Synthesis X. Bao et al. Paper

Synthesis of 3-Formylbenzenesulfonyl Chloride Derivatives

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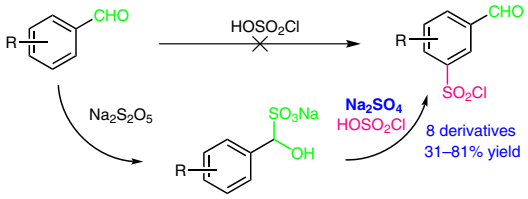

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Abstract A synthetic route to 3-formylbenzenesulfonyl chloride derivatives from the corresponding benzaldehydes has been developed. The key step in this procedure is the conversion of aldehyde bisulfite adducts to target compounds via a two-stage reaction in the presence of Na_2SO_4. A series of 3-formylbenzenesulfonyl chloride derivatives were prepared by this method and identified by chemical derivatization method.

Key words 3-formylbenzenesulfonyl chloride, aldehyde sodium bisulfite, chlorosulfonation, two-stage reaction, chemical derivatization method

3-Formylbenzenesulfonyl chloride derivatives are valuable synthetic building blocks for chemical and pharmaceutical industries. They participate in the preparation of many bioactive compounds, such as anticancer,[1] antimalarial,[2] antidiabetic,[3] antihypertensive,[4] anti-inflammatory,[5] neurological diseases drugs,[6] etc. 3-Formylbenzenesulfonyl chloride and 4-ethoxy-3-formylbenzenesulfonyl chloride are key intermediates for the preparation of Belinostat (anticancer drug)[7] and Sildenafil (erectile dysfunction drug),[8] respectively (Figure 1).

However, only a few synthetic routes to 3-formylbenzenesulfonyl chloride derivatives are reported. Yamaguchi et al. disclosed a method for the synthesis of 3-formyl-4-methoxybenzenesulfonyl chloride.[4] In this method, benzaldehyde was used as the starting material, which was first reacted with triethyl orthoformate to produce the acetal, followed by chlorosulfonylation process to provide the target sulfonyl chloride in a 72% total yield. Zhao et al. reported that salicylaldehyde protected by aniline could afford 3-formyl-4-hydroxybenzenesulfonyl chloride via chlorosulfonation and in situ deprotection during workup.[9] In these two methods, acetal and Schiff base are the synthetic strategies used to mask the reactive aldehyde group. Liu et al. developed another method for the directly preparation of 4-ethoxy-3-formylbenzenesulfonyl chloride by the reaction of chlorosulfonic acid with 2-ethoxybenzaldehyde.[10] The problem associated with these methods is the impaired substrates containing hydroxyl or alkoxy group (Scheme 1).

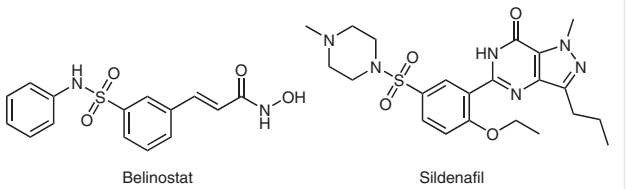
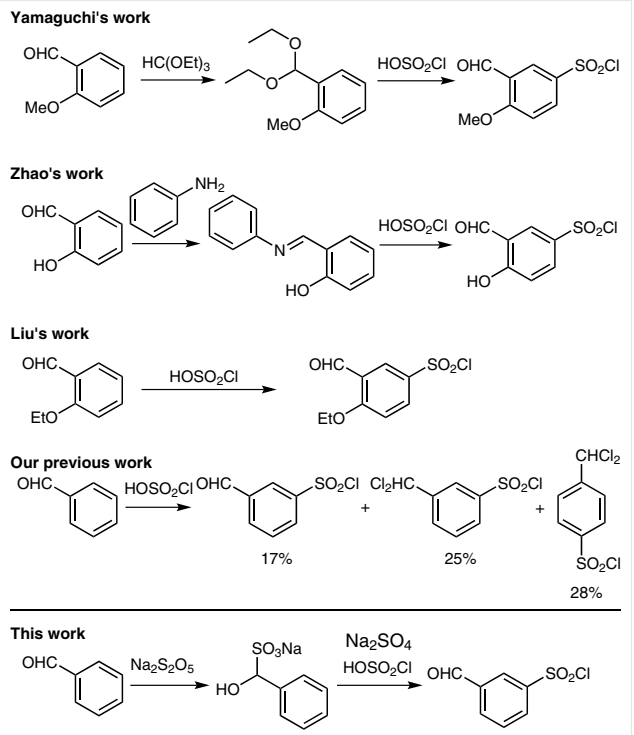


