Quantum Chemical Modeling of Chiral Catalysis. Part 15. On the Role of Hydride-Bridged Borane - Alkoxyborane Complexes in the Catalytic Enantioselective Reduction of Ketones Promoted by Chiral Oxazaborolidines

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Abstract: - Hydride-bridged borane - alkoxyborane complexes of oxazaborolidines were investigated by means of *ab initio* molecular orbital methods (RHF). The complexes were found to be stable in the absence of Lewis basic solvents. In the presence of a Lewis basic solvent the borane - alkoxyborane complexes were predicted to decompose leading to the formation of borane - solvent complexes of the oxazaborolidines. A new class of oxazaborolidine catalysts, of which the mechanism of regeneration would be based on borane - borane hydride exchange, was invented.

INTRODUCTION

Chiral oxazaborolidines **1** able to form borane *N*-adducts (**2**, Scheme I) catalyze the reduction of ketones to produce secondary alcohols with high enantioselectivity.[1] The history, present results and most important applications of 1,3,2-oxazaborolidines in enantioselective syntheses have been recently summarized in two reviews.[1]

Coordination of a ketone to **2** has been proposed to lead to the formation of **3** in which a hydride transfer could occur giving rise to the formation of **4** (Scheme I).[1,2] Computational studies on this mechanism[3-6] imply **4** to be unstable (on the basis of an inspection of a simple model of **4**).[3d] Reactions of **4** were found[3d] to lead either to the opening of the oxazaborolidine ring or to the formation of **5** (Scheme I). Elimination of the alkoxyborane moiety from **5** would regenerate the catalyst. Therefore, the catalytic cycle of the oxazaborolidine catalyzed reduction of ketones could be represented as "**1** -> **2** -> **3** -> **4** -> **5** -> **1** etc." (Scheme I). Computational studies also indicate that oxazaborolidines could form hydride-bridged aggregates with borane.[5a] As **2** and alkoxyboranes could form analogous hydride-bridged aggregates an alternative mechanism for the oxazaborolidine catalyzed reduction of ketones can be devised.[6] The mechanism is based on a new regeneration pathway (*via* **6**, Scheme I).[6]

Borane - solvent complexes (e.g. H$_3$B•THF) present in the reaction mixture could react with the unstable intermediate (**4**) or insert to the oxazadiboretane ring of **5** giving rise to the formation of a hydride-bridged complex **6** (Scheme I). The complex (**6**) could decompose producing **2** and an alkoxyborane derivative of the newly formed secondary alcohol R$_L$R$_S$CHOH (effectively a simple borane - borane hydride exchange had taken place). Consequently, the catalytic cycle of oxazaborolidine catalyzed reduction of ketones could be represented also as "**2** -> **3** -> **4** -> **6** -> **2** etc." or "**2** -> **3** -> **4** -> **5** -> **6** -> **2** etc." (Scheme I).[6] On the other hand, if the alkoxyborane would coordinate back to **2** the catalyst would be inhibited by its own product. This is interesting in the light of recent discoveries of Cai *et al.*[7] They have shown that the enantioselectivity of reduction of ketones (by stoichiometric amounts of **2**) increases if the reduction is performed in the presence of triethylamine. Cai *et al.* suggest that the alkoxyborane derivative of the newly formed chiral secondary alcohol would be trapped by triethylamine and therefore its involvement in further reduction reactions would be prevented.[7]

This new mechanism involving **6** could also allow one to invent a new class of oxazaborolidine type of catalysts for the enantioselective reduction of ketones.[6] In this respect two facts related to these mechanisms are worth of noticing. For instance, rotation of the borane moiety of **2** is not restricted [e.g. the energy of borane *N*-adduct of 1,3,2-oxazaborolidine of which the N-BH$_3$ group is in a staggered conformation is only 4 kJ mol^{-1} lower than that of

the eclipsed system (6-31G*//6-31G*)[5a]. Furthermore, it is not know how the performance of the oxazaborolidine catalyzed reduction of ketones correlates with the orientation of the borane coordinated to the nitrogen of the oxazaborolidine. If it would be possible to run the catalytic reduction through 6 there would be no need for breaking the bond between the hydride delivering borane moiety and the nitrogen of the oxazaborolidine ring. Consequently, properly substituted more bridged/fused systems of which the borane is bound to the skeleton of the catalyst by an inert alkyl (aryl) spacer (e.g. 7 or 8) could be used as catalysts.

