5256 *J. Org. Chem.* **2001,** *66,* 5256−5258

Iron-Catalyzed Reaction of Propargyl Sulfides and Trimethylsilyldiazomethane

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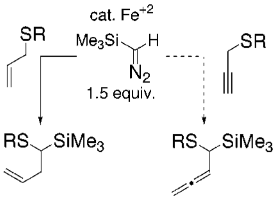
Received March 7, 2001

Introduction

Iron is the most abundant metal in the cosmos, yet catalytic applications of iron in C−C bond formation are rare. Some examples include Fischer−Tropsch chemistry, ene carbocyclizations,[1] cross-coupling reactions of Grignard reagents,[2] and some limited examples of cyclopropanation.[3] Bach and co-workers have recently shown that iron efficiently catalyzes the addition/[2,3]-rearrangement of allyl sulfides and $BocN_3$, leading to C−N bond formation.[4] This process was later shown to be efficient with allyl sulfides, iron catalysts, and trimethylsilyldiazomethane, leading to C−C bond formation (Scheme 1).[5] Unlike reactions with traditional metal catalysts such as rhodium, copper, cobalt, or palladium, reactions with ferrous salts give good yields without syringe pump addition of the diazo compound or a large excess of reagents.

Scheme 1

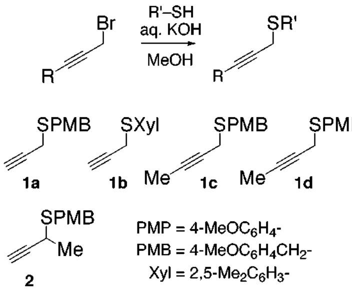


The reaction of allyl sulfides, iron salts, and Me_3SiCHN_2 generates α-silyl sulfides that can be unveiled as aldehydes or used directly in Peterson olefination reactions.[6] An important property of silicon, the ability to enhance the nucleophilicity of pi systems, is not expressed in the homoallylsilane products. In contrast, homoallenylsilanes, available from a [2,3]-rearrangement (Scheme 1), are poised to take advantage of the silicon effect.[7] Copper and rhodium-catalyzed reactions of propargyl derivatives[8] with diazomethane and α-diazoesters have been previously reported; this work describes the efficient formation of homoallenylsilanes by the iron-catalyzed reaction of propargyl sulfides with trimethylsilyldiazomethane.

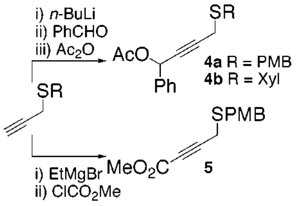
Results and Discussion

Synthesis of Substrates. Propargyl sulfides **1a**−**d** and **2** were synthesized by alkylation of the corresponding thiolates in yields ranging from 58 to 94% (Scheme 2). Sulfides **1a**−**d** were prepared from propargyl bromides, whereas substrate **2** was prepared from a propargyl mesylate.[9] The termini of **1a** and **1b** were functionalized by deprotonation with 1.1 equiv of *n*-butyllithium and addition of benzaldehyde at −78 °C.[10] The resulting propargyl alcohols **3a** and **3b** (not shown) were then protected by acetylation. Propynoate **5** was prepared by formation of the Grignard salt of alkyne **1b** followed by acylation with methyl chloroformate (Scheme 3).[11] Since xylyl derivative **1b** lacked polar functionality, the conversion to ester **4b** was essential for chromatographic purification of products of the iron-catalyzed reaction.

Scheme 2



Scheme 3



Reaction Conditions. Propargyl sulfide **1c** was subjected to the iron-catalyzed addition/rearrangement reaction with Me_3SiCHN_2. To ensure reliable results in these reactions, the propargyl sulfide substrate first had to be heated for 1.5 h in 1,2-dichloroethane with the 5 mol % catalyst precursor, typically $dppeFeCl_2$, prior to addition of Me_3SiCHN_2. Shorter incubation times may be effective, but were not investigated. A 2.5 equiv portion of Me_3SiCHN_2 was added as a 2.0 M solution in hexanes, and the reaction was stirred at reflux (3 h) until TLC

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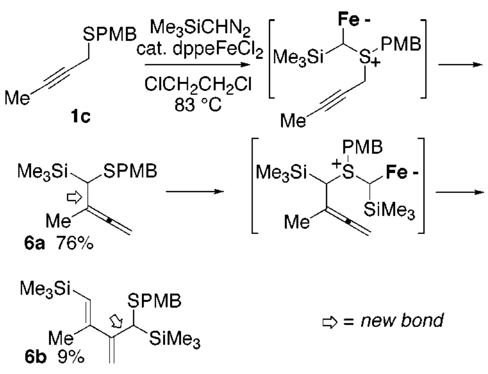
10.1021/jo010247u CCC: $20.00

