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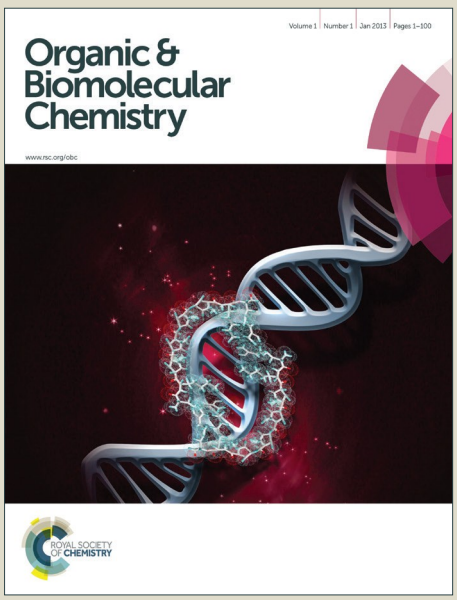

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ARTICLE

Iodine-Catalyzed Thiolation of Electron-Rich Aromatics Using Sulfonyl Hydrazides as Sulfenylation Reagents

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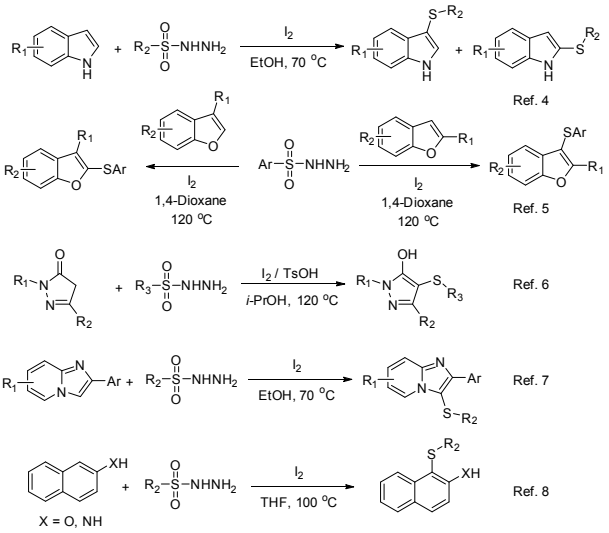
Iodine-catalyzed thiolation of electron-rich aromatics, including substituted anisole, thioanisole, phenol, toluene, and naphthalene, using sulfonyl hydrazides as sulfenylation reagents was developed. Sulfonothioates, the products of decomposition of sulfonyl hydrazides in the presence of iodine, are proposed as the major sulfenylation species in this transformation.

Introduction

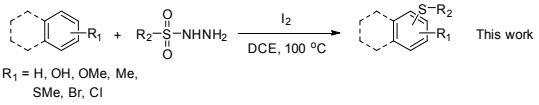
Carbon-sulfur (C–S) bond formation has emerged as a key step in the syntheses of natural products, pharmaceuticals, and organic materials.[1] Significant research is being pursued on the development of new C–S bond formation reactions, with emphasis on identifying new sulfenylation reagents.[2] In the past two years, sulfonyl hydrazides have been developed as environmentally friendly sulfenylation reagents that are stable, readily accessible, and odor-free.[3] Following Tian's report on indole sulfenylation (Scheme 1),[4] several research groups, including ours, have used sulfonyl hydrazides for the thiolation of electron-rich heterocycles such as benzofurans,[5] pyrazolones,[6] and imidazo[1,2-a]pyridines,[7] as well as naphthols and naphthylamines.[8] Although transition metal-catalyzed sulfenylation of arenes has been reported,[9, 10] metal-free sulfenylation of electron-rich benzene and naphthalene by sulfonyl hydrazides has not yet been reported. In this paper, we report the iodine-catalyzed thiolation of substituted anisole, thioanisole, phenol, toluene, and naphthalene using sulfonyl hydrazides as sulfenylation reagents (Scheme 2).

Results and discussion

First, we treated anisole **1a** with 4-methylbenzenesulfonohydrazide **2a** using iodine as the catalyst in 1,4-dioxane at 120 °C and the desired sulfenylation product **3aa** was obtained in 28% yield (Table 1, Entry 1). To optimize the reaction conditions, we tested various solvents such as 1,2-dichloroethane (DCE), ethanol (EtOH), toluene and *N*,*N*-dimethylformamide (DMF) (Table 1, Entries 2-5) and found that DCE gave the best result (Table 1, Entry 5). Brønsted acids have been reported to promote the decomposition of sulfonyl hydrazides.[5b] However, when *p*-toluenesulfonic acid (TsOH) was used as an additive, the yield was not improved (Table 1, Entry 6). To further optimize the reaction conditions, we varied the reactant concentration and iodine catalyst loading, and found that changing the reactant concentration had great effect on the reaction yield. When the concentration of **2a** was increased from 2.0 M to 6.7 M,



Scheme 1 Sulfenylation of electron-rich heterocycles, naphthols, and naphthylamines



Scheme 2 Sulfenylation of electron-rich benzenes and naphthalenes

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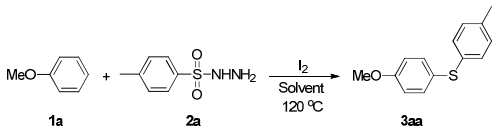
the yield increased from 70% to 79% (Table 1, Entries 5, 7, 8). However, further increase in the concentration led to diminished yield (Table 1, Entries 9, 10). We also found that decreasing the catalyst loading from 0.2 equiv. to 0.1 equiv. did not have any notable effect on the yield (Table 1, Entry 11). However, further decreasing catalyst loading to 0.05 equiv. led to a lower yield (Table 1, Entry 12). This suggests that 0.1 equiv. of the iodine catalyst is required for the optimal product yield. Finally, the equivalent amount of **2a** was examined: 1.2 equiv. of **2a** was sufficient for the reaction, giving 82% product yield (Table 1, Entries 11, 13-15). Thus, the optimal reaction conditions were as follows: **1a**, 2.0 mmol; **2a**, 2.4 mmol; I_2, 0.2 mmol; DCE, 0.3 mL; temperature, 120 °C.

