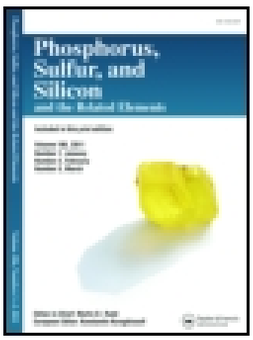

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ISSN: 1042-6507 (Print) 1563-5325 (Online) Journal homepage: http://www.tandfonline.com/loi/gpss20

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To cite this article: Xing-Song Zhang & Xiao-Hong Zhang (2015): Mild Synthesis of n-Acylsulfenamides from Arylamides and Disulfides, Phosphorus, Sulfur, and Silicon and the Related Elements, DOI: 10.1080/10426507.2015.1012670

To link to this article: http://dx.doi.org/10.1080/10426507.2015.1012670

MILD SYNTHESIS OF *N*-ACYLSULFENAMIDES FROM ARYLAMIDES AND DISULFIDES

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Abstract An efficient and new method was developed to synthesize *N*-acylsulfenamides *via* NaH-promoted sulfenylation of benzamides with readily available disulfides under mild conditions. A series of *N*-acylsulfenamides were easily obtained in moderate to high yields. Moreover, the obtained *N*-acylsulfenamides were used as thiolating reagents in the synthesis of sulfenylpyrroles and 3-sulfenylbenzofurans.

Keywords *N*-acyl sulfenamides, sulfenylation, thiolating reagents

INTRODUCTION

Sulfenamide derivatives have aroused much interest because of their practical application in biochemistry and pharmacological chemistry,[1] including antibacterial agents,[2] enzyme inhibition,[3] and as the prodrugs of carbamazepine,[4] metformin[5] or NH-acidic compounds.[6] Moreover, sulfenamides were also potential precursors for the synthesis of numerous pharmaceuticals and agrochemicals owing to their unique S-N bonds.[7] For example, *N*-(phenylthio)phthalimide,[8] *N*-(phenylthio)succinimide[9] and 1,2-benzisothiazolin-3-one[10] were used as versatile thiolating reagents in the synthesis of diverse sulfur-containing molecules. However, only limited efficient methods have been reported for the synthesis of *N*-acyl sulfenamides,[11] possibly due to the difficult formation of S-N bonds. For example, to date *N*-acylsulfenamides are usually obtained by the reaction of amides with the toxic and unstable sulfenyl chlorides,[12] which are generally prepared by chlorination of thiols or disulfides with poisonous / corrosive chlorine gas (Scheme 1, eq. 1). An alternative method was the acylation of not easily available arenesulfenamides using acyl chlorides as acylation reagent.[13] However, a sulfenyl chloride is also required for the synthesis of the arenesulfenamides (Scheme 1, eq. 2).[14] It is well-known that the use of both sulfenyl chlorides and acyl chlorides, would inevitability bring about environmental pollution.

Therefore, the development of ñgreenò and efficient strategies for the synthesis of *N*-acylsulfenamides is highly desired. Based on the aforementioned synthetic methods and considering the weak acidity of amides, we envisage that *N*-acylsulfenamides could be prepared *via* the sulfenylation of benzamides with a disulfide with the aid of base. Fortunately, the reaction proceeded smoothly to provide a series of *N*-acylsulfenamides in moderate to high yields when using NaH as the base under mild conditions. The obtained *N*-acylsulfenamides can also act as useful thiolating reagents to achieve diverse sulfur compounds. Herein, we describe our results in detail.

RESULTS AND DISCUSSION

We began our study with the reaction between benzamide andh phenyl disulfide to explore the optimal reaction conditions (Table 1). Benzamide was initially treated with NaH (1 equiv.) in THF at room temperature for about 1 h, then phenyl disulfide (1.5 equiv.) was added and the mixture was stirred for another 36 h, giving the aimed product *N*-(phenylthio)benzamide (**3**) in 30% yield (entry 1). We supposed that the low yield was caused by the low loading of NaH. Therefore, the amount of NaH was increased to 2 and 3 equivalents, and the yields sharply increased to 52% and 96%, respectively (entries 2-3). When 4 equivalents of NaH were used, no obvious yield improvement was observed (entry 4). Subsequently, the loading of phenyl disulfide was screened. We found that *N*-(phenylthio)benzamide was obtained in lower yields

when we used 1.0 and 1.2 equivalents disulfide (entries 5-6). Besides, shortening the reaction times to 24 h (12 h) also led to lower yields (entries 7-8). If benzamide, diphenyl disulfide and NaH were added into the reaction system at the same time, only a 25% yield of *N*-(phenylthio)benzamides was isolated (entry 3). The results showed that the sulfenylation proceed *via* the base-deprotonation of benzamide to form the benzamide anion, which then reacted with diphenyl disulfide to give the target molecules. Thus, the optimal condition was finally identified as following: benzamide (1.0 equiv.) was initially treated with NaH (3 equiv.) in THF (3.0 mL) at room temperature for 1 h, then diphenyl disulfide (1.5 equiv.) was added and the mixture was stirred for another 36 h at room temperature.

