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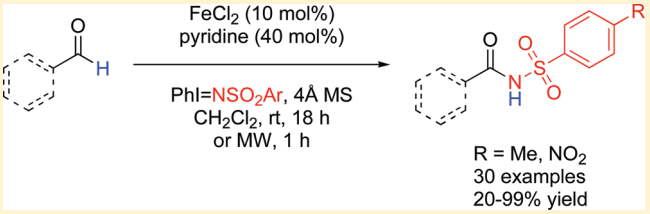
Iron(II)-Catalyzed Amidation of Aldehydes with Iminoiodinanes at Room Temperature and under Microwave-Assisted Conditions

Thi My Uyen Ton, Ciputra Tejo, Stefani Tania, Joyce Wei Wei Chang, and Philip Wai Hong Chan*

Division of Chemistry and Biological Chemistry, School of Physical and Mathematical Sciences, Nanyang Technological University, Singapore 637371, Singapore

Supporting Information

ABSTRACT: A method for the amidation of aldehydes with PhI=NTs/PhI=NNs as the nitrogen source and an inexpensive iron(II) chloride + pyridine as the *in situ* formed precatalyst under mild conditions at room temperature or microwave assisted conditions is described. The reaction was operationally straightforward and accomplished in moderate to excellent product yields (20−99%) and with complete chemoselectivity with the new C−N bond forming only at the formylic C−H bond in substrates containing other reactive functional groups. By utilizing microwave irradiation, comparable product yields and short reaction times of 1 h could be accomplished. The mechanism is suggested to involve insertion of a putative iron-nitrene/imido group to the formylic C−H bond of the substrate via a H-atom abstraction/radical rebound pathway mediated by the precatalyst $[Fe(py)_4Cl_2]$ generated *in situ* from reaction of $FeCl_2$ with pyridine.



INTRODUCTION

Establishing methods to amides is an immensely important pursuit in organic synthesis due to the role of this functional group as a privileged pharmacophore and building block in a myriad of biomolecules as well as pharmaceutically interesting compounds.[1] Typically, amide bond synthesis has relied on the condensation of an amine with a carboxylic acid in the presence of a coupling reagent.[2] Although shown to be highly efficient, producing H_2O as potentially the only byproduct, the utility of this approach has been lessened by the need for an extra step to convert the carboxylic acid to a more reactive derivative. This not only generates additional byproduct but also, in some cases, synthetic complications in the activated intermediates. For this reason, the development of alternative synthetic strategies to this ubiquitously important functional group has received an immense amount of attention over the years.[3−13] This has hitherto included Staudinger ligation,[4] Beckmann rearrangement of oximes,[5] aminocarbonylation of haloarenes, alkenes, and alkynes,[6] oxidative amidation of alcohols[7] and aldehydes,[8] hydrative amide synthesis with alkynes,[9] and amidation of ketones and thioacids with azides.[10]

As part of our efforts to develop new methods for amide bond synthesis, we recently reported one approach that relied on nitrene insertion at the formyl C−H bond of aldehydes with PhI=NTs as the nitrogen source and [Ru(TTP)(CO)] as the catalyst.[11] At about the same time, Chan and co-workers reported the same C−N bond forming process could be accomplished with $TsNH_2$ in the presence of $[Rh_2(esp)_2]$ (esp = α,α,α′,α′-2-tetramethyl-1,3-benzenedipropionate) as the catalyst and $PhI(OC(O)tBu)_2$ as the oxidant.[12] Thought to proceed via a highly reactive metal-nitrene/imido species, in both synthetic strategies the corresponding acyl sulfonamides were afforded in good to excellent yields. We subsequently showed that a more practical copper(I) halide catalyzed version of this reaction could be realized.[13] While less expensive and more ecologically benign than ruthenium, a drawback of this latter approach was the need to develop two distinct catalytic Cu(I) systems to achieve a broad substrate scope that included aromatic compounds. Thus, it remains a challenge to develop a synthetic method that can effect such reactions for a wide range of substrates in a manner that improves or at least maintains the practical and biocompatible nature of the catalytic system employed. In this regard, we envisioned that establishing an iron-mediated approach to this important amide forming reaction could hold promise as the basis to readdressing this shortcoming.[14] Recently, iron complexes and salts have come under renewed scrutiny in the field of amidation and aziridination of activated C−H and C=C bonds of alkanes and alkenes due to their low cost and less toxic nature when compared to other transition metals.[15,16] However, the use of iron catalysis to mediate the analogous nitrogen atom or group insertion reactions at the formylic C−H bond of aldehydes to our knowledge has, thus far, remained unexplored. Herein, we report the use of the *in situ* formed complex $[FeCl_2(py)_4]$ (py = pyridine) for amidation of a wide variety of aldehydes with $PhI{=}NSO_2Ar$ at room temperature and under microwave-assisted conditions (Scheme 1). The acyl sulfonamide products were afforded in moderate to excellent yields comparable to those reported for the analogous Ru(II)- and Cu(I)-promoted reactions.

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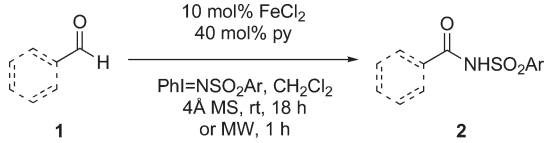
Scheme 1. Iron(II)-Catalyzed Amidation of Aldehydes with PhI=NTs at Room Temperature or under Microwave Irradiation (MW)



RESULTS AND DISCUSSION

In view of the challenges still posed by aromatic aldehydes in the analogous Cu(I)- and Ru(II)-catalyzed reactions, we began by examining the amidation of benzaldehyde **1a** by a variety of Fe(II) and Fe(III) salts, and the results are depicted in Table 1. This revealed that treating **1a** with 10 mol % of $FeCl_2$ (99.5% purity),[17] pyridine (0.4 equiv), and 2 equiv of PhI=NTs as the nitrogen source in CH_2Cl_2 at room temperature for 18 h gave the best result (entry 1). Under these conditions, *N*-tosylbenzamide **2a** was afforded in 90% yield that was found to be comparable to product yields of 83−93% obtained for the analogous amidations of **1a** with PhI=NTs mediated by Cu(I), Rh(II,II), and Ru(II).[11−13] Lower product yields of 74−78% were obtained when we employed a lower catalyst loading of 5 mol % or 1.5 equiv of PhI=NTs (entries 2 and 3). Likewise, conducting the reaction with benzene in place of CH_2Cl_2 as the solvent led to a comparable product yield of 73% (entry 4). In marked contrast, the analogous reactions with $TsNH_2$ + $PhI(OAc)_2$ or chloramine-T trihydrate ($TsNClNa\cdot 3H_2O$) + PhI=O as the nitrogen source were also found to give low product yields along with **3a** in 8−35% yield (entries 8 and 9). Similarly, low product yields along with recovery of **1a** and/or the imine adduct were found when the reaction was performed with 1.5 equiv of PhI=NTs in other solvent systems or with other pyridyl-based ligands (entries 5−7 and 11−14). In our hands, only the analogous reaction of **1a** with PhI=Ts mediated by $FeCl_2$ and DMAP afforded **2a** in a comparable yield of 88% (entry 10). An inspection of entries 15−21 in Table 1 also revealed the reaction to proceed less effectively with other Fe(II) and Fe(III) salts in the presence or absence of a ligand. In these reactions, the imine byproduct was additionally furnished in yields of 8−55%. More notably, the use of $Fe(OTf)_2$ was the only instance that was found to be superior than $FeCl_2$ in mediating the amidation process under ligand free conditions, furnishing **2a** in 50% yield (entry 20). However, repeating this reaction with pyridine gave a lower product yield of 28% (entry 15). Additionally, the contrasting activities exhibited by $FeCl_2$ and $FeCl_3$ suggested it was unlikely that these latter reactions proceeded via a common catalytically active iron species (entries 1 and 17 vs 16 and 21).

To define the scope of the present procedure, we next turned our attentions to the reactions of a variety of aldehydes (Table 2). In general, these experiments showed that with the $FeCl_2$ and pyridine combination, reaction of **1a** with PhI=NNs gave **2b** and a variety of substituted aromatic aldehydes PhI=NTs afforded the corresponding acyl sulfonamides **2c**−**o** in moderate to excellent yields (entries 1−14). This hitherto included substrates with a pendant Br, Cl, or MeO group at the *para* positon of the aromatic, which were previously shown to give the corresponding amide products in moderate yields of 47−65% in the analogous Cu(I)-mediated reactions.[13] Under our conditions, the $FeCl_2$-mediated reaction of 1-naphthaldehyde was the only

Table 1. Optimization of Reaction Conditions[a]

entry	catalyst	ligand	solvent	yield (%) 2a	yield (%) 3a
1	$FeCl_2$	pyridine	CH_2Cl_2	90	
2[b]	$FeCl_2$	pyridine	CH_2Cl_2	78	
3[c]	$FeCl_2$	pyridine	CH_2Cl_2	74	
4[c]	$FeCl_2$	pyridine	C_6H_6	73	
5[c]	$FeCl_2$	pyridine	PhMe	40	
6[c]	$FeCl_2$	pyridine	CH_3CN	27	
7[c]	$FeCl_2$	pyridine	1,4-dioxane	[d,e]	
8[f]	$FeCl_2$	pyridine	CH_2Cl_2	25	35
9[g]	$FeCl_2$	pyridine	CH_2Cl_2	59	8
10	$FeCl_2$	DMAP	CH_2Cl_2	88	
11	$FeCl_2$	2-picolinic acid	CH_2Cl_2	36	10
12	$FeCl_2$	quinaldic acid	CH_2Cl_2	11	36
13	$FeCl_2$	2,6-pyridinedicarboxylic acid	CH_2Cl_2	[d]	48
14	$FeCl_2$	quinoline	CH_2Cl_2	27[h]	33
15	$Fe(OTf)_2$	pyridine	CH_2Cl_2	28	32
16	$FeCl_3$	pyridine	CH_2Cl_2	49[h]	
17	$FeCl_2$		CH_2Cl_2	35	42
18	$FeBr_2$		CH_2Cl_2	28	15
19	$Fe(OAc)_2$		CH_2Cl_2	26	51
20	$Fe(OTf)_2$		CH_2Cl_2	50	49
21	$FeCl_3$		CH_2Cl_2	24	55

[a] Unless otherwise stated, all reactions were carried out for 18 h at rt in the presence of powdered 4 Å MS (400 mg) with [Fe]:py:**1a**:PhI=NTs molar ratio = 1:4:10:20. [b] Reaction conducted with 5 mol % of $FeCl_2$. [c] Reaction conducted with 1.5 equiv of PhI=NTs. [d] No reaction based on TLC and ^{1}H NMR analysis of the crude mixture. [e] Near quantitative recovery of **1a**. [f] PhI=NTs was replaced by $PhI(OAc)_2$ and $TsNH_2$. [g] PhI=NTs was replaced by PhIO and $TsNClNa\cdot 3H_2O$. [h] Recovery of **1a** in 40−50% yield.

example of a sterically demanding substrate that was found to deliver the amidation product in a moderate yield of 46% (entry 14). On the other hand, reactions of a variety of alkyl aldehydes examined were found to afford the corresponding acyl sulfonamide products **2p**−**z** in good to excellent yields (entries 15−25). A similar outcome was found for reactions of aliphatic aldehydes containing an alkene functional group (entries 26−29). More notably, in these reactions where either a competing aziridination or tertiary C−H amidation process was a potential problem, the corresponding acyl sulfonamides **2e**, **2q**−**r**, **2u**−**w**, **2α**−***ε*** were furnished as the sole product in yields of 48−99%. The only substrates examined that failed or found to be less effective in our hands were **1m** and **1x** and the carbaldehydes of furan and thiophene **1*ζ*** and **1*η*** (entries 12, 23, and 31−32). Under the standard conditions, reaction of **1x** was found to lead to the formation of toluene on the basis of ^{1}H NMR and ESI-MS measurements of the crude mixture, whereas **1m** and **1*ζ*** resulted in their recovery and **1*η*** afforded **2*η*** in 20% yield.

