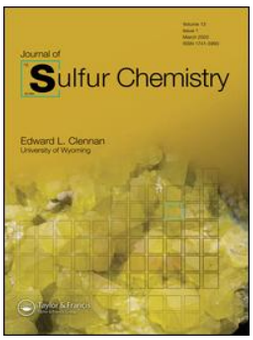

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$NaClO_2$-mediated preparation of pyridine-2-sulfonyl chlorides and synthesis of chiral sulfonamides

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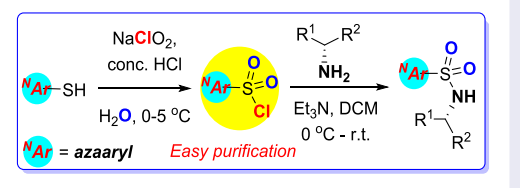
ABSTRACT

A simple method to prepare azaarenesulfonyl chlorides by $NaClO_2$-mediated oxidative chlorination of azaarenethiols have been developed, with water as the solvent. Easy purification by simple extraction and concentration gives the products in good yields. The azaarenesulfonyl chlorides readily undergo condensation with chiral amines to afford chiral sulfonamides.



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1. Introduction

Pyridine-2-sulfonyl groups have found wide applications in both organic syntheses and medicinal chemistry. From a synthetic perspective, they are widely used as directing groups in transition-metal-catalyzed sp^2 C−H activation of arylamines and azaarenes[1–8], as well as sp^3 C−H activation of amino acids or aliphatic amines, by forming bidentate 2-pyridinesulfonamide derivatives [9–11]. In addition, 2-pyridinesulfonyl groups play an important role in some stereoselective reactions such as Arrayás and Carretero's anti-stereocontrolled ring-opening of azabicyclic alkenes [12] and Toru's enantioselective C−C bond formation to sulfonylimines [13]. Some useful reagents such as Hu's difluoromethylation reagent [14–16] and Doyle's deoxyfluorination reagent [17] also have a pyridine-2-sulfonyl group as a key structural motif. In medical chemistry, various reports have demonstrated that the drug candidates with *N*-pyridinesulfonyl groups display good

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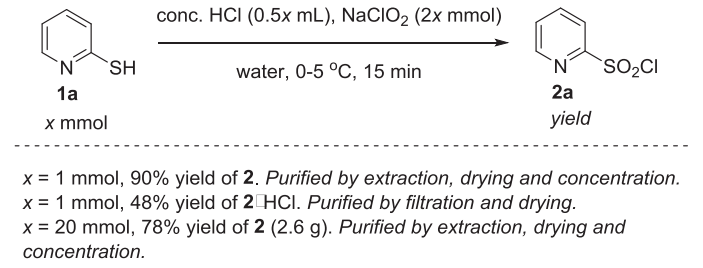
bioactivities [18–20], 2-Pyridinesulfonyl chlorides are the most important precursors to introduce the pyridinesulfonyl groups, and their syntheses have received much attention. Generally, oxidative chlorination of 2-thiopyridines with aqueous sodium hypochlorite solution (bleach) [21–23], in addition to chlorine gas [24–26] and Oxone-KCl [27], is always harnessed to achieve this goal. However, as demonstrated by Pu's [28] and our groups [29], the instability of bleach and the ambiguous content of efficient chlorine sometimes cause disappointed results, and titration is always recommended before use. In addition, the low chlorium content in bleach and a largely excessive amount of water also renders the large-scale operation less convenient. To overcome this problem, Pu and coworkers turned to 2,4-dichloro-5,5-dimethyl hydantoin, and organic waste was generated as byproduct [28]. Out of our background in developing new reactions via oxidation of low-valent organosulfur compounds with halogenium oxidants [29–37], we turned to the solid sodium chlorite, which has already been evidenced as efficient oxidizing reagent to convert aldehydes to carboxylic acids [38,39] and *S*-alkyl isothiourea salts into the corresponding sulfonyl chlorides [30]. In this work, by use of sodium chlorite, we have developed a clean and more efficient synthesis of 2-pyridinesulfonyl chlorides, and have demonstrated their application in synthesizing some chiral sulfonamides.

