Convenient and Environment-Friendly Synthesis of Sulfonyl Chlorides from *S*-Alkylisothiourea Salts via *N*-Chlorosuccinimide Chlorosulfonation

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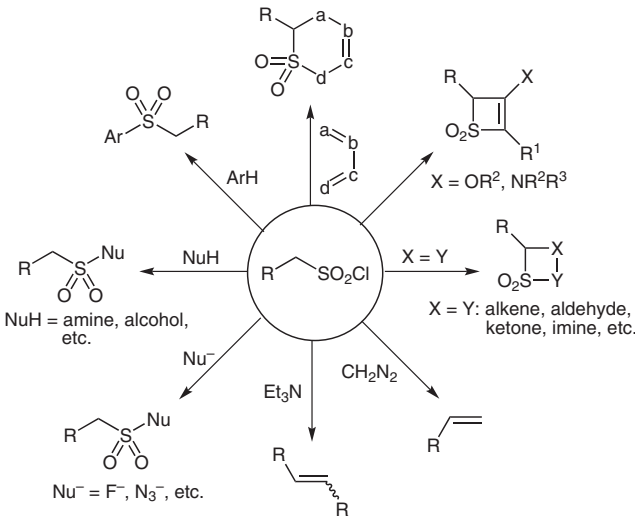
Abstract: A convenient, practical, and environmentally friendly method for the synthesis of sulfonyl chlorides has been developed. Structurally diverse sulfonyl chlorides were synthesized in moderate to excellent yields from *S*-alkylisothiourea salts, which can be easily prepared from readily accessible alkyl halides or mesylates and inexpensive thiourea, via *N*-chlorosuccinimide chlorosulfonation. In large-scale syntheses, the byproduct succinimide from 'waste water' can be conveniently converted into the starting reagent *N*-chlorosuccinimide with sodium hypochlorite (bleach) to make the method sustainable.

Key words: sulfonyl chloride, *S*-alkylisothioruea, *N*-chlorosuccinimide, chlorosulfonation, synthesis

Alkanesulfonyl chlorides are a class of significantly important compounds that have been widely applied as intermediates in synthetic organic chemistry and as building blocks in medicinal chemistry.[1] An important source of the sulfonyl group, alkanesulfonyl chlorides, are involved in many reactions for the construction of various molecules containing the sulfonyl group (Scheme 1).[2] For example, in the presence of base, alkanesulfonyl chlorides can react with compounds containing unsaturated bonds, such as imines,[2d–h] aldehydes,[2i] ketones,[2j] electron-rich olefins[2k–m] and alkynes,[2n–p] and diene-type reagents,[2u–w] to form the corresponding four- and six-membered ring systems. Sulfonyl chlorides can react with alkenes and arenes with aluminum trichloride catalysis to produce the corresponding sulfones.[2x–aa] Sulfonyl chlorides can also be attacked by a series of nucleophiles.[1a–d] For example, reactions with alcohols and amines generate sulfonates and sulfonamides, respectively.[2a,b] In the pharmaceutical field, sulfonamides are common subunits in many medicines,[3] therefore, these reactions have been widely used to construct bioactive structures. Nucleophilic displacements of sulfonyl chlorides with fluoride and azide anions can give sulfonyl fluorides[2s] and sulfonyl azides,[2t] respectively. These derivatives play an important role in both synthetic and medicinal chemistry, and the latter have been reported to possess bioactivity.[2s] Additionally, reactions of alkanesulfonyl chlorides with diazomethane can yield terminal olefins,[2q] while treatment of alkanesulfonyl chlorides with a base such as triethylamine can afford symmetrical olefins.[2r]