Figure 1 Structures of Belinostat and Sildenafil

Besides, commercially available 3-formylbenzenesulfonyl chloride derivatives are rare and most of them are expensive. And in our previous work,[11] we observed that the reaction of benzaldehyde and chlorosulfonic acid was inefficient for the preparation of 3-formylbenzenesulfonyl chloride. As shown in Scheme 1, only a small amount of target compound was obtained because of the generation of benzal chlorides as reported in literature.[12] Several attempts were made to prepare 3-formylbenzenesulfonyl chloride including acetal and Schiff base, but to no avail. Therefore, the development of general protocols for the preparation of 3-formylbenzenesulfonyl chloride derivatives appears to be desirable. In this paper, encouraged by Lu et al.'s report that potassium sulfate could be conducive to the preparation of benzenesulfonyl chloride,[13] we optimized a reaction of aldehyde bisulfite adducts and chlorosulfonic acid to prepare 3-formylbenzenesulfonyl chlorides and further evaluated the general applicability of this method.

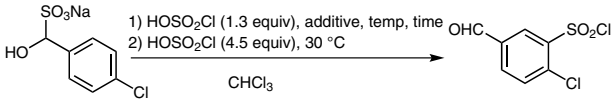


Scheme 1 Synthetic route of 3-formylbenzenesulfonyl chloride derivatives

Aldehyde bisulfite adduct was obtained according to the literature procedure.[14] Then additive, ground in advance, and the bisulfite adduct were suspended in chloroform and stirred well. Chlorosulfonic acid (1.3 equiv) was slowly dropped into the suspension and the mixture was reacted under appropriate temperature. After no starting material was detected by TLC, an additional amount of chlorosulfonic acid (4.5 equiv) was slowly added and the mixture was stirred at 30 °C for 4.5 hours. When the reaction was deemed complete, the product was isolated by column chromatography.

As shown in Table 1, we investigated the temperature of first stage: by raising the temperature, a remarkable increase in yield was observed, but when it rose to 60 °C, no improvement was observed at higher temperatures (Table 1, entries 1–4). And the reaction with incremental amount of potassium sulfate afforded a higher yield, and it reached a maximum (49–53%) when treated with more than 1 equivalent of potassium sulfate (entries 3–7). Meanwhile, several experiments were performed to investigate the influence of the type of additives (entries 9–18). Sodium sulfate, monopotassium phosphate, and potassium fluoride gave results similar to those obtained with potassium sulfate (46–53%). Almost no target compound was obtained with sodium sulfite and sodium carbonate, which might be due to the water generated from these salts retarding the reaction. Sodium bisulfate, potassium chloride, and sodium chloride gave results comparable to that obtained with no additive.

Table 1 Optimization of the Reaction Conditions

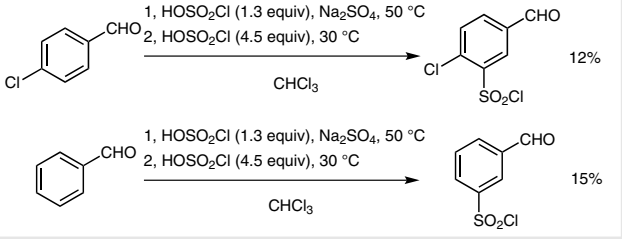


Entry	Additive (equiv)	Temp (°C)	Time (h)	Yield (%)[a]
1	K_2SO_4 (0.7)	30	14	23
2	K_2SO_4 (0.7)	40	9.5	28
3	K_2SO_4 (0.7)	50	6	44
4	K_2SO_4 (0.7)	60	6	41
5	K_2SO_4 (1)	50	6	49
6	K_2SO_4 (1.3)	50	6	52
7	K_2SO_4 (1.5)	50	6	53
8	K_2SO_4 (1.5)	60	6	47
9	Na_2SO_4 (1.3)	50	6	53
10	Na_2SO_4 (1.5)	50	6	50
11	KH_2PO_4 (1.3)	50	6	50
12	KF (1.3)	50	6	46
13[b]	Na_2SO_3 (1.3)	50	14	–
14[b]	Na_2CO_3 (1.3)	50	14	–
15	$NaHSO_4$ (1.3)	50	6	10
16	KCl (1.3)	50	6	9
17	NaCl (1.3)	50	6	8
18	–	50	6	8

[a] Isolated yield after flash column chromatography.
[b] Almost no target compound was observed by TLC.

