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Kinetic Studies on the Reaction of Chlorosulfonyl Isocyanate with Monofluoroalkenes: Experimental Evidence for Both Stepwise and Concerted Mechanisms and a Pre-equilibrium Complex on the Reaction Pathway

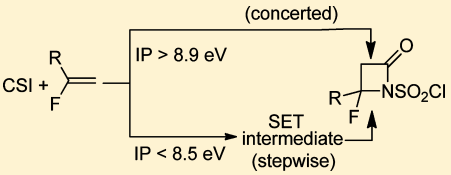
Dale F. Shellhamer,* Summer A. Bunting, Kelli R. Hickle, Parker C. Horn, Jacob C. Milligan, Danielle E. Shipowick, Lincoln B. Smith, David J. Vandenbroek, Marc C. Perry, and Jerry A. Boatz†

Department of Chemistry, Point Loma Nazarene University, San Diego, California 92106-2899, United States

†Air Force Research Laboratory, Edwards Air Force Base, California 93524-7680, United States

Supporting Information

ABSTRACT: Chlorosulfonyl isocyanate (CSI) is reported to react with hydrocarbon alkenes by a stepwise dipolar pathway to give *N*-chlorosulfonyl-*β*-lactams that are readily reduced to *β*-lactams. Substitution of a vinyl hydrogen for a vinyl fluorine changes the dynamics for reaction with CSI so that a concerted pathway is favored. Rate constants were measured for reactions of CSI with monofluoroalkenes and some hydrocarbon alkenes. Activation parameters for two hydrocarbon alkenes and two monofluoroalkenes support this change in mechanism. A plot generated from the natural log of rate constants vs ionization potentials (IP) indicates that fluoroalkenes with IP values >8.9 eV react by a concerted process. Electron-rich monofluoroalkenes with IP values <8.5 eV were found to react by a single-electron transfer (SET) pathway. Hydrocarbon alkenes were also found to react by this dipolar stepwise SET intermediate rather than the previously accepted stepwise dipolar pathway. Data support a pre-equilibrium complex on the reaction pathway just before the rate-determining step of the concerted pathway and a SET intermediate for the stepwise reactions. When the reactions are carried out at lower temperatures, the equilibrium shifts toward the complex or SET intermediate enhancing the synthetic utility of these reactions. Kinetic data also support formation of a planar transition state rather than the orthogonal geometry as reported for ketene [2 + 2] cycloadditions.



1. INTRODUCTION

Chlorosulfonyl isocyanate (CSI) is the most reactive and versatile isocyanate,[1a,b,c] and it reacts with alkenes to give *N*-chlorosulfonyl-*β*-lactams that are readily reduced to *β*-lactams.[2a,b,3a−c] This reaction sequence can provide a synthetic route to *β*-lactam antibiotics[4a] and cholesterol-lowering drugs.[4b] Reactions of CSI with hydrocarbon alkenes are reported to proceed through open-ion dipolar intermediates.[1,3a,b] Speculation of a concerted pathway with CSI and hydrocarbon alkenes has been proposed,[3b] but a one-step pathway has not been demonstrated experimentally.[3c] In a recent paper, we found that substituting a hydrogen for a fluorine on the *π*-bond of an alkene changes the reaction pathway with CSI from a stepwise to a concerted process.[5] Data supporting a concerted process for reaction of CSI with monofluoroalkenes include: (a) reactions with *E* and *Z* fluoroalkenes are stereospecific; (b) neat reactions or reactions run at high molar concentration of CSI and monofluoroalkenes do not give 2:1 uracil products as observed with some hydrocarbon alkenes when very stable open-ion dipolar intermediates are formed;[2a,c] and (c) a concerted pathway is supported by quantum chemical calculations with CSI and vinyl fluoride.

In this paper, we provide kinetic data that experimentally support the concerted pathway over a stepwise process for reaction of CSI with electron-deficient monofluoroalkenes that have high ionization potentials (IP > 8.9 eV). A single electron transfer (SET) process is indicated for reaction of CSI with electron-rich monofluoroalkenes with IP values <8.5 eV (Scheme 1). We define the calculated cutoff ionization potential for monofluoroalkenes where this change in mechanism occurs with CSI as the electrophile. Hydrocarbon alkenes are also found to react by the dipolar SET intermediate rather than the previously accepted dipolar pathway[1,3a,b] described in Scheme 2. We found that the synthetic utility of this sluggish electrophile (CSI) can be improved by shifting the equilibrium toward the complex or toward the SET intermediate at lower temperatures.