Scheme 1 Diverse reactions of alkanesulfonyl chlorides

As a result of their great importance and wide applications in laboratory-scale synthesis and industrial production, several groups have developed methods for the synthesis of sulfonyl chlorides.[4,5] In general, sulfonyl chlorides can be accessed by the chlorination of the corresponding sulfonic acids or their sodium salts with chlorinating reagents,[4] or by the oxidative chlorination of sulfur-containing compounds, including thiols, disulfides, thioacetates, and thiocarbamates, with oxidative chlorinating reagents.[5] The first method has many drawbacks, such as harsh reaction conditions, long reaction time, low functional group tolerance, the use of excess chlorinating reagent, and acidic and/or toxic byproducts. Therefore, increased attention has been paid to the second method. This method, however, always involves the utilization of hazardous and toxic chlorine gas, which is not conveniently handled on a laboratory-scale operation. Hence, a series of mild oxidative chlorinating reagents hydrogen peroxide/thionyl chloride,[5a–d] ozone/thionyl chloride,[1g] sulfuryl chloride/potassium nitrate,[5e] bromine/phosphoryl chloride,[5f] *N*-chlorosuccinimide/hydrochloric acid,[5g–j] and chlorotrimethylsilane/potassium nitrate [5k] have been developed to circumvent the use of chlorine gas.[6] Nevertheless, most sulfur-containing substrates (thiols, disulfides, and thioacetates) or their precursors (e.g., thioacetic acid) employed in the mild oxidative chlorination step possess strong and repulsive odors; thiols can be detected at a level of 0.01 ppm by the human nose.[7] They are toxic pollut-

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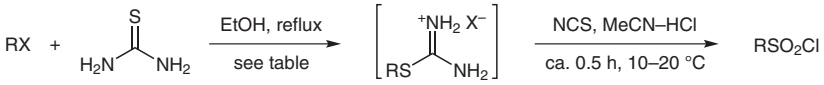
ants in the environment and they do great harm to human respiratory system. Therefore, the preparation of sulfonyl chlorides in an operationally simple and environmentally friendly way still remains a challenge.

In our opinion, the best strategy to overcome the drawbacks in the second method is to find an environmentally benign sulfur resource. Among many sulfur resources we considered, *S*-alkylisothiourea salts, which can be readily prepared from alkyl halides and thiourea, stand out as the best choice because of their odorless, clean, and harmless properties. The oxidative chlorosulfonation of *S*-alkylisothiourea salts to sulfonyl chlorides was first realized by Sprague and co-workers in 1937;[8] chlorine gas has been the predominant reagent for the chlorosulfonation of *S*-alkylisothiourea salts to sulfonyl chlorides.[9] Several oxidative chlorinating reagents were developed instead of chlorine gas, such as hydrogen peroxide/hydrochloric acid and potassium permanganate/hydrochloric acid in the synthesis of methanesulfonyl chloride from *S*-methylisothiourea salt,[10] hydrochloric acid treated silica gels and iodosobenzene in the solid synthesis of phenylmethanesulfonyl chloride from *S*-benzylisothiourea salt,[11] and sodium chlorate/hydrochloric acid in the synthesis of acyclic phthalimidoalkanesulfonyl chlorides from the corresponding *S*-phthalimidoalkylisothiourea salts.[12] Although suffering from different drawbacks, these facts convinced us that *S*-alkylisothiourea salts are suitable sulfur resources in our pursuit of an operationally simple and environmentally friendly synthesis of sulfonyl chlorides. Next, we searched for an efficient, facile, reliable, and operationally simple oxidative chlorinating reagent. Among so many oxidative chlorinating reagents involved in the preparation of sulfonyl chlorides, only two, *N*-chlorosuccinimide/hydrochloric acid [5g–j] and hydrogen peroxide/thionyl chloride,[5a–d] seem to be suitable candidates due to their easy access, safe handling, and simple operation. However, in our previous large-scale preparation of phenylmethanesulfonyl chloride (50-mmol scale) from phenylmethanethiol, we found that the reaction became uncontrollable with the hydrogen peroxide/thionyl chloride reagent. But under the *N*-chlorosuccinimide/hydrochloric acid oxidative chlorinating conditions, the reaction proceeded smoothly and gave a high yield. Hence, *N*-chlorosuccinimide/hydrochloric acid should be a suitable choice for transforming *S*-alkylisothiourea halides into sulfonyl chlorides. *S*-Alkylisothiourea halides are intermediates or precursors in the synthesis of thiols from alkyl halides. Herein, we present our results on the direct preparation of sulfonyl chlorides from *S*-alkylisothiourea halides by *N*-chlorosuccinimide oxidative chlorosulfonation.

