Tetrahedron 68 (2012) 10201–10208

Contents lists available at SciVerse ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

One-pot sequential combination of multi-component and multi-catalyst: synthesis of 5-aminobenzofurans from aminophenol and ketene acetals

Cheng-Wen Yang [a], Yue-Xia Bai [a], Ni-Tao Zhang [a], Cheng-Chu Zeng [a,*], Li-Ming Hu [a], Hong-Yu Tian [b]

[a] College of Life Science & Bioengineering, Beijing University of Technology, Beijing 100124, China
[b] School of Food Chemistry, Beijing Technology and Business University, Beijing 100048, China

ARTICLE INFO

Article history:
Received 22 June 2012
Received in revised form 18 September 2012
Accepted 21 September 2012
Available online 26 September 2012

Keywords:
Multi-catalyst
Oxidation
Cyclization
5-Aminobenzofurans
Alkene acetals

ABSTRACT

The reaction between *p*-aminophenols **1** and various ketene acetals **2** in the presence of hypervalent iodine is described. The results show that 2- and 3-substituted 5-sulfonamidobenzofurans **3** are obtained in moderate to good yields from *p*-aminophenols and ketene acetals.

1. Introduction

Natural and synthetic benzofurans are of great interest due to their various biological activities.[1] Moreover, they are used as electroluminescent materials, liquid crystals, and organic dyes in material chemistry.[2] As a consequence, newer and more efficient procedures are desirable for the syntheses of these compounds.

Structurally, benzofurans can be constructed either through [4+2] cycloaddition of furan derivatives and dienophiles[3] or starting from benzene derivatives.[4] The Michael addition and subsequent cyclization of benzoquinone with active methylene derivatives may provide an alternative approach for the synthesis of benzofurans.[5] Engler and co-workers elegantly explored the Lewis acid-promoted reaction of 2-alkoxy-1,4-benzoquinones,[6] quinone-1,4-diimine,[7] and quinone monoimine derivatives[8] with styrenyl systems yielding primarily either 2-aryl-2,3-dihydrobenzofuran or -dihydroindole products. Recently, Liu and co-workers reported that the Michael addition and cyclization of ketene dithioacetals and 1,4-benzoquinones activated by $CuBr_2$ and $BF_3{\cdot}OEt_2$ gave 5-hydroxybenzofurans.[9] On the other hand, others and we have demonstrated that the electrochemical oxidation of catechols in the presence of polarized alkenes can generate polyhydroxylated benzofurans or indoles in a sequence of reactions beginning with anodic oxidation followed by an intermolecular Michael reaction, a second anodic oxidation and an intramolecular Michael reaction.[10]

Based on the above understanding, we hypothesize that the in situ oxidation of 4-aminophenol derivatives using hypervalent iodine[11] ought to generate quinone monoimine **1**–**O**. When this type of reactive intermediate is treated with a polarized alkene in the presence of dual catalysis, 5-aminobenzofurans may be produced (Fig. 1). In the present work, we describe the efficient synthesis of highly functionalized 5-aminobenzofurans from simple starting material under mild conditions in a two-step, one-pot process.

2. Results and discussion

2.1. Synthesis of starting ketene *S,S*-acetals and *N,S*-acetals

α-Benzoyl ketene *S,S*-acetals **2a**–**d** (see Table 2) were prepared from acetophenone and methanedithione[12]; α-acetyl-, α-amino-carbonyl-, α-nitro-, and α-cyano-ketene *S,S*-acetals (**2e**–**h**; Table 2) were prepared according to known procedures.[13]

For the synthesis of *N,S*-acetals (**2i**–**q**), we note that a literature indicated that a mixture of *S,N*- and *N,N*-ketals, which were difficult to separate, was always afforded. Therefore, *n*-BuLi was used to generate exclusively the mono-substituted *N,S*-acetals.[14] However, after extensive optimization of the experimental conditions, we were delightedly to find that the desired *N,S*-acetal could be selectively obtained by refluxing equivalent amounts of the

* Corresponding author. Fax: +86 10 67392001; e-mail address: zengcc@bjut.edu.cn (C.-C. Zeng).

0040-4020/$ – see front matter © 2012 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.tet.2012.09.090

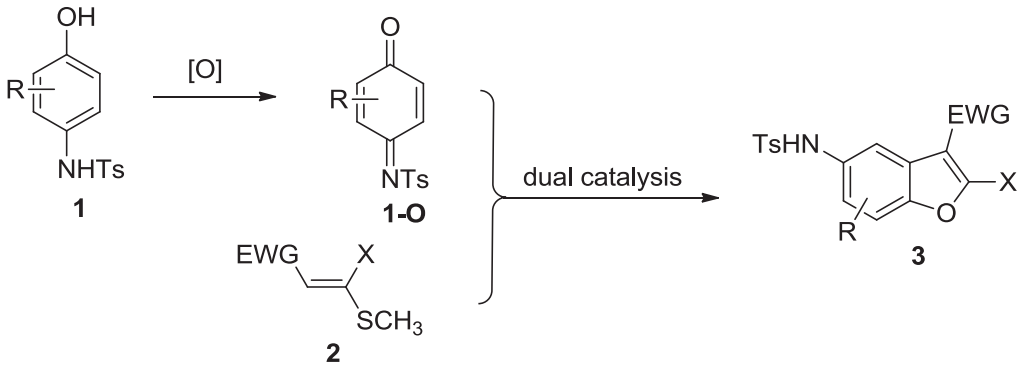
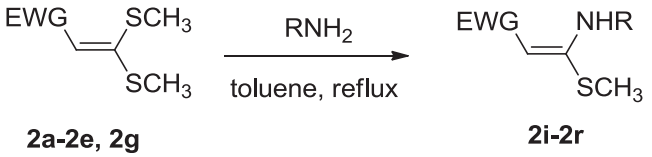


Fig. 1. A two-step, one-pot approach for the synthesis of 5-aminobenzofurans **3**.

S,*S*-acetals and the desired amines in toluene for 16 h (45–70% yields; note Scheme 1).



Scheme 1. The synthesis of *N*,*S*-acetals **2i**–**q**.

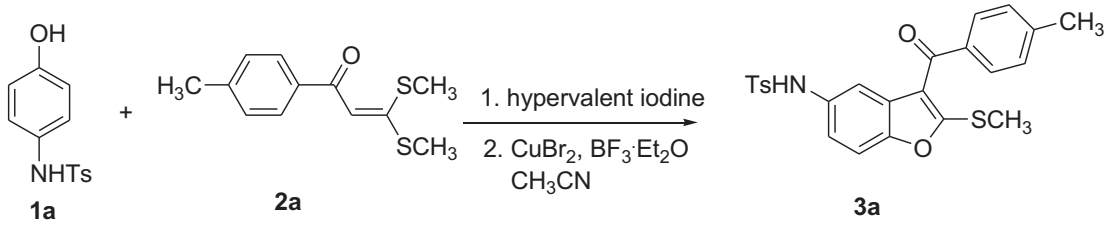
2.2. Synthesis of benzofurans

Our evaluation of the possibility of achieving a one-pot, two-step synthesis of benzofurans from aminophenol derivatives and acetals commenced by using the sulfonamide-protected aminophenol **1a** and *para*-methylbenzoyl *S*,*S*-acetal **2a** as model compounds (Scheme 2). In a first experiment, the reaction of **1a** with **2a** was allowed to proceed at room temperature in the presence of 1 equiv of $PhI(OCOCF_3)_2$ as oxidant and the dual catalysts ($BF_3\cdot Et_2O$ and $CuBr_2$). This led to the desired benzofuran **3a** in only 11% yield (Table 1, entry 1). The use of longer reaction times (from 12 to 48 h) did not lead to an increase in yield. However, under the same conditions, the yield of **3a** increased to 24% when $PhI(OAc)_2$ was used as the oxidant (Table 1, entry 2).

Since the starting material, **1a**, was not fully consumed, we reasoned that these low yields might have arisen because an insufficient amount of oxidant was used. In accord with this idea, the use of 1.5 equiv of $PhI(OAc)_2$ showed that the starting material was consumed in 1.5 h and the yield of **3a** increased to 48% (Table 1, entry 3); the use of 2 equiv of oxidant resulted in a decrease to 36% in yield (Table 1, entry 4).

