JOC The Journal of Organic Chemistry

Article

Nickel-Catalyzed Regio-selective Cleavage of Csp2-S Bonds: Method for the Synthesis of Tri- and Tetra-Substituted Alkenes

Jinyang Chen, Sihai Chen, Xinhua Xu, Zhi Tang, Chak-Tong Au, and Renhua Qiu

J. Org. Chem., **Just Accepted Manuscript** • Publication Date (Web): 21 Mar 2016

Just Accepted

ACS Publications

The Journal of Organic Chemistry is published by the American Chemical Society.
1155 Sixteenth Street N.W., Washington, DC 20036

Nickel-Catalyzed Regio-selective Cleavage of C_{sp2}-S Bonds: Method for the Synthesis of Tri- and Tetra-Substituted Alkenes

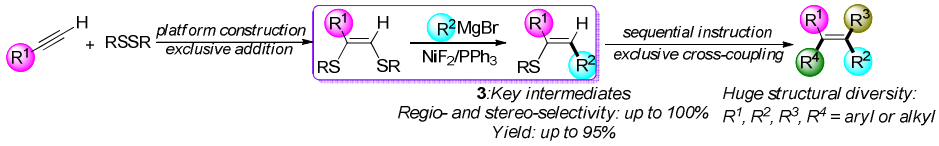
Jinyang Chen, Sihai Chen, Xinhua Xu*, Zhi Tang, Chak-Tong Au, Renhua Qiu*

State Key Laboratory of Chemo/Biosensing and Chemometrics, College of Chemistry and Chemical Engineering, Hunan University, Changsha, 410082, P.R. of China

xhx1581@hnu.edu.cn, renhuaqiu@hnu.edu.cn

RECEIVED DATE (to be automatically inserted after your manuscript is accepted if required according to the journal that you are submitting your paper to)

ABSTRACT

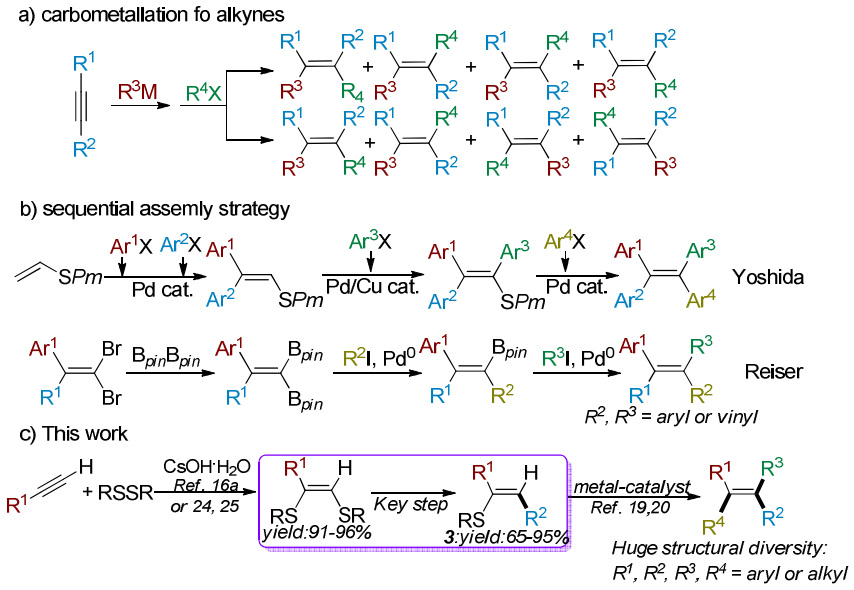


We describe here an efficient route for the synthesis of (*Z*)-vinylic sulfides 3 *via* the highly regio- and stereo-selective coupling of (*Z*)-1,2-diaryl(alkyl)thio alkenes and Grignard Reagents over a Ni-catalyst under mild conditions. (*Z*)-Vinylic sulfides 3 are important intermediates in the synthesis of tri- and tetra-substituted 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 resource. The protocol provides a general method that is highly regio- and stereo-selective for the synthesis of a diversity of tri- and tetra-substituted 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 of which each 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 tetra-substituted alkenes[6], the potential of huge structural diversity has not been fully exploited. For the preparation of tri- and tetra-substituted alkenes, the carbonmetallation of alkynes (Scheme 1a) is generally accepted as the most widely used method[7], disregard of the problems of poor stereo-selectivity[7a,7b] and the lack of structural flexibility[7d]. Compared to the carbonmetallation approach, the sequential assembly strategy using configuration-fixed heteroatoms (E)[8a] or halogen substituted[8b] alkenes as platforms has the advantages of high regio-selectivity and structural flexibility. However, there are only two pioneering works[8] and the studies were on substituents of aryl 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 tetra-substituted alkenes.

Scheme 1. General methods for synthesis of tri- and tetra-substituted alkenes.



Last decade, in the area of transition metal-catalyzed cross-coupling reactions, the C–E (S, Se, or Te) bond cleaving reactions have attracted considerable attention as they provide a good way to form new C–C bond with configuration retention[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 mult-substituted alkenes are vinylic chalcogenides[9a-e]. However, until now, most of the synthetic applications focus on vinylic monochalcogenides[9] and there are few on vinylic dichalcogenides[15]. It is because when vinylic dichalcogenides were treated with nucleophilic reagents, it was hard to control the cleavage of two C–E bonds regio-selectively. 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 stereo-selective reactions of terminal alkynes and diaryl(alkyl) disulfides (diselenides and ditellurides) catalyzed by cesium hydroxide under mild conditions. Due to difference in the activity of C_{sp2}–S and C_{sp2}–Se (Te) bonds, (*Z*)-vinylic selenossulfides (tellurossulfides) can be used as effective platform molecules for the stereoselective synthesis of tri- and tetra-substituted alkenes[17]. However, purification is a problem because the stereoisomers of (*Z*)-vinylic selenossulfides (tellurossulfides) are similar in polarity[18].

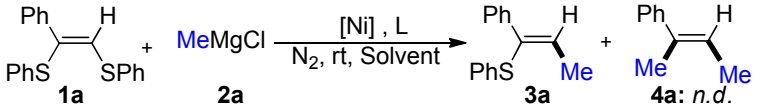
During our attempt to develop a better way to synthesize tri-substituted alkenes by using (*Z*)-1,2-aryl(alkyl)thio alkenes as platforms, we observed that the coupling of (*Z*)-1,2-aryl(alkyl)thio alkenes with Grignard Reagents occurs only on C^1_{sp2}–S bond of (*Z*)-1,2-aryl(alkyl)thio alkenes, and forms (*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 tetra-substituted alkenes *via* the arylation (alkylation) of C–S[19] and C–H[20] bonds. To our knowledge, highly regio-selective coupling of (*Z*)-1,2-diaryl(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 regio-selective coupling of (*Z*)-1,2-diaryl(alkyl)thio alkenes with Grignard

Reagents catalyzed by Ni-catalysts, and their application in the preparation of tri- and tetra-substituted alkenes.

