



Metal-Free Deoxygenation of Carbohydrates**

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Abstract: The conversion of readily available cellulosic biomass to valuable feedstocks and fuels is an attractive goal but a challenging transformation that requires the cleavage of multiple nonactivated C–O bonds. Herein, the Lewis acid tris(pentafluorophenyl)borane ($B(C_6F_5)_3$) is shown to catalyze the metal-free hydrosilylative reduction of monosaccharides and polysaccharides to give hydrocarbons with reduced oxygen content. The choice of the silane reductant influences the degree of deoxygenation, with diethylsilane effecting the complete reduction to produce hexanes while tertiary silanes give partially deoxygenated tetraol and triol products.

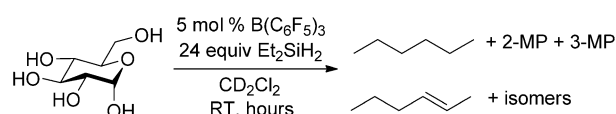
The ubiquity of petroleum-based materials in everyday products has driven a growing interest in developing renewable sources for important feedstocks and fuels.^[1] As many feedstocks and fuels are composed of hydrocarbons or partially oxygenated hydrocarbons, one natural source for their production might be cellulosic biomass, which is readily available but requires deoxygenation for further use,^[2] a need with significant inherent challenges.^[3]

We recently reported that the hydrosilylative reduction of glucose to a mixture of hexane isomers can be catalyzed by a (POCOP)IrH⁺ species ([{(POCOP)IrH(acetone)}]⁺[B(C₆F₅)₄][−], **1**; POCOP = 2,6-[PO(*t*Bu)₂]₂C₆H₃), with Et₂SiH₂ serving as the terminal hydride source.^[4] Reported herein are investigations showing that the commercially available Lewis acid tris(pentafluorophenyl)borane ($B(C_6F_5)_3$, **2**), a known catalyst for the hydrosilylative reduction of primary and secondary alcohols,^[5] also catalyzes the hydrosilylative reduction of carbohydrates (Scheme 1),^[6] and moreover that the reaction can be tuned to selectively deoxygenate glucose to value-added products.

When unprotected carbohydrates are utilized, the deoxygenation is preceded by an in situ conversion of the alcohols

to silyl ethers (with concomitant H₂ evolution). For this reason experiments to contrast the deoxygenation activity of catalysts **1** and **2** used sugars that were preprotected (Figure 1), while experiments to gauge the breadth of the substrate scope of **2** used unprotected sugars for convenience. ¹³C NMR analysis, which proved the most useful method for monitoring C–O bond cleavage, indicated that the metal-free borane-catalyzed reaction proceeds faster at the 5 mol% catalyst level than the iridium-catalyzed version at the same loading. For example, after one hour at room temperature, the $B(C_6F_5)_3$ -catalyzed deoxygenation of per-TMS-protected glucose (**TMS-3**) displayed exclusively deoxygenated products by ¹³C NMR spectroscopy, while oxygenates persisted in the iridium-catalyzed reaction (Figure 1).

In both cases, however, the reactions eventually proceeded to a point where all observable C–O bonds had been cleaved. Like the (POCOP)IrH⁺-catalyzed deoxygenation, the $B(C_6F_5)_3$ -catalyzed deoxygenation yields a product mixture that is dominated by hexane isomers, principally *n*-



Scheme 1. Example of $B(C_6F_5)_3$ -catalyzed hydrosilylative carbohydrate deoxygenation. 2-MP = 2-methylpentane, 3-MP = 3-methylpentane.

