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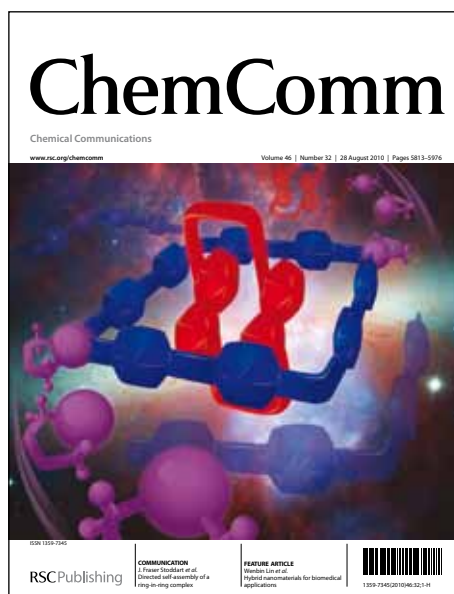
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Unprecedented Organocatalytic Reduction of Lignin Model Compounds to Phenols and Primary Alcohols Using Hydrosilanes†

Elias Feghali and Thibault Cantat*

The first metal–free reduction of lignin model compounds is described. Using inexpensive Et_3SiH, PMHS and TMDS hydrosilanes as reductants, α–O–4 and β–O–4 linkages are
10 **reduced to primary alcohols and phenols under mild conditions using $B(C_6F_5)_3$ as an efficient catalyst.**

While 98% of organic chemicals currently derive from fossil carbon feedstocks, the utilization of renewable carbon sources has been identified as one of the major challenges facing the
15 chemical industry for the next decades.[1] In this context, CO_2 and biomass are attractive alternatives to oil and gas, for the production of chemicals.[2] Yet, these renewable feedstocks have a lower carbon/oxygen ratio than petrochemicals and their reduction is therefore required to increase their energy
20 content and promote their deoxygenation.[3] In particular, lignin results from the radical polymerization of the *p*-coumaryl, coniferyl and sinapyl alcohols and the catalytic depolymerization of this complex biopolymer by reduction of the ether linkages would offer an attractive source of
25 aromatics (Figure 1).[4] The homogeneous catalytic reduction of biomass–based compounds is therefore attracting increased attention.[5] In this regard, hydrosilylation appears as an attractive alternative to hydrogenation strategies to achieve the selective reduction of the strong C–O ether bond under
30 mild reduction conditions. Indeed the slightly polar and weaker Si–H bond (bond dissociation energy (BDE) of 92 kcal/mol in SiH_4) is easier to activate than the strong non-polar H–H bond (BDE of 104 kcal/mol).[6] In fact, the Lewis acid $B(C_6F_5)_3$ is a potent catalyst for the reduction of carbonyl
35 derivatives, alcohols and ethers.[7,8] Nonetheless, the utilization of this methodology is mostly limited to organic chemistry

synthesis and its potential has not been explored for the reduction of poly–functional substrates such as lignin. Recently, the C–O bond cleavage in aryl–ether derivatives
40 relevant to lignin reductive depolymerization has been explored, using stoichiometric amounts of alkoxide salts. with Et_3SiH.[9] Herein, we report the first organocatalytic reduction of lignin model compounds. The methodology utilizes inexpensive hydrosilanes as reductants, with $B(C_6F_5)_3$
45 as the organic catalyst.