With the optimal reaction conditions determined, the scope of disulfides was next investigated (Table 2). As expected, various aryl disulfides worked well under the reaction conditions. A range of functional groups, such as methyl, methoxy, fluoro, chloro, and nitro substituents were tolerated in this sulfenylation procedure. Generally, electron-withdrawing groups on the phenyl ring of disulfides were beneficial for the transformation, whereas electron-donating substituents decreased the efficiency (products **4-12**). For example, the disulfides with chloro, and nitro groups gave the *N*-acylsulfenamides in more than 79 % yields (products **8-12**), while disulfides bearing methyl and methoxy moieties generated the corresponding products in less than 60%

yields (products **4** and **5**). To our delight, treatment of the 1,2-di(pyridin-2-yl)disulfide and 1,2-di(thiophen-2-yl)disulfide with benzamide also afforded the sulfenamides **13** and **14** in 41% and 59 % yields, respectively.

Subsequently, a series of arylamides bearing different substituents on the phenyl groups were evaluated. The results disclosed that the reaction seemed to be insensitive to the electronic effects on the phenyl ring of the arylamides. For instance, both arylamides with electron-donating substituents (such as methyl and methoxyl groups) and those bearing electron-withdrawing groups (including fluoro, chloro and bromo) can furnish the desired products **15-19**, **22** in moderate to high yields. However, arylamides bearing strong electron-withdrawing groups, such as NO_2 and CF_3, reacted with diphenyl disulfide to give products **20** and **21** in lower yields of 40% and 37%, respectively. Gratifyingly, both α-naphthamide and 2-iodobenzamide can undergo the reaction, providing the corresponding *N*-acylsulfenamides **24** and **25** in 21% and 28% yields. It is noteworthy that the reaction conditions are compatible with aliphatic amides. Cyclohexanecarboxamide and butyramide, for instance, underwent the reaction with diphenyl disulfide to furnish the products **26**, **27** in 38 % and 42 % yields, respectively. Meanwhile, 4-methylbenzamide was also successfully reacted with bis(2-chlorophenyl), bis(3,5-dichlorophenyl) and bis(4-nitrophenyl) disulfide, to afford the compounds **28-29** in good yields.

The successful synthesis of *N*-acylsulfenamides encouraged us to extend their application as sulfur sources for other reactions. As we know, pyrroles[15] and benzofurans[16] are important classes of heterocyles with naturally occurrence and biological activities. There are different methods available in the literature for the synthesis of sulfenyl pyrroles[17] and 3-sulfenylbenzofurans.[18] Sulfenyl chlorides or thiols are commonly used as sulfenylating reagents. But we wished to use *N*-acylsulfenamides as new sulfenylating reagents for the synthesis of sulfenylpyrroles and 3-sulfenylbenzofurans. We found that 2-phenylthio-1*H*-pyrrole (**30**) was obtained in high yield under mild conditions when 2 mol% of $AlCl_3$ (Scheme 2, eq. 3) was used as catalyst. Moreover, the electrophilic cyclisation of 2-alkynylanisoles with *N*-(phenylthio)benzamide was accomplished well to give the target molecule **31** in 83% yield in the presence of 1.0 equivalent of $FeCl_3$ at low temperature (Scheme 2, eq. 4). The results demonstrated that *N*-acylsulfenamides can act as efficient and new sulfur sources to provide a series of sulfur-containing compounds.

CONCLUSION

In summary, we have developed an efficient and mild method for the synthesis of *N*-acylsulfenamides *via* sulfenylation of carboxamides with readily available disulfides under mild conditions. A series of *N*-acylsulfenamides with various groups can be obtained in moderate

to high yields. Moreover, *N*-acylsulfenamides could be used as new thiolating reagents to access to a variety of sulfur compounds, such as sulfenylpyrroles and 3-sulfenylbenzofurans.

EXPERIMENTAL

Materials and methods

Chemicals were either used as purchased or purified by standard techniques. NaH was used as 60% dispersion in mineral oil. NMR spectroscopy was performed on a Bruker Avance-500 spectrometer operating at 500 MHz (^{1}H NMR) and 125 MHz (^{13}C NMR) using $CDCl_3$ and Actone-D_6 as the solvent with tetramethylsilane (TMS) as an internal standard at room temperature. The high resolution mass spectrometer was Waters Micromass GCT Premier (ESI). Melting points were determined on a digital melting-point apparatus from Beijing TECH Instrument CO. LTD and are uncorrected. All reactions are performed under air atmosphere. Column chromatography was performed using EM Silica gel 60 (300-400 mesh).

Typical experimental procedure for NaH promoted sulfenylation of benzamides with disulfide

The benzamide (0.2 mmol), NaH (3 equiv.) and dry THF (3 mL) were added to a two necked flask in turn and stirred at room temperature for 1h. Then disulfide (1.5 equiv.) was added into the mixture and stirred for another 36 h at room temperature. During the whole reaction process, the system was kept turbid owing to the difficult solubility of NaH in THF.