Microwave irradiation has been extensively documented in recent years as a method to accelerate transition metal catalyzed

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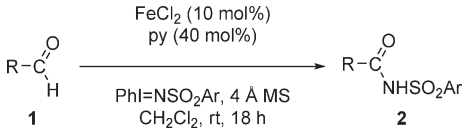
reactions and their potential for scale-up applications.[18] With this in mind, we also investigated the iron mediated transformation of aldehydes to amides under microwave assisted conditions with **1a**, **1o**, **1v**, **1β**, **1ε**, and **1η** chosen as representative examples, as shown in Scheme 2. In the presence of 10 mol % of $FeCl_2$, pyridine (0.4 equiv) and PhI=NTs (2 equiv) in CH_2Cl_2 and microwave irradiation for 1 h, these subtrates provided the corresponding acyl sulfonamide products in yields of 38−99%, comparable to those obtained at room temperature.

The preferential formation of toluene for the amidation of **1x** mentioned earlier in entry 23 in Table 2 led us to speculate on the possible involvement of a radical species in the present Fe(II)-catalyzed reactions. This would be not inconceivable in view of the fact that it has been previously reported that decarbonylation of a phenylacetyl radical has been measured in the order of $k_d = 5.2 \times 10^7\ s^{-1}$ at 25 °C.[19] The premise that the amidation proceeds via a radical intermediate would be consistent with our findings showing the detection of only the aldehyde based on TLC and ^1H NMR analysis of the crude reaction mixture of **1a** + PhI=NTs exposed to 10 mol % of $FeCl_2$, 40 mol % of pyridine, and the radical scavenger butylhydroxytoluene (BHT) under the standard conditions. Indeed, this is further supported by competitive rate studies under the conditions shown in Figure 1.

Table 2. Iron(II)-Catalyzed Amidation of Aldehydes 1a−η[a]



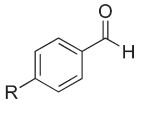
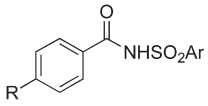
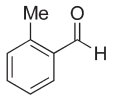
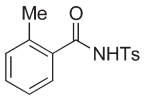
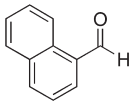
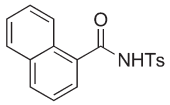
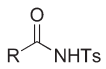
entry	substrate	product	yield (%)
1[b]	 **1a**, **c-m**	 **2b**, R = H, Ar = *p*-$NO_2C_6H_4$	94
2		**2c**, R = OMe, Ar = *p*-$CH_3C_6H_4$	77
3		**2d**, R = ^{t}Bu, Ar = *p*-$CH_3C_6H_4$	95
4		**2e**, R = ^{i}Pr, Ar = *p*-$CH_3C_6H_4$	92
5		**2f**, R = Me, Ar = *p*-$CH_3C_6H_4$	94
6		**2g**, R = Ph, Ar = *p*-$CH_3C_6H_4$	82
7		**2h**, R = Br, Ar = *p*-$CH_3C_6H_4$	83
8		**2i**, R = Cl, Ar = *p*-$CH_3C_6H_4$	82
9		**2j**, R = F, Ar = *p*-$CH_3C_6H_4$	99
10		**2k**, R = CF_3, Ar = *p*-$CH_3C_6H_4$	65
11		**2l**, R = CO_2Me, Ar = *p*-$CH_3C_6H_4$	99
12		**2m**, R = NO_2, Ar = *p*-$CH_3C_6H_4$	-[c]
13	 **1n**	 **2n**	78
14	 **1o**	 **2o**	46
15		**2p**, R = Et	99
16		**2q**, R = ^{i}Pr	99
17	 **1p-t**	 **2r**, R = ^{i}Bu	95
18		**2s**, R = ^{t}Bu	70
19		**2t**, R = ^{n}Hex	90
20		**2u**, *n* = 1	96

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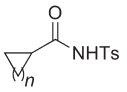
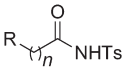
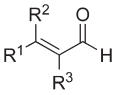
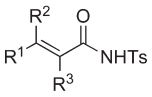
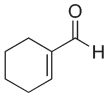
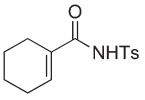
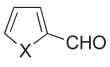
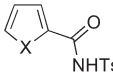
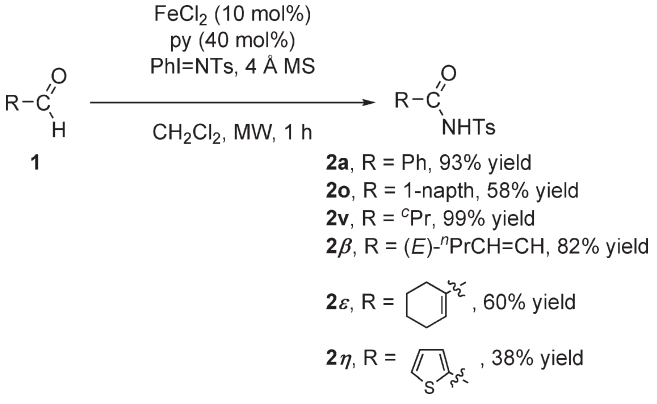
Table 2. Continued

entry	substrate	product	yield (%)
21		 **2v**, $n = 3$	99
22	**1u-w**	**2w**, $n = 4$	90
23		**2x**, $n = 1$, R = Ph	-[d]
24		 **2y**, $n = 2$, R = Ph	61
25	**1x-z**	**2z**, $n = 2$, R = CO_2Me	50
26		**2α**, $R^1 = R^2 = Me$, $R^3 = H$	77
27		 **2β**, $R^1 = {}^n$Pr, $R^2 = R^3 = H$	83
28		**2γ**, R^1 = Ph, $R^2 = R^3 = H$	48
29	**1α-δ**	**2δ**, R^1 = Et, R^2 = H, R^3 = Ph	78
30		 **2ε**	51
31	**2ε** 	**2ζ**, X = O	-[e]
32	**2ζ-η**	 **2η**, X = S	20

[a] Unless otherwise stated, all reactions were carried out for 18 h at rt in the presence of powdered 4 Å MS with $FeCl_2$ (99.5% purity):[17]py:**1**:PhI=NTs molar ratio = 1:4:10:20. [b] PhI=NTs was replaced by PhI=NNs. [c] Trace amount (<1%) of product detected on the basis of ^{1}H NMR analysis of the crude mixture but not isolated. [d] Toluene detected on the basis of GC and ^{1}H NMR analysis. [e] No reaction based on TLC and ^{1}H NMR analysis of the crude mixture.

Scheme 2. Iron(II)-Catalyzed Amidation of Aldehydes with PhI=NTs under Microwave Irradiation



This revealed a $\log(k_{rel})$ value of −0.103 that suggested there were no significant electronic effects in the amidation process. With the exception of **1m**, the absence of such effects would also account for our earlier results showing aromatic aldehyde amidation to proceed well regardless of the presence of an electron-withdrawing or electon-donating group depicted in entries 2−11 in Table 2. Additionally, the near zero reaction constant is comparable to that found for manganese corrole catalyzed alkene aziridinations reported by Abu-Omar and co-workers in which a nonpolar transition state and a radical-type mechanism was proposed.[20]

In view of recent works showing the true catalytic species in the reported cross-coupling reactions to be due to trace amounts of Cu and Pd in the iron salts,[21] this possibility was next examined with **1a** and **1k** as the test substrates under the conditions described in Table 3. This initially revealed the amidation of **1a** with PhI=NTs in the presence of 0.05 mol % of Cu_2O as the catalyst gave the corresponding imine **3a** as the sole product and recovery of the aldehyde in 29% and 71% yield, respectively (entry 3). Repeating this process with **1k** in place of **1a** and 1 mol % of the metal oxide as well as chloride and triflate salts of Cu(I) and Cu(II) was found to give a similar outcome (entries 5−9). In all of these reactions, the corresponding imine **3k** was preferentially afforded in near quantitative yields. The analogous reactions with 1 mol % of either $Pd(PPh_3)_4$ or $Pd(OAc)_2$ were also found to lead to the exclusive formation of the imine adduct in 58−61% yield and recovery of the substrate in 39−42% yield (entries 10 and 11). In marked contrast, the acyl sulfonamide products **2a** and **2k** were obtained in respective yields of 92% and 70% when we carried out the corresponding reactions of **1a** and **1k** with 10 mol % of $FeCl_2$ of 99.99% purity[17] (entries 1 and 4). Likewise, reaction of **1a** with 10 mol % of $[FeCl_2(py)_4]$, prepared following literature procedure and structurally determined by X-ray crystallography (see Figure S40 in the Supporting Information),[22] was found to deliver **2a** in 93% yield (entry 2). The product yields and chemoselectivities obtained

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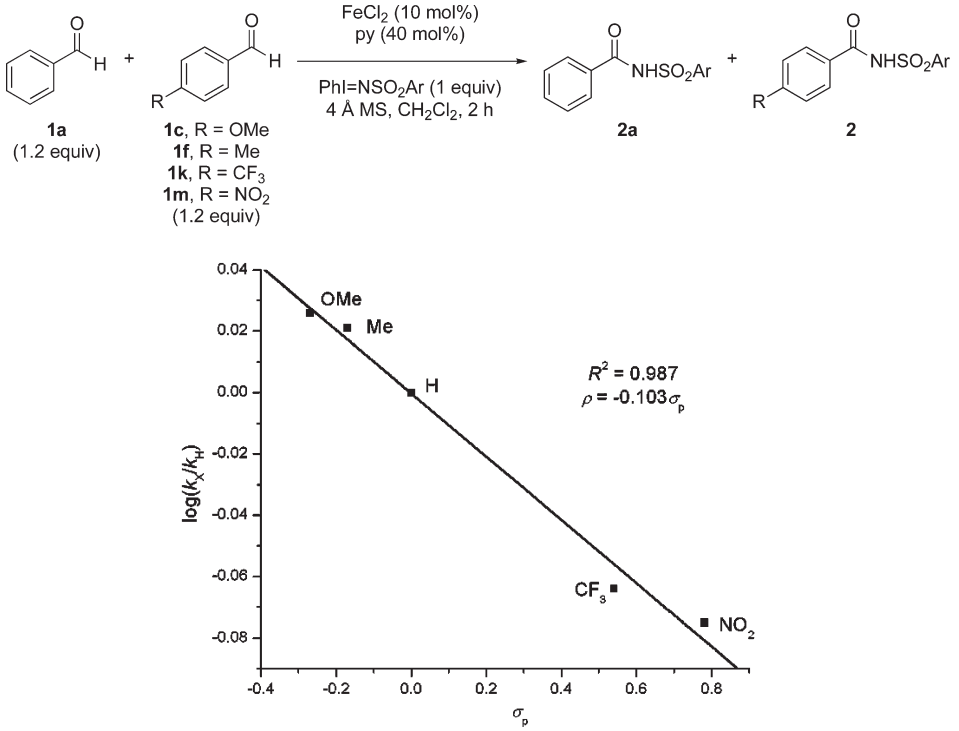
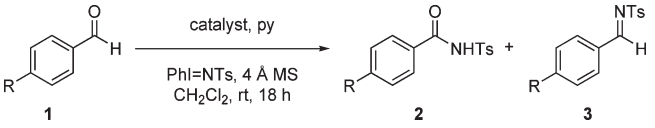


Figure 1. Linear free-energy correlation of log k_X/k_H versus σ_p plot for amidation of *para*-substituted aldehydes **2a**, **2c**, **2f**, **2k**, and **2m**.