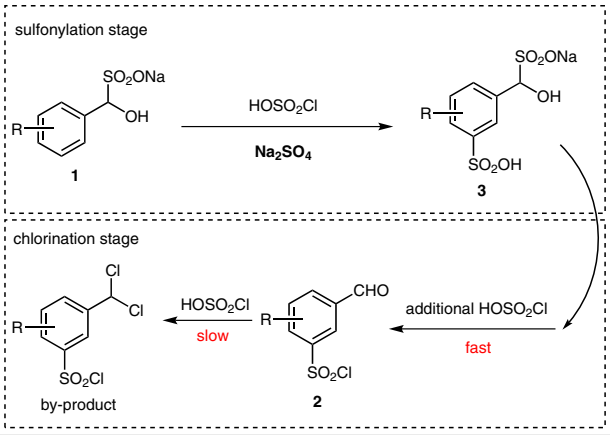
Although a satisfactory result was obtained via the reaction of aldehyde bisulfite adduct and chlorosulfonic acid in the presence of sodium sulfate, the starting material sodium α-hydroxybenzenemethanesulfonic acid was not commercially available. And in order to better understand the effect of sodium sulfate, we employed aromatic aldehydes as starting materials (Scheme 2). Unfortunately, 4-chlorobenzaldehyde could not be converted into the corresponding 3-formylbenzenesulfonyl chloride at 30 °C, while a complex mixture of product was formed in the first stage at 50 °C. And the reaction of benzaldehyde also gave an unsatisfactory yield, which was equivalent to our previous work. The poor results indicated that sodium sulfate did not retard the chlorination of the aldehyde.

Based on the above results, a plausible effect of Na_2SO_4 on the present reaction is outlined in Scheme 3. The buffering effect of the Na_2SO_4 prevented deprotection of the aldehyde during the sulfonylation stage at a slightly high temperature, and the bisulfate adduct prevented chlorination of



Scheme 2 Aromatic aldehydes employed as starting materials

the aldehyde. In detail, bisulfite adduct **1** did not convert to aldehyde smoothly in the first stage of the reaction, which might be due to Na_2SO_4 influencing the acidity of the reaction mixture. After the formation of sulfonic acid **3**, it gets converted into sulfonyl chloride **2** and bisulfite adduct was converted into aldehyde along with the addition of more chlorosulfonic acid. And the chlorination reaction rate of sulfonic acid might be faster than that of aldehyde group. Thus, 3-formylbenzenesulfonyl chloride **2** was the main product together with small amounts of benzal chloride.

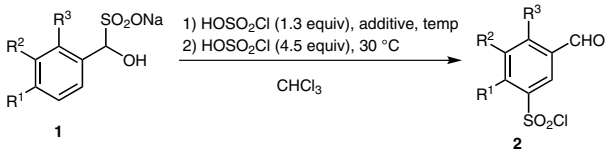


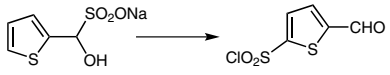
Scheme 3 Proposed mechanism for the formation of sulfonyl chlorides

The general applicability of this method was further evaluated for structurally diverse bisulfite adducts (Table 2). The aromatic nucleus with electron-donating substituents were smoothly converted into the corresponding benzenesulfonyl chlorides in good yields, while the aromatic nucleus with electron-withdrawing groups had the opposite effect. Isophthalaldehyde, 3-nitrobenzaldehyde, and 4-methyl-3-nitrobenzaldehyde were also used as substrates, but no target compound was obtained. As for these substrates, 1.3 equivalents of chlorosulfonic acid could not produce the intermediate sulfonic acid in the first stage, and 2.5 equivalents chlorosulfonic acid made the reaction mixture more complex.

The structures of these target compounds were confirmed by NMR, IR spectra, and electrospray ionization mass spectrometry (ESI-MS) analyses. When ESI-MS analyses were recorded in an Agilent 1100 Series MSD Trap SL, the quasi-molecular ion of arylsulfonyl chlorides was not observed, but quasi-molecular ion of sulfonic acids was very clear. Then the products were determined to be not sulfonic acids based on their TLC properties as well as by comparison with the authentic sulfonic acids. We postulated that arylsulfonyl chlorides hydrolyzed to the corresponding sulfonic acids when subjected to ESI-MS analyses (Figure 2).