2. Results and discussion

According to the optimal conditions in our previous work [30], we initially tried the reaction on a 1-mmol scale, by dissolving 2-thiopyridines **(1a)** in concentrated hydrochloric acid and subsequent addition of the aqueous sodium chlorite solution at low temperature. The reaction was completed after 15 min upon addition of sodium chlorite, as indicated by TLC analysis. In light of the fact that reagent $NaClO_2$ and byproduct NaCl dissolve well in water while the product 2-pyridinesulfonyl chloride **2a** dissolves well in organic solvents, we first tried the purification by extraction with dichloromethane, drying over Na_2SO_4 and then concentrated under vaccum. Gratifyingly, desired product **2a** was obtained as a colorless oil in 90% yield. We also found that a yellow solid, which was later identified as 2-(chlorosulfonyl) pyridin-1-ium chloride, precipitated during the reaction. Another purification in a parallel reaction by filtrating the precipitates and drying at vacuum gave the hydrochloride salt of **2a** in 48% yield. When the solid hydrochloride of **2a** was dissolved in dichloromethane and then concentrated under vacuum, dehydrochlorination occurred. These two purifications gave the corresponding products in good purity, as indicated by their ^{1}H NMR spectra. As for the oxidative chlorination mechanism, our previous work suggested that the Cl and O atoms in **2a** came from sodium chlorite and water molecules, respectively [30]. Scheme 1.

The preparation was easy to scale up. On a 20-mmol scale, **2a** was prepared in a yield of 78% (2.6 g). It is noteworthy that 2-pyridinesulfonyl chloride was not so stable. After immediate purification, it was colorless. However, after being stored in a refrigerator at -4°C for two days, it became yellow. After one week, it became brown. However, our further experiments revealed that the change of color did not affect its further application (*vide post*).

With the optimal procedure, 6-methylpyridine-2-sulfonyl chloride (**2b**) and 4-methylpyridine-2-sulfonyl chloride (**2c**) were readily synthesized in satisfactory 89% and 55% yields, respectively, from the corresponding 2-thiopyridines **1b** and **1c**. Although we



Scheme 1. Trials in synthesizing 2-pyidinesulfonyl chloride.

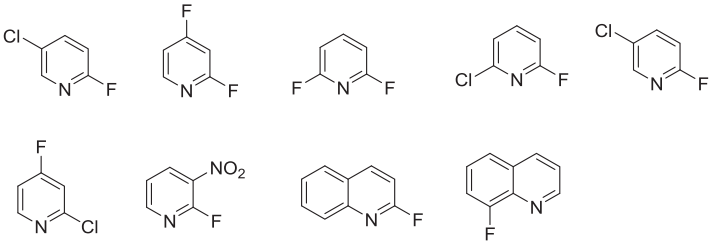


Figure 1. Failed examples for preparing azaarenethiols.

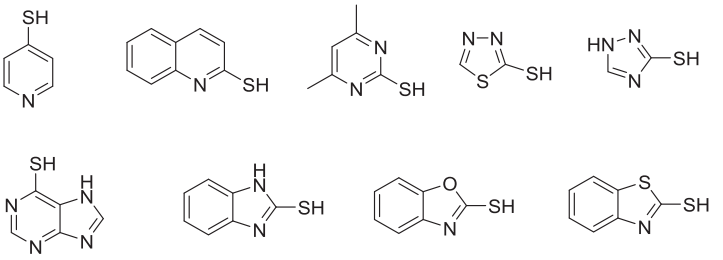
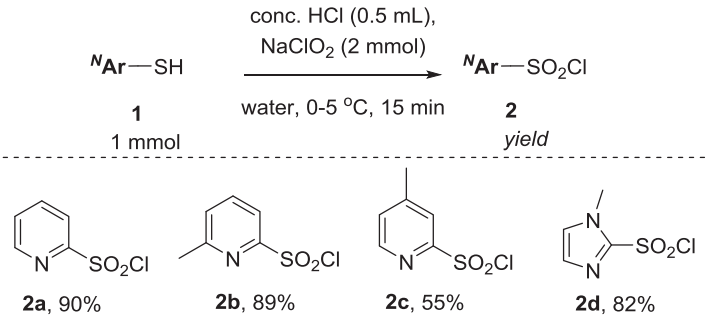


Figure 2. Failed examples for preparing azaarenesulfonyl chlorides.