RESULTS AND DISCUSSION

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

Table 1. Optimization of reaction conditions [a]

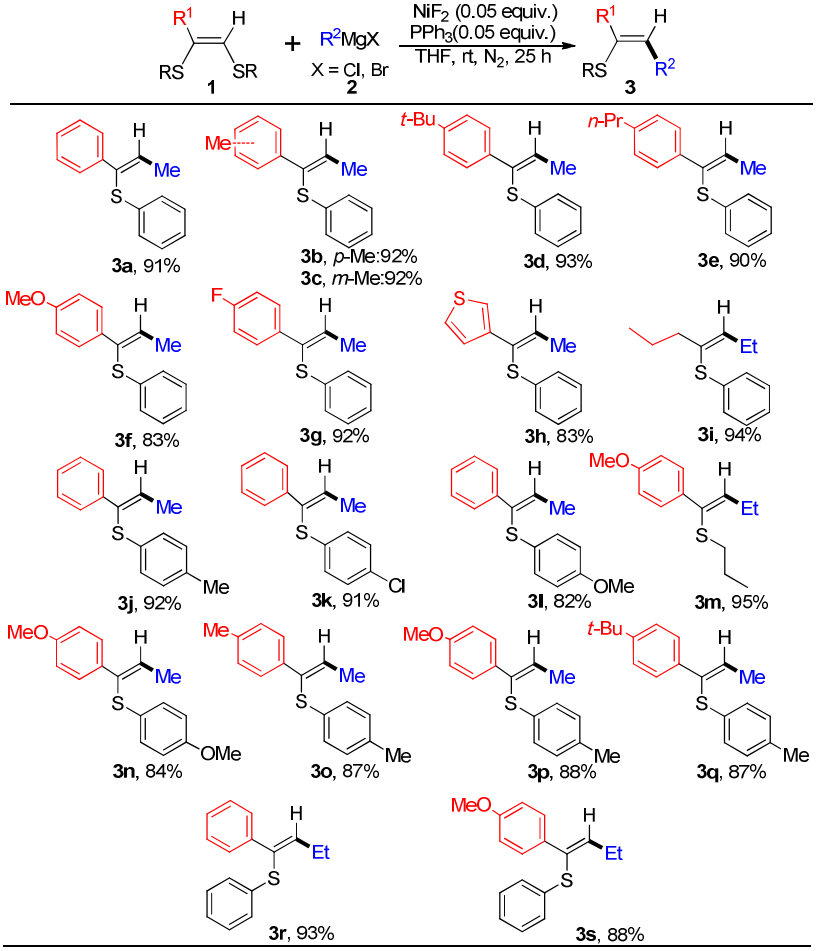


Entry	[Ni] (equiv.)	L (equiv.)	Conditions	Yield (**3a**) [b] (%)
1	$NiCl_2$ (1.0)	PPh_3 (1.0)	THF, rt, 10 h	46
2	None	PPh_3 (1.0)	THF, rt, 10 h	0
3	$NiCl_2$ (1.0)	None	THF, rt, 10 h	0
4	$NiCl_2$ (1.0)	PCy_3(1.0)	THF, rt, 10 h	26
5	$NiCl_2$ (1.0)	Xantphos (0.5)	THF, rt, 10 h	34
6	$NiBr_2$ (1.0)	PPh_3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

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

After 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, entriy 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 rusults 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 $^{\circ}$C, there was reduction of product yield to 80%, and generation of by-product. 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). And after H_2O_2 oxidation, diphenyl disulfide is obtained as the major by-product with a yield of 72%. When excess amount of methylmagnesium chloride **2a** was used, several other by-products such as biphenyl, toluene and diphenyl disulfide were detected. Thus the optimized reaction conditions are: 0.05 equiv. of NiF_2 and 0.05 equiv. of PPh_3, 1.0 equiv. of **1a** and 1.25 equiv. of **2a** in THF at rt under nitrogen for 25 h.

Table 2. Reaction Scope of 1,2-diarylthio Aromatic Acetylene[a]

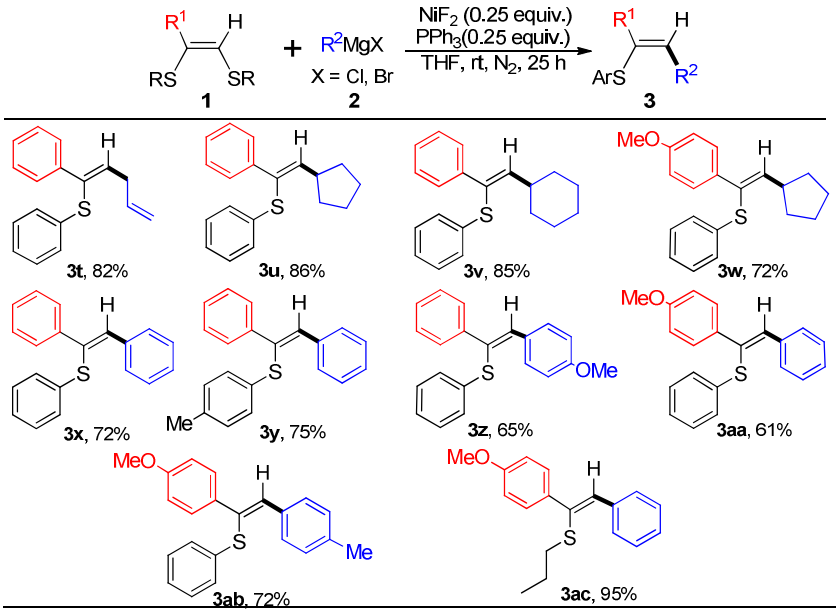


[a] Reaction conditions: **1** (0.2 mmol), **2** (0.25 mmol), NiF_2 (0.01 mmol), PPh_3 (0.01 mmol), THF (1.0 mL), N_2 , rt, 25 h.