Table 3. Determining the Potential Role of Trace Amounts of Cu and Pd in the Aldehyde Amidation Process[a]



entry	substrate	catalyst	product	yield (%)
1[b]	**1a**, R = H	$FeCl_2$	**2a**	92
2[c]	**1a**, R = H	$[FeCl_2(py)_4]$	**2a**	93
3[d]	**1a**, R = H	Cu_2O	**3a**	29[e]
4[b]	**1k**, R = CF_3	$FeCl_2$	**2k**	70
5	**1k**, R = CF_3	Cu_2O	**3k**	99
6	**1k**, R = CF_3	CuCl	**3k**	99
7	**1k**, R = CF_3	CuOTf	**3k**	99
8	**1k**, R = CF_3	$Cu(OTf)_2$	**3k**	99
9	**1k**, R = CF_3	$CuCl_2$	**3k**	99
10	**1k**, R = CF_3	$Pd(PPh_3)_4$	**3k**	61[e]
11	**1k**, R = CF_3	$Pd(OAc)_2$	**3k**	58[e]

[a] Unless otherwise stated, all reactions were carried out for 18 h at rt in the presence of powdered 4 Å MS with catalyst:py:**1**:PhI=NTs molar ratio = 0.1:0.4:10:20. [b] Reaction conducted with 10 mol % of $FeCl_2$ of 99.99% purity[17] and 40 mol % of py. [c] Reaction conducted with 10 mol % of $[FeCl_2(py)_4]$ and in the absence of py. [d] Reaction conducted with 0.05 mol % of Cu_2O and 0.2 mol % of py. [e] Recovery of aldehyde in 39−71% yield.

in these latter control experiments were also found to be comparable to those reported for the same substrates in Tables 1 and 2 using 99.5% pure $FeCl_2$ as the catalyst.[17] More importantly, the contrasting reactivities observed in Table 3 provided evidence that trace amounts of Cu and Pd impurities present in $FeCl_2$ used in this work are not the catalytically active species.

On the basis of the above results, we tentatively propose the present iron(II)-catalyzed amidation of aldehydes with PhI=NTs to proceed by C−H bond functionalization as outlined in Scheme 3.[15,23] This could involve the initial formation of the precatalyst $[FeCl_2(py)_4]$ from reaction of $FeCl_2$ with pyridine. Further reaction of this newly formed iron complex with PhI=NSO_2Ar then generates the putative highly reactive [Fe]=NSO_2Ar species **A**.[15k,23] In contrast to the analogous CuI-catalyzed aldehyde amidation reactions,[13] subsequent insertion of the nitrene/imido group from this intermediate to the formylic C−H bond of the substrate via a H-atom abstraction/radical rebound pathway is then thought to deliver the amide product **2**. The obtained product chemoselectivities are in good agreement with recent DFT calculations by Bolm and Shaik showing amidation is favored over aziridination when the nitrogen substituent contains an electron-withdrawing group and steric effects having little influence in these reactions.[23a] The role of pyridine as a ligand in the catalytic system that tempers the Lewis acidity of $FeCl_2$ through coordination to the metal center and *in situ* formation of $[FeCl_2(py)_4]$ is evident in a number of experiments examined in this work. First is the formation of only the acyl sulfonamide product for reactions of **1** conducted in the presence of the iron(II) salt and pyridine or $[FeCl_2(py)_4]$ under the various conditions described in Tables 1−3. In contrast, both **2a** and **3a** were observed on either removing the nitrogen heterocycle from the reaction conditions or replacing it with less basic ligands when we examined the amidation of **1a** (entries 11−14 and 17 in Table 1). We surmise the origin of the imine byproduct could be due to iron catalyzed hydrolysis of PhI=NTs to $TsNH_2$ by H_2O,[24] followed by condensation of this newly formed aryl sulfonamide with the aldehyde in the presence of the Lewis acidic metal salt.[25]

Given previous works demonstrating iron-catalyzed hydrolysis of the iminoiodinane to the aryl sulfonamide by H_2O to occur via iron-nitrene/imido species of the type **A** and/or **B**,[24]

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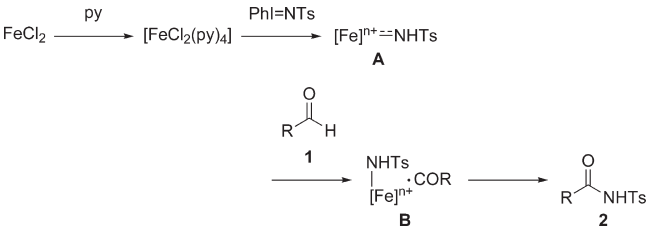
Scheme 3. Tentative Reaction Pathway for C−N Bond Formation



the competitive formation of the imine byproduct also implies the involvement of such intermediates in our reactions. Indeed, this speculation was supported by ^{1}H NMR measurements of an equimolar CD_2Cl_2 sample of $[FeCl_2(py)_4]$ and PhI=NTs (see Figure S37 in the Supporting Information). The resultant dark brown homogeneous solution was found to be diamagnetic with well-resolved ^{1}H NMR signals at normal fields that showed the methyl and *ortho* and *meta* aromatic C−H resonances of the tosyl group shifted downfield by 0.10−0.35 ppm relative to the respective signals in PhI=NTs and $TsNH_2$. Subsequent addition of **1a** to this CD_2Cl_2 sample then led to the detection of **2a** by ^{1}H NMR and TLC analysis.

Although further NMR analysis and mass spectrometry was not able to elucidate the exact structure of **A**, measurement of the deuterium kinetic isotope effect with **1a** and benzaldehyde-d_6 as the test substrates revealed a k_H/k_D value of 4.4 based on LC−MS analysis. This suggested that C−H bond cleavage resulting in the formation of the proposed radical species **B** is most probably the rate-determining step. This value is also comparable to k_H/k_D values reported for the analogous CuI-catalyzed benzaldehyde amidation reaction,[13] nitrene/imido insertion into the dibenzyl ether in the presence of CuCl as catalyst,[26] and [Ru(TMP)(NNs)$_2$] (H_2TMP = 5,10,15,20-tetramesitylporphyrin)-mediated amidation of ethyl benzene.[27]

While the above results are consistent with a H-atom abstraction/radical rebound pathway depicted in Scheme 3, other possible pathways were considered but discounted on the basis of the following control experiments. In addition to acting as a ligand to form the tetrapyridyliron(II) complex, we considered the possibility that pyridine could react with PhI=NTs and formation of the nitrene transfer agent *N*-tosyliminopyridine **4** shown in Figure 2.[28] With this in mind, the reaction of **1a** with an authentic sample of **4** in the presence of the iron catalyst under the standard conditions was first examined. Analysis of the resultant crude reaction mixture by TLC and ^{1}H NMR analysis showing only the presence of the aldehyde substrate led us to conclude the involvement of such a nitrene transfer agent to be less likely. Similarly, the competitive formation of the imine byproduct **3a** under certain conditions mentioned in Table 1 or its subsequent oxidation derivative **5** shown in Figure 2 led us to consider pathways in which these intermediates could be involved.[29] However, our findings showing only the recovery of the starting material for the respective reactions of **3a** and **5** exposed to 10 mol % of $FeCl_2$ and 40 mol % of pyridine under the standard conditions led us to also rule out the possibility of amide bond formation occurring via such intermediates. The direct conversion of the aldehyde to the amide functional group was further supported by our findings for the reaction of **1a** labeled with ^{13}C at the aldehyde position in CD_2Cl_2 under the standard

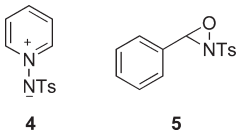


Figure 2. Possible amidation intermediates **4** and **5**.

conditions (see Figure 35 in the Supporting Information). Monitoring the progress of the reaction by ^{13}C NMR spectroscopy revealed the presence of two major signals in aliquots taken from the reaction mixture. These were, namely, that of the labeled benzaldehyde substrate ^{13}C-**1a** decreasing in intensity and that of labeled amide product ^{13}C-**2a** increasing in intensity.

CONCLUSION

In summary, an efficient and practical iron-catalyzed synthetic route to acyl sulfonamides based on nitrene/imido insertion into the formylic C−H bond of aldehydes has been reported. These results show that the reaction tolerates a structurally diverse set of starting aldehydes and compliment earlier works mediated by Ru(II) and Cu(I) catalysts. While the product yields and chemoselectivities obtained are also comparable, the present method was shown to benefit from a low-cost and extremely simple catalytic system generated *in situ* from iron(II) chloride and pyridine and withstand microwave irradiation to achieve short reaction times. Similarly as for the analogous copper-catalyzed amidation reactions, our studies suggest the reaction to proceed by rate-determining insertion of an iron-nitrenoid species into the aldehydic C−H bond. However, it differs in that the C−N bond-forming process is more likely to follow a radical rather than a concerted mechanistic pathway.

