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Iron(III) chloride (FeCl₃)-catalyzed electrophilic aromatic substitution of chlorobenzene with thionyl chloride (SOCl₂) and the accompanying auto-redox in sulfur to give diaryl sulfides (Ar₂S): Comparison to catalysis by aluminum chloride (AlCl₃)

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ABSTRACT

The Lewis acids MCl₃ (M = Fe and Al)-catalyzed electrophilic aromatic (ArH) substitution reactions with thionyl chloride (SOCl₂) have been shown to give diaryl sulfoxide (Ar₂SO) and the reduced diaryl sulfide (Ar₂S). Under various selected conditions, the FeCl₃-catalyzed reactions of chlorobenzene gave substantially much higher percent yields of Ar₂S (Ar = *p*-ClC₆H₄) than the reactions catalyzed by AlCl₃, showing that FeCl₃ facilitates the reduction in the sulfur center of SOCl₂. A d_π → p_π* back bond between Fe(III) and the O=S group is thought to be responsible for enhancement of the reduction.

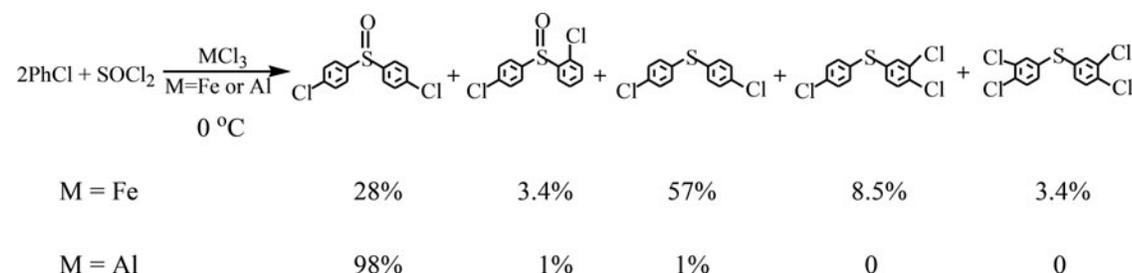
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Iron catalysis; auto-redox, aromatic; CH substitution; chlorobenzene; d_π-p_π* bonding

GRAPHICAL ABSTRACT



Introduction

Iron(III) chloride (FeCl₃) is a good Lewis acid and has been very widely and effectively employed as a catalyst in a variety types of organic chemical reactions.¹ Of these types of reactions, particularly interesting to us are the FeCl₃-catalyzed electrophilic aromatic substitution (EAS) reactions.^{1,2} As part of the efforts made in this scenario, we have previously carried out the reaction of benzene with selenyl chloride (SeOCl₂) in the presence of FeCl₃ as a catalyst, and the reaction was found to give a mixture of diphenyl selenide (Ph₂Se) and diphenyl diselenide (Ph₂Se₂) without the formation of diphenyl selenoxide (Ph₂SeO).³ We demonstrated that the formations of Ph₂Se and Ph₂Se₂ occur via an EAS mechanism which is accompanied by auto-redox processes on the selenium center facilitated by FeCl₃ (Figure 1).³ In this work, we extend the FeCl₃-catalyzed EAS reactions to thionyl chloride (SOCl₂), the sulfur analogue of SeOCl₂.

Previously, we have studied aluminum chloride (AlCl₃)-catalyzed EAS reactions of SOCl₂, and both diaryl sulfoxides (Ar₂SO, Ar=C₆H₅, *p*-CH₃C₆H₄, *o*-CH₃C₆H₄, and *p*-ClC₆H₄) and diaryl sulfides (Ar₂S, Ar=C₆H₅, *p*-CH₃C₆H₄, *o*-CH₃C₆H₄,

p-ClC₆H₄, and *p*-HOC₆H₄) were produced in different percent yields depending on reaction conditions without formation of diphenyl disulfide (Ph₂S₂) under any conditions.^{3,4} The formations of Ar₂SO and Ar₂S were demonstrated^{3,4} to take place via the EAS and auto-redox on sulfur which are analogous to those involved in the FeCl₃-catalyzed EAS of SeOCl₂ as shown in Figure 1. In the present work, we study the FeCl₃-catalyzed reactions of SOCl₂ with chlorobenzene (PhCl). We have found that at the same conditions (temperature and the manner of mixing starting materials) all the FeCl₃-catalyzed reactions gave substantially much higher percent yields of diaryl sulfide Ar₂S (Ar = *p*-ClC₆H₄) than the reactions catalyzed by AlCl₃, showing that FeCl₃ facilitates the auto-redox process on the sulfur center in the reactions of PhCl with SOCl₂. The findings are unique, and we believe it is worthy to report them in the present article.