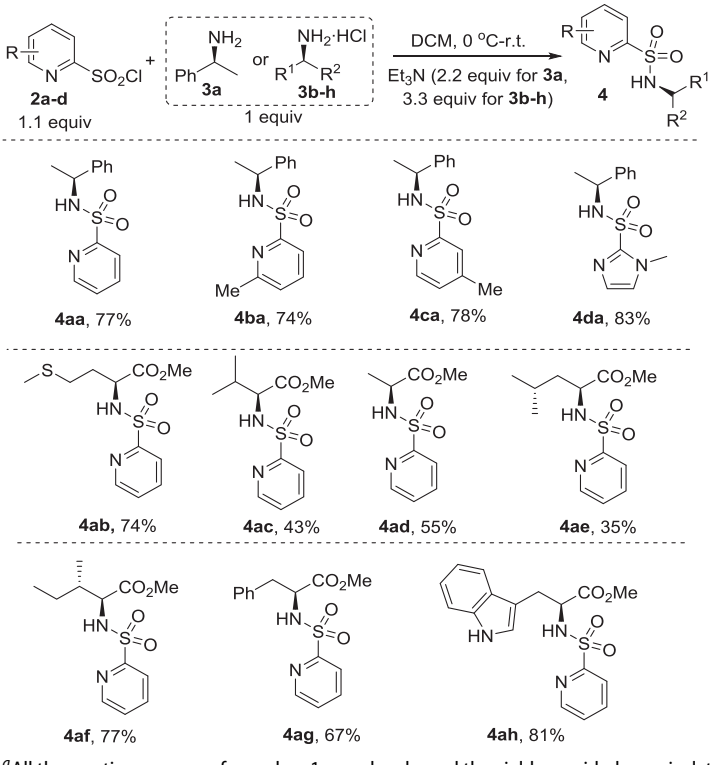
believe that this is a good method to synthesize various substituted pyridine-2-sulfonyl chlorides, the current substrate scope is severely limited by the deficient resources of different 2-thiopyridines (see Figure 1 in the Experimental section). Other heteroarenethiols were also tested under the optimal conditions (see Figure 2 in the Experimental section). However, only the reaction of 1-methyl-1*H*-imidazole-2-thiol (**1d**) gave desired sulfonyl chloride **2d** in 82% isolated yield, while the others gave desulfurative chlorination products or complex decomposed chlorination products, with complete consumption of the heteroarenethiols. Scheme 2.

With the sulfonyl chlorides in hand, we used them in the synthesis of chiral sulfonamides. The four azaarenesulfonyl chlorides **2a-d** readily reacted with L−1-phenylethylamine (**3a**) to deliver desired chiral sulfonamides **4aa**-**4da** in 74-83% yields. Next, we sought to explore the scope of chiral amines. A number of enantiopure amino acid esters salts **3b**-**h** were tested, using pyridine-2-sulfonyl chloride as the sulfonyl donor. The reactions of methyl L-methioninate (**3b**), methyl L-valinate (**3c**), and methyl L-alaninate



Scheme 2. Preparation of some azaarenesulfonyl chlorides.

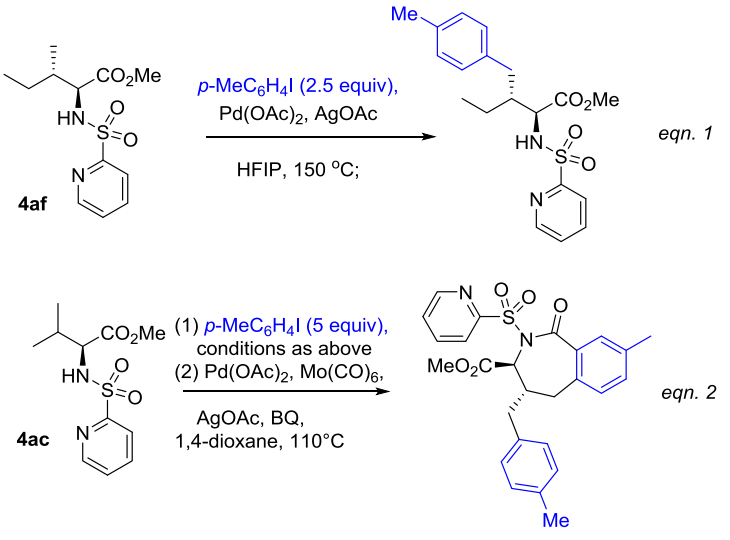
Table 1. Use of azaareneslfonyl chlorides to prepare chiral sulfonamides[a].