EXPERIMENTAL SECTION

General Remarks. All reactions were performed under a nitrogen atmosphere at ambient temperature unless otherwise stated. PhI=NTs,[30] PhI=O,[31] and [Ru(TTP)CO][32] (H_2TTP = *meso*-tetrakis(*p*-tolyl)porphyrin) were prepared according to known literature procedures. Unless specified, all reagents and starting materials were purchased from commercial sources and used as received; $FeCl_2$ used in this work was of either 99.5% or 99.99% purity.[17] Solvent were purified prior to use following literature procedures; CH_2Cl_2 and MeCN were purified prior to use by distilling over CaH_2; pyridine was distilled over KOH and benzaldehyde was distilled under reduced pressure. Analytical thin layer chromatography (TLC) was performed using precoated silica gel plate. Visualization was achieved by UV−vis light (254 nm) followed by treatment with ninhydrin stain and heating. Flash chromatography was performed using silica gel using a gradient solvent system (EtOAc/*n*-hexane as eluant). Unless otherwise stated, ^{1}H and ^{13}C NMR spectra were measured on a 300 MHz spectrometer. Unless otherwise stated, chemical shifts (ppm) were recorded in $CDCl_3$ solution with tetramethylsilane (TMS) as the internal reference standard. Multiplicities are given as s (singlet), bs (broad singlet), d (doublet), dt (doublet of triplet), t (triplet), bt (broad triplet), tt (triple of triplets), q (quartet), dd (doublet of doublets), quin (apparent quintet) or m (multiplet). The number of protons (*n*) for a given resonance is indicated by *n*H, and coupling constants are reported as a *J* value in Hz. Low resolution mass spectra were determined on a mass spectrometer and reported as a ratio of mass to charge (*m*/*z*). High resolution mass spectra (HRMS) were obtained using a LC−HRMS mass spectrometer. Kinetic isotope measurements were conducted on a benchtop atmospheric pressure LC−MS mass spectrometer with 0.1%

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formic acid in 95:5 H_2O:/MeCN as the mobile phase. Reactions conducted under microwave conditions were carried out with a CEM Discover Labmate microwave synthesizer with an internal IR sensor located at the bottom of the cavity, irradiation at 2450 MHz and temperature, power and pressure settings at 25 °C, 200 W and 17 bar, respectively.

General Procedure for $FeCl_2$ + Pyridine Catalyzed Amidation of Aldehydes with PhI=NTs or PhI=NNs. To a suspension of $FeCl_2$ (0.05 mol) and powdered 4 Å MS (400 mg) in CH_2Cl_2 (2 mL) was added pyridine (0.2 mmol). After 5 min of stirring, PhI=NTs or PhI=NNs (1 mmol) was added followed by addition of the aldehyde (0.5 mmol). The reaction was stirred at room temperature for 18 h (or 1 h under microwave conditions), after which the crude mixture was filtered through Celite, washed with EtOAc, evaporated to dryness, and purified by silica gel flash column chromatography (*n*-hexanes/EtOAc as eluant) to give the acyl sulfonamide product.

***N*-Tosylbenzamide (2a)[6c].** White solid; ^{1}H NMR δ 9.83 (bs, 1H), 8.03 (d, J = 8.1 Hz, 2H), 7.84 (d, *J* = 7.5 Hz, 2H), 7.48 (t, *J* = 7.2 Hz, 1H), 7.36 (t, *J* = 7.5 Hz, 2H), 7.30 (d, *J* = 8.1 Hz, 2H), 2.39 (s, 3H); ^{13}C NMR δ 164.6, 145.2, 135.5, 133.5, 131.1, 129.7, 128.9, 128.6, 128.0, 21.7; MS (ESI) *m*/*z* 276 $[M + H]^+$.

***N*-(4-Nitrophenylsulfonyl)benzamide (2b)[33].** White solid; ^{1}H NMR (CD_3COCD_3, 400 MHz) δ 8.45 (d, *J* = 8.8 Hz, 2H), 8.37 (d, *J* = 8.8 Hz, 2H), 7.95 (d, *J* = 7.6 Hz, 2H), 7.62 (t, *J* = 7.6 Hz, 1H), 7.48 (t, *J* = 8.0 Hz, 2H); ^{13}C NMR δ 165.8, 150.7, 145.6, 133.2, 132.1, 129.8, 128.6, 128.4, 124.1; MS (ESI) *m*/*z* 307 $[M + H]^+$.

4-Methoxy-*N*-tosylbenzamide (2c)[6c]. White solid; ^{1}H NMR δ 9.21 (bs, 1H), 8.02 (d, *J* = 8.4 Hz, 2H), 7.82 (d, *J* = 8.4 Hz, 2H), 7.31 (d, *J* = 8.1 Hz, 2H), 6.89 (d, *J* = 8.7 Hz, 2H), 3.82 (s, 3H), 2.42 (s, 3H); ^{13}C NMR δ 163.8, 145.1, 135.7, 130.0, 129.6, 128.6, 126.5, 123.3, 114.1, 55.5, 21.7; MS (ESI) *m*/*z* 306 $[M + H]^+$.

4-*tert*-Butyl-*N*-tosylbenzamide (2d)[34]. White solid; ^{1}H NMR δ 9.69 (bs, 1H), 8.05 (d, *J* = 8.1 Hz, 2H), 7.79 (d, *J* = 8.1 Hz, 2H), 7.40 (d, *J* = 8.4 Hz, 2H), 7.32 (d, *J* = 8.1 Hz, 2H), 2.41 (s, 3H), 1.27 (s, 9H); ^{13}C NMR δ 164.4, 157.3, 145.1, 135.7, 129.6, 128.6, 128.2, 127.9, 125.8, 35.1, 31.0, 21.7; MS (ESI) *m*/*z* 332 $[M + H]^+$.

4-Isopropyl-*N*-tosylbenzamide (2e). White solid; mp 155−157 °C; ^{1}H NMR δ 9.36 (bs, 1H), 8.05 (d, *J* = 8.4 Hz, 2H), 7.79 (d, *J* = 8.4 Hz, 2H), 7.31 (d, *J* = 8.4 Hz, 2H), 7.23 (d, *J* = 8.4 Hz, 2H), 2.89 (quin, *J* = 6.9 Hz, 1H), 2.40 (s, 3H), 1.19 (d, *J* = 6.9 Hz, 6H); ^{13}C NMR δ 164.7, 155.0, 145.1, 135.7, 129.6, 128.7, 128.6, 128.3, 126.9, 34.2, 23.6, 21.7; IR (neat, cm^{-1}) 3273, 3020, 2964, 1697, 1608, 1427, 1215, 1166, 1070; MS (ESI) *m*/*z* 318 $[M + H]^+$; HRMS (ESI) calcd for $C_{17}H_{20}NO_3S$ 318.1164, found 318.1164.

4-Methyl-*N*-tosylbenzamide (2f)[6c]. White solid; ^{1}H NMR δ 9.56 (bs, 1H), 8.04 (d, *J* = 8.4 Hz, 2H), 7.73 (d, *J* = 8.1 Hz, 2H), 7.32 (d, *J* = 8.1 Hz, 2H), 7.18 (d, *J* = 8.1 Hz, 2H), 2.41 (s, 3H), 2.34 (s, 3H); ^{13}C NMR δ 164.5, 145.1, 144.4, 135.6, 129.6, 129.5, 128.6, 128.3, 128.0, 21.7, 21.6; MS (ESI) *m*/*z* 290 $[M + H]^+$.

4-Phenyl-*N*-tosylbenzamide (2g). White solid; mp 200−202 °C; ^{1}H NMR δ 9.07 (bs, 1H), 8.07 (d, *J* = 8.4 Hz, 2H), 7.87 (d, *J* = 8.4 Hz, 2H), 7.65 (d, *J* = 8.4 Hz, 2H), 7.58 (d, *J* = 8.1 Hz, 2H), 7.46−7.35 (m, 5H), 2.44 (s, 3H); ^{13}C NMR δ 164.5, 145.5, 144.6, 139.4, 137.1, 130.7, 129.4, 129.0, 128.8, 128.4, 128.3, 127.1, 127.0, 20.6; IR (neat, cm^{-1}) 3286, 3018, 1697, 1606, 1425, 1334, 1215, 1165; MS (ESI) *m*/*z* 352 $[M + H]^+$; HRMS (ESI) calcd for $C_{20}H_{18}NO_3S$ 352.1007, found 352.0991.

4-Bromo-*N*-tosylbenzamide (2h)[13]. White solid; ^{1}H NMR δ 9.53 (bs, 1H), 8.02 (d, *J* = 8.4 Hz, 2H), 7.70 (d, *J* = 8.4 Hz, 2H), 7.54 (d, *J* = 8.4 Hz, 2H), 7.35 (d, *J* = 8.1 Hz, 2H), 2.44 (s, 3H); ^{13}C NMR δ 163.4, 145.0, 134.9, 131.8, 129.6, 129.3, 129.1, 128.2, 21.3; MS (ESI) *m*/*z* 354 $[M + H]^+$.

4-Chloro-*N*-tosylbenzamide (2i)[13]. Pale yellow solid; ^{1}H NMR (500 MHz) δ 9.63 (bs, 1H), 8.02 (d, *J* = 8.4 Hz, 2H), 7.78 (d, *J* = 8.4 Hz, 2H), 7.39−7.26 (m, 4H), 2.44 (s, 3H); ^{13}C NMR (125 MHz) δ 163.5, 145.4, 140.0, 135.1, 129.6, 129.4, 129.3, 129.1, 128.5, 21.6; MS (ESI) *m*/*z* 310 $[M + H]^+$.

4-Fluoro-*N*-tosylbenzamide (2j)[35]. White solid; ^{1}H NMR δ 9.70 (bs, 1H), 8.02 (d, *J* = 8.1 Hz, 2H), 7.87 (dd, *J* = 8.4, 5.1, 2H), 7.33 (d, *J* = 8.1 Hz, 2H), 7.07 (t, *J* = 8.4 Hz, 2H), 2.43 (s, 3H); ^{13}C NMR δ 163.6, 145.4, 135.3, 130.8, 130.6, 129.7, 128.6, 127.3, 116.2, 115.9, 21.7. MS (ESI) *m*/*z* 294 $[M + H]^+$.

4-Trifluoromethyl-*N*-tosylbenzamide (2k)[6c]. White solid; ^{1}H NMR δ 9.78 (bs, 1H), 8.02 (d, *J* = 8.2 Hz, 2H), 7.96 (d, *J* = 8.1 Hz, 2H), 7.65 (d, *J* = 8.2 Hz, 2H), 7.35 (d, *J* = 8.1 Hz, 2H), 2.44 (s, 3H); ^{13}C NMR δ 163.5, 145.7, 135.1, 134.6, 134.4, 129.8, 128.7, 128.5, 125.9, 125.8, 125.1, 21.7; MS (ESI) *m*/*z* 344 $[M + H]^+$.

4-Acetoxy-*N*-tosylbenzamide (2l). White solid; mp 138−139 °C; ^{1}H NMR δ 9.39 (bs, 1H), 8.02 (d, *J* = 8.1 Hz, 2H), 7.83 (d, *J* = 8.7 Hz, 2H), 7.34 (d, *J* = 8.4 Hz, 2H), 7.14 (d, *J* = 8.7 Hz, 2H), 2.43 (s, 3H), 2.32 (s, 3H); ^{13}C NMR δ 163.4, 154.6, 145.3, 129.7, 129.5, 128.7, 122.2, 21.7, 21.1; IR (neat, cm^{-1}) 3018, 2399, 1759, 1705, 1602, 1425, 1165, 1066; MS (ESI) *m*/*z* 318 $[M + H]^+$; HRMS (ESI) calcd for $C_{16}H_{16}NO_5S$ 334.0749, found 334.0762.

