JOC *Note*

Iron(II)-Catalyzed Sulfimidation and [2,3]-Sigmatropic Rearrangement of Propargyl Sulfides with *tert*-Butoxycarbonyl Azide. Access to *N*-Allenylsulfenimides

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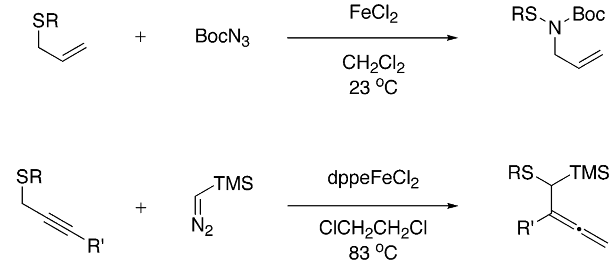
Abstract: The iron(II)-catalyzed Bach reaction of *tert*-butoxycarbonyl azide ($BocN_3$) and allyl sulfides has been extended to include propargyl sulfides, which give *N*-allenylsulfenimide products. Using 10 mol % $dppeFeCl_2$ as catalyst the reaction proceeds at 0 °C with a number of different propargyl sulfides in 31−73% isolated yield. The reaction is limited by product instability toward catalyst and termination of the catalytic cycle by excess $BocN_3$. *N*-Allenylsulfenimide **2b** smoothly undergoes catalytic hydrogenation and a Diels−Alder reaction with cyclopentadiene.

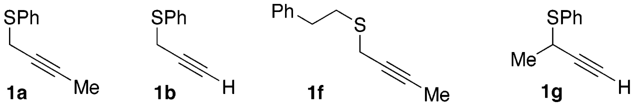
Metal-catalyzed nitrogen atom transfer reactions have attracted considerable attention due to their ability to efficiently construct synthetically valuable intermediates. Since the initial report of Kwart and Kahn,[1] continued research has resulted in the development of practical methods for the catalytic aziridination of olefins.[2−7] The related catalytic sulfimidation reaction[8−13] has also emerged as a valuable tool, particularly in the context of preparing allylic sulfimides, which undergo [2,3]-sigmatropic rearrangement to give allylic sulfenamides.[8,14−16] With the exception of TsN_3[12,16] and a lone carbonyl azide[14] example, azides have been ineffective as imido group donors for metal-catalyzed aziridinations and sulfimidations. Nitrene precursors such as *N*-(*p*-tolylsulfonyl)iminophenyliodinane ($PhI{=}NTs$)[17,18] have typically been employed with greater success. Bach and Körber demonstrated that $FeCl_2$ can catalyze the reaction of *N*-*tert*-butoxycarbonyl azide ($BocN_3$) with allylic sulfides to give *N*-Boc-protected *N*-allylamines (Scheme 1).[15] These results suggested that iron catalysis could provide access to reactive intermediates derived directly from the reaction of azides and sulfides. Since our group has shown that propargyl sulfides are good partners for the iron-catalyzed Kirmse reaction with trimethylsilyldiazomethane (Scheme 1),[19] we investigated their use in the iron-catalyzed Bach reaction with $BocN_3$.

SCHEME 1



Preparation of Propargyl Substrates. Propargyl sulfides **1a**, **1b**, and **1f** were prepared by reaction of the appropriate propargyl bromide and thiolate, whereas the α-branched sulfide **1g** was prepared from the mesylate derived from 2-butynol (Scheme 2).[20] Internal alkynes were prepared from propargyl sulfides by deprotonation with *n*-BuLi at −78 °C and reaction with either TMS−chloride (sulfide **1c**)[21] or benzaldehyde (sulfide **1d**) (Scheme 3).[22] The alcohol **1d** was acylated with acetic anhydride to give the acetate **1e** (Scheme 3). $BocN_3$ was prepared according to the literature procedure.[23]

SCHEME 2



Reaction Conditions. Bach has prepared *N*-allylsulfenimides by dissolving the allyl sulfide and $BocN_3$ in CH_2Cl_2 and adding solid $FeCl_2$ to initiate the reaction. When these conditions were applied to propargyl sulfide **1a**, the desired *N*-allenylsulfenimide **2a** was obtained in 49% yield (Scheme 4). The reaction was relatively slow, with product formation occurring over 15 h. As previously observed by Bach, no reaction occurs without catalyst.