[a] All the reactions were performed on 1-mmol scale, and the yields provided were isolated yields from column chromatography on silica gel.

(**3d**) gave desired products **4ab**, **4ac**, and **4ad** in 74%, 43% and 55% yields, respectively. In addition, L-alaninate (**3e**), L-isoleucinate (**3f**), and L-phenylalaninate (**3 g**) also readily underwent the condensation to give chiral sulfonamides **4ae**, **4af**, **4af** in respective 35%, 77%, and 67% yields. Notably, the NH moiety in the indolyl ring of L-tryptophanate (**3 h**) did react with **2a**, while the NH_2 moiety adjacent to the ester group exclusively underwent the displacement to give **4ah** in 81% yields. Table 1.

The synthesized chiral sulfonamides have found indispensable application in the C−H activation field. For example, Carretero and coworkers found that the direct Pd-catalyzed



Scheme 3. Selected important applications of the chiral sulfonamides.

γ-arylation of **4af** occurred readily, with the *N*-(2-pyridyl) sulfonyl as directing group (Scheme 3, eqn. 1) [9]. In 2019, the same group discovered a general method to construct seven-membered ring through cascade Pd-catalyzed γ-C(sp^3)-H arylation and C(sp^2)–H carbonylation of **4ac** using $Mo(CO)_6$ as the CO source (Scheme 3, eqn. 2) [11].

3. Conclusion

We have described a simple method to prepare some azaarenesulfonyl chlorides by $NaClO_2$-mediated oxidative chlorination of azaarenethiols. Water is used as the solvent, and the products are purified by simple extraction and concentration. Some pyridine-2-sulfonyl chlorides and 1-methyl-1*H*-imidazole-2-sulfonyl chloride are successfully obtained. The azaarenesulfonyl chlorides readily undergo condensation with chiral amines to afford chiral sulfonamides, which serve as important substrates in C–H activation/functionalization, with the azaaryl moieties as directing groups.

4. Experimental section

4.1. General

All the chemicals and solvents were used directly as received. TLC analyses were performed on Yantai Chemical Co., Ltd. silica gel GF_{254} plates with petroleum ether (PE) and ethyl acetate (EA), and the plates were visualized with UV light. Products were purified with column chromatography using Qingdao Ocean Chemical Co., Ltd. silica gel (200-300 mesh) with PE and EA as eluents. Melting points were obtained on a Yanaco MP-500 melting point apparatus and are uncorrected. The specific rotation analysis was measured by Anton Paar MCP200 Polarimeter. IR spectra were taken on a Bruker FT-IR spectrometer on KBr pellets. ^1H and ^{13}C spectra were recorded on a Bruker 400 MHz spectrometer as CDCl3

solution with TMS as an internal standard. HRMS data were obtained with an Agilent LC/MS TOF mass spectrometer.

1-Methyl-1*H*-imidazole-2-thiol and pyridine-2-thiol are commercially available.

4.2. General procedure for the synthesis of pyridine-2-thiols

Prepared according to Thirtle's procedure [40]. In a 25-ml dry round-bottom flask, 1 mmol of substituted 2-fluoropyridine, 1.2 mmol of NaSH (96 mg, 70% content by weight,1.2 mol), and 10 ml of 1,2-propylene glycol were refluxed for 2 h. The reaction was cooled to room temperature. The system was washed with 10 ml of brine, extracted with ethyl acetate, dried with $NaSO_4$, and concentrated in vacuum. The resultant residue was further purified by column chromatography on silica gel (PE:EA = 2:1) to obtain the corresponding products.

4.2.1. 4-methylpyridine-2-thiol (1b)

Known compound, CAS No. 18368-65-5. Yellow liquid; Yield 88 mg, 70%; R_f = 0.25 (PE: EA = 2:1, *v/v*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 13.6 (1H, s), 7.46 (1H, d, J = 6.4 Hz), 7.4(1H, s), 6.59 (1H, dd, J = 6.8, 1.2 Hz), 2.25 (3H, s).