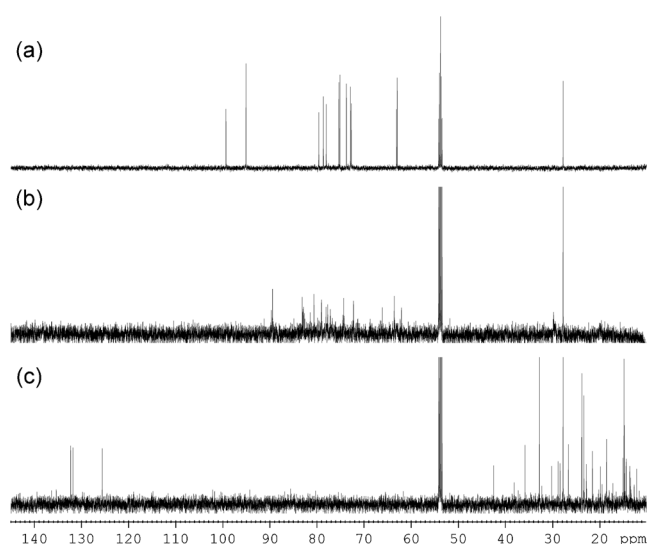


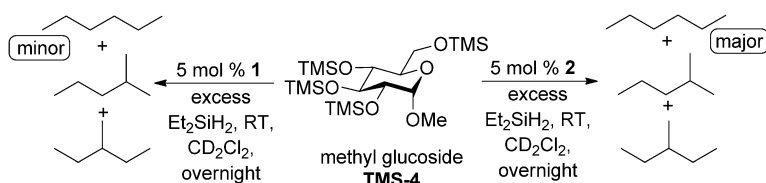
Figure 1. 150 MHz ¹³C{¹H} NMR spectra of a) **TMS-3** starting material with cyclooctane standard, b) reaction mixture from the hydrosilylative reduction of **TMS-3** catalyzed by 5 mol% **1** with 20 equiv of Et₂SiH₂ after 1 hour, c) reaction mixture from the hydrosilylative deoxygenation of **TMS-3** catalyzed by 5 mol% **2** with 20 equiv Et₂SiH₂ after 1 hour.

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[**] M.P.M. thanks the National Research Council for a postdoctoral fellowship, L.L.A. thanks the Progress Energy Foundation/UNC Institute for the Environment, M.R.G. thanks the Department of Energy (DE-FG02-05ER15630), and J.J.B. thanks the Army Research Office for funding.

Supporting information for this article is available on the WWW under <http://dx.doi.org/10.1002/ange.201306864>.



Scheme 2. Iridium- versus borane-catalyzed deoxygenation of **TMS-4**.

hexane, 2-methylpentane (2-MP), and 3-methylpentane (3-MP). The observation of 2-MP and 3-MP points to the likelihood of alkyl shifts and carbenium ions in the deoxygenation sequence.^[7]

While catalysts **1** and **2** were able to effect complete deoxygenation, the hydrocarbon product distribution was different in several cases. For example, the $B(C_6F_5)_3$ -catalyzed deoxygenation of **TMS-3** affords a significant quantity of hexene isomers in addition to the alkanes observed in the iridium-catalyzed hydrosilylation. Additionally, for TMS-protected methyl glucoside (**TMS-4**), the product distribution arising from the iridium-catalyzed reaction favored the alkyl-shifted 2-MP and 3-MP isomers,^[4] while the major deoxygenation product of **TMS-4** under $B(C_6F_5)_3$ catalysis was *n*-hexane (Scheme 2 and Figure S7 in the Supporting Information). The build-up of hexene isomers for **2** but not for **1** is also a point of differentiation (Figure 1). As recently discussed,^[6] studies by Brookhart et al. for **1**^[8] and by the Piers, McRae, and Gevorgyan groups for **2**^[5] indicate that there are numerous similarities and some differences between these two catalysts. The commercial availability of **2** and ease of handling were considered major benefits, prompting an exploration of its reactivity with a range of carbohydrates.