Although the exact structure of lignin depends on its origin, it is already recognized that ether functional groups represent about two-thirds of its linkages. Typically, hardwood lignin
50 contains 60% β–O–4 and 5–10% α–O–4 linkages, while 5–5', 4–O–5 and β–β groups represent the remaining linkages (Figure 1).[10] The reduction of benzylphenylether (**1**), a model for the α–O–4 linkage, was first undertaken, using Et_3SiH. Catalyst $B(C_6F_5)_3$ promotes the complete reduction of **1**
55 within 2 h, at 25 °C, with a low loading of 2 mol% and using 1 equiv. of Et_3SiH (Eq. 1). As expected from the seminal work of the Piers and Gevorgyan groups, the alkyl–O bond in **1** is selectively reduced while the aryl–O bond is left untouched, leading to the formation of phenoxysilane **2** and
60 toluene, in 60% yield.[7] Interestingly, under these electrophilic conditions, mono– and bis–benzylated phenoxysilanes (**3**) are formed in 40% yield, resulting from Friedel–Crafts like alkylation.[11] Noticeably, when a model of the β–O–4 linkage (**4**) is utilized, this methodology also allows a complete
65 reduction, with a very high selectivity. In fact, **4a** is reduced to phenylethane and **2** in 94% yield and the formation of Friedel–Crafts products is reduced significantly (6% **6a**) (Eq. 2). **4b**, a model for the coniferyl derivative of **4a**, is reduced similarly to phenylethane and silylated catechol **5b** in 94%
70 yield, the additional methoxy group being reduced to methane under the applied conditions (Eq. 2).
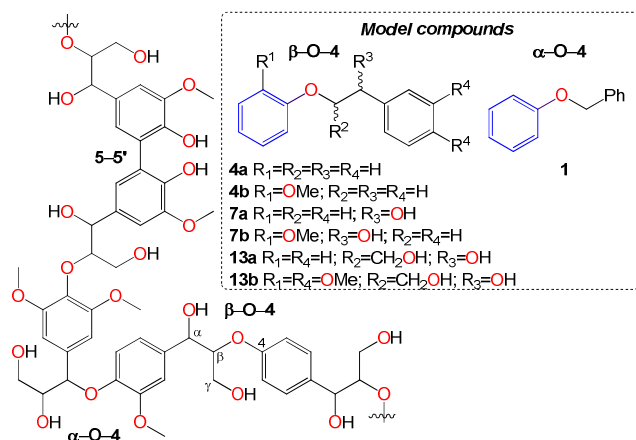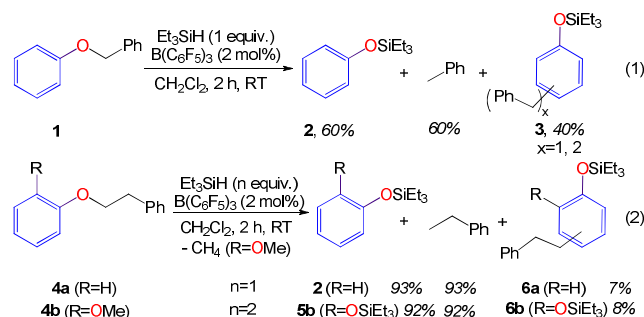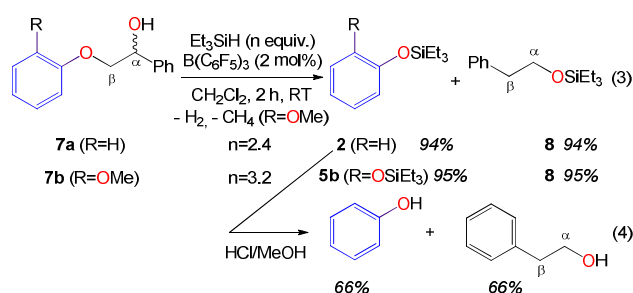

Fig. 1. Representative structure of a lignin fragment and molecular models of the α–O–4 and β–O–4 linkages utilized in this study.

Scheme 1. Proposed pathways for the reduction of **7a** to **2a** and **8**.