2. RESULTS AND DISCUSSION

Concerted vs Stepwise Pathways. Rate data at various temperatures for reaction of CSI with monofluoroalkenes **1**−**8** (Figure 1) are given in Table 1. Figure 2 is a plot of natural logarithm rate constants (ln *k*) vs vertical ionization potentials (IP) for reactions of CSI with monofluoroalkenes at 28.6 °C. The IP values were calculated at the MP2/6-311 G(d,p)

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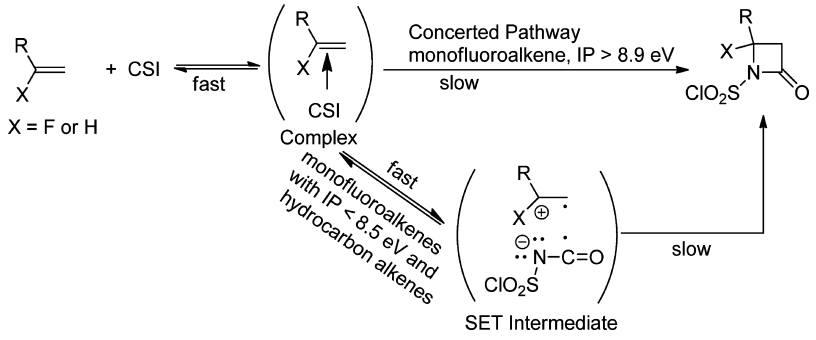
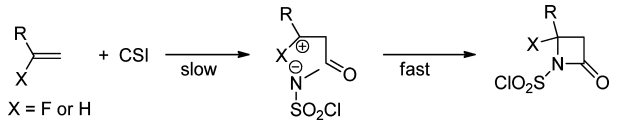
Scheme 1. Postulated Reaction Pathways for Chlorosulfonyl Isocyanate with Monofluoroalkenes and Hydrocarbon Alkenes



Scheme 2. Pathway for Reaction of CSI with Alkenes. Previously Accepted Stepwise Dipolar Pathway



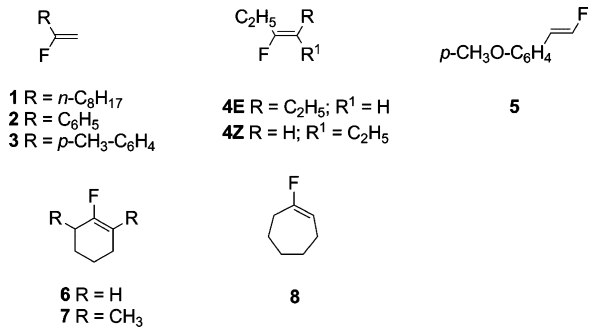


Figure 1. Monofluoroalkenes.

level.[6a−e,7] Higher level (CCSD and CR-CCL(2,3)[8]) ionization potential calculations are comparable to those calculated at the MP2/6-311 G(d,p) level (Table 1). The less electron-rich monofluoroalkenes **1**, **2**, **4E**, **4Z**, **6**, and **8** with IP > 8.9 eV form a line on the ln *k* vs IP graph (Figure 2) because they are reacting by a common concerted pathway as describer in our earlier paper.[5] Electron-rich monofluoroalkenes *α*-fluoro-*p*-methylstyrene (**3**) and *β*-fluoro-*p*-methoxystyrene (**5**), with IP values less than 8.5 eV, are reacting slower than expected, and they fail to correlate indicating that they are not reacting by a concerted pathway (Figure 2). CSI reactions with **3** and **5** should be faster than the concerted reaction with the less electron-rich *α*-fluorostyrene (**2**) if both **3** and **5** are reacting by a pathway leading to dipolar intermediates like those reported for hydrocarbon alkenes.[1,3a,b] Furthermore, reaction of CSI through a stepwise dipolar intermediate with **3** should be faster than **2** if the dipolar stepwise process of **3** is to compete with or dominate the rate for the concerted pathway with **2**. However, monofluoroalkenes **3** and **5** fall below rather than above the extended line for concerted reactions with CSI in Figure 2 which is inconsistent with the previously accepted pathway described in Scheme 2. Perhaps a rapid single electron transfer (SET) reaction occurs with electron-rich alkenes like **3** and **5** as described in Scheme 1. The last step then becomes rate determining, and it gives rise to the smaller rate constants for **3** and **5** relative to **2** in Table 1 and for the blue data points from **3** and **5** that are below the extended line of concerted reactions in Figure 2.

To test for a SET pathway, we treated *α*-fluorostyrenes **2** and **3** with the radical inhibitor TEMPO, and the results are given in Table 2. TEMPO had no effect on the reaction progress for the concerted reaction with **2**. *α*-Fluoro-*p*-methylstyrene (**3**) reacts much slower with TEMPO, indicating that a radical species is on the reaction pathway (Scheme 1, SET pathway). These findings caused us to consider the possibility that hydrocarbon alkenes might also be reacting by the stepwise SET mechanism proposed in Scheme 1. Reaction progress of CSI with the hydrocarbon alkenes styrene, 3-ethyl-2-pentene, and even the less electron-rich 1-hexene are all significantly interrupted by TEMPO (Table 2). Thus. the previously accepted stepwise dipolar mechanism shown in Scheme 2 is not supported by our data and the stepwise SET pathway is indicated for reaction of CSI with hydrocarbon alkenes and for monofluoroalkenes with IP values <8.5 eV (Scheme 1). Monofluoroalkenes with IP values >8.9 eV react by a concerted pathway. Perhaps the concerted reaction of CSI with electron-deficient monofluoroalkenes can be explained by the increase in oxidation potential of the fluoroalkenes with IP values >8.9 eV such that the SET intermediate does not form. A more detailed description of the SET pathway will be investigated by our ongoing quantum chemical calculations.

