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Quantum Chemical Modeling of Chiral Catalysis. Part 13. On the Role of Borane *O*-Adducts in the Enantioselective Reduction of Ketones Catalyzed by Chiral Oxazaborolidines

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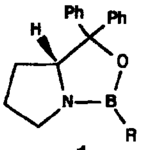
Abstract: - Plausible reactions of Lewis bases (ketones and ethers) with borane *O*-adducts of chiral oxazaborolidines used as catalysts in the enantioselective reduction of ketones were investigated by means of *ab initio* MO methods. Properties of the *O*-adducts were found to be different from those of the corresponding *N*-adducts. The *O*-adducts were not able to form complexes with ketones and ethers similar to those of the corresponding *N*-adducts proposed to be essential for the performance of oxazaborolidines as chiral catalysts in the enantioselective reduction of ketones.

INTRODUCTION

Chiral oxazaborolidines **1** are known to induce highly enantioselective catalytic reduction of ketones in the presence of Lewis acidic borane derivatives able to donate a hydride (CBS reduction). The history, present results and most important applications of 1,3,2-oxazaborolidines in enantioselective syntheses have been recently summarized in two review articles.[1]



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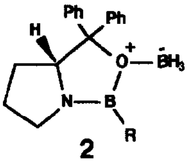


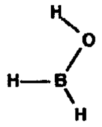
2

Although **1** has been found to react with borane to form an *N*-adduct[2] one may not be able to generalize the *N*-adducts to be the exclusive products formed as oxazaborolidines react with borane. Theoretically also formation of borane *O*-adducts **2** could be possible (a mixture of *N*- and *O*-adducts of which the latter could be present in small amounts). The role of analogs of **2** in formation of the minor enantiomer in the oxazaborolidine catalyzed reduction of ketones has been considered lately.[3] Although another pathway was predicted[3] to be more probably responsible for the formation of the minor enantiomer it can be difficult to confirm experimentally whether **2** would play any role in this catalytic process as the *O*-adduct **2** could be present in much smaller amounts in mixtures of borane and **1** than the corresponding *N*-adduct. However, as methods of theoretical chemistry do not suffer from this limitation they can be used for studies on properties of **2**.

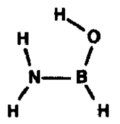
As the key steps of the mechanism of this catalytic enantioselective reduction based on the formation of borane *N*-adducts of **1** has been studied by means of molecular orbital calculations[4-6] it could be useful to determine whether the same mechanistic steps would be possible also in the case of the corresponding borane *O*-adducts (**2**). Relative stabilities of several plausible isomeric borane - oxazaborolidine complexes including one model of 2 have been recently estimated by means of computational methods.[6] The aim of this work was to study adducts of ethers (THF is the most common solvent used in these reductions)[1] and ketones to 2.

MODELS AND COMPUTATIONAL METHODS

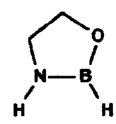
Modeling techniques similar to those applied in the case of previous studies of this series[4d] were employed. The following simple systems were used as models: **1'a**, **1'b** and **1'c** as models of **1**; **2'a**, **2'b** and **2'c** as models of **2**; **3'a**, **3'b** and **3'c** as models of complexes of ethers with **2** (water as a model of ethers), and **4'a**, **4'b** and **4'c** as models of complexes of ketones with **2** (formaldehyde as a model of ketones).



1'a

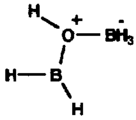


1'b

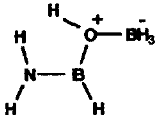


1'c

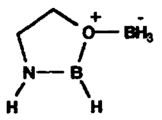
Standard *ab initio* MO calculations (RHF) were carried out by using the Gaussian 80 series of programs at the 3-21G, 4-31G, 6-31G, 4-31G* and 6-31G* levels.[7] Properties of the models **1'a-c** and **2'c** have been discussed in the literature.[4-6] No other calculations on the structures **2'a-b**, **3'a-c** or **4'a-c** appeared to have been published whereas the corresponding analogs of *N*-adducts have been characterized by using *ab initio* MO methods.[4-6]



