. When the amounts of catalyst and ligand were increased to 0.25 equiv, the reactions of (*Z*)-vinylic disulfides with both larger alkyl-substituted and aryl-substituted Grignard reagents gave the corresponding products in moderate to good yields (Table 3). A closer inspection of the results reveal that alkyl-substituted (e.g., cyclopentyl and cyclohexyl) Grignard reagents of large size performed more poorly than those (e.g., Me, Et, allyl) of small size (**3t**−**w**, 72−86%). It is noted that the yields of the cross-coupling with aryl-substituted Grignard reagents are moderate, mainly due to the steric hindrance and homocoupling of arylmagnesium bromide (**3x**−**ab**, 61−75%). A smaller functional group (propyl) bonded to the sulfur atom can accelerate the cross-coupling, giving the corresponding product in 95% yield (**3ac**).

The method can be carried out on a larger scale, and the yield percentages of the desired products decrease only slightly in comparison with those for the small scale (0.2 mmol). The coupling of (*Z*)-1,2-bis(phenylthio)styrene (**1a**; 640 mg, 2.0 mmol) and methylmagnesium chloride (**2a**; 1.0 mL, 2.5 mmol)

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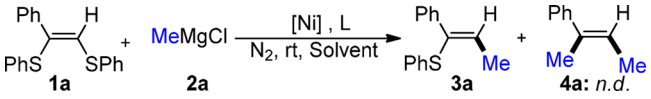
Table 1. Optimization of Reaction Conditions[a]



entry	[Ni] (amt (equiv))	L (amt (equiv))	conditions	yield of 3a[b] (%)
1	$NiCl_2$ (1.0)	PPh_3 (1.0)	THF, room temp, 10 h	46
2	none	PPh_3 (1.0)	THF, room temp, 10 h	0
3	$NiCl_2$ (1.0)	none	THF, room temp, 10 h	0
4	$NiCl_2$ (1.0)	PCy_3 (1.0)	THF, room temp, 10 h	26
5	$NiCl_2$ (1.0)	Xantphos (0.5)	THF, room temp, 10 h	34
6	$NiBr_2$ (1.0)	PPh_3 (1.0)	THF, rt, 10 h	42
7	$Ni(acac)_2$ (1.0)	PPh_3 (1.0)	THF, room temp, 10 h	21
8	NiF_2 (1.0)	PPh_3(1.0)	THF, room temp, 10 h	88
9	NiF_2 (1.0)	ddpe (1.0)	THF, room temp, 10 h	trace
10	$Ni(OAc)_2$ (1.0)	PPh_3 (1.0)	THF, room temp, 10 h	67
11	NiF_2 (0.5)	PPh_3 (0.5)	THF, room temp, 10 h	75
12	NiF_2 (0.25)	PPh_3 (0.25)	THF, room temp, 10 h	58
13	NiF_2 (0.1)	PPh_3(0.1)	THF, room temp, 10 h	42
14	NiF_2(0.1)	PPh_3 (0.1)	THF, room temp, 25 h	94
15	NiF_2 (0.1)	PPh_3 (0.1)	THF, room temp, 30 h	94
16	**NiF_2 (0.05)**	**PPh_3 (0.05)**	**THF, room temp, 25 h**	**94 (91)**[c]
17	NiF_2 (0.05)	PPh_3 (0.05)	THF, room temp, 30 h	94
18	NiF_2 (0.025)	PPh_3 (0.025)	THF, room temp, 35 h	88
19	NiF_2 (0.025)	PPh_3 (0.025)	THF, 50 °C, 15 h	80
20	NiF_2 (0.05)	PPh_3 (0.05)	toluene, room temp, 25 h	72
21	NiF_2 (0.05)	PPh_3 (0.05)	DCM, room temp, 25 h	60
22[d]	NiF_2 (0.05)	PPh_3 (0.05)	THF, room temp, 25 h	94
23[e]	NiF_2 (0.05)	PPh_3 (0.05)	THF, room temp, 25 h	94

[a]Reaction conditions unless specified otherwise: **1a** (0.2 mmol), **2a** (1.0 mmol), solvent (1.0 mL), N_2. [b]GC yields. [c]Isolated yields. [d]0.50 mmol of **2a** was used. [e]0.25 mmol of **2a** was used.

using NiF_2 (9.7 mg, 0.1 mmol) and PPh_3 (26.2 mg, 0.1 mmol) affords (*Z*)-1-(phenylthio)-2-methylstyrene (**3a**; 398 mg) in 88% yield (90% on a 20 mmol scale) (Scheme 2).

Recently, a number of methods for stereoselective synthesis of tri- and tetrasubstituted alkenes were reported,[21] but it is hard to control the chemo- and regioselectivity of products. According to previous studies,[19,20] (*Z*)-vinylic sulfides **3** are important intermediates in the preparation of tri- and tetrasubstituted alkenes. Here, we use the synthesis of (*Z*)-tamoxifen as an example to illustrate the application of (*Z*)-vinylic sulfides **3** for the production of tri- and tetrasubstituted alkenes. First compound **3y** is obtained readily by following the method described so far. Then, through bromination[20a] and Pd-catalyzed coupling[20b] of compound **3y**, there is the formation of alkene **5**, which is converted to (*Z*)-tamoxifen in high chemo- and regioselectivity using $NiCl_2$(dppe) as catalyst[12d] (Scheme 3).

To shed light on the mechanism of the cross-coupling reaction, some control experiments and NMR experiments were conducted. Comparing the four equations in Scheme 4, one can see that fluorine plays an important role. As shown in eqs 3 and 4, the outcome of the process catalyzed by NiF_2 appears to be different from that catalyzed by $NiCl_2$. Traditionally, the coupling includes steps of Ni(0) formation, oxidative addition, and reductive elimination. To further understand the mechanism, the coupling of (*Z*)-1,2-bis(phenylthio)styrene and methylmagnesium chloride in THF-d_8 using NiF_2/PPh_3 as catalyst was examined hourly by NMR spectroscopy. From the ^{31}P NMR spectra of $Ni(PPh_3)_4$ and those of the coupling mixture, it is confirmed that there is no Ni^0 at the start of the coupling reaction (see Figure 1 in the Supporting Information). From the ^{19}F NMR spectra of the reaction mixture, the signal of ^{19}F can be observed within the first 1 h but cannot be seen afterward. The phenomenon implies that the fluorine exists not only as an inorganic salt but also as an organic intermediate during the coupling reaction and is finally converted to MgFCl (see Figure 2 in the Supporting Information). The intensity of the Me signal (^1H NMR, δ 2.07) of the desired product increases in the first 8.0 h before reaching a constant value (see Figure 3 in the Supporting Information). Analyzing the ^{13}C NMR spectra (see Figure 4 in the Supporting Information), one can see that the peak of the carbon that is bonded to the hydrogen of (*Z*)-1,2-bis(phenylthio)styrene at δ 125.8 shifts to high field to δ 125.3, plausibly due to the replacement of PhS (an electron-withdrawing group) by Me. The signals at δ −5.37 and −49.9 (^{31}P NMR) ascribable to PPh_3 and $Ni^{II}(PPh_3)_2X_2$, respectively, exist during the whole process. Upon the complete consumption of (*Z*)-1,2-bis(phenylthio)styrene after 8 h, a ^{31}P NMR signal at δ 31.6 consistent with the Ni^0 signal of authentic $Ni^0(PPh_3)_4$ is observed. In addition, with the formation of diphenyl disulfide after oxidation, it is deduced that PhSMgCl is formed during the coupling process.

On the basis of the results described above and those of previous reports,[22] a mechanism is proposed as depicted in Figure 2. First Ni complex ***A*** is formed when MeMgCl (**2a**) is treated with NiF_2 in the presence of PPh_3. The coordination of compound **1a** to the nickel center of ***A*** followed by ligand exchange gives intermediate ***B***. It is worth pointing out that C^2 is stabilized by the the hyperconjugation of the aryl group or the electron-donating effect of the alkyl group. The insertion of nucleophile (Me^-) and electrophile (FNi^+) into C^1 and C^2, respectively, gives intermediate ***C***. The steric hindrance of the nucleophiles and electrophiles obviously affects the addition, in agreement with the results shown in Tables 2 and 3. The elimination of PhSNiF from intermediate ***C*** furnishes species ***D*** and the final coupling product **3a** exclusively in the form of the *Z* isomer. Then species ***D*** reacts with MeMgCl to give PhSMgCl and species ***A*** (cycle 1, slow) or MgFCl and species ***E*** (cycle 2, fast), and species ***E*** coordinates with **1a** to afford intermediate ***F***. With the insertion of PhSNiF into ***F***, there is the generation of intermediate ***G***, which gives product **3a** and species ***H*** via elimination. The species ***H*** reacts with another portion of MeMgCl to give PhSMgCl and species ***E***, effectively promoting the coupling reaction as a result.