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 *m*- and *p*-positions of the phenyl ring of aromatic ethylene affect the cross-coupling only slightly, affording the corresponding products in good to excellent yields (**3a**-**3g**, 83%-93%). The cross-coupling of 1,2-diphenylthio-4-(*t*-butyl)styrene with methylmagnesium chloride proceeds well with good yield (**3d**, 93%), suggesting that the steric effect of 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-diphenylthio thiophene alkene and (*Z*)-1,2-diphenylthio pentene, affording the corresponding products (**3h**, **3i**) in 83% and 94% yield, respectively. And the electron-donating and electron-withdrawing substituted functional groups at the phenyl ring bonded to the sulfur atom only slightly affects the cross-coupling

reaction (**3j-3q**, 82%-95%). Good yields also obtained when (*Z*)-vinylic disulfides were treated with ethylmagnesium chloride under the optimal conditions (**3r** and **3s**, 93% and 88%, respectively). The structure of product **3i** was determined by examining its NOESY H–H and COSY H–H interactions (SI), and the results show that the cross-coupling of (*Z*)-1,2-diaryl(alkyl)thio alkenes with Grignard Reagents occurs stereoselectively to give exclusively *Z*-isomers.

Table 3. Reaction Scope of Grignard Reagents [a]

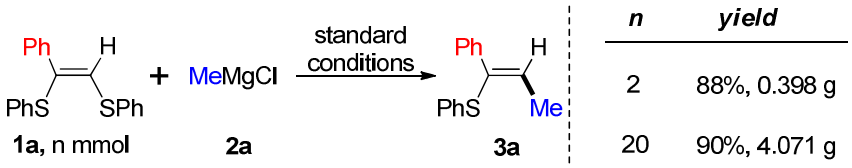


[a] Reaction conditions: **1** (0.2 mmol), **2** (0.25 mmol), NiF_2 (0.05 mmol), PPh_3 (0. 05 mmol), THF (1.0 mL), N_2 , rt, 25 h.

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. By increasing the amount of catalyst and ligand to 0.25 equiv., the reactions of (*Z*)-vinylic disulfides with both larger alkyl-substituted and aryl-substituted Grignard Reagents give 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 poorer than those (e.g. Me, Et, allyl) of small size (3t-3w, 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 aryl magnesium bromide (**3x-3ab**, 61%-75%). Smaller functional group (propyl)

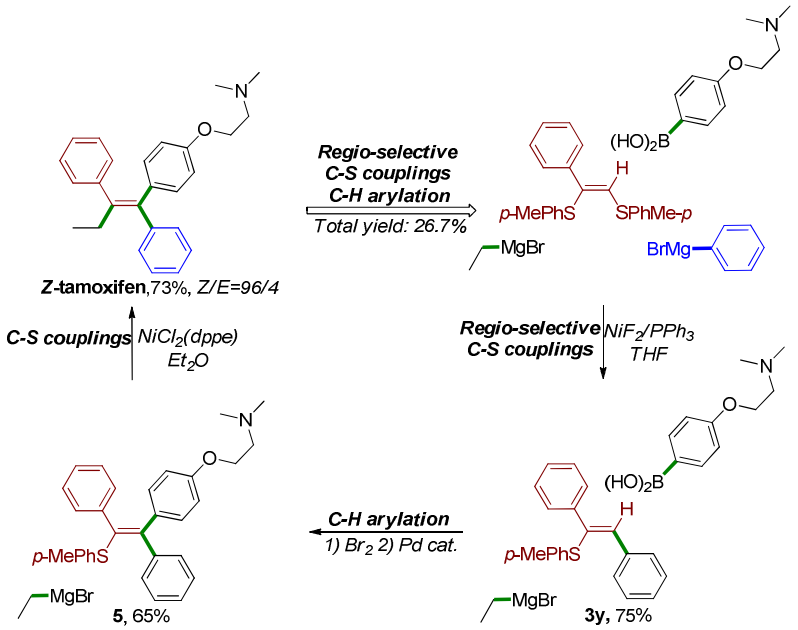
bonded to the sulfur atom can accelerate the cross-coupling, giving the corresponding product in 95% yield (**3ac**).

Scheme 2. Larger-scale synthesis of 3a.



The method can be carried out on a larger scale, and the yield percentage of the desired products decrease only slightly comparing with that of the small scale (0.2 mmol). The coupling of (*Z*)-1,2-diphenylthio styrene **1a** (640 mg, 2.0 mmol) and methylmagnesium chloride **2a** (1.0 mL, 2.5 mmol) using NiF_2 (9.7 mg, 0.1 mmol) and PPh_3 (26.2 mg, 0.1 mmol) affords (*Z*)-1-phenylthio-2-methyl styrene **3a** (398 mg) in 88% yield (90% in 20 mmol scale) (Scheme 2).

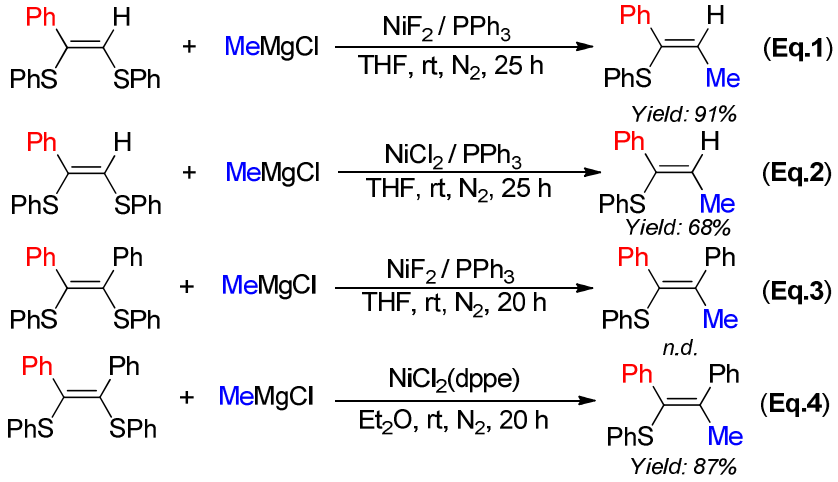
Scheme 3. Synthesis of (*Z*)-tamoxifen using product 3y as starting material.



Recently, a number of methods for stereoselective synthesis of tri- and tetra-substituted alkenes were reported[21], but it is hard to control the chemo- and regio-selectivity of products. According to previous studies[19,20], (*Z*)-Vinylic sulfides **3** are important intermediates in the preparation of tri- and

tetra-substituted 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 tetra-substituted alkenes. First compound **3y** is obtained readily 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 regio-selectivity using $NiCl_2$(dppe) as catalyst[12d] (Scheme 3).