Employment of $B(C_6F_5)_3$ in combination with diethylsilane enabled the deoxygenation of a wide range of glycosidic substrates. While complete deoxygenation was observed by ^{13}C NMR spectroscopy in all cases, the relative yields of alkane and alkene products were dependent on the substrate, catalyst, and protecting group (Figure 2). The proportion of alkyl-shifted C6 products was greatest for 1-deoxyglucose (**5**)

and smallest for the ring-opened glucitol (**6**) (Figure 2).^[4] Intriguingly, the relative proportions of 2-MP and 3-MP were also substrate dependent, with 2-deoxyglucose providing a disproportionately high amount of 3-MP. In all cases, other C6 hydrocarbons including methylcyclopentane, cyclohexane, 2,2-dimethylbutane, and 2,3-dimethylbutane were either not observed or present in quantities too small to be reliably quantified by

NMR spectroscopy.

As noted above, the iridium catalyst **1** reacted to give little detectable elimination, whereas the borane catalyst **2** gave significant elimination (up to 20% overall yield). Spiking product mixtures with authentic samples revealed that alkenes observed in the ^{13}C NMR spectra of the $B(C_6F_5)_3$ -catalyzed reactions included *trans*-2-hexene > *trans*-3-hexene > *cis*-2-hexene, with *cis*-3-hexene not being observed in any appreciable quantity. Because the absolute yield of alkenes was small, not exceeding a sum of 25%, a correlation between the quantity of hexenes and experimental parameters was challenging.

A full accounting for the mass balance of the completely deoxygenated products was hampered both by the volatility of the products and the complexity of the mixture. Looking at only the aforementioned hexane and hexene isomers, a sum of the products consistently gave an estimated total yield between 60 and 90% for various sugar substrates, although the absolute yield of each hydrocarbon typically varied 5–10% between trials. This variability also characterized the product ratios in most of the runs.^[9] ^{13}C NMR spectra revealed the wide variety of species contributing to the total mass balance, and although several products including C2–C4 hydrocarbons were identified by GC–MS analysis, many remain unidentified. Additionally, while ^{19}F NMR spectroscopy revealed minor catalyst decomposition during the experiment, the addition of a second portion of carbohydrate and silane after the first portion had been fully consumed showed the second portion of carbohydrate to be reduced in good yield (80%). Catalysis also continued in the presence of

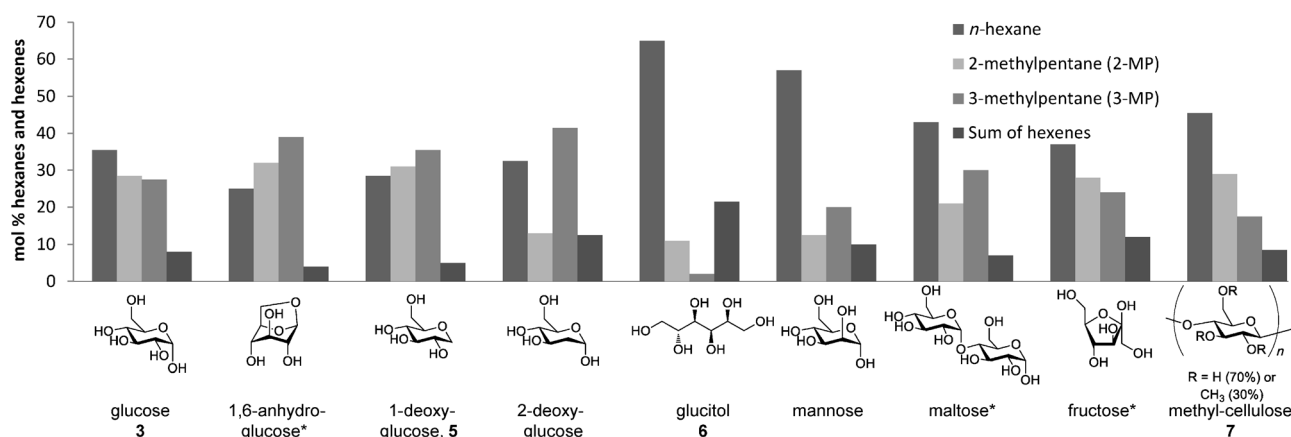
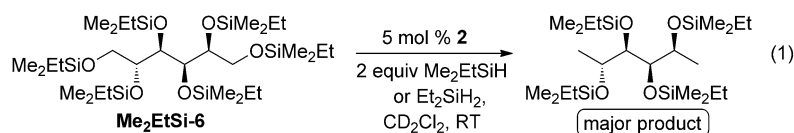


