Lewis Acid Catalysis

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Si–H Bond Activation: Bridging Lewis Acid Catalysis with Brookhart's Iridium(III) Pincer Complex and $B(C_6F_5)_3$**

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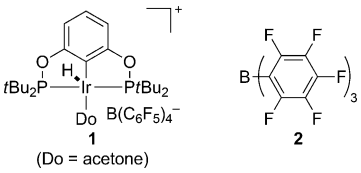
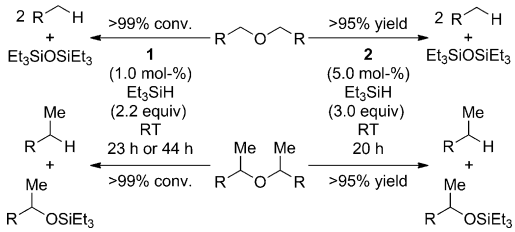
deoxygenation · Lewis acids · pincer complexes · Si–H bond activation · silicon

Dedicated to Professor Helmut Schwarz on the occasion of his 70th birthday

Reduction with Si–H compounds is an important method in synthetic organic chemistry because of the mild reaction conditions compared to established classic methods.[1] In regard to catalytic versions, recent studies by the Brookhart research group[2] on cationic iridium(III) pincer complex **1** and reports by Piers and co-workers[3] using tris(pentafluorophenyl)borane (**2**) are currently garnering increased attention. Both systems were shown to catalytically activate silanes, thereby creating an electrophilic silicon intermediate that is able to react with a wide variety of nucleophiles.[4,5] Of these, ethers (and alcohols) are particularly attractive, as their reductive deoxygenation[5a,b,e] is also relevant to the defunctionalization of biomass, such as carbohydrates.[6] The aim of this Highlight is to describe the similarities between the two catalysts, by using a full deoxygenation of an ether as an example, and to identify the possible limitations not yet addressed.



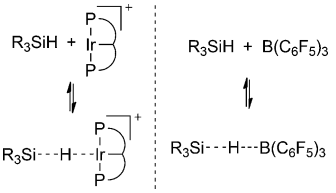
Gevorgyan, Yamamoto, and co-workers demonstrated more than a decade ago that $B(C_6F_5)_3$ (**2**) in combination with Et_3SiH reductively cleaves ethers.[5a,b,e] Almost ten years later, Brookhart and co-workers used **1** as a catalyst in the same transformation.[2c] Both systems were applicable to the exhaustive reduction of primary ethers, thereby affording two molecules of the corresponding alkane at room temperature (Scheme 1, top). Reduction of secondary and even tertiary ethers stopped at the alcohol oxidation level under



Scheme 1. Catalytic reductive cleavage of ethers with **1**/Et_3SiH[2c] (left) and **2**/Et_3SiH[5a,b] (right).

equally mild reaction conditions, thus yielding one molecule of the alkane and one molecule of the less basic silyl ether (Scheme 1, bottom). Higher temperatures failed to drive these deoxygenations to completion.

The mechanism of both catalyst systems was extensively studied in the hydrosilylation of carbonyl compounds.[2b,e,3c,7] A closer look at the catalytic cycles reveals the parallels of the two, especially with respect to the mode of Si–H bond activation.[2b,7] Brookhart and co-workers were even able to prove spectroscopically as well as crystallographically that the Si–H bond coordinates to the iridium center of **1** to form an η^1 rather than an η^2-σ complex.[2b] Such direct evidence is still elusive for the $B(C_6F_5)_3$-catalyzed Si–H bond activation, but has been proposed by Rendler and Oestreich as part of their mechanistic elucidation of the crucial Si–H bond activation step in the Piers hydrosilylation[3a,c] of carbonyl groups.[7] The stereochemical course of the reaction at the silicon atom was shown, by using a silane with a stereogenic silicon atom, to proceed through inversion, which corresponds to an S_N2-Si mechanism and excludes an S_N1-Si-type hydride abstraction (Scheme 2).



Scheme 2. Si–H bond activation by **1** (left) and **2** (right).

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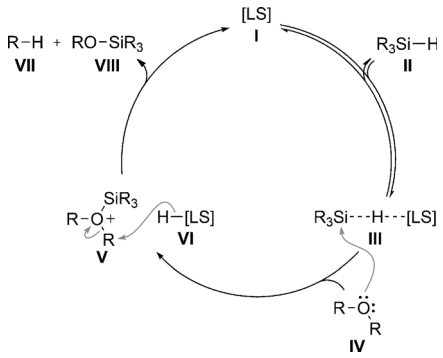
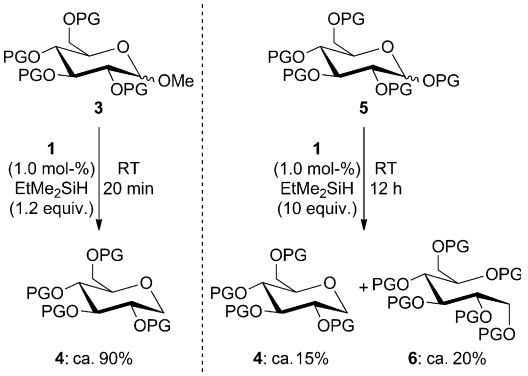
The mechanism of the Lewis acid-promoted reductive deoxygenations is believed to have the same general features as the reduction of carbonyl compounds. Brookhart and co-workers also elucidated the mechanism in full detail for the catalysis with **1**.[2c] Lewis acid **I** (either cationic **1** or neutral **2**) reversibly activates the Si–H bond of **II** to generate the η^1-σ complex **III**. The electrophilic silicon atom in **III** is then transferred to the ether oxygen atom in **IV**, thereby forming the oxonium ion **V** along with neutral (from **1**) or anionic (from **2**) hydride **VI**. Hydride transfer from **VI** to a carbon atom adjacent to the oxygen atom in **V** releases the alkane **VII** and the silyl ether **VIII** (Scheme 3).