Since the formation of the benzofuran framework is believed to occur via a two-step, one-pot sequence, we reasoned that the order of addition of the reagents should play an important role in the success of the process. To test this idea, **1a** and the oxidant, $PhI(OAc)_2$, were first mixed at room temperature, followed by the addition of **2a** and co-catalysts under the conditions reported above[9] 10 min later. This change significantly improved the reaction outcomes and 61% of **3a** was isolated (entry 5). On the basis of these results, the optimized condition was found to use a 1.0:1.5:1.0 ratio of **1a** to $PhI(OAc)_2$ to **2a**, with 2.0 mol % of $CuBr_2$ and 10 mol % of $BF_3\cdot Et_2O$ as catalysts (in 4.0 mL MeCN)[9] and at room temperature; the preferred order of addition proved to be aminophenol **1a** and $PhI(OAc)_2$, followed by the addition of ketene acetals **2**, $BF_3\cdot Et_2O$ and $CuBr_2$ 10 min later.

Then, the scope of this two-step, one-pot benzofuran synthesis was investigated under the optimized conditions. As shown in Table 2, the α-methoxybenzoyl ketene *S*,*S*-acetal **2b** afforded adduct **3b** in 65% yield (entry 2). Similarly, **3c** and **3d** were generated in 52% and 49% yields, respectively, from α-benzoyl ketene *S*,*S*-acetal **2c** and **2d**,



Scheme 2. The synthesis of **3a** from sulfonamide-protected aminophenol **1a** and *p*-methylbenzoyl *S*,*S*-acetal **2a**.

Table 1
Optimization of conditions for the synthesis of **3a** from sulfonamide-protected aminophenol **1a** and *p*-methylbenzoyl *S*,*S*-acetal **2a**

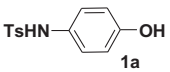
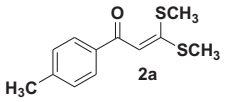
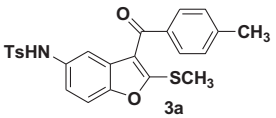
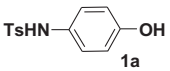
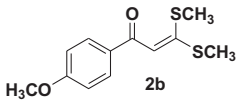
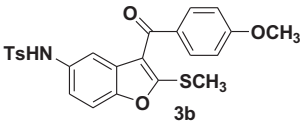
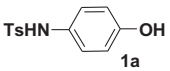
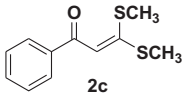
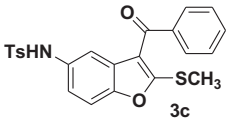
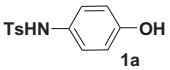
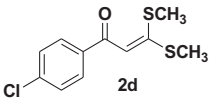
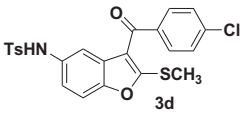
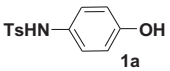
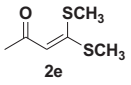
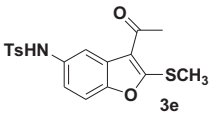
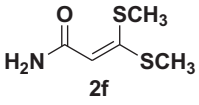
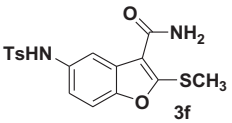
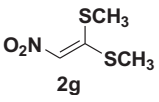
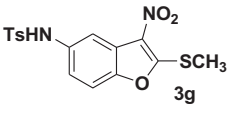
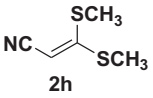
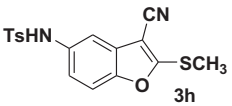
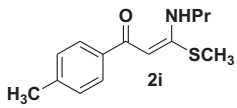
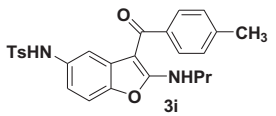
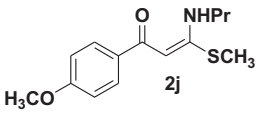
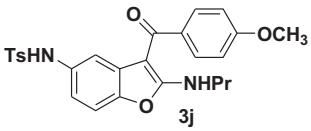
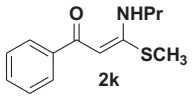
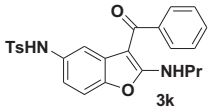
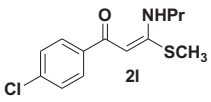
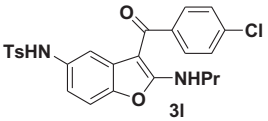
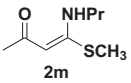
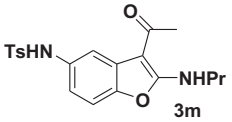
Entry	Oxidant	Ratio of oxidant	Addition sequence	Time (h)	Yield (%)
1	$PhI(OCOCF_3)_2$	1.0 equiv	Method a	12	11
2	$PhI(OAc)_2$	1.0 equiv	Method a	12	24
3	$PhI(OAc)_2$	1.5 equiv	Method a	1.5	48
4	$PhI(OAc)_2$	2.0 equiv	Method a	1.5	36
5	$PhI(OAc)_2$	1.5 equiv	Method b	1.5	61

Method a: **1a**, **2a** and oxidant were firstly added followed by the addition of catalysts $BF_3\cdot Et_2O$ and $CuBr_2$ 10 min later.
Method b: **1a** and oxidant were firstly added followed by the addition of **2a**, $BF_3\cdot Et_2O$, and $CuBr_2$ 10 min later.

although in a bit lower yields (entries 3 and 4). To investigate the influence of the electron-withdrawing group (EWG) on the reaction yield, acetyl-, aminocarbonyl-, nitro-, and cyano-substituted ketene *S*,*S*-acetals **2e**– **h** were also synthesized and allowed to react with **1a** under the same conditions; it was observed that the stronger of the electron-withdrawing properties of the EWG, the higher of the yields. For example, when the EWG are acetyl- or aminocarbonyl-, **2e** and **2f** gave 42% and 35% of corresponding benzofurans **3e** and **3f** (entries 5–6). However, the yields of the corresponding benzofurans **3g** and **3h** increased to 61% and 63% yields, respectively, when the EWG is replaced by nitro or cyano groups, (entries 7–8).

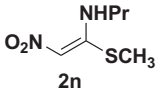
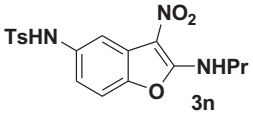
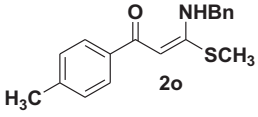
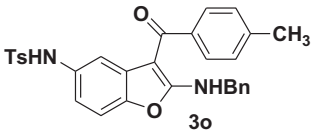
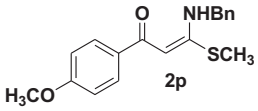
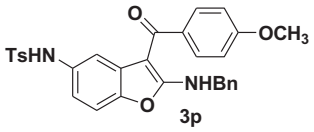
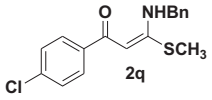
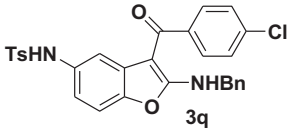
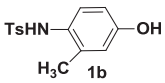
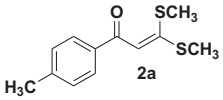
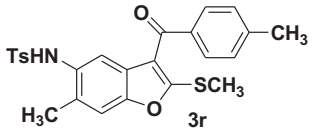
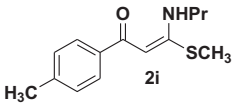
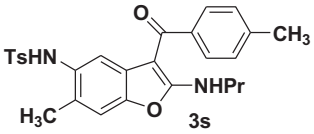
Subsequently, the ketene *N*,*S*-acetals were subjected to reaction with **1a** in the presence of $PhI(OAc)_2$ as oxidant. As shown in Table 2