Table 1 Optimization of conditions for I_2-catalyzed reaction of **1a** with **2a.**[a]



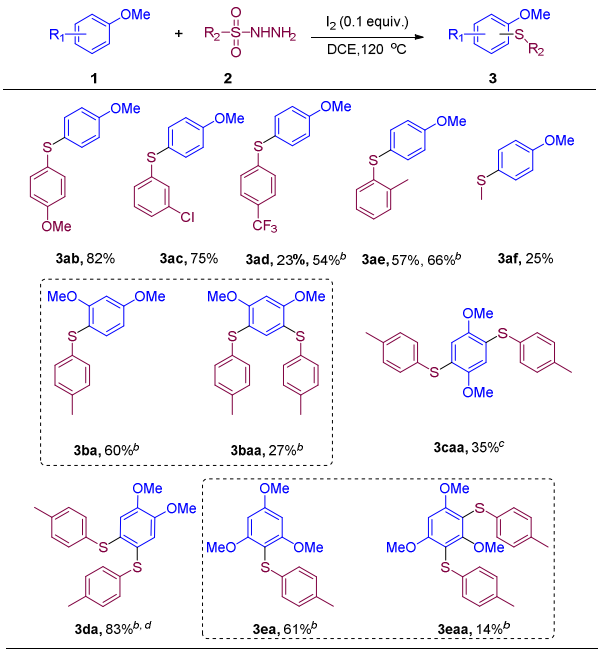
1a 2a 3aa

Entry	I_2 (eq.)	**2a** (eq.)	Solvent (mL)	Solvent	Yield (%)
1	0.2	1.5	1.0	1,4-Dioxane	28
2	0.2	1.5	1.0	EtOH	4
3	0.2	1.5	1.0	Toluene	57
4	0.2	1.5	1.0	DMF	0
5	0.2	1.5	1.0	DCE	70
6	0.2	1.5	1.0	DCE	64[b]
7	0.2	1.5	0.5	DCE	75
8	0.2	1.5	0.3	DCE	79
9	0.2	1.5	0.2	DCE	72
10	0.2	1.5	0	DCE	70
11	0.1	1.5	0.3	DCE	77
12	0.05	1.5	0.3	DCE	27
13	0.1	1.2	0.3	DCE	82
14	0.1	1.1	0.3	DCE	77
15	0.1	1.0	0.3	DCE	72

[a] Reaction conditions: **1a** (2.0 mmol), **2a** (2.0-3.0 mmol), iodine (0.1-0.4 mmol) solvent (0-1.0 mL). [b] TsOH (2.0 mmol) was added.

With the optimized conditions in hand, we extended the reaction to a series of anisole and sulfonyl hydrazides; the results are presented in Table 2. Most of the reactions afforded the corresponding anisole thioethers in moderate to good yields. The reaction of anisole proceeded as expected with *meta*-, *ortho*-, and *para*-substituted aryl sulfonyl hydrazides, as well as with aryl sulfonyl hydrazides with electron-withdrawing and electron-donating groups, to give the corresponding mono-thioethers (**3ab**, **3ac**, **3ad**, and **3ae**). However, aliphatic sulfonyl hydrazides such as methanesulfonohydrazide **2f** afforded the product in relatively low yield. Notably, when an aryl sulfonyl hydrazide bearing a strong electron-withdrawing group **2d** and an *ortho*-substituted aryl sulfonyl hydrazide **2e** were used as substrates, decreasing the reaction temperature to 100 °C increased the product yields. Next the use of methoxy-substituted anisole in the reaction was examined. 1,3-Dimethoxybenzene **1b** and 1,3,5-trimethoxybenzene **1e** afforded both the corresponding mono- and di-thioethers, while 1,4-dimethoxybenzene **1c** and 1,2-dimethoxybenzene **1d** gave only the corresponding di-thioether.

Table 2 I_2-catalyzed cross coupling with a series of anisoles and sulfonyl hydrazides.[a]



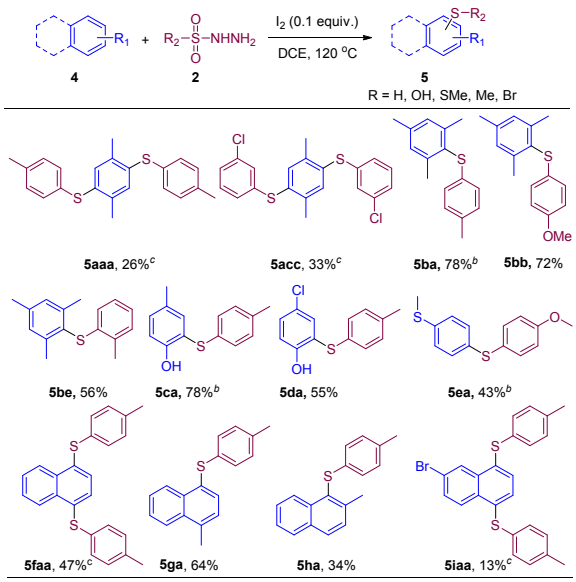
[a] Reaction conditions: **1a-c** (2.0 mmol), **2b-f** (2.4 mmol), I_2 (0.2 mmol), DCE (0.3 mL), 120 °C.
[b] The reaction was carried out in 100 °C.
[c] 4.8 mmol of **2a** was used.
[d] The yield was calculated using sulfonyl hydrazide as reference.

Finally, to broaden the substrate scope of this transformation, we tested other electron-rich aromatics using the optimized conditions. The results are summarized in Table 3. Substituted toluene (**4a** and **4b**), substituted phenol (**4c** and **4d**), thioanisole (**4e**), naphthalene (**4f**), and substituted naphthalene (**4g**-**4i**) underwent coupling with various aryl sulfonyl hydrazides (**2a**-**2c**) to give the corresponding mono- and di-sulfenylation products. In the case of substituted toluenes, *p*-xylene afforded di-sulfenylation products **5aaa** and **5acc**, albeit in poor yields. Mesitylene resulted in the formation of mono-thioethers **5ba**, **5bb**, and **5be** in moderate to good yields. 4-Methylphenol and 4-chlorophenol gave 2-sulfenylation products **5ca** and **5da**, respectively, while thioanisole gave the 4-sulfenylation product **5ea** in moderate to good yields. Moreover, when we used naphthalene and 2-bromonaphthalene as substrates, the corresponding 1, 4-disulfenylation products (**5faa** and **5iaa**) were obtained. However, 1-methylnaphthalene and 2-methylnaphthalene gave only mono-sulfenylation products (**5ga** and **5ha**).