Then the resulting mixture was filtered and washed with EtOAc to give the solvent, which was concentrated in vacuo and the residue was purified by flash column chromatography on a silica gel to give the desired product.

2-(Phenylthio)-1*H*-pyrrole. Pyrrole (0.4 mmol), *N*-(phenylthio)benzamide (0.2 mmol), $AlCl_3$ (2 mol%) and DMA (2 mL) were put in a two necked flask and stirred at 90 °C for 16 h and then cooled to room temperature. The solution was extracted with EtOAc (3 x 10 mL) and the combined organic extracts washed with brine (3 x 10 mL) before being dried over $MgSO_4$ and concentrated. The solvent was concentrated in vacuo and the residue was purified by flash column chromatography on a silica gel to give the desired product.

2-Phenyl-3-(phenylthio)benzofuran. 1-Methoxy-2-(phenylethynyl)benzene (0.2 mmol), *N*-(phenylthio)benzamide (1.2 equiv.), $FeCl_3$ (1.0 equiv.) and CH_2Cl_2 (3 mL) were put in a two necked flask in turn and stirred at 50 °C for 24 h, and then cooled to room temperature. The solvent was concentrated in vacuo and the residue was purified by flash column chromatography on silica gel to give the desired product.

***N*-(Phenylthio)benzamide (3)[13]**

***N*-(p-Tolylthio)benzamide (4)[13]**

***N*-[(4-Methoxyphenyl)thio]benzamide (5).** White solid, m. p. 104-106 °C. ^{1}H NMR ([D_6]acetone) δ 9.24 (s, 1H), 7.96 (d, J = 8.5 Hz, 2H), 7.59-7.55 (m, 1H), 7.50-7.46 (m, 4H), 6.93-6.90(m, 2H), 3.78 (s, 3H). ^{13}C NMR ([D_6]acetone) δ 169.1, 160.7, 134.9, 132.8, 131.5,

130.9, 129.4, 128.6, 115.4, 55.7; HRMS (ESI): calcd. for $C_{14}H_{14}NO_2S^+$ ($[M+H]^+$): 260.0740, found: 260.0744.

***N*-[(2-Fluorophenyl)thio]benzamide (6).** Yellow solid, m. p. 99-100 °C. ^{1}H NMR ([D_6]acetone) δ 9.23 (s, 1H), 8.04-8.03 (m, 2H), 8.03 (d, J = 1.5 Hz, 1H), 7.64-7.61 (m, 1H), 7.55-7.52 (m, 2H), 7.33-7.29 (m, 1H), 7.27-7.23 (m, 1H), 7.20-7.12 (m, 2H).^{13}C NMR ([D_6]acetone) δ 169.2, 158.6 (d, J = 240.0 Hz), 134.4, 133.2, 129.5, 128.8, 128.7 (d, J = 7.5 Hz), 127.7 (d, J = 16.3 Hz), 127.2 (d, J = 2.5 Hz), 125.8 (d, J=3.8 Hz), 116.2 (d, J=20.0 Hz); HRMS (ESI): calcd. for $C_{13}H_{11}FNOS^+$ ($[M+H]^+$): 248.0540, found: 248.0544.

***N*-[(3-Fluorophenyl)thio]benzamide (7).** White solid, m. p. 100-102 °C. ^{1}H NMR ([D_6]acetone) δ 9.39 (s,1H), 8.05-8.03 (m,2H), 7.65-7.61 (m, 1H), 7.55-7.52 (m, 2H), 7.40-7.35 (m, 1H), 7.12-7.10 (m, 1H), 7.05-7.03 (m, 1H), 6.95-6.91 (m, 1H). ^{13}C NMR ([D_6]acetone) δ 169.1, 164.0 (d, J = 245.0 Hz), 143.9 (d, J = 7.5 Hz), 134.4, 133.2, 131.6 (d, J = 8.8 Hz), 129.5, 128.8, 120.1 (d, J = 3.8 Hz), 113.4 (d, J = 21.3 Hz), 111.1 (d, J = 23.8 Hz); HRMS (ESI): calcd. for $C_{13}H_{11}FNOS^+$ ($[M+H]^+$): 248.0540, found: 248.0539.

***N*-[(4-Chlorophenyl)thio]benzamide (8)[13]**

***N*-[(2-Chlorophenyl)thio]benzamide (9).** White solid, m. p. 129-131 °C. ^{1}H NMR (CD_3Cl) δ 7.88 (d, J = 7.0 Hz, 2H), 7.60 (bs, 1H), 7.57-7.54 (m, 1H), 7.45-7.42 (m, 2H), 7.29-7.27 (m, 1H), 7.19-7.07 (m, 3H). ^{13}C NMR ([D_6]acetone). δ 169.1, 137.3, 133.0, 132.8, 129.7, 129.2,

129.0, 127.8, 127.4, 127.2, 124.8; HRMS (ESI): calcd. for $C_{13}H_{11}ClNOS^+$ ($[M+H]^+$): 264.0244, found: 264.0253.

