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# Hydroxylic Solvents as Hydrogen Atom Donors in Radical Reactions

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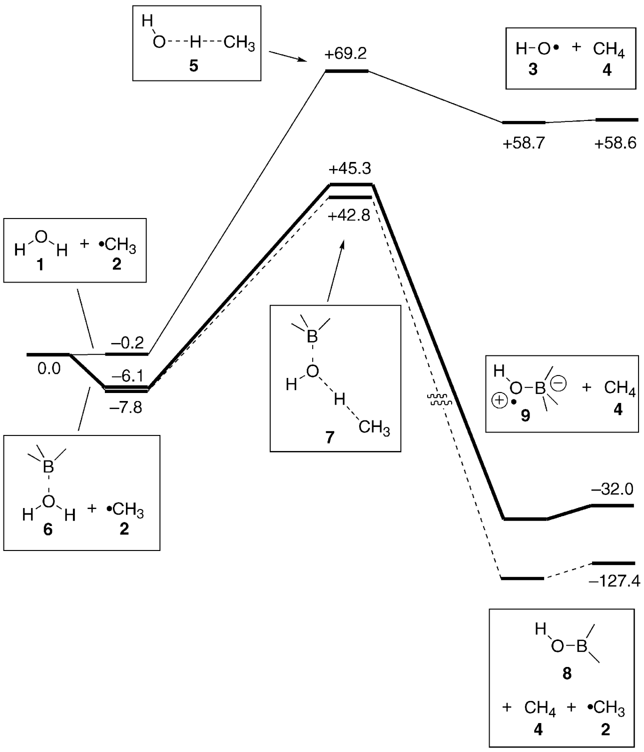
Hydrogen-transfer reactions between methyl radicals and protic solvents, such as water and ethanol, have been studied at the G3(MP2)-RAD level of theory. The typically high barriers for hydrogen abstraction from the OH group are lowered dramatically on complexation of protic solvents with $BMe_3$. The barrier lowering is found to be a consequence of the unique properties of trialkylboranes, acting as Lewis acids towards the closed-shell solvent, but as electron donors towards the evolving oxygen-centered radicals.

## Introduction

Synthetically, environmentally, or biologically important radical reactions often proceed through chain mechanisms. Among the key steps in these chain processes are reactions between radicals and hydrogen-atom donors. In synthetically important reactions this involves the use of thiols, tin hydrides or silanes as the source of hydrogen, while anitoxidant vitamins such as α-tocopherol assume this role in biological systems.[1–6] Water or protic solvents, such as alcohols, are usually not considered to be competitive hydrogen-atom donors due to the high homolytic H–O bond energy.[7] Various groups have recently reported that coordination of hydroxy groups to a Lewis acid (LA) leads to a dramatic change in the kinetic and thermodynamic aspects of the homolytic H–O bond dissociation process,[8–11] turning even water (**1**) into a good hydrogen-atom source. In order to identify the origin of this effect and to explore the generality of this concept, we are studying here the reaction of methyl radical (**2**) with hydroxylic solvents in the absence and the presence of Lewis acids.

## Results and Discussion

The reaction of water (**1**) with methyl radical (**2**) to yield hydroxyl radical (**3**) and methane (**4**) represents the smallest possible model system in which this effect can be explored. This reaction is endothermic by $\Delta H_{298}$ = 58.6 kJ mol$^{-1}$ as calculated at the G3(MP2)-RAD level of theory, in good agreement with the experimental value of $\Delta H_{298}$ = 57.6 kJ mol$^{-1}$ (Scheme 1).[12] The transition state **5** for this process is located 69.2 kJ mol$^{-1}$ above the separate reactants. Reaction of radical **2** with water–trimethylborane complex **6**, in contrast, proceeds through transition state **7** to yield $HOBMe_2$ (**8**), methane (**4**) and a new methyl radical (**2**) in a single step. The overall reaction is now exothermic



Scheme 1. Reaction pathways for hydrogen abstraction from water (**1**) (solid line) and water–borane complex **6** (dashed line) by methyl radical (**2**). Results obtained with frozen B–C bond lengths are indicated by a grey line. Enthalpies (in kJ mol$^{-1}$) obtained at the G3(MP2)-RAD level of theory are given relative to the separate reactants.

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by $-127.4\ \mathrm{kJ\,mol^{-1}}$ and faces a barrier of $+42.8\ \mathrm{kJ\,mol^{-1}}$. After accounting for differences in the strength of the substrate complexes, the borane-induced barrier lowering thus amounts to $19\ \mathrm{kJ\,mol^{-1}}$.