Scheme I
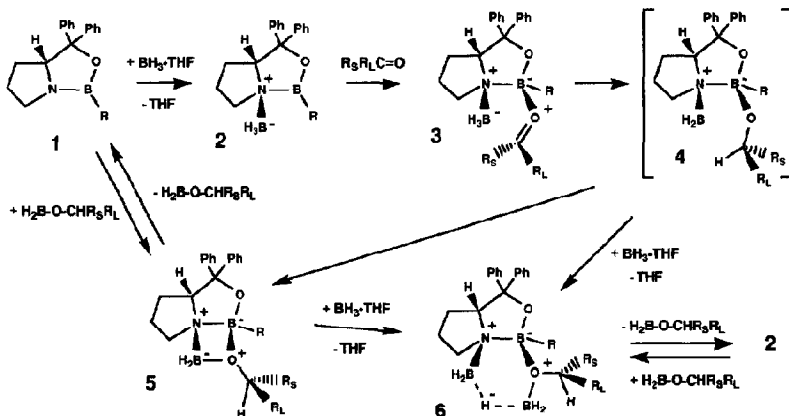
Although the performance of 7, 8, or other related systems is not yet known this type of intramolecular borane adducts may have properties more advantageous than those of the parent oxazaborolidines (1). Namely, Mathre *et al.*[8] have discovered that borane adducts of oxazaborolidines can be significantly more stable than the parent oxazaborolidines. Altogether, as knowing properties of hydride-bridged systems analogous to 6 would be of importance for understanding the mechanism of the oxazaborolidine catalyzed reduction of ketones and for the development of new and better catalysts probing the formation of 6 was attempted by means of *ab initio* MO methods.
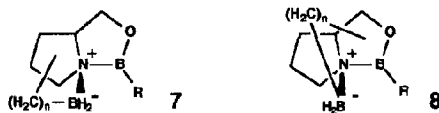
MODELS AND COMPUTATIONAL METHODS

The models used in this study were as follows: 1'a-c as models of catalysts 1, 2'a-c as models of borane *N*-adducts 2; 5'a-c as models of 5; 6'a-c, 6''a-c as models of 6; H_2B-OH, H_2B-OCH_3 as models of alkoxyboranes. Modeling techniques applied were similar to those of previous studies of this series.[3d] Standard *ab initio* calculations (RHF) were carried out by using the Gaussian 80[9] series of programs at the 3-21G, 4-31G, 6-31G, 4-31G* and 6-31G* levels. No other calculations on the structures 6'a-c, 6''a-c appear to have been published. Properties of 1'a-c, 2'a-c, 5'a-c and the alkoxyborane models have been described in previous reports of this series.[3-5]

RESULTS AND DISCUSSION

The optimized structures of 6'a and 6'b are depicted in Figure 1. The optimized structure of 6'c (and its

conformer 6'c') is presented in Figure 2. Total energies and dipole moments of 1'a-c, 2'a-c, 5'a-c, 5''a-c, 6'a-c, 6'c' and 6''a-c are shown in Table 1. The energies of formation of analogs of 6 are shown in Tables 2 and 3, the degrees of sp^3 hybridization of the hydride-bridged borons in Table 4 and the charge transfer values in Table 5.
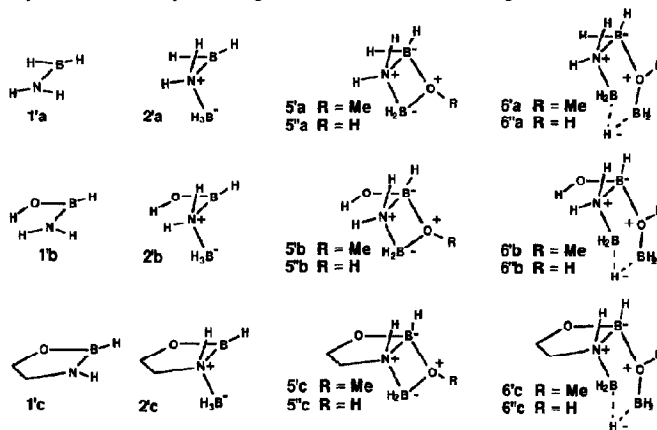
[Chemical structure diagrams: 1'a, 2'a, 5'a R = Me / 5''a R = H, 6'a R = Me / 6'a R = H; 1'b, 2'b, 5'b R = Me / 5''b R = H, 6'b R = Me / 6'b R = H; 1'c, 2'c, 5'c R = Me / 5''c R = H, 6'c R = Me / 6'c R = H]