***N*-[(3-Chlorophenyl)thio]benzamide (10).** White solid, m. p. 130-131 °C. ^{1}H NMR ([D$_6$]acetone) δ 9.29 (s, 1H), 8.08-8.06 (m, 2H), 7.66-7.63 (m, 1H), 7.56-7.53 (m, 2H), 7.40-7.38 (m, 1H), 7.32-7.29 (m, 1H), 7.20-7.16 (m, 2H). ^{13}C NMR ([D$_6$]acetone) δ 169.1, 139.3, 134.3, 133.1, 130.2, 129.5, 128.8, 128.4, 127.9, 127.3, 124.4; HRMS (ESI): calcd. for $C_{13}H_{11}ClNOS^+$ ($[M+H]^+$): 264.0244, found: 264.0253.

***N*-[(3,5-Dichlorophenyl)thio]benzamide (11).** White solid, m. p. 129-131 °C. ^{1}H NMR ([D$_6$]acetone) δ 9.44(s, 1H), 8.06-8.05 (m, 2H), 7.66-7.63 (m, 1H), 7.56-7.53 (m, 2H), 7.26-7.25 (m, 3H). ^{13}C NMR ([D$_6$]acetone). δ 169.0, 145.6, 136.1, 134.0, 133.4, 129.6, 128.9, 126.3, 122.3; HRMS (ESI): calcd. for $C_{13}H_{10}Cl_2NOS^+$ ($[M+H]^+$): 297.9855, found: 297.9869.

***N*-[(4-Nitrophenyl)thio]benzamide (12).**[13] Yellow solid, m. p. 144-146 °C. ^{1}H NMR ([D$_6$]acetone) δ 8.15 (d, J = 9.0 Hz, 2H), 7.91 (d, J = 7.5 Hz, 2H), 7.64-7.61 (m, 1H), 7.53-7.50 (m, 3H), 7.30 (d, J = 9.0 Hz, 2H). ^{13}C NMR ([D$_6$]acetone) δ 168.7, 148.3, 146.1, 133.3, 132.5, 129.2, 127.9, 124.4, 123.0; HRMS (ESI): calcd. for $C_{13}H_{11}N_2O_3S^+$ ($[M+H]^+$): 275.0485, found: 275.0502.

***N*-(Pyridin-2-ylthio)benzamide (13).** Yellow solid, m. p. 67-69 °C. ^{1}H NMR ([D$_6$]acetone) δ 9.34 (s, 1H), 8.41-8.39 (m, 1H), 8.08-8.06 (m, 2H), 7.71-7.68 (m, 1H), 7.67-7.62 (m, 1H), 7.57-7.53 (m, 2H), 7.23-7.21 (m, 1H) 7.12-7.09 (m, 1H). ^{13}C NMR ([D$_6$]acetone) δ 169.0, 163.1,

150.1 137.8, 134.6, 133.1, 129.5, 128.8, 120.9, 117.8; HRMS (ESI): calcd. for $C_{12}H_{11}N_2OS^+$ ($[M+H]^+$): 231.0587, found: 231.0592.

***N*-(Thiophen-2-ylthio)benzamide (14).** White solid, m.p. 168-169 °C. ^{1}H NMR ([D$_6$]acetone) δ 9.31 (s, 1H), 7.10 (d, J = 7.0 Hz, 2H), 7.66-7.65 (m, 1H), 7.57-7.54 (m, 1H), 7.48-7.45 (m, 2H), 7.44-7.43 (m, 1H), 7.06-7.04 (m, 1H). ^{13}C NMR ([D$_6$]acetone) δ 168.7, 137.9, 136.3, 134.7, 133.2, 132.9, 129.4, 128.6, 128.2; HRMS (ESI): calcd. for $C_{11}H_{10}NOS_2^+$ ($[M+H]^+$): 236.0198, found: 236.0199.

4-Methyl-*N*-(phenylthio)benzamide (15). White solid, m. p. 140-142 °C. ^{1}H NMR ([D$_6$]acetone) δ 9.22 (s, 1H), 7.93 (d, J = 8.5 Hz, 2H), 7.33-7.28 (m, 6H), 7.19-7.16 (m, 1H), 2.40 (s, 3H). ^{13}C NMR ([D$_6$]acetone) δ 169.0, 143.6, 141.0, 131.8, 130.0, 129.8, 128.8, 126.9, 124.9, 21.4; HRMS (ESI): calcd. for $C_{14}H_{14}NOS^+$ ($[M+H]^+$): 244.0791, found: 244.0799.