Table 2
Yields of benzofurans **3**

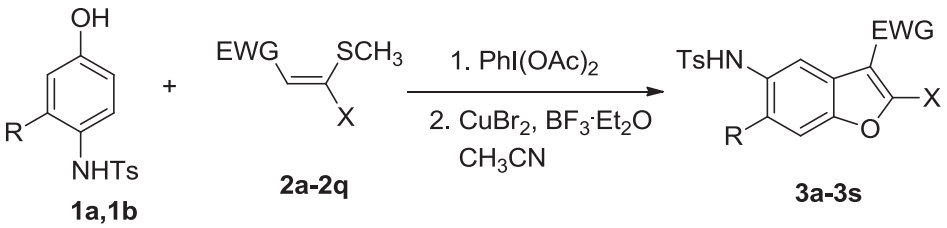
Entry	1	Ketene acetal	Product	Yield (%)
1	 1a	 2a	 3a	61
2	 1a	 2b	 3b	65
3	 1a	 2c	 3c	52
4	 1a	 2d	 3d	49
5	 1a	 2e	 3e	42
6	1a	 2f	 3f	35
7	1a	 2g	 3g	61
8	1a	 2h	 3h	63
9	1a	 2i	 3i	55
10	1a	 2j	 3j	72
11	1a	 2k	 3k	54
12	1a	 2l	 3l	49
13	1a	 2m	 3m	58

(*continued on next page*)

Table 2 (*continued*)

Entry	1	Ketene acetal	Product	Yield (%)
14	**1a**	 **2n**	 **3n**	47
15	**1a**	 **2o**	 **3o**	73
16	**1a**	 **2p**	 **3p**	76
17	**1a**	 **2q**	 **3q**	64
18	 **1b**	 **2a**	 **3r**	69
19	**1b**	 **2i**	 **3s**	64

and Scheme 3, the reaction of ketene *N*,*S*-acetals **2i**–**n**, wherein one $-SCH_3$ group was substituted by NHPr, and **1a** under the same conditions afforded moderate to good yields of corresponding benzofurans **3i**–**n**. In addition, benzylamino-substituted ketene *N*,*S*-acetals **2o**–**q** also generated benzofurans **3o**–**q** in good yield (64–76%). monoimine through binding to the imide and forms the dihydrofuran; whereas a dihydroindole is the main product using excess amounts of Ti(IV) as the promoter due to its binding to the C-1 carbonyl group of 4-(*N*-benzenesulfonyl)monoimine. Together with the structural identification of the products in the present

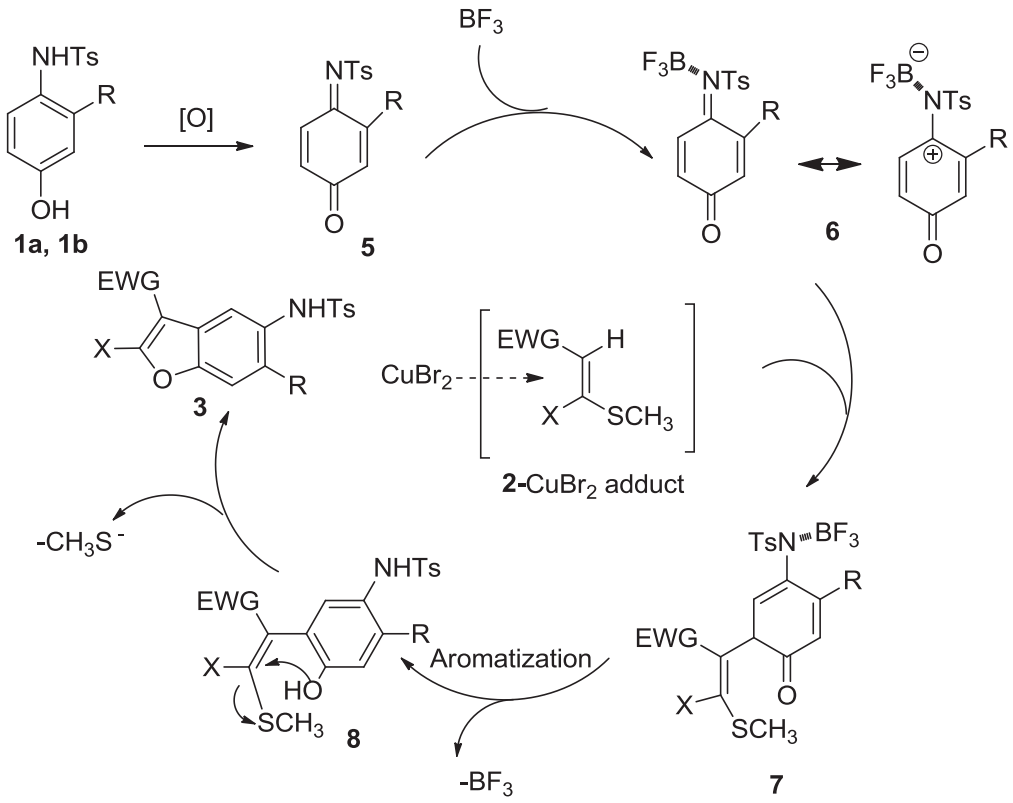


Scheme 3. Synthesis of benzofurans **3a**–**s**.

Finally, methyl-substituted aminophenol **1b** was investigated. As shown in Table 2, benzofurans **3r** and **3s** were obtained in 69% and 64% yield, respectively.

2.3. Reaction mechanism

For the Lewis acid promoted reaction of 4-(*N*-benzenesulfonyl) quinone monoimine derivatives and styrenes, the nature of the Lewis acid promoter determines the regioselectivity, leading to the formation of dihydrofuran or dihydroindoles.[6b,8a] When $BF_3 \cdot OEt_2$ is used as the Lewis acid, it activates the 4-(*N*-benzenesulfonyl) work, we can propose an oxidation and [3+2] cycloaddition sequence for the construction of benzofurans **3**. As illustrated in Scheme 4, the oxidation of *N*-(4-hydroxyphenyl)-benzenesulfonamide **1a** and **1b** gives quinone monoimine **5**, which is coordinated by BF_3 to the benzenesulfonyl nitrogen atom to produce intermediate **6**. On the other hand, the ketene acetals **2** are activated by $CuBr_2$ to form **2**-$CuBr_2$ adduct. The Michael addition of $CuBr_2$-activated ketene acetals **2** to **6** at its *ortho*-position of the carbonyl group, followed by aromatization, generates intermediate **8**. Finally, the intramolecular nucleophilic vinylic substitution (S_NV) reaction produce benzofurans **3**.[9,15]



Scheme 4. A proposed reaction mechanism for the formation of benzofurans from *p*-tosylaminophenol and ketene acetals.

3. Conclusion

In summary, we have developed a one-pot, two-step sequence involving the combination of a multi-component and multi-catalysis strategy for the synthesis of 5-aminobenzofurans from aminophenols and ketene acetals. The reaction is initiated from the oxidation of aminophenol by hypervalent iodine to form a quinone monoimine. The intermediate is activated in situ by BF_3 at the benzenesulfonyl nitrogen atom to induce a regioselective Michael addition with ketene acetals activated by $CuBr_2$. Following intramolecular S_NV reaction, 5-aminobenzofurans are formed in moderate to good yields. This method provides an environmentally benign access to 5-aminobenzofurans with several active functional groups for further derivatization under mild reaction conditions.

4. Experimental

4.1. General

All melting points (mp) were measured with an XT4A Electrothermal apparatus equipped with a microscope and are uncorrected. Infrared spectra (IR) were recorded as thin films on KBr plates on a Bruker IR spectrophotometer and are expressed in ν (cm^{-1}). ^1H and ^{13}C NMR spectra were recorded on an AV 400 M Bruker spectrometer (400 MHz for ^1H frequency, 100 MHz for ^{13}C frequency) in solvent ($CDCl_3$ or DMSO-d_6) with TMS as an internal reference. MS data (ESI) were recorded on a Bruker esquire 6000 mass spectrometer. HR-MS (TOF-EI) were recorded on a GCT CA 127 Micronass UK mass spectrometer. All solvents were of commercial quality and were dried and purified by standard procedures. *N*-(4-hydroxyphenyl)benzenesulfonamides (**1a** and **1b**) were synthesized following reference procedures.[16]

4.2. General procedure for the synthesis of ketene *N,S*-acetals 2i–q

To a 100 mL round bottomed flask equipped with a magnetic stirrer and a condenser were added ketene *S,S*-acetals (20 mmol) and amine (20 mmol) dissolved in 30 mL of toluene. The reaction mixture was heated to reflux for about 16 h and then cooled to room temperature. After removal of the solvents under reduced pressure, 50 mL of water was added to the flask and the mixture was extracted using ethyl acetate (3×200 mL). The combined organic layers were washed with brine (2×50 mL) and dried over anhydrous $MgSO_4$. The desired ketene *N,S*-acetals were obtained after column chromatography eluted by petroleum ether and ethyl acetate.