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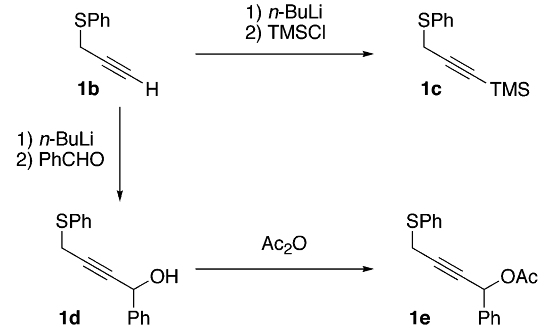
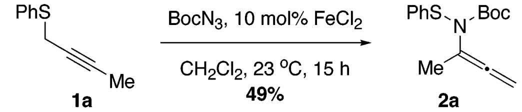
10.1021/jo0340410 CCC: $25.00

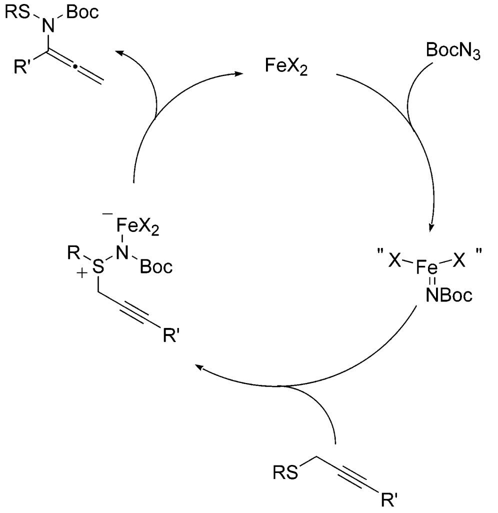
SCHEME 3



SCHEME 4



SCHEME 5



The reaction was also attempted with $PdCl_2(PhCN)_2$[14] as catalyst, but was unsuccessful.

Since $FeCl_2$ has poor solubility under the reaction conditions, we hypothesized that better results might be achieved using a completely soluble catalyst. In solvents that solubilize $FeCl_2$ such as MeCN and DMF, no reaction was observed, but when dppe$FeCl_2$ was dissolved in refluxing 1,2-dichloroethane and then cooled to room temperature, the reaction proceeded in 15 min to give product **2a** in 54% yield. Immediately following the addition of propargyl sulfide **1a** and $BocN_3$ to the catalyst solution, violent nitrogen evolution was observed and the reaction mixture became hot. Although obvious nitrogen evolution ceased after 3 min, product continued to form over 15 min. At 0 °C, nitrogen evolution was less vigorous and ceased after approximately 5 min. *N*-Allenylsulfenimide **2a** was isolated in 70% yield after 6 h (comparable yields are obtained when the reaction is run for 2 h).

Catalyst deactivation was hypothesized to be the cause of incomplete conversion of sulfide, as $BocN_3$ was present at the end of the reaction (by GC-MS). The reaction with sulfide **1a** was run at 0 °C and an additional 5 mol % of catalyst was added after 2 h as a solution in 1,2-dichloroethane. The majority of the starting material was consumed (3% recovered vs 14% with no added catalyst), confirming that catalyst had been deactivated during the course of the reaction.

Since initial evolution of nitrogen gas was not accompanied by consumption of starting material, we believe a stable Fe·NBoc complex is formed (Scheme 5).[15] The stable complex may be an iron–nitrene precursor[24] or an iron–nitrene[25] that reacts with sulfide to produce a sulfimide that rearranges to the *N*-allenylsulfenimide product and liberates the iron catalyst to continue the catalytic cycle.