Relative rates also support a change in mechanism for CSI reactions with monofluoroalkenes. Concerted reactions of CSI tend to react faster than the stepwise reactions with substrates of similar structure. For example, *α*-fluoro-*p*-methylstyrene (**3**) should react faster than alpha-fluorostyrene (**2**) if both fluorostyrenes are reacting by the same mechanism. However, *α*-fluoro-*p*-methylstyrene **3** is reacting 0.5 times slower than **2** (Table 3). Thus, **3** (IP = 8.46 eV) reacts slower than **2** (IP = 8.88 eV) because they are reacting by different pathways. CSI reactions with monofluoroalkenes like **2** that have IP values greater than 8.9 eV will react by a concerted mechanism. Monofluoroalkenes with IP values lower than 8.5 eV like **3** will proceed by a stepwise SET process rather than the accepted dipolar reaction pathway[1,3a,b] previously reported for hydrocarbon alkenes (Scheme 2). Monofluoroalkenes with IP values between 8.5 and 8.9 eV most likely have competing pathways, and 1-fluoro-2,6-dimethylcyclohexene (**7**) with an IP value of 8.74 eV may contain a minor competing concerted pathway. When the datum point of **7** vs. its IP value is plotted in Figure 2 it clearly falls below the line as expected for the two-step pathway. The fluorocyclohexene **7** may also be reacting slower than expected due to steric effects in the rate determining step for either pathway.

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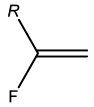
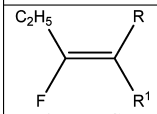
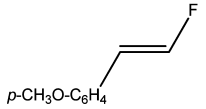
Table 1. Rate Constants (L/mol s) for Reactions of CSI with Monofluoroalkenes and Calculated Ionization Potentials (eV) of Monofluoroalkenes

Monofluoroalkene	Temperature (°C)	Rate Constant (l/mol s)	Ionization Potential IP (eV)[a]	IP (eV)	IP (eV)[c]
 **1** R = *n*-C_8H_{17}	28.6	$3.6 \pm 0.3 \times 10^{-5}$	9.60	9.43	…..
1	34.0	$5.8 \pm 0.2 \times 10^{-5}$			
1	39.0	$1.3 \pm 0.06 \times 10^{-4}$			
1	44.0	$5.6 \pm 0.7 \times 10^{-4}$			
2 R = C_6H_5	14.7	$4.4 \pm 0.7 \times 10^{-4}$			
2	20.0	$1.3 \pm 0.06 \times 10^{-3}$			
2	24.0	$2.5 \pm 0.4 \times 10^{-3}$			
2	28.6	$3.7 \pm 0.4 \times 10^{-3}$	8.88	9.10	9.14
3 R = *p*-$CH_3C_6H_4$	14.9	$2.3 \pm 0.3 \times 10^{-3}$ [d]			
3	28.6	$1.8 \pm 0.08 \times 10^{-3}$	8.46	8.37	8.36
 **4E** R = C_2H_5; R^1 = H	28.6	$2.9 \pm 0.1 \times 10^{-4}$	9.14	8.95	8.98
4Z R = H; R^1 = C_2H_5	28.6	$2.6 \pm 0.4 \times 10^{-5}$	9.16	8.97	8.99
 **5**	28.6	$3.5 \pm 0.2 \times 10^{-4}$	7.92	7.86	7.82
6 1-Fluorocyclohexene[e]	28.6	$3.5 \pm 0.1 \times 10^{-5}$,	9.19	9.00	9.03
7 1-Fluoro-2,6-dimethyl-cyclohexene	28.6	$8.5 \pm 0.97 \times 10^{-6}$	8.74	8.54	8.56
8 1-Fluorocycloheptene[e]	28.6	$5.0 \pm 0.4 \times 10^{-4}$ [d],	9.03	….	….

[a]Vertical ionization potentials, calculated at the MP2/6-311G(d,p) level. [b]Vertical ionization potentials, calculated at the CCSD/6-311G(d,p)//MP2/6-311G(d,p) level. [c]Vertical ionization potentials, calculated at the CR-CCL(2,3)/6-311G(d,p)//MP2/6-311(d,p) level. [d]An average of only two runs. [e]Kinetic data by ^{19}F NMR with 4-fluoroanisole as internal standard.