*4.2.1. (E)-3-Methylthio-3-propylamino-1-p-tolylprop-2-en-1-one (**2i**).*[17] Yellowish powder, mp: 35–37 °C; yield: 65%. ^1H NMR (400 MHz, $CDCl_3$): δ 1.05 (t, 3H, J=7.2 Hz, CH_3), 1.75–1.77 (m, 2H, CH_2), 2.40 (s, 3H, CH_3), 2.49 (s, 3H, SCH_3), 3.38 (m, 2H, CH_2), 5.62 (s, 1H, C=CH), 7.23 (d, 2H, J=8.0 Hz, Ar–H), 7.78 (d, 2H, J=8.0 Hz, Ar–H), 11.94 (br, 1H, NH).

*4.2.2. (E)-1-(4-Methoxyphenyl)-3-methylthio-3-propylaminoprop-2-en-1-one (**2j**).*[17] Yellowish powder, mp: 43–44 °C; yield: 69%. ^1H NMR (400 MHz, $CDCl_3$): δ 1.04 (t, 3H, J=7.2 Hz, CH_3), 1.68–1.77 (m, 2H, CH_2), 2.48 (s, 3H, SCH_3), 3.33–3.38 (m, 2H, CH_2), 3.85 (s, 3H, OCH_3), 5.62 (s, 1H, C=CH), 6.92 (d, 2H, J=8.8 Hz, Ar–H), 7.85 (d, 2H, J=8.8 Hz, Ar–H), 11.81 (br, 1H, NH).

*4.2.3. (E)-3-Methylthio-1-phenyl-3-propylaminoprop-2-en-1-one (**2k**).*[17] Yellowish liquid, yield: 60%. ^1H NMR (400 MHz, $CDCl_3$): δ 1.05 (t, 3H, J=7.2 Hz, CH_3), 1.71–1.77 (m, 2H, CH_2), 2.49 (s, 3H, SCH_3), 3.35–3.40 (m, 2H, CH_2), 5.66 (s, 1H, C=CH),

7.39–7.45 (m, 3H, Ar–H), 7.87 (d, 2H, *J*=8.8 Hz, Ar–H), 11.91 (br, 1H, NH).

*4.2.4. (E)-1-(4-Chlorophenyl)-3-methylthio-3-propylaminoprop-2-en-1-one (**2l**).*[17] Yellowish powder, mp: 68–70 °C; yield: 60%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.04 (t, 3H, *J*=7.2 Hz, CH_3), 1.69–1.76 (m, 2H, CH_2), 2.49 (s, 3H, SCH_3), 3.34–3.39 (m, 2H, $NHCH_2$), 5.60 (s, 1H, C=CH), 7.37 (d, 2H, *J*=8.8 Hz, Ar–H), 7.79 (d, 2H, *J*=8.8 Hz, Ar–H), 11.91 (br, 1H, NH).

*4.2.5. (E)-4-Methylthio-4-propylaminobut-3-en-2-one (**2m**).* Yellowish liquid, yield: 41%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.98 (t, 3H, *J*=7.6 Hz, CH_3), 1.61–1.70 (m, 2H, CH_2), 2.05 (s, 3H, CH_3), 2.35 (s, 3H, SCH_3), 3.26 (m, 2H, $NHCH_2$), 4.95 (s, 1H, C=CH), 11.35 (br, 1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6): δ 18.9, 28.7, 42.8, 59.0, 71.5, 95.4, 163.0, 194.8; IR (KBr): ν 2923, 2879, 1610, 1571 cm^{-1}; ESI-MS: *m*/*z* 172.0 [M−1]$^-$.

*4.2.6. (E)-N-[1-(Methylthio)-2-nitrovinyl]propan-1-amine (**2n**).*[18] Yellow powder, mp: 64–65 °C; yield: 68%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.02 (t, 3H, *J*=7.2 Hz, CH_3), 1.71–1.77 (m, 2H, CH_2), 2.45 (s, 3H, SCH_3), 3.38–3.42 (m, 2H, $NHCH_2$), 6.59 (s, 1H, C=CH), 10.58 (br, 1H, NH).

*4.2.7. (E)-3-Benzylamino-3-methylthio-1-p-tolylprop-2-en-1-one (**2o**).*[19] Yellowish powder, mp: 83–84 °C; yield: 63%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.50 (s, 3H, SCH_3), 4.63 (d, 2H, *J*=5.6 Hz, CH_2), 5.70 (s, 1H, C=CH), 7.28–7.33 (m, 1H, Ar–H), 7.34–7.40 (m, 6H, Ar–H), 7.81 (d, 2H, *J*=8.4 Hz, Ar–H), 12.21 (br, 1H, NH).

*4.2.8. (E)-3-Benzylamino-1-(4-methoxyphenyl)-3-methylthioprop-2-en-1-one (**2p**).*[19] Pink powder, mp: 43–44 °C; yield: 71%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.49 (s, 3H, SCH_3), 3.87 (s, 3H, OCH_3), 4.63 (d, 2H, *J*=5.6 Hz, CH_2), 5.70 (s, 1H, C=CH), 6.93 (d, 2H, *J*=8.8 Hz, Ar–H), 7.29–7.34 (m, 5H, Ar–H), 7.78 (d, 2H, *J*=8.4 Hz, Ar–H), 12.15 (br, 1H, NH).

*4.2.9. (E)-3-Benzylamino-1-(4-chlorophenyl)-3-methylthioprop-2-en-1-one (**2q**).*[19] Yellowish powder, mp: 92–93 °C; yield: 59%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.49 (s, 3H, SCH_3), 4.63 (d, 2H, *J*=5.6 Hz, CH_2), 5.70 (s, 1H, C=CH), 6.93 (d, 2H, *J*=8.8 Hz, Ar–H), 7.29–7.34 (m, 5H, Ar–H), 7.78 (d, 2H, *J*=8.4 Hz, Ar–H), 12.15 (br, 1H, NH).

4.3. General procedure for the synthesis of benzofurans 3a–s

To a 50 mL round bottomed flask containing *N*-(4-hydroxyphenyl)-benzenesulfonamide (1 mmol) dissolved in 10 mL of acetonitrile was added dropwise $PhI(OAc)_2$ (483 mg, 1.5 mmol) in 5 mL of CH_2Cl_2 and 0.1 mL of 1 mol/L $BF_3\cdot Et_2O$. After stirring at room temperature for 10 min, ketene *S*,*S*-acetals or *N*,*S*-acetals (1 mmol) and $CuBr_2$ (4.6 mg, 0.02 mmol) were added and the solution was continued to stir, while monitoring the reaction by TLC. After the completion of the reaction (about 30 min), the solvent was evaporated under reduced pressure and 20 mL of saturated sodium carbonate aqueous was added. CH_2Cl_2 was used to extract (3×20 mL), the combined organic layers were washed with brine and dried over anhydrous $MgSO_4$. The expected benzofurans were obtained after column chromatography; elution used a mixed solvent of petroleum ether and acetone.

*4.3.1. N-[3-(4-Methylbenzoyl)-2-(methylthio)benzofuran-5-yl]-4-methyl-benzene-sulfonamide (**3a**).* Yield: 61%; mp: 159–161 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 2.33 (s, 3H, CH_3), 2.44 (s, 3H, CH_3), 2.62 (s, 3H, SCH_3), 7.01 (dd, 1H, *J*=8.8 Hz, *J*=2.0 Hz, Ar–H), 7.05 (d, 1H, *J*=1.6 Hz, Ar–H), 7.31 (d, 2H, *J*=8.8 Hz, Ar–H), 7.33 (d, 2H, *J*=8.8 Hz, Ar–H), 7.50 (d, 2H, *J*=8.0 Hz, Ar–H), 7.52 (d, 1H, *J*=8.8 Hz, Ar–H), 7.56 (d, 2H, *J*=8.0 Hz, Ar–H), 10.10 (s, 1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6): δ 14.1, 21.4, 21.7, 111.8, 112.8, 116.7, 118.3, 127.1, 127.2, 128.9, 129.7, 130.0, 134.7, 136.4, 136.9, 143.3, 143.6, 152.1, 163.7, 189.4; IR (KBr): ν 3434, 2923, 1608 cm^{-1}; ESI-MS: *m*/*z* 449.8 [M−1]$^-$, 473.9 [M+Na]$^+$; HREI-MS (*m*/*z*) calcd for $C_{24}H_{21}NO_4S_2$ (M) 451.0912, found 451.0920.