Although mechanisms for the sulfonyl hydrazide-based sulfenylation have been proposed by many groups,[3d, 3i, 4, 5b] the actual sulfenylation species generated from sulfonyl hydrazides are not very clear because the proposed sulfenylation intermediates were unstable and could not be isolated and characterized.[4] To further understand the reaction mechanism and determine the sulfenylation species produced, we investigated the decomposition of **2a** under the optimized reaction conditions, and obtained 1,2-di-*p*-tolyldisulfane **6a** and *S*-*p*-tolyl 4- methylbenzenesulfonothioate **7a** in 43% and 55% yields, respectively. Table 4 summarizes the results

obtained when using **6a**, **7a**, and 4-methylbenzenesulfinic acid **8a**, a previously reported decomposition product of **2a**,[4] as well as the

Table 3 I_2-catalyzed sulfenylation of electron-rich aromatics with aryl sulfonyl hydrazides.[a]

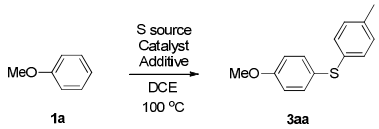


[a] Reaction conditions: **1a-c** (2.0 mmol), **2b-f** (2.4 mmol), I_2 (0.2 mmol), DCE (0.3 mL), 120 °C.
[b] The reaction was carried out in 100 °C.
[c] The yield was calculated using sulfonyl hydrazide as reference.

results obtained with combinations of **6a**/**7a** and **6a**/**8a** as the sulfenylation reagents in the reaction with **1a**. We found that **6a** did not react with **1a** to afford the desired **3aa** product (Table 4, Entry 1), unless 0.1 equiv. of iodine (Table 4, Entries 2) was added. Notably, when H_2O_2 was used as an additive to oxidize **6a** to **7a**, the yield was improved from 19% to 42%, which suggests that **7a** is a more efficient sulfenylation reagent in this reaction (Table 4, Entry 3). Further, **7a** could not be transformed into **3aa** in the absence of a catalyst or additive; however, when 0.1 equiv. of iodine was used as a catalyst, **7a** coupled with **1a** to produce the desired product in 65% yield (Table 4, Entries 4, 5). Interestingly, HI, which is proposed to be generated from the decomposition of sulfonyl hydrazide by iodine,[4] catalyzed the transformation of **7a** to **3aa** in 70% yield (Table 4, Entry 6). Notably, when a combination of 0.3 equiv. **6a** and 0.3 equiv. **7a** was used for sulfenylation, an excellent product yield of 87% was obtained (Table 4, Entry 7). It is known that **6a** reacts with **8a** to produce **7a**;[11] hence, the combination of **6a** and **8a** was tested as the sulfur source. When 0.6 equiv. of **6a** was combined with 0.1 equiv. of **8a**, the desired product was obtained in 15% yield in the absence of the iodine catalyst and in 31% yield in the presence of the iodine catalyst (Table 4, Entries 8, 9). Notably, increasing the loading of **8a** led to an increase in the yields. Additionally, **7a** increased in amount during the reaction but disappeared when the reaction was completed (Table 4; Entries 10, 11). Finally, when only **8a** was used as the sulfenylation reagent,[12] the desired products were obtained in 43% and 44% yield in the presence of iodine and HI as the catalyst, respectively. (Table 4; Entries 12, 13). Based on these data, we propose that **7a** is the major sulfenylation species in this reaction.

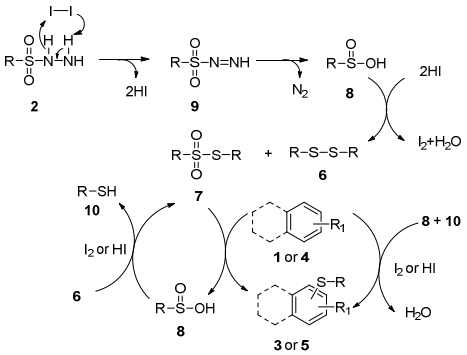
A possible mechanism of this transformation, based on our experimental observations and those reported in the literature,[3d, 4] is proposed in Scheme 3. Sulfonyl hydrazide **2** ultimately decomposes into disulfide **6** and thiosulfonate **7**. Two intermediates are formed when iodine is used as the catalyst: sulfonyl diazene **9** and sulfinic acid **8**. The key intermediate **7** reacts with electron-rich aromatics **1** or **4** to produce the sulfenylation compound **8** as well as products **3** or **5** when iodine or HI is added. Intermediate **8** then reacts with **6** to yield **7** and thiophenol **10**. The combination of **10** and **8** can be used as the sulfur source to convert substrates into the sulfenylation products in the presence of iodine, as confirmed in the following two experiments. 1) When 0.6 equiv. of **8a** and 0.6 equiv. of 4-methylbenzenethiol **10a** were used as the sulfur source, in the presence of iodine and at 100 °C, the desired sulfenylation product **3aa** was obtained in 70 % yield. 2) When **10a** was reacted with benzenesulfinic acid **8a'** instead of **8a** as the sulfur source, sulfenylation products **3aa** and (4-methoxyphenyl)(phenyl)sulfane **3aa'** were formed in 48% and 34% yield, respectively (Scheme 4).[13]

Table 4. Reaction of anisole **1a** with three decomposition products of sulfonyl hydrazides **2a**.[a]