As reported previously by different workers, diaryl sulfoxides and sulfides have many important applications in organic synthesis and biomedical aspects.^{5–10} Our findings in the role of FeCl₃ in facilitating the auto-redox of sulfur are also significant and have contributed new aspects to the iron catalysis.

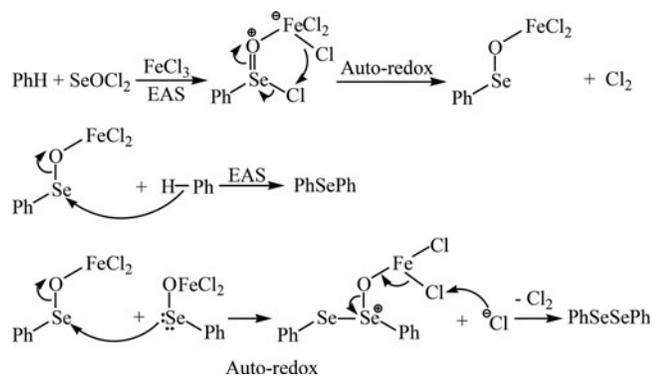


Figure 1. The FeCl₃-catalyzed reaction of benzene with SeOCl₂ giving Ph₂Se and Ph₂Se₂ via an EAS reaction and subsequent auto-redox processes on selenium.³

Results and discussion

The FeCl₃-catalyzed reactions of PhCl with SOCl₂ and comparison to the AlCl₃ catalysis

Table 1 shows the product distributions for the MCl₃ (M = Fe and Al)-catalyzed reactions of PhCl with SOCl₂ in different conditions (temperature, manner of mixing the starting materials, and molar ratio of the starting materials). At both 0°C and 25°C (Entries 1 and 2), the reactions catalyzed by FeCl₃ gave a total of five products; two isomers of diaryl sulfoxides and three reduced diaryl sulfides, with the total percentage (normalized) of the diaryl sulfides being about 69% and 57% at 0°C and 25°C, respectively. By contrast, the AlCl₃-catalyzed reactions at these temperatures mainly gave two sulfoxide isomers with only 1% and 7% (normalized) diaryl sulfide formed at 0°C and 25°C, respectively. When the temperature was further raised to 80°C (Entries 3 and 4), the FeCl₃-catalyzed reactions only gave the reduced diaryl sulfide products without formation of sulfoxide, while the AlCl₃-catalyzed reactions mainly gave two isomers of diaryl sulfoxide with only 6% diaryl sulfide formed. All these

results demonstrate that by comparison to the AlCl₃ catalysis, utilization of FeCl₃ as a catalyst substantially facilitated the auto-redox process on sulfur so that the diaryl sulfides became the major products.

In addition to the auto-redox on sulfur to lead to the formation of (4-ClC₆H₄)₂S, the FeCl₃-catalyzed reactions of PhCl with SOCl₂ led to the formations of further chlorinated diaryl sulfide products (4-ClC₆H₄)S(3,4-Cl₂C₆H₃) and (3,4-Cl₂C₆H₃)₂S (Table 1). It is a remarkable feature observed for the reactions. At an elevated temperature (80°C) (Entries 3 and 4), formations of (4-ClC₆H₄)S(3,4-Cl₂C₆H₃) and (3,4-Cl₂C₆H₃)₂S became the major processes. When the molar ratio of PhCl : SOCl₂ : FeCl₃ = 2:1:1 (Entry 4), the molar percentages (normalized) of (4-ClC₆H₄)₂S, (4-ClC₆H₄)S(3,4-Cl₂C₆H₃), and (3,4-Cl₂C₆H₃)₂S in the product were 7%, 52%, and 41%, respectively. When the molar ratio of PhCl : SOCl₂ : FeCl₃ became 1:1:1, as the quantity of PhCl decreased and the quantity of SOCl₂ increased relatively, the percentage of (3,4-Cl₂C₆H₃)₂S in the product substantially increased coincident with the decrease in (4-ClC₆H₄)S(3,4-Cl₂C₆H₃), and the molar percentages (normalized) of (4-ClC₆H₄)₂S, (4-ClC₆H₄)S(3,4-Cl₂C₆H₃), and (3,4-Cl₂C₆H₃)₂S in the product became 3%, 24%, and 73%, respectively (Entry 3).