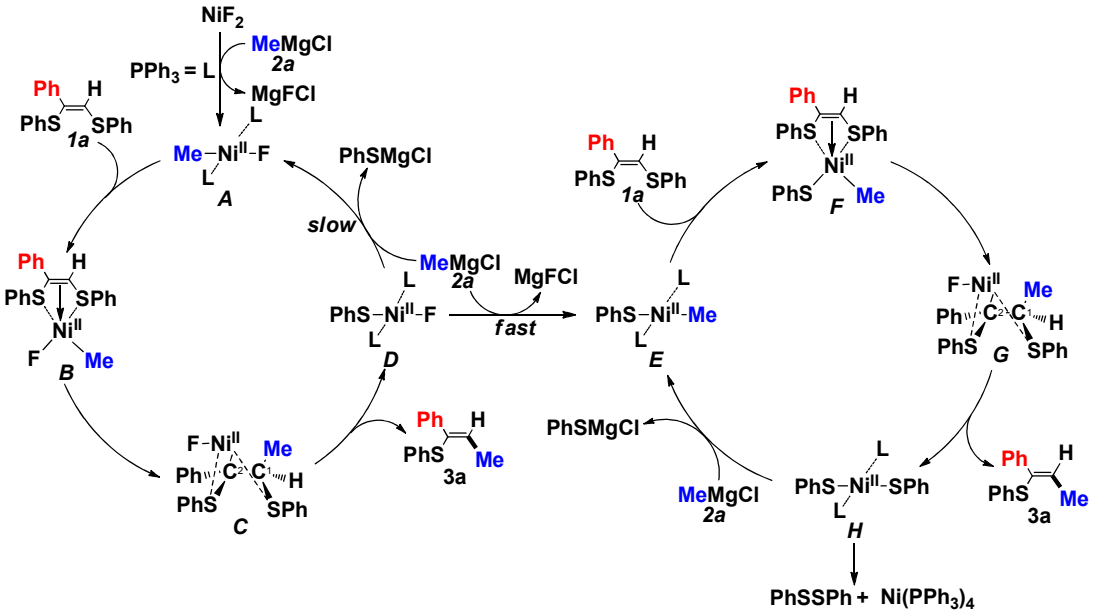
Scheme 4. Control experiments for mechanism study.



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-diphenylthio styrene and methylmagnesium chloride in THF-*d8* 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 the absence of Ni^0 at the start of the coupling reaction (see Figure 1 in SI). From the ^{19}F NMR spectra of the reaction mixture, the signal of ^{19}F can be observed within the first hour but cannot be seen afterward. The phenomenon implies that the fluorine exists not only as inorganic salt but also as organic intermediate during the coupling reaction, and finally converted to MgFCl (see Figure 2 in SI). The intensity of the Me signal (^{1}H NMR, δ = 2.07) of

the desired product increases in the first 8.0 h before reaching constant (see Figure 3 in SI). Analyzing the ^{13}C NMR spectra (see figure 4 in SI), one can see that the peak of the carbon that is bonded to the hydrogen of (*Z*)-1,2-diphenylthio styrene at δ 125.8 shifts highfield to δ 125.3, plausibly due to the replacement of PhS (an electron drawing group) by Me. The signals at δ -5.37 and δ -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-diphenylthio styrene at the 8th hour, a ^{31}P NMR signal at δ 31.6 consistent with the Ni^0 signal of authentic $Ni^0(PPh_3)_4$ is observed. Also, with the formation of diphenyl disulfide after oxidation, it is deduced that PhSMgCl is formed during the coupling process.

Figure 2. Proposed mechanism of the cross-coupling.



Based on 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 hyperconjugation of aryl or electron-donating effect of alkyl. The insertion of nucleophile (Me^-) and electrophile (FNi^+) into C^1 and C^2, respectively, give 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 *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 then species ***E*** coordinates with **1a** to afford intermediate ***F***. With the insertion of PhSNiF into ***F***, there is the generation of intermediate ***G*** that 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 regio-selectivity *via* the direct Ni-catalyzed cross-coupling of (*Z*)-1,2-diaryl(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 demonstrated that (*Z*)-tamoxifen can be successfully synthesized in high regio- and stereo-selectivity using (*Z*)-vinylic sulfides **3** as starting material. 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 resource.

EXPERIMENTAL SECTION

General information

Unless noted, all reactions were conducted in Schlenk tubes under an atmosphere of nitrogen. Dry DCM (CH_2Cl_2), toluene and THF (tetrahydrofuran) and THF-d_8 were purified according to the standard methods. Reactions were monitored by thin layer chromatography (TLC) using gel 60 F_{254} pre-coated plates. Visualization was accomplished with UV lamp or I_2 stain. Silica gel 300-400 mesh size 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

$^{13}C\{^{1}H\}$ NMR spectra were recorded on 400 MHz and 100 MHz NMR plus spectrometer using residue solvent peaks as internal standards, respectively. Mass spectra (MS) were obtained using EI mass spectrometer. High resolution mass spectra (HRMS) were measured on an electron ionization (EI) mass spectrometry.

General procedure for the synthesis of (Z)-1,2-diarl(alkyl)thio alkenes 1[16a]

Terminal alkynes (2.0 mmol), diaryl disulfides (1.0 mmol) were added, under nitrogen, to a solution of cesium hydroxide monohydrate (0.5 mmol, 25 mol%) in DMF (2 mL). The resulting solution was stirred at room temperature for 20 hours under nitrogen atmosphere. Then, the reaction mixture was diluted with water (30 mL), and extracted with ethyl acetate (30 mL ×3). The combined organic phase was 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-diphenylthiostyrene (**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); $^{13}C\{^{1}H\}$ 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)-1,2-diphenylthio(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); $^{13}C\{^{1}H\}$ 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)-1,2-diphenylthio(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); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 137.6, 136.1, 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-diphenylthio(4-(t-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-diphenylthio(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-diphenylthio(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-diphenylthio(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-di(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); $^{13}C\{^1H\}$ 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-di(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 ^{o}C overnight. After completion of the reaction, the no consumed pentene was distilled off on a rotary evaporator. The residue was purified by flash chromatography with a hexane-chloroform mixture as an eluent to afford (*Z*)-1,2-di(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); $^{13}C\{^1H\}$ 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-di(4-methylphenylthio)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); $^{13}C\{^1H\}$ 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-di(4-chlorophenylthio)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); $^{13}C\{^1H\}$ 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-di(4-methoxyphenylthio)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-di(n-propylthio) (4-methoxy styrene) (**1m**)*[25]: $Ni(acac)_2$ (0.18 mmol, 46 mg), (n-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 homogeneous brown solution was formed. 4-methoxy phenylacetylene (6.0 mmol, 792 mg) was added to the solution and the reaction was carried out at 100 ^{o}C under stirring until complete conversion of the n-Pr_2S_2. After finish, the residue was purified by flash chromatography to afford (Z)-1,2-di(*n*-propylthio) (4-methoxy styrene) (**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-di(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-di(4-methylphenylthio)(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, 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-di(4-methylphenylthio)(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-di(4-methylphenylthio)(4-(t-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-3s

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 rt under N_2. The reaction mixture was stirred at rt for 25 h. After completion of reaction, the solution was quenched with H_2O_2 (1.0 mL), and stirred at rt for 3 h. The resulting mixture was extracted with dichloromethane, and the combined organic layers were dried over anhydrous Na_2SO_4, subject to filtration, and concentrated *in vacuo*. The residue was purified by flash chromatography on silica gel (petroleum ether) to afford the desired products **3a-3s**.