Though **4a** is a popular model for the β–O–4 linkage in lignin, it features a low degree of functionality which may not be fully representative of the outcome of the reaction. Moreover, the B(C$_6$F$_5$)$_3$ catalyzed hydrosilylation of ethers has been mostly limited to molecules with no additional functional groups. The reduction of model **7**, featuring an hydroxyl group at the α position, was therefore carried out, using Et$_3$SiH (3 equiv.) and 2 mol% B(C$_6$F$_5$)$_3$, at RT. The reduction of alcohols with the hydrosilane/B(C$_6$F$_5$)$_3$ system is well documented and occurs in conditions similar to ethers.[6] Nonetheless, while the ether linkage is cleaved in **7** to afford the phenoxysilane derivatives **5**, the hydroxyl function is maintained and **8** is obtained in >94% yield after 2 h at RT. Hydrolysis of **8** affords the corresponding phenol and 2-phenylethanol in 66% isolated yield (see ESI). While primary alcohols are generally more reactive than secondary alcohol, including in hydrosilylation chemistry, the selective formation of **8** from the polyfunctional substrate **7** is surprising.[7] Two pathways, depicted in Scheme 1, may account for this reaction chemistry. Both routes share a first dehydrogenative silylation of the O–H bond in **7a** to afford **9a**, which was observed experimentally (see ESI). Electrophilic activation of Et$_3$SiH by the borane catalyst, in the presence of **9a**, leads to the [**10a$^+$**,HB(C$_6$F$_5$)$_3$$^-$] ion pair.[12] Cation **10a$^+$** may either evolve to a cationic epoxide **11a$^+$** (route A) or undergo a semipinacol rearrangement (*via* **12a$^+$**, route B) prior to its reduction to **8a**. DFT calculations were carried out so as to examine the kinetics involved in each path (Figure 2). Interestingly, both kinetics and thermodynamics favor the semipinacol rearrangement, with an activation enthalpy of 14.2 kcal/mol (*vs* 18.2 kcal/mol for route A). Given the low activation energy difference between the two pathways, isotopic labeling studies were conducted. Reduction of **7a** with Et$_3$Si–D affords
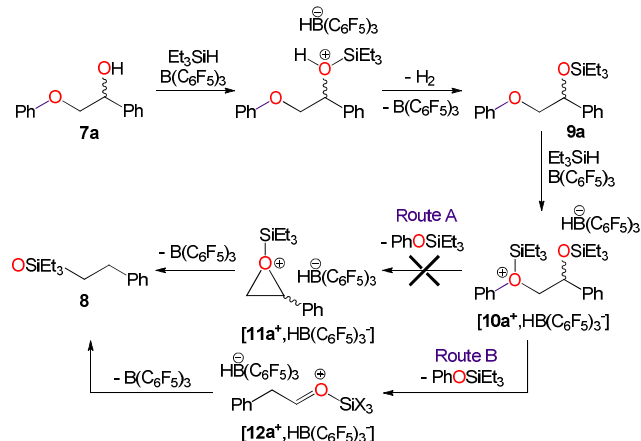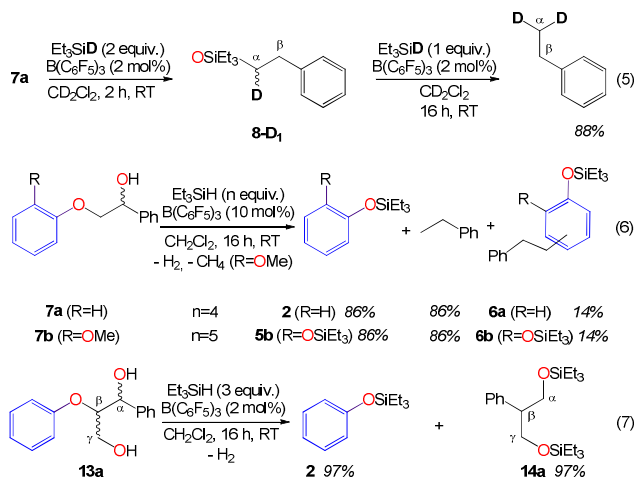
8-D$_1$ with a deuterium atom at the α position, therefore ruling out the involvement of **11a$^+$** in the rearrangement of **10a$^+$** (Eq. 5).

Importantly, complete reduction of **7** to phenylethane and **5** is feasible and achieved quantitatively in the presence of 10 mol% B(C$_6$F$_5$)$_3$ and an excess Et$_3$SiH (4 equiv.), after 16 h at RT (Eq. 6). This transformation shows that, a protected primary alcohol accumulates at short reaction times, from the hydrosilylation of **7**, which can be further deoxygenated after prolonged reaction times. The formation of a primary alcohol was also observed from the more realistic model molecule **13a**. Indeed, hydrosilylation of the α,γ–hydroxylated model **13a** with Et$_3$SiH provides the bis–silylated alcohol **14a** in quantitative yield after 16 h at RT (Eq. 7). Again, the formation of **14a** results from a semipinacol rearrangement, which was established through labeling studies (Eqs 8 and 9). The reduction of **13a–D$_2$**, featuring two deuterium atoms at the γ position, to **14a–D$_2$** shows that the phenyl ring migrates (Eq. 8), while the reduction of **13a** to **14a–D$_1$** with Et$_3$SiD confirms that the α position is the reduction site (Eq. 9). It is noteworthy that **14a** exhibits a low reactivity towards reduction and only small amounts of 1-phenylpropane (≈21%) were observed after 32 h at RT, in the presence of an excess Et$_3$SiH (8 equiv.) and 15 mol% B(C$_6$F$_5$)$_3$.

Polymethylhydrosiloxane (Me$_3$Si(OSiMeH)$_n$OSiMe$_3$, PMHS) and tetramethyldisiloxane (Me$_2$SiHOSiHMe$_2$, TMDS) are especially attractive reductants for further developments of this methodology. Indeed, these hydrosilanes are by–products of the silicone industry and are cost–efficient (2-5 € per
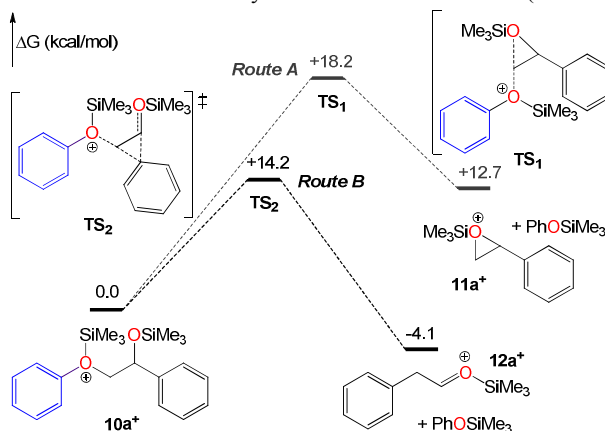