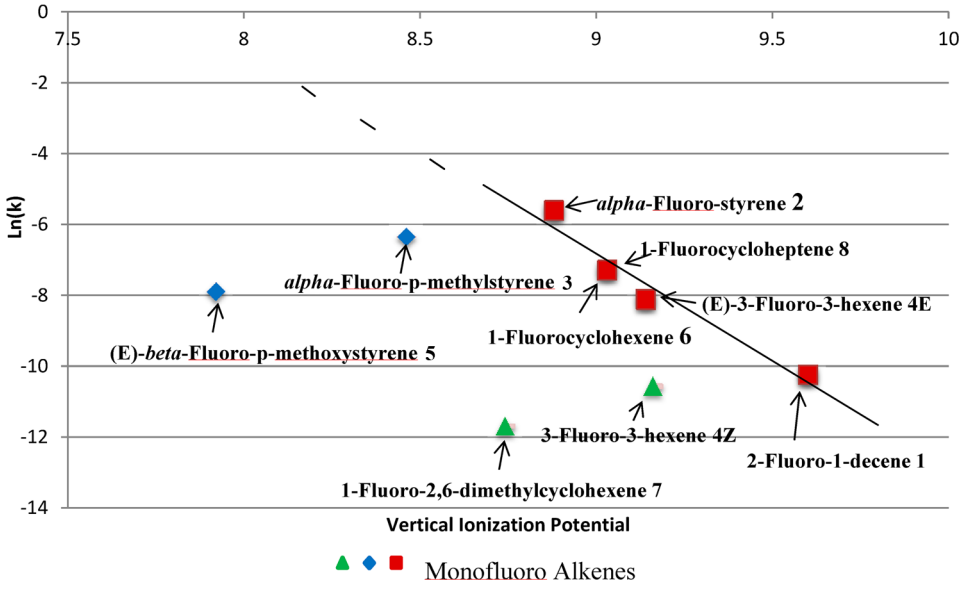


Figure 2. Natural log of rate constants vs ionization potential. Ionization potential calculated at the MP2/6-311G(d,p) level; see Table 1.

Rate constants for the hydrocarbons styrene and 1-decene at several temperatures are given in Table 4. Data in Table 5 compare the activation enthalpies for concerted reactions of CSI with two monofluoroalkenes and for CSI reactions of two hydrocarbon alkenes that are reacting by a stepwise SET pathway. The Arrhenius plots (Figure 3) for 2-fluoro-1-decene (**1**) and 1-decene show that 1-decene reacting by a stepwise pathway has a higher activation enthalpy ($\Delta H^{\ddagger}$ = 41.9 vs 32.7 kcal/mol). Reactions of CSI with styrene and α-fluorostyrene (**2**) also give linear Arrhenius plots above room temperature

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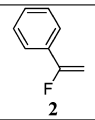
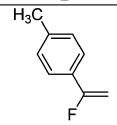
Table 2. Reaction Progress of Chlorosulfonyl Isocyanate with Alkenes

Alkene	Time for Completion at Room Temperature	
	With TEMPO[a]	Without TEMPO
 **2**	No Effect[b]	Same as with TEMPO[b]
 **3**	60 % Reacted in 20 hrs.[b]	Complete in 5 min.[b]
Styrene[c]	25 % Reacted in 45 hrs.	Complete in 2.5 hrs.
3-Ethyl-2-pentene[d]	60 % Reacted in 1 hr.	< 1 min.
1-Hexene[d]	No Reaction in 1 week	90 % Reacted in 1 week

[a]1 equiv each: TEMPO/alkene/CSI. [b]Reaction progress followed by ^{19}F NMR with *p*-fluoroanisole as internal standard. [c]Reaction progress followed by ^{1}H NMR with toluene as internal standard. [d]Reaction progress followed by ^{1}H NMR with bromobenzene as internal standard.

Table 3. Relative Rates Comparing Concerted and Stepwise Pathways for Reaction of CSI with Alkenes

alkene	rate constants (L/mol s)	relative rate
α-fluoro-*p*-methylstyrene (**3**)[a]/ *α*-fluorostyrene (**2**)[a]	$(1.8 \pm 0.08) \times 10^{-3}$/ $(3.7 \pm 0.4) \times 10^{-3}$	0.5
1-fluorocyclohexenes[a] **6**/**7**	$(3.5 \pm 0.1) \times 10^{-5}$/ $(8.5 \pm 0.97) \times 10^{-6}$	4.1
α-fluorostyrene (**2**)[a]/ 2-fluoro-1-decene (**1**)[a]	$(3.7 \pm 0.4) \times 10^{-3}$/ $(3.6 \pm 0.3) \times 10^{-5}$	103
styrene[b]/1-decene[a]	$(3.3 \pm 0.002) \times 10^{-3}$/ $(2.8 \pm 0.2) \times 10^{-6}$	1179

[a]Rate constant from Table 1 at 28.6 °C. [b]Rate constant from Table 4 at 28.6 °C.

