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Improved Synthetic Utility of a Sluggish Electrophile: Reaction of Chlorosulfonyl Isocyanate with Unreactive and Reactive Alkenes

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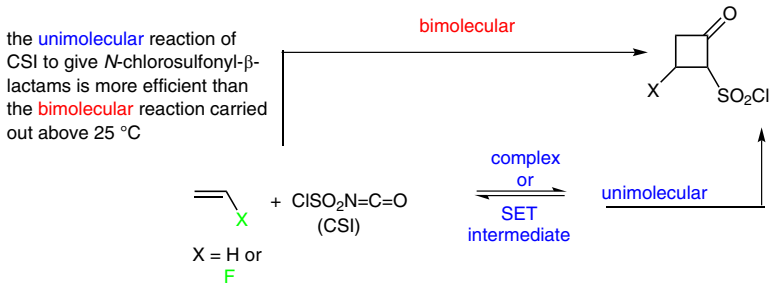

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Abstract Chlorosulfonyl isocyanate (CSI) is a sluggish electrophile in reactions with electron-deficient alkenes or with many monofluoroalkenes. The efficiency of these reactions is improved at temperatures between –15 and 25 °C because, at these temperatures, CSI and the alkene are in equilibrium with an intermediate. A unimolecular reaction of the intermediate at a temperature between –15 and 25 °C is more efficient than the bimolecular reaction of the dissociated reagents above room temperature. This finding provides a method for improving the reactions of CSI with unreactive alkenes.

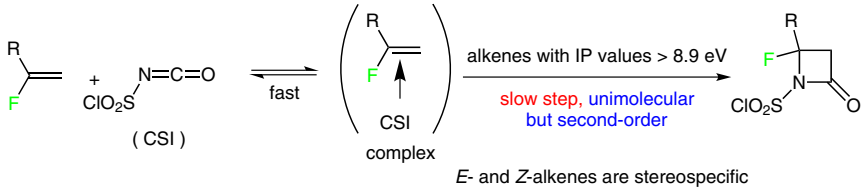
Key words electrophilic additions, alkenes, amides, radical cations, complexes, cycloadditions

Chlorosulfonyl isocyanate ($ClSO_2NCO$; CSI) is a highly versatile and reactive isocyanate,[1] but it is unreactive with electron-deficient alkenes. CSI reacts with alkenes to give *N*-chlorosulfonyl β-lactams that can be readily reduced to the corresponding β-lactams (azetidin-2-ones).[2,3] This reaction sequence provides a synthetic route to a wide range of products, including β-lactam antibiotics,[4a–e] potential cholesterol-lowering drugs,[4f] and various derivatives from ring-opening chlorosulfonyl reactions,[1e,f,2c,3b–d,4g,h] from nitrogen alkylations of the reduced azetidin-2-ones,[3e] from oxygen alkylations to give imino ethers,[3c,4i] from free-radical ring-opening reactions,[4j] and from allylations of the *N*-chlorosulfonyl β-lactams.[4k]

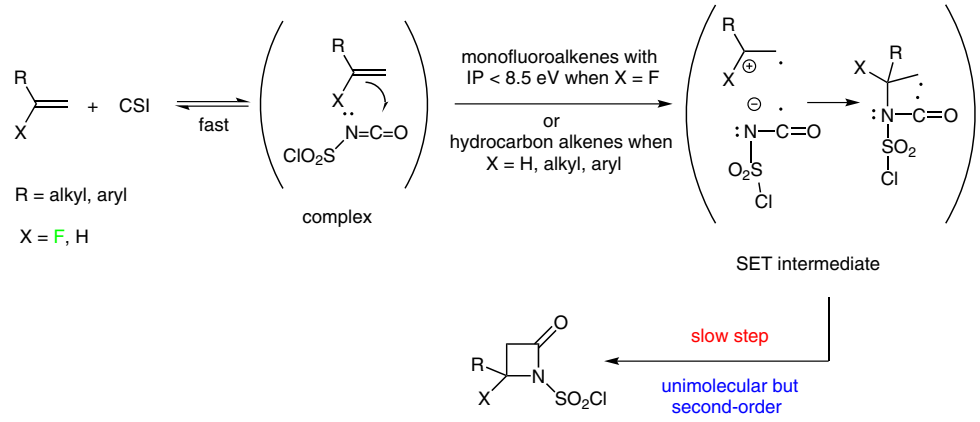
We recently reported that reactions of CSI below room temperature show nonlinear Arrhenius relationships in which the rate of the reaction increases as a result of a pre-equilibrium (Schemes 1 and 2).[5a] Cooling the reaction mixture to below room temperature drives the equilibrium toward a complex or a single-electron transfer (SET) intermediate that increases the reaction rate, as shown by the nonlinear Arrhenius plots.[5a,6] Our kinetic studies also showed that monofluoroalkenes with an ionization potential (IP) of more than 8.9 eV react by a concerted pathway (Scheme 1),[5a] whereas alkenes with IP values of less than 8.5 eV react by the SET pathway (Scheme 2).[5a,6]