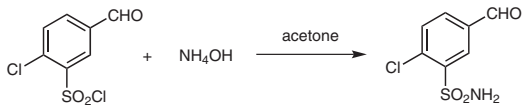
Table 2 Scope of the Present Method for the Formation of 3-Formylbenzenesulfonyl Chlorides



Product	Temp (°C)	R^1	R^2	R^3	Yield (%)[a]
2a	50	Cl	H	H	53
2b	60	Cl	H	Cl	31
2c	30	H	H	H	69
2d	30	Me	H	H	74
2e	20	MeO	H	H	80
2f	20	MeO	$ClCH_2CH_2O$	H	77
2g	20	OCH_2O		H	81
2h	20				72
2i	60	H	CHO	H	–[b]
2j	60	H	NO_2	H	–[b]
2k	60	Me	NO_2	H	–[b]

[a] Isolated yield after flash column chromatography.
[b] No target compound was obtained.

As shown in Figure 2, the IR spectrum (b) and ^1H NMR spectrum (c) further confirmed that the product obtained from this method was not 2-chloro-5-formylbenzenesulfonic acid. The sulfonic acid was obtained according to a modified literature procedure.[15] These products were not stable enough to undergo certain instrumental analysis, such as mass spectrometry, so we employed chemical derivatization method to confirm the structure. When **2a** was reacted with aqueous ammonia,[16] 2-chloro-5-formylbenzenesulfonamide (**3a**) was obtained as a white solid in high yield (Scheme 4). This conversion verified indirectly that **2a** was 2-chloro-5-formylbenzenesulfonyl chloride.



Scheme 4 Reaction of **2a** and aqueous ammonia

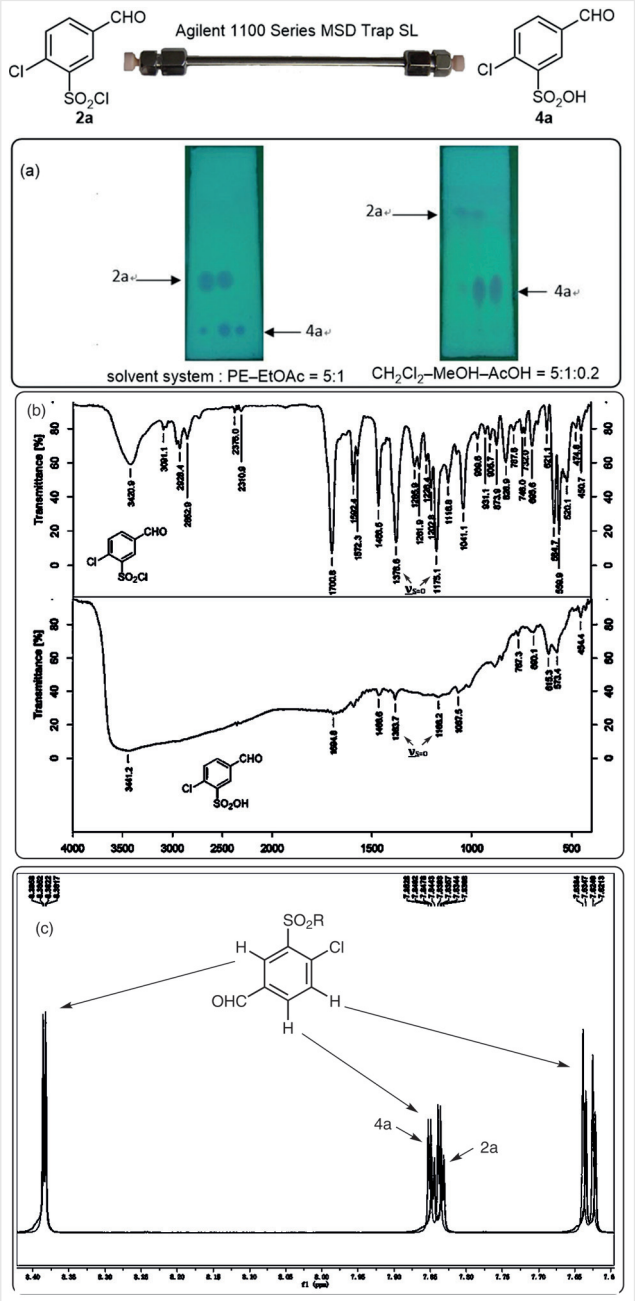


Figure 2 2-Chloro-5-formylbenzenesulfonyl chloride (**2a**) hydrolyzed to 2-chloro-5-formylbenzenesulfonic acid (**4a**). (a) TLC properties of **2a** and **4a**; (b) IR spectrum of **2a** and **4a**; (c) ^{1}H NMR spectra of **2a** and **4a**.