We first examined our assumption by submitting *S*-benzylisothiourea chloride to *N*-chlorosuccinimide/hydrochloric acid chlorosulfonation conditions. *S*-Benzylisothiourea chloride was readily prepared by refluxing benzyl chloride with thiourea in ethanol for 30 minutes. After removal of the solvent, the crude product was directly subjected to oxidative chlorosulfonation without further purification. On the basis of the fact that both the *S*-alkylisothiourea chloride and the phenylmethanethiol contain only one sulfur atom, we used the reaction conditions optimized by Nishiguchi et al.[5h] for our reaction. Gratifyingly, the desired product phenylmethanesulfonyl chloride (**3a**) was obtained in 96% yield with very high efficiency (Table 1, entry 1). Most importantly, the troublesome problem caused by the strong odor of thiol derivatives in previous oxidative chlorination methods was successfully circumvented.

Table 1 Synthesis of Structurally Diverse Alkanesulfonyl Chlorides[a]



1 **2** **3**

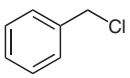
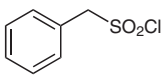
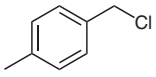
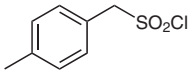
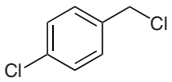
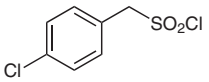
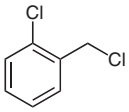
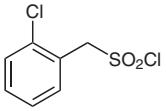
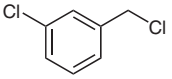
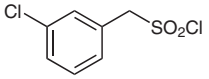
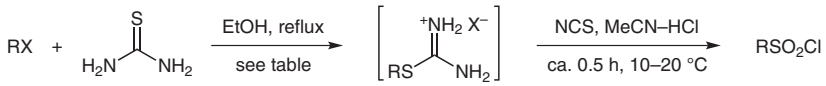
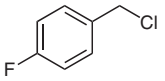
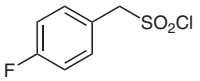
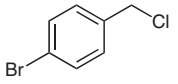
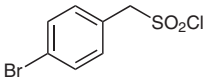
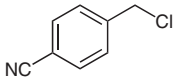
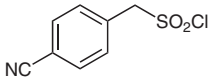
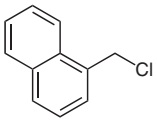
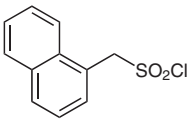
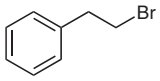
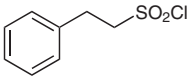
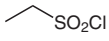
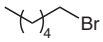
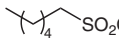
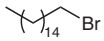
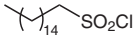
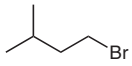
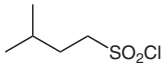
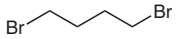
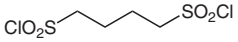
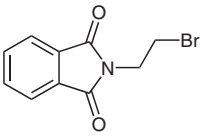
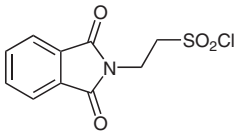
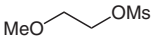
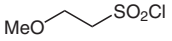
Entry	Alkyl halide or mesylate	Time[b] (h)	Product	Yield[c] (%)
1	**1a** 	0.5	**3a** 	96
2	**1b** 	0.5	**3b** 	98
3	**1c** 	0.5	**3c** 	98
4	**1d** 	0.5	**3d** 	99
5	**1e** 	0.5	**3e** 	98

Table 1 Synthesis of Structurally Diverse Alkanesulfonyl Chlorides[a] (continued)



1 **2** **3**

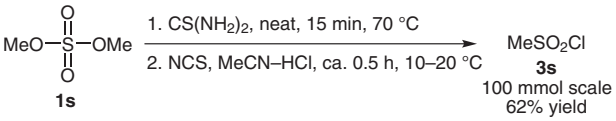
Entry	Alkyl halide or mesylate	Time[b] (h)	Product	Yield[c] (%)
6	**1f** 	0.5	**3f** 	98
7	**1g** 	0.5	**3g** 	97
8	**1h** 	0.5	**3h** 	24
9	**1i** 	0.5	**3i** 	75[d]
10	**1j** 	1	**3j** 	92
11	**1k** 	1	**3k** 	78
12	**1l** 	1	**3l** 	98
13[e]	**1m** 	1	**3m** 	95
14	**1n** 	1	**3n** 	85
15	**1o** 	1	**3o** 	45
16[e,f]	**1p** 	1	**3p** 	99
17	**1q** 	1	**3q** 	62[g]
18	**1r** 	1	**3r** 	90

[a] Reaction conducted on a 5-mmol scale using equimolar alkyl halide and thiourea.
[b] Reflux time of alkyl halide and thiourea in EtOH.
[c] Isolated yield obtained by flash chromatography for 2 steps.
[d] Starting material **1i** (25%) was recovered.
[e] Reaction conducted at 30–40 °C.
[f] The amounts of thiourea, NCS, 2 M HCl, and MeCN were doubled.
[g] *N*-(2-Bromoethyl)phthalimide (30%) was recovered.