*4.3.2. N-[3-(4-Methoxybenzoyl)-2-(methylthio)benzofuran-5-yl]-4-methylbenzene-sulfonamide (**3b**).* Yellowish powder, yield: 65%; mp: 130–131 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 2.32 (s, 3H, CH_3), 2.62 (s, 3H, SCH_3), 3.88 (s, 3H, OCH_3), 7.03–7.06 (m, 4H, Ar–H), 7.31 (d, 2H, *J*=7.6 Hz, Ar–H), 7.50–7.54 (m, 3H, Ar–H), 7.66 (d, 2H, *J*=7.6 Hz, Ar–H), 10.12 (s, 1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6): δ 14.2, 21.4, 56.0, 111.8, 112.8, 114.4, 117.0, 118.2, 127.1, 127.4, 130.0, 131.3, 131.4, 134.7, 136.9, 143.6, 152.1, 162.6, 163.3, 188.3; IR (KBr): ν 3435, 3172, 2934, 1599 cm^{-1}; ESI-MS: *m*/*z* 465.8 [M−1]$^-$, 467.8 [M+1]$^+$, 489.8 [M+Na]$^+$; HREI-MS (*m*/*z*) calcd for $C_{24}H_{21}NO_5S_2$ (M) 467.0861, found 467.0869.

*4.3.3. N-[3-Benzoyl-2-(methylthio)benzofuran-5-yl]-4-methylbenzene-sulfonamide (**3c**).* Yellowish powder, yield: 52%; mp: 156–157 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 2.32 (s, 3H, CH_3), 2.63 (s, 3H, SCH_3), 6.98–7.02 (m, 2H, Ar–H), 7.31 (d, 2H, *J*=7.6 Hz, Ar–H), 7.48–7.56 (m, 5H, Ar–H), 7.64 (d, 2H, *J*=7.6 Hz, Ar–H), 7.68–7.71 (m, 1H, Ar–H), 10.14 (br, 1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6): δ 14.0, 21.4, 111.8, 112.6, 116.4, 118.1, 127.0, 127.1, 128.5, 129.2, 130.0, 132.9, 134.8, 136.9, 139.2, 143.6, 152.1, 164.5, 189.8; IR (KBr): ν 3436, 3242, 2920, 1600 cm^{-1}; ESI-MS: *m*/*z* 435.8 [M−1]$^-$, 437.8 [M+1]$^+$, 459.7 [M+Na]$^+$; HREI-MS (*m*/*z*) calcd for $C_{23}H_{19}NO_4S_2$ (M) 437.0756, found 437.0762.

*4.3.4. N-[3-(4-Chlorobenzoyl)-2-(methylthio)benzofuran-5-yl]-4-methylbenzene-sulfonamide (**3d**).* Yellowish powder, yield: 49%; mp: 169–171 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 2.33 (s, 3H, CH_3), 2.64 (s, 3H, SCH_3), 6.99 (d, 1H, *J*=2.0 Hz, Ar–H), 7.03 (dd, 1H, *J*=8.8 Hz, *J*=2.0 Hz, Ar–H), 7.33 (d, *J*=8.0 Hz, 2H, Ar–H), 7.51 (d, 2H, *J*=8.4 Hz, Ar–H), 7.54 (d, 1H, *J*=8.8 Hz, Ar–H), 7.59 (d, 2H, *J*=8.8 Hz, Ar–H), 7.66 (d, 2H, *J*=8.8 Hz, Ar–H), 10.15 (br, 1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6): δ 14.0, 21.4, 111.8, 112.4, 116.1, 118.1, 126.9, 127.1, 129.3, 130.1, 130.4, 134.9, 136.9, 137.6, 137.9, 143.6, 152.1, 164.9, 188.6; IR (KBr): ν 3436, 3227, 2941, 1612, 1592 cm^{-1}; ESI-MS: *m*/*z* 469.8 [M−1]$^-$, 471.7 [M+1]$^+$, 493.7 [M+Na]$^+$; HREI-MS (*m*/*z*) calcd for $C_{23}H_{18}NO_4S_2Cl$ (M) 451.0366, found 451.0373.

*4.3.5. N-[3-Acetyl-2-(methylthio)benzofuran-5-yl]-4-methylbenzene-sulfonamide (**3e**).* Yield: 42%; mp: 147–149 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 2.31 (s, 3H, CH_3), 2.48 (s, 3H, SCH_3), 2.67 (s, 3H, $COCH_3$), 6.99–7.01 (m, 1H, Ar–H), 7.32 (d, 2H, *J*=8.0 Hz, Ar–H), 7.49 (d, 1H, *J*=8.8 Hz, Ar–H), 7.61 (d, 2H, *J*=8.0 Hz, Ar–H), 7.62 (s, 1H, Ar–H), 10.20 (s, 1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6): δ 13.7, 21.4, 31.1, 111.6, 113.0, 116.8, 117.8, 126.8, 127.3, 130.1, 135.0, 136.9, 143.6, 152.0, 163.8, 192.0; IR (KBr): ν 3435, 3101, 2985, 2917, 1706, 1602 cm^{-1}; ESI-MS: *m*/*z* 373.8 [M−1]$^-$, 375.9 [M+1]$^+$, 397.8 [M+Na]$^+$; HREI-MS (*m*/*z*) calcd for $C_{18}H_{17}NO_4S_2$ (M) 375.0599, found 375.0603.

*4.3.6. 5-(4-Methylphenylsulfonamido)-2-(methylthio)benzofuran-3-carboxamide (**3f**).* Yield: 35%; mp: 235–236 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 2.29 (s, 3H, CH_3), 2.58 (s, 3H, SCH_3), 6.97 (d, 1H, *J*=8.8 Hz, Ar–H), 7.29 (d, 2H, *J*=7.6 Hz, Ar–H), 7.42 (d, 1H, *J*=8.8 Hz, Ar–H), 7.58 (d, 2H, *J*=8.0 Hz, Ar–H), 7.57 (s, 1H, Ar–H), 9.94 (s, 1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6): δ 15.2, 21.4, 111.5, 113.6, 118.6, 127.2, 130.0, 134.3, 137.0, 143.6, 152.1, 156.3, 164.3; IR (KBr): ν 3449, 3368, 2921, 1641 cm^{-1}; ESI-MS: *m*/*z* 375.0 [M−1]$^-$, 377.0 [M+1]$^+$, 376.5 [M+Na]$^+$; HREI-MS (*m*/*z*) calcd for $C_{17}H_{16}N_2O_4S_2$ (M) 376.0552, found 376.0557.

*4.3.7. N-[2-(Methylthio)-3-nitrobenzofuran-5-yl]-4-methyl-benzene-sulfonamide (**3g**).* Yield: 61%; mp: 193–195 °C; ^{1}H NMR

(400 MHz, DMSO-d_6): δ 2.31 (s, 3H, CH_3), 2.76 (s, SCH_3), 7.14 (d, 1H, *J*=8.0 Hz, Ar–H), 7.33–7.71 (m, 6H, Ar–H), 10.42 (s, 1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6): δ 13.5, 21.4, 111.0, 112.5, 118.7, 121.6, 127.2, 128.8, 130.1, 136.3, 136.8, 143.8, 150.6, 165.8; IR (KBr): ν 3435, 3241, 1599 cm^{-1}; ESI-MS: *m*/*z* 376.6 $[M-1]^-$; HREI-MS (*m*/*z*) calcd for $C_{16}H_{14}N_2O_5S_2$ (M) 378.0344, found 378.0351.

*4.3.8. N-[3-Cyano-2-(methylthio)benzofuran-5-yl]-4-methylbenzenesulfonamide (**3h**).* Yield: 63%; mp: 184–186 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 2.32 (s, 3H, CH_3), 2.76 (s, SCH_3), 7.12 (dd, 1H, *J*=2.0 Hz, 8.8 Hz, Ar–H), 7.24 (d, 1H, *J*=1.6 Hz, Ar–H), 7.35 (d, 2H, *J*=8.4 Hz, Ar–H), 7.57–7.60 (m, 3H, Ar–H), 10.39 (s, 1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6): δ 15.2, 21.4, 111.0, 112.7, 112.9, 119.4, 126.9, 127.2, 127.3, 130.2, 135.7, 136.7, 143.8, 151.6, 164.5; IR (KBr): ν 3450, 3241, 2922, 1623 cm^{-1}; ESI-MS: *m*/*z* 357.0 $[M-1]^-$, 359.0 $[M+1]^+$, 381.0 $[M+Na]^+$; HREI-MS (*m*/*z*) calcd for $C_{17}H_{14}N_2O_3S_2$ (M) 358.0446, found 358.0450.