General procedure for the synthesis of 3t-3ac

Grignard Reagents (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 rt under N_2. The reaction mixture was stirred at rt for 25 h. After completion of reaction, the solution was quenched with H_2O_2 (1.0 mL), and stirred at rt for 3 h. The resulting mixture was extracted with dichloromethane, and the combined organic layers were dried over anhydrous Na_2SO_4, subject to filtration, and concentrated *in vacuo*. The residue was purified by flash chromatography on silica gel (petroleum ether) to afford the desired products **3t-3ac**.

*(Z)-1-phenylthio-2-methyl styrene (**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 calc. for $C_{15}H_{14}S$ 226.0811, found 226.0840.

*(Z)-1-phenylthio-2-methyl (4-methylstyrene) (**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 calc. for $C_{16}H_{16}S$ 240.0967, found 240.0964.

*(Z)-1-phenylthio-2-methyl (3-methylstyrene) (**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 calc. for $C_{16}H_{16}S$ 240.0964, found 240.0963.

*(Z)-1-phenylthio-2-methyl (4-(t-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 calc. 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 calc. for $C_{18}H_{20}S$ 268.1280, found 268.1273.

*(Z)-1-(phenylthio)-2-methyl(4-methoxystryrene) (**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 calc. for $C_{16}H_{16}OS$ 256.0916, found 256.0916.

*1-(phenylthio)-2-methyl-4-fluorostryrene (**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, $^1J_{C\text{-}F}$ = 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 calc. 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 calc. 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 calc. for $C_{13}H_{18}S$ 206.1152, found 206.1154.

(Z)-1-(4-methylphenylthio)-2-methyl stryrene (***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 calc. for $C_{16}H_{16}S$ 240.0967, found 240.0963.

(Z)-1-(4-chlorophenylthio)-2-methylstryrene ***(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 calc. for $C_{15}H_{13}ClS$ 260.0421, found 260.0413.

(Z)-1-(4-methoxyphenylthio)-2-methylstryrene ***(3l)***. Yellow oil; yield: 82% (41.7 mg). ^1H 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); $^{13}C\{^1H\}$ 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 calc. for $C_{16}H_{16}OS$ 256.0924, found 256.0926.

(Z)-1-propylthio-2-ethyl(4-methoxystryrene) ***(3m)***. Yellow oil; yield: 95% (41.8 mg). ^1H 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); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 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 calc. for $C_{14}H_{20}OS$ 236.1278, found 236.1276.

(Z)-1-(4-methoxyphenylthio)-2-methyl(4-methoxystryrene) ***(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 calc. for $C_{17}H_{18}O_2S$ 286.1037, found 286.1032.

(Z)-1-(4-methylphenylthio)-2-methyl(4-methylstryrene) ***(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); $^{13}C\{^{1}H\}$ 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 calc. for $C_{17}H_{18}S$ 254.1124, found 254.1116.

(Z)-1-(4-methylphenylthio)-2-methyl(4-methoxystryrene) ***(3p)****.* Yellow oil; yield: 88% (47.4 mg). ^{1}H 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); $^{13}C\{^{1}H\}$ 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 calc. for $C_{17}H_{18}OS$ 270.1127, found 270.1124.

(Z)-1-(4-methylphenylthio)-2-methyl(4-(t-butyl)stryrene) ***(3q)****.* Yellow oil; yield: 87% (50.7 mg). ^{1}H 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); $^{13}C\{^{1}H\}$ 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 calc. for $C_{20}H_{24}S$ 296.1641, found 296.1645.

(Z)-1-phenylthio-2-ethylstryrene ***(3r)****.* Yellow oil; yield: 93% (44.6 mg). ^{1}H 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); $^{13}C\{^{1}H\}$ 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 calc. for $C_{16}H_{16}S$ 240.0967, found 240.0962.

*(Z)-1-phenylthio-2-ethyl(4-methoxystryrene) (**3s**)*. Light yellow oil; yield: 88% (47.5 mg). ^{1}H 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{^{1}H} 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 calc. for $C_{17}H_{18}OS$ 270.1175, found 270.1173.

*(Z)-1-phenylthio-2-allylstryrene (**3t**)*. Yellow oil; yield: 82% (41.3 mg). ^{1}H 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{^{1}H} 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 calc. for $C_{17}H_{16}S$ 252.1045, found 252.1047.

*(Z)-1-phenylthio-2-cyclopentylstryrene (**3u**)*. Yellow oil; yield: 86% (48.1 mg). ^{1}H 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{^{1}H} 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 calc. for $C_{19}H_{20}S$ 280.1280, found 280.1275.

*(Z)-1-phenylthio-2-cyclohexylstryrene (**3v**)*. Light yellow oil; yield: 85% (50.0 mg). ^{1}H 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{^{1}H} 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 calc. for $C_{20}H_{22}S$ 294.1416, found 294.1418.

(Z)-1-phenylthio-2-cyclopentyl(4-methoxystryrene) ***(3w)***. Light yellow oil; yield: 72% (44.6 mg). ^{1}H 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{^{1}H} 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 calc. for $C_{20}H_{22}OS$ 310.1452, found 310.1450.

(Z)-1-phenylthio-2-phenylstryrene ***(3x)***[26]. Light yellow oil; yield: 72% (41.5 mg). ^{1}H 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{^{1}H} 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 calc. for $C_{20}H_{16}S$ 288.1052, found 288.1050.

(Z)-1-(4-methylphenylthio)-2-phenylstryrene ***(3y)***. Light yellow oil; yield: 75% (45.3 mg). ^{1}H 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{^{1}H} 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 calc. for $C_{21}H_{18}S$ 302.1125, found 302.1127.

(Z)-1-phenylthio-2-(4-methoxyphenyl)stryrene ***(3z)***. Light yellow oil; yield: 65% (41.3 mg). ^{1}H 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 calc. for $C_{21}H_{18}OS$ 318.1073, found 318.1080.

(Z)-1-phenylthio-2-phenyl(4-methoxystryrene) ***(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 calc. for $C_{21}H_{18}OS$ 318.1154, found 318.1156.