We used these findings to improve the synthetic utility of reactions of CSI with a wide range of reactive and unreactive alkenes in several solvents. Previously reported yields of *N*-chlorosulfonyl β-lactam products from CSI and electron-deficient hydrocarbon alkenes or unreactive monofluoroalkenes were poor.[1e,f,5b] An improved synthesis of *N*-chlorosulfonyl β-lactams and *N*-chlorosulfonyl β-fluorolactams is desirable because the corresponding reduced β-lactams have a wide range of potential uses.[1e,f,2c,3a–e,4a–k]

The alkenes that we investigated in this study are listed in Table 1. The results listed in Table 1 for 4-chlorostyrene (**1**) represent a thorough study of the reactions of CSI (Table 1, entries 1–21). After entry 22, Table 1 lists only the optimal reaction conditions along with a few selected reactions for alkenes **2** through **13**. For these alkenes, more-detailed sets of data for their reactions with CSI (like those given in



Scheme 1 Concerted pathway for the reaction of chlorosulfonyl isocyanate with alkenes



Scheme 2 Proposed single-electron-transfer stepwise pathway for the reaction of chlorosulfonyl isocyanate with alkenes

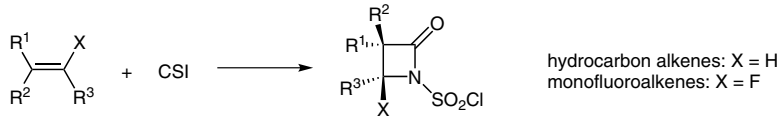
Table 1, entries 1–21, for alkene **1**) are available in the Supporting Information. In Table 1,T_{max} is the low temperature that gives the best product yield for analytical reactions run in an NMR tube. Preparative reactions run at the T_{max} temperature were conducted on a 6 mmol scale and are shown in bold face in Table 1.

Microwave initiation of the reaction of CSI with 4-chlorostyrene (**1**) or other unreactive electron-deficient alkenes has not been productive because the polar *N*-chlorosulfonyl β-lactam products decompose at temperatures above 60 °C.[6] Graf reported that 4-chlorostyrene (**1**) reacts poorly, but gave no details.[1e,f] We previously reported the reaction of 4-chlorostyrene (**1**) with CSI in dichloromethane at 55 °C and isolated the *N*-chlorosulfonyl β-lactam product in 40% yield.[5a] On the basis of our kinetic study,[5a] we reduced the temperature for this reaction, and we found that the yield of the product from **1** and CSI was maximal (97% isolated) at 10 °C (T_{max}) (Table 1, entry 14). Toluene appears to be a good solvent, because Fülöp and co-workers reported that CSI reacts with **1** in toluene at room temperature to give a 58% yield of the lactam (entry 2).[3d] Increasing the temperature to 50 °C in toluene improved the yield and decreased the reaction time (entry 1). For this reaction, a higher temperature improved the outcome because the product from CSI and alkene **1** is more stable than most other *N*-chlorosulfonyl β-lactam products. However, reducing the temperature to 15 °C in toluene-d_8 gave an 80% yield (entry 3), comparable to that obtained at 50 °C (entry 1). At room temperature, the reaction of CSI with **1** in nitromethane, a more-polar solvent, also gave the lactam product, but it rearranged and decomposed in nitromethane at 25 °C (entry 17). At 10 or 0 °C in nitromethane, the *N*-chlorosulfonyl β-lactam product was stable during the short reaction time required for completion of the reaction (entries 18 and 19). Decreasing the temperature to 0 °C or less in toluene (entries 5 and 6), chloroform (entries 10 and 11), dichloromethane (entries 15 and 16), or nitromethane (entry 21) resulted in lower product yields and/or longer reaction times. These reactions show a linear Arrhenius behavior above room temperature[5a] or below –15 °C. Between room temperature and –15 °C, the equilibrium is shifting toward the complex or SET intermediate, which reacts in a more efficient manner than do the dissociated reagents (Scheme 2).[5a,6]