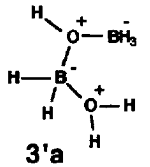
2'a



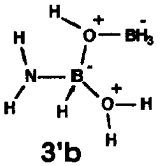
2'b



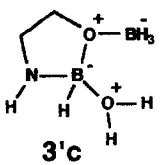
2'c



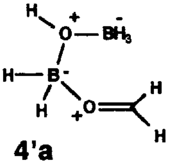
3'a



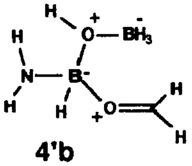
3'b



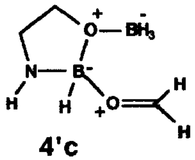
3'c



4'a



4'b



4'c

RESULTS AND DISCUSSION

Total energies and dipole moments calculated are summarized in Table 1. Energies of the formation of borane *O*-adducts **2'a-c** are shown in Table 2. Energies of the formation of water and formaldehyde complexes of these adducts are summarized in Table 3. Optimized structures of **3'a** and **4'a** (6-31G*//6-31G*) are shown in Figure 1 and those of **3'b** and **4'b** in Figure 2. Optimized structures of **3'c** and **4'c** (6-31G//6-31G) are shown in Figure 3.

Table 1. Total energies (E)[a] and dipole moments (D)[b] of the models 1'a-c, 2'a-c, 3'a-c and 4'a-c.

Structure	3-21G//3-21G		4-31G//4-31G		6-31G//6-31G		4-31G*//4-31G*		6-31G*//6-31G*	
	E[a]	D[b]	E	D	E	D	E	D	E	D
1'a	-100.76196	1.91	-101.17676	1.87	-101.27793	1.89	-101.22430	1.68	-101.32139	1.68
1'b	-155.55682	3.27	-156.19671	3.20	-156.35434	3.23	-156.25862	2.95	-156.40862	2.96
1'c	-232.01452	3.16	-232.95883	3.18	-233.19703	3.21	-233.07225	2.65	-233.29859	2.67
2'a	-127.02612	4.54	-127.54312	4.20	-127.67012	4.10	-127.59608	3.47	-127.71858	3.46
2'b	-181.82768	6.85	-182.56735	6.25	-182.75061	6.22	-182.63419	5.90	-182.80935	5.78
2'c	-258.28934	7.17	-259.33435	6.74	-259.59810	6.67	-259.45063	6.22	-259.70225	6.13
3'a	-202.66122	4.64	-203.47917	4.63	-203.68060	4.57	-203.55227	4.30	-203.74458	4.27
3'b	-257.43902	5.56	-258.48675	4.77	-258.74624	4.51	-258.58156	4.41	-258.82786	4.33
3'c	-333.90160	6.07	-335.25615	5.04	-335.59591	4.26	-335.39942	4.85	-335.72260	4.67
4'a	-240.27986	5.16	-241.25358	4.72	-241.49447	4.60	-241.36510	5.07	-241.59536	5.00
4'b	-295.06123	5.41	-296.26702	4.34	-296.56575	4.07	-296.39705	4.06	-296.68102	3.92
4'c	-371.52496	4.74	-373.03640	3.88	-373.41526	3.84	-	-	-	-
$H_3B{\cdot}OH_2$	-101.86336	5.28	-102.28057	4.92	-102.38267	4.86	-102.31848	4.28	-102.41525	4.26
$H_2C{=}O$	-113.22182	2.66	-113.69261	3.02	-113.80836	3.04	-113.75706	2.64	-113.86633	2.67
H_2O	-75.58596	2.39	-75.90864	2.49	-75.98536	2.51	-75.93900	2.18	-76.01075	2.20
H_3B	-26.23730	0.00	-26.34927	0.00	-26.37679	0.00	-26.36322	0.00	-26.39000	0.00

[a] Total energies given in hartrees. [b] Dipole moments given in debyes.

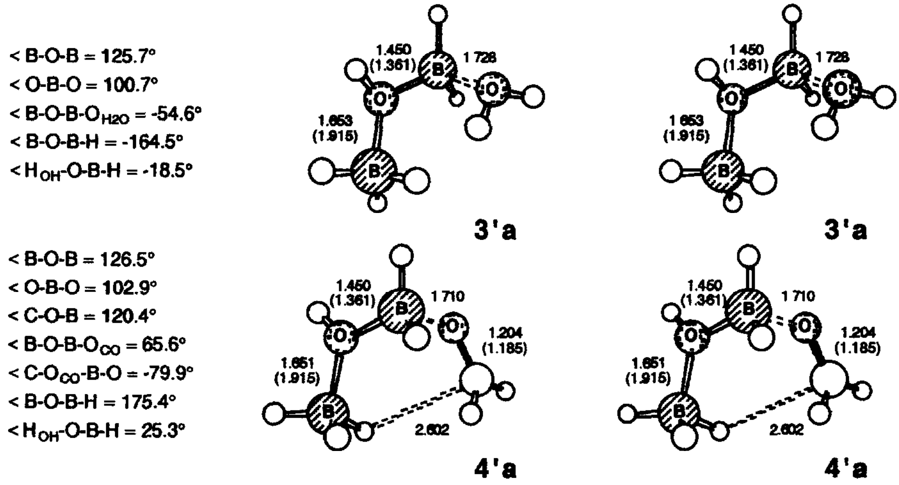


Figure 1. Stereo representations of the optimized (6-31G*//6-31G*) structures of adducts **3'a** and **4'a**. Some of the most important bond lengths [in Å] and bond angles [in degrees] are shown. The corresponding bond lengths of **2'a** (and formaldehyde in the case of **4'a**) are shown in parentheses.