4.2.2. 6-methylpyridine-2-thiol (1c)

Known compound, CAS No. 18368-57-5. Yellow liquid; Yield 62 mg, 49%; R_f = 0.3 (PE: EA = 2:1, *v/v*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 13.44 (1H, s), 7.33 (1H, d, J = 8.8 Hz), 7.23 (1H, dd, J = 6.8, 1.2 Hz), 6.47 (1H, d, J = 6.8 Hz), 2.42 (3H, s).

The reactions of the following fluoropyridines or fluoroquinolines under the above conditions failed.

4.3. General procedure for the synthesis of sulfonyl chlorides.

To a 5-mL round-bottom flask was sequentially added azaarenethiol (2.0 mmol) and concentrated HCl (12 mol/L, 1.0 mL) at 0 °C in an ice bath. Subsequently, sodium chlorite (426 mg, 85% content by weight, 4 mmol) dissolved in 1 mL of water, was added dropwise within 15 min. To maintain the inner temperature of reaction mixture to no more than 5 °C, ice was intermittently added to the flask. After another 15 min, the reaction mixture was extracted by CH_2Cl_2, dried over anhydrous Na_2SO_4 and concentrated in vacuum, and the corresponding crude azaarenesulfonyl chloride was obtained.

4.3.1. Pyridine-2-sulfonyl chloride (2a)

Known compound, CAS No. 66715-65-9. Yellow liquid; Yield: 160 mg, 90%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.81-8.79 (1H, m), 8.11-8.05 (2H, m), 7.72-7.68 (1H, m).

4.3.2. 6-Methylpyridine-2-sulfonyl chloride (2b)

Known compound, CAS No. 281221-71-4. Yellow liquid; Yield: 219 mg, 89%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (2H, d, J = 4.8 Hz), 7.51 (1H, t, J = 4.8 Hz), 2.72 (3H, s).

4.3.3. 4-Methylpyridine-2-sulfonyl chloride (2c)

Known compound, CAS No. 341008-95-5. Yellow liquid; Yield: 105 mg, 55%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.64 (1H, d, J = 5.2 Hz), 7.91 (1H, s), 7.48 (1H, dd, J = 5.2 Hz, 0.5Hz), 2.54 (3H, s).

4.3.4. 1-Methyl-1H-imidazole-2-sulfonyl chloride (2d):

Known compound, CAS No. 55694-81-0. Yellow liquid; Yield: 296 mg, 82%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23(1H, s), 7.19 (1H, s), 4.03 (1H, s).

The reactions of the following azaarenethiols under the above conditions failed.

4.4. General procedure for the synthesis of chiral sulfonamides

To a dry 25-mL round-bottom flask was added chiral amine or chiral amino acid ester salt (1.0 mmol) and the solution of triethylamine (222 mg, 2.2 mmol for chiral amines, or 334 mg, 3.3 mmol for amino acid ester salts) in 5 mL of CH_2Cl_2 at 0 °C in an ice bath. Then a solution of azaarenesulfonyl chloride (1.1 mmol) in 2.5 mL of CH_2Cl_2 was added dropwise. The mixture was slowly warmed to room temperature. Upon completion of the reactions (detected by TLC analysis), the reaction mixture was washed by water (3 × 5 mL), dried over $MgSO_4$, concentrated in vacuum. The residue was further purified by column chromatography with PE and EA as eluent to obtain the corresponding chiral sulfonamide.

4.4.1. (S)-N-(1-Phenylethyl) pyridine-2-sulfonamide (4aa)

Known compound, CAS No. 872874-24-3. White solid, mp 102-103°C, Lit.[13] 103.8–105.0 °C; Yield: 204 mg, 77%; Specific rotation $[\alpha]_D^{25}$ = - 44.4 (c = 0.25, CH_2Cl_2). Lit.[13] $[\alpha]_D^{20}$ =-42.3 (c = 0.29, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55 (1H, d, J = 4.8 Hz), 7.78-7.69 (2H, m), 7.38-7.32 (1H, m), 7.2-7.1 (5H, m), 5.53 (1H, d, J = 7.6 Hz), 4.60 (1H, qui, J = 7.2 Hz), 1.47 (1H, d, J = 6.8 Hz); ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.8, 149.7, 141.6, 137.6, 128.4, 127.4, 126.3, 126.2, 122.1, 77.3, 77.0, 76.7, 54.2, 23.3. ESI-HRMS $[M+H]^+$ calcd for C13H15N2O2S$^+$ m/z 263.0849;found, 263.0849 (these two numbers are occasionally identical).

