# On the Possibility of Conversion of Alcohols to Ketones and Aldehydes by Phosphinoboranes $R_2PBR'R''$: A Computational Study

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Hydrogenation, the addition of hydrogen to unsaturated organic compounds, is undoubtedly one of the most important reactions in synthetic organic chemistry. Reactions of molecular hydrogen with transition-metal complexes, metal-catalyzed $H_2$ additions,[1] and transfer hydrogenations, in which hydrogen gas is replaced by, for example, 2-propanol or formic acid,[2] are well-known and frequently employed. Although the cost and potential toxicity of transition-metal catalysts, and the waste disposal issue of stoichiometirc reductions by the main group hydrides are among significant concerns that could be addressed by metal-free catalytic systems, hydrogenations under metal-free conditions[3] have been considerably less studied.

The enormous interest in environmentally benign fuels, the potential of hydrogen storage materials,[4] and the importance of the use of molecular hydrogen in fundamental chemical transformations[5] and biological processes[6] intensified the research focused on metal-free systems. More recently, promising main group species, such as amino- and phosphinoboranes, were studied experimentally[7] and theoretically.[8] It has recently been shown[9] that the combination of bulky electron-rich phosphides and electron-deficient B-$(C_6F_5)_2$ fragments produces phosphinoboranes $R_2P=BR'_2$ (**1**) that can undergo addition of dihydrogen to afford phosphine-borane complexes $R_2HP-BHR'_2$ (**1′**).
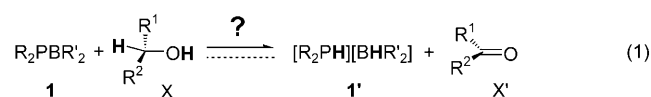
The uptake of $H_2$ by main-group species has potential to generate new types of hydrogen donors for metal-free hydrogenation. The uptake of hydrogen from a source other than gaseous $H_2$ is important in the context of the transfer hydrogenation. For these reasons, we initiated a theoretical study on the likelihood of the reaction of **1** with primary and secondary alcohols (Scheme 1). Herein, we suggest on
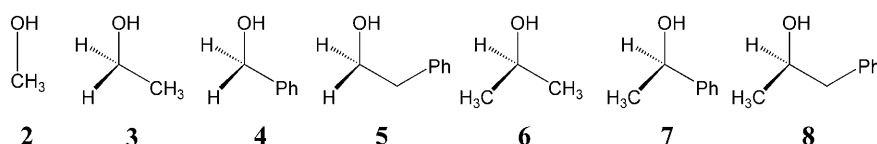


Scheme 1. Model substrates employed in theoretical study of the reaction given in Equation (1).

the basis of density functional calculations with the B3LYP and MPW1K density functionals[10] that such a reaction [Eq. (1)] is indeed quite plausible, affording phosphine-borate $(tBu)_2HP-BH(C_6F_5)_2$ (**1′**) and the corresponding carbonyl moieties. Furthermore, the reaction of **1** with methanol is predicted to afford formaldehyde (**2′**) in a reversible fashion. The potential of **1** as a metal-free mediator in hydrogenation of carbonyl moieties will be discussed further.



$$R_2PBR'_2 + H{-}\underset{R^2}{\overset{R^1}{\underset{X}{|}}}{-}OH \xrightarrow{\quad ? \quad} [R_2PH][BHR'_2] + \underset{R^2}{\overset{R^1}{|}}{=}O \qquad (1)$$

Computational optimization of **1** and **1′** with the B3LYP and MPW1K density functionals using the 6-31+G* basis set provided structures (see Figure S1 in the Supporting Information) in agreement with the crystallographic data.[9] Though bonds between B and P atoms are reproduced with some elongation for both **1** and **1′**, the difference between those is reproduced very accurately. The bond between B and P atoms in **1** compares fairly well with those seen experimentally for phosphinoboranes thought to contain a B=P bond.[11] Orbital population analysis carried out for **1** is con-

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sistent with the previously reported[9] significant localization of the HOMO, which is a B≡P π bonding orbital, on the phosphorus atom. The LUMO is the B≡P antibonding orbital, π*; the larger part of the electron density of which is localized on the B center with some involvement of two B-bound $(C_6F_5)_2$ groups (vide infra the discussion of the transition state for the uptake of $H_2$ by **1**).