In conclusion, we have prepared a class of 3-formylbenzenesulfonyl chlorides via the two-stage reaction of bisulfite adduct and chlorosulfonic acid. This process provides an alternative protocol to synthesize 3-formylbenzenesulfonyl chlorides from benzaldehydes with electron-donating or weak electron-withdrawing groups. The method has a relatively wide substrate scope and the presence of Na_2SO_4 is an important factor in improving the product yield.

Solvents were purchased from commercial suppliers and used without further purification. Melting points were determined with an X-4 apparatus and were uncorrected. NMR spectra were recorded on a Bruker Ascend 400 or Bruker Avance III 600 using TMS as an internal standard. Electrospray ionization mass spectrometry (ESI-MS) analyses was recorded in an Agilent 1100 Series MSD Trap SL. The high-resolution electrospray ionization mass spectrometry (HR-ESI-MS) analyses were run using a Bruker SolariX 7.0T instrument. All experiments were conducted under an argon atmosphere. Column chromatography and TLC (HG/T2354-92, GF254), which were used to monitor the reactions, were performed on silica gel.

Sodium α-Hydroxybenzenemethanesulfonic Acids 1; General Procedure

$Na_2S_2O_5$ (6.3 g, 33 mmol) was dissolved in H_2O (15 mL), and a small amount of insoluble substance was filtered off. Then, the filtrate was added to a solution of the respective aromatic aldehyde (47 mmol) in EtOH (30 mL) over 30 min under r.t. and the reaction mixture was stirred at 45–50 °C under an atmosphere of argon for 13 h. When the reaction was deemed complete with no aromatic aldehyde detected by TLC, the heterogeneous reaction mixture was cooled to r.t., stirred for 4 h, and the product was isolated by vacuum filtration. The product cake was washed with EtOH to give the product bisulfite adduct.

3-Formylbenzenesulfonyl Chlorides 2; General Procedure

A suspension of the above corresponding bisulfite adduct (2.0 mmol, 1 equiv) and anhyd Na_2SO_4 powder (2.6 mmol, 1.3 equiv) in $CHCl_3$ were stirred at 0–5 °C, and $HOSO_2Cl$ (2.6 mmol, 1.3 equiv) was added dropwise to the suspension, and the mixture was allowed to react under appropriate temperature (Table 2). After no starting material was detected by TLC, the mixture was cooled to 0–5 °C and $HOSO_2Cl$ (9.0 mmol, 4.5 equiv) was slowly added dropwise whilst maintaining the temperature below 30 °C. When the addition was complete, the reaction mixture was stirred at 30 °C. After the completion of the reaction, the mixture was slowly poured into crushed ice. The aqueous phase was removed, and the organic phase was washed with brine and dried (anhyd Na_2SO_4). The Na_2SO_4 was filtered off and the filtrate was concentrated under vacuum to afford crude **2**, which was purified by flash column chromatography to afford the desired 3-formylbenzenesulfonyl chloride.

2-Chloro-5-formylbenzenesulfonyl Chloride (2a)

Yield: 0.26 g (53%); white solid; mp 51–52 °C; R_f = 0.32 (PE–EtOAc, 5:1).

IR (KBr): 3039, 2928, 2853, 1701, 1592, 1466, 1379, 1175, 1041, 827 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 10.05 (s, 1 H), 8.20 (d, J = 2.0 Hz, 1 H), 7.88 (dd, J = 8.2, 2.0 Hz, 1 H), 7.64 (d, J = 8.2 Hz, 1 H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 190.6, 141.3, 138.8, 136.1, 135.3, 131.5, 130.4.

MS (ESI): m/z = 218.7, 220.7 [M – Cl + OH – H]$^-$.

HRMS (ESI): m/z [M – Cl + OH – H]$^-$ calcd for $C_7H_4ClO_4S$: 218.9523; found: 218.9524.

2,4-Dichloro-5-formylbenzenesulfonyl Chloride (2b)

Yield: 0.15 g (31%); off-white solid; mp 58–61 °C; R_f = 0.40 (PE–EtOAc, 5:1).

IR (KBr): 3089, 2961, 2875, 1694, 1573, 1442, 1386, 1188, 1081, 928 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 10.43 (s, 1 H), 8.66 (s, 1 H), 7.81 (s, 1 H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 186.0, 144.0, 140.8, 138.6, 134.7, 131.3, 131.2.