Table 1. Total energies (E)[a] and dipole moments (D)[b] of the models.

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	-81.04343	2.01	-81.37857	1.76	-81.46276	1.76	-81.40935	1.84	-81.48910	1.82
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	-107.29823	4.35	-107.73575	3.84	-107.84578	3.78	-107.78128	4.21	-107.88689	4.24
2'b	-181.82032	4.72	-182.55939	4.21	-182.74260	4.21	-182.63855	4.48	-182.81418	4.46
2'c	-258.28393	5.22	-259.32696	4.93	-259.59052	4.89	-259.45727	4.98	-259.70944	4.97
5'a	-220.65768	0.60	-221.53912	0.67	-221.76155	0.73	-221.63330	0.80	-221.84643	0.81
5''a	-181.84477	0.82	-182.57271	1.01	-182.75550	1.07	-182.64372	1.45	-182.81873	1.48
5'b	-295.17021	1.94	-296.35536	2.03	-296.65164	2.04	-296.47763	1.84	-296.76124	1.87
5''b	-256.35880	1.71	-257.39068	1.62	-257.64734	1.62	-257.49078	2.06	-257.73638	2.06
5'c	-371.63266	1.31	-373.12185	1.58	-373.49818	1.67	-	-	-	-
5''c	-332.82019	1.57	-334.15586	1.85	-334.49239	1.90	-334.30493	1.75	-334.62681	1.75
6'a	-246.91647	2.69	-247.90598	2.57	-248.15505	2.56	-248.01361	2.47	-248.25309	2.45
6''a	-208.10741	2.16	-208.94337	2.39	-209.15273	2.40	-209.03016	2.32	-209.23153	2.33
6'b	-321.42138	1.84	-322.71334	1.45	-323.03645	1.34	-322.85038	1.65	-323.16051	1.60
6''b	-282.61803	0.67	-283.75690	0.70	-284.03999	0.74	-283.87207	1.13	-284.14292	1.65
6'c	-397.89400	2.73	-399.48850	2.50	-399.89142	2.46	-	-	-	-
6'c' [c]	-397.88804	2.78	-399.48341	2.85	-399.88631	2.90	-	-	-	-
6''c	-359.08212	3.14	-360.52434	2.92	-360.88764	2.91	-	-	-	-
H₂B-O-H	-100.76196	1.91	-101.17676	1.87	-101.27793	1.89	-101.22430	1.68	-101.32139	1.68
H₂B-O-CH₃	-139.57090	2.16	-140.13955	2.08	-140.28052	2.06	-140.21037	1.71	-140.34556	1.71
H₂B-OH₂	-101.86336	5.28	-102.28057	4.92	-102.38267	4.86	-102.31848	4.28	-102.41525	4.26
H₂O	-75.58596	2.39	-75.90864	2.49	-75.98536	2.51	-75.93900	2.18	-76.01075	2.20
H₃B	-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. [c] A conformer of 6'c' (Figure 2).
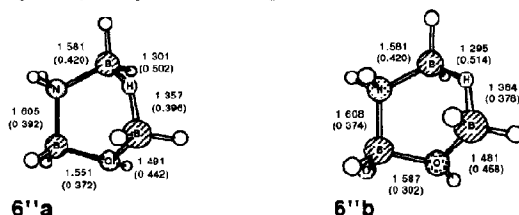
Structure and bonding

An inspection of structural parameters of the models of 6 reveals that these systems really are hydride-bridged [e.g. lengths of the B-H bonds of the bridges are 1.295 Å - 1.364 Å in the case of the optimized structures of 6''a-b (Figure 1) and 6'c and 6'c' (Figure 2)]. Bond lengths of the borane - oxazaborolidine moieties of the models are close to those of related hydride-bridged aminoborane adducts reported in the literature.[5a] Consequently, one could predict the

relative changes of the most important bonding interactions involved in the formation of **6** to be similar to those of the aminoborane adducts (Scheme II).