2-Methyl-*N*-tosylbenzamide (2n)[6c]. White solid; ^{1}H NMR δ 9.17 (bs, 1H), 8.00 (d, *J* = 8.4 Hz, 2H), 7.41 (d, *J* = 7.5, 1H), 7.34 (d, *J* = 8.1 Hz, 2H), 7.29−7.35 (m, 1H), 7.17 (d, *J* = 7.5, 1H), 7.13−7.18 (m, 1H), 2.44 (s, 3H), 2.33 (s, 3H); ^{13}C NMR δ 166.5, 145.2, 138.0, 135.6, 132.1, 131.8, 131.6, 129.6, 128.5, 127.5, 125.9, 21.7, 20.1; MS (ESI) *m*/*z* 290 $[M + H]^+$.

***N*-Tosyl-1-napthamide (2o)[6c].** Yellow solid; ^{1}H NMR δ 8.81 (bs, 1H), 8.17 (m, 1H), 8.04 (d, *J* = 8.4 Hz, 2H), 7.93 (d, *J* = 8.1 Hz, 1H), 7.82 (m, 1H), 7.65 (dd, *J* = 7.2, 0.9 Hz, 1H), 7.47−7.52 (m, 2H), 7.33−7.42 (m, 3H), 2.45 (s, 3H); ^{13}C NMR δ 165.9, 145.3, 135.5, 133.7, 132.9, 130.0, 129.9, 129.7, 128.6, 128.5, 127.9, 126.8, 126.6, 124.9, 124.4, 21.7; MS (ESI) *m*/*z* 326 $[M + H]^+$.

***N*-Tosylpropionamide (2p)[36].** White solid; ^{1}H NMR δ 8.85 (bs, 1H), 7.94 (d, *J* = 8.4 Hz, 2H), 7.33 (d, *J* = 8.1 Hz, 2H), 2.43 (s, 3H), 2.29 (q, *J* = 7.5 Hz, 2H), 1.06 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR δ 171.8, 145.2, 135.6, 129.7, 128.3, 29.5, 21.7, 8.2; MS (ESI) *m*/*z* 228 $[M + H]^+$.

3-Methyl-*N*-tosylbutanamide (2q)[37]. White solid; ^{1}H NMR δ 8.99 (bs, 1H), 7.95 (d, *J* = 8.3 Hz, 2H), 7.34 (d, *J* = 8.2 Hz, 2H), 2.41 (s, 3H), 2.10 (d, *J* = 6.3 Hz, 2H), 2.00−2.06 (m, 1H), 0.86 (d, *J* = 6.6 Hz, 6H); ^{13}C NMR δ 171.1, 145.2, 135.7, 129.7, 128.4, 45.3, 25.7, 22.3, 21.8; MS (ESI) *m*/*z* 256 $[M + H]^+$.

***N*-Tosylisobutyramide (2r)[37].** Pale yellow solid; ^{1}H NMR (400 MHz) δ 8.86 (bs, 1H), 7.95 (d, *J* = 8.1 Hz, 2H), 7.35 (d, *J* = 8.1 Hz, 2H), 2.39−2.46 (m, 4H), 1.09 (d, *J* = 7.2 Hz, 6H); ^{13}C NMR (100 MHz) δ 175.0, 145.4, 135.7, 129.9, 128.6, 35.9, 22.0, 18.8; MS (ESI) *m*/*z* 344 $[M + H]^+$.

***N*-Tosylpivalamide (2s)[38].** Pale yellow solid; ^{1}H NMR δ 8.68 (bs, 1H), 7.95 (d, *J* = 8.4 Hz, 2H), 7.33 (d, *J* = 8.4 Hz, 2H), 2.43 (s, 3H), 1.14 (s, 9H); ^{13}C NMR δ 176.0, 145.0, 135.6, 129.6, 128.4, 40.0, 26.7, 21.6; MS (ESI) *m*/*z* 256 $[M + H]^+$.

***N*-Tosylheptanamide (2t)[11].** Pale yellow solid; ^{1}H NMR δ 9.19 (bs, 1H), 7.96 (d, *J* = 8.1 Hz, 2H), 7.34 (d, *J* = 8.1 Hz, 2H), 2.44 (s, 3H), 2.23 (t, *J* = 7.5 Hz, 2H), 1.56 (t, *J* = 6.9 Hz, 2H), 1.20−1.26 (m, 6H), 0.82 (t, *J* = 6.9 Hz, 3H); ^{13}C NMR δ 171.5, 145.1, 135.6, 129.6, 128.3, 36.3, 31.3, 28.5, 24.3, 22.4, 21.7, 13.9; MS (ESI) *m*/*z* 284 $[M + H]^+$.

***N*-Tosylcyclopropanecarboxamide (2u)[11].** White solid; ^{1}H NMR δ 8.88 (bs, 1H), 7.95 (d, *J* = 8.1 Hz, 2H), 7.34 (d, *J* = 8.1 Hz, 2H), 2.44 (s, 3H), 1.56−1.51 (m, 1H), 1.02 (m, 2H), 0.87−0.83 (m, 2H); ^{13}C NMR δ 172.3, 145.1, 135.6, 129.6, 128.3, 21.7, 14.7, 9.7; MS (ESI) *m*/*z* 240 $[M + H]^+$.

***N*-Tosylcyclopentanecarboxamide (2v)[11].** White solid; ^{1}H NMR δ 8.67 (bs, 1H), 7.94 (d, *J* = 8.4 Hz, 2H), 7.33 (d, *J* = 8.1 Hz, 2H), 2.62 (m, 1H), 2.43 (s, 3H), 1.51−1.82 (m, 8H); ^{13}C NMR δ 173.9,

145.0, 135.7, 129.6, 128.3, 45.5, 29.6, 25.9, 21.7; MS (ESI) m/z 268 $[M + H]^+$.

***N*-Tosylcyclohexanecarboxamide (2w)[37].** White solid; ^{1}H NMR δ 8.12 (bs, 1H), 7.93 (d, J = 8.1 Hz, 2H), 7.33 (d, J = 8.4 Hz, 2H), 2.44 (s, 3H), 2.13 (tt, J = 11.6, 3.5 Hz, 1H), 1.76 (t, J = 13.8 Hz, 4H), 1.63 (bd, J = 9.9 Hz, 2H), 1.12−1.40 (m, 6H); ^{13}C NMR δ 173.7, 145.0, 135.6, 129.6, 128.3, 45.1, 28.7, 25.4, 25.2, 21.7; MS (ESI) m/z 282 $[M + H]^+$.

3-Phenyl-*N*-tosykpropanamide (2y)[11]. White solid; ^{1}H NMR δ 8.96 (bs, 1H), 7.89 (d, J = 8.4 Hz, 2H), 7.31 (d, J = 8.1 Hz, 2H), 7.18−7.25 (m, 3H), 7.04 (d, J = 7.5 Hz, 2H), 2.86 (t, J = 7.7, 2H), 2.54 (t, J = 7.7, 2H), 2.44 (s, 3H); ^{13}C NMR δ 170.2, 145.2, 139.6, 135.5, 129.6, 128.6, 128.4, 128.3, 126.5, 38.0, 30.3, 21.7; MS (ESI) m/z 304 $[M + H]^+$.

Methyl 4-(4-methylphenylsulfonamido)-4-oxobutanoate (2z)[39]. White solid; ^{1}H NMR δ 9.00 (bs, 1H), 7.93 (d, J = 8.4 Hz, 2H), 7.34 (d, J = 8.1 Hz, 2H), 3.65 (s, 3H), 2.58−2.60 (m, 4H), 2.44 (s, 3H); ^{13}C NMR (100 MHz) δ 173.0, 169.7, 145.1, 135.6, 129.6, 128.3, 52.1, 31.0, 28.2, 21.7; MS (ESI) m/z 286 $[M + H]^+$.

3-Methyl-*N*-tosylbut-2-enamide (2α)[40]. Pale yellow solid; ^{1}H NMR δ 8.87 (bs, 1H), 7.96 (d, J = 8.1 Hz, 2H), 7.33 (d, J = 8.1 Hz, 1H), 5.62 (s, 1H), 2.43 (s, 3H), 2.10 (s, 3H), 1.84 (s, 3H); ^{13}C NMR δ 163.4, 160.2, 144.7, 135.9, 129.6, 128.3, 115.5, 27.6, 21.6, 20.5; MS (ESI) m/z 254 $[M + H]^+$.

(*E*)-*N*-Tosylhex-2-enamide (2β)[41]. Yellow oil; ^{1}H NMR δ 9.29 (bs, 1H), 7.96 (d, J = 8.4 Hz, 2H), 7.32 (d, J = 8.1 Hz, 2H), 6.98 (dt, J = 15.4, 7.0 Hz, 1H), 5.85 (d, J = 15.4 Hz, 1H), 2.41 (s, 3H), 2.14 (q, J = 7.0 Hz, 2H), 1.37−1.44 (m, 2H), 0.86 (t, J = 7.3 Hz, 3H); ^{13}C NMR δ 163.5, 151.0, 145.1, 135.7, 129.6 128.4, 121.4, 34.3, 21.7, 21.1, 13.6; MS (ESI) m/z 268 $[M + H]^+$.

***N*-Tosylcinnamamide (2γ)[42].** White solid; ^{1}H NMR δ 8.00 (d, J = 8.4 Hz, 2H), 7.69 (d, J = 15.6 Hz, 2H), 7.46 (m, 3H), 7.33−7.38 (m, 5H), 6.44 (d, J = 15.8, 1H), 2.43 (s, 3H); ^{13}C NMR δ 163.2, 146.0, 145.2, 135.7, 133.7, 131.0, 129.7, 129.0, 128.5, 128.4, 117.3, 21.7; MS (ESI) m/z 302 $[M + H]^+$.

2-Phenyl-*N*-tosylpent-2-enamide (2δ). White solid, mp 118−120 °C ^{1}H NMR δ 7.93 (d, J = 8.3 Hz, 2H), 7.46−7.38 (m, 3H), 7.33 (d, J = 8.1 Hz, 2H), 7.10 (d, J = 1.56 Hz, 2H), 7.03 Hz (t, J = 7.7 Hz, 1H), 2.43 (s, 3H), 1.96 (quin, J = 7.6 Hz, 2H), 0.93 (t, J = 7.5 Hz, 3H); ^{13}C NMR δ 163.7, 147.9, 145.0, 135.6, 133.5, 133.3, 129.6, 129.5, 129.4, 128.9, 128.6, 23.0, 21.7, 13.0; IR (neat, cm^{-1}) 3365, 3284, 3022, 2970, 2933, 1701, 1627, 1597, 1492, 1406, 1342, 1215, 1176, 1145; MS (ESI) m/z 330 $[M + H]^+$; HRMS (ESI) calcd for $C_{18}H_{20}NO_3S$ 330.1164, found 330.1164.