Figure 2. Hydrosilylative defunctionalization of representative carbohydrates. The proportions of each of the hexane and hexene products are reported as a percentage of the total. Alkane and alkene yields were determined by semiquantitative ^{13}C NMR spectroscopy, corroborated in select cases by GC analysis (see the Supporting Information for details and absolute yields). General reaction conditions: 5 mol % catalyst **2**, 24 equiv of Et_2SiH_2 , RT, 18 h. Data are the average of two trials, except where * denotes the result of one trial.

small amounts of added water (6 equiv relative to $B(C_6F_5)_3$), which was quickly hydrosilylated to provide dry reaction conditions, indicating that rigorous drying of catalyst, substrate, or solvent is not necessary. Polymethylhydrosiloxane, $(-(OSiMe(H))_n-)$, an inexpensive waste product of the silicone industry, also reduces carbohydrates under $B(C_6F_5)_3$ catalysis to give hexane and hexene isomers in 80% yield.^[10]

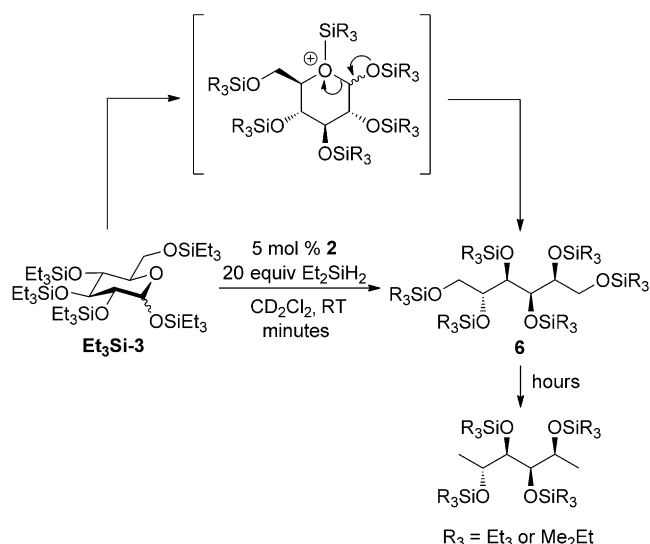
Reactions in chlorobenzene and methylene chloride both resulted in facile reduction of glucose and a good yield of the fully deoxygenated products in similar proportions. Although the reaction mixture appeared homogeneous when pentane was used as the solvent, the rate and yield of the reaction was dramatically reduced, perhaps speaking to the importance of generating reactive ion pairs during silane activation and/or oxygen abstraction. The rate and yield of the reaction were also reduced with the tertiary silane Me_2EtSiH , indicating a significant steric effect. This difference is evident in the reduction of Me_2EtSi -protected glucitol (**Me₂EtSi-6**) with Me_2EtSiH , which proceeds with only partial consumption of C–O bonds after 1 week [Eq. (1)]. Under these conditions it is evident that reduction of primary C–O bonds is kinetically favored, though other minor products are also observed. In



contrast, complete reduction of **Me₂EtSi-6** occurs with Et_2SiH_2 after only 2 h.