After the successful preparation of phenylmethanesulfonyl chloride, we synthesized a series of important sulfonyl chlorides by the same protocol. The results are presented in Table 1. The extension of the substrate scope commenced with the modification of the phenyl ring of benzyl chloride. Introducing the electron-donating methyl group in the phenyl ring of benzyl chloride did not affect the reaction efficiency and the desired product **3b** was obtained in 98% yield (entry 2). Reactions of various halo-modified benzyl chlorides also proceeded smoothly in excellent yields varying from 97 to 99%, regardless of the halogen and its position (entries 3–7). However, when the stronger electron-withdrawing cyano group was introduced at the *para* position, the yield decreased drastically to 24% (entry 8), presumably due to the high reactivity of 4-cyanophenylmethanesulfonyl chloride (**3h**) with water. The preparation of naphthalen-1-ylmethanesulfonyl chloride (**3i**) was performed successfully in 75% yield (entry

9). 2-Phenylethanesulfonyl chloride (**3j**) was obtained in a good 92% yield (entry 10). Considering the importance of aliphatic alkanesulfonyl chlorides in synthetic chemistry and the field of surfactants, we examined the use of our method in the synthesis of these compounds. Ethane- (**3k**), hexane- (**3l**), and hexadecanesulfonyl chlorides (**3m**) were readily prepared in 78%, 98%, and 95% yields, respectively (entries 11–13). The lower yield of ethanesulfonyl chloride was presumably attributed to the incomplete reaction of bromoethane with thiourea because of the volatility of bromoethane. Branched 3-methylbutane-1-sulfonyl chloride (**3n**) was also accessed in a satisfactory 85% yield (entry 14). Not only primary but also a secondary sulfonyl chloride, butane-2-sulfonyl chloride (**3o**), was synthesized, albeit in a moderate 45% yield (entry 15); this moderate yield was a result of elimination from 2-bromobutane when it was refluxed with thiourea.[8] Surprisingly, butane-1,4-disulfonyl dichloride (**3p**), which was prepared previously in a low yield from butane-1,4-dithiol by oxidative chlorosulfonation with hazardous chlorine gas[13] or from sodium butane-1,4-disulfonate with a toxic chlorinating reagent,[14] was readily synthesized in an excellent 99% yield (entry 16). Finally, we wished to synthesize β-functionalized sulfonyl chlorides. It is noteworthy that the N-protected β-aminoethanesulfonyl chloride **3q**, which is widely used as a building block in the synthesis of sulfonopeptides,[15] was accessed in a moderate 62% yield. In addition to alkyl halides, the functionalized mesylate **1r** was also examined; refluxing mesylate **1r** with thiourea for 30 minutes and then chlorosulfonation with *N*-chlorosuccinimide gave sulfonyl chloride **3r** in a good 90% yield (entry 18). The results indicate that not only alkyl halides, but also compounds with good leaving groups are suitable substrates for the preparation of sulfonyl chlorides by our method.

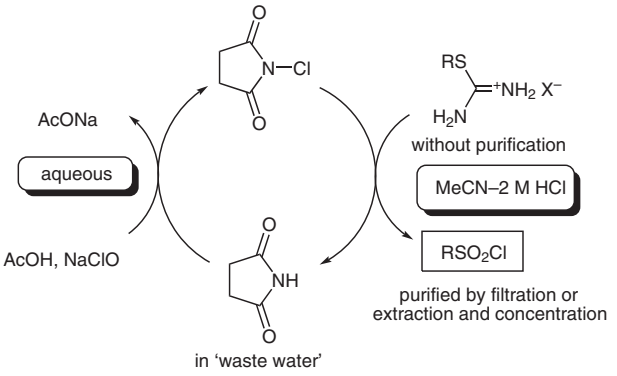
Regarding the significant importance and wide application of methanesulfonyl chloride in both synthetic and pharmaceutical fields, we then directed our effort to the large-scale synthesis of methanesulfonyl chloride. In consideration of the high volatility and high cost of iodomethane, we decided to use dimethyl sulfate in its place. Heating dimethyl sulfate with thiourea without solvent at 70 °C for 15 minutes afforded a white solid that was directly subjected to the oxidative chlorosulfonation conditions to give the desired product, methanesulfonyl chloride (**3s**), in 62% yield (Scheme 2). Based on our previous studies that almost all the aliphatic halides and mesylates were consumed completely, a convenient method to purify methanesulfonyl chloride was devised. In the workup process of the large-scale synthesis, after removal of the acetonitrile at 1.34 mbar and 15 °C, a large amount of water was added, following this the mixture was extracted with diethyl ether, the ethereal extracts were dried, and the solvents were removed. By this method, methanesulfonyl chloride was obtained in high purity as indicated by ^{1}H NMR and no further purification was required. The workup process presents a general, convenient method for the isolation and purification of oily alkanesulfonyl chlorides that are generally purified by operationally complex, poorly secure, and yield-lowering vacuum distillation.