Scheme 3. Unified catalytic cycle of the reductive ether cleavage with silanes using cationic iridium(III) complex **1**[2c] or neutral $B(C_6F_5)_3$ (**2**); LA = Lewis acid.

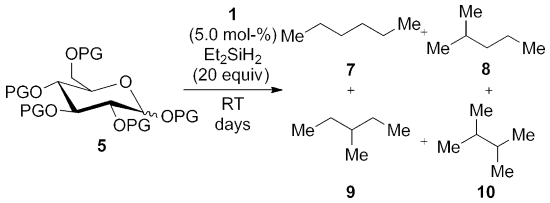
Despite the limitation of both catalyst systems to the full reduction of primary ethers, Gagné and co-workers were just recently able to advance this method further. These authors successfully applied Brookhart's catalyst **1** to the exhaustive reduction of silicon-protected glucose derivatives.[8] As expected, **1** catalyzed the cleavage of the OMe group in glucose **3** chemoselectively to afford **4** in high yield within minutes (Scheme 4, left). Compound **3** was used as a mix of α and β anomers, and competition experiments with substoichiometric amounts of silane revealed different reaction rates, with the equatorial anomer reacting almost exclusively.



Scheme 4. Reduction of protected glucose derivatives **3** and **5** catalyzed by **1** (PG = $EtMe_2Si$).

Remarkably, subjecting persilylated glucose **5** to the same reaction setup also resulted in the reductive cleavage of C–O bonds (Scheme 4, right). Conversion was still low at prolonged reaction times, even in the presence of excess silane, but this result by itself is noteworthy. Brookhart and co-workers had reported that secondary silyl ethers are not reduced further.[2c] Another surprise is the fact that the formation of **4** was accompanied by the formation of D-glucitol **6**.

The low chemoselectivity for the cleavage of the protected alcohol at the C-1 position is somewhat counterintuitive (**5**→**4** versus **5**→**6**), as an enhanced stability of the resulting oxocarbenium ion ought to favor exocyclic C–O bond scission (as seen exclusively for **3**→**4**). This unexpected finding prompted the authors to probe the exhaustive reduction of **5** (Scheme 5). Indeed, at a higher catalyst loading and with



Scheme 5. Exhaustive reduction of a persilylated glucose **5** (PG = $EtMe_2Si$).

a more reactive silane (Et_2SiH_2 versus $EtMe_2SiH$), deoxygenation proceeded to a mixture of fully reduced hexane derivatives with *n*-hexane (**7**), 2-methylpentane (**8**), 3-methylpentane (**9**), and 1,2-dimethylbutane (**10**) as the main components (all assigned by ^{13}C NMR spectroscopy through comparison with authentic samples). Moreover, in situ monitoring of the defunctionalization of protected glucose **3** was insightful. It was quickly transformed into **4** (Scheme 4, left) but, as the signal intensity of this C-1-deoxygenated intermediate decreases, no new distinct sets of signals were detected until the reaction had progressed to a late stage when the signals of the fully reduced hexanes began to appear. This is a strong indication that the defunctionalization does not proceed through one or two distinct intermediates, but a large number of different isomers. The reason for the branching is still unclear. However, a comparison of the deoxygenation of **4** and of a separately prepared sample of D-glucitol **6** showed that the reduction of the latter leads to the preferred formation of *n*-hexane (**7**), thus suggesting that the pyranose **4** stemming from either **3** or **5** is likely to initiate the branching.

The study by Gagné and co-workers is an excellent contribution to the fascinating field of defunctionalization chemistry.[9] One obvious question, however, remains unaddressed. A deoxygenation catalyzed by **1** starting from the free alcohol, namely, from unprotected glucose, would be ideal, but this aspect is only vaguely commented on in a footnote.[8] Dehydrogenative Si–O coupling catalyzed by **1** might be problematic because of the formation of dihydrogen followed by its oxidative addition to **1**.[10] $B(C_6F_5)_3$ (**2**) is superior in this case. Piers and co-workers reported such

coupling reactions for all types of alcohols (including diols) more than ten years ago,[3b] but would it work with polyols? One final comment should be made, there are now several transformations that are catalyzed by either Brookhart's cationic iridium(III) pincer complex **1**[2,8] or $B(C_6F_5)_3$ (**2**)[3–5,7] but a systematic comparison of the two catalysts is still rare. It might be about time to classify these and other Lewis acids that activate or are likely to activate Si–H bonds through η^1-σ coordination.

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[9] We note here that Brookhart and co-workers had already applied the **1**/Et_3SiH system at elevated temperatures to the fragmentation of poly(ethylene glycol) with success (cf. Scheme 1, left).[2c]

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