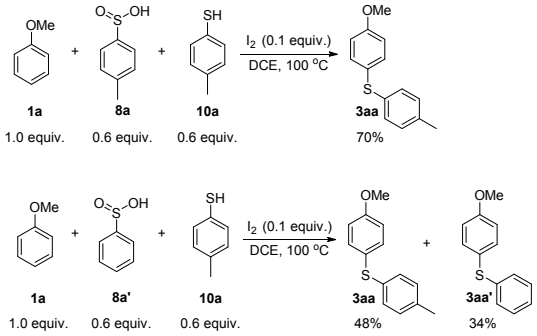


Entry	S source **A**	S source **B**	Catalyst	Additive	Yield (%)
1	**6a** (0.6 eq.)	—	—	—	0
2	**6a** (0.6 eq.)	—	I_2 (0.1 eq.)	—	19
3	**6a** (0.6 eq.)	—	I_2 (0.1 eq.)	H_2O_2 (1.5 eq.)	42
4	**7a** (0.6 eq.)	—	—	—	0
5	**7a** (0.6 eq.)	—	I_2 (0.1 eq.)	—	65
6	**7a** (0.6 eq.)	—	—	HI (0.1 eq.)	70
7	**6a** (0.3 eq.)	**7a** (0.3 eq.)	I_2 (0.1 eq.)	—	87
8	**6a** (0.6 eq.)	**8a** (0.1 eq.)	—	—	15
9	**6a** (0.6 eq.)	**8a** (0.1 eq.)	I_2 (0.1 eq.)	—	31
10	**6a** (0.6 eq.)	**8a** (0.2 eq.)	I_2 (0.1 eq.)	—	52
11	**6a** (0.6 eq.)	**8a** (0.3 eq.)	I_2 (0.1 eq.)	—	72
12	—	**8a** (1.2 eq.)	I_2 (0.1 eq.)	—	43
13	—	**8a** (1.2 eq.)	HI (0.1 eq.)	—	44

[a] Reaction conditions: **1a** (1.0 mmol), S source (0.3-0.6 mmol), iodine (0-0.1 mmol), additive (0-1.5 eq.), solvent (0.3 mL), 100 °C.



Scheme 3 Proposed reaction pathway



Scheme 4 Sulfenylation of anisole using **8a**, **8a'**, and **10a** as sulfur sources

Experimental

1) General methods and material

All solvents were distilled prior to use. Unless otherwise noted, chemicals were used as received without further purification. For chromatography, 200−300 mesh silica gel was employed. ^{1}H and ^{13}C{^{1}H} NMR spectra were recorded at 400 MHz and 100 MHz respectively. Chemical shifts are reported in ppm using tetramethylsilane as internal standard. IR spectra were recorded in wave numbers (cm^{-1}) with a FT-IR spectrometer. HRMS was performed on an FTMS mass instrument. Melting points are reported as uncorrected.

2) The synthesis and spectral data of the sulfenylation products

General Procedure: The I_2-catalyzed reactions between electron-rich aromatics 1a, 1b, 1d, 1e; 4a-i and sulfonyl hydrazides 2a-f (Table 2, 3). Electron-rich aromatics (2.0 mmol), sulfonyl hydrazides (2.4 mmol) and I_2 (50.8 mg, 0.2 mmol) and DCE (0.3 mL) were mixed in a sealed tube. The mixture was stirred at 120 °C or 100 °C until electron-rich aromatics disappeared detected by TLC. Then, the solvent was evaporated under reduced pressure and the residue was purified by silica gel column chromatography to afford the pure product.

(4-methoxyphenyl)(p-tolyl)sulfane (3aa)[14]**:** After purification by silica gel column chromatography (PE : DCM = 15 : 1, PE = petroleum ether, DCM = CH_2Cl_2), compound **3aa** was isolated as a pale yellow oil (379 mg, 82%): R_f (PE : EA = 30 : 1) = 0.63; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36 (dd, *J* = 6.8 Hz, 2.0 Hz, 2H), 7.13 (dd, *J* = 6.8 Hz, 2.0 Hz, 2H), 7.06 (d, *J* = 6.8 Hz, 2H), 6.87 (dd, *J* = 6.8 Hz, 2.0 Hz, 2H), 3.80 (s, 3H), 2.30 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 159.4, 136.1, 134.3, 129.7, 129.4, 125.6, 114.8, 55.3, 21.0.

bis(4-methoxyphenyl)sulfane (3ab)[15]***:*** After purification by silica gel column chromatography (PE:DCM = 5:1), compound **3ab** was isolated as a pale yellow oil (404 mg, 82%): R_f (PE : EA = 30 : 1) = 0.48; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.28 (dd, *J* = 6.8 Hz, 2.0 Hz, 4H), 6.84 (dd, *J* = 6.8 Hz, 2.0 Hz, 4H), 3.79 (s, 6H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 158.9, 132.7, 127.4, 114.7, 55.3.

(3-chlorophenyl)(4-methoxyphenyl)sulfane (3ac)[16]**:** After purification by silica gel column chromatography (PE : DCM = 100 : 1), compound **3ac** was isolated as a pale yellow oil (378 mg, 75%): R_f (PE : EA = 30 : 1) = 0.6; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43 (dd, *J* = 6.8 Hz, 2.0 Hz, 2H), 7.12-7.15 (m, 1H), 7.08 (d, *J* = 8.0 Hz, 1H), 7.07 (s, 1H), 7.00 (d, *J* = 8.0 Hz, 1H), 6.92 (dd, *J* = 6.8 Hz, 2.0 Hz, 2H), 3.84 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 160.3, 141.3, 136.1, 134.8, 129.8, 127.0, 125.5, 125.4, 122.6, 115.2, 55.4.

(4-methoxyphenyl)(4-(trifluoromethyl)phenyl)sulfane (3ad)[2]**:** After purification by silica gel column chromatography (PE : DCM = 100 : 1), compound **3ad** was isolated as a white solid (131 mg, 23% for 120 °C), (308 mg, 54% for 100 °C): R_f (PE : EA = 30 : 1) = 0.7; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.47 (d, *J* = 8.8 Hz, 2H), 7.43 (d, *J* = 8.4 Hz, 2H), 7.13 (d, *J* = 8.4 Hz, 2H), 6.95 (d, *J* = 8.8 Hz, 2H), 3.85 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 160.7, 114.8, 136.6, 127.2 (q, *J* = 32.0 Hz, 1C), 126.5, 125.6 (q, *J* = 4.0 Hz, 1C), 124.2 (q, *J* = 270 Hz, 1C), 121.8, 115.4, 55.4.

(4-methoxyphenyl)(o-tolyl)sulfane (3ae)[3]**:** After purification by silica gel column chromatography (PE : DCM = 100 : 1), compound **3ae** was isolated as a colorless oil (264 mg, 57% for 120 °C), (305 mg, 66% for 100 °C): R_f (PE : EA = 30 : 1) = 0.68; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32 (dd, *J* = 6.8 Hz, 2.0Hz, 2H), 7.17 (d, *J* = 6.8 Hz, 1H), 7.03-7.11 (m, 2H), 6.98 (d, *J* = 6.8 Hz, 1H), 6.89 (dd, *J* = 6.8 Hz, 2.0Hz, 2H), 3.81 (s, 3H), 2.38 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 159.5, 137.01, 137.03, 134.5, 130.2, 129.1, 126.4, 126.1, 124.5, 115.0, 55.3, 20.3.