Graf reported that *p*-nitrostyrene (**2**) and 2,6-dichlorostyrene (**3**) barely reacted with CSI, however, he did not report the yields of these reactions.[1e,f] In nitromethane as solvent, **2** and **3** gave moderate to low product yields at 50–55 °C (Table 1, entries 22 and 23). The reactions of CSI with **2** or **3** did not show improved results below room temperature. Alkenes that are unreactive because of the presence of strongly electron-withdrawing substituents, such as styrenes **2** and **3**, require the polar solvent nitromethane to give products. These results suggest that very strongly electron-deficient styrenes may not function as electron donors to give SET intermediates, as shown in Scheme 2, because their ionization potentials (IPs) and oxidation potentials are too high for the transfer of an electron to CSI. 4-Chlorostyrene (**1**) has a calculated IP of 8.47 eV,[7b] and it reacts with CSI by the SET pathway.[5a] Monofluoroalkenes with IP values greater than 8.9 eV react through a concerted pathway.[5a] Styrenes **2** and **3** have calculated IP values of 10.0 eV[7a] and 10.5 eV,[7c] respectively, suggesting that they might react by a concerted pathway because they cannot function as electron donors to CSI. Styrenes **2** and **3** might be the first hydrocarbon alkenes to show a reaction by a concerted pathway, and they were the least reactive alkenes from which we were able to obtain *N*-chlorosulfonyl β-lactam products with CSI in the current study.

The more-reactive styrene (**4**) and CSI gave the best results at 0 °C in nitromethane as solvent (Table 1, entry 24). Kinetic data show that, in dichloromethane, styrene reacts 7.8 times faster at 0.5 °C than it does at 25 °C;[5a,6] those data were confirmed by our measured reaction times for completion of the reaction (see Supporting Information). The

Table 1 Synthetic Utility of Reactions of CSI at Lower Temperatures



hydrocarbon alkenes: X = H
monofluoroalkenes: X = F

Entry	Alkene	Solvent	Temp (°C)	Time	Yield[a] (%)	Ref.
1	4-chlorostyrene (**1**)	toluene-d_8	50	2.5 h	85	
2	4-chlorostyrene (**1**)	toluene	25	24 h	58	3d
3	4-chlorostyrene (**1**)	toluene-d_8	15[b]	16 h	80	
4	**4-chlorostyrene (1)**	**toluene**	**15[b]**	**16 h**	**70[c]**	
5	4-chlorostyrene (**1**)	toluene-d_8	0	22 h	75	
6	4-chlorostyrene (**1**)	toluene-d_8	–15	24 h	–[d]	
7	4-chlorostyrene (**1**)	$CDCl_3$	50	4 h	30	
8	4-chlorostyrene (**1**)	$CDCl_3$	25	5 h	55	
9	4-chlorostyrene (**1**)	$CDCl_3$	10	7 h	50	
10	4-chlorostyrene (**1**)	$CDCl_3$	0	7 h	45	
11	4-chlorostyrene (**1**)	$CDCl_3$	–10[b]	1 d	75	
12	4-chlorostyrene (**1**)	CD_2Cl_2	50	1 h	30	
13	**4-chlorostyrene (1)**	**CH_2Cl_2**	**25[b]**	**4 h**	**95[c]**	
14	**4-chlorostyrene (1)**	**CH_2Cl_2**	**10[b]**	**7 h**	**97[c]**	
15	4-chlorostyrene (**1**)	CD_2Cl_2	0	3 h	50	
16	4-chlorostyrene (**1**)	CD_2Cl_2	–10	30 h	75	
17	4-chlorostyrene (**1**)	CD_3NO_2	25	5 min	36[e]	5a
18	4-chlorostyrene (**1**)	CD_3NO_2	10	5 min	80[f]	
19	4-chlorostyrene (**1**)	CD_3NO_2	0[b]	5 min	80[f]	5a
20	**4-chlorostyrene (1)**	**$MeNO_2$**	**0[b]**	**10 min**	**80[c,f]**	5a
21	4-chlorostyrene (**1**)	CD_3NO_2	–15	5 min	–[f,g]	
22	4-nitrostyrene (**2**)	CD_3NO_2	55	24 h	25[h]	
23	2,6-dichlorostyrene (**3**)	CD_3NO_2	50	1 week	30	
24	styrene (4)	CD_3NO_2	0[b]	20 min	90	
25	*trans*-β-methylstyrene (5)	CD_3NO_2	10[b]	2.5 h	95	
26	*trans*-β-methylstyrene **5**	toluene-d_8	25	30 h	90	
27	***trans*-β-methylstyrene 5**	**CH_2Cl_2**	**25**	**5 h**	**85[c]**	
28	*cis*-stilbene (**6**)	CD_3NO_2	10[b]	30 d	80 (*cis*/*trans* = 1:1)	
29	*cis*-stilbene (**6**)	toluene-d_8	25	30 d	60 (*cis*/*trans* = 2:1)	
30	*cis*-stilbene (**6**)	$CDCl_3$	25	41 d	60 (*cis*/*trans* = 1:1)	
31	**hex-1-ene (7)**	**CH_2Cl_2**	**10[b]**	**14 d**	**99[c]**	
32	*trans*-hex-3-ene (**8**)	CD_3NO_2	25[b]	2 d	50[e]	
33	**2-methylbut-2-ene (9)**	**toluene**	**–10[b]**	**1 h**	**91[c]**	
34	**methylenecyclohexane (10)**	**CH_2Cl_2**	**0[b]**	**30 min**	**87[c]**	
35	α-fluorostyrene (**11**)	toluene	10[b]	2 h	95[i]	
36	α-fluorostyrene (**11**)	toluene	–20	13 h	95[j]	5b
37	α-fluoro-4-methylstyrene (**12**)	CH_2Cl_2	25	4 h	80[e,i]	
38	2-fluorodec-1-ene (**13**)	$MeNO_2$	15[b]	3 h	80[i]	
39	2-fluorodec-1-ene (**13**)	toluene	–10	8 d	80[i]	