4.4.2. (S)-6-Methyl-N-(1-phenylethyl) pyridine-2-sulfonamide (4ba):

Transparent solid, mp 157–160 °C; Yield: 206 mg, 74%; Specific rotation $[\alpha]_D^{25} = +24.0$ (c = 1.0; CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64-7.56 (2H, m), 7.19-7.07 (6H, m), 5.34 (1H, d, J = 7.6 Hz), 4.56 (1H, qui, J = 7.2 Hz), 2.49 (3H, s), 1.49 (3H, d, J = 6.8 Hz); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.4, 156.8, 141.7, 137.6, 128.2, 127.8, 127.3, 126.1, 126.1, 125.8,119.1, 54.1, 24.0, 23.4. FT-IR (film, cm^{-1}): 3273, 2979, 2930, 1593, 1452, 1329, 1206, 1131, 1118, 1095, 965. ESI-HRMS $[M+H]^+$ calcd for $C_{14}H_{17}N_2O_2S^+$ m/z 277.1005; found, 277.1002.

4.4.3. (S)-4-Methyl-N-(1-phenylethyl) pyridine-2-sulfonamide (4ca):

Transparent solid, mp: 154–156 °C; Yield: 217 mg, 78%; Specific rotation $[\alpha]_D^{25} = +32.0$ (c = 1.0; CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63-7.57 (2H, m), 7.19-7.09 (6H, m), 5.34 (1H, d, J = 7.7 Hz), 4.56 (1H, qui, J = 7.1 Hz), 2.49 (3H, s), 1.49(3H, d, J = 6.9 Hz); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.4, 156.8, 141.7, 137.6, 128.2, 127.4, 126.1, 126.1, 119.1, 54.2, 24.1, 23.4. FT-IR (film, cm^{-1}): 3275, 2976, 2928, 1594, 1452, 1329, 1206, 1128, 1117,

1090, 966 cm^{-1}. HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{14}H_{17}N_2O_2S^+$ *m/z* 277.1005; found, 277.1006.

4.4.4. (S)-1-methyl-N-(1-phenylethyl)-1h-imidazole-2-sulfonamide (4da)

White solid, mp 112–114 °C; Yield: 220 mg, 83%; Specific rotation $[\alpha]_D^{25} = +91.2$ ($c = 0.4$; CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26-7.15 (5H, m), 6.97 (2H, m), 6.72 (1H, s), 4.69 (1H, qui, $J = 6.4$ Hz), 3.65 (3H, s), 1.51 (3H, d, $J = 7.2$ Hz), ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.8, 142.4, 128.8, 127.7, 126.5, 124.6, 54.7, 35.3, 23.5. FT-IR (film, cm^{-1}): 3258, 3065, 2974, 2926, 2854, 1459, 1342, 1186, 1148, 302, 632 cm^{-1}. HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{12}H_{16}N_3O_2S^+$ *m/z* 266.0958; found, 266.0960.

4.4.5. Methyl (pyridin-2-ylsulfonyl)-L-Methioninate (4ab)

White solid, mp = 91-92 °C; Yield: 225 mg, 74%; Specific rotation $[\alpha]_D^{25} = +26.0$ ($c = 0.25$, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.65 (1H, d, $J = 4.8$ Hz), 7.97 (1H, d, $J = 8.0$ Hz), 7.92 (1H, t, $J = 8.0$ Hz), 7.52-7.47 (1H, m), 5.77 (1H, d, $J = 8.8$ Hz), 4.45 (1H, td, $J = 8.4$ Hz, $J = 4.8$ Hz), 3.62 (3H, s), 2.65-2.55 (2H, m), 2.18-2.04 (1H, m), 2.07 (3H, s), 2.01-1.91 (1H, m); ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.8, 157.6, 149.6, 138.3, 126.8, 121.9, 77.3, 77.0, 76.7, 55.7, 52.6, 32.8, 29.6, 15.3. FT-IR (film, cm^{-1}): 3257, 2954, 2919, 1737, 1579, 1427, 1344, 1179. ESI-HRMS $[M+H]^+$ calcd for $C_{11}H_{17}N_2O_4S_2^+$ *m/z* 305.0635; found, 305.0624.