(4-methoxyphenyl)(methyl)sulfane (3af)[17]**:** After purification by silica gel column chromatography (PE : DCM = 100 : 1), compound **3af** was isolated as a yellow oil (76 mg, 25%). R_f (PE : EA = 30 : 1) = 0.72; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.27 (dd, *J* = 6.8 Hz, 2.0 Hz, 2H), 6.85 (d, *J* = 6.8 Hz, 2.0 Hz, 2H), 3.79 (s, 3H), 2.44 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 158.2, 130.2, 128.7, 114.6, 55.3, 18.0.

(2,4-dimethoxyphenyl)(p-tolyl)sulfane (3ba)[18]**:**

(4,6-dimethoxy-1,3-phenylene)bis(p-tolylsulfane) (3baa)**:** After purification by silica gel column chromatography (PE : EA = 100 : 1), compound **3ba** and compound **3baa** were isolated as a white solid (310 mg, 60%) and as a white solid (205 mg, 27%) respectively. For **3ba**: mp (melting point) = 69-70 °C; R_f (PE : EA = 30 : 1) = 0.4; IR (film): 2942, 1594, 1490, 1463, 1303, 1209, 1162, 1075, 1031, 804 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.24 (d, *J* = 8.4 Hz, 1H), 7.10 (d, *J* = 8.4 Hz, 2H), 7.05 (d, *J* = 8.4 Hz, 2H), 6.51 (d, *J* = 2.4 Hz, 1H), 6.46 (dd, *J* = 8.4 Hz, 2.4 Hz, 1H), 3.82 (s, 6H), 2.29 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 161.3, 159.8, 135.7, 135.4, 133.4, 129.6, 129.0, 113.6, 105.3, 99.2, 55.9, 55.4, 21.0; HRMS (ESI, m/z): calcd for $C_{15}H_{16}O_2S$ $[M]^+$ 260.0866, found 260.0868, calcd for $C_{15}H_{16}NaO_2S$ $[M+Na]^+$ 283.0763, found 283.0765. For **3baa:** mp (melting point) = 111-112 °C; R_f (PE : EA = 30 : 1) = 0.18; IR (film): 2923, 2842, 1576, 1491, 1365, 1274, 1207, 1028, 806 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.15 (s, 1H), 7.09 (d, *J* = 8.4 Hz, 4H), 7.02 (d, *J* = 8.4 Hz, 4H), 6.52 (s, 1H), 3.88 (s, 6H), 2.30 (s, 6H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 159.4, 138.3, 136.2, 132.1, 129.9, 129.7, 114.8, 96.1, 56.2, 21.0; HRMS (ESI, m/z): calcd for $C_{22}H_{22}O_2S_2$ $[M]^+$ 382.1056, found 382.1059, calcd for $C_{22}H_{22}NaO_2S_2$ $[M+Na]^+$ 405.0953, found 405.0955.

(2,5-dimethoxy-1,4-phenylene)bis(p-tolylsulfane) (3caa)**:** **1c** (276 mg, 2.0 mmol), **2a** (893 mg, 4.8 mmol) and I_2 (50.8 mg, 0.2 mmol) and DCE (0.3 mL) were mixed in a sealed tube. The mixture was stirred at 120 °C until **1c** disappeared detected by TLC. Then, the solvent was evaporated under reduced pressure and the residue was purified by silica gel column chromatography (PE : CH_2Cl_2 = 5 : 1) to get compound **3caa** (264 mg, 35%) as a white solid: mp (melting point) = 162-163 °C; R_f (PE : EA = 30 : 1) = 0.43; IR (film): 2952, 1490, 1438, 1365, 1205, 1037, 812, 777 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.28 (d, *J* = 8.0 Hz, 4H), 7.14 (d, *J* = 8.0 Hz, 4H), 6.57 (s, 2H), 3.64 (s, 6H), 2.35 (s, 6H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 151.5, 137.6, 132.1, 130.2, 130.3, 124.3, 113.8, 56.5, 21.1; HRMS (ESI, m/z): calcd for $C_{22}H_{23}O_2S_2$ $[M+H]^+$ 383.1134, found 383.1141, calcd for $C_{22}H_{22}NaO_2S_2$ $[M+Na]^+$ 405.0953, found 405.0958.

***(4,5-dimethoxy-1,2-phenylene)bis(p-tolylsulfane) (3da)*:** After purification by silica gel column chromatography (PE : EA = 50 :1), compound **3da** was isolated as a pale yellow solid (380 mg, 83%): mp (melting point) = 99-100 °C; R_f (PE : EA = 30 : 1) = 0.2; IR (film): 2930, 1489, 1436, 1252, 1207, 1178, 1035, 806 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.19 (d, *J* = 8.0 Hz, 4H), 7.10 (d, *J* = 8.0 Hz, 4H), 6.77 (s, 2H), 3.71 (s, 6H), 2.32 (s, 6H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 148.9, 136.8, 132.4, 130.6, 129.9, 129.2, 115.5, 56.0, 21.1; HRMS (ESI, m/z): calcd for $C_{22}H_{23}O_2S_2$ $[M+H]^+$ 383.1134, found 383.1141, calcd for $C_{22}H_{22}NaO_2S_2$ $[M+Na]^+$ 405.0953, found 405.0959.