[a] Yield by ^1H NMR with toluene as internal standard (unless otherwise stated).
[b] T_{max} (The temperature that gave the best yield in the shortest reaction time).
[c] Isolated yield (6.0 mmol scale).
[d] Only 40% of the alkene reacted.
[e] The yield was low because the product rearranged and decomposed under these conditions.
[f] $CDCl_3$ was added at the completion of the reaction to dissolve the *N*-chlorosulfonyl β-lactam product.
[g] Only 20% of the alkene reacted.
[h] The *N*-chlorosulfonyl β-lactam carbonyl group was observed at 1820 cm^{-1}. On reduction of the crude reaction mixture with $NaHSO_3/NaHCO_3$, the carbonyl group of the reduced β-lactam appeared at 1764 cm^{-1}.
[i] Yield by ^{19}F NMR with *o*- or *p*-fluoroanisole as internal standard.
[j] Isolated yield on a 1.0 mmol scale.

efficiency of this reaction is maximized when the preequilibrium is shifted toward the SET intermediate at 0 °C in nitromethane (Scheme 2).

Other kinetic data[8] show that styrene (**4**) reacts 12.5 times faster than the more-electron-rich *trans*-β-methylstyrene (**5**); this was confirmed by the results shown in Table 1 (entries 24 and 25). The slower reactions rate of CSI with *trans*-β-methylstyrene (**5**) compared with styrene (**4**) is due to an in-plane stepwise transition state that is sensitive to steric effects from the vinyl methyl group on **5**.[5b] We found that the best yield of *N*-chlorosulfonyl β-lactam product from **5** in the shortest reaction time was obtained in nitromethane at 10 °C (entry 25). Toluene and dichloromethane as solvents also provide good results at 25 °C (entries 26 and 27). When the reduced reactivity of an alkene with CSI is caused by steric effects, less-polar solvents generally give good yields without the decomposition that sometimes accompanies reactions of CSI in nitromethane. The synthetic utility of reactions of **5** is degraded below 10 °C in nitromethane and below 25 °C in less-polar solvents.

CSI is even less reactive with *cis*-stilbene (**6**) than with *trans*-β-methylstyrene (**5**) (Table 1, entries 25 and 28). Steric factors in the stepwise transition state again contribute to the reduced rate of the reaction of CSI with *cis*-stilbene (**6**). Reactions of CSI with stilbenes are stereoselective,[9] whereas reactions with *cis*- or *trans*-β-methylstyrenes and *cis*- or *trans*-hex-3-enes are stereospecific.[10] The best yield of the *N*-chlorosulfonyl β-lactam product from the reaction of CSI with *cis*-stilbene (**6**) was obtained in nitromethane at 10 °C (entry 28). The reaction of *cis*-stilbene (**6**) with CSI also gave good yields at 25 °C in toluene (entry 29) or chloroform (entry 30), but the product yields were lower in less-polar solvents than they were in nitromethane at 10 °C.