As already observed[6] in the case of formation of **2'c** also the borane transfer from oxygen of the solvent (water as a model of the solvent) to the oxygen of **1'a-b** appears to require energy (Table 2). Energies of the formation of *O*-adducts are not highly positive but the difference between the energies of formation of *N*- and

O-adducts appears to be more significant [e.g. the energy of formation of **2'c** was calculated to be +2 kJ mol^{-1} (6-31G*//6-31G*) whereas the difference of the energy of formation of **2'c** and that of the corresponding borane *N*-adduct (-17 kJ mol^{-1}) was 19 kJ mol^{-1}, Table 2]. These results, together with those of earlier works,[6] clearly indicate formation of borane *N*-adducts to be favored over that of the corresponding *O*-adducts.

$< B\text{-}O\text{-}B = 129.8°$
$< O\text{-}B\text{-}O = 82.6°$
$< B\text{-}O\text{-}B\text{-}O_{H2O} = -74.2°$
$< H_{OH}\text{-}O\text{-}B\text{-}N = -7.8°$
$< H\text{-}B\text{-}N\text{-}H = -8.0°$
$< B\text{-}O_{OH}\text{-}B\text{-}N = -174.4°$
$< O_{H2O}\text{-}B\text{-}N = 102.5°$
$< O_{OH}\text{-}B\text{-}N = 120.4°$

$< B\text{-}O\text{-}B = 129.9°$
$< O\text{-}B\text{-}O = 86.7°$
$< C\text{-}O\text{-}B = 112.0°$
$< B\text{-}O\text{-}B\text{-}O_{CO} = 89.7°$
$< H_{OH}\text{-}O\text{-}B\text{-}N = 9.2°$
$< H\text{-}B\text{-}N\text{-}H = 7.3°$
$< B\text{-}O_{OH}\text{-}B\text{-}N = -171.7°$
$< C_{CO}\text{-}O\text{-}B\text{-}O = -75.7°$
$< O_{CO}\text{-}B\text{-}N = 99.0°$
$< O_{OH}\text{-}B\text{-}N = 121.0°$

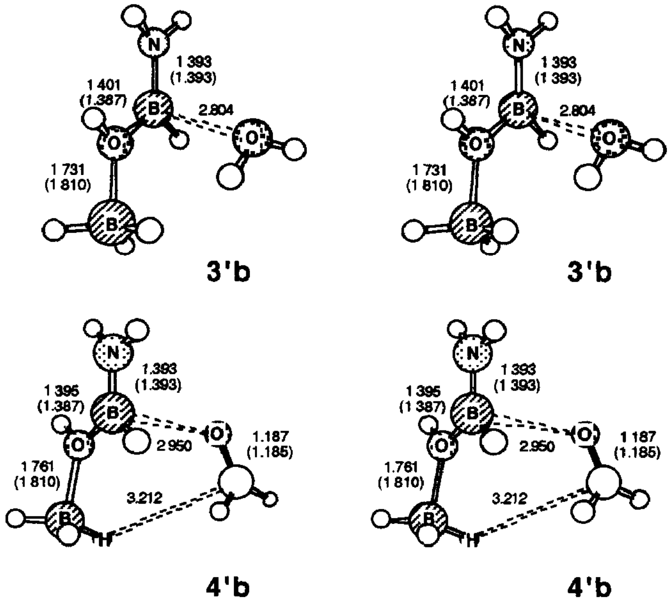


Figure 2. Stereo representations of the optimized (6-31G*//6-31G*) structures of adducts **3'b** and **4'b**. Some of the most important bond lengths [in Å] and bond angles [in degrees] are shown. The corresponding bond lengths of **2'b** (and formaldehyde in the case of **4'b**) are shown in parentheses.