Table 4. Rate Constants (L/mol s) for Reactions of CSI with Styrene and 1-Decene

hydrocarbon alkene	temp (°C)	rate constant (L/mol s)
styrene[a]	37.0	$(3.5 \pm 0.05) \times 10^{-2}$
	33.0	$(1.1 \pm 0.1) \times 10^{-2}$
	28.6	$(3.3 \pm 0.02) \times 10^{-3}$
	25[b]	$1^{b} \times 10^{-3}$
	7.9	$(1.9 \pm 0.3) \times 10^{-3}$
	0.5	$(7.8 \pm 0.9) \times 10^{-3}$
1-decene[c]	40.0	$(1.4 \pm 0.1) \times 10^{-5}$
	37.0	$(1.2 \pm 0.1) \times 10^{-5}$
	33.0	$(4.8 \pm 0.2) \times 10^{-6}$
	28.6	$(2.8 \pm 0.2) \times 10^{-6}$

[a]In methylene chloride, by GC with chlorobenzene as internal standard. [b]Data from Clauss, K. *Liebigs Ann. Chem.* **1969**,*722*, 110. [c]In deuterochloroform by NMR with toluene as internal standard.

Table 5. Activation Enthalpies for Reaction of CSI with Alkenes

alkene	transition state	$\Delta H^{\ddagger}$ (kcal/mol)
2-fluoro-1-decene (1)	concerted	32.7
decene	stepwise	41.9
α-fluorostyrene (2)	concerted	26.4
styrene	stepwise	53.7

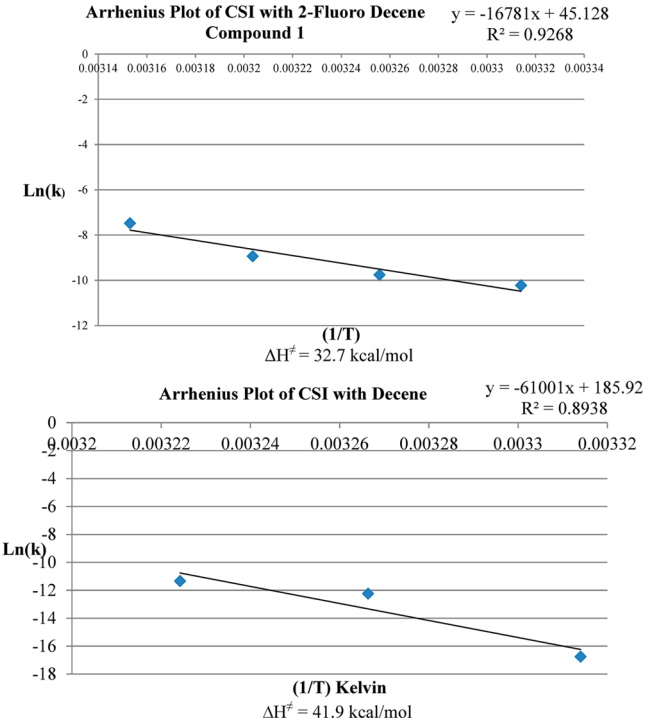


Figure 3.

(Figure 4). The activation enthalpy is considerably higher for the stepwise pathway of styrene (53.7 k cal/mol) than its monofluoroalkene counterpart *α*-fluorostyrene (**2**) at 26.4 kcal/mol. The lower activation enthalpy for *α*-fluorostyrene (**2**) compared to styrene and 2-fluoro-1-decene (**1**) vs 1-decene support a concerted pathway for both fluoroalkenes. A concerted reaction of **2** with CSI is indicated even though a stabilized diradical fluoro-benzylic cation intermediate could be supported as indicated for styrene and *α*-fluoro-*p*-methylstyrene (**3**). Our experimental kinetic data are consistent for CSI reacting by a concerted pathway with electron-deficient monofluoroalkenes, and a concerted reaction was also demonstrated by our quantum chemical transition-state calculations with CSI and vinyl fluoride.[5]

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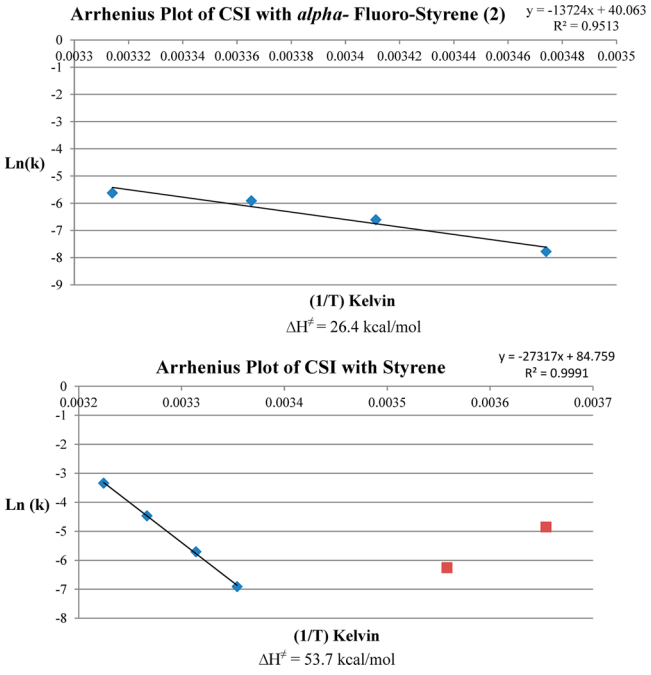


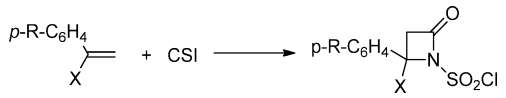
Figure 4.