(Z)-1-phenylthio-2-(4-methylphenyl) (4-methoxystryrene) ***(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 calc. 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 (45), 226 (26), 216 (77), 197 (16), 116 (83), 151 (72), 135 (11), 115 (8), 91 (8), 63 (6); HRMS calc. for $C_{18}H_{20}OS$ 284.1272, found 284.1275.

The experimental procedure for larger-scale synthesis of 3a

Methyl magnesium chloride (1.0 mL, 2.5 mmol) was added to a mixture of (*Z*)-1,2-diphenylthio 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 rt under N_2. The reaction mixture was stirred at rt 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, subject to filtration, and concentrated *in vacuo*. The residue was purified by flash chromatography on silica gel (petroleum ether) to afford (*Z*)-1-phenylthio-2-methyl styrene **3a** as 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-methylphenylthio)-2-phenylstryrene (2.0 mmol) and glacial acetic acid (4.0 mL), and the reaction mixture was stirred at rt for 2 h. Upon completion of reaction, the product was filtered out and recrystallized from 95% ethanol to give (*E*)-1-phenylthio-2-bromo toluylene in 75% yield. Then $Pd(PPh_3)_4$ (5.0 mmol%) was added to a solution of (*E*)-1-phenylthio-2-bromo toluylene (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 nitrogen amosphere. The reaction solution was stirred at 150 ^oC for 16 h. Upon completion of reaction, the desired product (compound **5**) was obtained by column chromatography in 87% yield. ^1H 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); $^{13}C\{^1H\}$ 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 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).

The procedure for the NMR experiment

Methyl magnesium chloride (0.3 mmol, 2.5 mol/L in THF) was added to 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 methyl magnesium chloride (THF-d_8) was added to a Low Pressure/Vacuum Valve **(**PLV) NMR sample tube containing a mixture of (*Z*)-1,2-diphenylthio 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 rt under N_2. The reaction mixture was examined in hourly intervals by NMR spectroscopy.

ACKNOWLEDGMENT

This work was supported by the National Natural Science Foundation of China (Nos. 21273068 and 21373003, J1210040), and the Fundamental Research Funds for the Central University, Hunan University. All authors thank Prof. Nobuaki Kambe and Dr. Takanori Iwasaki of Osaka University for helpful discussion. C.T. Au thanks HNU for an adjunct professorship.

Supporting Information:

^{1}H NMR and ^{13}C{^{1}H} NMR spectra of compounds **1a**-**1q**, **3a**–**3ac**, compound **5** and (*Z*)-tamoxifen. This material is available free of charge via the Internet at http://pubs.acs.org.

REFERENCES

(1) Witing, G.; Geissler, G. *Justus Liebigs Ann. Chem.* **1953**, 44: see also Staudinger, H.; Meyer, J. *Helv. Chim. Acta.* **1919**, *2*, 619.

(2) (a) Robertson, D. W.; Katzenellenbogen, J. A.; Hayes, J. R.; Katzenellenbogen, B. S. *J. Med. Chem.* **1982**, *25*, 167. (b) Levenson, A. S.; Jordan, V. C. *Eur. J. Cancer* **1999**, *35*, 1974. (c) Mckinley, N. F.; O'Shea, D. F. *J. Org. Chem.* **2006**, *71*, 9552. (d) Caturla, F.; Amat, M.; Reinoso, R. F.; Córdoba, M.; Warrellow, G. *Bioorg. Med. Chem. Lett.* **2006**, *16*, 3209. (e) Wadman, M. *Nature* **2006**, *440*, 277. (f) Prasit, P.; Wang, Z.; Brideau, C.; Chan, C.-C.; Charleson, S.; Cromlish, W.; Ethier, D.; Evans, J. F.; Ford-Hutchinson, A. W.; Gauthier, J. Y. *Bioorg. Med. Chem. Lett.* **1999**, *9*, 1773. (g) Zhang, Y.-H.; Shi, B.-F.; Yu, J.-Q. *J. Am. Chem. Soc.* **2009**, *131*, 5072. (h) Higman, C. S.; Lummiss, J. A. M.; Fogg, D. E. *Angew. Chem. Int. Ed.* **2016**, *55*, 3552.

(3) (a) Oonishi, Y.; Ogura, J.; Sato, Y. *Tetrahedron Lett.* **2007**, *48*, 7505. (b) Coulter, M. M.; Dornan, P. K.; Dong, V. M. *J. Am. Chem. Soc.* **2009**, *131*, 6932. (c) Moragas, T.; Cornella, J.; Martin, R. *J. Am. Chem. Soc.* **2014**, *136*, 17702. (d) Wu, P.; Wang, L.; Wu, K.; Yu, Z. *Org. Lett.* **2015**, *17*, 868.

(4) (a) Cahiez, G.; Moyeux, A.; Poizat, M. *Chem. Commun.* **2014**, *50*, 8982. (b) Takahashi, A.; Kirio, Y.; Sodeoka, M.; Sasai, H.; Shibasaki, M. *J. Am. Chem. Soc.* **1989**, *111*, 643.

(5) (a) You, W.; Li, Y.; Brown, M. K. *Org. Lett.* **2013**, *15*, 1610. (b) Takizawa, S.; Arteaga, F. A.; Kishi, K.; Hirata, S.; Sasai, H. *Org. Lett.* **2014**, *16*, 4162. (c) Landelle, G.; Champagne, P. A.; Barbeau, X.; Paquin, J.-F. *Org. Lett.* **2009**, *11*, 681. (d) Xie, M.; Wang, J.; Gu, X.; Sun, Y.; Wang, S. *Org. Lett.* **2006**, *8*, 431. (e) Pospíšil, J.; Pospíšil, T.; Markó, I. E. *Org. Lett.* **2005**, *7*, 2373.

(6) (a) Wu, J.; Yoshikai, N. *Angew. Chem. Int. Ed.* **2016**, *128*, 344. (b) Nishihara, Y.; Miyasaka, M.; Okamoto, M.; Takahashi, H.; Inoue, E.; Tanemura, K.; Takagi, K. *J. Am. Chem. Soc.* **2007**, *129*, 12634. (c) Yang, Y.; Wang, L.; Zhang, F.; Zhu, G.o *J. Org. Chem.* **2014**, *79*, 9319. (d) Rummelt, S.