Table 2. Energies of the formation (ΔE)[a,b] of borane *O*-adducts **2'a-c**.[c]

Reaction	$\Delta E^{a,d}$				
	3-21G	4-31G	6-31G	4-31G*	6-31G*
1'a + $H_3B{\bullet}OH_2$ -> 2'a + H_2O	+35	+15	+13	+20	+19
1'b + $H_3B{\bullet}OH_2$ -> 2'b + H_2O	+15 (+36)	+4 (+25)	+3 (+24)	+10 (-1)	+10 (-2)
1'c + $H_3B{\bullet}OH_2$ -> 2'c + H_2O	+7 (+21)	-9 (+10)	-10 (+10)	+3 (-14)	+2 (-17) [e]

[a] Energies given in kJ mol^{-1} [b] $H_3B{\bullet}OH_2$ used as a model of $H_3B{\bullet}THF$. [c] Energies of the formation of the corresponding borane *N*-adducts are shown in parentheses (from. ref. 4c). [e] From. ref 6

Although the formation of borane *O*-adducts was found to be less advantageous than that of the corresponding *N*-adducts (Table 2) energies of the formation of water and formaldehyde complexes of the *O*-adducts[8] are not much different from those of the corresponding *N*-adducts (Table 3). However, inspection of the optimized structures of **3'b** / **4'b** (Figure 2) and **3'c** / **4'c** (Figure 3), charges and HOMO and LUMO energies of the borane adducts shown in the Scheme reveals that the borane *O*-adducts **2'b** and **2'c** cannot form, in contrast to the corresponding borane *N*-adducts,[4,5c-d] tightly bound complexes with water or formaldehyde and that the formaldehyde cannot be activated in the same way as in the corresponding complexes of borane *N*-

adducts[4,5c-d]). This conclusion is supported by the following five observations:

1) Distances between the acidic boron of the borane *O*-adduct moiety and the basic oxygen of water / formaldehyde are too long in all **3'b-c** and **4'b-c** (longer that 2.8 Å, Figures 2 and 3) to represent any significant chemical binding (the distances are also much longer than those found in the corresponding water[4c] / formaldehyde[4,5c-d] complexes of borane *N*-adducts).
2) Changes of lengths of the B_{ring}-O and B_{ring}-N bonds are much less significant in the case of the formation of water / formaldehyde complexes **3'b-c** and **4'b-c** than those observed in the case of formation of related *N*-adducts[4,5c-d] [e.g. as the complex **3'c** forms the B_{ring}-N bond shortens only by 0.004 Å and the B_{ring}-O bond lengthens by 0.008 Å (on the basis of 6-31G//6-31G, Figure 3; the corresponding changes are 0.005 and 0.009 Å at the 6-31G* level, respectively); the analogous reaction of the corresponding borane *N*-adduct lengthens the B_{ring}-N and B_{ring}-O bonds by 0.083 and 0.064 Å (on the basis of 6-31G//6-31; at the 6-31G* level the corresponding changes are 0.079 and 0.059 Å[4c]].
3) The lowest unoccupied molecular orbitals (LUMO) of *O*-adducts **2'b-c** reside higher in energy than those of the corresponding *N*-adducts [e.g. E(LUMO) of **2'c** is 0.58 eV higher than that of the corresponding *N*-adduct (6-31G*//6-31G*), the Scheme]. This implies borane *O*-adducts to be weaker Lewis acids than the corresponding *N*-adducts.
4) The ring boron of borane *O*-adducts is less positive than that of the corresponding *N*-adducts [e.g. the charge of B_{ring} of **2'c** is 0.024 lower than that of the corresponding *N*-adduct (6-31G*//6-31G*), the Scheme]. This implies borane *O*-adducts to be weaker Lewis acids than the corresponding *N*-adducts.
5) The resonance B-N <-> $B^-=N^+$ inactivating B_{ring} (**A** and **A'**, the Scheme) remains intact as *O*-adducts of oxazaborolidines form [e.g. in the case of the formation of **2'c** the B_{ring}-N bond shortens only by 0.009 Å (6-31G//6-31G, Figure 3, ref. 4a)] whereas in the formation of the corresponding borane *N*-adducts the resonance **A** disappears lengthening the B_{ring}-N bond substantially [e.g. by 0.085 Å in the case of the borane *N*-adduct of **1'c** (6-31G*//6-31G*)[4a]] and shortening also the B_{ring}-O bond [e.g. by 0.029 Å in the case of the borane *N*-adduct of **1'c** (6-31G*//6-31G*),[4a] compare the resonance **B** (the Scheme)].