Scheme II

X = O, n = 1
X = N, n = 2

S = bond strengthened
W = bond weakened
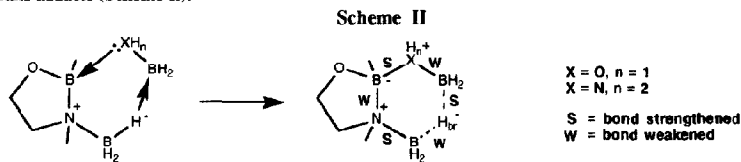
One of the bonding interactions undergoing significant changes as complexes **6** form (Scheme II) is the N-B_{BH_3} interaction. This interaction appears to be much stronger in the hydride-bridged complexes (**6**) than in the corresponding borane adducts (**2**). In the former class of structures N-B_{BH_3} bonds are shorter and Mulliken overlap populations higher than in the latter one. For example, at the 6-31G* level, the N-B_{BH_3} bonds of **6''a-b** are 1.581 Å long (overlap populations 0.420, Figure 1) whereas the corresponding bonds of **2'a** and **2'b** are 1.826 and 1.765 Å long[3a] (overlap populations[4a] 0.161 and 0.160). The same conclusion can be drawn also as results of calculations carried out without polarization functions are compared [e.g. at the 6-31G level, the N-B_{BH_3} bond of **6'c** is 1.594 Å long (overlap population 0.188, Figure 2) whereas the N-B_{BH_3} bond of **2'c** is 1.750 Å long[3d] (overlap population 0.030). As observed in the case of related aminoborane adducts,[5a] it would be rational to attribute tightening of the N-B_{BH_3} binding to a decrease of other acid - base interactions of the N and B_{BH_3} atoms.

On the basis of changes of bonding interactions depicted in Scheme II the B-N bond of the oxazaborolidine ring should lengthen/weaken as adducts analogous to **6** form. A comparison of lengths of the B-N bonds of the oxazaborolidine rings of **6'c** and **2'c** reveals that the B-N bond of **2'c** (1.490 Å, 6-31G//6-31G)[3d] is 0.142 Å shorter than that of **6'c** (1.632 Å, Figure 2). Similar conclusions can be drawn if Mulliken overlap populations of the models are compared [e.g. the B-N overlap of the oxazaborolidine moiety is 0.436 in the case of **2'c** (6-31G//6-31G)[5a] whereas the corresponding overlap is only 0.222 in **6'c** (Figure 2)].

6''a   **6''b**

Figure 1. The optimized (6-31G*//6-31G*) structures of **6''a** and **6''b**. Some of the most important bond lengths [in Å] and the corresponding Mulliken overlap populations (in parentheses) are shown.

An inspection of structural changes related to the ring B-H_{br} bonds (Scheme II) is trivial in the case of the B_O-H_{br} bond (predicted to shorten/strengthen) as it forms in the reaction. The B_N-H_{br} bond should lengthen/weaken (Scheme II). A comparison of lengths of the B_N-H_{br} bonds of **6'a-c**, **6'c'**, **6''a-c** and B-H bonds of the BH_3 moieties of **2'a-c** indicates that the bridging hydrogen of **6** would be less tightly bound to its adjacent borons than the corresponding hydrogen of **2** [e.g. the B_N-H_{br} bond of **6'c** is 1.306 Å long (Figure 2) whereas lengths of the B-H bonds of the BH_3 moiety of **2'c** are within the range of 1.202 - 1.206 Å].