■ CONCLUSIONS

We developed a convenient method for the synthesis of (*Z*)-vinylic sulfides **3** with high regioselectivity via the direct Ni-

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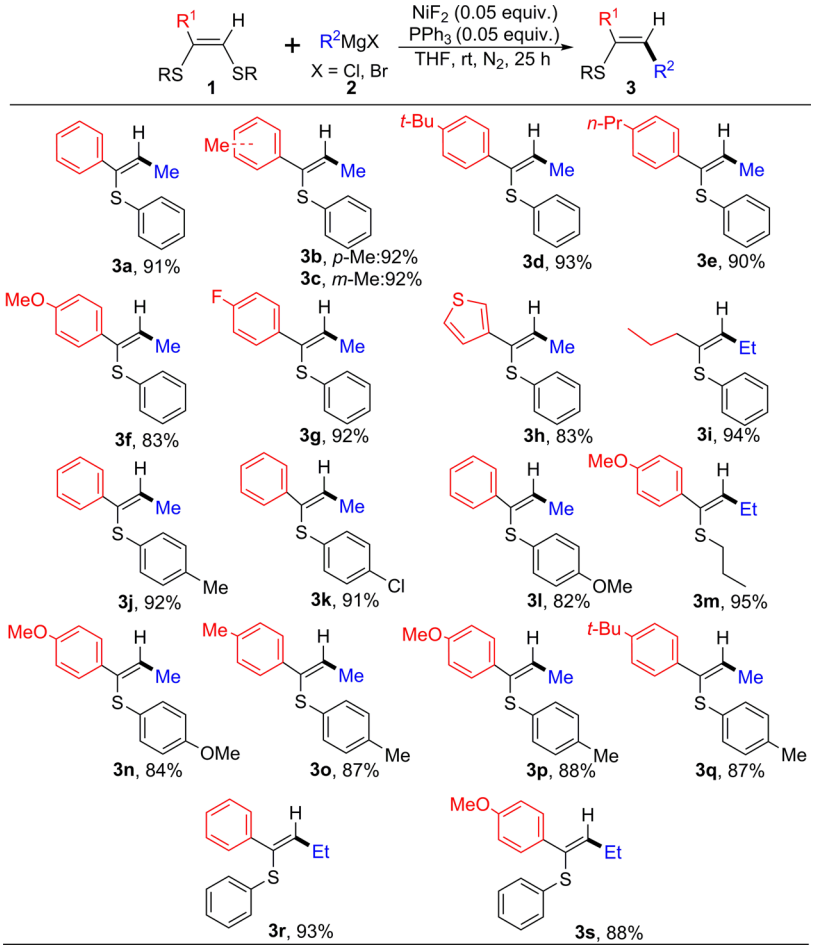
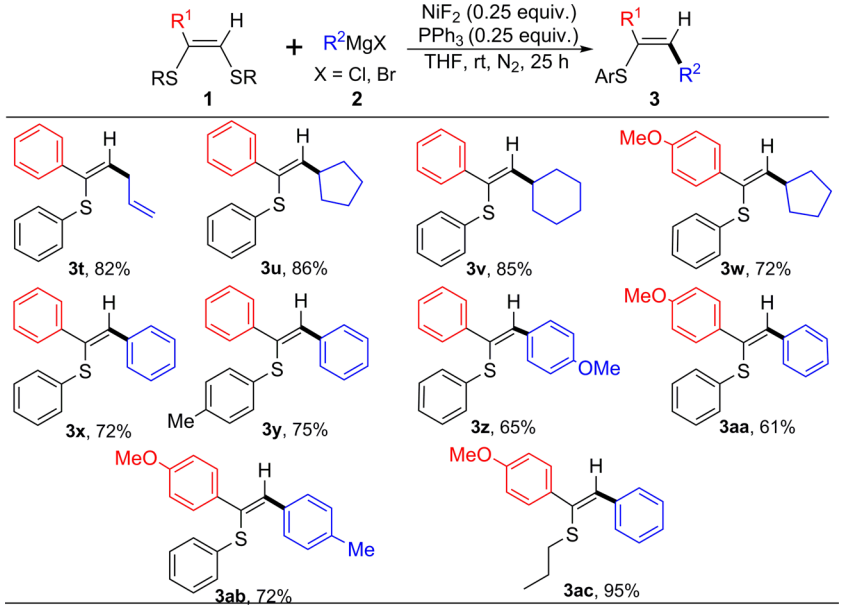
Table 2. Reaction Scope of 1,2-Diarylthio Aromatic Acetylenes[a]



[a]Reaction conditions: **1** (0.2 mmol), **2** (0.25 mmol), NiF_2 (0.01 mmol), PPh_3 (0.01 mmol), THF (1.0 mL), N_2, room temperature, 25 h.

Table 3. Reaction Scope of Grignard Reagents[a]



[a]Reaction conditions: **1** (0.2 mmol), **2** (0.25 mmol), NiF_2 (0.05 mmol), PPh_3 (0. 05 mmol), THF (1.0 mL), N_2, room temperature, 25 h.

catalyzed cross-coupling of (*Z*)-1,2-bis(aryl(alkyl)thio)alkenes with Grignard reagents. The method utilizes easily available starting materials, offers operational simplicity, and enjoys a broad substrate scope as well as functionality tolerance. We also

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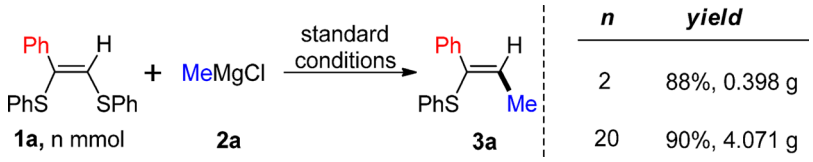
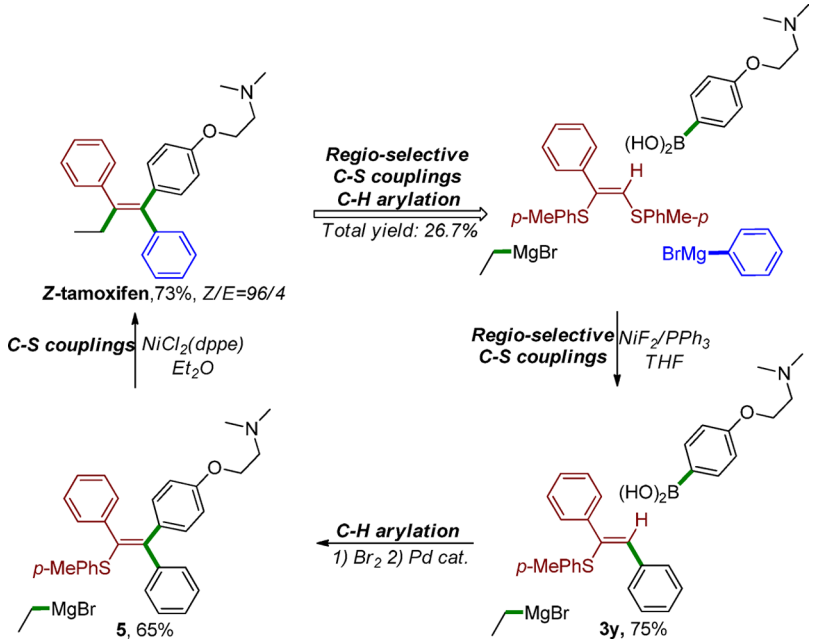
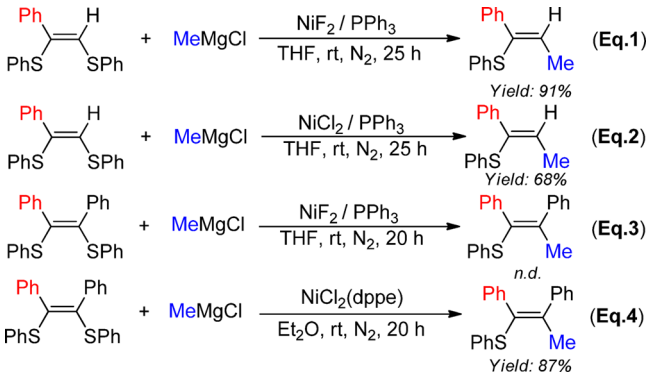
Scheme 2. Larger-Scale Synthesis of 3a



Scheme 3. Synthesis of (*Z*)-Tamoxifen using Product 3y as Starting Material



Scheme 4. Control Experiments for Mechanism Study



demonstrated that (*Z*)-tamoxifen can be successfully synthesized in high regio- and stereoselectivity using (*Z*)-vinylic sulfides **3** as starting materials. As directing groups, the organosulfur groups can be converted to diaryl(alkyl) disulfides via the oxidation of the reaction solution in air or with H_2O_2, hence avoiding the waste of the sulfur resources.