Styrene (**4**) reacts about 10^3 times faster with CSI than does the monosubstituted alkene hex-1-ene (**7**) or the disubstituted alkene *trans*-hex-3-ene (**8**).[8] The optimal conditions for the reaction of CSI with hex-1-ene (**7**) involved a temperature of 10 °C in dichloromethane; in this case the yield was quantitative (Table 1, entry 31). Steric effects in the reaction of CSI with *trans*-hex-3-ene (**8**) rendered reactions in toluene or dichloromethane impracticable. The reaction in nitromethane at room temperature was faster, but the yield suffered as a result of decomposition of the product (entry 32). The overall best yield (74%) for the reaction of CSI with **8** is that reported by Moriconi and co-workers, who used diethyl ether as the solvent.[2c]

2-Methylbut-2-ene (**9**) is 25 times more reactive with CSI than is styrene (**4**).[8] Rates of reactions of CSI with methylenecyclohexane (**10**) were comparable those with 2-methylbut-2-ene (**9**) (Table 1, entries 33 and 34). These more reactive alkenes show improved product yields at lower temperatures, indicating that the preequilibrium is shifted toward the SET intermediate. Reaction yields for both **9** and **10** were maximal in toluene as solvent at –10 °C and +10 °C, respectively (entries 33 and 34).

Monofluoroalkenes **11**, **12**, and **13** were chosen for this study because **12** reacts with CSI by the SET process, like most hydrocarbon alkenes, whereas **11** and **13** react by a concerted pathway.[5a] [2,2,6,6-Tetramethylpiperidin-1-yl)oxyl (TEMPO) inhibits the reaction of CSI with **12**, but does not inhibit the concerted reactions of **11** or **13**.][5a] Monofluoroalkene **12** is more electron-rich than **11**, but it reacts 0.5 times more slowly than **11** because these two monofluoroalkenes react by different pathways.[5a] The change in mechanism for the reaction of CSI with monofluoroalkenes occurs between calculated vertical IPs of 8.5 and 8.9 eV.[5a] Alkene **12** has an IP of 8.46 eV and reacts by the SET pathway (Scheme 2). α-Fluorostyrene (**11**), which has a higher IP of 8.88 eV, is the most electron-rich and reactive monofluoroalkene that reacts by the concerted pathway (Scheme 1).[5a] Of the alkenes that were studied, monofluoroalkene **13** is the most electron-deficient and least reactive alkene that reacts with CSI by a concerted mechanism, and it has an IP of 9.60 eV.[5a]

The reaction of α-fluorostyrene (**11**) with CSI in dichloromethane gave the *N*-chlorosulfonyl β-fluorolactam product in 65% yield.[5b] The optimal conditions for the reaction of **11** with CSI were found to be 10 °C in toluene; these gave a 95% yield of the *N*-chlorosulfonyl β-fluorolactam product (Table 1, entry 35). Lowering the temperature to below 10 °C with **11** decreased the yield (see Supporting Information). At –20 °C, however, the yield from the reaction of CSI with **11** returned to 95% (entry 36). The reaction of CSI with **11** in toluene at the higher temperature of 10 °C is more efficient, in that the reaction time is shorter (entries 35 and 36). 4-Methyl-α-fluorostyrene (**12**) reacts by the stepwise pathway,[5a] and the best results were obtained at 25 °C in dichloromethane (entry 37). 2-Fluorodec-1-ene (**13**) reacts about 100 times more slowly than styrene, but it reacts slightly faster than dec-1-ene.[5a,8] Conditions for the reaction of **13** were optimal at 15 °C in nitromethane (entry 38). Presumably, the concentration of the complex in Scheme 1 is maximized for CSI and **13** at 15 °C in nitromethane and at –10 °C in toluene (entry 39).

