Tetrahedron: Asymmetry Vol. 2, No. 1, pp. 63-74, 1991
Printed in Great Britain

0957-4166/91 $3.00+.00
Pergamon Press plc

Quantum Chemical Modeling of Chiral Catalysis. On the Mechanism of Catalytic Enantioselective Reduction of Carbonyl Compounds by Chiral Oxazaborolidines

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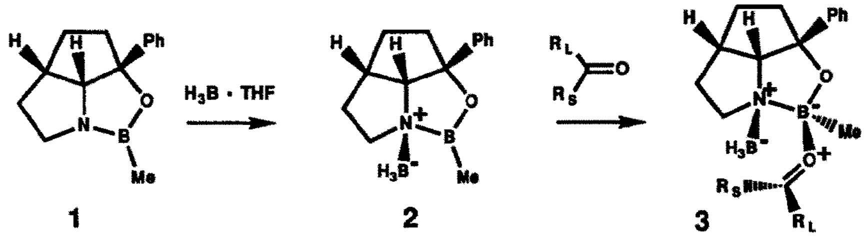
(*Received* 6 *December* 1990)

Abstract: - Energies of formation and structural parameters of two model systems of oxazaborolidine type of chiral reduction catalysts (CBS reduction), their borane adducts, and formaldehyde complexes of the borane adducts were calculated by using ab initio molecular orbital methods. Energies of the formation of formaldehyde complexes in which the borane and carbonyl were *cis* about the B-N bond of the oxazaborolidine ring were found to be slightly positive. The corresponding *trans* coordination was found to be repulsive. A new class of potential chiral catalysts which also contain the substructure O-B-N was found.

INTRODUCTION

Recently discovered chiral catalysts, e.g. **1**, (also called "chemzymes") have been reported to be highly effective for the enantioselective reduction of ketones (CBS reduction).[1] Although a reasonable reaction mechanism has been suggested for the catalysis,[1] there are still details left which might be clarified further.

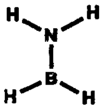
Oxazaborolidines react with $BH_3{\bullet}THF$ to form Lewis acid-base adducts, e.g. **2**. These adducts are assumed to form complexes with ketones, e.g. **3**, in which an intramolecular hydride transfer from the N-BH_3 moiety to the carbonyl occurs.[1]



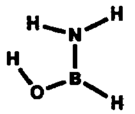
1 2 3

The main goal of the work summarized in this paper was to study structural properties of the analogs **1'a-c** of **1**, the analogs **2'a-c** of **2**, the analogs **3'a-b** of **3**, and the complex **4**, their energies of formation, their stabilities, and also conformational energies of **3'b** by using ab initio molecular orbital methods.

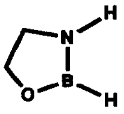
In addition to our preliminary reports,[2] previous calculations have being published only for **1'a** and the nitrogen analog of **1'b**,[3a-c] aminoborane analogs of **2'a**,[3d-e] and for analogs of **4**.[3f] Standard optimization procedures were utilized. All calculations were done by using the Gaussian 80 series of programs at the 3-21G, 4-31G, 4-31G* and 6-31G* levels.[4] The molecules $H_3B{\bullet}NH_3$, $H_3B{\bullet}OH_2$ (which was used as a model of BH_3•THF), BH_3, H_2O, $H_2C=O$ and NH_3 were calculated for reference purposes. The results were practically equal to those reported in the literature.[5] This modeling approach was taken because computing an entire catalyst systems (e.g. **1**, **2** and **3**) would have been far beyond the scope of normal accurate ab initio calculations.



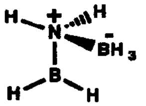
1'a



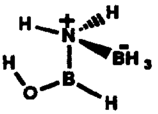
1'b



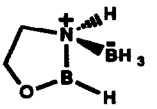
1'c



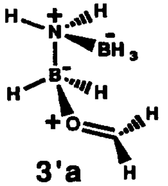
2'a



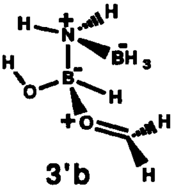
2'b



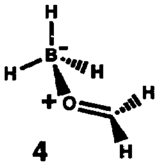
2'c



3'a



3'b



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RESULTS AND DISCUSSION

Stereo representations of the 6-31G* optimized structures and the most important bond lengths of **2'a-c** are shown in Scheme 1 and the stereo representations of the 6-31G* optimized structures of **3'a** and **3'b** in Scheme 2. The total energies and dipole moments calculated are summarized in Table 1. The net atomic charges of the most important structural moieties accompanied with the HOMO/LUMO energies are shown in Table 2. Energies of the formation of borane adducts **2'a-c** and energies of the coordination of formaldehyde to borane adducts **2'a-b** and BH_3 (i.e. energies of the formation of **3'a-b** and **4**) are shown in Table 3.