One key component of the barrier lowering mechanism is certainly the dramatic change in the reaction enthalpy of $-186\ \mathrm{kJ\,mol^{-1}}$, which is very close to the value of $-180\ \mathrm{kJ\,mol^{-1}}$ obtained recently by Wiberg et al. at the G3 level of theory.[8] The generation of a new methyl radical through cleavage of one of the C–B bonds is also essential for the propagation of synthetically useful radical-chain mechanisms. However, inspection of the transition-state structure **7** indicates that cleavage of the C–B bond has hardly begun at the stage of hydrogen transfer to radical **2** (1.649 Å in transition state **7** vs. 1.607 Å in reactant complex **5**; Figure 1), implying that the barrier lowering may be due to more than just the combination of two bond-cleavage processes. This interpretation is also supported by the results of calculations, in which the C–B bond lengths have been frozen at the values of reactant complex **6** (grey line in Scheme 1). The reaction barrier is hardly affected by this constraint ($+42.8$ vs. $+45.3\ \mathrm{kJ\,mol^{-1}}$), while the reaction enthalpy is now significantly less favourable at $-32.0\ \mathrm{kJ\,mol^{-1}}$. Analysis of the spin and charge distribution in the system lacking $BMe_3$ is in full accord with the known electrophilic nature of the OH radical. The partial charge of $-0.47$ e of the OH fragment in water is reduced to $-0.26$ e in transition state **5** and eventually becomes neutral in the hydroxyl radical **3** at the end of the reaction sequence. Complexation of water by the Lewis acid $BMe_3$ exacerbates the problem, reducing the partial charge of the OH fragment in complex **6** to $-0.33$ e. However, on proceeding along the reaction pathway, the $BMe_3$ Lewis acid transforms itself from an electron acceptor to an effective electron donor, leading to partial charges of the OH fragment in transition state **7** of $-0.22$ e and in product **8** of $-0.38$ e. The actual electron donor in this system is one of the borane methyl groups reducing its partial charge from $-0.32$ e in the reactant complex to practically zero at the end of the reaction. This argument can be recast into an molecular orbital picture involving the $\sigma$(B–C) bond as the donor and the SOMO of the reacting O···H···C frament as the acceptor.

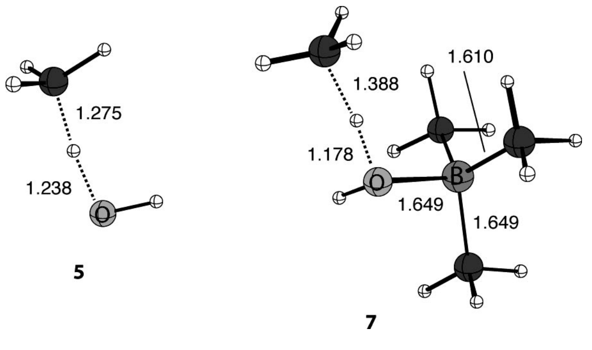


Figure 1. Structures of transition states **5** and **7** [UB3LYP/6-31G(d)].