Transition states for alcohol oxidation have been located for all substrates in Scheme 1 and all transition states were found to be concerted. Typical transition states of alcohol oxidation are shown in Figure 1; a detailed account of all
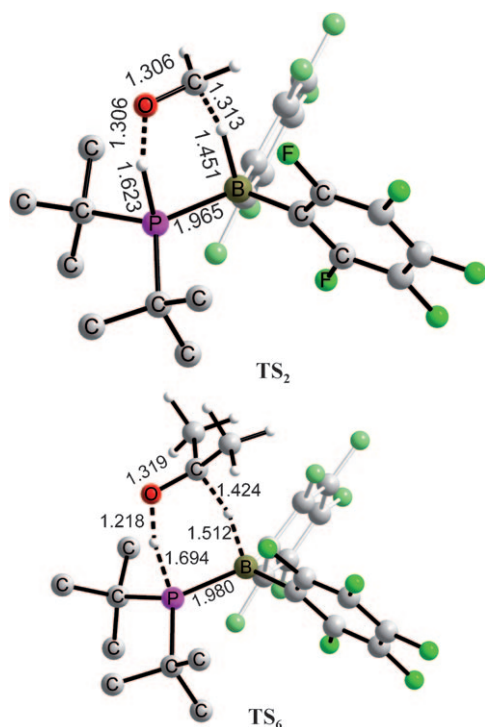


Figure 1. Typical transition states of alcohol oxidation ([Eq. (1)]) by **1**: **TS₂** and **TS₆** for methanol and 2-propanol, respectively; the B3LYP/6-31+G* level of theory. Hydrogen atoms of P-bound $t$Bu groups are omitted for clarity. All distances are in Å. Transition states for all other substrates (see Scheme 1) and all MPW1K computations of transition states and stationary complexes are reported in the Supporting Information.

transition states at the B3LYP and MPW1K levels of theory is given in the Supporting Information. According to the principle of microscopic reversibility, the concerted transition states $TS_x$ (Figure 1) are valid for the dehydrogenation of alcohols by complex **1** as well as for the reversed process of the hydrogenation of the corresponding ketone or aldehyde by **1′**.

Since the electron lone pair of the P atom is "trapped" by the Lewis acidity of the $(C_6F_5)_2$-coordinated B atom,[13] the dehydrogenation of alcohols by **1** is concerted: the proton transfer between the P and O atoms is synchronized with the hydride transfer between B and C atoms (Scheme 2A). The latter effectively displaces the phosphorus electron lone
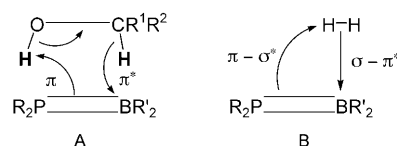


Scheme 2. A) The concerted mechanism of the hydrogenation/dehydrogenation reaction given in Equation (1). B) The mechanism of the $H_2$ activation by **1** according to the MO analysis of the reacting species and **TS2**.

pair. The same mechanism is valid for the $H_2$ uptake by **1** (Scheme 2B).

Key features of all presently located transition states for alcohol oxidation by **1** are as follows: 1) the C−O bond is longer than that in the oxidized product, but is shorter than the C−O bond in the starting substrate; 2) the B−P bond is longer than that in **1** but is shorter than the B−P bond in **1′**; 3) P−H and B−H bonds are elongated with respect to those in **1′**, whereas O−H and C−H bonds are elongated with respect to those in the starting material (see details in Table S1 in the Supporting Information). According to the molecular orbital (MO) analysis, the electron density of the C−H bond is donated to the B≡P π* antibonding orbital, whereas the P-based B≡P π binding orbital of **1** interacts with the LUMO of methanol, which has definitive O−H antibonding character; in this concerted process the B≡P bond transforms into a single bond with the synchronized creation of the C≡O bond (Scheme 2A).