M.; Preindl, J.; Sommer, H.; Fürstner, A. *Angew. Chem. Int. Ed.* **2015**, *54*, 6241. (e) Trost, B. M.; Cregg, J. J. *J. Am. Chem. Soc.* **2015**, *137*, 620. (f) Saini, V.; O'Dair, M.; Sigman, M. S. *J. Am. Chem. Soc.* **2015**, *137*, 608. (g) Xiao, J.; Yang, J.; Chen, T.; Han, L.-B. *Chem. Commun.* **2016**, doi**:** 10.1039/c5cc10005d. (h) Schirmer, M.-L.; Adomeit, S.; Spannenberg, A.; Werner, T. *Chem. Eur. J.* **2016**, *22*, 1. (i) Zhu, G.; Kong, W.; Feng, H.; Qian, Z. *J. Org. Chem.* **2014**, *79*, 1786. (j) Jiao, J.; Nakajima, K.; Nishihara, Y. *Org. Lett.* **2013**, *15*, 3294. (k) Jiao J.; Hyodo, K.; Hu, H.; Nakajima, K.; Nishihara, Y. *J. Org. Chem.* **2014**, *79*, 285.

(7) (a) Itami, K.; Kamei, T.; Yoshida, J. *J. Am. Chem. Soc.* **2003**, *125*, 14670. (b) Denmark, S. E.; Kallemeyn, J. M. *J. Am. Chem. Soc.* **2006**, *128*, 15958. (c) Tsuji, H.; Ueda, Y.; Ilies, L.; Nakamura, E. *J. Am. Chem. Soc.* **2010**, *132*, 11854. (d) Alfaro, R.; Parra, A.; Alemán, J.; Ruano, J. L. G.; Tortosa, M. *J. Am. Chem. Soc.* **2012**, *134*, 15165. (e) Suero, M. G.; Bayle, E. D.; Collins, B. S. L.; Gaunt, M. J. *J. Am. Chem. Soc.* **2013**, *135*, 5332.

(8) (a) Itami, K.; Mineno, M.; Muraoka, N.; Yoshida, J. *J. Am. Chem. Soc.* **2004**, *126*, 11778. (b) Reiser, O. *Angew. Chem. Int. Ed.* **2006**, *45*, 2838.

(9) (a) Yang, F.-L.; Ma, X.-T.; Tian, S.-K. *Chem. Eur. J.* **2012**, *18*, 1582. (b) Itami, K.; Higashi, S.; Mineno, M.; Yoshida, J. *Org. Lett.* **2005**, *7*, 1219. (c) Erdelmeier, I.; Gais, H.-J. *J. Am. Chem. Soc.* **1989**, *111*, 1125. (d) Gais, H.-J.; Bulow, G. *Tetrahedron Lett.* **1992**, *33*, 465. (e) Yang, Q.; Wu, S.; Quan, Z.; Du, B.; Wang, M.; Li, P.; Zhang, Y.; Lei, Z.; Wang, X. *Tetrahedron* **2015**, *71*, 8462. (f) Sharma, S.; Pathare, R. S.; Maurya, A. K.; Gopal, K.; Roy, T. K.; Sawant, D. M.; Pardasani, R. T. *Org. Lett.* **2016**, *18*, 356. (g) Nordin, N.; Ariffin, A.; Daud, M. N.; Sim, Y.-L., *Tetrahedron* **2016**, doi:10.1016/j.tet.2015.10.077. (h) Bouchet, L. M.; Penenory, A. B.; Robert, M.; Arguello, J. E. *RSC Adv.* **2015**, *5*, 11753. (i) L. S. Liebeskind, J. Srogl, *Org. Lett.* **2002**, *4*, 979. (j) L. S. Liebeskind, J. Srogl, *J. Am. Chem. Soc.* **2000**, *122*, 11260.

(10) (a) Kauffmann, T. *Angew. Chem. Int. Ed. Engl.* **1982**, *21*, 410. (b) Seebach, D.; Beck, A. K. *Chem. Ber.* **1975**, *108*, 314. (c) Dabdoub, M. J.; Jacob, R. G.; Ferreira, J. T. B.; Dabdoub, V. B.; Marques,

F. de A. *Tetrahedron Lett.* **1999**, *40*, 7159. (d) Ogawa, A.; Tsuboi, Y.; Obayashi, R.; Yokoyama, K.; Ryu, I.; Sonoda, N. *J. Org.Chem.* **1994**, *59*, 1600. (e) Wu, X.; Zhang, J.; Liu, S.; Gao, Q.; Wu, A. *Adv. Synth. Catal.* **2016**, *358*, 218. (f) Quan, Z.-J.; Lv, Y.; Jing, F.-Q.; Jia, X.-D.; Huo, C.-D.; Wang, X.-C. *Adv. Synth. Catal.* **2014**, *356*, 325.

(11) (a) Mehta, V.P.; Modha, S. G.; Van der Eycken, E. *J. Org. Chem.* **2009**, *74*, 6870. (b) Zhou, X.; Luo, J.; Liu, J.; Peng, S.; Deng, G.-J. *Org. Lett.* **2011**, *13*, 1432. (c) Liu, B.; Guo, Q.; Cheng, Y.; Lan, J.; You, J. *Chem. Eur. J.* **2011**, *17*, 13415. (d) Wu, M.; Luo, J.; Xiao, F.; Zhang, S.; Deng, G.-J.; Luo, H.-A. *Adv. Synth. Catal.* **2012**, *354*, 335. (e) Wang, H.; Li, Y.; Zhang, R.; Jin, K.; Zhao, D.; Duan, C. *J. Org. Chem.* **2012**, *77*, 4849. (f) Tobisu, M.; Masuya, Y.; Baba, K.; Chatani, N. *Chem. Sci.* **2016**, doi: 10.1039/C5SC04890G.

(12) (a) Ishizuka, K.; Seike, H.; Hatakeyama, T.; Nakamura, M. *J. Am. Chem. Soc.* **2010**, *132*, 13117. (b) Eberhart, A. J.; Imbriglio, J. E.; Procter, D. J. *Org. Lett.* **2011**, *13*, 5882. (c) Ghaderi, A.; Iwasaki, T.; Fukupka, A.; Terao, J.; Kambe, N. *Chem. Eur. J.* **2013**, *19*, 2951. (d) Yang, Z.; Chen, X.; Kong, W.; Xia, S.; Zheng, R.; Luo, F.; Zhu, G. *Org. Biomol. Chem.* **2013**, *11*, 2175.

(13) (a) Li, H.-X.; Zhao, W.; Li, H.-Y.; Xu, Z.-L.; Wang, W.-X.; Lang, J.-P. *Chem. Commun.* **2013**, *49*, 4259. (b) Begouin, J.-M.; Rivard, M.; Gosmini, C. *Chem. Commun.* **2010**, *46*, 5972. (c) Quan, Z.-J.; Lv, Y.; Jing, F.-Q.; Jia, X.-D.; Huo, C.-D.; Wang, X.-C. *Adv. Synth. Catal.* **2014**, *356*, 325.