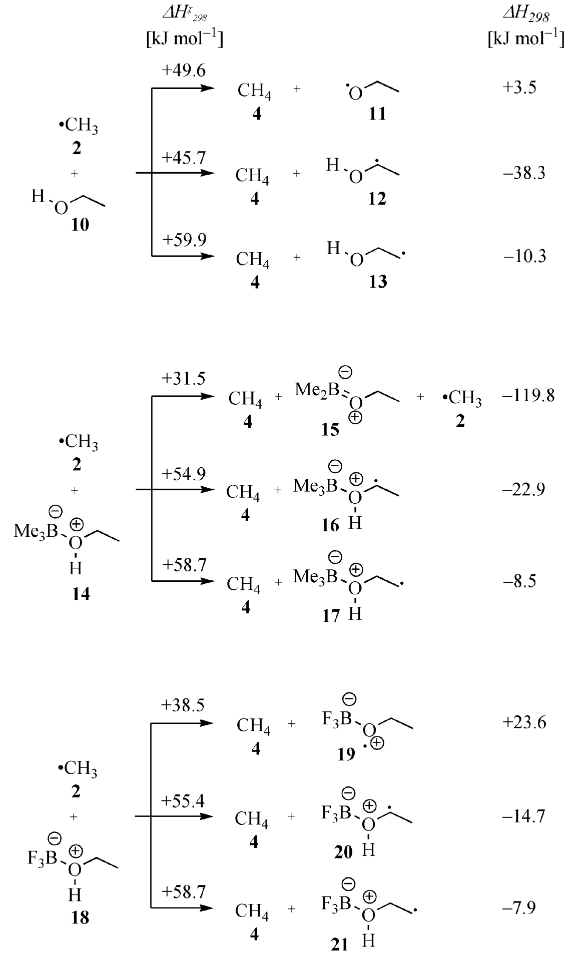
It has recently been shown by Newcomb et al. that hydrogen abstraction from borane–water complex **6** competes with hydrogen abstraction from free trimethylborane under experimental conditions.[11] The barrier calculated for hydrogen abstraction from trimethylborane is indeed very similar to that for hydrogen abstraction from borane–water complex **6** ($+43.4$ vs. $+42.8\ \mathrm{kJ\,mol^{-1}}$, Table 1). However, the former reaction is much less exothermic than the latter ($-34.7$ vs. $-127.4\ \mathrm{kJ\,mol^{-1}}$). Both of these processes will be subject to solvation effects under experimental conditions. Hydrogen abstraction from the methyl groups of free trimethylborane will most strongly be affected by association of the borane to a solvent or reactant molecule. Hydrogen abstraction from the methyl groups of borane–water complex **6**, which may be considered to be a realistic model for this situation, faces a significantly higher barrier than hydrogen abstraction from free borane ($+43.4$ vs. $+51.2\ \mathrm{kJ\,mol^{-1}}$), implying a detrimental solvent effect for this process. Hydrogen abstraction from the water molecule in complex **6** will most strongly be affected by coordination of the reacting water with a second water molecule. The reaction barrier calculated for hydrogen abstraction from the complex of trimethylborane with the water dimer is higher than that for complex **6** ($+46.0$ vs. $+42.8\ \mathrm{kJ\,mol^{-1}}$), but the solvent effect is smaller than that calculated for hydrogen abstraction from the borane alkyl groups. In assessing the relevance of these barrier heights for the reaction under experimental conditions it is important to recognize that the formation of borane–water complex **6** from its constituents is only weakly exothermic at $-10.5\ \mathrm{kJ\,mol^{-1}}$, while complexation of **6** with a second water molecule (formation of the borane–water dimer complex) is exothermic at $-32.40\ \mathrm{kJ\,mol^{-1}}$. Whether hydrogen abstraction occurs from borane–water complex **6** or from higher aggregates will thus be a matter of experimental design.

Table 1. Activation enthalpies ($\Delta H^{\neq}{}_{298}$) and reaction enthalpies ($\Delta H_{298}$) at 298.15 K for the reaction of $CH_3^{\cdot}$ with combinations of water and trimethylborane as calculated at the G3(MP2)-RAD level of theory (in $\mathrm{kJ\,mol^{-1}}$).

| Reactants | Products | $\Delta H^{\neq}{}_{298}$[a] | $\Delta H_{298}$[a] |
|---|---|---|---|
| $CH_3\cdot + H_2O$ | $CH_4 + HO\cdot$ | $+69.2$ | $+58.6$ |
| $CH_3\cdot + H_2OBMe_3$ | $CH_4 + HOBMe_2 + CH_3\cdot$ | $+42.8$ | $-127.4$ |
| $CH_3\cdot + H_2OBMe_3$ | $CH_4 + \cdot O(H)BMe_3$[b] | $+45.3$[b] | $-38.7$[b] |
| $CH_3\cdot + BMe_3$ | $CH_4 + BMe_2CH_2\cdot$ | $+43.4$ | $-34.7$ |
| $CH_3\cdot + H_2OBMe_3$ | $CH_4 + H_2OBMe_2CH_2\cdot$ | $+51.2$ | $-27.8$ |
| $CH_3\cdot + (H_2O)_2BMe_3$ | $CH_4 + (H_2O)HOBMe_2 + CH_3\cdot$ | $+46.0$ | $-109.4$ |

[a] With respect to separate reactants. [b] C–B distances constrained to those in reactant complex **6**.