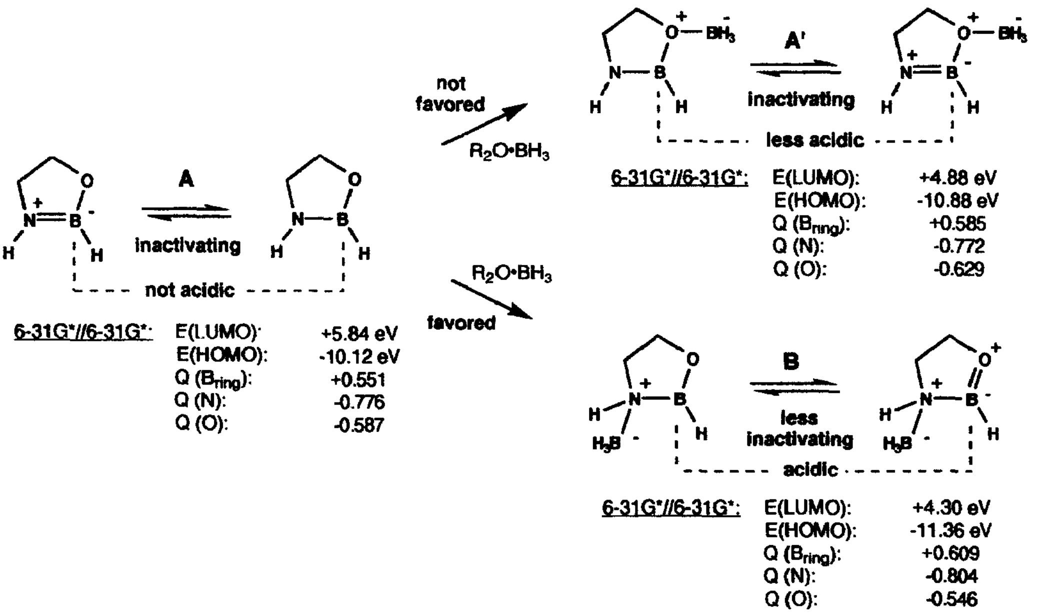
These five observations indicate B_{ring} of borane *O*-adducts of oxazaborolidines to be clearly less Lewis acidic than B_{ring} of the corresponding borane *N*-adducts. The ability of borane *O*-adducts of oxazaborolidines to bind Lewis bases appears to be low. In this respect borane *O*-adducts resemble clearly more the parent oxazaborolidines[4c] than the corresponding borane *N*-adducts.

Table 3. Energies (ΔE)[a] of the coordination of water[b] and formaldehyde[c] to borane, hydroxyborane and the borane adducts **2'a-c**.[d]

	3-21G	4-31G	6-31G	4-31G*	6-31G*
Reaction			$\Delta E^{a,e}$		
2'a + H_2O -> 3'a	-129 (-134)	-72 (-72)	-66 (-65)	-45 (-66)	-40 (-60) [f]
2'b + H_2O -> 3'b	-67 (-110)	-28 (-57)	-27 (-52)	-22 (-38)	-20 (-34) [g]
2'c + H_2O -> 3'c	-69 (-107)	-35 (-50)	-33 (-45)	-26 (-25)	-25 (-20) [g]
H_3B + H_2O -> $H_3B{\cdot}OH_2$	-105	-60	-54	-43	-38
$HO\text{-}BH_2$ + H_2O -> $HO\text{-}BH_2{\cdot}OH_2$	-54	-22	-19	-12	-10
2'a + $H_2C{=}O$ -> 4'a	-84 (-75)	-47 (-33)	-42 (-40)	-31 (-37)	-27 (-33) [f]
2'b + $H_2C{=}O$ -> 4'b	-31 (-39)	-19 (-3)	-18 (-3)	-15 (+4)	-14 (+8) [g]
2'c + $H_2C{=}O$ -> 4'c	-36 (-38)	-25 (-3)	-23 (+1)	-	- [g]
H_3B + $H_2C{=}O$ -> $H_3B{\cdot}O{=}CH_2$	-71	-41	-36	-34	-31
$H_3B\text{-}OH$ + $H_2C{=}O$ -> $HO\text{-}BH_2{\cdot}O{=}CH_2$	-28	-18	-16	-13	-12

[a] Energies given in kJ mol^{-1}. [b] Water used as a model of Lewis basic solvents. [c] Formaldehyde used as a model of ketones. [d] See Table 1. [e] Values of the corresponding reactions of the related *N*-adducts are shown in parentheses (ref. 4c). [f] Borane *N*-adduct of aminoborane as a Lewis acid (ref. 4c). [g] See ref. 8.