A series of experiments were performed to better understand the pathway(s) that lead to catalyst deactivation and/or limit the yield of *N*-allenylsulfenimide products. The two major factors that limit the reaction were found to be product instability toward the iron catalyst and termination of the catalytic cycle by excess $BocN_3$. When *N*-allenylsulfenimide **2a** and 10 mol % of dppe-$FeCl_2$ were stirred at room temperature for 15 min, half of the material was converted to products that did not move on silica gel and only 49% of the *N*-allenylsulfenimide was recovered. Iron-catalyzed decomposition of product seems to be the primary cause of incomplete mass balance. A low concentration of $BocN_3$ leads to higher catalyst turnover; when the typical reaction was repeated with slow addition of $BocN_3$, only trace amounts of starting sulfide were recovered and the *N*-allenylsulfenimide **2a** was isolated in 69% yield. Thus, when concentrations of $BocN_3$ are kept low, the catalyst remains active long enough to completely consume the starting material. When 2 equiv of $BocN_3$ was used in the reaction, the yield of *N*-allenylsulfenimide **2a** decreased to 49% and 41% unreacted sulfide was recovered, supporting the idea that the reaction of $BocN_3$ (which leads to catalyst destruction) competes with the reaction of sulfide.

To investigate the effect of the phosphine ligand, catalyst solutions were prepared by stirring dppp and dppf with $FeCl_2$ in refluxing dichloroethane until the $FeCl_2$ went into solution. When a solution of propargyl sulfide **1b** and $BocN_3$ was added to the chilled catalyst solution, *N*-allenylsulfenimide **2b** was formed in yields of 57% and 56%, respectively. These yields are slightly lower than those obtained with the preformed dppe$FeCl_2$ catalyst. Other iron(II) catalysts were examined in the sulfimidation/[2,3] rearrangement (FeF_2, $FeBr_2$, FeI_2, $Fe(acac)_2$, $Fe(OAc)_2$, and $FeBF_4·6H_2O$). None were completely soluble in refluxing 1,2-dichloroethane with the exception of $Fe(acac)_2$, which failed to catalyze the reaction. Despite incomplete solubility $FeBr_2$ and FeI_2 did produce *N*-allenylsulfenimide, but with low conversion. In addition to simple ferrous salts, a number of other insoluble catalysts were examined with dichloroethane as the reaction solvent ($AuBr_3$, $AuCl_3$, AuCl·DMS, CuBr, CuOTf·$^1/_2$PhH, $Cu(OTf)_2$, $HfCl_4$, $Mn(OAc)_2$, $NiCl_2$, (COD)$RuCl_2$, and $RuCl_3$) but, as expected, no reaction was observed. Several soluble metal catalysts were examined: AuCl·PPh_3, CuCN, CuI, $[(COD)IrCl]_2$, $Ir(acac)_3$, dppp$NiCl_2$, $Cl_2Ni(PPh_3)_2$, $Pd(acac)_2$, $Rh_2(OAc)_4$, and $Sn(OTf)_2$. $Pd(acac)_2$

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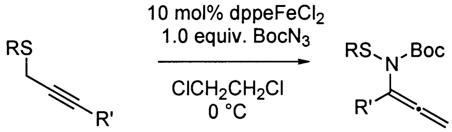
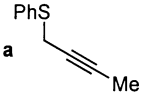
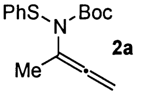
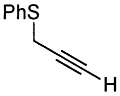
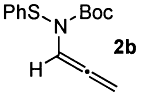
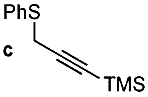
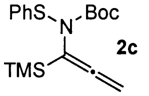
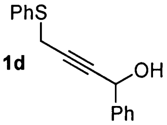
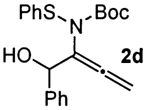
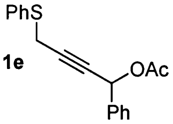
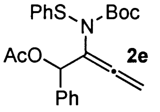
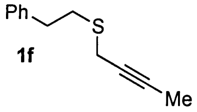
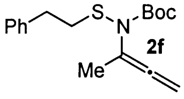
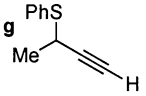
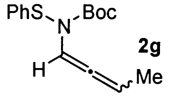
TABLE 1. Iron(II)-Catalyzed Sulfimidation/Rearrangement of Propargyl Sulfides