*4.3.9. N-[3-(4-Methylbenzoyl)-2-(propylamino)benzofuran-5-yl]-4-methyl-benzene sulfonamide (**3i**).* Yield: 55%; mp: 204–205 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 0.92 (t, 3H, *J*=7.6 Hz, CH_2CH_3), 1.62–1.67 (m, 2H, CH_2CH_3), 2.33 (s, 3H, CH_3), 2.44 (s, 3H, CH_3), 3.43–3.48 (m, 2H, $NHCH_2$), 6.62 (s, 1H, Ar–H), 6.68 (dd, 1H, *J*=8.8 Hz, 1.6 Hz, Ar–H), 7.23 (d, 1H, *J*=8.8 Hz, Ar–H), 7.29–7.31 (m, 4H, Ar–H), 7.40 (d, 2H, *J*=8.0 Hz, Ar–H), 7.44 (d, 2H, *J*=8.0 Hz, Ar–H), 9.12 (t, 1H, *J*=6.0 Hz, $NHCH_2$), 9.87 (s, 1H, $NHSO_2$); ^{13}C NMR (100 MHz, DMSO-d_6): δ 11.5, 21.4, 21.7, 23.3, 43.7, 92.7, 110.7, 111.6, 115.3, 127.2, 127.3, 127.5, 129.4, 129.9, 134.2, 137.0, 138.4, 140.8, 143.4, 146.1, 166.9, 188.2; IR (KBr): ν 3436, 3291, 3166, 2963, 1644, 1592 cm^{-1}; ESI-MS: *m*/*z* 460.9 $[M-1]^-$, 462.9 $[M+1]^+$, 484.9 $[M+Na]^+$; HREI-MS (*m*/*z*) calcd for $C_{26}H_{26}N_2O_4S$ (M) 462.1613, found 462.1620.

*4.3.10. N-[3-(4-Methoxybenzoyl)-2-(propylamino)benzofuran-5-yl]-4-methyl-benzenesulfonamide (**3j**).* Yellowish powder, yield: 72%; mp: 86–88 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 0.92 (t, 3H, *J*=7.2 Hz, CH_2CH_3), 1.62–1.67 (m, 2H, CH_2CH_3), 2.33 (s, 3H, CH_3), 3.45 (q, 2H, *J*=7.2 Hz, $NHCH_2$), 3.88 (s, 3H, OCH_3), 6.68 (d, 1H, *J*=2.0 Hz, Ar–H), 6.72 (dd, 1H, *J*=6.8 Hz, 2.0 Hz, Ar–H), 7.01 (d, 2H, *J*=8.8 Hz, Ar–H), 7.24 (d, 1H, *J*=8.4 Hz, Ar–H), 7.30 (d, 2H, *J*=8.0 Hz, Ar–H), 7.46 (d, 2H, *J*=7.2 Hz, Ar–H), 7.48 (d, 2H, *J*=7.2 Hz, Ar–H), 9.07 (t, 1H, *J*=7.2 Hz, $NHCH_2$), 9.87 (s, 1H, $NHSO_2$); ^{13}C NMR (100 MHz, DMSO-d_6): δ 11.5, 21.4, 23.3, 43.7, 55.8, 92.5, 110.7, 111.7, 114.1, 115.2, 127.2, 127.4, 129.5, 129.9, 133.5, 134.2, 137.0, 143.4, 146.1, 161.6, 166.8, 187.5; IR (KBr): ν 3438, 3158, 2961, 1643, 1603 cm^{-1}; ESI-MS: *m*/*z* 476.8 $[M-1]^-$, 479.0 $[M+1]^+$, 501.0 $[M+Na]^+$, 516.9 $[M+K]^+$; HREI-MS (*m*/*z*) calcd for $C_{26}H_{26}N_2O_5S$ (M) 478.1562, found 478.1568.

*4.3.11. N-[3-Benzoyl-2-(propylamino)benzofuran-5-yl]-4-methylbenzenesulfonamide (**3k**).* Yield: 54%; mp: 191–192 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 0.92 (t, 3H, *J*=7.6 Hz, CH_2CH_3), 1.61–1.70 (m, 2H, CH_2CH_3), 2.33 (s, 3H, CH_3), 3.47–3.49 (m, 2H, $NHCH_2$), 6.57 (d, 1H, *J*=1.6 Hz, Ar–H), 6.68 (dd, 1H, *J*=8.8 Hz, *J*=1.6 Hz, Ar–H), 7.24 (d, 1H, *J*=8.8 Hz, Ar–H), 7.29 (d, 2H, *J*=8.0 Hz, Ar–H), 7.43 (d, 2H, *J*=8.8 Hz, Ar–H), 7.47–7.63 (m, 5H, Ar–H), 9.16 (t, 1H, *J*=6.0 Hz, $NHCH_2$), 9.89 (s, 1H, $NHSO_2$); ^{13}C NMR (100 MHz, DMSO-d_6): δ 11.5, 21.4, 23.2, 43.8, 92.3, 110.7, 111.4, 115.3, 127.1, 127.2, 128.5, 129.0, 129.9, 131.0, 134.3, 137.0, 141.3, 143.4, 146.1, 166.9, 188.3; IR (KBr): ν 3435, 3099, 2929, 1648, 1593 cm^{-1}; ESI-MS: *m*/*z* 449.0 $[M+1]^+$, 471.0 $[M+Na]^+$, 486.9 $[M+K]^+$; HREI-MS (*m*/*z*) calcd for $C_{25}H_{24}N_2O_4S$ (M) 448.1457, found 448.1464.

*4.3.12. N-[3-(4-Chlorobenzoyl)-2-(propylamino)benzofuran-5-yl]-4-methylbenzene-sulfonamide (**3l**).* Yield: 49%; mp: 161–163 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 0.91 (t, 3H, *J*=7.2 Hz, CH_2CH_3), 1.62–1.67 (m, 2H, CH_2CH_3), 2.33 (s, 3H, CH_3), 3.45–3.47 (m, 2H, $NHCH_2$), 6.49 (s, 1H, Ar–H), 7.14 (d, 1H, *J*=8.4 Hz, Ar–H), 7.23–7.56 (m, 9H, Ar–H), 9.13 (t, 1H, *J*=6.0 Hz, $NHCH_2$), 9.93 (s, 1H, $NHSO_2$); ^{13}C NMR (100 MHz, DMSO-d_6): δ 11.5, 21.4, 23.2, 43.8, 92.7, 110.8, 111.0, 115.2, 127.0, 127.1, 129.1, 129.2, 129.9, 134.4, 135.6, 137.0, 139.9, 143.4, 146.1, 166.9, 186.8; IR (KBr): ν 3438, 3171, 2963, 1648, 1593 cm^{-1}; ESI-MS: *m*/*z* 480.8 $[M-1]^-$, 483.0 $[M+1]^+$, 504.9 $[M+Na]^+$, 520.9 $[M+K]^+$; HREI-MS (*m*/*z*) calcd for $C_{25}H_{23}N_2O_4SCl$ (M) 482.1067, found 482.1073.