The B_N-H_{br} bonds appear to be shorter than the adjacent B_O-H_{br} bonds in the case of all models of **6** [e.g. the B_N-H_{br} bond of **6''b** is 0.069 Å shorter than the adjacent B_O-H_{br} bond, Figure 1]. Also the Mulliken overlaps of B_N-H_{br} interactions are higher than those of B_O-H_{br} ones [e.g the B_N-H_{br} overlap of **6''b** is 0.514 whereas that of B_O-H_{br} is only 0.378, Figure 1]. Although these differences of lengths and overlap populations are smaller in the case of more strained systems (**6'c** and **6'c'**; Figure 2) the same relative differences can be found also in that group. Implications of these differences could be inspected also in the light of the resonance formulae A and B shown in Scheme III. Namely,

as the B_N-H_{br} bond was found to be shorter/stronger one could predict that the degree of sp^3 hybridization of B_N could be higher than that of B_O.
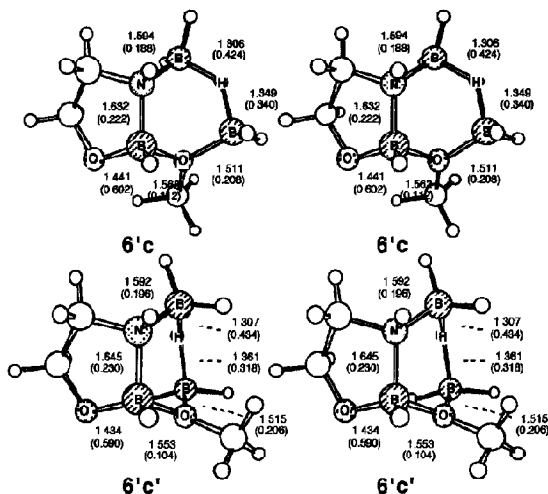

Figure 2. Stereo presentations of the optimized (6-31G//6-31G) structures of 6'c and 6'c'. Some of the most important bond lengths [in Å] and the corresponding Mulliken overlap populations (in parentheses) are shown.

The degrees of sp^3 hybridization (Table 4) of B_N $[T(B_N)]$ are indeed higher than those of B_O $[T(B_O)]$. The $T(B_N)$ and $T(B_O)$ values are also remarkably independent of the nature of the models and the basis sets used. All the $T(B_N)$ values are within the range of 60 - 64 % and those of $T(B_O)$ within the range of 49 - 53 %. The largest difference of the values calculated at the 6-31G and 6-31G* levels is 3 % (in the case of 6''b). Therefore, also the degrees of sp^3 hybridization indicate that these hydride-bridged systems (6) could be better presented by the resonance formula A than by B (Scheme III).

Table 2. Energies $(\Delta E)^a$ of the formation of hydride-bridged adducts 6'a-c, 6'c' and 6''a-c by insertion of borane to the alkoxy- and hydroxyborane adducts 5'a-c and 5''a-c.

						3-21G	4-31G	6-31G	4-31G*	6-31G*
Reaction								ΔE^a		
5'a	+	$H_3B\cdot OH_2$	->	6'a	+	H_2O	+49	+13	+10	+2	-6
5''a	+	$H_3B\cdot OH_2$	->	6''a	+	H_2O	+39	+3	0	-18	-22
5'b	+	$H_3B\cdot OH_2$	->	6'b	+	H_2O	+69	+37	+33	+18	+14
5''b	+	$H_3B\cdot OH_2$	->	6''b	+	H_2O	+48	+15	+12	-5	-5
5'c	+	$H_3B\cdot OH_2$	->	6'c	+	H_2O	+42	+14	+11	-	-
5'c	+	$H_3B\cdot OH_2$	->	6'c' [b]	+	H_2O	+58	+27	+24	-	-
5''c	+	$H_3B\cdot OH_2$	->	6''c	+	H_2O	+41	+9	+5	-	-
H_3B	+	H_2O	->	$H_3B\cdot OH_2$			-105	-60	-54	-43	-38

[a] Energies given in kJ mol^{-1}. [b] A conformer of 6'c'.