p-tolyl(2,4,6-trimethoxyphenyl)sulfane (3ea) [21]**:**

***(2,4,6-trimethoxy-1,3-phenylene)bis(p-tolylsulfane) (3eaa)*:** After purification by silica gel column chromatography (PE : EA = 50 : 1), compound **3ea** and **3eaa** were isolated as a white solid (354 mg, 61%) and as a white solid (113 mg, 14%) respectively. For **3ea**: R_f (PE : EA = 20 : 1) = 0.23; mp (melting point) = 120-121 °C; IR (film): 1580, 1490, 1226, 1206, 1161, 1123, 804, 739 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 6.93-6.98 (m, 4H), 6.21 (s, 2H), 3.86 (s, 3H), 3.80 (s, 6H), 2.25 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 162.7, 162.5, 135.0, 134.1, 129.2, 126.0, 99.4, 91.2, 56.3, 55.4, 20.8; HRMS (ESI, m/z): calcd for $C_{16}H_{19}O_3S$ $[M+H]^+$ 291.1049, found 291.1050, calcd for $C_{16}H_{18}NaO_3S$ $[M+Na]^+$ 313.0869, found 313.0871. For **3eaa**: R_f (PE : EA = 20 : 1) = 0.17; mp (melting point) = 142-144 °C; IR (film): 2928, 1571, 1491, 1369, 1212, 1116, 1097, 803 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 6.99 (s, 8H), 6.41 (s, 1H), 3.86 (s, 6H), 3.76 (s, 3H), 2.26 (s, 6H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 165.9, 163.3, 134.7, 134.6, 129.4, 126.6, 107.5, 92.5, 62.2, 56.3, 20.8; HRMS (ESI, m/z): calcd for $C_{23}H_{25}O_3S_2$ $[M+H]^+$ 413.1240, found 413.1245, calcd for $C_{23}H_{24}NaO_3S_2$ $[M+Na]^+$ 435.1059, found 435.1063.

(2,5-dimethyl-1,4-phenylene)bis(p-tolylsulfane) (5aaa) [19]**:** After purification by silica gel column chromatography (PE), compound **5aaa** was isolated as a white solid (110 mg, 26%): R_f (PE) = 0.55; mp (melting point) = 114-116 °C; IR (film): 2924, 1489, 1467, 1445, 1087, 1012, 805 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.16 (d, *J* = 8.0 Hz, 4H), 7.11 (d, *J* = 8.0 Hz, 4H), 7.03 (s, 2H), 2.33 (s, 6H), 2.24 (s, 6H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 137.0, 136.8, 133.9, 133.1, 131.5, 130.7, 130.0, 21.1, 19.9; HRMS (ESI, m/z): calcd for $C_{22}H_{23}S_2$ $[M+H]^+$ 351.1236, found 351.1232.

***(2,5-dimethyl-1,4-phenylene)bis((3-chlorophenyl)sulfane) (5acc)*:** After purification by silica gel column chromatography (PE), compound **5acc** was isolated as a white solid (153 mg, 33%): R_f (PE) = 0.76; mp (melting point) = 71-72 °C; IR (film): 2918, 1576, 1460, 1081, 774, 678 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.23 (s, 2H), 7.15-7.22 (m, 6H), 7.06 (d, *J* = 8.0 Hz, 2H), 2.28 (s, 6H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 138.8, 138.2, 135.4, 135.0, 132.9, 130.2, 128.7, 127.2, 126.5, 20.0; HRMS (ESI, m/z): calcd for $C_{20}H_{17}Cl_2S_2$ $[M+H]^+$ 391.0143, found 391.0149.

mesityl(p-tolyl)sulfane (5ba) [10]**:** After purification by silica gel column chromatography (PE : DCM = 100 : 1), compound **5ba** was isolated as a white solid (378 mg, 78%): R_f (PE) = 0.8; ^1H NMR (400 MHz, $CDCl_3$): δ 6.99 (s, 2H), 6.98 (d, *J* = 8.0 Hz, 2H), 6.82 (d, *J* = 8.0 Hz, 2H), 2.38 (s, 6H), 2.31 (s, 3H), 2.26 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 143.6, 139.0, 134.8, 134.2, 129.6, 129.3, 127.5, 125.7, 21.7, 21.1, 20.8.

mesityl(4-methoxyphenyl)sulfane (5bb) [9]**:** After purification by silica gel column chromatography (PE), compound **5bb** was isolated as a pale yellow solid (371mg, 72%). R_f (PE) = 0.35; ^1H NMR (400 MHz, $CDCl_3$): δ 6.98 (s, 2H), 6.90 (d, *J* = 8.8 Hz, 2H), 6.74 (d, *J* = 8.8 Hz, 2H), 3.74 (s, 3H), 2.39 (s, 6H), 2.30 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 157.4, 143.4, 138.9, 129.2, 129.0, 128.3, 127.6, 114.6, 55.3, 21.8, 21.1.

mesityl(o-tolyl)sulfane (5be) [20]**:** After purification by silica gel column chromatography (PE), compound **5be** was isolated as a pale yellow oil (271 mg, 56%): R_f (PE) = 0.85; IR (film): 2921, 1588, 1466, 1377, 1045, 851, 745 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.12 (d, *J* = 6.8 Hz, 1H), 7.02 (s, 2H), 6.90-6.99 (m, 2H), 6.39 (dd, *J* = 8.0 Hz, 1.2 Hz, 1H), 2.43 (s, 3H), 2.35 (s, 6H), 2.32 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 143.8, 139.1, 137.4, 134.6, 129.9, 129.3, 127.0, 126.4, 124.2, 124.0, 21.6. 21.1, 20.0; HRMS (ESI, m/z): calcd for $C_{16}H_{19}S$ $[M+H]^+$ 243.1202, found 243.1207.

4-methyl-2-(p-tolylthio)phenol (5ca) [21]**:** After purification by silica gel column chromatography (PE : DCM = 15 : 1), compound **5ca** was isolated as a colorless oil (363 mg, 78%): R_f (PE : EA = 30 : 1) = 0.5; ^1H NMR (400 MHz, $CDCl_3$): δ 7.31 (d, *J* = 2.0 Hz, 1H), 7.14 (dd, *J* = 8.4 Hz, 2.0 Hz, 1H), 6.99-7.05 (m, 4H), 6.94 (d, *J* = 8.4 Hz, 1H), 6.35 (s, 1H), 2.28 (s, 3H), 2.27 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 154.9, 136.6, 136.2, 132.7, 132.4, 130.4, 129.9, 127.5, 116.7, 115.2, 20.9, 20.3.