Figure 2. Computed pathways for the conversion of **10a$^+$** to **11a$^+$** and **12a$^+$**.

mole), non-toxic and moisture stable.[13] Additionally, the oxidation of TMDS provides a source of methicones, which are useful compounds in cosmetics.[14] Replacing Et_3SiH with PMHS or TMDS allows the complete reduction of **1**, **4a,b**,
[5] **7a,b** and **13a,b** (Eqs. 10-12 and S1-3 in the ESI). Importantly, TMDS is able to completely reduce **13a** to 1-phenylpropane (Eq. 12). In contrast, **14a** is obtained as the end-product with Et_3SiH (Eq. 7). This increased reactivity is attributed to the proximity of the two hydrides in TMDS, which facilitates the
[10] reduction of the C–O bonds. The catalytic activity of $B(C_6F_5)_3$ is maintained in the presence of water, as H_2O is readily dehydrogenated. In fact, Eq. 12 can be conducted successfully in the presence of water (10 mol%) with 16 equiv. TMDS to obtain **15a** in quantitative yield.
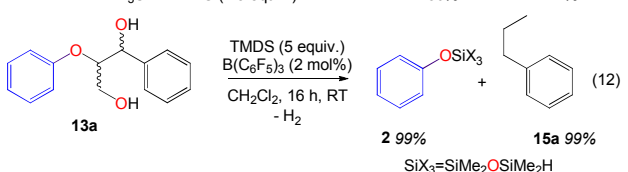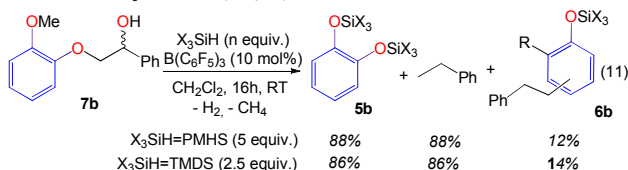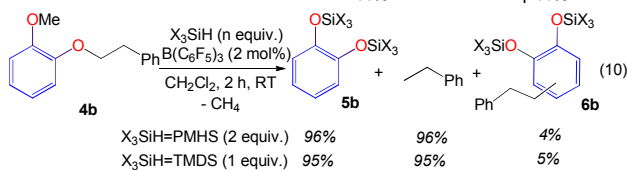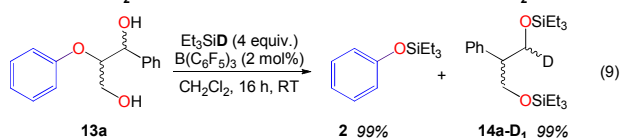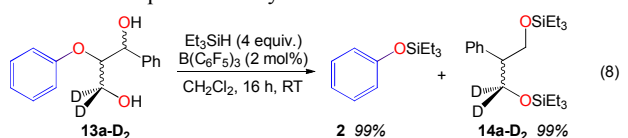
[15] In summary, we have reported the first organo–catalytic reduction of lignin model compounds. $B(C_6F_5)_3$ is a potent catalyst for the selective reduction of α–O–4 and β–O–4 linkages to phenol derivatives, *via* hydrosilylation. Active hydrosilanes include inexpensive and air stable PMHS and
[20] TMDS. Depending on the reductant, primary alcohols derivatives can be obtained selectively. Their formation is shown to involve a semipinacol rearrangement, based on DFT calculations and labeling studies. Further work will focus on extending this methodology to natural lignin.

[25] Acknowledgements

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Notes and references

CEA, IRAMIS, SIS2M, CNRS UMR 3299, CEA/Saclay, 91191 Gif-sur-Yvette, France. E-mail: thibault.cantat@cea.fr; Fax: +33 1 6908 6640; Tel: +33 1 6908 4338

[35] † Electronic supplementary information (ESI) available: General exprimental details, synthetic procedures and data for XXX, and computational details. For ESI see DOI: 10.1039/b000000x/

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GRAPHICAL ABSTRACT
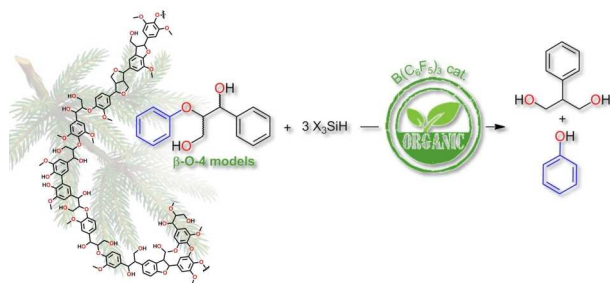
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