Also an inspection of the B-O bonds of hydride-bridged rings of the models of 6 provides evidence for the rational of the above conclusions drawn with respect to the structural changes (Scheme II) and resonance formulae (Scheme III). By analogy to the behaviour of related aminoborane adducts the B-O bond of alkoxyborane was predicted to lengthen/weaken as the alkoxyborane coordinates to a borane adduct of an oxazaborolidine (Scheme II). When the lengths of B-O bonds of the hydroxy- and methoxyborane moieties of the models of 6 were compared with those of

free hydroxy- and methoxyborane[3d] the former bonds turned out to be substantially longer [e.g. at the 6-31G level the B-O bond of methoxyborane is 1.358 Å long[3d] whereas in the case of 6'c the corresponding bond is 1.511 Å long (Figure 2)]. Furthermore, if the resonance formula A (Scheme III) represents 6 better than B then the oxygen of the alkoxyborane moiety should be more tightly bound to the boron of the alkoxyborane than to the boron ($B_{catal.}$) of the oxazaborolidine ring. The O-BH_2 bonds of the models of 6 are shorter (and the corresponding overlap populations higher) than the O-$B_{catal.}$ bonds [e.g. at the 6-31G level the lengths of the O-BH_2 and O-$B_{catal.}$ bonds of 6'c (Figure 2) are 1.511 Å (overlap 0.208) and 1.562 Å (overlap 0.112)]. In the case of 6''b the corresponding values (6-31G//6-31G) are 1.517 and 1.594 Å (overlaps 0.198 and 0.116). Inclusion of polarization functions increases this difference further [e.g. in the case of 6''b (Figure 1, 6-31G*//6-31G*) the lengths of the O-BH_2 and O-$B_{catal.}$ bonds are 1.481 Å (overlap 0.458) and 1.587 Å (overlap 0.302). .

Table 3. Energies (ΔE)[a] of the elimination of alkoxy- and hydroxyborane from hydride-bridged adducts 6'a-c, 6'c' and 6''a-c.[b]

| Reaction				3-21G	4-31G	6-31G	4-31G*	6-31G*
						ΔE[a,b]		
6'a	->	2'a	+ H_2B-O-CH_3	+124 (-10)	+81 (+9)	+76 (+11)	+58 (-8)	+54 (-6)
6''a	->	2'a	+ H_2B-O-H	+124 (-10)	+81 (+9)	+76 (+11)	+65 (-1)	+61 (+1)
6'b	->	2'b	+ H_2B-O-CH_3	+79 (-31)	+38 (-19)	+35 (-17)	+4 (-34)	+2 (-32)
6''b	->	2'b	+ H_2B-O-H	+94 (-16)	+55 (-2)	+51 (-1)	+24 (-14)	+19 (-15)
6'c	->	2'c	+ H_2B-O-CH_3	+103 (-4)	+58 (+8)	+54 (-9)	-	-
6'c'[c]	->	2'c	+ H_2B-O-CH_3	+87 (-20)	+45 (-5)	+41 (-4)	-	-
6''c	->	2'c	+ H_2B-O-H	+95 (-12)	+54 (+4)	+50 (+5)	-	-

[a] Energies given in kJ mol⁻¹. [b] The corresponding solvent corrected energies show in parentheses [corrected with respect to the formation of solvent complexes of the borane adducts 2'a-c; solvent (water as a model of the solvent) and borane *cis* about the oxazaborolidine ring, ref. 3c]. [c] A conformer of 6'c'.

Table 4. Degrees of sp^3 hybridization (T) of the hydride-bridged borons B_N and B_O of 6'a-c, 6'c' and 6''a-c.

	6-31G		6-31G*	
Structure	T(B_N)%	T(B_O)%	T(B_N)%	T(B_O)%
6'a	63	50	62	49
6''a	62	51	63	53
6'b	54	61	54	63
6''b	60	53	63	51
6'c	62	49	-	-
6'c'[a]	64	49	-	-
6''c	63	51	-	-

[a] A conformer of 6'c'.