If the barrier lowering for the homolytic H–O abstraction process is indeed connected to the effective stabilization of an emerging oxygen-centered radical through resonance and charge-transfer effects, it must be expected that the use of aliphatic alcohols instead of water leads to further reduction of the reaction barrier. This hypothesis was tested using ethanol (**10**) as the substrate, again in reaction with methyl radical (**2**). This system also offers the possibility to compare O–H and C–H abstraction processes within the same system. The reaction enthalpies for these transformations are given in Scheme 2. Product radical **12** is predicted to be most stable, followed by **13** and **11** based on the respective experimental heats of formation (with $\Delta H_{298,\mathrm{rel}}$ = 0.0, +28.2, and +43.3 kJ mol$^{-1}$).[12] This is in agreement with the observation that the gas-phase reaction of methyl radicals with ethanol leads to the exclusive formation of radical **12**.[18] Our evaluation of relative stabilities at the G3(MP2)-RAD level gives $\Delta H_{298,\mathrm{rel}}$ = 0.0, +28.0, and +41.8 kJ mol$^{-1}$, in close agreement with the experimental values.[19] The reaction barriers for these three pathways are not quite in line with reaction thermodynamics in that formation of **11** and **12** face almost identical barriers (+49.6 vs. +45.7 kJ mol$^{-1}$), while the barrier for formation of **13** is somewhat higher at +59.9 kJ mol$^{-1}$. Complexation of ethanol with $BMe_3$ as the Lewis acid couples the O–H abstraction process to B–Me cleavage in much the same way as was found for water before. Both bond-cleavage processes fall into a single kinetic step, the barrier of which is lower than that of the uncomplexed alcohol **10** by 18.1 kJ mol$^{-1}$ and with a reaction enthalpy of –119.8 kJ mol$^{-1}$.



Scheme 2. Hydrogen-transfer reactions between methyl radical (**2**) and ethanol (**10**) in the absence and the presence of Lewis acids ($BMe_3$, $BF_3$). Activation enthalpies $\Delta H^{\neq}_{298}$ and reaction enthalpies $\Delta H_{298}$ have been calculated at the G3(MP2)-RAD level (in kJ mol$^{-1}$).

Comparing these results to those obtained for borane–water complex **6**, we note that the reaction barrier is significantly lower for ethanol complex **14**, despite the fact that the reaction energies are slightly less favourable. The dramatic effect on both barrier and reaction enthalpy for O–H abstraction contrasts with comparatively minor effects on both C–H abstraction pathways. The barrier for hydrogen abstraction from C1 is raised through complexation with $BMe_3$ from +45.7 to +54.9 kJ mol$^{-1}$, while hydrogen abstraction from the C2 position is hardly affected at all (+59.9 vs. +58.7 kJ mol$^{-1}$). Can the barriers be further lowered using a stronger Lewis acid such as $BF_3$? This question was explored using the reaction of methyl radical (**2**) with ethanol–$BF_3$ complex **18**. Hydrogen abstraction from the OH group still proceeds through a lower barrier than in uncomplexed ethanol (+38.5 to +49.6 kJ mol$^{-1}$). The reaction is now, however, significantly endothermic at +23.6 kJ mol$^{-1}$ and does not produce a product radical suitable for chain propagation. Hydrogen abstraction from the C1 and C2 positions in complex **18** face similar barriers to those in complex **14**, indicating only a minor influence of the Lewis acid on these two pathways.

## Conclusions

The results obtained here underline the large potential of alcohol–borane complexes as potent hydrogen atom donors in radical reactions. Reaction barriers appear to be lowest when electron-rich alcohols are used in weakly coordinating solvents together with trialkylboranes as Lewis acids. The alkyl groups contained in the latter are integral parts of the barrier-lowering mechanism and highly critical for chain propagation.

## Computational Details

Geometry optimizations of ground and transition states have been performed at the UB3LYP/6-31G(d) basis set. Thermochemical corrections to 298.15 K have been calculated at the same level of theory using the rigid rotor/harmonic oscillator model. A scaling factor of 0.9806 has been used for this latter part. Relative enthalpies are obtained using the G3(MP2)-RAD(p) scheme proposed by Radom et al. This level of theory has recently been used to assess the stability of a wide variety of radicals.[7,20–22] All enthalpies cited in the text have been obtained at this level of theory, if not mentioned otherwise. The URCCSD(T)/6-31G(d)//B3LYP/6-31G(d) single-point calculations required for this latter method have been performed with MOLPRO,[23] all other calculations have been performed with Gaussian 03.[24]

**Supporting Information** (see footnote on the first page of this article): Structures and energies of all stationary points described in this paper.

## Acknowledgments

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