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

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The first metal–free reduction of lignin model compounds is described. Using inexpensive Et3SiH, PMHS and TMDS hydrosilanes as reductants, α–O–4 and β–O–4 linkages are reduced to primary alcohols and phenols under mild conditions using B(C6F5)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 chemical industry for the next decades.1 In this context, CO2 and biomass are attractive alternatives to oil and gas, for the production of chemicals.5 Yet, these renewable feedstocks have a lower carbon/oxygen ratio than petrochemicals and their reduction is therefore required to increase their energy content and promote their deoxygenation.1 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 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 mild reduction conditions. Indeed the slightly polar and weaker Si–H bond (bond dissociation energy (BDE) of 92 kcal/mol in SiH2) is easier to activate than the strong non-polar H–H bond (BDE of 104 kcal/mol).6 In fact, the Lewis acid B(C6F5)3 is a potent catalyst for the reduction of carbonyl 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 relevant to lignin reductive depolymerization has been explored, using stoichiometric amounts of alkoxide salts, with Et3SiH.9 Herein, we report the first organocatalytic reduction of lignin model compounds. The methodology utilizes inexpensive hydrosilanes as reductants, with B(C6F5)3 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 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 Et3SiH. Catalyst B(C6F5)3 promotes the complete reduction of 1 within 2 h, at 25 °C, with a low loading of 2 mol% and using 1 equiv. of Et3SiH (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 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 alklylation.11 Noticeably, when a model of the β–O–4 linkage (4) is utilized, this methodology also allows a complete 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% yield, the additional methoxy group being reduced to methane under the applied conditions (Eq. 2).

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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.
Nonetheless, while the ether linkage is cleaved in pathways, depicted in Scheme 1, may account for this reaction by the borane catalyst, in the presence of Hydrolysis of maintained and kinetics and thermodynamics favor the semipinacol kinetics involved in each path (Figure 2). Interestingly, both DFT calculations were carried out so as to examine the of including in hydrosilylation chemistry, the selective formation alcohols are generally more reactive than secondary alcohol, studies were conducted. Reduction of energy difference between the two pathways, isotopic labeling experimentally (see ESI). Electrophilic activation of Et\(_2\)SiH (3 equiv.) and 2 mol% B(C\(_2\)F\(_3\))\(_2\) at RT. The reduction of alcohols with the hydrosilane/B(C\(_2\)F\(_3\))\(_2\) system is well documented and occurs in conditions similar to ethers. Nonetheless, while the ether linkage is cleaved in 7 to afford the phenoxyisilane 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. 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 \([10a^+\text{HB}(C_2F_3)_2]^–\) 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\(_2\)F\(_3\))\(_2\) 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\(_2\)F\(_3\))\(_2\). Polyethyleneoxydisiloxane (Me\(_2\)Si(OSiMe\(_3\))\(_2\)OSiMe\(_2\)), PMHS) and tetramethyldisiloxane (Me\(_2\)SiO(SiMe\(_2\))\(_2\)), 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

![Scheme 1. Proposed pathways for the reduction of 7a to 2a and 8.](image)

![Figure 2. Computed pathways for the conversion of 10a\(^+\) to 11a\(^+\) and 12a\(^+\).](image)
proximity of the two hydrides in TMDS, which facilitates the
reduction of the C–O bonds. The catalytic activity of B(C₆F₃)₃ is
maintained in the presence of water, as H₂O 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.

In summary, we have reported the first organo–catalytic
reduction of lignin model compounds. B(C₆F₃)₃ is a potent
catalyst for the selective reduction of α–O–4 and β–O–4
linkages to phenol derivatives, via hydroisilylation. Active
hydroisilanes include inexpensive and air stable PMHS and
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.

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Notes and references

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