MS (ESI): *m*/*z* = 252.7, 254.7 [M – Cl + OH – H]$^-$.

HRMS (ESI): *m*/*z* [M – Cl + OH – H]$^-$ calcd for $C_7H_3Cl_2O_4S$: 252.9132; found: 252.9134.

3-Formylbenzenesulfonyl Chloride (2c)

Yield: 0.33 g (69%); light yellow oil; R_f = 0.25 (PE–EtOAc, 5:1).

IR (KBr): 3077, 2846, 2740, 1700, 1596, 1434, 1383, 1204, 1162, 1074, 897 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 10.13 (s, 1 H), 8.53 (s, 1 H), 8.31–8.26 (m, 2 H), 7.85 (t, *J* = 8.0 Hz, 1 H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 189.4, 145.4, 137.3, 135.3, 131.9, 130.8, 128.0.

MS (ESI): *m*/*z* = 184.7 [M – Cl + OH – H]$^-$.

HRMS (ESI): *m*/*z* [M – Cl + OH – H]$^-$ calcd for $C_7H_5O_4S$: 184.9915; found: 184.9914.

5-Formyl-2-methylbenzenesulfonyl Chloride (2d)

Yield: 0.36 g (74%); off-white solid; mp 65–67 °C; R_f = 0.36 (PE–EtOAc, 5:1).

IR (KBr): 3066, 2980, 2842, 1704, 1606, 1447, 1368, 1171, 1034, 913 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 10.06 (s, 1 H), 8.56 (d, *J* = 1.7 Hz, 1 H), 8.14 (dd, *J* = 7.9, 1.7 Hz, 1 H), 7.64 (d, *J* = 7.8 Hz, 1 H), 2.90 (s, 3 H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 191.3, 144.6, 142.9, 135.2, 134.6, 130.4, 127.8, 20.0.

MS (ESI): *m*/*z* = 198.5 [M – Cl + OH – H]$^-$.

HRMS (ESI): *m*/*z* [M – Cl + OH – H]$^-$ calcd for $C_8H_7O_4S$: 199.0071; found: 199.0071.

5-Formyl-2-methoxybenzenesulfonyl Chloride (2e)

Yield: 0.39 g (80%); white solid; mp 66–68 °C; R_f = 0.21 (PE–EtOAc, 2:1).

IR (KBr): 3111, 2954, 2851, 1699, 1598, 1497, 1369, 1167, 1008, 837 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 9.96 (s, 1 H), 8.48 (d, *J* = 2.1 Hz, 1 H), 8.25 (dd, *J* = 8.7, 2.1 Hz, 1 H), 7.29 (d, *J* = 8.7 Hz, 1 H), 4.18 (s, 3 H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 188.6, 161.4, 137.5, 132.3, 132.3, 128.9, 113.8, 57.4.

MS (ESI): *m*/*z* = 214.5 [M – Cl + OH – H]$^-$.

HRMS (ESI): *m*/*z* [M – Cl + OH – H]$^-$ calcd for $C_8H_7O_5S$: 215.0018; found: 215.0020.

3-(2-Chloroethoxy)-5-formyl-2-methoxybenzenesulfonyl Chloride (2f)

Yield: 0.38 g (77%); white solid; mp 79–81 °C; R_f = 0.26 (PE–EtOAc, 2:1).

IR (KBr): 3080, 2963, 2842, 1684, 1595, 1510, 1437, 1361, 1270, 1165, 1020, 865 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 9.93 (s, 1 H), 8.07 (d, *J* = 1.8 Hz, 1 H), 7.74 (d, *J* = 1.8 Hz, 1 H), 4.43–4.40 (m, 2 H), 4.29 (s, 3 H), 3.96–3.92 (m, 2 H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 190.7, 155.0, 148.2, 130.0, 127.5, 124.9, 111.1, 60.0, 56.3, 41.5.

MS (ESI): *m*/*z* = 292.7, 294.7 [M – Cl + OH – H]$^-$.

HRMS (ESI): *m*/*z* [M – Cl + OH – H]$^-$ calcd for $C_{10}H_{10}ClO_6S$: 292.9891; found: 292.9892.

6-Formylbenzo[*d*][1,3]dioxole-4-sulfonyl Chloride (2g)

Yield: 0.40 g (81%); white solid; mp 88–89 °C; R_f = 0.36 (PE–EtOAc, 2:1).