From the kinetic data[5a,8] and our time-to-completion study, the order of reactivity for SET reaction of CSI with alkenes is: **9** ≈ **10** > **4** ≈ **12** > **5** > **6** > **7** ≈ **8** > **1**. The least reactive alkenes in the SET pathway are 4-chlorostyrene (**1**), *cis*-stilbene (**6**), and the hydrocarbon alkenes **7** and **8**. Hydrocarbon alkenes **1**, **6**, **7**, and **8** are not as electron-deficient as **2** or **3**, and they show an improved performance at lower temperatures, indicating a shift in the equilibrium to the complex or SET intermediate. Hydrocarbon alkenes **5**, **6**, and **8**, which react slowly with CSI as a result of steric interactions, perform best in nitromethane as solvent, but they also react well in less-polar solvents. Steric effects are less noticeable in alkenes such as **9** and **10** because these are more reactive than alkenes **7** and **8**. The *N*-chlorosulfonyl β-fluorolactam from α-fluorostyrene **11** can be isolated at

low temperature,[5b] but the the corresponding product from **12** decomposes at or above room temperature (see Supporting Information).

This study has shown how recent observations of nonlinear Arrhenius behavior for the [2+2] cycloaddition of CSI with alkenes below room temperature can be used to improve the outcomes of reactions. Between room temperature and –15 °C, the rates increase because the preequilibrium shifts toward a complex or SET intermediate that reacts more efficiently. Furthermore, the *N*-chlorosulfonyl β-lactam products are less susceptible to rearrangement and decomposition when the reactions are carried out below room temperature. Above room temperature in nitromethane, decomposition can occur with many *N*-chlorosulfonyl β-lactam products, and isomerization is more prevalent at elevated temperatures for the *N*-chlorosulfonyl *cis*-β-lactam product from *cis*-stilbene. In their reactions with CSI, unreactive alkenes such as **2**, **3**, and **13** give the best results in the polar solvent nitromethane. Reactions of CSI with styrenes such as **2** and **3** do not benefit from lower temperatures because their preequilibrium does not shift sufficiently between 0 and –15 °C or because these alkenes are not sufficiently electron-rich to form a complex or SET intermediate. The styrenes **2** and **3** may be too electron-deficient to serve as electron donors to CSI, which is required for the formation of the SET intermediate. It is possible that styrenes **2** and **3** are the first hydrocarbon alkenes to be identified as reacting with CSI by a concerted process (Scheme 1) that is similar to that followed by monofluoroalkenes with IP values equal to or higher than that of α-fluorostyrene **11**.[5a]

The monofluoroalkenes used in this study were synthesized by the reported procedures.[11] Hydrocarbon alkenes and CSI were obtained from commercial sources. Solvents were dried over molecular sieves. Characterization data for all products in this study have been previously reported. ^{1}H NMR data were recorded by using a Varian Mercury spectrometer at 500 or 400 MHz in $CDCl_3$ as solvent with TMS as internal standard. High-field ^{1}H and ^{13}C NMR data for the *N*-chlorosulfonyl β-lactam products from alkenes **1**,[5a] **11**,[5b] and **13**[5b] were identical to those that we previously reported. High-field NMR data for the other products for which only low-field data or no published NMR data were available are reported below. IR spectra were recorded on a Thermo Electron (Nicolet) 4700 FT-IR spectrometer with an ATR attachment.

Kinetic Studies with NMR Monitoring

A dry NMR tube was charged with the appropriate solvent (0.5 mL), alkene (0.50 mmol), and toluene or PhCl (0.10 mmol) as internal standard. The initial NMR spectrum (t = 0) was recorded, and the alkene and internal standard peaks were integrated. CSI (92 mg, 56 μL, 0.65 mmol) was added at the appropriate temperature (Table 1), and the progress of the reaction of CSI with alkenes **1**–**10** was monitored by ^{1}H NMR. The progress of the reaction of the monofluoroalkenes **11**, **12**, and **13** was similarly monitored by ^{19}F NMR with 4-fluoroanisole as internal standard. In their IR spectra, all products showed a peak between1810 and 1830 cm^{-1} corresponding to a carbonyl group; this is definitive for the corresponding *N*-chlorosulfonyl β-lactams. Preparative reactions were performed on a 6.0 mmol scale in 6.0 mL of solvent. The progress of the preparative reactions was monitored by following the disappearance of the IR carbonyl frequency of CSI at ~2230 cm^{-1}.