EXPERIMENTAL SECTION

General Information. Unless noted, all reactions were conducted in Schlenk tubes under an atmosphere of nitrogen. Dry DCM (CH_2Cl_2), toluene, THF (tetrahydrofuran), and THF-d_8 were purified according to the standard methods. Reactions were monitored by thin-layer chromatography (TLC) using silica gel 60 F_{254} precoated plates. Visualization was accomplished with a UV lamp or I_2 stain. Silica gel of size 300−400 mesh was used for column chromatography using the combination of ethyl acetate and petroleum ether as eluent. Preparative thin-layer chromatography (TLC) was performed as described by Anderson.[23] ^{1}H NMR and $^{13}C\{^1H\}$ NMR spectra were recorded on 400 and 100 MHz NMR Plus spectrometers using residual solvent peaks as internal standards, respectively. Mass spectra (MS) were obtained using an EI mass spectrometer. High-resolution mass spectra (HRMS) were measured on an electron ionization (EI) mass spectrometer.

General Procedure for the Synthesis of (*Z*)-1,2-Diaryl(alkyl)-thioalkenes 1.[16a] Terminal alkynes (2.0 mmol) and diaryl disulfides (1.0 mmol) were added, under nitrogen, to a solution of cesium hydroxide hydrate (0.5 mmol, 25 mol %) in DMF (2 mL). The resulting solution was stirred at room temperature for 20 h under a nitrogen atmosphere. Then, the reaction mixture was diluted with water (30 mL) and extracted with ethyl acetate (30 mL × 3). The combined organic phases were dried over anhydrous Na_2SO_4 and concentrated in vacuo. The desired products **1** were obtained by flash chromatography using ethyl acetate/hexane as an eluent.

*(Z)-1,2-Bis(phenylthio)styrene (**1a**).*[16a] Light yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (d, J = 7.6 Hz, 2H), 7.47 (d, J = 7.2 Hz, 2H), 7.32 (t, J = 7.6 Hz, 2H), 7.28−7.20 (m, 6H), 7.15 (t, J = 8.0 Hz, 1H), 7.05 (t, J = 7.6 Hz, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 138.8, 136.6, 135.3, 134.8, 130.7, 129.4, 129.4, 129.0, 128.5, 128.3, 127.7, 127.7, 126.8, 126.0; MS (EI) m/z 320 (M^+, 55), 268 (18), 212 (100), 178 (61), 167 (43), 159 (28), 134 (28), 121 (33), 109 (20), 91 (16), 77 (29), 66 (144).

*(Z)-Bis(phenylthio)-4-methylstyrene (**1b**).* Light yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50−7.44 (m, 4H), 7.37−7.23 (m, 6H), 7.20−7.15 (m, 2H), 7.09−7.03 (m, 3H), 2.27 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 137.6, 136.0, 135.5, 134.9, 130.5, 129.3, 129.2, 128.9, 128.2, 127.5, 126.7, 125.8, 21.1; MS (EI) m/z 334 (M^+, 100), 225 (72), 210 (64), 192 (13), 167 (16), 147 (11), 115 (15), 109 (8), 91 (5), 65 (5).

*(Z)-Bis(phenylthio)-3-methylstyrene (**1c**).* Light yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (t, J = 8.4 Hz, 4H), 7.31 (t, J = 8.0 Hz, 2H), 7.26−7.22 (m, 3H), 7.19 (s, 1H), 7.14 (t, J = 8.0 Hz, 2H), 7.06−7.00 (m, 3H), 2.24 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 137.6, 136.1,

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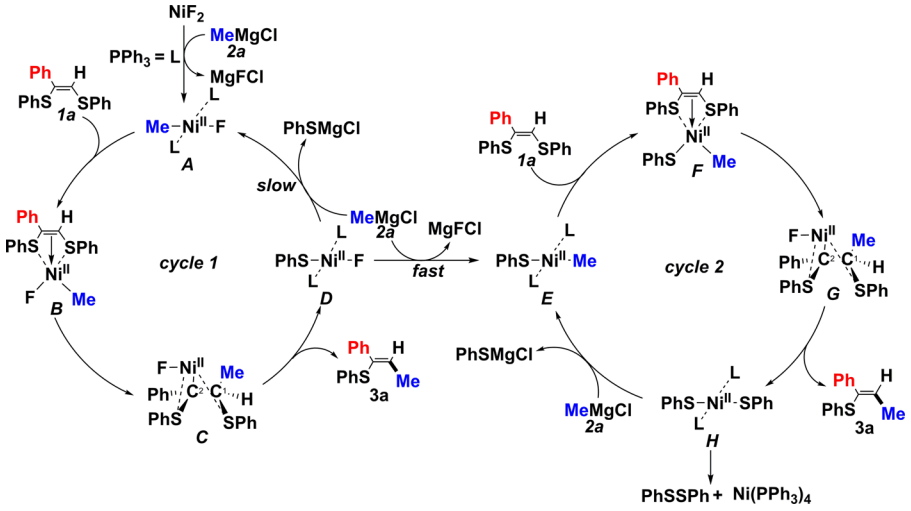

Figure 2. Proposed mechanism of the cross-coupling.

135.53, 135.48, 135.0, 130.6, 129.5, 129.4, 129.3, 129.0, 128.3, 127.6, 126.7, 125.9, 21.2; MS (EI) *m*/*z* 334 (M^+, 100), 225 (73), 210 (62), 192 (11), 167 (17), 147 (18), 115 (12), 109 (11), 91 (6), 65 (7).

*(Z)-1,2-Bis(phenylthio)-4-(tert-butyl)styrene (**1d**).* Light yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 (t, J = 8.0 Hz, 4H), 7.285−7.27 (m, 2H), 7.21−7.17 (m, 6H), 7.12 (t, J = 7.6 Hz, 2H), 7.01 (t, J = 7.2 Hz, 1H), 1.19 (s, 9H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 136.4, 136.1, 135.4, 135.1, 130.5, 129.3, 128.9, 127.9, 127.5, 126.3, 125.7, 125.4, 31.3; MS (EI) *m*/*z* 338 (M^+, 100), 229 (86), 208 (13), 196 (31), 183 (21), 165 (65), 139 (7), 109 (27), 77 (11), 65 (12).

*(Z)-1,2-Bis(phenylthio)-4-(n-propyl)styrene (**1e**).* Light yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46−7.44 (m, 4H), 7.29 (t, J = 7.6 Hz, 2H), 7.22 (t, J = 6.4 Hz, 4H), 7.13 (d, J = 7.6 Hz, 2H), 7.05−7.01 (m, 3H), 2.48 (t, J = 7.6 Hz, 2H), 1.58−1.53 (m, 2H), 0.87 (t, J = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 142.4, 136.4, 135.8, 135.5, 135.1, 130.6, 129.5, 129.4, 129.0, 128. 7, 128.2, 127.6, 126.7, 125.9, 37.7, 24.5, 14.0; MS (EI) *m*/*z* 362 (M^+, 100), 334 (16), 239 (61), 224 (45), 210 (11), 195 (16), 148 (5), 123 (4), 91 (3).

*(Z)-1,2-Bis(phenylthio)-4-methoxystyrene (**1f**).* Light yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 (d, J = 8.4 Hz, 4H), 7.36−7.32 (m, 2H), 7.29−7.23 (m, 3H), 7.17 (t, J = 8.0 Hz, 2H), 7.11−7.07 (m, 2H), 6.76 (d, J = 8.4 Hz, 2H), 3.74 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 159.3, 135.5, 134. 9, 134.0, 131.5, 130.4, 129.5, 129.3, 128.9, 128.3, 128.1, 127.4, 125.9, 113.8, 55.3; MS (EI) *m*/*z* 350 (M^+, 100), 241 (78), 226 (75), 210 (21), 197 (15), 165 (17), 151 (6), 132 (7), 110 (10), 89 (7), 77 (4), 66 (3).