*4.3.13. N-[3-Acetyl-2-(propylamino)benzofuran-5-yl]-4-methylbenzenesulfonamide (**3m**).* Yield: 58%; mp: 240–241 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 0.92 (t, 3H, *J*=7.2 Hz, CH_2CH_3), 1.54–1.63 (m, 2H, CH_2CH_3), 2.27 (s, 3H, CH_3), 2.30 (s, 3H, CH_3), 3.34–3.41 (m, 2H, $NHCH_2$), 6.73 (dd, 1H, *J*=8.4 Hz, 2.0 Hz, Ar–H), 7.16 (d, 1H, *J*=2.0 Hz, Ar–H), 7.21 (d, 1H, *J*=8.4 Hz, Ar–H), 7.32 (d, 2H, *J*=8.4 Hz, Ar–H), 7.62 (d, 2H, *J*=8.4 Hz, Ar–H), 8.72 (t, 1H, *J*=6.0 Hz, Ar–H), 10.01 (s, 1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6): δ 11.4, 21.4, 23.3, 29.3, 43.6, 93.5, 110.7, 111.2, 114.5, 127.3, 127.7, 130.0, 134.7, 143.5, 146.0, 165.4, 190.1; IR (KBr): ν 3435, 3240, 2968, 1667, 1490 cm^{-1}; EI-MS: *m*/*z* 386 $[M]^+$; HREI-MS (*m*/*z*) calcd for $C_{20}H_{22}N_2O_4S$ (M) 386.1300, found 386.1306.

*4.3.14. N-[3-Nitro-2-(propylamino)benzofuran-5-yl]-4-methyl-benzenesulfonamide (**3n**).* Yellowish powder, yield: 47%; mp: 199–201 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 0.89 (t, 3H, *J*=7.6 Hz, CH_2CH_3), 1.61–1.70 (m, 2H, CH_2CH_3), 2.31 (s, 3H, CH_3), 3.44–3.49 (m, 2H, $NHCH_2$), 6.92 (dd, 1H, *J*=8.8 Hz, 2.0 Hz, Ar–H), 7.32–7.63 (m, 6, Ar–H), 9.59 (t, 1H, *J*=6.4 Hz, NH), 10.21 (s, 1H, SO_2NH); ^{13}C NMR (100 MHz, DMSO-d_6): δ 11.4, 21.4, 22.8, 44.6, 109.1, 111.2, 111.3, 116.8, 122.8, 122.7, 127.2, 130.1, 135.6, 137.0, 143.6, 144.2, 161.0; IR (KBr): ν 3433, 3242, 2965, 1665, 1494, 1468, 1158, 1078 cm^{-1}; ESI-MS: *m*/*z*, 411.9 $[M+Na]^+$; HREI-MS (*m*/*z*) calcd for $C_{18}H_{19}N_3O_5S$ (M) 389.1045, found 389.1051.

*4.3.15. N-[2-(Benzylamino)-3-(4-methylbenzoyl)benzofuran-5-yl]-4-methyl-benzenesulfonamide (**3o**).* Yellowish powder. Yield: 73%; mp: 189–189 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 2.33 (s, 3H, CH_3), 2.44 (s, 3H, CH_3), 4.69 (d, 2H, *J*=7.2 Hz, $NHCH_2$), 6.63 (s, 1H, Ar–H), 6.68 (dd, 1H, *J*=8.8 Hz, 2.0 Hz, Ar–H), 7.22 (d, 1H, *J*=8.8 Hz, Ar–H), 7.26–7.44 (m, 13H, Ar–H), 9.51 (t, 1H, *J*=7.2 Hz, NH), 9.87 (s, 1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6): δ 21.4, 21.7, 45.6, 93.0, 110.8, 111.7, 115.4, 127.1, 127.5, 127.8, 129.0, 129.1, 129.4, 129.9, 130.0, 134.3, 137.0, 138.4, 138.8, 140.9, 141.0, 143.4, 146.1, 187.6; IR (KBr): ν 3434, 3249, 2921, 1643, 1182 cm^{-1}; ESI-MS: *m*/*z* 508.8 $[M-1]^-$, 511.0 $[M+1]^+$, 533.0 $[M+Na]^+$, 548.9 $[M+K]^+$; HREI-MS (*m*/*z*) calcd for $C_{30}H_{26}N_4O_4S$ (M) 510.1613, found 510.1618.

*4.3.16. N-[2-(Benzylamino)-3-(4-methoxybenzoyl)benzofuran-5-yl]-4-methyl-benzenesulfonamide (**3p**).* Yellowish powder. Yield: 76%; mp: 168–170 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 2.32 (s, 3H, CH_3), 3.88 (s, 3H, OCH_3), 4.69 (d, 2H, *J*=6.4 Hz, CH_2Ph), 6.68–6.72 (m, 2H, Ar–H), 7.00 (d, 2H, *J*=8.8 Hz, Ar–H), 7.22 (d, 1H, *J*=8.4 Hz, Ar–H), 7.25–7.40 (m, 7H, Ar–H), 7.45 (d, 2H, *J*=8.4 Hz, Ar–H), 7.49 (d, 2H, *J*=8.8 Hz, Ar–H), 9.45 (t, 1H, *J*=6.4 Hz, $NHCH_2$), 9.87 (s, 1H, $NHSO_2$); ^{13}C NMR (100 MHz, DMSO-d_6): δ 21.4, 45.6, 55.8, 92.9, 108.8, 110.7, 111.7, 115.4, 127.1, 127.5, 127.8, 128.1, 129.1, 129.4, 129.9, 134.3, 137.0, 138.4, 138.8, 140.9, 141, 143.4, 146.1, 187.6; IR (KBr): ν 3434, 2924, 1644, 1602 cm^{-1}; *m*/*z* 524.8 $[M-1]^-$, 527.0 $[M+1]^+$, 549.0 $[M+Na]^+$; HREI-MS (*m*/*z*) calcd for $C_{30}H_{26}N_2O_5S$ (M) 526.1562, found 526.1570.

*4.3.17. N-[2-(Benzylamino)-3-(4-chlorobenzoyl)benzofuran-5-yl]-4-methyl-benzenesulfonamide (**3q**).* Yellowish powder. Yield: 64%; mp: 109–111 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 2.32 (s, 3H, CH_2CH_3), 4.70 (s, 2H, $NHCH_2$), 6.50 (s, 1H, Ar–H), 6.71 (d, 2H,

J=7.6 Hz, Ar–H), 7.22–7.54 (m, 14H, Ar–H), 9.55 (s, 1H, NH), 9.93 (s, 1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6): δ 21.4, 45.6, 93.0, 110.9, 111.2, 115.3, 127.1, 127.8, 127.8, 129.0, 129.0, 129.1, 129.3, 129.9, 134.5, 135.7, 137.0, 138.7, 139.8, 143.4, 146.1, 166.5, 187.1; IR (KBr): ν 3434, 3256, 2922, 1643 cm^{-1}; ESI-MS: m/z 528.8 [M−1]$^-$, 531.0 [M+1]$^+$, 552.7 [M+Na]$^+$; HREI-MS (m/z) calcd for $C_{29}H_{23}N_2O_4SCl$ (M) 530.1067, found 530.1072.

*4.3.18. N-[6-Methyl-3-(4-methylbenzoyl)-2-(methylthio)benzofuran-5-yl]-4-methylbenzenesulfonamide (**3r**).* Yellowish powder. Yield: 69%; mp: 199–201 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 2.06 (s, 3H, CH_3), 2.35 (s, 3H, CH_3), 2.45 (s, 3H, CH_3), 2.63 (s, 3H, CH_3), 6.91 (s, 1H, Ar–H), 7.26 (d, 2H, J=8.0 Hz, Ar–H), 7.33 (d, 2H, J=8.0 Hz, Ar–H), 7.41 (d, 2H, J=8.0 Hz, Ar–H), 7.46 (s, 1H, Ar–H), 7.59 (d, 2H, J=8.0 Hz, Ar–H), 9.45 (s, 1H, $NHSO_2$); ^{13}C NMR (100 MHz, DMSO-d_6): δ 14.1, 18.5, 21.5, 21.7, 112.6, 116.7, 119.0, 124.8, 127.0, 128.9, 129.7, 129.9, 131.9, 132.0, 136.4, 138.0, 143.3, 153.4, 162.9, 189.2; IR (KBr): ν 3435, 2920, 1623, 837 cm^{-1}; ESI-MS: m/z 464.0 [M−1]$^-$, 466.0 [M+1]$^+$; HREI-MS (m/z) calcd for $C_{25}H_{23}NO_4S_2$ (M) 465.1068, found 465.1065.