Scheme 2 Large-scale synthesis of methanesulfonyl chloride

In previous small-scale (5 mmol) synthesis of sulfonyl chlorides, the products were isolated and purified by silica gel column chromatography. However, in large-scale synthesis, separation by column chromatography is not practical or economical. Inspired by the workup process in the preparation of methanesulfonyl chloride (**3s**), we also devised a convenient method for the purification of the solid alkanesulfonyl chlorides in large-scale preparations. Verification commenced with the 250-mmol scale synthesis of phenylmethanesulfonyl chloride (**3a**). After completion of the reaction, the acetonitrile was removed as described above, followed by the addition of large amount of water. The resultant white solid was filtered and dried to give desired product in 93% yield with very high purity. By using this workup procedure, we synthesized several solid alkanesulfonyl chlorides in good to excellent yields and high purity. The results are listed in Table 2.

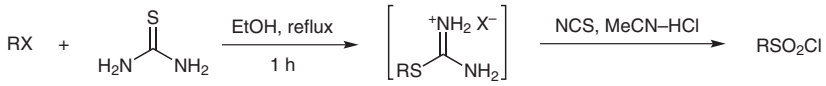
In the large-scale synthesis of alkanesulfonyl chlorides, the byproduct succinimide was left in the aqueous phase. Since *N*-chlorosuccinimide can be readily prepared on an industrial scale by treating succinimide with sodium hypochlorite and acetic acid in aqueous media,[16] we improved our method in a sustainable way by converting the byproduct succinimide from the 'waste water' into the starting reagent *N*-chlorosuccinimide. The process is outlined in Scheme 3.



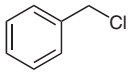
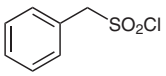
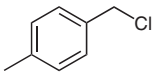
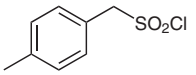
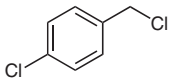
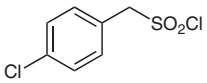
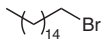
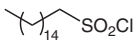
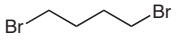
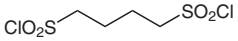
Scheme 3 Large-scale, convenient, and sustainable synthesis of sulfonyl chlorides by *N*-chlorosuccinimide chlorosulfonation

The detailed proposed mechanism for the formation of sulfonyl chlorides from *S*-alkylisothiourea salts via the *N*-chlorosuccinimide chlorosulfonation is shown in Scheme 4. In the presence of aqueous acidic solution, the *S*-alkylisothiourea salt is oxidized to the corresponding alkylsulfonyl methanimidamide salt **4** via two consecutive

Table 2 Large-Scale Synthesis of Alkanesulfonyl Chlorides[a]