Monofluoroalkenes that react by a concerted pathway are different from hydrocarbon alkenes of similar structure that proceed through a stepwise SET process. For example, α-fluorostyrene **2** reacts only 100 times faster than 2-fluoro-1-decene **1** (Table 3), while their hydrocarbon counterparts styrene and 1-decene show styrene reacting more than 1000 times faster than 1-decene (Table 3). The larger relative rate for styrene vs 1-decene compared to the concerted reaction of monofluoroalkenes **2** and **1** is due to stabilization of the benzyl carbocation in the more polar SET transition state with the hydrocarbon styrene as it progresses to the *N*-chlorosulfonyl-β-lactam product (Scheme 1, SET pathway). Quantum chemical calculations will be investigated to determine the nature of the SET intermediate and this proposed slow second step for the SET pathway.

Pre-Equilibrium. Scheme 1 describes the pre-equilibrium on the reaction pathway for CSI with alkenes. Experimental data to support formation of an SET intermediate from electron-rich monofluoroalkenes and hydrocarbon alkenes are as follows: (a) the very electron-rich monofluoroalkenes **3** and **5** have SET intermediates formed at room temperature as indicated by the intense color and their absorbance at 642 and 505 nm, respectively. The absorbance from **3** and **5** increases relative to the baseline as the temperature decreases due to a shift in the equilibrium toward the SET intermediate. This process is reversible since warming and cooling returns the absorbance to their previous values. (b) TEMPO interrupts the reaction progress of CSI with monofluoroalkene **3** and hydrocarbon alkenes. (c) Stepwise reactions of CSI with electron rich alkenes like styrene and α-fluoro-*p*-methylstyrene (**3**) react faster as the temperature decreases below room temperature where the SET intermediate forms (Tables 1 and 4). Data to support formation of a complex for the concerted reaction of CSI with electron-deficient monofluoroalkenes are as follows: (a) quantum chemical calculations show complexes of CSI with monofluoroalkenes **1** and **2** that are −6.0 and −6.8 kcal/mol thermodynamically more stable than their dissociated free reagents. (b) A complex rather than an SET intermediate is indicated for the reaction of α-fluorostyrene (**2**) with CSI because TEMPO does not inhibit the reaction progress (Table 2), and the intense color on mixing CSI with **2** is not observed.

We used this equilibrium shift of the SET intermediate at lower temperature to increase the synthetic utility of a sluggish and mediocre reaction with CSI. Graf reports that *p*-chlorostyrene reacts slowly and in poor yield with CSI, but he does not give experimental data.[1c] We found that CSI reacts with p-chlorostyrene at 55 °C in 18 h to give the *N*-chlorosulfonyl-β-lactam product **9** in 40% isolated yield (Table 6). Higher temperatures decompose the *N*-chlorosulfonyl-β-lactam product **9**. Reaction of CSI with the unreactive *p*-chlorostyrene at room temperature in nitromethane as solvent gives better results. The best results were obtained at 0 °C in nitromethane as solvent (Table 6). Below 0 °C the reaction time increased indicating that the equilibrium was completely shifted toward the intermediate around 0 °C. Similar results were found for the concerted reaction of CSI with α-fluorostyrene (**2**) where the reaction conditions are maximized at −15 °C. The complex from this concerted reaction must be completely formed with **2** around −15 °C because reaction progress decreases at −20 °C (Table 6).

Table 6. Synthetic Utility of CSI Reactions at Lower Temperatures



alkene	solvent	temp (°C)	reaction time	yield (%)
p-chlorostyrene	CH_2Cl_2	55	18 h	40[a]
p-chlorostyrene	CH_3NO_2	25	5 min	36[a]
p-chlorostyrene	CH_3NO_2	0	<5 min	80[a]
p-chlorostyrene	CH_3NO_2	−15	5 min	only 20% reacted[b]
α-fluorostyrene (2)	CH_3NO_2	0	1 h	25[c,d]
α-fluorostyrene (2)	CH_3NO_2	−10	0.75 h	35[c,d]
α-fluorostyrene (2)	CH_3NO_2	−15	0.5 h	60[c]
α-fluorostyrene (2)	CH_3NO_2	−20	0.75 h	50[c]

[a]Isolated yield. [b]On workup only 20% of *p*-chlorostyrene reacted. Analysis by ^{1}H NMR. [c]Yield by ^{19}F NMR with *p*-fluoroanisole as internal standard. [d]The yield is low because product **9** rearranges and decomposes during the reaction.