Scheme



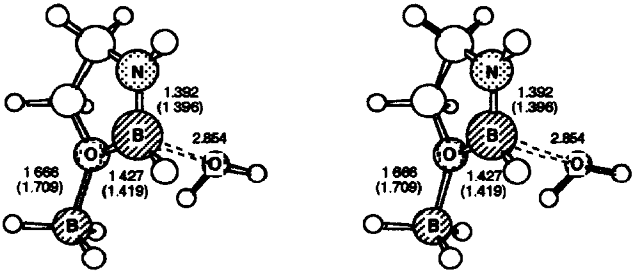
Merits of the inspection of structural features, charges HOMO and HOMO energies and resonance effects discussed above could be assessed further in the light of inspection of related properties of **2'a**. As the chemical behaviour of **2'a** appears to be different from that of **2'b** or **2'c** in that **2'a** can bind tightly both water and formaldehyde (formation of **3'a** and **4'a**, Figure 1) it is possible to make five observations, analogous to those described above, also in the case of **2'a**, **3'a** and **4'a**, as follows:

1) Binding between the acidic boron of the borane *O*-adduct moiety and the basic oxygen of water / formaldehyde is tight in the complexes **3'a** and **4'a** (lengths of the $B\text{-}O_{H_2O}$ and $B\text{-}O_{H_2CO}$ bonds are 1.728 Å and 1.710 Å , on the basis of 6-31G*//6-31G*, Figure 1). These values are rather close to those of the corresponding water and formaldehyde complexes of borane *N*-adducts (1.643 Å and 1.606 Å).[4c]
2) Changes of lengths of the B-O and C=O bonds of the hydroxyborane and formaldehyde moieties are significant in the case of the formation of **3'a** and **4'a** (significant changes imply tight binding between the Lewis acidic and basic moieties). The changes are similar to those observed in the case of the formation of related *N*-adducts[4c] [e.g. as the complex **3'a** forms the B-O bond of the hydroxyborane moiety lengthens by 0.089 Å and the C=O bond lengthens by 0.019 Å (Figure 1); an analogous reaction of the corresponding borane *N*-adduct lengthens the B-N bond of the aminoborane moiety by 0.229 Å and the C=O bond of the formaldehyde moiety by 0.026 Å (6-31G*//6-31G*)[4a]].
3) The lowest unoccupied molecular orbital (LUMO) of **2'a** resides much lower in energy than that of **2'b** or **2'c** [e.g. E(LUMO) of **2'a** is 3.20 eV (6-31G*//6-31G*) whereas that of **2'c** is 4.88 eV (the Scheme)]. Actually the LUMO energy of **2'a** is closer to that of borane (2.41 eV) or the corresponding borane *N*-adduct of aminoborane[4a] (2.94 eV, 6-31G*//6-31G*). This implies **2'a** to be a stronger Lewis acid than **2'b** or **2'c**.
4) Positive charge of boron of the hydroxyborane moiety of **2'a** is about as high as that of the corresponding borane *N*-adduct of aminoborane[4a] [e.g. at the 6-31G* level the charge of the sp^2 hybridized boron of

2'a is +0.365 whereas that of the borane *N*-adduct of aminoborane[4a] is +0.346]. This implies **2'a** to be as strong Lewis acid as the borane *N*-adduct of aminoborane has been predicted to be.[4a]

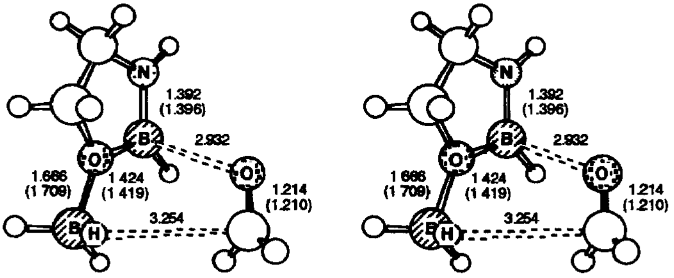
5) The resonance B-N <-> B^-=N^+ inactivating B_{ring} (**A** and **A'**, the Scheme) in the case of **2'b** and **2'c** is not present in **2'a**. Also the resonance B-O <-> B^-=O^+ stabilizing hydroxyborane disappears as **2'a** forms. Also this implies **2'a** to be a stronger Lewis acid than **2'b** or **2'c**.