4-Phenylazetidin-2-one

Competing polymerization of styrene (**4**) during its reaction with CSI made crystallization of the corresponding *N*-chlorosulfonyl β-lactam difficult. Consequently, the crude *N*-chlorosulfonyl β-lactam was reduced[2a] with $NaHSO_3$ to give 4-phenylazetidin-2-one, which was easier to crystallize. Freshly distilled styrene (1.04 g, 1.14 mL, 10.0 mmol) was dissolved in anhyd toluene (1.0 mL), and the stirred solution was cooled to 15 °C. CSI (1.41 g, 0.870 mL, 11.0 mmol) was added dropwise. After 15 min at 15 °C, the mixture was slowly added to ice-cold 2% aq $NaHCO_3$. The organic layer was separated and the aqueous layer was extracted with Et_2O (3 × 25 mL). The organic layers were combined, dried (Na_2SO_4), and concentrated under vacuum to give the crude product as a clear oil (IR: 1817 cm^{-1}). The crude product was dissolved in Et_2O (2 mL) and the soln was added dropwise to a vigorously stirred solution of $NaHSO_3$ (40 mg) and $NaHCO_3$ (360 mg) in H_2O (2 mL). The mixture was stirred for 15 min at r.t., the organic layer was separated, and the aqueous layer was extracted with Et_2O (3 × 25 mL). The organic layers were combined and dried (Na_2SO_4), and then the Et_2O was evaporated until the solution became cloudy. Crystallization gave white crystals; yield: 700 mg (4.8 mmol, 48%); mp 104–105 °C (Lit.[12] 104–105 °C).

IR (ATR): 1757 cm^{-1}.

The high-field NMR data agreed with those reported in the literature.[12]

2-Oxo-1-azaspiro[3.5]nonane-1-sulfonyl Chloride: Typical Preparative-Scale Procedure

A round-bottom flask equipped with a drying tube and magnetic stirrer bar was charged with methylenecyclohexane (**10**; 576 mg 6.00 mmol) and anhyd CH_2Cl_2 (6.0 mL) at 0 °C. CSI (863 mg, 535 μL, 6.10 mmol) was added dropwise. After 30 min at 0 °C, ice-water (25 mL) was added and the organic layer was separated. The aqueous layer was extracted with CH_2Cl_2 (2 × 5 mL), and the organic extracts were combined, washed with 2% aq $NaHCO_3$ (2 × 10 mL), and dried (Na_2SO_4). The solvent was removed under vacuum and the product was purified by column chromatography (silica gel, hexanes–EtOAc) to give white crystals; yield: 1.240 g (87%); mp 87.5–89.0 °C (Lit.[2b] 88–89 °C).

IR (ATR): 1810 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.02 (s, 2 H), 2.24 (m, 2 H), 2.01 (m, 4 H), 1.73 (m, 1 H), 1.27 (m, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 161.6, 70.9, 48.8, 34.4, 24.3, 23.9.

2-(4-Nitrophenyl)-4-oxoazetidine-1-sulfonyl Chloride

Prepared by the typical procedure from 4-chlorostyrene (**2**) (solvent: CD_3NO_2; reaction time: 24 h; temp: 55 °C) as a light-yellow oil; yield: 435 mg (1.50 mmol, 25%).

IR (ATR): 1817 cm^{-1}.

^{13}C NMR (125 MHz, $CDCl_3$): δ = 168.4, 140.2, 128.9, 128.2, 125.7, 50.4, 47.9.

2-(2,6-Dichlorophenyl)-4-oxoazetidine-1-sulfonyl Chloride

Prepared by the typical procedure from 2,6-dichlorostyrene (**3**) (solvent: CD_3NO_2; reaction time: 7 d; temp: 50 °C) as white crystals; yield: 565 mg (1.79 mmol, 30%); mp 107–108 °C.

IR (ATR): 1824 cm^{-1}.

^{13}C NMR (125 MHz, $CDCl_3$): δ = 160.6, 131.3, 130.7, 129.2, 127.5, 54.2, 44.0.

2-Methyl-4-oxo-2-phenylazetidine-1-sulfonyl Chloride

Prepared by the typical procedure from *trans*-β-methylstyrene (**5**) (solvent: CD_3NO_2; reaction time: 2.5 h; temp: 10 °C) as white crystals; yield: 1.46 g (5.70 mmol, 95%); mp 44–45 °C (Lit.[2c] 44–45 °C).

IR (ATR): 1817 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.42 (m, 5 H), 4.85 and 4.84 (s, 1 H), 3.48 and 3.47 (q, *J* = 7.5 Hz, 1 H), 1.49 (d, *J* = 7.5 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 165.8, 134.5, 129.7, 129.2, 126.6, 66.9, 55.8, 12.2.