Our previous work has shown that the auto-redox on sulfur in the AlCl₃-catalyzed EAS reactions of SOCl₂ and the auto-redox on selenium in the AlCl₃- and FeCl₃-catalyzed EAS reactions of SeOCl₂ gave a byproduct of Cl₂.^{3,4} Presumably and conceivably, the Cl₂ byproduct is also formed in the FeCl₃-catalyzed reaction of PhCl with SOCl₂. This is strongly evidenced by the observed chlorination of the aromatic rings (by Cl₂) to lead to the formations of (4-ClC₆H₄)S(3,4-Cl₂C₆H₃), and (3,4-Cl₂C₆H₃)₂S in all the FeCl₃-catalyzed reactions (Table 1). Comparing to the previously studied AlCl₃-catalyzed reactions,^{3,4} the production of Cl₂ in the FeCl₃-catalyzed reactions, along with the conversion of S(IV) in SOCl₂ to S(II) in Ar₂S, supports a similar, proposed auto-redox mechanism as

Table 1. Distributions of products formed in the MCl₃ (M = Fe and Al)-catalyzed reactions of PhCl with SOCl₂^a

	$2\text{PhCl} + \text{SOCl}_2 \xrightarrow[\text{M=Fe or Al}]{\text{MCl}_3} \text{Cl-C}_6\text{H}_4\text{-SO-C}_6\text{H}_4\text{-Cl} + \text{Cl-C}_6\text{H}_3(\text{Cl})_2\text{-SO-C}_6\text{H}_4\text{-Cl} + \text{Cl-C}_6\text{H}_4\text{-S-C}_6\text{H}_4\text{-Cl} + \text{Cl-C}_6\text{H}_3(\text{Cl})_2\text{-S-C}_6\text{H}_4\text{-Cl} + \text{Cl-C}_6\text{H}_3(\text{Cl})_2\text{-S-C}_6\text{H}_3(\text{Cl})_2\text{-Cl}$				
M = Fe	28%	3.4%	57%	8.5%	3.4%
M = Al ^b	98%	1%	1%	0	0
(Entry 1)	SOCl ₂ added dropwise to the PhCl/MCl ₃ mixture at 0°C PhCl : SOCl ₂ : MCl ₃ = 1:1:1 (molar ratio)				
M = Fe	39%	4%	38%	7%	12%
M = Al	76%	17%	7%	0	0
(Entry 2)	MCl ₃ added to the PhCl/SOCl ₂ mixture at 25°C PhCl : SOCl ₂ : MCl ₃ = 1:1:1 (molar ratio)				
M = Fe	0	0	3%	24%	73%
M = Al ^c	78%	16%	6%	0	0
(Entry 3)	SOCl ₂ added dropwise to the PhCl/MCl ₃ mixture at 80°C PhCl : SOCl ₂ : MCl ₃ = 1:1:1 (molar ratio)				
M = Fe	0	0	7%	52%	41%
M = Al	79%	21%	0	0	0
(Entry 4)	SOCl ₂ added dropwise to the PhCl/MCl ₃ mixture at 80°C PhCl : SOCl ₂ : MCl ₃ = 2:1:1 (molar ratio)				

^aAll the percentages are relative normalized yields (GC yields), determined by comparison of areas of the GC spectra of related components on the basis, as previously established,³ that the peak area is proportional to the number of moles of the component.

^bEssentially, only the *para*-isomer of diaryl sulfoxide was formed based on GC-MS analysis. The overall isolated percent yield was determined to be 63% by comparison of the actually recovered mass of the product with the theoretical yield of diaryl sulfoxide. Therefore, the absolute conversion yield of the *para*-isomer should be 62% (98% × 63%).

^cMainly, the *para*- and *ortho*-isomers of diaryl sulfoxide were formed with overall isolated percent yield being 80%. Therefore, the absolute conversion yields of the *para*-isomer and *ortho*-isomer should be 62% (78% × 80%) and 13% (16% × 80%), respectively.