*(Z)-1,2-Bis(phenylthio)-4-fluorostyrene (**1g**).* Light yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52−7.49 (m, 4H), 7.36 (t, J = 7.6 Hz, 2H), 7.31−7.29 (m, 1H), 7.24−7.14 (m, 5H), 7.09 (t, J = 6.8 Hz, 1H), 6.92 (t, J = 7.2 Hz, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 136.0, 135.1, 134.4, 130.7, 128.9, 128.5, 128.4, 127.7, 126.1, 115.4, 115.2; MS (EI) *m*/*z* 376 (M^+, 100), 319 (5), 267 (24), 251 (14), 211 (17), 178 (7), 167 (20), 143 (7), 128 (4), 115 (13), 110 (10), 77 (4), 57 (25).

*(Z)-1,2-Bis(4-phenylthio)-3-thienylenevinylene (**1h**).* Light yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (d, J = 7.6 Hz, 2H), 7.25−7.10 (m, 11H), 7.02 (t, J = 7.2 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 140.7, 136.1, 135.2, 135.0, 130.7, 129.4, 129.0, 127.9, 127.6, 126.1, 126.0, 125.4, 124.2, 122.2.

*(Z)-1,2-Bis(phenylthio)pent-1-ene (**1i**).*[24] A mixture of Ph_2S_2 (1.0 mmol, 218 mg) and PPh_3 (0.15 mmol, 47.2 mg) in a tube was heated by a hair dryer until the formation of a homogeneous melt. Then, $Pd(PPh_3)_4$ (0.01 mmol, 12 mg) was added to the melt and the mixture was shaken until complete dissolution of the salt and formation of a homogeneous dark brown melt. Pentene (1.5 mmol, 102 mg) was added to the melt, and the reaction mixture was stirred at 100 °C overnight. After completion of the reaction, the unconsumed pentene was distilled off on a rotary evaporator. The residue was purified by flash chromatography with a hexane−chloroform mixture as eluent to afford (*Z*)-1,2-bis(phenylthio)pent-1-ene (**1i**; 271 mg, 95%). Light yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42−7.21 (m, 8H), 6.57 (s, 1H), 2.22 (t, J = 7.2 Hz, 2H), 1.56−1.49 (m, 2H), 0.84 (t, J = 6.8 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 135.9, 134.0, 133.9, 130.5, 129.8, 129.5, 129.1, 129.0, 126.9, 126.8, 39.2, 21.8, 13.4.

*(Z)-1,2-Bis((4-methylphenyl)thio)styrene (**1j**).*[16a] Light yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (d, J = 7.6 Hz, 2H), 7.39 (d, J = 8.0 Hz, 2H), 7.23 (t, J = 7.6 Hz, 2H), 7.17−7.14 (m, 6H), 6.98 (d, J = 8.0 Hz, 2H), 2.35 (s, 3H), 2.23 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 138.9, 137.8, 136.9, 135.8, 131.8, 131.1, 131.0, 130.1, 129.7, 129.2, 128.6, 128.4, 127. 5, 126.8, 21.1, 21.0.

*(Z)-1,2-Bis(4-(chlorophenyl)thio)styrene (**1k**).* Light yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (d, J = 7.2 Hz, 2H), 7.43−7.40 (m, 2H), 7.34−7.32 (m, 2H), 7.26−7.21 (m, 3H), 7.15−7.13 (m, 4H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 138.2, 135.8, 133.9, 133.5, 133.1, 132.0, 131.9, 129.9, 129.5, 129.3, 1129.1, 128.6, 128.0, 126.8.

*(Z)-1,2-Bis(4-(methoxyphenyl)thio)styrene (**1l**).* Light yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50−7.44 (m, 4H), 7.23−7.12 (m, 3H), 6.99 (s, 1H), 7.88 (d, J = 7.2 Hz, 2H), 6.71 (d, J = 8.8 Hz, 2H), 3.79 (s, 3H), 3.69 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 159.7, 158.5, 138.9, 136.6, 133.3, 131.2, 129.8, 128.3, 127.4, 127.0, 125.8, 125.2, 55.4, 55.3.

*(Z)-1,2-Bis(n-propylthio)-4-methoxystyrene (**1m**).*[25] $Ni(acac)_2$ (0.18 mmol, 46 mg), $(n\text{-}Pr)_2S_2$ (6.0 mmol, 900 mg), and PBu_3 (1.8 mmol, 363.6 mg) were placed in a reaction vessel and stirred at room temperature until a homogeneous brown solution was formed. (4-Methoxyphenyl)acetylene (6.0 mmol, 792 mg) was added to the solution, and the reaction was carried out at 100 °C with stirring until complete conversion of the $n\text{-}Pr_2S_2$. After completion of the reaction, the residue was purified by flash chromatography to afford (*Z*)-1,2-bis(*n*-propylthio)-4-methoxystyrene (**1m**; 1.65 g, 72%). Light yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 (d, J = 6.8 Hz, 2H), 6.86 (d, J = 7.2 Hz, 2H), 6.41 (s, 1H), 3.82 (s, 3H), 2.77 (t, J = 7.6 Hz, 2H), 2.47 (t, J = 7.2 Hz, 2H), 1.75−1.69 (m, 2H), 1.51−1.46 (m, 2H), 1.03 (t, J = 7.2 Hz, 3H), 0.91 (t, J = 7.6 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 159.0, 132.0, 130.7, 130.3, 128.4, 113.8, 55.3, 36.3, 34.6, 27.9, 23.2, 13.2.

*(Z)-1,2-Bis(4-methoxyphenylthio)-4-methoxystyrene) (**1n**).* Light yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45−7.41 (m, 4H), 7.21 (d, J = 8.8 Hz, 2H), 6.90−6.86 (m, 3H), 6.73 (d, J = 8.0 Hz, 4H), 3.80 (s, 3H), 3.73 (s, 3H), 3.71 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 159.6, 159.0, 158.5, 134.1, 133.1, 134.5, 131.2, 129.8, 128.2, 126.1, 125.3, 114.9, 114.5, 113.7, 55.4, 55.3; MS (EI) *m*/*z* 410 (M^+, 56), 271 (100), 256 (44), 240 (28), 227 (29), 165 (7), 139 (56), 125 (18), 95 (13), 89 (7), 77 (6), 63 (5).

*(Z)-1,2-Bis(4-(methylphenyl)thio)-4-methylstyrene (**1o**).* Light yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39−7.33 (m, 4H), 7.19−7.09 (m, 6H), 6.97 (d, J = 8.0 Hz, 3H), 2.33 (s, 3H), 2.26 (s, 3 H), 2.21 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 139.0, 138.0, 137.8, 136.9,

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J. Org. Chem. 2016, 81, 3246−3255

135.8, 131.8, 131.3, 131.1, 130.1, 129.7, 129.3, 128.5, 128.4, 128.3, 127.4, 124.1, 21.5, 21.2, 21.1.

*(Z)-1,2-Bis(4-(methylphenyl)thio)-4-methoxystyrene (**1p**).* Light yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 (d, J = 7.6 Hz, 2H), 7.36 (d, J = 8.0 Hz, 2H), 7.14−7.11 (m, 4H), 7.01 (s, 1H), 6.94 (d, J = 8.0 Hz, 2H), 6.72 (d, J = 8.8 Hz, 2H), 3.67 (s, 3H), 2.31 (s, 3H), 2.19 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 159.2, 137.6, 135.8, 134.4, 132.1, 131.6, 131.3, 130.9, 130.1, 129.8, 129.4, 128.7, 128.1, 113.8, 55.3, 21.2, 21.1.

*(Z)-1,2-Bis(4-(methylphenyl)thio)-4-(tert-butyl)styrene (**1q**).* Light yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 (d, J = 8.4 Hz, 2H), 7.38 (d, J = 8.0 Hz, 2H), 7.27−7.25 (m, 3H), 7.19 (s, 1H), 7.17−7.15 (m, 4H), 7.00 (d, J = 8.0 Hz, 2H), 2.35 (s, 3H), 2.25 (s, 3H), 1.27 (s, 9H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 150.5, 137.6, 136.9, 136.2, 135.5, 131.9, 131.5, 130.9, 130.0, 129.7, 128.6, 128.1, 126.3, 125.3, 34.5, 31.2, 21.1, 21.0.