2-Oxo-3,4-diphenylazetidine-1-sulfonyl Chloride

Prepared by the typical procedure from *cis*-stilbene (**6**) (solvent: CD_3NO_2; reaction time: 30 d; temp 10 °C) as a red oil; yield: 145 mg (4.87 mmol 80%).

cis-Isomer

IR (ATR): 1811 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 5.20 (d, *J* = 7.5 Hz, 1 H), 5.72 (d, *J* = 7.5 Hz, 1 H), 7.06–7.18 (m, 10 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 163.3, 131.5, 129.3, 128.9, 128.6, 128.4, 128.3, 128.2, 127.3, 64.6, 62.1.

2-Butyl-4-oxoazetidine-1-sulfonyl Chloride

Prepared by the typical procedure from hex-1-ene (**7**) (solvent: CH_2Cl_2; reaction time: 14 d; temp: 10 °C) as a clear oil; yield: 1.34 g (5.94 mmol, 99%).

IR (ATR): 1814 cm^{-1}.

^1H NMR (500, MHz, $CDCl_3$) : δ = 4.34 (m, 1 H), 3.39 (dd, *J* = 17.5 and 7.0 Hz, 1 H), 2.98 (dd, *J* = 17.5 and 4.0 Hz, 1 H), 2.18 (m, 1 H), 1.78 (m, 1 H), 1.39 (m, 4 H), 0.94 (t, *J* = 7.0 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 161.9, 58.0, 43.4, 32.3, 26.8, 22.3, 13.8.

2-Butyl-4-oxoazetidine

2-Butyl-4-oxoazetidine-1-sulfonyl chloride was reduced with $NaHSO_3$/$NaHCO_3$ as described above for 4-phenylazetidin-2-one.

^1H NMR (500, MHz, $CDCl_3$) : δ = 6.86 (br s, 1 H), 3.59 (m, 1 H) (protons α to the carbonyl group showed both *syn*- and *anti*-absorptions) [3.04 and 3.03 (dd, *J* = 15.0, 0.5 Hz, 1 H)], [2.54 and 2.53 (dd, *J* = 15.0, 0.5 Hz, 1 H)], 1.65 (m, 2 H), 1.33 (m, 4 H), 0.91 (t, *J* = 7.0 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 168.9, 48.3, 43.4, 35.1, 28.4, 22.5, 14.0.

These spectra matched the published low-field NMR data.[3b]

2,3-Diethyl-4-oxoazetidine-1-sulfonyl Chloride

Prepared by the typical procedure from *trans*-hex-3-ene (**8**) (solvent: CD_3NO_2; reaction time: 2 d; temp: 25 °C) as a clear oil; yield: 676 mg (3.00 mmol, 50%).

IR (ATR): 1814 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = [3.98 and 3.97 (t, *J* = 7.5 Hz, 1 H], 3.10 (m, 1 H), 2.16–2.24 (m, 1 H), 1.76–1.95 (m, 3 H), 1.10 (t, *J* = 7.5 Hz, 3 H), 1.05 (t, *J* = 7.5 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 164.9, 64.5, 57.5, 25.5, 21.4, 11.2, 9.1.

2,2,3-Trimethyl-4-oxoazetidine-1-sulfonyl Chloride

Prepared by the typical procedure from 2-methylbut-2-ene (**9**) (solvent: toluene; reaction time: 1 h; temp: –10 °C) as waxy crystals; yield: 1.15 g (5.46 mmol, 91%); mp 44–45 °C (Lit.[2c] 44–45 °C).

IR (ATR): 1809 cm^{-1}.

^1H NMR (400, MHz, $CDCl_3$): δ (two isomers *syn* and *anti* to the chlorosulfonyl group) = [3.29 and 3.25 (q, *J* = 7.6 Hz, 1 H)], [1.76 and 1.75 (s, 3 H)], [1.65 and 1.64 (s, 3 H)]; [1.32 and 1.31 (d, *J* = 7.6 Hz, 3 H)].

^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.3, 69.8, 55.7, 26.4, 20.5, 8.9.

Attempts to isolate the *N*-chlorosulfonyl β-lactam product from 4-methyl-α-fluorostyrene (**12**) were unsuccessful because the product decomposed (see Supporting Information).

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Supporting Information

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