Scheme 4



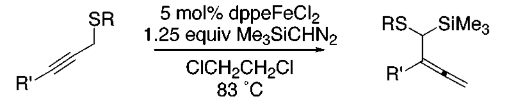
indicated complete consumption of starting material. Under these conditions, the desired homoallenylsilane **6a** was isolated in 76% yield. An additional product, diene **6b,** was obtained as a 2:1 mixture of *E* and *Z* isomers. The stereochemistry of the *Z* isomer was confirmed by the presence of a 15% NOE (2 s mixing time) from the C2 methyl to the C1 proton. Diene **6b** probably results from a second addition of Me_3SiCHN_2 to the homoallenyl sulfide moiety of **6a** as depicted in Scheme 4. While a third addition/rearrangement is possible, the corresponding products were not formed in sufficient amounts to isolate. Although the intermediates involved in this catalytic reaction have not been established, they may be analogous to intermediates involved in cyclopropanation by $CpFe(CO)_2{=}CH_2$, except that the process described in this work is catalytic in iron.[12] When the stoichiometry of Me_3SiCHN_2 was reduced from 2.5 to 1.3 equiv, the starting material was still completely consumed and the yield of allene **6a** increased to 85%; only a trace of diene **6b** was formed.

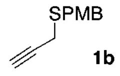
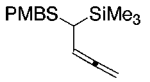
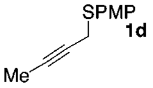
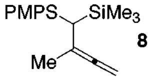
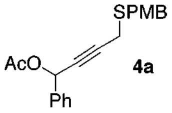
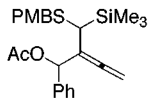
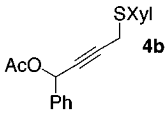
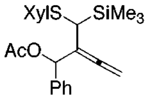
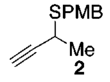
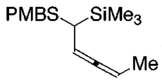
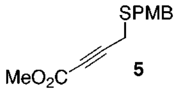
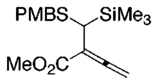
When the addition/rearrangement is carried out with alkyne **1c** using catalytic $FeBr_2$, the allene **6a** was isolated in 65% yield. Even though phosphine ligand is not required in the reaction there are two reasons to use $dppeFeCl_2$ rather than simple ferrous salts. First, $FeBr_2$ is sufficiently hygroscopic that it requires handling under argon or nitrogen. Second, simple ferrous halides have low solubility in chlorinated solvents, even when the thiother is present.

Substituent Effects. When the terminal alkyne **1b** was subjected to the rearrangement conditions, the reaction stopped after about 1.5 h even though about 10% of the starting material remained. Addition of an extra 0.25 equiv of Me_3SiCHN_2 led to consumption of the remaining starting material. The desired product **7a** was isolated in 73% yield, accompanied by 11% of diene **7b** (not shown) resulting from a second addition/rearrangement. Thus, the extra methyl in substrate **1c** was probably beneficial in minimizing diene formation. Additionally, aryl thioethers should be weaker donors than benzyl thioethers, yet the aryl thioether **1d** gives a yield similar to that of the benzyl thioether **1c**.

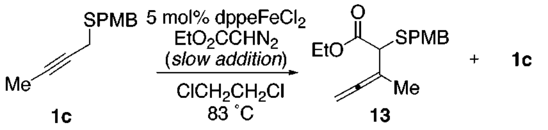
Formation of the initial ylide complex should play an important role in diastereoselection. The sulfur lone pairs of substrates **4a** and **4b** are diastereotopic, but are far from the stereogenic center. The chiral acetates **4a** and **4b** both gave good yields of allenes **9** and **10**, respectively, but as 1:1 mixtures of diastereomers. The juxtaposition of allylic acetate and allylsilane functional groups in products **9** and **10** may make them useful for palladium-catalyzed trimethylenemethane cycloaddition reactions.[13] In contrast to **4a** and **4b**, the stereogenic center of substrate **2** is proximal to the sulfur atom rather than distal. However, reaction of substrate **2** proceeds with a mere 2:1 diastereocontrol. As with substrate **1a**, the reaction stopped after 1.5 h leaving a substantial amount of starting material. Addition of an extra 0.75 equiv. Me_3SiCHN_2 helped to consume the starting material, but probably led to further consumption of the allene product. Ultimately, chiral allene **11** was isolated in 48% yield. Finally, the sensitive propynoate **5** was a poor substrate for the reaction. Allene product **12** was isolated in only 18% yield from a mixture of products.