4.4.6. Methyl (pyridin-2-ylsulfonyl)-L-Valinate (4ac)

Known compound, CAS No. 1384331-68-3. White solid, mp = 109-110 °C, Lit.[9] 109–109 °C; Yield: 117 mg, 43%; Specific rotation $[\alpha]_D^{25} = +13.6$ ($c = 0.25$, CH_2Cl_2), Lit. [9] $[\alpha]_D = +17$ ($c = 1$, CH_2Cl_2, no temperature given by this ref.). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.62 (1H d, $J = 4.4$ Hz), 7.95 (1H, d, $J = 7.6$ Hz), 7.88 (1H, t, $J = 7.6$ Hz), 7.49-7.43 (1H, m), 5.43 (1H, d, $J = 10.0$ Hz), 4.14 (1H, dd, $J = 10.0$, 5.0 Hz), 3.56 (3H, s), 2.16-2.04 (1H, m), 0.99 (3H, d, $J = 6.8$ Hz), 0.88 (3H, d, $J = 6.8$ Hz); ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.8, 157.8, 149.6, 138.0, 126.6, 121.7, 77.3, 77.0, 76.7, 62.0, 52.2, 31.7, 18.9, 17.3. ESI-HRMS $[M+H]^+$ calcd for C11H17N2O4S$^+$ *m/z* 273.0904; found, 273.0910.

4.4.7. Methyl (pyridin-2-ylsulfonyl)-L-Alaninate (4ad)

White solid, mp = 127-128 °C; Yield: 134 mg, 55%; Specific rotation $[\alpha]_D^{25} = -2.6$ ($c = 0.15$, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.65 (1H, d, $J = 4.0$ Hz), 7.96 (1H, d, $J = 8.0$ Hz), 7.89 (1H, t, $J = 7.8$ Hz), 7.50-7.45 (1H, m), 5.68 (1H, d, $J = 10.0$ Hz), 4.35 (1H, qui, $J = 7.6$ Hz), 3.62 (3H, s), 1.43 (1H, d, $J = 7.2$ Hz); ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.6, 157.9, 149.8, 138.0, 126.7, 121.7, 77.3, 77.0, 76.7, 52.6, 52.4, 20.1. FT-IR (film, cm^{-1}): 3170, 2994, 2957, 2890, 1471, 1580, 1460, 1435, 1424, 1351, 1213, 1180. ESI-HRMS $[M+H]^+$ calcd for $C_9H_{13}N_2O_4S^+$ *m/z* 245.0591; found, 245.0594.

4.4.8. Methyl (pyridin-2-ylsulfonyl)-L-Leucinate (4ae)

Known compound, CAS No. 1384331-70-7. White solid, mp = 80-81 °C, Lit.[9] 81–83 °C; Yield: 100 mg, 35%; Specific rotation $[\alpha]_D^{25} = -5.2$ ($c = 0.25$, CH_2Cl_2), Lit.[9] $[\alpha]_D = 0$ ($c = 1$, CH_2Cl_2, no temperature given by this ref.). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.64 (1H, d, $J = 4.8$ Hz), 7.97 (1H, d, $J = 8.0$ Hz), 7.89 (1H, t, $J = 7.6$ Hz), 7.50-7.44 (1H, m), 5.36 (1H, d, $J = 9.6$ Hz), 4.34-4.26 (1H, m), 3.56 (3H, s), 1.84 (1H, sep, $J = 6.8$ Hz), 1.54

(2H, t, J = 7.2 Hz), 0.93 (6H, d, J = 6.4 Hz); ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.8, 157.8, 149.7, 138.0, 126.6, 121.8, 77.3, 77.0, 76.7, 55.4, 52.3, 42.6, 24.3, 22.8, 21.4. ESI-HRMS $[M+H]^+$ calcd for C12H19N2O4S$^+$ m/z 287.1060; found, 287.1060 (these two numbers are occasionally identical).