Formation of the Borane Adducts

As shown in Scheme 1, the B(2)-N bond of the oxazaborolidine moiety of **1'c** and **1'b** lengthens and the B(2)-O(1) bond shortens as their borane adducts are formed. This is related to the decrease of electron density of the boron B(2) during formation of the adducts. The loss of the partial boron nitrogen double bond character [B-N <-> $B^-=N^+$] would be compensated by an enhanced interaction with the adjacent oxygen [B-O <-> $B^-=O^+$] causing the B-O bond to shorten. This compensation mechanism appears to be more important in the case of **1'c/2'c** (the B-O bond of **1'c** shortens twice as much as that of **1'b**) whereas lengthening of the B-N bond is closely similar in the case of both **1'b/2'b** and **1'c/2'c**. In the case of **1'a/2'a** the B(2)-N bond also lengthens but the effect is smaller.

Table 1. Total energies (E)[a] and dipole moments (D)[b] of catalyst models **1'a-c**, complexes **2'a-c**, **3'a-b**, **4**, $H_3B{\bullet}NH_3$ and $H_3B{\bullet}OH_2$.

Structure	3-21G//3-21G		4-31G//4-31G		4-31G*//4-31G*		6-31G*//6-31G*	
	E[a]	D[b]	E	D	E	D	E	D
1'a	-81.04343	2.01	-81.37857	1.76	-81.40935	1.84	-81.48910	1.82
1'b	-155.55682	3.27	-156.19671	3.20	-156.25862	2.95	-156.40862	2.96
1'c	-232.01452	3.16	-232.95883	3.18	-233.07225	2.65	-233.29859	2.67
2'a	-107.29823	4.35	-107.73575	3.84	-107.78128	4.21	-107.88689	4.24
2'b	-181.82032	4.72	-182.55939	4.21	-182.63855	4.48	-182.81418	4.46
2'c	-258.28393	5.22	-259.32696	4.93	-259.45727	4.98	-259.70944	4.97
3'a	-220.54866	3.68	-221.44102	3.60	-221.55240	3.53	-221.76572	3.50
3'b	-295.05704	2.52	-296.25298	3.21	-296.39390	3.00	-296.67764	2.95
4	-139.48641	5.78	-140.05755	5.48	-140.13337	5.38	-140.26800	5.37
$H_3B{\bullet}OH_2$	-101.86336	5.28	-102.28057	4.92	-102.31848	4.28	-102.41525	4.26
$H_3B{\bullet}NH_3$	-82.16629	5.70	-82.49789	5.52	-82.53244	5.59	-82.61180	5.58

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

Table 2. Net atomic charges of B(1), H(1), B(2), N, O(1), $O_{c=o}$ and $C_{c=o}$ of **1'a-c**, **2'a-c**, **3'a-b**, **4**, $H_3B{\bullet}NH_3$, $H_3B{\bullet}OH_2$, BH_3 and $H_2C{=}O$, and the HOMO/LUMO energies (6-31G*//6-31G*).[a]