Alkenes 1-decene, styrene, 2-fluoro-1-decene (**1**), and α-fluorostyrene (**2**) do not form complexes or SET intermediates at or above room temperature since their kinetic data are linear on the Arrhenius plots (Figures 3 and 4). The product study for reaction of CSI with α-fluorostyrene (**2**) is consistent with complex formation below 0 °C where the equilibrium is completely shifted to the complex around −15 °C (Table 6). The hydrocarbon styrene also begins to form its SET intermediate with CSI below room temperature at 7.9 and 0.5 °C (see the red data points in Figure 4 and the larger rate constants at these lower temperatures in Table 4). Complex or SET intermediate formation of CSI with alkenes must be on the reaction pathway just before the kinetic transition state. Formation of the complex or SET intermediate on a cul-de-sac not on the reaction pathway would lead to a decrease rather than an increase in reaction rate because the reagents would be diverted from the reaction pathway. An SET intermediate may

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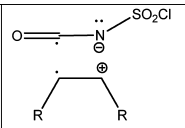
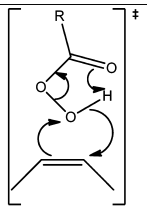
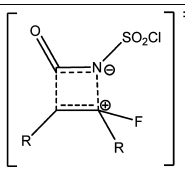
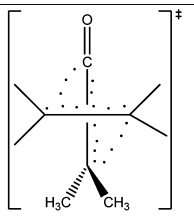
Table 7. Relative Rates for Electrophiles with Various Transition States

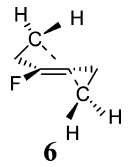
Compounds *cis/trans* , (E)/(Z) or Cycloalkenes	 Stepwise, *In* Plane Intermediate CSI [a]	 Concerted, In-Plane Per Acetic Acid [b]	 Concerted, In-Plane CSI [c]	 Concerted, Orthogonal Dimethylketene [d]
cis/trans Stilbenes [b]	…	1.6	…	…
cis/trans Oleic Acids [b]	…	1.1	…	…
4 (E) / 4 (Z) [c]	…	…	11.1	…
-Fluorocycloheptene **8** [c] 1-Fluorocyclohexene **6** [c]	…	…	14.3	…
Cycloheptene [b] Cyclohexene [b]	…	1.4	…	…
cis/trans 2-Butenes [d]	…	…	…	1250
cis/trans 3-Heptenes [a]	3	…	…	…
Cyclopentene [a] Cyclohexene [a]	3.6	…	…	…

[a]Data from ref 13. [b]Data from ref 11. [c]Relative rate calculated from data in Table 1. [d]Data from ref 12.

be formed directly from the isolated reagents rather than the complex as shown in Scheme 1. The nature of this proposed SET pathway is under investigation.

In-Plane Transition State. Concerted transition states for CSI and monofluoroalkenes are not orthogonal as reported for ketene cycloadditions where the orbitals mix by a [π^2(s) + π^2(a)] process.[9] A six-electron process involving the lone pair on nitrogen of CSI can be represented as [π^2(s) + π^2(s) + n^2(s)]. This six electron cyclization provides a concerted transition state where the fluoroalkene C=CF double bond and the O=C=N- moiety of CSI are in the same plane.[9] We considered a pseudopericyclic transition state like that proposed by Lemal[10a] and others[10b] where the orthogonal π-electrons on the carbonyl of CSI contribute to make the concerted in-plane transition state. Our calculated localized molecular orbital's of the cyclic [2 + 2] transition state for the cycloaddition of CSI to vinyl fluoride show that the carbonyl π-electrons were not perturbed.[5] There was however, significant mixing between the C−N π-bond in CSI and the nitrogen lone pair electrons on CSI which is consistent with a [π^2(s) + π^2(s) + n^2(s)] process.[5]

Relative rate values also provide experimental support for this in-plane concerted transition state described by our earlier calculations.[5] In-plane transition states show rather small relative rate values. Data in Table 7 give the relative rate of peracetic acid epoxidation[11] (in-plane, concerted transition state) for *cis/trans*-stilbenes as 1.6 and for *cis/trans* oleic/elaidic acids as 1.1. The concerted reaction of CSI with (*E*)-3-fluoro-3-hexene (**4E**) is on the line of the ln vs IP graph (Figure 2) and it reacts 11.1 times faster than **4Z** (Table 7). A relative rate of 11.1 from **4E**/**4Z** is small as expected for the steric effects from an in-plane concerted transition state with *E*/*Z* isomers. Dimethylketene[12] reacts by an orthogonal concerted transition state 1250 times faster with *cis*-butene than *trans*-butene (Table 7). Clearly CSI does not react through an orthogonal transition state. A small steric effect is also found with cyclohexenes. The monofluorocyclohexene **6** exists in a half-chair conformation (Figure 5), and the homoallylic methylene groups in **6** sterically lower the rate. For example, 1-fluorocycloheptene (**8**) reacts



6

Figure 5. Conformation of **6**.

14.3 times faster with CSI than 1-fluorocyclohexene (**6**) (Table 7). A similar trend was found for the steric involvement of the homoallylic methylene groups from peracetic acid epoxidation of cyclic alkenes where cycloheptene reacts 1.4 times faster than cyclohexene[11] through an in-plane concerted transition state (Table 7).