Under silane-limited conditions (1 equiv), we observed that Me_2EtSiH converted **Me₂EtSi-6** to 1,6-deoxyglucitol as the major product. On a preparative scale (0.8 mmol), treating unprotected **6** with 9 equiv of Me_2EtSiH in the presence of $B(C_6F_5)_3$ gave 1,6-deoxy glucitol in 70% yield (by in situ 1H NMR spectroscopy). The tetraol was isolated in 62% yield, with 2,3,4-hexanetriol (6:1 d.r., the product of one additional reduction) also contributing to the mass balance ($\approx 7\%$). With 2 equiv of Et_2SiH_2 , the product mixture was considerably more complex, but 1,6-deoxyglucitol was also identified as the major observed product by ^{13}C NMR spectroscopy ($> 50\%$, see Figure S11 in the Supporting Information). These data suggest that the reaction with Et_2SiH_2 may be inherently less selective or that the $O-SiEt_2(H)$ groups generated by silyl exchange may participate in further, presumably intramolecular, reductions. The selective reduction of primary over secondary C–O bonds parallels that observed for simple alcohols.^[5a,b]

Slowing the reaction further by using Et_3Si -protected glucose (**Et₃Si-3**) with Me_2EtSiH allowed us to observe the initial steps of the reaction for a ring-closed sugar. Curiously, the first step causes ring opening over the course of minutes to give spectroscopically identified glucitol (**6**) as the major product,^[11] and not reduction of the primary C₆ or anomeric C₁ positions. Ring opening was followed by a considerably slower (hours) reduction of the primary sites to give 1,6-



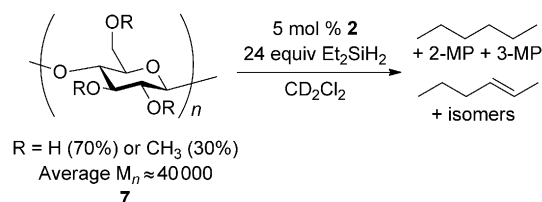
Scheme 3. **Et₃Si-3** is reduced first to glucitol (**6**) and then to 1,6-deoxy glucitol.

deoxyglucitol (Scheme 3).^[12] The preference for ring opening is likely the result of a comparatively increased Lewis basicity and steric accessibility of the pyranose oxygen.

Finally, the direct deoxygenation of cellulose has historically been limited by its low solubility and steric congestion, therefore often requiring pretreatment to separate the chains or cleave the glycosidic linkages before defunctionalization.^[13] Not surprisingly then, cellulose itself was completely insoluble and unreactive

under our conditions, even at elevated temperatures. Commercially available 30% methylated cellulose (**7**), however, was significantly more soluble. While displaying no apparent solubility in CH_2Cl_2 , this material is rapidly solubilized by the addition of $B(C_6F_5)_3$ and Et_2SiH_2 , which presumably silylates at least some of the unprotected hydroxy groups and allows for complete dissolution under reaction conditions. Although the degree of silyl versus methyl protection at the time of reduction is unknown, fully deoxygenated products are observable within 20 min (Scheme 4 and Figure 2), with yields reaching 80% after our 18 h assay. This suggests both that the method is exceptionally active and can consequently activate congested, minimally soluble substrates, and that the cellulose problem may be exclusively one of solubility.

In summary, we have demonstrated a new mild method for the metal-free deoxygenation of carbohydrates to give



Scheme 4. $B(C_6F_5)_3$ -catalyzed hydrosilylative deoxygenation of 30% methylcellulose (**7**). Major products observed by ^{13}C NMR spectroscopy.

mixtures of alkane and alkene hydrocarbons. The product distribution and rate of reduction are sensitive to substrate, solvent, silane, protecting group, and catalyst. This feature makes it possible to develop conditions for the selective deoxygenation of glucose to more valuable products like 1,6-deoxyglucitol. The mechanism of deoxygenation is currently under investigation.

Received: August 5, 2013

Published online: January 13, 2014

Keywords: biomass · carbohydrates · deoxygenation · hydrosilylation · renewable feedstocks

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