General Procedure for the Synthesis of 3a−s. Methyl(ethyl) magnesium chloride (0.25 mmol) was added to a mixture of (*Z*)-vinylic disulfides (0.2 mmol), NiF_2 (0.97 mg, 0.01 mmol), and PPh_3 (2.62 mg, 0.01 mmol) in dry THF (1.0 mL) at room temperature under N_2. The reaction mixture was stirred at room temperature for 25 h. After completion of the reaction, the solution was quenched with H_2O_2 (1.0 mL) and stirred at room temperature for 3 h. The resulting mixture was extracted with dichloromethane, and the combined organic layers were dried over anhydrous Na_2SO_4, subjected to filtration, and concentrated in vacuo. The residue was purified by flash chromatography on silica gel (petroleum ether) to afford the desired products **3a−s**.

General Procedure for the Synthesis of 3t−ac. Grignard reagent (0.25 mmol) was added to a mixture of (*Z*)-vinylic disulfides (0.2 mmol), NiF_2 (4.85 mg, 0.05 mmol), and PPh_3 (13.1 mg, 0.05 mmol) in dry THF (1.0 mL) at room temperature under N_2. The reaction mixture was stirred at room temperature for 25 h. After completion of the reaction, the solution was quenched with H_2O_2 (1.0 mL) and stirred at room temperature for 3 h. The resulting mixture was extracted with dichloromethane, and the combined organic layers were dried over anhydrous Na_2SO_4, subjected to filtration, and concentrated in vacuo. The residue was purified by flash chromatography on silica gel (petroleum ether) to afford the desired products **3t−ac**.

*(Z)-1-(Phenylthio)-2-methylstyrene (**3a**).* Light yellow oil: yield 91% (41.1 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (d, J = 7.6 Hz, 2H), 7.24−7.01 (m, 7H), 7.03−7.00 (m, 1H), 6.51 (q, J = 6.8 Hz, 1H), 2.08 (d, J = 6.8 Hz, 3H); ^{113}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 104.7, 136.1, 134.7, 134.2, 128.7, 128.2, 127.9, 127.5, 127.4, 125.3, 17.0; MS (m/z) 226 (M^+, 100), 211 (14), 117 (86), 110 (17), 91 (23), 77 (7), 65 (7); HRMS calcd for $C_{15}H_{14}S$ 226.0811, found 226.0840.

*(Z)-1-(Phenylthio)-2,4-dimethylstyrene (**3b**).* Light yellow oil: yield 92% (44.1 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29−7.26 (m, 2H), 7.07−7.04 (m, 5H), 6.96−6.90 (m, 2H), 6.41 (q, J = 6.8 Hz, 1H), 2.20 (s, 3H), 1.98 (d, J = 6.8 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 137.8, 137.2, 136.3, 133.9, 128.9, 128.7, 127.8, 127.2, 125.2, 21.1, 16.9; MS (m/z) 240 (M^+, 100), 225 (28), 117 (91), 91 (45), 65 (10); HRMS calcd for $C_{16}H_{16}S$ 240.0967, found 240.0964.

*(Z)-1-(Phenylthio)-2,3-dimethylstyrene (**3c**).* Light yellow oil: yield 92% (44.1 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53, 7.24−7.21 (m, 3H), 7.05 (d, J = 8.0 Hz, 2H), 6.94 (d, J = 8.0 Hz, 2H), 6.46 (q, J = 6.8 Hz, 1H), 2.22 (s, 3H), 2.08 (d, J = 6.8 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 104.7, 137.7, 136.3, 134.6, 134.2, 128.7, 128.3, 128.1, 128.0, 127.8, 125.2, 124.6, 21. 5, 16.9; MS (m/z) 240 (M^+, 100), 225 (26), 117 (90), 91 (48), 65 (8); HRMS calcd for $C_{16}H_{16}S$ 240.0964, found 240.0963.

*(Z)-1-(Phenylthio)-2-methyl-4-(tert-butyl)styrene (**3d**).* Light yellow oil: yield 93% (53.4 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 (d, J = 8.4 Hz, 2H), 7.19 (d, J = 8.8 Hz, 2H), 7.09−7.08 (m, 3H), 6.97−6.96 (m, 1H), 6.49 (q, J = 6.8 Hz, 1H), 1.99 (d, J = 6.8 Hz, 3H), 1.20 (s, 9H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 150.5, 137.8, 136.6, 134.7, 133.5, 128.7, 127.3, 126.8, 125.1, 125.0, 34.5, 31.3, 16.9; MS (m/z) 282 (M^+, 2), 277 (20), 268 (21), 226 (12), 211 (100), 183 (14), 152 (6), 115 (10), 91 (8), 57 (16); HRMS calcd for $C_{19}H_{22}S$ 282.1437, found 282.1432.

*(Z)-1-(Phenylthio)-2-methyl-4-(n-propyl)styrene (**3e**).* Yellow oil: yield 90% (48.2 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, J = 8.4 Hz, 2H), 7.14−7.10 (m, 4H), 7.04−7.01 (m, 3H), 6.50 (q, J = 6.8 Hz, 1H), 2.50 (t, J = 8.0 Hz, 2H), 2.05 (d, J = 6.8 Hz, 3H), 1.59−1.56 (m, 2H), 0.89 (t, J = 7.6 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 142.1, 138.1, 136.4, 134.1, 133. 9, 128.7, 128.3, 128.1, 127.7, 127.2, 125.1, 37.7, 24.4, 16.9, 13.9; MS (m/z) 268 (M^+, 15), 241 (11), 218 (8), 163 (9), 159 (30), 147 (100), 129 (12), 117 (17), 109 (11), 91 (21), 77 (12), 57 (12); HRMS calcd for $C_{18}H_{20}S$ 268.1280, found 268.1273.

*(Z)-1-(Phenylthio)-2-methyl-4-methoxystyrene (**3f**).* Yellow oil: yield 83% (42.3 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 (d, J = 8.4 Hz, 2H), 7.15−7.14 (m, 4H), 7.06−7.03 (m, 1H), 6.77 (d, J = 8.8 Hz, 2H), 6.43 (q, J = 6.8 Hz, 1H), 3.76 (s, 3H), 2.07 (d, J = 6.8 Hz, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 159.0, 136.2, 133.5, 133.2, 132.9, 128.7, 128.5, 127.8, 125.2, 113.5, 55.2, 16.8; MS (m/z) 256 (M^+, 36), 156 (6), 147 (100), 132 (12), 115 (18), 103 (11), 91 (24), 77 (8), 51 (4); HRMS calcd for $C_{16}H_{16}OS$ 256.0916, found 256.0916.

*1-(Phenylthio)-2-methyl-4-fluorostyrene (**3g**).* Yellow oil: yield 92% (44.9 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51−7.47 (m, 2H), 7.14−7.13 (m, 4H), 7.05−7.02 (m, 1H), 6.93−6.87 (m, 2H), 6.43 (d, J = 6.8 Hz, 1H), 2.08 (d, J = 6.8 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 162.2 (d, $^1J_{C-F}$ = 245.2 Hz), 136.7, 135.6, 134.2, 133.4, 129.0, 128.9, 128.8, 128.7, 128.2, 125.5, 115.1, 114.9, 16.9; MS (m/z) 244 (M^+, 63), 229 (7), 196 (4), 154 (18), 139 (47), 135 (100), 123 (40), 109 (54), 95 (17), 75 (7), 69 (13); HRMS calcd for $C_{15}H_{13}FS$ 244.0717, found 244.0709.

*(Z)-1-(Phenylthio)-2-methyl-3-thienylenevinylene (**3h**).* Yellow oil: yield 83% (35.6 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 (s, 1H), 7.25−7.23 (m, 1H), 7.18−7.17 (m, 5H), 7.09−7.04 (m, 1H), 6.64 (q, J = 6.8 Hz, 1H), 2.05 (d, J = 6.8 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 142.3, 136.3, 133.8, 128.8, 128.4, 127.4, 125.9, 125.6, 125.2, 122.4, 16.4; MS (m/z) 232 (M^+, 74), 217 (11), 199 (13), 184 (5), 160 (7), 127 (27), 123 (100), 110 (10), 97 (8), 79 (25), 51 (7); HRMS calcd for $C_{13}H_{12}S_2$ 232.0375, found 232.0370.