Scheme III
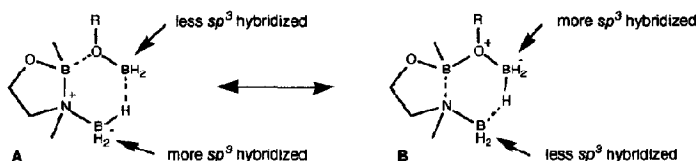
In amino- and alkoxyboranes the lone electron pair(s) of nitrogen(s) and/or oxygen(s) can interact with the empty $2p_z$ orbital of the boron. This interaction could be described by the resonance [B-X <-> B⁻=X⁺; (X=N,O)]. If the boron receives electron density from an external source (e.g. from a Lewis basic substance[3-5] coordinating to the boron) the B-X bond lengthens. Because the B-O bond of alkoxyborane was found to lengthen/weaken (Scheme II) it could be rational to predict that the alkoxyborane would receive electrons from the borane adduct (2). Indeed, all the charge transfer values (Table 5) of the models of 6 are negative (except that of 6'a; 6-31G*//6-31G*). In the case of related

borane adducts [$H_2B-O(H) \cdot BH_3$ and $H_2B-O(CH_3) \cdot BH_3$ in which BH_3 behaves as a monodentate acid and hydroxy- and methoxyborane as monodentate bases] charge transfer occurs to the opposite direction. On the other hand, in the case of 6 the alkoxyborane is playing a different role. As complexes 6 form, both the alkoxyborane and borane adducts behave as bidentate Lewis acid-base pairs, called also as Lewis dipoles[5a] (one end of the dipole is acidic and the other basic).

Table 5. Charge transfer to hydroxy- and methoxyboranes as they coordinate to models of borane adducts of oxazaborolidines (2'a-c) and borane.[a]

Structure	6-31G		6-31G*	
	Q($H_3C-O-BH_2$)	Q($H-O-BH_2$)	Q($H_3C-O-BH_2$)	Q($H-O-BH_2$)
6'a	-0.041	-	+0.098	-
6''a	-	-0.116	-	-0.066
6'b	-0.120	-	-0.116	-
6''b	-	-0.174	-	-0.111
6'c	-0.162	-	-	-
6'c' [b]	-0.145	-	-	-
6''c	-	-0.140	-	-
$H_2B-O(H) \cdot BH_3$	-	+0.102	-	+0.098
$H_2B-O(CH_3) \cdot BH_3$	+0.108	-	+0.105	-

[a] Negative/positive signs indicate that the species has received/donated electrons. [b] A conformer of 6'c'.

Conclusions partially contradictory to those discussed above can be drawn as the B-N bonds of the models of 6 are compared. If, in contrast to that proposed above, B depicts 6 better than A (Scheme III) then it could be rational to predicted the N-$B_{catal.}$ bond to be longer than its adjacent N-B_{BH_3} bond. However, the N-B_{catal} bonds are indeed about 0.3±0.1 Å longer in the case of all models and basis sets used. Similar results can be obtained as the Mulliken overlap populations of the B-N interactions of 6'a-b and 6''a-b are inspected. Lower B-N overlap populations always correspond to longer B-N bonds and *vice versa*. However, in the case of more strained and rigid models an opposite correlation can be found. Although the B-N bond of the oxazaborolidine moiety of 6'c (or 6'c') is longer than the adjacent N-B_{BH_3} bond the Mulliken overlap population of the former is higher (Figure 2). It looks also as if this difference in the correlation of overlaps and bond lengths between the flexible models 6'a-b, 6''a-b and more strained ones (6'c, 6'c' and 6''c) would not depend on the nature of the basis sets used as the same correlation was observed in the case of the more flexible models at both the 6-31G and 6-31G* levels. Altogether, as the models 6'c, 6'c' and 6''c resemble 6 more closely than 6'a-b, 6''a-b one could conclude that also the results of the comparison of Mulliken overlap populations of the B-N bonds imply the resonance formula A (Scheme III) to represent 6 better than B would do.

A comparison of bond and torsion angles of the models of 6 reveals that some values are very closely similar in the case of all the models whereas others may vary considerably. At the 6-31G level the O-B-H_{br} and N-B-H_{br} bond angles are 104.4° ±0.5° and 107.0° ±0.5° in the case of all the optimized models (the corresponding values provided at the 6-31G* level are within 107.5° ±0.5° and 107.9 ±1.0°, respectively). On the other hand, at the 6-31G level the B-O-B bond angles are 121.9° ±6.1°, the B-N-B angles 118.0° ±4.0°, the N-B-O angles 102.9° ±3.4° and the B-H_{br}-B angles, surprisingly, 139.8° ±9.2°. Variation ranges of the torsion angles are much larger. Therefore, one could conclude that structural parameters may vary as far as the bridging hydride can form an angle of 107.5° ±0.5° to the O-BH_2 bond and an angle of 107.9 ±1.0° to the N-B_{BH_3} bond. Furthermore, all the hydride-bridged rings of the models of 6 studied, except that of 6'b, were found to be in boat conformations. The ring system of 6'b was almost planar.