***N*-Tosylcyclohex-1-enecarboamide (2ε).** White solid, mp 164−166 °C; ^{1}H NMR δ 8.76 (bs, 1H), 7.98 (d, J = 8.4 Hz, 2H), 7.33 (d, J = 8.1 Hz, 2H), 6.77 (s, 1H), 2.43 (s, 3H), 2.16 (m, 4H), 1.57 (m, 4H);^{13}C NMR δ 165.2, 144.9, 139.1, 135.8, 131.8, 129.5, 128.5, 25.8, 23.6, 21.72, 21.69, 21.1; IR (neat, cm^{-1}) 3275, 3018, 1693, 1417, 1215, 1161; MS (ESI) m/z 280 $[M + H]^+$; HRMS (ESI) calcd for $C_{14}H_{18}NO_3S$ 280.1007, found 280.1015.

***N*-Tosylthiophene-2-carboxamide (2η)[6c].** White solid; ^{1}H NMR δ 8.04 (d, J = 8.2 Hz, 2H), 7.71 (d, J = 3.5 Hz, 1H), 7.59 (d, J = 4.7 Hz, 1H), 7.35 (d, J = 8.1 Hz, 2H), 7.07 (t, J = 4.39 Hz, 1H), 2.43 (s, 3H); ^{13}C NMR δ 158.7, 145.3, 135.9, 135.4, 133.7, 131.1, 129.6, 128.6, 128.2, 21.7; MS (ESI) m/z 282 $[M + H]^+$.

Phenyl-*N*-tosylmethanimine (3a)[43]. ^{1}H NMR (400 MHz) δ 9.03 (s, 1H) 7.94−7.88 (m, 4H), 7.62 (t, J = 7.4 Hz, 1H) 7.49 (d, J = 7.7 Hz, 2H), 7.36 (d, J = 8.1 Hz, 2H), 2.44 (s, 3H); ^{13}C NMR (100 MHz) δ 170.1, 144.6, 135.2, 135.0, 132.4, 131.3, 129.8, 129.2, 128.1, 21.7; MS (ESI) m/z 260 $[M + H]^+$.

Procedure for Amidation of 1a with PhI═NTs in the presence of $FeCl_2$ + Pyridine and BHT. To a suspension of $FeCl_2$ (0.05 mol) and powdered 4 Å MS (400 mg) in CH_2Cl_2 (2 mL) was added pyridine (0.2 mmol). After 5 min of stirring, PhI═NTs (1 mmol) and BHT (0.75 mmol) followed by **1a** (0.5 mmol) were added. The reaction was stirred at room temperature for 18 h, after which the crude mixture was filtered through Celite, washed with EtOAc, and evaporated to dryness. The reaction mixture was then analyzed by ^{1}H NMR spectroscopy.

Procedure for Competitive Rates Studies. To a suspension of $FeCl_2$ (0.05 mol) and powdered 4 Å MS (400 mg) in CH_2Cl_2 (2 mL) was added pyridine (0.2 mmol). After 5 min of stirring, PhI═NTs (0.5 mmol) was added followed by a solution of benzaldehyde (0.6 mmol) and *p*-substituted benzaldehyde (0.6 mmol). After 2 h, the solution was assayed via GC analysis.

Procedure for the Amidation of 1a or 1k with PhI═NTs Mediated by a Variety of Copper and Palladium Catalysts. To a suspension of the copper or palladium catalyst stated in Table 3 (5 μmol) and powdered 4 Å MS (400 mg) in CH_2Cl_2 (2 mL) was added pyridine (0.02 mmol). After 5 min of stirring, PhI═NTs (1 mmol) followed by **1a** (0.1 mmol) or **1k** (0.5 mmol) was added, and the resultant reaction mixture was stirred at room temperature for 18 h. On completion, the reaction mixture was filtered through Celite, washed with EtOAc, and evaporated to dryness. The crude mixture was then analyzed by ^{1}H NMR spectroscopy.

(4-(Trifluoromethyl)phenyl)-*N*-tosylmethanimine (3k)[44]. ^{1}H NMR δ 9.09 (s, 1H), 8.06 (d, J = 7.8 Hz, 2H), 7.91 (d, J = 8.5 Hz, 2H), 7.76 (d, J = 8.2 Hz, 2H), 7.38 (d, J = 8.1 Hz, 2H); 2.45 (s, 3H); ^{13}C NMR δ 168.5, 145.1, 137.5, 131.4, 130.3, 129.9, 128.2, 126.1, 21.7; MS (ESI) m/z 328 $[M + H]^+$.

Procedure for the Synthesis of $[FeCl_2(py)_4]$[22]. Pure iron powder (0.09 mol) was slowly and carefully added to 15 mL of 5 M HCl [**CAUTION**: a large volume of H_2(g) is evolved on addition to HCl and care should be exercised] over a period of 45 min. When all of the H_2(g) was evolved, MeOH (20 mL, sodium-dried) was added, and under a dry nitrogen atmopshere, the solution was filtered into a flask containing 100 mL of pyridine (purified by distillation in a dry N_2 atmosphere prior to use). Intensely yellow crystals of tetrakis-(pyridyl)iron(II) chloride separated out immediately from the solution and were allowed to stand overnight under a dry N_2 atmosphere. The crystals were then filtered off, recrystallized from distilled pyridine, and dried in a vacuum desiccator. IR (neat, cm^{-1}) 3420, 3312, 3198, 1605, 1487, 1223, 1042, 756, 694.

Procedure for Amidation Reaction of 1a with $[FeCl_2(py)_4]$. To a suspension of tetrakis(pyridyl)iron(II) chloride (0.05 mmol), PhI═NTs (1 mmol), and powdered 4 Å MS (400 mg) in 2 mL of CH_2Cl_2 was added **1a** (0.5 mmol). The reaction was stirred at room temperature for 18 h, after which the mixture was filtered through Celite, washed with EtOAc, evaporated to dryness, and purified by silica gel flash column chromatography to furnish **2a** as the sole product.

Procedure for Reaction of $[Fe(py)_4Cl_2]$ + PhI═NTs. To a yellow suspension of $[Fe(py)_4Cl_2]$ (25 μmol) in CD_2Cl_2 (1 mL) was added PhI═NTs (0.1 mmol). The mixture was stirred at room temperature and under N_2. After 10 min, a homogeneous brown solution was obtained and assayed via ^{1}H NMR spectroscopy (See Figure S37 in the Supporting Information).

Procedure for Kinetic Isotope Study. To a suspension of $FeCl_2$ (25 μmol) and powdered 4 Å MS (400 mg) in CH_2Cl_2 (2 mL) was added pyridine (0.1 mmol). After 5 min of stirring, PhI═NTs (0.25 mmol) was added followed by a solution of benzaldehyde (0.3 mmol) and d_6-benzaldehyde (0.3 mmol). After 2 h, the solution was assayed via LC−MS analysis.

Procedure for the Synthesis of 3a[43]. To a solution of benzaldehyde **1a** (10 mmol) and *p*-toluenesulfonamide (10 mmol) in 50 mL of CH_2Cl_2 was added trifluoroacetic anhydride (11 mmol). The reaction was refluxed for 12 h after which the reaction mixture was poured into cold water, extracted with CH_2Cl_2, dried with $MgSO_4$, evaporated to dryness, and recrystallized to give the title compound as a white solid in 81% yield.

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Procedure for the Synthesis of 4[28a]**.** To a suspension of [Ru(TTP)CO] (0.2 mmol, 0.1 equiv) and PhI=NTs (3 mmol, 1.5 equiv) in 2 mL of CH_2Cl_2 in the presence of powdered 4 Å molecular sieves (400 mg) was added pyridine (2 mmol, 1 equiv). The reaction was stirred at 30 °C until completion based on TLC analysis, after which the reaction mixture was cooled to room temperature, filtered, evaporated to dryness, and purified by silica gel flash column chromatography (CH_2Cl_2/acetone as eluant) to afford the product in 63% yield. ^{1}H NMR δ 8.45 (d, J = 5.7 Hz, 2H), 7.96 (t, J = 7.8, 1H), 7.54−7.61 (m, 4H), 7.15 (d, J = 8.2 Hz, 2H), 2.34 (s, 3H); ^{13}C NMR δ 145.2, 141.7, 138.9, 138.6, 129.3, 127.1, 126.9, 21.4; MS (ESI) m/z 249 $[M + H]^+$.

Procedure for the Synthesis of 5[29]**.** To a suspension of powdered KOH (7 mmol) and *m*-chloroperoxybenzoic acid (2.2 mmol) in 1 mL of CH_2Cl_2 was added a solution of **3** (2 mmol) in 3 mL of CH_2Cl_2. After 5 min, the suspension was filtered, evaporated to dryness, and dried under vacuum to afford the product as a white solid in 90% yield. ^{1}H NMR δ 7.93 (d, J = 8.4 Hz, 2H), 7.37−7.46 (m, 7H), 5.44 (s, 1H), 2.49 (s, 3H); ^{13}C NMR δ 162.3, 146.4, 131.5, 131.4, 130.6, 130.1, 129.4, 128.7, 128.3, 76.3, 21.9; MS (ESI) m/z 276 $[M + H]^+$.

Procedure for $FeCl_2$-Catalyzed Reaction of 1a with 4. To a suspension of $FeCl_2$ (0.05 mmol), **4** (1 mmol), and powdered 4 Å MS (400 mg) in 2 mL of CH_2Cl_2 was added **1a** (0.5 mmol). The reaction was stirred at room temperature for 18 h, after which the mixture was filtered through Celite, washed with EtOAc, and evaporated to dryness. The reaction mixture was then analyzed by ^{1}H NMR spectroscopy.

Procedure for $FeCl_2$ + Pyridine Catalyzed Reaction of 3a or 5. A suspension of $FeCl_2$ (0.05 mmol), pyridine (0.2 mmol), and powdered 4 Å MS (400 mg) were stirred for 5 min in 2 mL of CH_2Cl_2. On completion, PhI=NTs or $PhI(OAc)_2$ (1 mmol) and **3a** or **5** (0.5 mmol) were added. The reaction was stirred at room temperature for a further 18 h, after which the mixture was filtered through Celite, washed with EtOAc, and evaporated to dryness. The reaction mixture was then analyzed by ^{1}H NMR spectroscopy.

Procedure for ^{13}C-Benzaldehyde *in Situ* Monitoring Experiment. To a suspension of $FeCl_2$ (0.05 mmol) and powdered 4 Å MS (400 mg) in CD_2Cl_2 (2 mL) was added pyridine (0.2 mmol). After stirring for 5 min, PhI=NTs (1 mmol) and ^{13}C-benzaldehyde (0.5 mmol) were added. The crude reaction mixture was then filtered through Celite, diluted with CD_2Cl_2, and monitored by ^{13}C NMR spectroscopy. This process was repeated by taking subsequent aliquots at 4, 12, and 18 h and subjecting the resultant CD_2Cl_2 solutions of the crude reaction to ^{13}C NMR spectroscopic analysis.