< B-O-B = -129.3°
< O-B-O = 76.0°
< B-O-B-O_{H2O} = 80.5°
< C_{ring}-O-B-N = 6.6°
< H-B-N-H = 4.8°
< B-O_{ring}-B-N = 180.0°
< O_{H2O}-B-N = 102.4°
< O_{ring}-B-N = 106.8°



3'c **3'c**

< B-O-B = 129.9°
< O-B-O = 88.7°
< C-O-B = 109.8°
< B-O-B-O_{CO} = -76.4°
< C_{ring}-O-B-N = -5.7°
< H-B-N-H = -5.2°
< B-O_{ring}-B-N = 178.3°
< C_{CO}-O-B-O = 69.5°
< O_{CO}-B-N = 104.9°
< O_{ring}-B-N = 106.8°



4'c **4'c**

Figure 3. Stereo representations of the optimized (6-31G//6-31G) structures of adducts 3'c and 4'c. Some of the most important bond lengths [in Å] and bond angles [in degrees] are shown. The corresponding bond lengths of 2'c (and formaldehyde in the case of 4'c) are shown in parentheses.

On the basis of the above inspection of properties of borane *O*-adducts **2'a**, **2'b**, **2'c**, the corresponding borane *N*-adducts, and the water and formaldehyde complexes of these adducts one may clearly draw a conclusion that the chemical behaviour of borane *O*-adduct of hydroxyborane (**2'a**, which could be considered as a general model of borane adducts of alkoxyboranes) resembles that of borane and borane *N*-adducts of oxazaborolidines, species which have been calculated to form tightly bound complexes with Lewis basic ethers and ketones[4,5d] and which all are present in the reaction mixture of oxazaborolidine catalyzed enantioselective reduction of ketones. Behaviour of borane *O*-adducts of oxazaborolidines, however, clearly resembles that of the corresponding oxazaborolidines[4c] in that neither oxazaborolidines nor their borane *O*-adducts are able to form tightly bound complexes with Lewis bases (e.g. water and formaldehyde). This all clearly implies the borane *O*-adducts of oxazaborolidines, if formed under some conditions, to have no catalytic function similar to that of the corresponding borane *N*-adducts. Furthermore, results of the inspection of **3'a** and **4'a** imply alkoxyboranes, products of the enantioselective reduction of ketones catalyzed by oxazaborolidines, to catalyze the reduction of ketones too. In other words, as the products of the oxazaborolidine catalyzed reaction may catalyze their own formation the enantiomeric excess of the reduction would depend also on the nature of the product as a catalyst and not only on the nature of the ketone as a substrate to the oxazaborolidine catalyst. Confirmation of this hypothesis would require experimental studied on the influence of alkoxyboranes to the enantiomeric excess of oxazaborolidine catalyzed reduction of ketones to be carried out.

In addition to the properties of **2'a-c**, **3'a-c** and **4'a-c** discussed above the role of electric dipole moment in the formation of **3'b-c** and **4'b-c** could be worth of considering as dipole moment has been proposed[4c] to play an important role in the formation of water / formaldehyde complexes of borane *N*-adducts of **1'a-c**. Orientation of the dipole moment of borane *N*-adducts of oxazaborolidines was proposed to determine the direction in which Lewis bases are allowed to approach the Lewis acidic center of the adducts.[4c]

The electric dipole moments shown in Table 1 indicate borane coordinating to the ring oxygen of oxazaborolidine to induce a substantial increase in the moment of the system being formed [e.g. dipole moment of **1'c** is 2.67 D whereas that of **2'c** is 6.13 D (6-31G*//6-31G*), Table 1]. Actually, dipole moments of both the borane *O*-adducts and *N*-adducts[4-6] are so high that any reaction of the adducts enhancing the moment would be hardly possible (e.g. coordination of Lewis bases to the borane *N*-adduct of **1'c** *trans* about the ring[4c]). This conclusion has important consequences. Namely, as the geometry of borane *O*-adducts is practically planar the main components of the dipole moments of the *O*-adducts reside in the $(\text{N-B-O})_{\text{ring}}$ plane (e.g. the moment of **2'c**, Figure 4, part A). Consequently, only such reactions in which a Lewis base approaches the borane *O*-adduct in the $(\text{N-B-O})_{\text{ring}}$ plane (from the direction collinear with the dipole moment vector of the *O*-adduct, Figure 4, part A) decreasing the electric dipole moment of the system would be advantageous.