4-Methoxy-*N*-(phenylthio)benzamide (16). White solid, m. p. 131-133 °C. ^{1}H NMR ([D$_6$]acetone) δ 9.15 (s, 1H), 8.03-8.01 (m, 2H), 7.33-7.30 (m, 2H), 7.28-7.27 (m, 2H), 7.19-7.15 (m, 1H), 7.05-7.03 (m, 2H), 3.88 (s, 3H). ^{13}C NMR ([D$_6$]acetone) δ 168.4, 163.9, 141.2, 130.8, 129.8, 126.8, 126.7, 124.9, 114.7, 55.9; HRMS (ESI): calcd. for $C_{14}H_{14}NO_2S^+$ ($[M+H]^+$): 260.0740, found: 260.0745.

4-Fluoro-*N*-(phenylthio)benzamide (17). Yellow solid, m. p. 124-126 °C.^{1}H NMR ([D$_6$]acetone) δ 9.33 (s, 1H), 8.12-8.10 (m, 2H), 7.35-7.27 (m, 6H), 7.21-7.17 (m, 1H). ^{13}C NMR ([D$_6$]acetone) δ 168.1, 166.0 (d, J = 248.8 Hz), 140.7, 131.5(d, J = 8.8 Hz), 131.0 (d, J = 2.5 Hz)

129.8, 127.0, 125.2, 116.4 (d, J = 21.3 Hz); HRMS (ESI): calcd. for $C_{13}H_{11}FNOS^+$ ($[M+H]^+$): 248.0540, found: 248.0542.

4-Chloro-*N*-(phenylthio)benzamide (18). White solid, m. p. 159-161 °C. ^{1}H NMR ([D$_6$]acetone) δ 9.38 (s, 1H), 8.03 (d, J = 8.5 Hz, 2H), 7.57-7.55 (m, 2H), 7.34-7.30 (m, 4H), 7.21-7.38 (m, 1H). ^{13}C NMR ([D$_6$]acetone) δ 168.2, 140.6, 138.9, 133.3, 130.6, 129.9, 129.6, 127.1, 125.3; HRMS (ESI): calcd. for $C_{13}H_{11}ClNOS^+$ ($[M+H]^+$): 264.0244, found: 264.0253.

4-Bromo-*N*-(phenylthio)benzamide (19). Yellow solid, m. p. 163-164 °C. ^{1}H NMR ([D$_6$]acetone) δ 9.39 (s, 1H), 7.96 (d, J = 8.5 Hz, 2H), 7.72-7.71 (m, 2H), 7.35-7.30 (m, 4H), 7.21-7.17 (m, 1H). ^{13}C NMR ([D$_6$]acetone) δ 168.3, 140.5, 133.7, 132.6, 130.7, 129.8, 127.2, 127.1, 125.2; HRMS (ESI): calcd. for $C_{13}H_{11}BrNOS^+$ ($[M+H]^+$): 307.9739, found: 307.9754.

4-Nitro-*N*-(phenylthio)benzamide (20). Yellow solid, m. p. 146-147 °C. ^{1}H NMR ([D$_6$]acetone) δ 9.63 (s, 1H), 8.37 (d, J = 8.5 Hz, 2H), 8.25 (d, J = 8.0 Hz, 2H), 7.36-7.35 (m, 4H), 7.23-7.20 (m, 1H). ^{13}C NMR ([D$_6$]acetone) δ 167.9, 151.0, 140.2, 140.1, 130.2, 129.9, 127.4, 125.6, 124.6; HRMS (ESI): calcd. for $C_{13}H_{11}N_2O_3S^+$ ($[M+H]^+$): 275.0485, found: 275.0502.

***N*-(Phenylthio)-4-(trifluoromethyl)benzamide (21).** Yellow solid, m. p. 175-176 °C. ^{1}H NMR ([D$_6$]acetone) δ 9.55 (s, 1H), 8.22 (d, J = 8.0 Hz, 2H), 7.88 (d, J=8.0 Hz, 2H), 7.35-7.34 (m, 4H), 7.22-7.19 (m, 1H). ^{13}C NMR ([D$_6$]acetone) δ 168.3, 140.3, 138.3, 133.8 (q, J = 32.5

Hz), 129.9, 129.6, 127.2, 126.5 (q, *J*= 3.8 Hz), 127.1 (q, *J* = 270 Hz), 125.4; HRMS (ESI): calcd. for $C_{14}H_{11}F_3NOS^+$ ($[M+H]^+$): 298.0508, found: 298.0510.

3,5-Difluoro-*N*-(phenylthio)benzamide (22). White solid, m. p. 106-107 °C. ^{1}H NMR ([D_6]acetone) δ 9.45 (s, 1H), 7.65 (d, *J* = 8.5 Hz, 2H), 7.34-7.33 (m, 4H), 7.31-7.29 (m, 1H), 7.23-7.19 (m, 1H). ^{13}C NMR ([D_6]acetone) δ 167.0, 163.8 (dd, *J* = 246.3, 11.3 Hz), 140.1, 138.0(t, *J* = 8.4 Hz), 129.9, 127.3, 125.6, 112.1 (dd, *J* = 20.0, 6.3 Hz), 108.2 (t, *J* = 25.0 Hz); HRMS (ESI): calcd. for $C_{13}H_{10}F_2NOS^+$ ($[M+H]^+$): 266.0446, found: 266.0453.