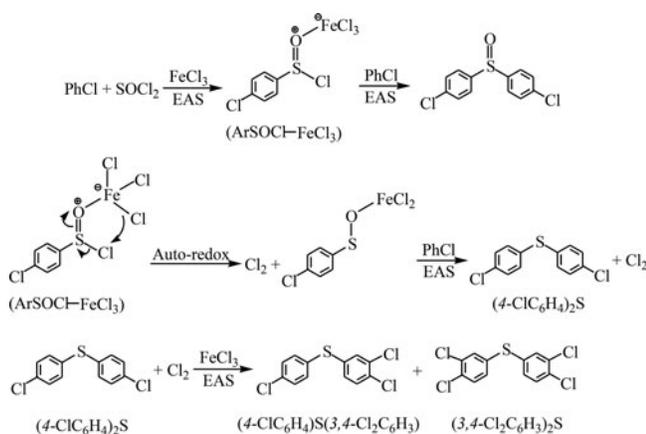


Figure 2. Mechanism for the FeCl₃-catalyzed reaction of PhCl with SOCl₂.

shown in Figure 2.¹¹ The overall process is demonstrated in Figure 2.

Previously, we have identified chlorination of PhOH to form minor *p*-ClC₆H₄OH in the course of an AlCl₃-catalyzed reaction of phenol (PhOH) with SOCl₂ giving (*p*-HOC₆H₄)₂S and the Cl₂ by-product as a result of the auto-redox on sulfur.³ By comparison of the reaction with the molar ratio of PhCl : SOCl₂ : FeCl₃ = 2:1:1 (Entry 4) and the reaction with the molar ratio of PhCl : SOCl₂ : FeCl₃ = 1:1:1 (Entry 3) at 80°C (Table 1), as the relative quantity of SOCl₂ increased and became excess and the relative quantity of PhCl decreased and became deficit, the extent of chlorination on the aromatic rings of the initially formed (4-ClC₆H₄)₂S was enhanced. As a result, the 1:1:1 reaction (Entry 3) gave much higher percentage (73%) of (3,4-Cl₂C₆H₃)₂S than that (41%) of (3,4-Cl₂C₆H₃)₂S produced in the 2:1:1 reaction (Entry 4). As the percentage of (3,4-Cl₂C₆H₃)₂S was getting higher, the percentage of (4-ClC₆H₄)S(3,4-Cl₂C₆H₃) in the product was getting correspondingly lower.

The iron(III) d-orbital facilitated intramolecular auto-redox processes on sulfur in the FeCl₃-catalyzed EAS reactions of SOCl₂

The studies of MCl₃ (M = Fe and Al)-catalyzed reactions of PhCl with SOCl₂ have shown that under the same conditions, the FeCl₃-catalyzed reactions always produce much higher percent yields of diaryl sulfides than the reactions catalyzed by AlCl₃. Under certain conditions (Table 1 Entries 3 and 4, reactions at 80°C), all the products generated from the FeCl₃-catalyzed reactions are diaryl sulfides without formation of diaryl sulfoxides, while the AlCl₃ catalyzed reactions, on the other hand, give diaryl sulfoxides as major products. This shows that the utilization of FeCl₃ as a catalyst for the EAS reactions of SOCl₂ greatly facilitates the intramolecular auto-redox on sulfur (Figure 2) to lead to formation of diaryl sulfides. We believe that this effect is accomplished via the iron(III) d-orbital participation in the overall reactions.

The symmetry of the empty p_π* orbital (the antibonding π* orbital) in the S=O bond domain of the ArSOCl-FeCl₃ intermediate (Figure 2) matches the symmetry of the filled d_π orbital in the iron atom. Therefore, the d_π and p_π* orbitals can overlap

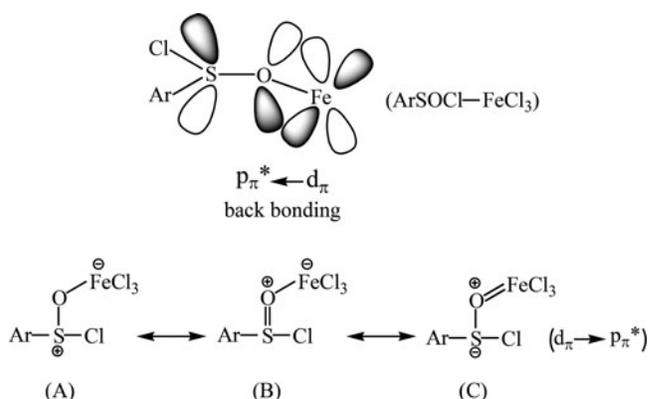


Figure 3. The d_π-p_π* back bonding between Fe(III) and S=O in the ArSOCl-FeCl₃ adduct molecule and possible resonance structures of ArSOCl-FeCl₃. The d_π (d_{yz}) orbital is perpendicular to the FeCl₃ molecule plane (the *xy*-plane).