It is instructive to compare the reaction in Equation (1) with the recently discovered[9] uptake of $H_2$ by **1** [Eq. (2)].

$$(t\text{Bu})_2P=B(C_6F_5) \ + \ H_2 \rightarrow (t\text{Bu})_2HP-BH(C_6F_5) \qquad (2)$$
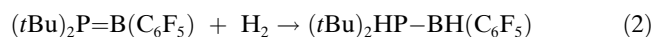
Though the DFT study of the potential surface of the $H_2$ uptake by **1** has already been carried out,[9] the geometry of the corresponding transition state has yet to be reported. For that reason, and to be able to draw comparison at the same level of theory, we have located the transition state for the activation of $H_2$ by **1** (Figure 2).
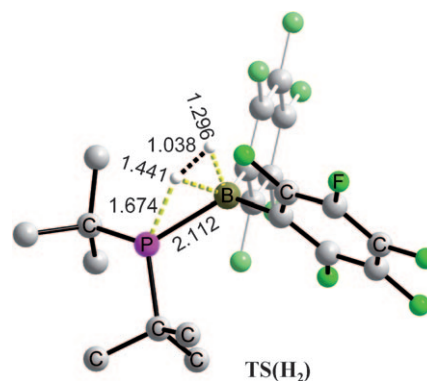


Figure 2. The transition state of the $H_2$ uptake by **1**. Hydrogen atoms of P-bound $t$Bu groups are omitted for clarity. All distances are in Å.

In the nonpolar solvent toluene, we have obtained a barrier of 27.6 kcal mol$^{-1}$ for **TS(H$_2$)** with respect to the total energy of the reacting species H$_2$ and **1**. This barrier is comparable to computationally predicted barriers for the oxidation of alcohols (vide infra Table 1). The exothermicity of the direct H$_2$ uptake by **1** is −31 kcal mol$^{-1}$. It is noteworthy that the transition state of the heterolytic H−H bond cleavage by the Lewis base–Lewis acid pair, [($t$Bu)$_3$P][B(C$_6$F$_5$)$_3$], lies about 10 kcal mol$^{-1}$ above the total energy of the reactants, and the reaction is highly exothermic ($\Delta E \approx -26$ kcal mol$^{-1}$).[8a]

The transition state structure **TS(H$_2$)** (Figure 2) reveals that 1) the P−H bond is about to be formed and one hydrogen atom is shared between the P and B centers; 2) the substantially elongated H−H bond, the H−H distance is about 1 Å, is almost parallel to the B−P bond; 3) the B−P bond itself is elongated with respect to those in **1** and **2**; 4) the H−H bond cleavage occurs in the vicinity of the B atom. The Hessian of the transition state has been used to determine the intrinsic reaction coordinate. The exploration of the potential surface along this reaction coordinate in the direction of the reacting species confirmed the previously reported[9] alignment of H−H and B−P bonds already at quite a large B−H distance of about 2.4 Å.

As already known in the heterolytic cleavage of the H−H bond by frustrated Lewis pairs,[7b] the dihydrogen acts as a mediator for the electron transfer between the P center (the Lewis base) and the B center (the Lewis acid). The electron transfer from the electron lone pair of the P atom to the empty σ*(H$_2$) orbital, and the electron transfer from the σ(H$_2$) orbital to the empty p orbital of B occur simultaneously.[8a] The boron's Lewis acidity attracts the phosphorus electron lone pair in **1**. The MO analysis of **TS(H$_2$)** and the reacting species shows that the H$_2$−(B−P) interaction is B-centered to displace the electron lone pair of the P atom and to optimize the orbital overlap for σ(H$_2$)→π*(1) and σ*(H$_2$)→π(1) concerted electron donations.

To test a simpler system, we have located the analogue of **TS(H$_2$)** for the simplified complex (CH$_3$)$_2$P=B(CF$_3$)$_2$ (**9**).[11] The transition state is shown in Figure S6 in the Supporting Information. The barrier for the H$_2$ uptake by **9** is 17 kcal mol$^{-1}$ in the gas phase and about 20 kcal mol$^{-1}$ in toluene. This is an important indication that at least from the theoretical perspective analogues of **1** may prove to be useful for applications requiring H$_2$ uptake.