2-Chloro-6-nitro-*N*-(phenylthio)benzamide (23). Yellow solid, m. p. 169-170 °C. ^{1}H NMR $(CD_3)_2SO$) δ 10.42 (s, 1H), 8.24 (d, *J* = 9.0 Hz, 1H), 8.05-8.03 (m, 1H), 7.79-7.76 (m, 1H), 7.44-7.38 (m, 4H), 7.27-7.23 (m, 1H). ^{13}C NMR [$(CD_3)_2SO$] δ 169.9, 165.5, 146.4, 138.4, 135.8, 131.9, 131.7, 128.9, 126.5, 124.8, 123.6; HRMS: calcd. for $C_{13}H_{10}ClN_2O_3S^+$ ($[M+H]^+$): 309.0095, found: 309.0103.

***N*-(Phenylthio)-1-naphthamide (24).** White solid, m. p. 121-123 °C. ^{1}H NMR ($CDCl_3$) δ 8.29 (s, 1H), 7.97 (d, *J* = 8.0 Hz, 1H), 7.89-7.88 (m, 1H), 7.70-7.69 (m, 1H), 7.58-7.53 (m, 3H), 7.49-7.45 (m, 3H), 7.37-7.34 (m, 2H), 7.24-7.23 (m, 1H). ^{13}C NMR ($CDCl_3$) δ 170.7, 138.5, 133.7, 131.7, 130.1, 129.6, 129.2, 128.4, 127.6, 127.3, 126.7, 126.2, 125.5, 125.2, 124.6; HRMS (ESI): calcd. for $C_{17}H_{14}NOS^+$ ($[M+H]^+$): 280.0791, found: 280.0792.

2-Iodo-*N*-(phenylthio)benzamide (25). White solid, m. p. 127-129 °C. ^{1}H NMR ([D_6]acetone) δ 9.12 (s, 1H), 7.96 (d, *J* = 8.0 Hz, 1H), 7.53-7.46 (m, 4H), 7.38 (t, *J* = 8.0 Hz, 2H),

7.26-7.22 (m, 2H). ^{13}C NMR ([D$_6$]acetone) δ 171.3, 143.0, 140.8, 140.3, 132.3, 129.8, 129.2, 129.1, 127.3, 125.8, 92.9; HRMS (ESI): calcd. for $C_{13}H_{11}INOS^+$ ([M+H]$^+$): 355.9601, found: 355.9616.

***N*-(Phenylthio)cyclohexanecarboxamide (26).** White solid, m. p. 119-121 °C. ^{1}H NMR ($CDCl_3$) δ 7.81 (s, 1H), 7.21 (t, J = 7.5 Hz, 2H), 7.14-7.09 (m, 3H), 2.35-2.30 (m, 1H), 1.82-1.79 (m, 2H), 1.70-1.68 (m, 2H), 1.60-1.59 (m, 1H), 1.47-1.40 (m, 2H), 1.21-1.11 (m, 3H). ^{13}C NMR ($CDCl_3$) δ 178.7, 139.3, 128.8, 126.2, 124.6, 45.5, 29.7, 25.6, 25.5; HRMS (ESI): calcd. for $C_{13}H_{18}NOS^+$ ([M+H]$^+$): 236.1104, found: 236.1101.

***N*-(Phenylthio)butyramide (27).** White solid, m. p. 50-52 °C. ^{1}H NMR ($CDCl_3$) δ 8.05 (s, 1H), 7.22-7.19 (m, 2H), 7.15-7.14 (m, 2H), 7.12-7.09 (m, 1H), 2.27 (t, J = 7.5 Hz, 2H), 1.64-1.58 (m, 2H), 0.85 (t, J = 7.5 Hz, 3H). ^{13}C NMR ($CDCl_3$) δ 176.0, 139.1, 128.8, 126.3, 124.8, 38.3, 19.1, 13.6; HRMS (ESI): calcd. for $C_{10}H_{14}NOS^+$ ([M+H]$^+$): 196.0791, found: 196.0781.

***N*-[(3,5-Dichlorophenyl)thio]-4-methylbenzamide (28).** Yellow solid, m. p. 118-120 °C. ^{1}H NMR ([D$_6$]acetone) δ 9.40 (s, 1H), 7.95 (d, J = 8.0 Hz, 2H), 7.34 (d, J = 8.0 Hz, 2H), 7.24 (t, J = 2.0 Hz, 1H), 7.22 (d, J = 2.0 Hz, 2H), 2.41 (s, 3H). ^{13}C NMR ([D$_6$]acetone) δ 168.9, 145.8, 144.0, 136.1, 131.2, 130.2, 128.9, 126.2, 122.2, 21.5; HRMS (ESI): calcd. for $C_{14}H_{12}Cl_2NOS^+$ ([M+H]$^+$): 312.0011, found: 312.0023.