■ ASSOCIATED CONTENT

Supporting Information. Technical specifications for $FeCl_2$ of 99.5% and 99.99% purity, ^{1}H and ^{13}C NMR spectra for all starting materials and products, and CIF file of $[FeCl_2(py)_4]$. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author
*E-mail: waihong@ntu.edu.sg.

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■ REFERENCES

(1) (a) Schneider, C. *Angew. Chem., Int. Ed.* **2009**, *48*, 2082. (b) Friestad, G. K.; Mathies, A. K. *Tetrahedron* **2007**, *63*, 2541. (c) Baker, D. D.; Chu, M.; Oza, U.; Rajgarhia, V. *Nat. Prod. Rep.* **2007**, *24*, 1225.(d) Fraxedas, J. *Molecular Organic Materials: From Molecules to Crystalline Solids*; Cambridge University Press: Cambridge, 2006. (e) Hili, R.; Yudin, A. K. *Nat. Chem. Biol.* **2006**, *2*, 284. (f) Boaen, N. K.; Hillmyer, M. A. *Chem. Soc. Rev.* **2005**, *34*, 267. (g) Banerjee, S.; Hemraj-Benny, T.; Wong, S. S. *Adv. Mater.* **2005**, *17*, 17.(h) Kleeman, A.; Angel, J. *Pharmaceutical Substances: Syntheses, Patents, Applications*, 4th ed.; Georg Thieme: Stuttgart, 2001. (i) *Comprehensive Natural Products Chemistry*; Barton, D. H. R., Nakanishi, K., Meth-Cohn, O., Eds; Elsevier: Oxford, 1999; Vol. 4. (j) Henkel, T.; Brunne, R. M.; Müller, H.; Reichel, F. *Angew. Chem., Int. Ed.* **1999**, *38*, 643. (k) Humphrey, J. M.; Chamberlin, A. R. *Chem. Rev.* **1997**, *97*, 2243.(l) Craig, P. N. *Comprehensive Medicinal Chemistry*; Drayton, C. J., Ed.; Pergamon Press: New York, 1991. (m) Southon, I. W.; Buckingham, J. *Dictionary of Alkaloids*; Saxton, J. E., Ed.; Chapman and Hall: London, 1989.

(2) (a) Valeur, E.; Bradley, M. *Chem. Soc. Rev.* **2009**, *28*, 606. (b) Montalbetti, C. A. G. N.; Falque, V. *Tetrahedron* **2005**, *61*, 10827. (c) Salvatore, R. N.; Yoon, C. H.; Jung, K. W. *Tetrahedron* **2001**, *57*, 7785. (d) Larock, R. C. *Comprehensive Organic Transformation*; VCH: New York, 1999. (e) Bailey, P. D.; Collier, I. D.; Morgan, K. M. *Comprehensive Organic Functional Group Transformations*; Katrizky, A. R., Meth-Cohn, O., Rees, C. W., Eds.; Pergamon: Cambridge, 1995. (f) *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: Oxford, 1991.

(3) (a) Albericio, F. *Curr. Opin. Chem. Biol.* **2004**, *8*, 211. (b) Bray, B. L. *Nat. Rev. Drug Discovery* **2003**, *2*, 587.

(4) (a) Damkaci, F.; Deshong, P. *J. Am. Chem. Soc.* **2003**, *125*, 4408. (b) Saxon, E.; Bertozzi, C. R. *Science* **2000**, *287*, 2007. (c) Nilsson, B. L.; Kiessling, L. L.; Raines, R. T. *Org. Lett.* **2000**, *2*, 1939.

(5) (a) Ramalingan, C.; Park, Y.-T. *J. Org. Chem.* **2007**, *72*, 4536. (b) Owston, N. A.; Parker, A. J.; William, J. M. J. *Org. Lett.* **2007**, *9*, 2599. (c) Park, S.; Chio, Y.; Han, H.; Yang, S. H. *Chem. Commun.* **2003**, 1936.

(6) For selected examples, see: (a) Martinelli, J. R.; Clark, T. P.; Watson, D. A.; Munday, R. H.; Buchwald, S. L. *Angew Chem., Int. Ed.* **2007**, *46*, 8460. (b) Uenoyama, Y.; Fukuyama, T.; Nobuta, O.; Matsabara, H.; Ryu, I. *Angew. Chem., Int. Ed.* **2005**, *44*, 1075. (c) Wu, X.; Roenn, R.; Gossas, T.; Larhed, M. *J. Org. Chem.* **2005**, *70*, 3094. (d) Knapton, D. J.; Meyer, T. Y. *Org. Lett.* **2004**, *6*, 687. (e) Nanayakkara, P.; Alper, H. *Chem. Commun.* **2003**, 2384. (f) Ali, B. E.; Tijani, J. *Appl. Organomet. Chem.* **2003**, *17*, 921. (g) Lee, S. I.; Son, S. U.; Chung, J. K. *J. Chem. Soc., Chem. Commun.* **2002**, 1320. (h) Uozumi, Y.; Arii, T.; Watanabe, T. *J. Org. Chem.* **2001**, *66*, 5272. (i) Lin, T.-S.; Alper, H. *Angew. Chem., Int. Ed.* **2001**, *40*, 779. (j) Okura, K.; Kai, H.; Alper, H. *Tetrahedron: Asymmetry* **1997**, *8*, 2307. (k) Beller, M.; Cornils, B.; Frohning, C. D.; Kohlpainter, C. W. *J. Mol. Catal. A: Chem.* **1995**, *104*, 17.

(7) For selected examples, see: (a) Dam, J. H.; Osztrovszky, G.; Nordstrøm, L. U.; Madsen, R. *Chem.—Eur. J.* **2010**, *16*, 6820. (b) Ghosh, S. C.; Muthaiah, S.; Zhang, Y.; Xu, X.; Hong, S. H. *Adv. Synth. Catal.* **2009**, *351*, 2643. (c) Zweifel, T.; Naubron, N.-V.; Grutzmacher, H. *Angew. Chem., Int. Ed.* **2009**, *48*, 559. (d) Nordstrom, L. U.; Vogt, H.; Madsen, R. *J. Am. Chem. Soc.* **2008**, *130*, 17672. (e) Gunanathan, C.; Ben-David, Y.; Milstein, D. *Science* **2007**, *266*, 790.

(8) For selected examples, see: (a) Ekoue-Kovi, K.; Wolf, C. *Chem.—Eur. J.* **2008**, *14*, 6302. (b) Wang, J.; Li, J.; Xu, F.; Shen, Q. *Adv. Synth. Catal.* **2009**, *351*, 1361. (c) Wang, L.; Fu, H.; Jiang, Y.; Zhao, Y. *Chem.—Eur. J.* **2008**, *14*, 10722. (d) Suto, Y.; Yamagiwa, N.; Torisawa, Y. *Tetrahedron Lett.* **2008**, *49*, 5732. (e) Seo, S.; Marks, T. *Org. Lett.* **2008**, *10*, 317. (f) Fang, C.; Qian, W.; Bao, W. *Synlett* **2008**, 2529. (g) Yoo, W.; Li, C. *J. Am. Chem. Soc.* **2006**, *128*, 13064. (h) Tillack, A.; Rudloff, I.; Beller, M. *Eur. J. Org. Chem.* **2001**, 523.

(i) Naota, T.; Murahashi, S. *Synlett* **1991**, 693. (j) Tamaru, Y.; Yamada, Y.; Yoshida, Z. *Synthesis* **1983**, 474. (k) Nakagawa, K.; Onoue, H.; Minami, K. *Chem. Commun.* **1966**, 17.

(9) (a) Cassidy, M. P.; Raushel, J.; Fokin, V. V. *Angew. Chem., Int. Ed.* **2006**, *45*, 3154. (b) Cho, S.; Yoo, E.; Bae, I; Chang, S. *J. Am. Chem. Soc.* **2005**, *127*, 16046.

(10) For selected examples, see: (a) Yadav, J. S.; Reddy, B. V. S.; Reddy, U. V. S.; Praneeth, K. *Tetrahedron Lett.* **2008**, *49*, 4742. (b) Hassankhani, A. *Synth. Commun.* **2006**, *36*, 2211. (c) Fazio, F.; Wong, C.-H. *Tetrahedron Lett.* **2003**, *44*, 9083. (d) Rosen, T.; Lico, I. M.; Chu, D. T. W. *J. Org. Chem.* **1988**, *53*, 1580.

(11) Chang, J. W. W.; Chan, P. W. H. *Angew. Chem., Int. Ed.* **2008**, *47*, 1138.

(12) Chan, J.; Baucom, K. D.; Murry, J. A. *J. Am. Chem. Soc.* **2007**, *129*, 14106.

(13) Chang, J. W. W.; Ton, T. M. U.; Tania, S.; Taylor, P. C.; Chan, P. W. H. *Chem. Commun.* **2010**, *46*, 922.

(14) For recent reviews on iron catalysis, see: (a) Sun, C.-L.; Li, B.-J.; Shi, Z.-J. *Chem. Rev.* **2011**, *111*, 1293. (b) Sarhan, A. A. O.; Bolm, C. *Chem. Soc. Rev.* **2009**, *38*, 2730. (c) Czaplik, W. M.; Mayer, M.; Cvengros, J.; Jacobi von Wangelin, A. *ChemSusChem.* **2009**, *2*, 396.(d) Plietker, B. In *Iron Catalysis in Organic Chemistry*; Plietker, B., Ed.; Wiley-VCH: Weinheim, Germany, 2008. (e) Enthaler, S.; Junge, K.; Beller, M. *Angew. Chem., Int. Ed.* **2008**, *47*, 3317. (f) Sherry, B. D.; Fürstner, A. *Acc. Chem. Res.* **2008**, *41*, 1500. (g) Correa, A.; Garcia Mancheno, O.; Bolm, C. *Chem. Soc. Rev.* **2008**, *37*, 1108. (h) Bolm, C.; Legros, J.; Le Paih, J.; Zani, L. *Chem. Rev.* **2004**, *104*, 6217.

(15) For recent reviews, see: (a) Collet, F.; Dodd, R. H.; Dauban, P. *Chem. Commun.* **2009**, 5061. (b) Fantauzzi, S.; Caselli, A.; Gallo, E. *Dalton Trans.* **2009**, 5434. (c) Díaz-Requejo, M. M.; Pérez, P. J. *Chem. Rev.* **2008**, *108*, 3379. (d) Davies, H. M. L.; Manning, J. R. *Nature* **2008**, *451*, 417. (e) Davies, H. M. L. *Angew. Chem., Int. Ed.* **2006**, *45*, 6422. (f) Li, Z. G.; He, C. *Eur. J. Org. Chem.* **2006**, 4313. (g) Dick, A. R.; Sanford, M. S. *Tetrahedron* **2006**, *62*, 2439. (h) Lebel, H.; Leogane, O.; Huard, K.; Lectard, S. *Pure Appl. Chem.* **2006**, *78*, 363.(i) Espino, C. G.; Du Bois, J. In *Modern Rhodium-Catalyzed Organic Reactions*; Evans, P. A., Ed.; Wiley-VCH: Weinheim, 2005; p 379. (j) Davies, H. M. L.; Long, M. S. *Angew. Chem., Int. Ed.* **2005**, *44*, 3518. (k) Müller, P.; Fruit, C. *Chem. Rev.* **2003**, *103*, 2905.