1 **2** **3**

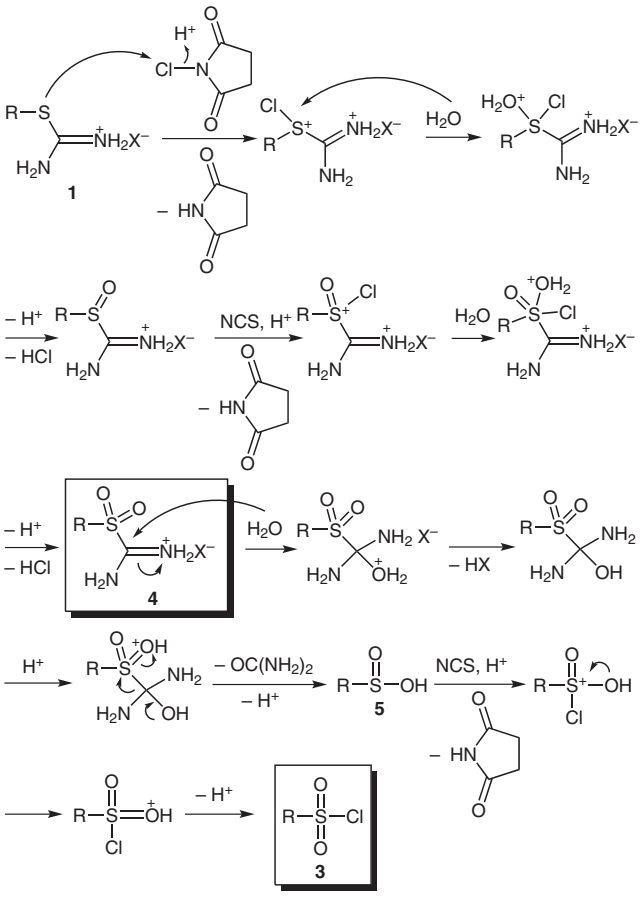
Entry	RX		Product		Yield[b] (%)
1	**1a**		**3a**		93
2	**1b**		**3b**		86
3	**1c**		**3c**		96
4[c]	**1m**		**3m**		92
5[c,d]	**1p**		**3p**		99

[a] Entry 1 was conducted on a 250-mmol scale, and entries 2–5 on a 50-mmol scale, based on starting materials.
[b] Isolated yield for 2 steps.
[c] Reaction conducted at 30–40 °C.
[d] The amounts of thiourea, NCS, 2 M HCl, and MeCN were doubled.

oxidation steps by *N*-chlorosuccinimide. Due to the high electrophilicity of the methanimidamide salt moiety with an electron-withdrawing sulfonyl group, the intermediate **4** undergoes a facile reaction with water. Consequently, through a sequence of attack by water, leaving of X^- anion, proton transfer, and leaving of protonated urea, **4** is converted into the corresponding sulfinic acid **5**, similar to the process in the oxidation of xanthates.[17] Sulfinic acid **5** undergoes a further *N*-chlorosuccinimide oxidation and elimination of a proton to give rise to the corresponding sulfonyl chloride **3**.

In conclusion, we have developed an operationally simple and environmentally friendly method for the synthesis of various sulfonyl chlorides from alkyl halides (including their equivalents sulfonates and sulfates) and thiourea. The method shows very high efficiency and most desired products are obtained in satisfactory to excellent yields. Compared with reported methods, our method has the advantages that it is not only operationally simple and environmentally friendly, but also purification in large-scale syntheses is easy and the byproduct can be sustainability converting into the starting reagent.

All the starting materials, solvents and reagents were used directly as received, without further purification. Melting points were obtained on a Yanaco MP-500 melting point apparatus and are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker 400 spectrometer with TMS as an internal standard in $CDCl_3$ solution and the chemical shifts (δ) are reported in parts per million (ppm). TLC separations were performed on silica gel GF_{254} plates, and the plates were visualized with UV light. For the column chromatography purification of the sulfonyl chlorides that do not contain chromagenic groups, Et_3N was used to detect the products. Petroleum ether (bp 60–90 °C) = PE.



Scheme 4 Proposed mechanism for the formation of sulfonyl chlorides from *S*-alkylisothiourea salts via *N*-chlorosuccinimide chlorosulfonation

Sulfonyl Chlorides 3a–r; General Procedure
Alkyl halide (or sulfonate) (5 mmol) and thiourea (0.387 g, 5 mmol) were refluxed together in EtOH (5 mL) for the time indicated in Table 1. After removal of EtOH at reduced pressure, the obtained solid or sticky oil was slowly added to a mixture of NCS (2.67 g, 20 mmol for alkyl chloride/mesylate; 3.34 g, 25 mmol for alkyl bromide), 2 M HCl (1.35 mL for alkyl chloride/mesylate, 1.62 mL for alkyl bromide), and MeCN (8 mL) in a 10 °C water bath to maintain the internal temperature between 10 and 20 °C. When the reaction was complete (~15 min), Et_2O (15 mL) was added and the resulting solution was partitioned by addition of H_2O (15 mL). The organic phase was separated, dried (Na_2SO_4), and concentrated under reduced pressure. The residue was subjected to flash column chromatography (silica gel; PE–EtOAc, 5:1) to afford the desired product.