4-Methyl-*N*-[(4-nitrophenyl)thio]benzamide (29). Yellow solid, m. p. 145-147 °C. ^{1}H NMR ([D$_6$]acetone) δ 9.45 (s, 1H), 8.18 (d, J = 9.0 Hz, 2H), 7.97 (d, J = 8.0 Hz, 2H), 7.45 (d, J =

9.0 Hz, 2H), 7.36 (d, J = 8.0 Hz, 2H), 2.42 (s, 3H). ^{13}C NMR ([D$_6$]acetone) δ 168.9, 150.9, 146.5, 144.1, 131.2, 130.2, 129.0, 124.9, 123.4, 21.5; HRMS (ESI): calcd. for $C_{14}H_{13}N_2O_3S^+$ ($[M+H]^+$): 289.0641, found: 289.0648.

2-(Phenylthio)-1*H*-pyrrole (30).[17c]

2-Phenyl-3-(phenylthio)benzofuran (31).[18a]

ACKNOWLEDGMENTS

The authors thank the National Natural Science Foundation of China (No. 21302144 and No. 21272177).

SUPPLEMENTARY DATA

Supplementary data associated with this article can be found online.

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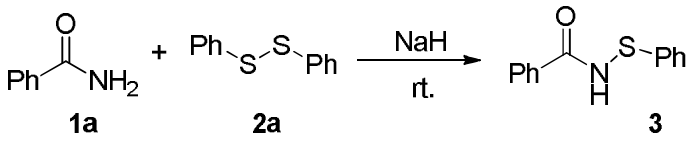
Table 1 Optimization of the reaction conditions [a]

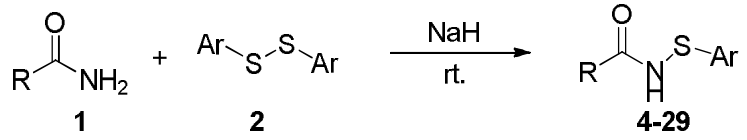


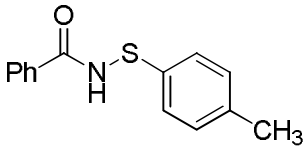
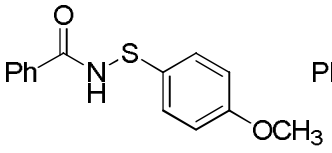
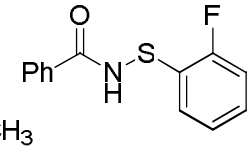
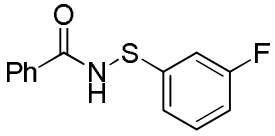
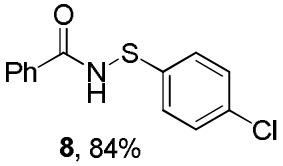
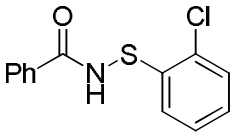
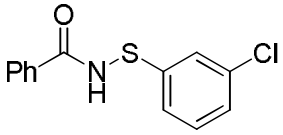
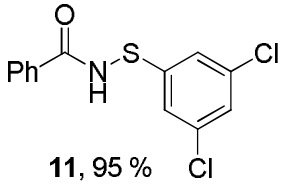
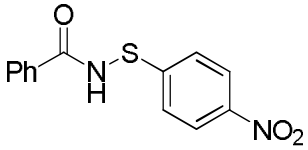
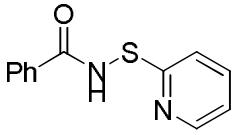
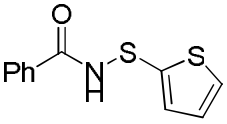
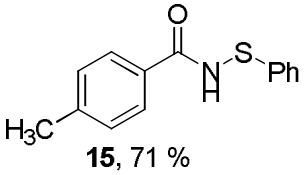
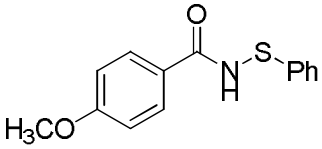
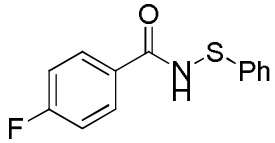
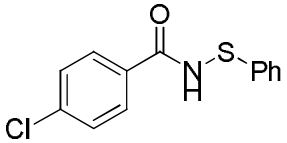
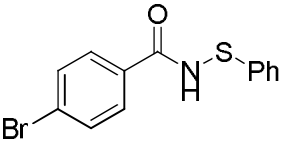
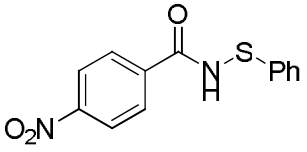
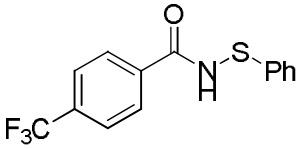
1a **2a** **3**

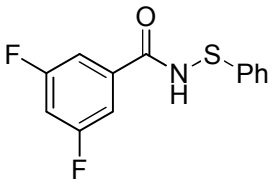
Entry	NaH (eq)	Disulfide (eq)	Time (h)	Yield (%)[b]
1	1	1.5	36	30
2	2	1.5	36	52
3	3	1.5	36	95, 25[c]
4	4	1.5	36	96
5	3	1.0	36	80
6	3	1.2	36	85
7	3	1.5	24	84
8	3	1.5	12	72

[a] the mixture of benzamide **1a** (0.2 mmol) and NaH was stirred in THF (3 mL) for 1 h, then diphenyl disulfide **2a** was added and stirred for another indicated time at room temperature. [b] isolated yield. [c] benzamide, phenyl disulfide and NaH were added into the reaction system at the same time.