An interesting question is what the thermodynamics of the hydrogenation reactions [Eq. (1)] are (herein, all energies are computed with the B3LYP and MPW1K functionals using the 6-31++G** basis set). The potential energy profiles of the reactions in Equation (1) are summarized in the Table 1 for a series of alcohols (Scheme 1); all relative energies are calculated with respect to a weakly bound adduct of reactants, for example, complex **1** and an alcohol).

It turns out that the barrier for the dehydrogenation of alcohols by **1** is comparable to the potential energy barrier of H$_2$ uptake by **1**. However the direct H$_2$ uptake is computed to be much more exothermic. Both the barrier and the exo-

Table 1. Oxidation reactions ([Eq. (1)]) in toluene for all substrates from Scheme 1, entries 1–7, and the uptake of dihydrogen, entry 8. MPW1K data are in square brackets. Primary alcohols, entries 1–4, are highlighted in italic. All energies are in kcal mol$^{-1}$.

| Entry | Hydrogen source | Barrier [kcal mol$^{-1}$] | $\Delta E$ [kcal mol$^{-1}$] |
|---|---|---|---|
| 1 | *2* | 29 [24] | −2 [−5] |
| 2 | *3* | 26 [27] | −11 [−10] |
| 3 | *4* | 27 [28] | −16 [−14] |
| 4 | *5* | 29 [27] | −10 [−9] |
| 5 | 6 | 19 [15] | −15 [−20] |
| 6 | 7 | 28 [29] | −18 [−17] |
| 7 | 8 | 30 [33] | −15 [−14] |
| 8 | H$_2$ | 28 [25] | −31 [−36] |

thermicity of the reaction increases slightly with the increase of the polarity of the solvent: solvent corrections are about −1.8 kcal mol$^{-1}$ in toluene and about −3.1 kcal mol$^{-1}$ in dichloromethane.

DFT calculations firmly suggest that the reaction of **1** with primary and secondary alcohols should be occurring, though it most certainly requires elevated temperatures to be efficient. It is most noteworthy that the dehydrogenation of methanol by **1** should be reversible at elevated temperatures: it is only slightly exothermic in toluene (Table 1, entry 1) at the B3LYP level of theory, though the MPW1K calculations predict a somewhat larger exothermicity for this reaction. The reaction of **1** with the simplest secondary alcohol **6**, which has been previously employed as a hydrogen source in metal-catalyzed transfer hydrogenations,[2] should also be possible, but the process is unlikely to be reversible even at elevated temperatures. However, it is noteworthy that the oxidation of 2-propanol by **1** has the lowest potential energy barrier both for the B3LYP and MPW1K density functional calculations. Oxidation of ethanol (**3**) and 2-phenyl-1-ethanol (**5**) is predicted to be moderately exothermic.

Remarkably, the energy barriers for the two different hydrogen uptake reactions involving complex **1** ([Eq. (1)] and [Eq. (2)]) are very similar, suggesting that all of them are more efficient at elevated temperatures. However, the exothermicity of these reactions is very different. While the oxidation of methanol to formaldehyde by **1** is only slightly exothermic and reasonably reversible, oxidation of more complex alcohols is more exothermic and probably much less reversible. The direct H$_2$ uptake by **1** is very exothermic and irreversible even under significantly elevated temperatures.

Combining Equations (1) and (2), we suggest the catalytic process that converts formaldehyde to methanol under elevated temperatures and with the appropriately high concentration of H$_2$ in the solution. From the mechanistic standpoint, the direct bonding between B and P atoms in **1′** allows the concerted reduction of the C=O double bond in formaldehyde by the {PH$^+$, BH$^-$} couple. The exothermicity of the H$_2$ uptake and the high barrier, **TS(H$_2$)**, guarantees the irreversibility of the hydrogen-related part of the cycle. The generalization of the proposed process is shown in Scheme 3.