effectively in sideways to form a d_π → p_π* back bond between the iron and oxygen atoms in ArSOCl-FeCl₃ (Figure 3). As a result, the d_π electrons in iron flow into the S=O p_π* orbital to partially neutralize the positive charge in sulfur decreasing its electrophilicity. The resonance structure (C) in Figure 3 results from the d_π → p_π* back bonding and further demonstrates the electron transfer from iron to sulfur. Consequently, the sulfur center in ArSOCl-FeCl₃ cannot be attacked efficiently by the nucleophilic aromatic ring in PhCl to make Ar₂SO (Ar = *p*-ClC₆H₄). Instead, the intramolecular auto-redox process in ArSOCl-FeCl₃, as shown in Figure 2, becomes more prominent, much faster than the EAS of ArH with ArSOCl-FeCl₃, to give Ar₂S as the major or sole product and the Cl₂ by-product. We believe that this accounts for the role of FeCl₃ in facilitating the auto-redox processes in the FeCl₃-catalyzed EAS reactions of SOCl₂. Recently, we have found that by comparison with the AlCl₃ catalysis, the FeCl₃-catalyzed reaction of benzene with SeOCl₂, the selenium analogue of SOCl₂, generated higher yield of the reduced Ph₂Se₂ indicating a similar role of FeCl₃ in facilitating the analogous auto-redox on selenium in the EAS reactions of SeOCl₂.³

Conclusions

In this work, the previously established FeCl₃-catalyzed EAS reaction of SeOCl₂³ has been extended to SOCl₂ (the sulfur analogue) and the results are compared to the catalysis by AlCl₃. Under the same conditions, including reaction temperature, the molar ratio of the reactants, and the manner of mixing starting materials, the FeCl₃-catalyzed reactions of PhCl with SOCl₂ have been found to give substantially much higher percent yields of diaryl sulfides Ar₂S (Ar = 4-ClC₆H₄) than the reactions catalyzed by AlCl₃, showing that FeCl₃ facilitates the auto-redox in the sulfur center of SOCl₂. A d_π → p_π* back bond between the iron and oxygen atoms in the ArSOCl-FeCl₃ intermediate formed in the first step of EAS reaction is proposed to account for the enhancement of the auto-redox by FeCl₃. The d_π electrons in iron can be transferred into the empty S=O p_π* orbital to decrease the electrophilicity in sulfur. As a result, the sulfur center in ArSOCl-FeCl₃ becomes much less reactive towards an aromatic ring. Instead, the intramolecular auto-redox in ArSOCl-FeCl₃

takes place predominately to give Ar₂S as the major or a sole product.

Iron catalysis has been shown to play very important roles in organic chemistry.^{1,2} We believe that our present research has made contributions of new and interesting aspects to this significant area.

Experimental

Chemical reagents

Thionyl chloride (SOCl₂) (purified) from J. T. Baker Chemical Company was used. Chlorobenzene (PhCl) (99%) were obtained from Sigma Aldrich. Granular anhydrous aluminum chloride (AlCl₃) (99%, extra pure) was obtained from Acros Organics. Powdery iron(III) chloride (FeCl₃) (98%), diethyl ether (solvent), dichloromethane (99.9%, the solvent for GC-MS samples), and anhydrous sodium sulfate (99.5%, drying agent) were purchased from Fisher Scientific Company.

The GC-MS measurements

Reaction products were identified using a Varian CP-3800 gas chromatograph-Varian Saturn 2200 mass spectrometer. The sample of each product was prepared in an approximate 1% (m/m) dilution in dichloromethane. One-microliter of the solution was injected onto a Chrompack CP-SIL 8-CB 30 m × 0.25 mm capillary column using a He carrier gas of 1.0 mL/min, a 1/100 injection split ratio, and a temperature ramp of 150°C to 240°C (10°C/min). All chemical compounds were eluted in 10 min. The individual compounds contained in each product, including Ar₂SO (Ar = *p*-ClC₆H₄), ArSOAr' (Ar, Ar' = *p*-ClC₆H₄, *o*-ClC₆H₄), Ar₂S (Ar = 4-ClC₆H₄, and 3,4-Cl₂C₆H₃), and ArSOAr' (Ar, Ar' = 4-ClC₆H₄, 3,4-Cl₂C₆H₃), were identified by comparison of their mass spectra with those on the available NIST database. Their molar percentages (normalized) in the product were estimated, as previously established,³ by comparing the related GC peak areas on such a basis that the peak area is proportional to the number of moles of the related compound.