Methanesulfonyl Chloride (3s)
Dimethyl sulfonate (6.31 g, 50 mmol) and thiourea (7.62 g, 100 mmol) were heated at 70 °C for 15 min to afford a white solid that was washed with Et_2O to remove excess dimethyl sulfonate. This solid was slowly added to a mixture of NCS (53.4 g, 400 mmol), 2 M HCl (27 mL), and MeCN (160 mL) following the general procedure. After completion of the reaction, MeCN was removed on a rotary evaporator (15 °C/1.33 mbar). A large amount of H_2O was added and the aqueous solution was extracted with Et_2O; the ether extract was dried (Na_2SO_4) and the solvent was removed to afford methanesulfonyl chloride (**3s**) (7.09 g, 62%) as a colorless oil that did not require further purification.

Large-Scale Preparation of Phenylmethanesulfonyl Chloride (3a); Typical Procedure
BnCl (31.65 g, 250 mmol) and thiourea (19.03 g, 250 mmol) were refluxed together in EtOH (250 mL) for 1 h. After removal of EtOH at reduced pressure, the obtained solid was slowly added to a mixture of NCS (133.53 g, 1000 mmol), 2 M HCl (67.5 mL), and MeCN (400 mL) over 30 min following the general procedure. After completion of the reaction, the MeCN was removed on a rotary evaporator (15 °C/1.33 mbar). Then H_2O (300 mL) was added, and the white solid was filtered and dried under an infrared lamp to afford **3a** (44.33 g, 93%), which did not require further purification.

Conversion of Succinimide to *N*-Chlorosuccinimide
To a 3-necked round-bottom flask equipped with a thermometer and a 100-mL addition funnel was sequentially added AcOH (10.5 mL), H_2O (20 mL), and 'waste water' (35 mL) containing succinimide (ca. 80 mmol). The mixture was cooled in an ice-water bath to make sure the internal temperature was less than 5 °C. Bleach (50 mL, 10%) was slowly added through the addition funnel. During the addition, the inner temperature was controlled to be less than 8 °C. When the addition was complete, the mixture was stirred for a further 1 h, the mixture was filtered, and the filter cake was washed with H_2O (30 mL) and dried under an infrared lamp to give *N*-chlorosuccinimide (9.6 g, yield ca. 90%) as a white powder; mp 150–152 °C (Lit.[16] 148–150 °C).

All the sulfonyl chlorides synthesized are known compounds. The ^{1}H NMR spectra and melting points for the solid products are identical with those reported.

Phenylmethanesulfonyl Chloride (3a)
Colorless crystals; on a 5-mmol scale, yield: 0.910 g (96%); on a 250-mmol scale, yield: 44.33 g (93%); mp 90–91 °C (Lit.[5h] 91–93 °C).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.45–7.40 (m, 5 H), 4.83 (s, 2 H).

***p*-Tolylmethanesulfonyl Chloride (3b)**
Colorless crystals; on a 5-mmol scale, yield: 1.051 g (98%); on a 50-mmol scale, yield: 8.56 g (86%); mp 84–85 °C (Lit.[18] 73–75 °C).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.38–7.26 (m, 4 H), 4.83 (s, 2 H), 2.39 (s, 3 H).

(4-Chlorophenyl)methanesulfonyl Chloride (3c)
Colorless crystals; on a 5-mmol scale, yield: 1.020 g (98%); on a 50-mmol scale, yield: 10.76 g (96%); mp 90–92 °C (Lit.[5h] 92–93 °C).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.46–7.42 (m, 4 H), 4.83 (s, 2 H).

(2-Chlorophenyl)methanesulfonyl Chloride (3d)
Colorless crystals; yield: 1.110 g (99%); mp 59–61 °C (Lit.[19] 55–59 °C).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.61–7.35 (m, 4 H), 5.12 (s, 2 H).

(3-Chlorophenyl)methanesulfonyl Chloride (3e)
Colorless crystals; yield: 1.100 g (98%); mp 74–76 °C (Lit.[20] 72–73 °C).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.48–7.37 (m, 4 H), 4.83 (s, 2 H).