IR (KBr): 3091, 2929, 2839, 1689, 1595, 1473, 1377, 1257, 1160, 1041, 888 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 9.88 (s, 1 H), 7.89 (d, *J* = 1.5 Hz, 1 H), 7.61 (d, *J* = 1.5 Hz, 1 H), 6.41 (s, 2 H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 188.1, 151.2, 150.3, 131.6, 125.6, 125.5, 111.5, 105.2.

MS (ESI): *m*/*z* = 228.8 [M – Cl + OH – H]$^-$.

HRMS (ESI): *m*/*z* [M – Cl + OH – H]$^-$ calcd for $C_8H_5O_6S$: 228.9811; found: 228.9812.

5-Formylthiophene-2-sulfonyl Chloride (2h)

Yield: 0.35 g (72%); yellow oil; R_f = 0.45 (PE–EtOAc, 5:1).

IR (KBr): 3101, 2855, 2747, 1685, 1519, 1425, 1384, 1169, 1073, 1019, 818 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 10.05 (s, 1 H), 7.94 (d, *J* = 4.1 Hz, 1 H), 7.79 (d, *J* = 4.1 Hz, 1 H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 182.6, 150.6, 150.0, 134.2, 133.7.

MS (ESI): *m*/*z* = 190.7 [M – Cl + OH – H]$^-$.

HRMS (ESI): *m*/*z* [M – Cl + OH – H]$^-$ calcd for $C_5H_3O_4S_2$: 190.9478; found: 190.9478.

2-Chloro-5-formylbenzenesulfonamide (3a)[17]

A solution of 2-chloro-5-formylbenzenesulfonyl chloride (**2a**; 0.1 g, 0.4 mmol) in acetone (1 mL) was added dropwise to aq ammonia (5 mL, 25%) below 5 °C, then the mixture was stirred at 0–5 °C for 2.5 h. When TLC analysis indicated the disappearance of **2a**, the solid obtained was collected by filtration, washed with H_2O (5 mL). The filter cake was dried in a vacuum oven at 50 °C to afford **3a** as an off-white solid; yield: 0.09 g (97%); mp 167–170 °C; R_f = 0.19 (PE–EtOAc, 2:1).

^{1}H NMR (DMSO-d_6, 600 MHz): δ = 10.08 (s, 1 H), 8.46 (d, *J* = 2.0 Hz, 1 H), 8.12 (dd, *J* = 8.2, 2.0 Hz, 1 H), 7.90 (d, *J* = 8.2 Hz, 1 H).

MS (ESI): *m*/*z* = 217.8, 219.8 [M – H]$^-$.

2-Chloro-5-formylbenzenesulfonic Acid (4a)[18]

4-Chlorobenzaldehyde (0.5 g, 3.6 mmol) was added to fuming H_2SO_4 (2 mL) at r.t. The mixture was stirred and heated at 60 °C for 7.5 h. After the completion of the reaction as monitored by TLC, the sirupy liquid was poured slowly with stirring into crushed ice (20 g). The aqueous solution was extracted with EtOAc (2 × 20 mL). The organic layers were combined and dried (anhyd Na_2SO_4). The Na_2SO_4 was filtered off and the filtrate was concentrated under vacuum to afford crude **4a**, which was recrystallized from EtOH–H_2O to afford pure white crystals of **4a**; yield: 0.57 g (73%); mp >300 °C; R_f = 0.35 (CH_2Cl_2–MeOH–AcOH, 5:1:0.2).

IR (KBr): 3441, 1695, 1466, 1434, 1384, 1166, 1067 cm^{-1}.

^{1}H NMR (DMSO-d_6, 600 MHz): δ = 10.01 (s, 1 H), 8.38 (d, *J* = 2.1 Hz, 1 H), 7.84 (dd, *J* = 8.1, 2.1 Hz, 1 H), 7.63 (d, *J* = 8.1 Hz, 1 H).

MS (ESI): m/z = 218.8, 220.8 [M – H]$^-$.