*4.3.19. N-[6-Methyl-3-(4-methylbenzoyl)-2-(propylamino)benzofuran-5-yl]-4-methylbenzenesulfonamide (**3s**).* Yellowish powder. Yield: 64%; mp: 194–197 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 0.93 (t, 3H, J=7.2 Hz, CH_2CH_3), 1.61–1.71 (m, 2H, CH_2CH_3), 2.06 (s, 3H, CH_3), 2.02 (s, 3H, CH_3), 2.37 (s, 3H, CH_3), 2.43 (s, 3H, CH_3), 3.45–3.50 (m, 2H, $NHCH_2$), 6.53 (s, 1H, Ar–H), 7.20 (s, 1H, Ar–H), 7.22–7.41 (m, 8H, Ar–H), 9.15 (t, 2H, J=6.4 Hz, Ar–H), 9.23 (s, 1H, $NHSO_2$); ^{13}C NMR (100 MHz, DMSO-d_6): δ 11.6, 18.3, 21.5, 21.6, 23.3, 43.8, 92.4, 112.0, 117.7, 124.7, 127.0, 127.5, 129.0, 129.3, 129.8, 131.2, 138.1, 138.4, 140.7, 143.1, 147.5, 166.8, 187.8; IR (KBr): ν 3450, 3288, 2970, 1641 cm^{-1}; ESI-MS: m/z 475.0 [M−1]$^-$, 477.1 [M+1]$^+$, 499.0 [M+Na]$^+$; HREI-MS (m/z) calcd for $C_{27}H_{28}N_2O_4S$ (M) 478.1770, found 478.1767.

Acknowledgements

This work was supported by grants from the National Basic Research Program of China (No. 2009CB930200), The National Key Technology R&D Program (2011BAD23B01), Beijing Natural Science Foundation (No. 7112008) and Beijing City Education Committee (KM201010005009). We also thank Mrs. Jinchao Wei in Institute of Chemistry, CAS, for the HREI-MS measurement.

References and notes

1. (a) Mendonca, P. P.; Araujo, A. R.; Young, M. C. M.; Giesbrecht, A. M. *Phytochemistry* **2000**, *55*, 597–601; (b) Sheen, W. S.; Tsai, I. L.; Teng, C. M.; Chen, I. S. *Phytochemistry* **1994**, *36*, 213–215; (c) Shikishima, Y.; Takaishi, Y.; Honda, G.; Ito, M.; Takeda, Y.; Kodzhimatov, O. K.; Ashurmetov, O.; Le, K. H. *Chem. Pharm. Bull.* **2001**, *49*, 877–880.
2. (a) Hwu, J. R.; Chuang, K. S.; Chuang, S. H.; Tsay, S. C. *Org. Lett.* **2005**, *7*, 1545–1548; (b) Jung, I.; Lee, J. K.; Song, K. H.; Song, K.; Kang, S. O.; Ko, J. *J. Org. Chem.* **2007**, *72*, 3652–3658; (c) Zhang, F. M.; Yun, G. L.; Zhang, J. M.; Yang, C. D. *Chin. J. Liquid Crystals and Displays* **2010**, *1*, 5–10 (in Chinese).
3. (a) Benitez, A.; Herrera, F. R.; Romero, M.; Talamas, F. X.; Muchowski, J. M. *J. Org. Chem.* **1996**, *61*, 1487–1492; (b) Asao, N.; Aikawa, H. *J. Org. Chem.* **2006**, *71*, 5249–5253.
4. (a) Lu, B.; Wag, B.; Zhang, Y. H.; Ma, D. W. *J. Org. Chem.* **2007**, *72*, 5337–5341; (b) Mattson, E.; Scheidt, K. A. *J. Am. Chem. Soc.* **2007**, *129*, 4508–4509; (c) Duan, X. F.; Zeng, J.; Zhang, Z. B.; Zi, G. F. *J. Org. Chem.* **2007**, *72*, 10283–10286.
5. Adams, R.; Whitaker, L. *J. Am. Chem. Soc.* **1956**, *78*, 658–660.
6. (a) Engler, T. A.; Combrink, K. D.; Letavic, M. A.; Lynch, K. O.; Ray, J. E., Jr. *J. Org. Chem.* **1994**, *59*, 6567–6587; (b) Engler, T. A.; Wei, D.; Letavic, M. A.; Combrink, K. D.; Reddy, J. P. *J. Org. Chem.* **1994**, *59*, 6588–6599.
7. Engler, T. A.; Meduna, S. P.; LaTessa, K. O.; Chai, W. *J. Org. Chem.* **1996**, *61*, 8598–8603.
8. (a) Engler, T. A.; Chai, W.; LaTessa, K. O. *J. Org. Chem.* **1996**, *61*, 9297–9308; (b) Engler, T. A.; Scheibe, C. M. *J. Org. Chem.* **1998**, *63*, 6247–6253; (c) Engler, T. A.; Wanner, J. *J. Org. Chem.* **2000**, *65*, 2444–2457.
9. Liu, Y.-J.; Wang, M.; Yuan, H.-J.; Liu, Q. *Adv. Synth. Catal.* **2010**, *352*, 884–892.
10. (a) Tabaković, I.; Grujić, Z.; Bejtovi&cacute, Z. *J. Heterocycl. Chem.* **1983**, *20*, 635–638; (b) Golabi, S. M.; Nematollahi, D. *J. Electroanal. Chem.* **1997**, *420*, 127–134; (c) Shamsipur, M.; Davarani, S. S. H.; Nematollahi, D. *J. Heterocycl. Chem.* **2006**, *43*, 1673–1677; (d) Fakhari, A. R.; Nematollahi, D.; Shamsipur, M.; Makarem, S.; Davarani, S. S. H.; Alizadeh, A.; Khavasi, H. R. *Tetrahedron* **2007**, *63*, 3894–3898; (e) Zeng, C. C.; Liu, F. J.; Ping, D. W.; Hu, L. M.; Cai, Y. L.; Zhong, R. G. *J. Org. Chem.* **2009**, *74*, 6386–6389; (f) Zeng, C. C.; Ping, D. W.; Xu, Y. S.; Hu, L. M.; Zhong, R. G. *Eur. J. Org. Chem.* **2009**, 5832–5840.
11. For the application of hypevalent iodine, see review: (a) Pouységu, L.; Deffieux, D.; Quideau, S. *Tetrahedron* **2010**, *66*, 2235–2261; (b) Richardson, R. D.; Wirth, T. *Angew. Chem., Int. Ed.* **2006**, *45*, 4402–4404; (c) Zhdankin, V. V.; Stang, P. J. *Chem. Rev.* **2008**, *108*, 5299–5358.
12. Huang, Z. T.; Zhang, P. C. *Synth. Commun.* **1990**, *20*, 1399–1407.
13. (a) Yin, Y.-B.; Zhang, Q.; Liu, Q.; Liu, Y.; Sun, S.-G. *Synth. Commun.* **2007**, *37*, 703–711; (b) Rao, H. S. P.; Sakthikumar, L.; Vanitha, S.; Kumar, S. S. *Tetrahedron Lett.* **2003**, *44*, 4701–4704.
14. (a) Kumar, A.; Aggarwal, V.; Ila, H.; Junjappa, H. *Synthesis* **1980**, 748–751; (b) Singh, O. M.; Junjappa, H.; Ila, H. *J. Chem. Soc., Perkin Trans. 1* **1997**, *23*, 3561–3565.
15. For a nice review about S_NV reaction, see: Bernasconi, C. F.; Rappoport, Z. *Acc. Chem. Res.* **2009**, *42*, 993–1003 recent examples, see (a) Chikhalikar, S.; Bhawe, V.; Ghotekar, B.; Jachak, M.; Ghagare, M. *J. Org. Chem.* **2011**, *76*, 3829–3836; (b) Bella, M.; Schultz, M.; Milata, V. *ARKIVOC* **2012**, 242–251; (c) Ibis, C.; Tuyun, A. F. *Curr. Org. Synth.* **2011**, *8*, 861–871.
16. Jackson, S. K.; Banfield, S. C.; Kerr, M. A. *Org. Lett.* **2005**, *7*, 1215–1218.
17. Zhang, T.; Jia, Y.-M.; Yan, S.-J.; Yu, C.-Y.; Huang, Z.-T. *ARKIVOC* **2009**, 156–170.
18. Reddy, T. I.; Bhawal, B. M.; Rajappa, S. *Tetrahedron* **1993**, *49*, 2101–2108.
19. (a) Kumar, A.; Aggarwal, V.; ILa, H.; Junjappa, H. *Synthesis* **1980**, 748–751; (b) Gupta, A. K.; ILa, H.; Junjappa, J. *Synthesis* **1988**, 284–286.