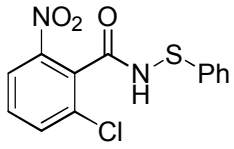
Table 2. The synthesis of N-acyl sulfenamides from the reaction of benzamides with disulfides [a, b]



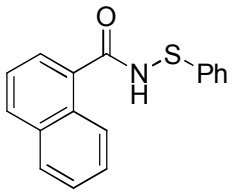
 **4**, 60%	 **5**, 32%	 **6**, 43 %
 **7**, 42%	 **8**, 84%	 **9**, 82%
 **10**, 94 %	 **11**, 95 %	 **12**, 79 %
 **13**, 41%	 **14**, 59%	 **15**, 71 %
 **16**, 55 %	 **17**, 52 %	 **18**, 67 %
 **19**, 96 %	 **20**, 40 %	 **21**, 37 %



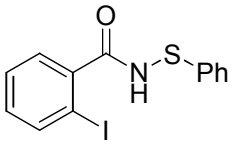
22, 63 %



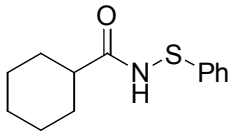
23, 72 %



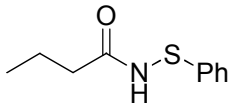
24, 21 %



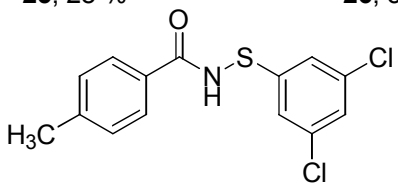
25, 28 %



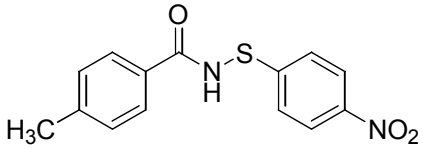
26, 38 **%**



27, 42 %

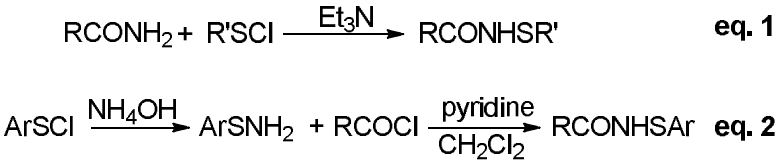


28, 93 %

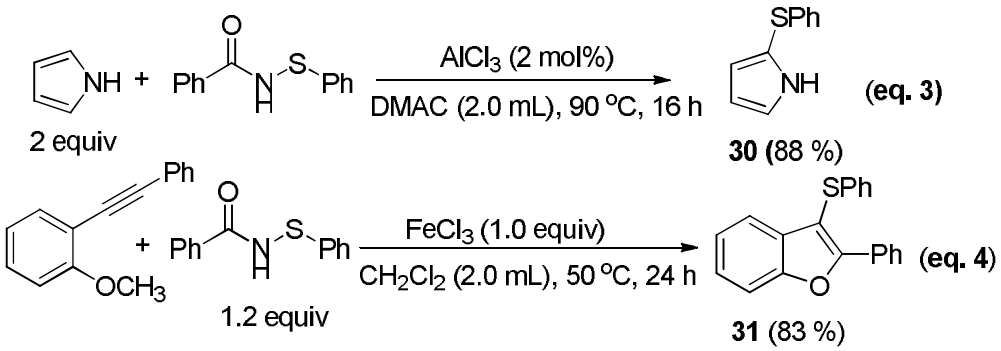


29, 79 %

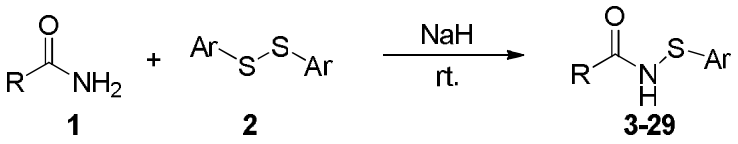
[a] the mixture of amide **1** (0.2 mmol), NaH (3 equiv.) was stirred in THF (3 mL) for 1 h, then disulfide **2** (1.5 equiv.) was added and stirred for another 36 h at room temperature. [b] isolated yield.



Scheme 1 The common processes for the synthesis of *N*-acylsulfenamides



Scheme 2 The application of *N*-(phenylthio)benzamide as new thiolation reagent



1 **2** **3-29**