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Supporting Information

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Primary Data

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References

(1) (a) Finn, P. W.; Bandara, M.; Butcher, C.; Finn, A.; Hollinshead, R.; Khan, N.; Law, N.; Murthy, S.; Romero, R.; Watkins, C.; Andrianov, V.; Bokaldere, R. M.; Dikovska, K.; Gailite, V.; Loza, E.; Piskunova, I.; Starchenkov, I.; Vorona, M.; Kalvinsh, I. *Helv. Chim. Acta* **2005**, *88*, 1630. (b) Cervi, G.; Magnaghi, P.; Asa, D.; Avanzi, N.; Badari, A.; Borghi, D.; Caruso, M.; Cirla, A.; Cozzi, L.; Felder, E.; Galvani, A.; Gasparri, F.; Lomolino, A.; Magnuson, S.; Malgesini, B.; Motto, I.; Pasi, M.; Rizzi, S.; Salom, B.; Sorrentino, G.; Troiani, S.; Valsasina, B.; O'Brien, T.; Isacchi, A.; Donati, D.; D'Alessio, R. *J. Med. Chem.* **2014**, *57*, 10443.
(2) Oliveira, M. E.; Cenzi, G.; Nunes, R. R.; Andrighetti, C. R.; Valadão, D. M. S.; Reis, C.; Simões, C. M. O.; Nunes, R. J.; Júnior, M. C.; Taranto, A. J.; Sanchez, B. A. M.; Viana, G. H. R.; Varotti, F. P. *Molecules* **2013**, *18*, 15276.
(3) Paal, M.; Ruehter, G.; Schotten, T. Patent PCT Int. Appl. WO 0078726, **2000**.
(4) Yamaguchi, Y.; Menear, K.; Cohen, N.; Maha, R.; Cumin, F.; Schnell, C.; Wood, J. M.; Maibaum, J. *Bioorg. Med. Chem. Lett.* **2009**, *19*, 4863.
(5) Lowe, C.; Dyke, H. J.; Hanghan, A. F.; Galvin, F. C. A.; Morgan, T.; Picken, C. L. Patent PCT Int. Appl. WO 0174786, **2001**.
(6) Zimmerman, S. S.; Khatri, A.; Garnier-Amblard, E. C.; Mullasseril, P.; Kurtkaya, N. L.; Gyoneva, S.; Hansen, K. B.; Traynelis, S. F.; Liotta, D. C. *J. Med. Chem.* **2014**, *57*, 2334.
(7) Wang, Q.; Luo, J.; Cao, Y.; Zhang, L.; Li, C.; Yuan, Q. *Faming Zhuanli Shenqing Gongkai Shuomingshu* Patent CN105367455, **2016**.
(8) Achmatowicz, O.; Balicki, R.; Chmielowiec, U.; Zaworska, A.; Szelejewski, W.; Magielka, S.; Glowacka, S.; Wysoczynska, M.; Dzikowska, J.; Bober, L.; Landsberg, J.; Falkowski, C.; Roznerski, Z.; Marczak, B.; Kempa, A. Patent PCT Int. Appl. WO 0122918, **2001**.
(9) Zhao, T.; Grützke, M.; Götz, K. H.; Druzhenkob, T.; Huhn, T. *Dalton Trans.* **2015**, *44*, 16475.
(10) Liu, Y.; Zhang, Z. *Faming Zhuanli Shenqing Gongkai Shuomingshu* Patent CN1454892, **2003**.
(11) Bao, X.; Song, D.; Qiao, X.; Zhao, X.; Chen, G. *Org. Process Res. Dev.* **2016**, *20*, 1482.
(12) Wolfson, A.; Shokin, O.; Tavor, D. *J. Mol. Catal. A: Chem.* **2005**, *226*, 69.
(13) Lu, J.; Ma, H.; Han, B.; Lu, B.; Bao, X. *Faming Zhuanli Shenqing Gongkai Shuomingshu* Patent CN 102633696 A, **2012**.
(14) (a) Faul, M.; Larsen, R.; Levinson, A.; Tedrow, J.; Vounatsos, F. *J. Org. Chem.* **2013**, *78*, 1655. (b) Knight, C. J.; Millan, D. S.; Moses, I. B.; Robin, A. A.; Selby, M. D. *Org. Process Res. Dev.* **2012**, *16*, 697.
(15) Weston, A. W.; Suter, C. M. *Org. Synth.* **1941**, *21*, 27.
(16) (a) Frost, C. G.; Hartley, J. P.; Griffin, D. *Synlett* **2002**, 1928. (b) *Hawley's Condensed Chemical Dictionary*, 13th ed.; Lewis, R. J. Sr., Ed.; Wiley: New York, **1997**, 1113.
(17) Wei, W.; Cheng, D.; Liu, J.; Li, Y.; Ma, Y.; Li, Y.; Yu, S.; Zhang, X.; Li, Z. *Org. Biomol. Chem.* **2016**, *14*, 8356.
(18) Marzolph, G.; Blank, H. U. Ger. Offen DE 3016186, **1981**.