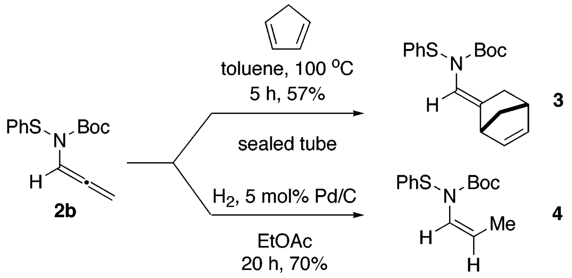


Sulfide	Time (h)	Product	% yield / % rec. SM
1a 	6	 **2a**	70 / 14
1b 	2	 **2b**	73 / 17
1c 	4.5	 **2c**	52 / 21
1d 	2.5	 **2d**	53 / 19
1e 	2	 **2e**	69 / 13
1f 	5	 **2f**	31 / 44
1g 	2	 **2g**	52 / 18

was the only catalyst that reacted with $BocN_3$ and a propargyl sulfide, but gave numerous products, none of which appeared to correspond to a nitrene transfer product. To our knowledge, the Bach[15] reaction with iron(II) halides and the Migita[14] reaction of Pd(II) (which was ineffective with propargyl sulfides and $BocN_3$) are the only reactions in which metals efficiently catalyze nitrene transfer reactions from azidoformates.

Substituent Effects. Propargyl sulfides **1a**−**f** were prepared to test the sensitivity of the sulfimidation/rearrangement reaction toward different functionality. Terminal alkyne **1b** was expected to form an *N*-allenylsulfenimide product that would be more reactive toward the iron catalyst, but allene **2b** was isolated in 73% yield (Table 1). The trimethylsilyl-substituted alkyne **1c** was prepared to test the effect of steric hindrance distal to sulfur and also provides a unique functional handle for further elaboration; the TMS−allene **2c** was isolated in 52% yield. Tolerance of polar functionality was tested with alcohol **1d** and acetate **1e**, which were converted to the homoallenyl alcohol **2d** and homoallenyl acetate **2e** in 53% and 69% isolated yields, respectively. Phenethyl sulfide **1f**, which is more nucleophilic than an aryl sulfide, shows the lowest conversion of all sulfides studied; alkyl sulfide **2f** was isolated in 31% yield. The effect of branching α to sulfur was tested with propargyl sulfide **1g**; chiral allene **2g** was isolated in 52% yield. Bach has suggested that α-branching decreases the nucleophilicity of sulfur,[15] a possible explanation for the poor yield of **2g**.

SCHEME 6



Reactivity of *N*-Allenylsulfenimides. Simple dialkyl allenamines are prone to hydrolysis and polymerization, making them difficult to prepare and handle.[26] Hsung and co-workers have prepared allenamides that are considerably more stable and easier to handle and have used them for [4+2] cycloadditions and a tandem *m*-CPBA oxidation/[4+3] cycloaddition.[27−29] The *N*-allenylsulfenimides produced in this study were purified by silica gel chromatography. However, neat *N*-allenylsulfenimides are not completely stable to storage even at −20 °C. In contrast, solutions of *N*-allenylsulfenimides in aprotic solvents such as benzene, hexane, or ether may be stored for over a month at −20 °C without significant decomposition.