*(Z)-4-(Propylthio)-3-heptene (**3i**).* Yellow oil: yield 94% (40.7 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26−7.25 (m, 4H), 7.17−7.14 (m, 1H), 5.90 (t, J = 6.8 Hz, 1H), 2.37−2.30 (m, 2H), 1.52−1.46 (m, 2H), 1.00 (t, J = 7.6 Hz, 3H), 0.82 (t, J = 7.6 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 138.5, 135.8, 132.2, 129.1, 128.7, 125.6, 39.6, 23.3, 21.6, 14.0, 13.3; MS (m/z) 206 (M^+, 65), 191 (35), 177 (15), 161 (34), 136 (64), 97 (100), 77 (35), 51 (14); HRMS calcd for $C_{13}H_{18}S$ 206.1152, found 206.1154.

*(Z)-1-(4-(Methylphenyl)thio)-2-methylstyrene (**3j**).* Yellow oil: yield 92% (44.1 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (d, J = 7.6 Hz, 2H), 7.26−7.17 (m, 3H), 7.05 (d, J = 8.0 Hz, 2H), 6.94 (d, J = 8.0 Hz, 2H), 6.46 (q, J = 6.8 Hz, 1H), 2.22 (s, 3H), 2.08 (d, J = 6.8 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 140.8, 135.2, 134.8, 134.0, 132.4, 129.6, 128.4, 128.2, 127.5, 127.4, 21.0, 16.9; MS (m/z) 240 (M^+, 100), 225 (27), 121 (41), 147 (88), 91 (47), 65 (7); HRMS calcd for $C_{16}H_{16}S$ 240.0967, found 240.0963.

*(Z)-1-(4-(Chlorophenyl)thio)-2-methylstyrene (**3k**).* Yellow oil: yield 91% (47.3 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (d, J = 7.2 Hz, 2H), 7.25−7.19 (m, 3H), 7.09−7.08 (m, 4H), 6.51 (q, J = 6.8 Hz, 1H), 2.08 (d, J = 6.8 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 140.2, 134.9, 134.0, 131.2, 129.5, 129.3, 128.8, 128.3, 127.6, 127.3, 16.9; MS (m/z) 260 (M^+, 40), 225 (7), 144 (8), 121 (17), 117 (100), 108 (4), 91 (28), 65 (5); HRMS calcd for $C_{15}H_{13}ClS$ 260.0421, found 260.0413.

*(Z)-1-(4-9Methoxyphenyl)thio)-2-methylstyrene (**3l**).* Yellow oil: yield 82% (41.7 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 (d, J = 7.6 Hz, 2H), 7.25−7.15 (m, 4H), 7.10 (d, J = 7.6 Hz, 2H), 6.68 (d, J = 7.6 Hz, 2H), 6.35 (q, J = 6.8 Hz, 1H), 3.70 (s, 3H), 2.09 (d, J = 6.8 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 158.1, 140.7, 135.8, 132.6, 130.9, 128.0, 127.6, 127.3, 126.2, 114.4, 55.2, 16.7; MS (m/z) 256 (M^+, 26), 207 (4), 147 (100), 135 (96), 132 (10), 115 (21), 103 (15), 91 (36), 77 (28), 65 (13); HRMS calcd for $C_{16}H_{16}OS$ 256.0924, found 256.0926.

*(Z)-1-(Propylthio)-2-ethyl-4-methoxystyrene (**3m**).* Yellow oil: yield 95% (41.8 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 (d, J = 8.0 Hz, 2H), 6.79 (d, J = 8.0 Hz, 2H), 5.83 (t, J = 7.2 Hz, 1H), 3.74 (s, 3H), 2.42−2.35 (m, 2H), 2.27 (t, J = 7.2 Hz, 2H), 1.37−1.32 (m, 2H), 0.99 (t, J = 7.6 Hz, 3H), 0.80 (t, J = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ

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J. Org. Chem. 2016, 81, 3246−3255

159.0, 136.2, 134.7, 133.2, 129.0, 113.6, 55.3, 34.0, 23.9, 23.1, 14.0, 13.1; MS (m/z) 236 (M^+, 67), 207 (12), 194 (35), 161 (100), 128 (28), 107 (42), 75 (28); HRMS calcd for $C_{14}H_{20}OS$ 236.1278, found 236.1276.

(Z)-1-(4-(Methoxyphenyl)thio)-2-methyl-4-methoxystyrene (**3n**). Yellow oil: yield 84% (47.9 mg); ^1H NMR (400 MHz, $CDCl_3$) δ 7.42 (d, J = 7.2 Hz, 2H), 7.10 (d, J = 8.8 Hz, 2H), 6.76−6.68 (m, 4H), 6.26 (q, J = 6.8 Hz, 1H), 3.75 (s, 3H), 3.71 (s, 3H), 2.07 (d, J = 6.8 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 135.5, 133.4, 129.8, 129.5, 129.1, 129.0, 128. 7, 128.6, 115.0, 114.8, 21.1, 20.9, 16.8; MS (m/z) 286 (M^+, 26), 147 (100), 115 (13), 103 (6), 91 (15), 77 (5); HRMS calcd for $C_{17}H_{18}O_2S$ 286.1037, found 286.1032.

(Z)-1-(4-(Methylphenyl)thio)-2-methyl-4-methylstyrene (**3o**). Light yellow oil: yield 87% (44.2 mg); ^1H NMR (400 MHz, $CDCl_3$) δ 7.43 (d, J = 8.0 Hz, 2H), 7.15−7.13 (m, 1H), 7.06−7.02 (m, 4H), 6.95 (d, J = 8.4 Hz, 2H), 6.44 (q, J = 6.8 Hz, 1H), 2.28 (s, 3H), 2.22 (s, 3H), 2.08 (d, J = 6.8 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 137.9, 137.1, 135.0, 134.4, 133.3, 132.5, 129.5, 128.8, 128.1, 127.2, 60.4, 21.0, 14.2; MS (m/z) 254 (M^+, 98), 240 (17), 135 (32), 131 (100), 115 (34), 105 (5), 91 (34), 77 (6), 65 (5); HRMS calcd for $C_{17}H_{18}S$ 254.1124, found 254.1116.

(Z)-1-(4-(Methylphenyl)thio)-2-methyl-4-methoxystyrene (**3p**). Yellow oil: yield 88% (47.4 mg); ^1H NMR (400 MHz, $CDCl_3$) δ 7.38 (d, J = 7.2 Hz, 2H), 6.96 (d, J = 8.0 Hz, 2H), 6.87 (d, J = 8.4 Hz, 2H), 6.67 (d, J = 8.8 Hz, 2H), 6.28 (q, J = 6.8 Hz, 1H), 3.65 (s, 3H), 2.13 (s, 3H), 1.97 (d, J = 6.8 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 159.0, 135.1, 133.7, 133.3, 132.3, 129.5, 128.5, 128.2, 113.5, 55.2, 20.9, 16.8; MS (m/z) 270 (M^+, 45), 255 (12), 224 (52), 175 (37), 163 (35), 148 (17), 123 (26), 107 (100), 72 (18); HRMS calcd for $C_{17}H_{18}OS$ 270.1127, found 270.1124.

(Z)-1-(4-(Methylphenyl)thio)-2-methyl-4-(tert-butyl)styrene (**3q**). Yellow oil: yield 87% (50.7 mg); ^1H NMR (400 MHz, $CDCl_3$) δ 7.26−7.23 (m, 2H), 7.06 (d, J = 8.0 Hz, 2H), 6.96 (d, J = 8.0 Hz, 2H), 6.51 (q, J = 6.8 Hz, 1H), 2.22 (s, 3H), 2.05 (d, J = 6.8 Hz, 3H), 1.27 (s, 9H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 150.4, 138.0, 134.9, 134.1, 134.0, 132.9, 129.5, 129.1, 127.7, 126.9, 125.1, 34.5, 31.3, 20.9, 16.9; MS (m/z) 296 (M^+, 13), 175 (100), 161 (64), 147 (18), 123 (12), 115 (14), 91 (27), 77 (8), 57 (23); HRMS calcd for $C_{20}H_{24}S$ 296.1641, found 296.1645.