4.4.9. Methyl (pyridin-2-ylsulfonyl)-L-Isoleucinate (4af)

Known compound, CAS No. 1423218-69-2. White solid, mp = 95-96 °C, Lit. [9] 97–99 °C; Yield: 220 mg, 77%; Specific rotation $[\alpha]_D^{25} = +23.5$ (c = 0.2, CH_2Cl_2), Lit. [9] $[\alpha]_D = +25$ (c = 1, CH_2Cl_2, no temperature given by this ref.). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.63 (1H, d, J = 4.8 Hz), 7.96 (1H, d, J = 7.6 Hz), 7.89 (1H, t, J = 7.8 Hz), 7.50-7.42 (1H, m), 5.39 (1H, t, J = 9.4 Hz), 4.19 (1H, dd, J = 9.6, 5.2 Hz), 3.56 (3H, s), 1.87-1.80 (1H, m), 1.50-1.38 (1H, m), 1.26-1.12 (1H, m), 0.95 (3H, d, J = 7.2 Hz), 0.95 (3H, d, J = 7.4 Hz); ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.8, 157.8, 149.7, 138.0, 126.6, 121.8, 77.3, 77.0, 76.7, 61.3, 52.1, 38.6, 24.6, 15.3, 11.3. ESI-HRMS $[M+H]^+$ calcd for C12H19N2O4S$^+$ m/z 287.1060; found, 287.1062.

4.4.10. Methyl (pyridin-2-ylsulfonyl)-L-Phenylalaninate (4ag) [41]

Known compound, CAS No. 1440515-06-9. Colorless solid, mp = 79-81 °C; Yield: 173 mg, 67%; Specific rotation $[\alpha]_D^{25} = +17.6$ (c = 0.5, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.61 (1H, d, J = 4.8 Hz,), 8.12 (1H, s), 7.94-7.82 (2H, m), 7.45 (1H, t, J = 6.0 Hz), 7.28-7.19 (3H, m), 7.11 (2H, d, J = 6.4 Hz), 5.40 (1H, d, J = 8.8 Hz), 4.63 (1H, dt, J = 8.8, 5.6 Hz), 3.56 (3H, s), 3.12 (2H, d, J = 5.6 Hz); ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.2, 157.8, 149.8, 138.0, 135.0, 129.4, 128.5, 127.2, 126.6, 121.6, 77.3, 77.0, 76.7, 57.5, 52.3, 39.7. ESI-HRMS $[M+H]^+$ calcd for C15H17N2O4S$^+$ m/z 321.0904; found, 321.0905.

4.4.11. Methyl (pyridin-2-ylsulfonyl)-L-Tryptophanate (4ah)

White solid, mp = 102-105 °C; Yield: 290 mg, 81%; Specific rotation $[\alpha]_D^{25} = +7.0$ (c = 0.5, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53 (1H, d, J = 4.8 Hz), 8.12 (1H, s), 7.87 (1H, d, J = 7.6 Hz), 7.79 (1H, t, J = 7.6 Hz), 7.47 (1H, d, J = 8.0 Hz), 7.42-7.34 (1H, m), 7.31 (1H, d, J = 8.0 Hz,), 7.16 (1H, t, J = 7.6 Hz), 7.10-7.03 (2H, m), 5.47 (1H, d, J = 8.4 Hz), 4.63 (1H, dt, J = 8.4, 5.6 Hz), 3.52 (3H, s), 3.31 (2H, d, J = 5.2 Hz); ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.6, 157.5, 149.7, 137.8, 136.1, 127.2, 126.5, 123.4, 122.2, 121.6, 119.6, 118.5, 111.2, 109.0, 77.3, 77.0, 76.7, 56.8, 52.4, 29.5. FT-IR (film, cm^{-1}): 3267, 3062, 2953, 2926, 1744, 1579, 1497, 1455, 1428, 1346, 1176, 1121, 745, 702. ESI-HRMS $[M+H]^+$ calcd for $C_{17}H_{18}N_3O_4S^+$ m/z 360.1013; found, 360.1017.

Disclosure statement

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