On the energies of the formation of hydride-bridged borane - alkoxyborane adducts of oxazaborolidines

The energies of formation of 6'a-c and 6''a-c by insertion of borane to 5'a-c and 5''a-c are shown in Table 2 [borane from borane - solvent complex (e.g. $H_3B \cdot THF$); water as a model[3c] of the solvent]. At the 6-31G* level the energies are low but negative (except in the case of 5'b -> 6'b); at the 6-31G level the energies are positive but low. Therefore, it could be reasonable to predict the borane transfer energies to be close to zero. This implies the formation of 6 via 5 to be controlled more by factors related to kinetics than those related to thermodynamics.

Dipole moments of all the models of 6 (Table 1) are significantly lower than those of the corresponding analogs of

2 (e.g. the moment of **6'c** is 2.46 D whereas that of **2'c** is 4.89 D; 6-31G//6-31G). Thus, stabilities of **6** (as those of **5**)[3d] could be predicted to be less dependent on the Lewis basicity of solvent than the corresponding analogs of **2**. Similar changes of dipole moments have been observed earlier in the case of formation of several other Lewis acid - base complexes of oxazaborolidines.[3-5]

The energies shown in Table 3 imply that in the absence of Lewis basic solvents the borane adduct **2** could "drown" in the alkoxyborane being formed in the reduction. Namely, energies of the formation of alkoxyborane adducts (**6**) appear to be much more advantageous than those of the ketone adducts[3] (**3**, Scheme 1). For example, the energy of coordination of hydroxyborane to **2'b** (formation of **6''b**) is -51 kJ mol^{-1} (6-31G//6-31G, Table 3) whereas the corresponding energy of coordination of formaldehyde[3c] to **2'b** is -3 kJ mol^{-1}. In the case of more strained systems the difference is not significantly smaller [e.g. the energy of coordination of hydroxyborane to **2'c** is -50 kJ mol^{-1} (6-31G//6-31G, Table 3) whereas the energy of coordination[3c] of formaldehyde to **2'c** is +1 kJ mol^{-1}].

In the presence of Lewis basic solvents (e.g. THF) the relative stability of **2** and **6** changes. At the 6-31G* level the solvent corrected energies of the formation of **6'b** and **6''b** are +32 and +15 kJ mol^{-1} (Table 3). The corresponding values of **6'a** and **6''a** are close to zero. At the 6-31G level the solvent corrected energies of the formation of **6'a**, **6''a**, **6'c**, **6'c'** and **6''c** are negative but low (Table 3). These results indicate that in the presence of a Lewis basic solvent the solvent would replace the alkoxyborane moiety of **6** giving rise to the formation of borane - solvent complex[3c] of the corresponding oxazaborolidine. On the basis of these results one could predict that the catalytic reduction of ketones with intramolecular borane adducts (**7**, **8**, or related analogs) could be achievable with respect to thermodynamics. Nevertheless, in order to obtain good catalysts of this class rates of the borane - borane hydride transfer should be much faster than the rates of non-catalytic reductions. Kinetics of the borane - borane hydride transfer has not yet been studied.

CONCLUSIONS

Results of this work indicate that in the absence of Lewis basic solvents borane - alkoxyborane complexes (**6**) may form as alkoxyboranes coordinate to borane adducts of oxazaborolidines or as borane inserts to an oxazadiboretane ring. In the presence of a Lewis basic solvent the complexes (**6**) would decompose giving rise to the formation of borane - solvent adducts of the corresponding oxazaborolidines. These reactions would offer a new regeneration pathway for the enantioselective reduction of ketones catalyzed by oxazaborolidines and a challenge of developing a new class of oxazaborolidine catalysts (e.g. **7**, **8** or related analogs in which the borane moiety delivering the hydride to the ketone being reduced would be covalently bound to the catalysts by an inert spacer).

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