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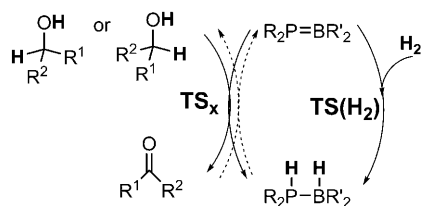


Scheme 3. Illustration of the plausible coupling/competition between irreversible uptake of $H_2$ by $R_2P=BR'R''$ complex oxidation of alcohols, including a plausible hydrogenation of a carbonyl moiety by a $[R_2PH]$-$[BHR'R'']$ complex.

It is noteworthy that the process proposed in Scheme 3 could in principle provide the possibility for the stereospecific hydride addition to an aldehyde, where the stereospecificity is achieved by means of specifically designed steric interactions between C-bound $R^2$ and $R^1$ groups of an aldehyde and unequivalent B-bound groups R' and R'' of **1**. While positive experimental and theoretical verification of our hypothesis of reversible reaction of **1** with alcohols might not be trivial and considering that **1'** does not favor the reversed reaction [Eq. (1)] for computationally tested carbonyl moieties listed in Scheme 1, other than formaldehyde, similar phosphinoboranes with less steric congestion of the P and B centers might exhibit desirable reactivity. It also becomes apparent that tuning and matching of the Lewis acidity of the B-center and the Lewis basicity of a partner-center might be a key for achieving the reversed reaction.

In conclusion, the work considers the reactivity of recently discovered phosphinoborane complexes. For the first time, we address the likelihood of the dehydrogenation of primary and secondary alcohols by $(tBu)_2PB(C_6F_5)_2$, and the hydrogenation of carbonyl moieties by $(tBu)_2HP-BH(C_6F_5)_2$ by means of density functional calculations. The comparison of the MPW1K- and B3LYP-based data reveals good agreement between these two computational methods. 1) Based on detailed characterization of transition states and intermediates, we have found that the proposed hydrogenation/dehydrogenation is certainly plausible at least in the case of simple acceptors, such as formaldehyde and possibly acetone, though it certainly requires elevated temperatures to be efficient. We predict that the process is concerted. 2) We have found that this hydrogenation/dehydrogenation reaction is nearly thermoneutral and therefore reversible under elevated temperatures in the case of formaldehyde/methanol; this leads us to hypothesize that $R_2PBR'R''$ complexes could in theory act as metal-free catalysts for racemization of alcohols. 3) We have also characterized the transition state and the thermodynamics of the irreversible uptake of $H_2$ by $(tBu)_2PB(C_6F_5)_2$. 4) We have found that oxidation of more complex primary alcohols, such as ethanol and 2-phenyl-1-ethanol, is only moderately exothermic, but still is most likely not easily reversible within the present design of the B=P complex **1**. 5) Finally, we envision a plausible mechanism for the hydrogenation of aldehydes and possibly ketones that combines irreversible uptake of $H_2$ by $R_2PBR'R''$

and the equilibration reaction of $R_2PBR'R''$ and $[R_2PH]$-$[HBR'R'']$ with alcohols and aldehydes/ketones, respectively.

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[10] Brief computational details: Gas-phase geometry optimizations of all intermediates and transition states were performed by using the

B3LYP and MPW1K functionals with the split-valence double-zeta basis set, 6-31+G*, augmented with diffuse and polarization functions. All transition states were characterized by one single imaginary vibrational frequency along the proper reaction coordinate; intrinsic reaction coordinate scans were employed for the exploration of the potential surfaces. The larger basis set 6-31++G** was used to obtain final electronic energies and Gibbs free energies of all complexes employing geometries obtained at the 6-31+G* base set level. See details in the Supporting Information.

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[12] Solvent effects are accounted for within the self-consistent reaction field model (PCM), see details in the Supporting information.

[13] The difference in the behavior of the phosphorus electron lone pair in **1** and in $R_2P(C_6F_4)B(C_6F_5)_2$ (**3′**) is immediately noticeable since unlike **3′** complex **1** does not form distinctive $P-H_{(O)}$ bonds with an alcohol, see details in the Supporting Information.