(16) For selected examples of iron-catalyzed amidation and aziridination of C−H and C═C bonds, see: (a) Wang, H.; Wang, Y.; Peng, C.; Zhang, J.; Zhu, Q. *J. Am. Chem. Soc.* **2010**, *132*, 13217. (b) Liu, Y.; Che, C.-M. *Chem.—Eur. J.* **2010**, *16*, 10494. (c) Jana, S.; Clements, M. D.; Sharp, B. K.; Zheng, N. *Org. Lett.* **2010**, *12*, 3736. (d) King, E. R.; Betley, T. A. *Inorg. Chem.* **2009**, *48*, 2361. (e) Klotz, K. L.; Slominski, L. M.; Riemer, M. E.; Phillips, J. A.; Halfen, J. A. *Inorg. Chem.* **2009**, *48*, 801. (f) Mayer, A. C.; Salit, A.-F; Bolm, C. *Chem. Commun.* **2008**, 5975. (g) Shen, M.; Driver, T. G. *Org. Lett.* **2008**, *10*, 3367. (h) Liu, P.; Wong, E. L.-M.; Yuen, A. W.-H.; Che, C.-M. *Org. Lett.* **2008**, *10*, 3275. (i) Wang, Z.; Zhang, Y.; Fu, H.; Jiang, Y.; Zhao, Y. *Org. Lett.* **2008**, *10*, 1863. (j) Nakanishi, M.; Salit, A.-F.; Bolm, C. *Adv. Synth. Catal.* **2008**, *350*, 1835. (k) Yan, S. Y.; Wang, Y.; Shu, Y. J.; Liu, H. H.; Zhou, X. G. *J. Mol. Catal. A* **2006**, *248*, 148. (l) Vyas, R.; Gao, G.-Y.; Harden, J. D.; Zhang, X. P. *Org. Lett.* **2004**, *6*, 1907. (m) Heuss, B. D.; Mayer, M. F.; Dennis, S.; Hossain, M. M. *Inorg. Chim. Acta* **2003**, *342*, 301. (n) Simkhovich, L.; Gross, Z. *Tetrahedron Lett.* **2001**, *42*, 8089.

(17) Please refer to the Supporting Information for details of the impurities found in 99.5% and 99.99% pure $FeCl_2$.

(18) For recent reviews, see: (a) Roberts, B. A.; Strauss, C. R. *Acc. Chem. Res.* **2005**, *38*, 653. (b) Larhed, M.; Moberg, C.; Hallberg, A. *Acc. Chem. Res.* **2002**, *35*, 717. For selected examples, see:(c) Alvarez, H. M.; Loupy, A.; Calderon, O.; Perez, E. *Tetrahedron* **2006**, *62*, 2616. (d) Alvarez, H. M.; Barbosa, D. P.; Fricks, A. T.; Aranda, D. A. G.; Valdés, R. H.; Antunes, O. A. C. *Org. Process Res. Dev.* **2006**, *10*, 941. (e) Dos Santos, A. A.; Wendler, E. P.; Marques, F. A.; Simonelli, F. *Lett. Org. Chem.* **2004**, *1*, 47. (f) Alvarez, H. M.; Plutín, A. M; Rodríguez, Y.; Perez, E.; Loupy, A. *Synth. Commun.* **2000**, *30*, 1067. (g) Alvarez, H. M.; Perez, E.; Plutín, A. M; Morales, M.; Loupy, A. *Tetrahedron Lett.* **2000**, *41*, 1753.

(19) Griller, D.; Ingold, K. U. *Acc. Chem. Res.* **1980**, *13*, 317.

(20) Zdilla, M. J.; Abu-Omar, M. M. *J. Am. Chem. Soc.* **2006**, *128*, 16971.

(21) (a) Bedford, R. B.; Nakamura, M.; Gower, N. J.; Haddow, M. F.; Hall, M. A.; Huwe, M.; Hashimoto, T.; Okopie, R. A. *Tetrahedron Lett.* **2009**, *50*, 6110. (b) Larsson, P.-F.; Correa, A.; Carril, M.; Norrby, P.-O.; Bolm, C. *Angew. Chem., Int. Ed.* **2009**, *48*, 5691. (c) Buchwald, S. L.; Bolm, C. *Angew. Chem., Int. Ed.* **2009**, *48*, 5586.

(22) (a) Carlino, S.; Hudson, M. J.; Locke, W. J. *J. Mater. Chem.* **1997**, *7*, 813. (b) Long, G. J.; Clarke., P. J. *Inorg. Chem.* **1978**, *17*, 1394.

(23) The involvement of a [Fe]═NSO_2Ar species has also been reported in other iron-mediated amidations and aziridinations; see refs 16e, 16h, 16l, 16m and (a) Moreau, Y.; Chen, H.; Derat, E.; Hirao, H.; Bolm, C.; Shaik, S. *J. Phys. Chem. B* **2007**, *111*, 10288. (b) Klinker, E. J.; Jackson, T. A.; Jensen, M. P.; Stubna, A.; Juhász, G.; Bominaar, E. L.; Münck, E.; Que, L., Jr. *Angew. Chem., Int. Ed.* **2006**, *45*, 7394. (c) Jensen, M. P.; Mehn, M. P.; Que, L., Jr. *Angew. Chem., Int. Ed.* **2003**, *42*, 4357. (d) Mahy, J. P; Bedi, G.; Battioni, P.; Mansuy, D. *J. Chem. Soc., Perkin Trans. 2* **1988**, 1517. (e) Mahy, J. P; Battioni, P.; Bedi, G.; Mansuy, D.; Fischer, J.; Weiss, R.; Morgenstern-Badarau, I. *Inorg. Chem.* **1988**, *27*, 353. (f) Mahy, J. P; Battioni, P.; Mansuy, D. *J. Am. Chem. Soc.* **1986**, *108*, 1079. (g) Svatis, E. W.; Dawson, J. H.; Breslow, R.; Gellman, S. H. *J. Am. Chem. Soc.* **1985**, *107*, 6427. (h) Mansuy, D.; Mahy, J. P.; Dureault, A.; Bedi, G.; Battioni, P. *Chem. Commun.* **1984**, 1161. (i) White, R. E.; McCarthy, M.-B. *J. Am. Chem. Soc.* **1984**, *106*, 4922.

(24) For iron catalyzed hydrolysis of PhI═NTs to $TsNH_2$ by H_2O, see refs 23e, 23f, 23h, 23i and O'Connor, K. J.; Wey, S.-J.; Burrows, C. J. *Tetrahedron Lett.* **1992**, *33*, 1001.

(25) Wu, X.-F.; Vovard-Le Bray, C.; Bechki, L.; Darcel, C. *Tetrahedron* **2009**, *65*, 7380.

(26) Albone, D. P.; Challenger, S.; Derrick, A. M.; Fillery, S. M.; Irwin, J. L.; Parsons, C. M.; Takada, H.; Taylor, P. C.; Wilson, D. J. *Org. Biomol. Chem.* **2005**, *3*, 107.

(27) Leung, S. K.-Y.; Tsui, W.-M.; Huang, J.-S.; Che, C.-M.; Liang, J.-L; Zhu, N. *J. Am. Chem. Soc.* **2005**, *127*, 16629.

(28) (a) Jiang, Y.; Zhou, G.-C.; He, G.-L.; He, L.; Li, J.-L.; Zheng, S.-L. *Synthesis* **2007**, 1459. (b) Jain, S. L.; Sharma, V. B.; Sain, B. *Tetrahedron Lett.* **2003**, *44*, 4385. (c) Evans, D. A.; Bilodeau, M. T.; Faul, M. M. *J. Am. Chem. Soc.* **1994**, *116*, 2742.

(29) Garcia-Ruano, J. L.; Aleman, J.; Fajardo, C.; Parra, A. *Org. Lett.* **2005**, *7*, 5493.

(30) Yamada, Y.; Yamamoto, T.; Okawara, M. *Chem. Lett.* **1975**, 361.

(31) Dauban, P.; Saniere, L.; Tarrade, A.; Dodd, R. H. *J. Am. Chem. Soc.* **2001**, *123*, 7701.

(32) (a) Falvo, R. E.; Mink, L. M. *J. Chem. Educ.* **1999**, *76*, 237. (b) Li, Z.-Y.; Huang, J.-S.; Che, C.-M.; Chang, C.-K. *Inorg. Chem.* **1992**, *31*, 2670. (c) Rillema, D. P.; Nagle, J. K.; Barringer, L. F., Jr.; Meyer, T. J. *J. Am. Chem. Soc.* **1981**, *103*, 56. (d) Adler, A. D.; Longo, F. R.; Finarelli, J. D.; Goldmacher, J.; Assour, J.; Korsakoff, L. *J. Org. Chem.* **1967**, *32*, 476.

(33) Yates, M. H.; Kallman, N. J.; Ley, C. P.; Wei, J. N. *Org. Process Res. Dev.* **2009**, *13*, 255.

(34) Klemarczyk, P. T.; Brantl, K. R.; Messana, A. D., U.S. Patent US 6958368 B1 20051025, 2005, 15.

(35) Joshi, G. *J. Indian Chem. Soc.* **1962**, *39*, 140.

(36) Kemp, A. D.; Stephen, H. *J. Chem. Soc.* **1948**, 110.

(37) Baumann, T.; Bachle, M.; Brase, S. *Org. Lett.* **2006**, *8*, 3797.

(38) Leca, D.; Song, K.; Amatore, M.; Fensterbank, L.; Lacote, E.; Malacria, M. *Chem.—Eur. J.* **2004**, *10*, 906.

(39) Konev, V. F.; Eremina, Z. G.; Maslennikov, A. I.; Kaliman, V. A.; Verdyan, A. I. *Farm. Zh. (Kiev)* **1985**, *5*, 49.

(40) Homsi, F.; Rosseau, G. *J. Org. Chem.* **1999**, *64*, 81.

(41) Cook, C. H.; Cho, Y. S.; Jew, S. S.; Chung, G. H. *Soul Taehakkyo Yakhak Nonmunjip* **1985**, *10*, 66.

(42) Reddy, C. R.; Mahipal, B.; Yaragorla, S. R. *Tetrahedron Lett.* **2007**, *48*, 528.

(43) (a) Palomo, C.; Oiarbide, M.; Halder, R.; Laso, A.; Lopez, R. *Angew. Chem., Int. Ed.* **2006**, *45*, 117. (b) Lee, K. Y.; Lee, C. G.; Kim, J. N. *Tetrahedron Lett.* **2003**, *33*, 1231.
(44) Wang, C.-J.; Shi, M. *J. Org. Chem.* **2003**, *68*, 6229.