Table 1. Iron-Catalyzed of Reaction withPropargyl Sulfides and Me_3SiCHN_2



Sulfide	Time (h)	Product	Yield
 **1b**	1	 **7**	73%
 **1d**	7	 **8**	78%
 **4a**	0.5	 **9**	73%
 **4b**	1	 **10**	90%
 **2**	5	 **11**	48%
 **5**	5	 **12**	18%

Scheme 5



1.3 equiv. EtO_2CCHN_2 7% 78%
6.7 equiv. EtO_2CCHN_2 21% 67%

Me_3SiCHN_2 is more efficient than ethyl diazoacetate in the iron-catalyzed addition/rearrangement reaction (Scheme 5). Dimerization is the primary competing

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pathway that reduces the yield of allene product.[5,14] The bulk of Me_3SiCHN_2 makes dimerization less favorable compared to sulfonium ylide formation. In contrast, the smaller ethyl diazoacetate is more likely to form dimer.

Conclusions

In summary, propargyl sulfides were shown to be efficient partners for the iron-catalyzed addition/rearrangement reaction with Me_3SiCHN_2. Yields of the allenyl α-silylsulfides were generally between 48 and 90%, except for propynoate **5**, which gave a low yield. Adding Me_3SiCHN_2 after premixing the catalyst with the sulfide substrate gave significantly higher yields and lower reaction times than comparable reactions without premixing. While dppe$FeCl_2$ was a convenient catalyst precursor, phosphine ligand was not required for the reaction. Larger substituents on the alkyne gave allene products in higher yields, presumably because they disfavor a second addition/rearrangement. Low diastereoselection was observed when a stereogenic center was adjacent to sulfur, while no diastereoselectivity was seen when stereogenic centers were far. Yields of allene products were enhanced when bulky Me_3SiCHN_2 was used compared to the smaller ethyl diazoacetate.

Experimental Section

General Preparation of Allenes. To a solution of propargyl sulfide **1c** (0.160 g, 0.77 mmol) in anhydrous 1,2-dichloroethane (7.7 mL) was added dppe$FeCl_2$ (0.020 g, 0.038 mmol), and the resulting solution was heated to reflux. After 1.5 h, Me_3SiCHN_2 (0.48 mL, 0.96 mmol, 2.0 M solution in hexanes) was added, and the solution was maintained at reflux for 1 h. The reaction mixture was cooled to room temperature, filtered through a plug of silica gel (80:20 ethyl acetate/hexanes), and concentrated in vacuo to afford a brown oil. Purification by silica gel chromatography (85:15 hexanes/benzene) gave allene **6a** as a clear colorless oil (0.190 g, 85%).

6a: $R_f = 0.33$ (85:15 hexanes/benzene); IR (thin film) 2954, 1951, 841 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.21 (dd, $J = 8.8$, 2.8 Hz, 2H), 6.82 (dd, $J = 8.8$, 2.8 Hz, 2H), 4.66 (dqd, $J = 10.0$, 3.2, 0.4 Hz, 1H), 4.62 (dqd, $J = 10.0$, 3.2, 0.8 Hz, 1H), 3.80 (s, 3H), 3.60 (s, 2H), 2.59 (m, 1H), 1.74 (t, $J = 3.2$ Hz, 3H), 0.04 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 207.5, 158.4, 130.4, 130.2, 113.6, 97.6, 73.7, 55.2, 36.3, 35.6, 16.8, −2.0; LRMS (EI) m/z (relative intensity) 292(29), 171(51), 121(99), 73(100); HRMS (CI/NH_3) m/z calcd for $C_{16}H_{24}OSSi$ (M^+) 292.1317, found 292.1320. Anal. Calcd for $C_{16}H_{24}OSSi$: C, 65.70; H, 8.27. Found: C, 65.47; H, 8.18.

Acknowledgment. We thank the National Science Foundation (CHE 9623903). Additional support was provided by Eli Lilly and the Dupont Aid to Education Program. D.L.V.V. is a fellow of the Alfred P. Sloan Foundation.

Supporting Information Available: Experimental procedures, ^1H NMR spectra, and other characterization data for all new compounds. NOE spectra for stereochemical assignment of dienes **6b**. This material is available free of charge via the Internet at http://pubs.acs.org.

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