The *N*-allenylsulfenimide products (**2a**, **2b**, and **2c**) were unreactive with a variety of electrophiles at ambient temperature (e.g., $PhCHO/SnCl_2$, triphosgene, and PhNCO). Reaction with stronger electrophiles such as Br_2 or $BF_3{\cdot}Et_2O/PhCHO$ resulted in numerous unidentifiable products. Removal of the benzenesulfanyl group with $NaBH_4$ gave intermediates that were too reactive to isolate. Likewise, the attempted removal of the Boc group with TFA gave numerous unisolable products. Both the benzenesulfanyl and Boc groups appear to have a deactivating effect on reactivity; as soon as either was removed, the intermediates became too reactive for isolation or functionalization in situ.

The *N*-allenylsulfenimide **2b** was reacted with cyclopentadiene to give the Diels−Alder adduct **3** (Scheme 6). To the best of our knowledge, the work of Hsung[27,28] and the work of Tamaru[30,31] represent the only other examples of [4+2] cycloadditions with allenamides. These allenamides underwent inverse electron demand [4+2]

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[27] Wei, L.-L.; Xiong, H.; Douglas, C. J.; Hsung, R. P. *Tetrahedron Lett.* **1999**, *40*, 6903.

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cycloaddition at the internal allenyl double bond. In contrast, we observed normal electron demand [4+2] cycloaddition at the terminal allenyl double bond. Heterogeneous catalytic hydrogenation of **2b** successfully gave the *Z*-enamide **4** in 70% isolated yield, despite the presence of sulfur. The syn addition of hydrogen was confirmed by the diagnostic 7.9 Hz coupling constant between vinylic protons of enamine **4**.

In conclusion, we have shown that Bach reaction of $BocN_3$ with allyl sulfides works efficiently with propargyl sulfides when $dppeFeCl_2$ is used as the catalyst precursor. The resulting *N*-allenylsulfenimides are sufficiently stable that they can be used in Diels−Alder reactions or hydrogenated to *Z*-enamides.

Experimental Section

Representative Procedure: *N*-Allenylsulfenimide, 2a. To a flame-dried round-bottom flask equipped with a magnetic stir bar was added $dppeFeCl_2$ (53 mg, 0.10 mmol) and 1,2-dichloroethane (0.9 mL). The resulting mixture was heated to reflux and stirred under N_2 until a clear brown solution was obtained. The solution was allowed to cool to room temperature and was then cooled to 0 °C in an ice bath. A solution of propargyl sulfide **1a** (162 mg, 1.0 mmol) and *tert*-butoxycarbonyl azide (143 mg, 1.0 mmol) in 0.1 mL of 1,2-dichloroethane was added via syringe to the cooled catalyst solution. The reaction mixture was stirred under N_2 at 0 °C for 6 h (comparable yields are obtained with a reaction time of 2 h). The crude oil was purified by silica gel chromatography with gradient elution (1→3% EtOAc/hexanes) to yield **2a** as a clear oil (193 mg, 70%): ^1H NMR (500 MHz, $CDCl_3$, 298 K) δ 7.27−7.35 (m, 4H), 7.17−7.20 (m, 1H), 4.90 (q, $J = 3.2$ Hz, 2H), 1.95 (t, $J = 3.2$ Hz, 3H), 1.47 (s, 9H); ^{13}C NMR (125 MHZ, $CDCl_3$, 298 K) δ 207.5, 155.2, 138.8, 128.9, 126.8, 125.7, 110.4, 82.4, 80.4, 28.2, 18.6; IR (thin film) 3061, 2979, 2931, 1717, 1585, 1292 cm^{-1}; TLC R_f 0.40 (10% EtOAc/hexanes); GC-MS (CI/NH_3) *m/z* (rel intensity) 278 (10), 239 (38), 178 (100); HRMS (CI/NH_3) *m/z* calcd for $C_{15}H_{20}NO_2S$ $[M + H]^+$ 278.1214, found 278.1206.

Acknowledgment. We thank NSF CHE 9623903 and the Alfred P. Sloan Foundation for financial support. K.L.G. is a recipient of a graduate fellowship sponsored by Pharmacia Corp.

Supporting Information Available: Experimental procedures and characterization data for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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