The MCl₃ (M = Fe and Al)-catalyzed reactions of PhCl with SOCl₂

Approach 1: The reactions were conducted in the fumehood at 0°C with the molar ratio of PhCl : SOCl₂ : MCl₃ being 1:1:1 and usage of SOCl₂ approximately 10 mmol [PhCl (1.13 g, 10.0 mmol), SOCl₂ (1.19 g, 10.0 mmol), and AlCl₃ (1.33 g, 10.0 mmol) or FeCl₃ (1.62 g, 10.0 mmol)]. For each reaction, SOCl₂ was added dropwise to the PhCl-MCl₃ (M = Fe or Al) mixture in a large test tube (80 mL) with constant stirring (For the AlCl₃-catalyzed reaction, SOCl₂ was added after the granular AlCl₃ had been mostly crushed). The reaction took place quickly, indicated by bubbling (formation of HCl) as above. After all the SOCl₂ was added, the reaction went to completion (in about 2 h), indicated by the cessation of bubbling. Then iced water (40 mL) was poured into the reaction mixture. This was followed by the addition of diethyl ether (20 mL). All the contents were transferred into a separatory funnel and shaken well

to ensure that the organic product had been fully extracted into the ether phase. The ether and water phases were separated. The water phase was extracted by diethyl ether (20 mL) again. Then all the ether solutions were combined and dried by anhydrous sodium sulfate. The dried ether solution was filtered off and left in the fumehood. Eventually, all the diethyl ether solvent evaporated, giving the final reaction product. The product was then characterized by GC-MS, and the results are shown in Table 1 (Entry 1).

Approach 2: The reactions were conducted in the fumehood at 25°C with the molar ratio of PhCl : SOCl₂ : MCl₃ being 1:1:1 and usage of SOCl₂ approximately 10 mmol (as above). For the FeCl₃-catalyzed reactions, powdery FeCl₃ was added in 10 aliquots to the PhCl-SOCl₂ mixture in a large test tube (80 mL). The reaction took place quickly, indicated by bubbling as above. After all the FeCl₃ was added, the reaction went to completion, indicated by the cessation of bubbling. Then the aqueous work-up was performed as above. The final product was characterized by GC-MS, and the results are shown in Table 1 (Entry 2). For the AlCl₃-catalyzed reactions, granular AlCl₃ was added piecewise to the PhCl-SOCl₂ mixture in a large test tube (80 mL) as follows: First, one piece of AlCl₃ was added and gas (HCl) bubbles started to form immediately. The piece of AlCl₃ was crushed using a stirring rod. When most of the pieces of AlCl₃ had dissolved and bubbling occurred very slowly, another piece of AlCl₃ was added. All the AlCl₃ granules were eventually added into the PhCl-SOCl₂ mixture piece-by-piece. The reaction went to completion, indicated by the cessation of bubbling after all the AlCl₃ had been added. Then an aqueous work-up was performed as above. The final product was characterized by GC-MS, and the results are shown in Table 1 (Entry 2).

Approach 3: The reactions were conducted in the fumehood at 80°C with the molar ratio of PhCl : SOCl₂ : MCl₃ being 1:1:1 and usage of SOCl₂ approximately 10 mmol (as above). For each reaction, SOCl₂ was added dropwise to the PhCl-MCl₃ (M = Fe or Al) mixture in a large test tube with constant stirring (For the AlCl₃-catalyzed reaction, SOCl₂ was added after the granular AlCl₃ had been mostly crushed). The procedure and observations were the same as those for the above reactions conducted at 0°C. The final product was characterized by GC-MS, and the results are shown in Table 1 (Entry 3).

Approach 4: The reactions were conducted in the fumehood at 80°C with the molar ratio of PhCl : SOCl₂ : MCl₃ being 2:1:1 and usage of SOCl₂ approximately 10 mmol [PhCl (2.26 g, 20.1 mmol), SOCl₂ (1.19 g, 10.0 mmol), and AlCl₃ (1.33 g, 10.0 mmol) or FeCl₃ (1.62 g, 10.0 mmol)]. For each reaction, SOCl₂ was added dropwise to the PhCl-MCl₃ (M = Fe or Al) mixture in a large test tube with constant stirring (For the AlCl₃-catalyzed reaction, SOCl₂ was added after the granular AlCl₃ had been mostly crushed). The procedure and observations were the same as those for the above 1:1:1 reactions at 80°C (Approach 3). The final product was characterized by GC-MS, and the results are shown in Table 1 (Entry 4).

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