(14) (a) Reddy, V. P.; Kumar, A. V.; Wapna, K. S.; Rao, K. R. *Org. Lett.* **2009**, *11*, 951. (b) Chen, F.J.; Liao, G.; Li, X.; Wu, J.; Shi, B.-F. *Org. Lett.* **2014**, *16*, 5644. (c) Qiao, Z.; Liu, H.; Xiao X.; Fu, Y.; Wei, J.; Li, Y.; Jiang, X. *Org. Lett.* **2013**, *15*, 2594. (d) Reddy, V. P.; Qiu, R.; Iwasaki, T.; Kambe, N. *Org. Lett.* **2013**, *15*, 1290. (e) Reddy, V. P.; Kumar, A. V.; Wapna, K. S.; Rao, K. R. *Org. Lett.* **2009**, *11*, 1697. (f) Schneider, C. C.; Godoi, B.; Prigol, M.; Nogueira, C. W.; Zeni, G. *Organometallics* **2007**, *26*, 4252. (g) Zeni, G.; Stracke, M. P.; Nogueira, C. W.; Braga, A. L.; Menezes, P. H.; Stefani, H. A. *Org. Lett.* **2004**, *6*, 1135. (h) Qiao, Z.; Wei, J.; Jiang, X. *Org. Lett.* **2014**, *16*, 1212. (i) Rao, W.-H.; Shi, B.-F. *Org. Lett.* **2015**, *7*, 2784.

(15) (a) Dabdoub, M. J.; Begnini, M. L.; Guerrero, P. G. Jr.; Baroni, A. C. M. *J. Org. Chem.* **2000**, *65*, 61. (b) Silveira, C. C.; Perin, G.; Braga, A. L.; Dabdoub, M. J.; Jacob, R. G. *Tetrahedron* **1999**, *55*, 7421.

(16) (a) Xia, X.; Zou, K. B.; Li, R. X.; Zhang, Z. Y.; Shao, L. L.; Fang, D. W.; Xu, X. H. *Acta Chim. Sinica* **2008**, *66*, 1749. (b) Chen, J.; Tang, Z.; Qiu, R.; He, Y.; Wang, X.; Li, N.; Yi, H.; Au, C.-T.; Yin, S.-F.; Xu, X. *Org. Lett.* **2015**, *17*, 2162.

(17) (a) Alves, D.; Schumacher, R. F.; Brandão, R.; Nogueira, C. W.; Zeni, G. *Synlett* **2006**, 1035. (b) Dabdoub, M. J.; Dabdoub, V. B.; Pereira, M. A.; Baroni, A. C. M.; Marques, F. A.; de Oliveira, P. R.; Guerrero, P. G. Jr. *Tetrahedron Lett.* **2010**, *51*, 5141. (c) Farhat, S.; Zouev, I.; Marek, I. *Tetrahedron* **2004**, *60*, 1329.

(18) Ogawa, A.; Obayashi, R.; Ine, H.; Tsuboi, Y.; Sonoda, N.; Hirao, T. *J. Org. Chem.* **1998**, *63*, 881.

(19) (a) Gerard, J.; Hevesi, L. *Tetrahedron* **2004**, *60*, 367. (b) Metzger, A.; Melzig, L.; Despotopoulou, C.; Knochel, P. *Org. Lett.* **2009**, *11*, 4228. (c) Itami, K.; Higashi, S.; Mineno, M.; Yoshida, J. *Org. Lett.* **2005**, *7*, 1219. (d) Ishizuka, K.; Seike, H.; Hatakeyama, T.; Nakamura, M. *J. Am. Chem. Soc.* **2010**, *132*, 13117. (e) Eberhart, A. J.; Imbriglio, J. E.; Procter, D. J. *Org. Lett.* **2011**, *13*, 5882.

(20) (a) Jana, D.; Ghorai, B. K. *Tetrahedron* **2012**, *68*, 7309. (b) Nunes, C. M.; Steffens, D.; Monteiro, A. L. *Synlett.* **2007**, *1*, 0103.

(21) (a) Saini, V.; O'Dair, M.; Sigman, M. S. *J. Am. Chem. Soc.* **2015**, *137*, 608. (b) Molinaro, C.; Scott, J. P.; Shevlin, M.; Wise, C.; Ménard, A.; Gibb, A.; Junker, E. M.; Lieberman, D. *J. Am. Chem. Soc.* **2015**, *137*, 999. (c) Ragno, D.; Bortolini, O.; Fantin, G.; Fogagnolo, M.; Giovannini, P. P.; Massi, A. *J. Org. Chem.* **2015**, *80*, 1937. (d) Shoda , T.; Kato, M.; Harada, R.; Fujisato, T.; Okuhira, K.; Demizu, Y.; Inoue, H.; Naito, M.; Kurihara, M. *Bioorg. Med. Chem.* **2015**, *23*, 3091. (e) Itoh, T.; Shimizu, Y.; Kanai, M. *Org. Lett.* **2014**, *16*, 2736. (f) Xue, F.; Zhao, J.; Andy Hor, T. S.; Hayashi, T. *J. Am. Chem. Soc.* **2015**, *137*, 3189. (g) Kotek, V.; Dvořáková, H.; Tobrman, T. *Org. Lett.* **2015**, *17*, 608; (h) Ganapathy, D.; Sekar, G. *Org. Lett.* **2014**, *16*, 3856. (i) Drapeau, M. P.; Fabre, I.; Grimaud, L.; Ciofini, I.; Ollevier, T.; Taillefer, M. *Angew. Chem. Int. Ed.* **2015**, *127*,10733.

(22) (a) Takise, R.; Muto, K.; Yamaguchi, J.; Itami, K. *Angew. Chem. Int. Ed.* **2014**, *53*, 6791. (b) Wang, G.-W.; Miao, T. *Chem. Eur. J.* **2011**, *17*, 5787. (c) Wang, G.-W.; Miao, T. *Chem. Eur. J.* **2011**, *17*, 5787.

(23) Anderson, N. H. J. *Lipia Res*. **1968**, *10*, 316.

(24) Ananikov, V. P.; Kabeshov, M. A.; Beletskaya, I. P. *Russian Chemical Bulletin* **2005**, *54*, 576.

(25) Ananikov, V. P.; Gayduk, K. A.; Beletskaya, I. P.; Khrustalev, V. N.; Antipin, M. Y. *Chem. Eur. J.* **2008**, *14*, 2420.

(26) Taniguchi, T.; Fujii, T.; Idota, A.; Ishibashi, H. *Org. Lett.* **2009**, *11*, 3298.

(27) Kumar, A. B. V. K.; Rao, K. S. V. K.; Maheswara, M.; Subha, M. C. S.; Cui, S.; Jin, D.; Lee, Y-III. *Bull. Korean. Chem. Soc.* **2008**, *29*, 2291.