(4-Fluorophenyl)methanesulfonyl Chloride (3f)[21]
Colorless crystals; yield: 1.022 g (98%); mp 66–67 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.49–7.13 (m, 4 H), 4.84 (s, 2 H).

(4-Bromophenyl)methanesulfonyl Chloride (3g)[22]
Colorless crystals; yield: 1.311 g (97%); mp 125–127 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.61–7.35 (m, 4 H), 4.81 (s, 2 H).

(4-Cyanophenyl)methanesulfonyl Chloride (3h)
Colorless crystals; yield: 0.254 g (24%); mp 105–106 °C (Lit.[23] 102–103 °C).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.78–7.62 (m, 4 H), 4.91 (s, 2 H).

Naphthalen-1-ylmethanesulfonyl Chloride (3i)
Yellowish oil; yield: 0.676 g (75% brms).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.08–7.51 (m, 7 H), 5.39 (s, 2 H).

2-Phenylethanesulfonyl Chloride(3j)[24]
Yellowish oil; yield: 0.934 g (92%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.38–7.20 (m, 5 H), 3.99–3.88 (m, 2 H), 3.36–3.30 (m, 2 H).

Ethanesulfonyl Chloride (3k)[8]
Yellowish oil; yield: 0.501 g (78%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.74 (q, *J* = 7.3 Hz, 2 H), 1.57 (t, *J* = 7.3 Hz, 3 H).

Hexane-1-sulfonyl Chloride (3l)[8]
Yellowish oil; yield: 0.904 g (98%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.76–3.65 (m, 2 H), 2.08–1.98 (m, 2 H), 1.50–1.35 (m, 6 H), 0.91 (t, *J* = 6.2 Hz, 3 H).

Hexadecane-1-sulfonyl Chloride (3m)
Colorless crystals; on a 5-mmol scale, yield: 1.540 g (95%); on a 50-mmol scale, yield: 14.95 g (92%); mp 51–52 °C (Lit.[8] 52–53 °C).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.75–3.51 (m, 2 H), 2.06–2.02 (m, 2 H), 1.49–1.26 (m, 26 H), 0.88 (t, *J* = 6.2 Hz, 3 H, CH_3).

3-Methylbutane-1-sulfonyl Chloride (3n)[25]
Yellowish oil; yield: 0.726 g (85%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.76–3.65 (m, 2 H), 1.96–1.88 (m, 2 H), 1.84–1.74 (m, 1 H), 0.99 (d, *J* = 6.4 Hz, 6 H).

Butane-2-sulfonyl Chloride (3o)[8]
Yellowish oil; yield: 0.352 g (45%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.50 (ddq, *J* = 6.7, 7.4, 7.4 Hz, 1 H), 2.26 (ddq, *J* = 7.4, 14.4, 7.4 Hz, 1 H), 1.77 (ddq, *J* = 7.4, 14.4, 7.4 Hz, 1 H), 1.57 (dd, *J* = 6.7, 25 Hz, 3 H), 1.12 (dd, *J* = 7.4, 7.4 Hz, 3 H).

Butane-1,4-disulfonyl Dichloride (3p)[13,14]
Prepared using 1,4-dibromobutane (**1p**, 5 mmol), thiourea (10 mmol), NCS (40 mmol), 2 M HCl (3.24 mL), and MeCN (16 mL).

Colorless crystals; on a 5-mmol scale, yield: 1.274 g (99%); on a 50-mmol scale, yield: 12.05 g (99%); mp 89–90 °C (Lit.[13] 86 °C).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.85–3.75 (m, 4 H), 2.32–2.27 (m, 4 H).

2-Phthalimidoethanesulfonyl Chloride (3q)
Colorless crystals; yield: 0.848 g (62%); mp164–166 °C (Lit.[26] 160–161 °C).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.91–7.76 (m, 4 H), 4.38–4.31 (m, 2 H), 4.18–4.07 (m, 2 H).

2-Methoxyethanesulfonyl Chloride (3r)[27]
Yellowish oil; yield: 0.714 g (90%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.97–3.94 (m, 4 H), 3.43 (s, 3 H).

Methanesulfonyl Chloride (3s)[10]
Colorless oil; yield: 7.09 g (62%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.68 (s, 3 H).

Acknowledgment

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Supporting Information for this article is available online at http://www.thieme-connect.com/ejournals/toc/synthesis.

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