***4-chloro-2-(p-tolylthio)phenol (5da)*:** After purification by silica gel column chromatography (PE : EA = 200 : 1), compound **5da** was isolated as a yellow oil (275 mg, 55%): R_f (PE : EA = 30 : 1) = 0.3; IR (film): 3418, 1491, 1468, 1275, 1190, 820, 803, 725 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.48 (d, *J* = 2.4 Hz, 1H), 7.28 (dd, *J* = 8.8 Hz, 2.4 Hz, 1H), 7.04-7.09 (m, 4H), 6.97 (d, *J* = 8.8 Hz, 1H), 6.45 (s, 1H), 2.29 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 155.6, 137.0, 135.3, 131.7, 131.0, 130.2, 128.3, 125.4, 119.3, 116.6, 20.9; HRMS (ESI, m/z): calcd for $C_{13}H_{12}ClOS$ $[M+H]^+$ 251.0292, found 251.0296.

1-methoxy-4-(4-(methylthio)phenylthio)benzene (5ea) [22]**:** After purification by silica gel column chromatography (PE : DCM = 5 : 1), compound **5ea** was isolated as a pale yellow solid (224 mg, 43%): mp (melting point) = 41-43 °C; R_f (PE : EA = 30 : 1) = 0.6; IR (film): 2920, 1591, 1493, 1476, 1246, 1172, 1106, 1031, 828, 808 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.37 (dd, *J* = 6.8 Hz, 2.0 Hz, 1H), 7.11-7.16 (m, 4H), 6.88 (dd, *J* = 6.8 Hz, 2.0 Hz, 2H), 3.81 (s, 3H), 2.45 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 159.6, 136.3, 134.7, 134.6, 129.4, 127.4, 124.9, 114.9, 55.3, 16.1; HRMS (ESI, m/z): calcd for $C_{14}H_{15}OS_2$ $[M+H]^+$ 263.0559, found 263.0565.

1,4-bis(p-tolylthio)naphthalene (5faa) [9]**:** After purification by silica gel column chromatography (PE), compound **5faa** was isolated as a white solid (209 mg, 47%): R_f (PE) = 0.48; ^1H NMR (400 MHz, $CDCl_3$): δ 8.40 (dd, *J* = 6.8 Hz, 3.2 Hz, 2H), 7.55 (dd, *J* = 6.8 Hz, 3.2 Hz, 2H), 7.30 (s, 2H), 7.21 (d, *J* = 8.0 Hz, 4H), 7.10 (d, *J* = 8.0 Hz, 4H), 2.32 (s, 6H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 137.2, 133.4, 133.0, 131.4, 131.1, 130.1, 129.5, 127.0, 125.7, 21.1.

***(4-methylnaphthalen-1-yl)(p-tolyl)sulfane (5ga)*:** After purification by silica gel column chromatography (PE), compound **5ga** was isolated as a yellow oil (340 mg, 64%): R_f (PE) = 0.67; IR (film): 2919, 1491, 1378, 1088, 829, 804, 757 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.43 (dd, *J* = 8.0 Hz, 1.6 Hz, 1H), 8.02 (dd, *J* = 7.6 Hz, 2.0 Hz, 1H), 7.50-7.56 (m, 3H), 7.26 (d, *J* = 7.6 Hz, 1H), 7.07-7.09 (m, 2H), 7.01 (d, *J* = 8.0 Hz, 2H), 2.70 (s, 3H), 2.27 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 135.9, 135.6, 133.63, 133.56, 133.4, 132.2, 129.8, 129.6, 129.1, 126.7, 126.4, 126.3, 126.1, 124.7, 20.9, 19.5; HRMS (ESI, m/z): calcd for $C_{18}H_{16}S$ $[M]^+$ 264.0967, found 264.0971, calcd for $C_{18}H_{17}S$ $[M+H]^+$ 265.1046, found 265.1049.

***(2-methylnaphthalen-1-yl)(p-tolyl)sulfane (5ha)*:** After purification by silica gel column chromatography (PE), compound **5ha** was isolated as a yellow oil (180 mg, 34%): R_f (PE) = 0.75; IR (film): 2920, 1491, 1085, 1016, 803, 775, 742 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.56 (d, *J* = 8.0 Hz, 1H), 7.82-7.85 (m, 2H), 7.42-7.51 (m, 3H), 6.94 (d, *J* = 8.0 Hz, 2H), 6.84 (d, *J* = 8.0 Hz, 2H), 2.65 (s, 3H), 2.23 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 142.7, 135.8, 134.6, 134.5, 132.9,

129.8, 129.6, 128.9, 128.2, 127.6, 127.1, 126.3, 125.4, 22.2, 20.8; HRMS (ESI, m/z): calcd for $C_{18}H_{16}S$ $[M]^+$ 264.0967, found 264.0972, calcd for $C_{18}H_{17}S$ $[M+H]^+$ 265.1046, found 265.1049.

***(6-bromonaphthalene-1,4-diyl)bis(p-tolylsulfane) (5iaa)*:** After purification by silica gel column chromatography (PE), compound **5iaa** was isolated as a pale yellow oil (71 mg, 13%): R_f (PE) = 0.46; IR (film): 2923, 1594, 1491, 1329, 987, 826, 807 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.59 (d, *J* = 2.0 Hz, 1H), 8.26 (d, *J* = 9.2 Hz, 1H), 7.61 (dd, *J* = 9.2Hz, 2.0 Hz, 1H), 7.28 (s, 2H), 7.23 (dd, *J* = 6.4 Hz, 2.0 Hz, 2H), 7.19 (dd, *J* = 6.4 Hz, 2.0 Hz, 2H), 7.09-7.13 (m, 4H), 2.33 (s, 3H), 2.32 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 137.6, 137.5, 134.3, 133.6, 133.0, 131.6, 131.5, 131.2, 131.0, 130.7, 130.4, 130.3, 130.22, 130.17, 129.8, 128.0, 127.6, 121.7, 21.09, 21.07; HRMS (ESI, m/z): calcd for $C_{24}H_{20}BrS_2$ $[M+H]^+$ 451.0184, found 451.0188.

Conclusions

In conclusion, we developed an efficient iodine-catalyzed cross-coupling reaction of sulfonyl hydrazides with electron-rich aromatics, including substituted anisole, thioanisole, phenol, toluene, and naphthalene, via direct C–H functionalization. This study not only broadened the scope of sulfenylation reactions with sulfonyl hydrazides as reagents from electron-rich heterocycles to general electron-rich aromatics, but also demonstrated that sulfonothioates were the major sulfenylation species in this transformation.