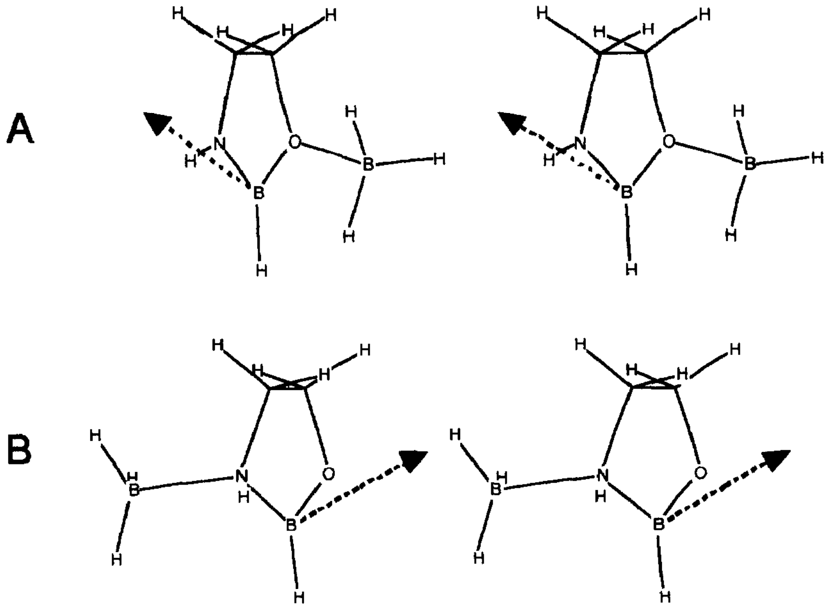


Figure 4. Stereo representations of the orientation of dipole moment vectors (dashed arrows) of the optimized structures of borane *O*- (part A) and *N*-adducts (part B, from ref. 4c) of 1,3,2-oxazaborolidine (6-31G*//6-31G*).

However, in the case of *O*-adducts all those "dipole-allowed" reactions in which the Lewis base approaches the borane *O*-adduct in the $(N\text{-}B\text{-}O)_{ring}$ plane would require the ring boron to place its all four adjacent neighbors to the same plane and, furthermore, the approaching Lewis base would overlap with the borane moiety before it would be at a binding distance from B_{ring}. Both of these requirements would be impossible to meet. Therefore, borane *O*-adducts of oxazaborolidines cannot bind Lewis bases in the same way as the corresponding *N*-adducts would do [in the case of the borane *N*-adducts Lewis bases are allowed, in contrast to the corresponding borane *O*-adduct, to approach the borane adduct from a direction perpendicular to the plane of the oxazaborolidine ring (from a direction collinear with the dipole moment vector of the *N*-adduct, Figure 4, part B) giving rise to the formation of desired complexes in which the atoms adjacent to the sp^3 hybridized ring boron would reside in a favorable tetrahedral arrangement].[4c]

At glance, the role of dipole moment in the formation of complexes of borane *O*-adducts with Lewis bases discussed above may look somewhat strange. Namely, the borane adduct of hydroxyborane (**2'a**) can, despite of the same orientational limitations of its dipole moment as those of **2'c**, bind Lewis bases such as water and formaldehyde (formation of **3'a** and **4'a**, Figure 1). On the other hand, this is not surprising as **2'a** is not rigid the B-O bond of the hydroxyborane moiety can rotate to meet the geometrical requirements emanating from the need of minimizing the total electric dipole moment of the system being formed. Furthermore, the values of B_{BH3}-O-B-O_{H2O} and B_{BH3}-O-B-O_{H2CO} torsion angles of **3'a** and **4'a** (Figure 1) are clearly smaller than those of rigid **3'c** and **4'c** (Figures 2 and 3). Nevertheless, rigidity may not be the most important factor behind the loose binding observed between the Lewis acidic and basic counterparts in water and formaldehyde complexes of borane *O*-adducts of oxazaborolidine and related models. Namely, the model **2'b** was not able to bind water or formaldehyde although its skeleton should be less rigid than that of **2'c**. In the light of these observations one could draw a conclusion that the resonance effects depicted in the Scheme could be more important in the deactivation of the ring boron of borane *O*-adducts of oxazaborolidines than effects related to dipole moment (Figure 4). A more thorough estimation of the relative importance of these effects would require further studies on properly selected series of models of alkoxy- and dialkoxyboranes. Computational studies on the properties of these chiral catalysts continue.

CONCLUSIONS

All the results of this study imply borane *O*-adducts of oxazaborolidines to be, in contrast to the corresponding *N*-adducts, unable to form complexes with Lewis bases such as ethers or carbonyl compounds. Consequently, borane *O*-adducts of oxazaborolidines can be predicted to be practically inactive as catalysts in the enantioselective reduction of ketones.

Hydroxyborane was found to form complexes with borane and formaldehyde similar to those proposed to be the key intermediates in the oxazaborolidine catalyzed reduction of ketones. This implies that the products of the oxazaborolidine catalyzed reduction of ketones (alkoxyboranes) catalyze their own formation under condition of the oxazaborolidine catalysis.

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8. As electron correlation has not been taken into account in this work energies of all complexes which have long "bonds" between Lewis basic and basic centers must be treated with caution.