Relative rate data also support an in-plane transition state for hydrocarbon alkenes reacting by a stepwise process. Reactions of CSI with the *cis/trans* 3-heptenes[13] have the *cis*-alkene reacting 3 times faster than *trans*-3-hexene (Table 7). The homoallylic methylene groups in cyclohexene again show the expected steric effect of an in-plane stepwise transition state since CSI reacts 3.6 times faster with cyclopentene than cyclohexene (Table 7).[13] Relative rate data and quantum chemical calculations[5] are consistent with CSI reacting through in-plane transition states for both stepwise and concerted pathways.

3. CONCLUSION

Kinetic measurements have shown that reactions of monofluoroalkenes with IP values >8.9 eV react by a concerted pathway. The concerted pathway may result from an increase in the oxidation potential of the electron-deficient monofluoroalkenes (IP > 8.9 eV) such that formation of the SET intermediate does not occur. Monofluoroalkenes with IP values <8.5 eV react by a stepwise pathway, and they are reacting slower than expected for a classical stepwise dipolar pathway. The slower than expected rate for reaction of CSI with electron-rich monofluoroalkenes is best explained by a stepwise SET dipolar pathway. Monofluoroalkenes with IP values between 8.5 and 8.9 eV most likely have competing pathways.

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Hydrocarbon alkenes were also found to react by the SET dipolar mechanism rather than the previously accepted stepwise dipolar pathway.[1,3a,b] Our kinetic data indicate that a complex or an SET intermediate, depending on the alkene, is on the reaction pathway and we used this discovery to enhance the synthetic utility of CSI reactions. Reaction of CSI with *p*-chlorostyrene was greatly improved by shifting the equilibrium toward the SET intermediate at lower temperature. The concerted reaction of CSI with **2** was also greatly improved by shifting the equilibrium toward the complex at lower temperature. We will continue to investigate the synthetic utility of shifting the equilibrium to enhance the usefulness of reactions with CSI and other less reactive isocyanate electrophiles. Our data also support an in-plane transition state for both the stepwise and concerted [2 + 2] reactions of CSI with alkenes.

4. EXPERIMENTAL SECTION

Monofluoroalkenes were synthesized and distilled as described previously.[5] *p*-Methoxy-*β*-fluorostyrene (**5**) was stored as a standard solution in methylene chloride after distillation since neat samples decomposed over time. The hydrocarbon styrenes were distilled prior to use. CSI was used from a fresh bottle and it was distilled prior to use every 3−5 days after opening. Methylene chloride was dried over sieves. Glassware was dried in the oven and then allowed to cool in a desiccator. Reliable kinetic data with CSI is a challenge as evidenced by the spread in rate constants reported by Clauss for reaction of CSI with hydrocarbon alkenes.[13] Our kinetic procedures were validated by reproducing data reported by Clauss for the reaction of CSI with hydrocarbon alkenes.[13] Second order kinetic data were obtained by following the disappearance of our monofluoroalkenes using gas chromatography with chlorobenzene, or in some cases 1,4-dichlorobenzene as internal standard. Disappearance of monofluoroalkenes **1** and **2** was followed by GC, and those kinetic data were also confirmed by following the disappearance of these monofluoroalkenes by ^{19}F NMR at 28.6 °C with 4-fluoroanisole as internal standard. For the cyclic monofluoroalkenes **6**, **7**, and **8**, only rate data by ^{19}F NMR at 28.6 °C were obtained.

Plots of $y = 1/(b_o - a_o)\ \ln a_o(b_o - x)/b_o(a_o - x)$ vs time[14] gave linear data. Better data were obtained for the slower reactions with 1-decene when they were run under pseudo-first-order conditions with CSI in excess. Rate constants listed in Table 1 are from an average of at least three kinetic runs unless indicated. Quantum chemical calculations to obtain IP values and thermodynamic data for complex formation of **1** and **2** were performed using second order perturbation theory[6a−e,7,8a,b] as described in our previous paper.[5]

Improved Procedure. Synthesis of *p*-Chlorophenylazetidin-2-one-*N*-sulfonyl Chloride (9). To 1.0 mmol of *p*-chlorstyrene in 2 mL of nitromethane with stirring at 0 °C was added 1.5 mmol of CSI. After 5 min, the reaction mixture was poured into water. The solid was filtered, washed with water then nitromethane and dried, mp 82−87 °C, crude yield 80%, lit.[1c] 82−84 °C). Combustion analysis and melting point data are given in the literature.[1c] Spectral data for **9**: IR (solid) 1817 cm^{-1}; ^{1}H NMR 400 MHz ($CDCl_3$) δ = 3.28 (dd, J = 16.8, 3.9 Hz, 1 H), 3.74 (dd, J = 16.8, 6.6 Hz, 1H), 5.28 (dd, J = 6.6, 3.9 Hz, 1H), 7.42 (m, 4H); ^{13}C 100 MHz ($CDCl_3$) δ = 47.1, 58.3, 128.2, 129.5, 133.1, 135.9, 161.4 ppm.

■ ASSOCIATED CONTENT

Supporting Information

Kinetic data and spectral data for **9**. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: dshellha@pointloma.edu.

Notes

The authors declare no competing financial interest.

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