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Notes and references

1 For recent reviews: (a) C. Shen, P. Zhang, Q. Sun, S. Bai, T. S. A. Hor and X. Liu, *Chem. Soc. Rev*. 2015, **44**, 291. (b) H. Liu and X. Jiang, *Chem. - Asian J.* 2013, **8**, 2546. (c) I. P. Beletskaya and V. P. Ananikov, *Chem. Rev.* 2011, **111**, 1596. (d) T. Kondo and T.-A. Mitsudo, *Chem. Rev*. 2000, **100**, 3205.

2 For selected recent examples: (a) X. Gao, X. Pan, J. Gao, H. Jiang, G. Yuan and Y. Li, *Org. Lett.* 2015, **17**, 1038. (b) T. Miao, P. Li, Y. Zhang and L. Wang, *Org. Lett.* 2015, **17**, 832. (c) M. W. Johnson, S. W. Bagley, N. P. Mankad, R. G. Bergman, V. Mascitti and F. D. Toste, *Angew. Chem. Int. Ed*. 2014, **53**, 4404. (d) X. Zhang, W. Zeng, Y. Yang, H. Huang and Y. Liang, *Org. Lett.* 2014, **16**, 876. (e) J. T. Reeves, K. Camara, Z. S. Han, Y. Xu, H. Lee, C. A. Busacca and C. H. Senanayake, *Org. Lett.* 2014, **16**, 1196. (f) V. G. Pandya and S. B. Mhaske, *Org. Lett.* 2014, **16**, 3836. (g) F. Xiao, H. Chen, H. Xie, S. Chen, L. Yang and G.-J. Deng, *Org. Lett*. 2014, **16**, 50. (h) Y. Xu, X. Tang, W. Hu, W. Wu and H. Jiang, *Green Chem*. 2014, **16**, 3720.

3 For selected examples: (a) G. Rong, J. Mao, H. Yan, Y. Zheng and G. Zhang, *J. Org. Chem.* 2015, **80**, 4697. (b) M. Zhang, P. Xie, W. Zhao, B. Niu, W. Wu, Z. Bian, C. U. Pittman and A. Zhou, *J. Org. Chem.* 2015, **80**, 4176. (c) W. Yu, P. Hu, Y. Fan, C. Yu, X. Yan, X. Li and X. Xu, *Org. Biomol. Chem.* 2015, **13**, 3308. (d) T.-T. Wang, F.-L. Yang and S.-K. Tian, *Adv. Synth. Catal.* 2015, **357**, 928. (e) K. Xu, V. Khakyzadeh, T. Bury and B. Breit, *J. Am. Chem. Soc.* 2014, **136**, 16124. (f) J. Zhang, Y. Shao, H. Wang, Q. Luo, J. Chen, D. Xu and X. Wan, *Org. Lett*. 2014, **16**, 3312. (g) S. Guo, W. He, J. Xiang and Y. Yuan, *Chem. Commun.* 2014, **50**, 8578. (h) F.-L. Yang, F.-X. Wang, T.-T. Wang, Y.-J. Wang and S.-K. Tian, *Chem. Commun.* 2014, **50**, 2111. (i) R. Singh, D. S. Raghuvanshi and K. N. Singh, *Org. Lett.* 2013, **15**, 4202. (j) N. Singh, R. Singh, D. S. Raghuvanshi and K. N. Singh, *Org. Lett.* 2013, **15**, 5874. (k) X. Li, X. Xu, P. Hu, X. Xiao and C. Zhou, *J. Org. Chem.* 2013, **78**, 7343.

4 F.-L. Yang and S.-K. Tian, *Angew. Chem., Int. Ed.* 2013, **52**, 4929.

5 X. Zhao, L. Zhang, X. Lu, T. Li and K. Lu, J. Org. Chem. 2015, 80, 2918.

6 (a) J. Sun, J.-K. Qiu, Y.-L. Zhu, C. Guo, W.-J. Hao, B. Jiang and S.-J. Tu, *J. Org. Chem.* 2015, **80**, 8217. (b) X. Zhao, L. Zhang, T. Li, G. Liu, H. Wang and K. Lu, Chem. Commun. 2014, 50, 13121.

7 A. Hajra, A. K. Bagdi, S. Mitra and M. Ghosh, *Org. Biomol. Chem.* 2015, **13**, 3314.

8 X. Kang, R. Yan, G. Yu, X. Pang, X. Liu, X. Li, L. Xiang and G. Huang, *J. Org. Chem.* 2014, **79**, 10605.

9 P. Saravanan and P. Anbarasan, *Org. Lett.* 2014, **16**, 848.

10 X. Li, Y. Xu, W. Wu, C. Jiang, C. Qi and H. Jiang, *Chem. - Eur. J.* 2014, **20**, 7911.

11 S. Oae, T. Takata and Y. H. Kim, *Tetrahedron*, 1981, **37**, 37.

12 C.-R. Liu and L.-H. Ding, *Org. Biomol. Chem.* 2015, **13**, 2251.

13 Because **3aa** and **3aa'** could not be separated by silica gel column chromatography, the yield was calculated by NMR.

14 A. Martin, D. Nelson, S. Meiries, A. Slawin and S. Nolan, *Eur. J. Org. Chem.* 2014**,** 3127.

15 D. J. C. Prasad and G. Sekar, *Org. Lett.* 2011, **13**, 1008.

16 S. Saba, J. Rafique and A. Braga, *Adv. Synth. Catal.* 2015, **357**, 1446.

17 Y. Jang, K. Kim and H. Jeon, *J. Org. Chem.* 2013, **78**, 6328.

18 C. D. Prasad, S. J. Balkrishna, A. Kumar, B. S. Bhakuni, K. Shrimali, S. Biswas and S. Kumar, *J. Org. Chem*. 2013, **78**, 1434.

19 M. Hojo and R. Masuda, *Synth. Commun.* 1975, **5**, 173.

20 G. Montaudo and P. Finocchiaro, *J. Mol. Struct.* 1972, **14**, 53.

21 Y. Liao, P. Jiang, S. Chen, H. Qi and G. Deng, *Green Chem*. 2013, **15**, 3302.

22 A. Pinchart, C. Dallaire, A. Van Bierbeek and M. Gingras, *Tetrahedron Lett.* 1999, **40**, 5479.