(Z)-1-(Phenylthio)-2-ethylstyrene (**3r**). Yellow oil: yield 93% (44.6 mg); ^1H NMR (400 MHz, $CDCl_3$) δ 7.55 (d, J = 8.4 Hz, 2H), 7.23−7.09 (m, 7H), 7.02−6.99 (m, 1H), 6.42 (t, J = 7.2 Hz, 1H), 2.57−2.50 (m, 2H), 1.09 (t, J = 7.2 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 141.7, 140.5, 132.7, 128.7, 128.2, 128.1, 127.5, 125.3, 24.5, 13.9; MS (m/z) 240 (M^+, 17), 211 (7), 133 (37), 115 (18), 110 (23), 105 (15), 91 (100), 77 (17), 57 (13), 79 (25), 51 (7); HRMS calcd for $C_{16}H_{16}S$ 240.0967, found 240.0962.

(Z)-1-(Phenylthio)-2-ethyl-4-methoxystyrene (**3s**). Light yellow oil: yield 88% (47.5 mg); ^1H NMR (400 MHz, $CDCl_3$) δ 7.40 (d, J = 8.4 Hz, 2H), 7.07−7.01 (m, 4H), 6.94−6.91 (m, 1H), 6.66 (d, J = 8.4 Hz, 2H), 6.25 (t, J = 7.6 Hz, 1H), 3.63 (s, 3H), 2.47−2.40 (m, 2H), 1.0 (t, J = 7.6 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 159.1, 140.1, 136.4, 133.0, 132.1, 128.7, 128.6, 128.0, 125.2, 113.6, 55.2, 24.5, 14.0; MS (m/z) 270 (M^+, 8), 185 (4), 161 (100), 128 (44), 117 (38), 107 (15), 91 (36), 66 (14); HRMS calcd for $C_{17}H_{18}OS$ 270.1175, found 270.1173.

(Z)-1-(Phenylthio)-2-allylstyrene (**3t**). Yellow oil: yield 82% (41.3 mg); ^1H NMR (400 MHz, $CDCl_3$) δ 7.55 (d, J = 7.6 Hz, 2H), 7.35- 7.27 (m, 1H), 7.24 (s, 1H), 7.20−7.13 (m, 5H), 7.03 (t, J = 6.8 Hz, 1H), 6.40 (t, J = 7.2 Hz, 1H), 5.92−5.86 (m, 1H), 5.15−5.04 (m, 2H), 3.31 (t, J = 6.4 Hz, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 140.2, 136.5, 135.70, 134.69, 131.1, 129.2, 128.7, 128.4, 128.2, 127.7, 127.6, 125.5, 115.8, 35.2; MS (m/z) 252 (M^+, 10), 239 (16), 199 (15), 175 (8), 157 (13), 128 (19), 105 (100), 77 (53), 51 (19); HRMS calcd for $C_{17}H_{16}S$ 252.1045, found 252.1047.

(Z)-1-(Phenylthio)-2-cyclopentylstyrene (**3u**). Yellow oil: yield 86% (48.1 mg); ^1H NMR (400 MHz, $CDCl_3$) δ 7.55 (d, J = 7.2 Hz, 2H), 7.24−7.20 (m, 2H), 7.16−7.10 (m, 5H), 7.02 (d, J = 6.8 Hz, 1H), 6.37 (d, J = 9.2 Hz, 1H), 3.34−3.28 (m, 1H), 1.91−1.88 (m, 2H), 1.74−1.59 (m, 4H), 1.43−1.37 (m, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 145.8, 140.4, 136.4, 131.7, 128.7, 128.1, 127.9, 127.43, 127.38, 125.2, 42.0, 33.6, 25.6; MS (m/z) 280 (M^+, 100), 212 (17), 203 (18), 184 (5), 171 (45), 141 (46), 129 (60), 121 (37), 91 (38), 77 (8), 67 (7); HRMS calcd for $C_{19}H_{20}S$ 280.1280, found 280.1275.

(Z)-1-(Phenylthio)-2-cyclohexylstyrene (**3v**). Light yellow oil: yield 85% (50.0 mg); ^1H NMR (400 MHz, $CDCl_3$) δ 7.54 (d, J = 7.2 Hz, 2H), 7.22−7.09 (m, 5H), 7.01 (t, J = 7.2 Hz, 1H), 6.25 (d, J = 9.2 Hz, 1H), 2.94−2.86 (m, 1H), 1.77−1.70 (m, 4H), 1.34−1.19 (m, 6H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 145.7, 140.3, 136.2, 131.3, 128.6, 128.1, 128.1, 127.5, 127.4, 125.3, 39.9, 32.8, 26.0, 25.7; MS (m/z) 294 (M^+, 100), 217 (26), 212 (28), 185 (21), 161 (14), 141 (34), 128 (36), 117 (28), 115 (23), 103 (15), 91 (24), 71 (14); HRMS calcd for $C_{20}H_{22}S$ 294.1416, found 294.1418.

(Z)-1-(Phenylthio)-2-cyclopentyl-4-methoxystyrene (**3w**). Light yellow oil: yield 72% (44.6 mg); ^1H NMR (400 MHz, $CDCl_3$) δ 7.51 (d, J = 8.8 Hz, 2H), 7.17−7.14 (m, 4H), 7.05−7.01 (m, 1H), 6.78 (d, J = 8.8 Hz, 2H), 6.29 (d, J = 9.2 Hz, 1H), 3.75 (s, 3H), 3.34−3.28 (m, 1H), 1.94−1.88 (m, 2H), 1.86−1.58 (m, 4H), 1.44−1.37 (m, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 159.0, 144.1, 136.6, 132.9, 130.8, 128.6, 128.5, 127.9, 125.2, 113.5, 55.2, 41.9, 33.7, 25.6; MS (m/z) 310 (M^+, 77), 279 (8), 242 (11), 201 (89), 159 (36), 145 (16), 133 (35), 121 (100), 115 (25), 110 (45), 91 (17), 77 (18), 67 (15); HRMS calcd for $C_{20}H_{22}OS$ 310.1452, found 310.1450.

(Z)-1-(Phenylthio)-2-phenylstyrene (**3x**).[26] Light yellow oil: yield 72% (41.5 mg); ^1H NMR (400 MHz, $CDCl_3$) δ 7.32−7.29 (m, 8H), 7.22−7.20 (m, 2H), 7.13−7.10 (m, 3H), 7.04−7.02 (m, 2H), 6.97 (s, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 143.4, 142.6, 140.4, 137.4, 130.4, 129.6, 128.6, 128.2, 128.2, 128.0, 127.6, 127.5, 127.4, 136.7; MS (m/z) 288 (M^+, 48), 211 (28), 198 (38), 178 (100), 109 (54), 102 (15), 77 (26); HRMS calcd for $C_{20}H_{16}S$ 288.1052, found 288.1050.

(Z)-1-(4-(Methylphenyl)thio)-2-phenylstyrene (**3y**). Light yellow oil: yield 75% (45.3 mg); ^1H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, J = 7.6 Hz, 2H), 7.61 (d, J = 7.6 Hz, 2H), 7.37−7.33 (2, 4H), 7.25−7.23 (m, 4H), 7.13 (s, 1H), 7.07 (d, J = 8.0 Hz, 2H), 6.89 (d, J = 8.0 Hz, 2H), 2.17 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 141.1, 136.9, 135.8, 135.4, 135.1, 131.5, 129.6, 129.5, 128.18, 128.17, 128.15, 128.0, 127.84, 127.77, 21.0; MS (m/z) 302 (M^+, 35), 256 (23), 246 (12), 178 (100), 152 (14), 123 (20), 105 (18), 91 (13), 77 (22), 63 (5), 51 (9); HRMS calcd for $C_{21}H_{18}S$ 302.1125, found 302.1127.

(Z)-1-(Phenylthio)-2-(4-methoxyphenyl)styrene (**3z**). Light yellow oil: yield 65% (41.3 mg); ^1H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, J = 8.8 Hz, 2H), 7.63 (d, J = 7.2 Hz, 2H), 7.27−7.23 (m, 2H), 7.20−7.19 (m, 4H), 7.11 (t, J = 8.0 Hz, 2H), 7.02 (t, J = 7.6 Hz, 1H), 6.89 (d, J = 8.8 Hz, 2H), 3.82 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 159.3, 141.4, 135.9, 135.6, 131.8, 131.1, 129.4, 128.7, 128.2, 127.8, 127.6, 125.6, 113.6, 55.3; MS (m/z) 318 (M^+, 100), 209 (43), 197 (31), 194 (17), 165 (29), 139 (5), 91 (6); HRMS calcd for $C_{21}H_{18}OS$ 318.1073, found 318.1080.

(Z)-1-(Phenylthio)-2-phenyl-4-methoxystyrene (**3aa**).[27] Light yellow oil: yield 61% (38.8 mg); ^1H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, J = 7.6 Hz, 2H), 7.58 (d, J = 7.6 Hz, 2H), 7.36−7.32 (m, 2H), 7.26−7.23 (m, 1H), 7.19−7.09 (m, 5H), 7.03−7.00 (m, 1H), 7.78 (t, J = 8.4 Hz, 2H), 3.74 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 159.5, 137.0, 135.6, 134.4, 134.1, 133.4, 129.5, 129.2, 128.9, 128.7, 128.2, 127.6, 125.7, 113.6, 55.3; MS (m/z) 318 (M^+, 55), 209 (100), 194 (18), 165 (34), 151 (20), 139 (5), 110 (4), 84 (33), 77 (5); HRMS calcd for $C_{21}H_{18}OS$ 318.1154, found 318.1156.

(Z)-1-(Phenylthio)-2-(4-methylphenyl)-4-methoxystyrene (**3ab**). Light yellow oil: yield 72% (47.8 mg); ^1H NMR (400 MHz, $CDCl_3$) δ 7.62 (d, J = 8.0 Hz, 2H), 7.58 (d, J = 8.4 Hz, 2H), 7.17−7.09 (m, 7H), 7.04−7.02 (m, 1H), 6.78 (t, J = 8.8 Hz, 2H), 3.76 (s, 3H), 2.35 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 159.4, 137.6, 135.8, 134.7, 134.1, 133.6, 132.9, 129.4, 129.1, 128.84, 128.75, 128.6, 125.6, 113.6, 55.2, 21.3; MS (m/z) 332 (M^+, 56), 223 (100), 208 (20), 193 (7), 178 (13), 165 (18), 151 (24), 115 (6); HRMS calcd for $C_{22}H_{20}OS$ 332.1235, found 332.1236.

(Z)-1-(Propylthio)-2-phenyl-4-methoxystyrene (**3ac**). Light yellow oil: yield 95% (54.1 mg); ^1H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, J = 7.6 Hz, 2H), 7.52 (d, J = 8.4 Hz, 2H), 7.36 (t, J = 7.6 Hz, 2H), 7.25−7.24 (m, 1H), 6.92 (d, J = 8.4 Hz, 2H), 6.74 (s, 1H), 3.84 (s, 3H), 2.39 (t, J = 7.2 Hz, 2H), 1.47−1.42 (m, 2H), 0.82 (t, J = 7.2 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 159.4, 137.43, 137.35, 133.7, 129.54, 129.48, 128.0, 126.9, 113.7, 55.4, 34.9, 23.2, 13.3; MS (m/z) 284 (M^+, 100), 241

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J. Org. Chem. 2016, 81, 3246−3255

(45), 226 (26), 216 (77), 197 (16), 116 (83), 151 (72), 135 (11), 115 (8), 91 (8), 63 (6); HRMS calcd for $C_{18}H_{20}OS$ 284.1272, found 284.1275.

Experimental Procedure for Larger-Scale Synthesis of 3a. Methylmagnesium chloride (1.0 mL, 2.5 mmol) was added to a mixture of (*Z*)-1,2-bis(phenylthio)styrene (640 mg, 2.0 mmol), NiF_2 (9.7 mg, 0.1 mmol), and PPh_3 (26.2 mg, 0.1 mmol) in dry THF (6.0 mL) at room temperature under N_2. The reaction mixture was stirred at room temperature for 25 h. Upon completion, the reaction was quenched by H_2O_2 (5.0 mL), and the resulting mixture was extracted with dichloromethane. The organic layer was washed with water (30 mL × 3) and brine (30 mL × 1), and the separated aqueous phase was extracted with CH_2Cl_2 (30 mL × 2). The combined organic layers were dried over anhydrous Na_2SO_4, subjected to filtration, and concentrated in vacuo. The residue was purified by flash chromatography on silica gel (petroleum ether) to afford (*Z*)-1-(phenylthio)-2-methylstyrene (**3a**) as a light yellow oil (88%, 398 mg).

Experimental Procedure for the Synthesis of (*Z*)-Tamoxifen. *Procedure for the Synthesis of Compound* **5**. A mixture of Br_2 (2.0 mmol) and glacial acetic acid (2.0 mL) was added to a solution of (*Z*)-1-(4-(methylphenyl)thio)-2-phenylstyrene (2.0 mmol) and glacial acetic acid (4.0 mL), and the reaction mixture was stirred at room temperature for 2 h. Upon completion of the reaction, the product was filtered out and recrystallized from 95% ethanol to give (*E*)-1-(phenylthio)-2-bromotoluene in 75% yield. Then $Pd(PPh_3)_4$ (5.0 mmol %) was added to a solution of (*E*)-1-(phenylthio)-2-bromotoluene (1.0 mmol), 4-(*N*,*N*-dimethylethoxy)phenylboronic acid (2.0 mmol), Na_2CO_3 (2.0 mmol), and dry THF (3.0 mL) under a nitrogen amosphere. The reaction solution was stirred at 150 °C for 16 h. Upon completion of the reaction, the desired product (compound **5**) was obtained by column chromatography in 87% yield: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34−7.27 (m, 7H), 7.06−6.99 (m, 5H), 6.90−6.84 (m, 4H), 6.58 (d, J = 8.8 Hz, 2H), 3.99 (t, J = 5.6 Hz, 2H), 2.75 (t, J = 5.6 Hz, 2H), 2.35 (s, 6H), 2.19 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 157.4, 145.7, 144.1, 139. 6, 135.5, 135.1, 132.9, 132.2, 132.1, 131.1, 129.61, 129.56, 129.2, 128.1, 127.6, 127.2, 126.8, 113.6, 65.5, 58.0, 45.6, 21.0; MS (*m*/*z*) 465 (M^+, 91), 406 (7), 394 (8), 329 (7), 283 (8), 252 (23), 239 (13), 178 (8), 126 (6), 72 (88), 58 (100).

Procedure for the Synthesis of (Z)-Tamoxifen. EtMgCl (5.0 mL, 0.2 M in diethyl ether) was added to a mixture of compound **5** (100 mg, 0.1 mmol) and $NiCl_2$(dppe) (9.0 mg, 0.017 mmol) in diethyl ether (2.0 mL) under a nitrogen atmosphere, and the mixture was refluxed with stirring for 15 h. After addition of H_2O to the mixture, the residue was dissolved in Et_2O, and the solution was washed with H_2O and saturated sodium chloride and dried over anhydrous magnesium sulfate. Chromatography on silica gel (5% methanol in ethyl acetate) gave (*Z*)-tamoxifen (58.5 mg, 73% *Z*/*E* = 96/4): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33−7.12 (m, 10H), 6.77 (d, J = 8.8 Hz, 2H), 6.55 (d, J = 8.4 Hz, 2H), 3.91 (t, J = 5.6 Hz, 2H), 2.63 (t, J = 5.6 Hz, 2H), 2.45 (q, J = 7.2 Hz, 2H), 2.27 (s, 6H), 0.92 (t, J = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 156.8, 143.9, 142.5, 141.3, 138.3, 135.6, 131.9, 129.7, 129.5, 128.1, 127.9, 126.5, 126.0, 113.4, 65.7, 58.3, 45.9, 29.0, 13.6; MS (*m*/*z*) 371 (M^+, 18), 312 (4), 252 (24), 191 (6), 178 (5), 152 (3), 115 (3), 91 (5), 72 (33), 58 (100).

Procedure for the NMR Experiment. Methylmagnesium chloride (0.3 mmol, 2.5 mol/L in THF) was placed in a dry Schlenk tube under nitrogen. The solvent (THF) was removed in vacuo, and dry THF-d_8 (0.5 mL) was injected into the Schlenk tube under nitrogen. Then fresh methylmagnesium chloride (THF-d_8) was added to a low pressure/vacuum valve (PLV) NMR sample tube containing a mixture of (*Z*)-1,2-bis(phenylthio)styrene (32 mg, 0.1 mmol), NiF_2 (0.5 mg, 0.005 mmol), and PPh_3 (1.3 mg, 0.005 mmol) in dry THF-d_8 (0.5 mL) at room temperature under N_2. The reaction mixture was examined at hourly intervals by NMR spectroscopy.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b00203.

^{1}H NMR and ^{13}C{^{1}H} NMR spectra of compounds **1a**−**q**, **3a**−**ac**, **5**, and (*Z*)-tamoxifen (PDF)

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Notes

The authors declare no competing financial interest.

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