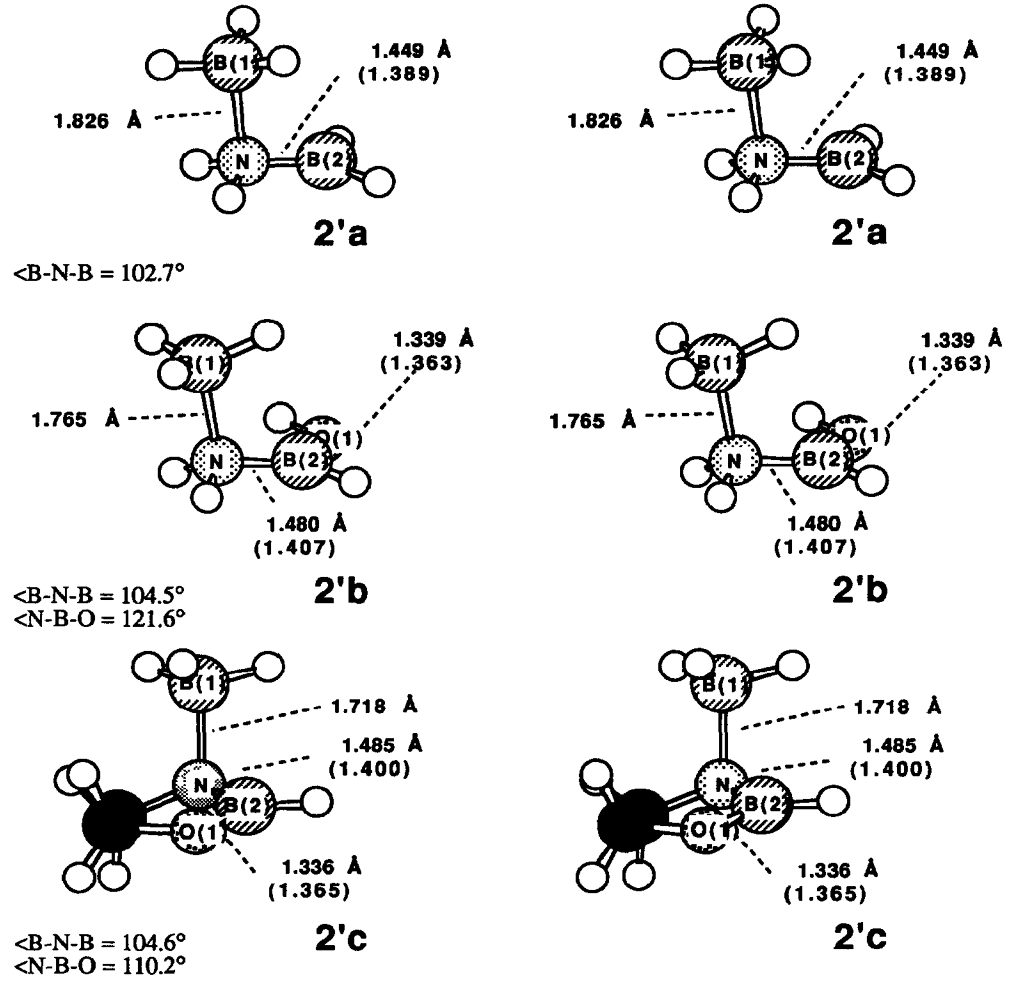
Structure	B(1)	H(1)	B(2)	N	O(1)	$O_{c=o}$	$C_{c=o}$	HOMO	LUMO
1'a	-	-	+0.265	-0.858	-	-	-	11.72	4.71
1'b	-	-	+0.545	-0.927	-0.694	-	-	11.26	5.84
1'c	-	-	+0.551	-0.776	-0.585	-	-	10.12	5.84
2'a	+0.077	-0.094[b]	+0.346	-0.906	-	-	-	11.76	2.94
2'b	+0.098	-0.106[b]	+0.595	-0.940	-0.658	-	-	11.54	4.50
2'c	+0.098	-0.114[b]	+0.609	-0.804	-0.546	-	-	11.31	4.28
3'a	+0.148	-0.208	+0.452	-0.919	-	-0.437	+0.175	10.94	2.14
3'b	+0.147	-0.195	+0.753	-0.942	-0.732	-0.463	+0.179	10.86	2.25
4	-	-	+0.183	-	-	-0.412	+0.148	11.61	2.35
$H_2C{=}O$	-	-	-	-	-	-0.416	+0.134	11.80	3.95
$H_3B{\bullet}OH_2$	+0.160	-0.102	-	-	-	-	-	11.80	4.27
$H_3B{\bullet}NH_3$	+0.104	-0.123	-	-0.933	-	-	-	11.12	4.65
BH_3	-	-0.041	+0.123	-	-	-	-	13.47	2.41

[a] Orbital energies are given in electron volts. [b] An average value of hydrogens of the BH_3 moiety.

Table 3. Energies of the formation (ΔE)[a] of adducts **2'a-c** and $H_3B{\bullet}NH_3$ and energies of the coordination of formaldehyde to **2'a-b** and borane (6-31G*//6-31G*).

Reaction							3-21G	4-31G	4-31G*	6-31G*
							ΔE[a]			
1'a	+	$H_3B{\bullet}OH_2$	->	**2'a**	+	H_2O	+59	+39	+20	+18
$H_2C{=}O$	+	$H_3B{\bullet}OH_2$	->	**4**	+	H_2O	+34	+19	+9	+7
1'b	+	$H_3B{\bullet}OH_2$	->	**2'b**	+	H_2O	+36	+25	-1	-3
1'c	+	$H_3B{\bullet}OH_2$	->	**2'c**	+	H_2O	+21	+10	-14	-17
NH_3	+	$H_3B{\bullet}OH_2$	->	$H_3B{\bullet}NH_3$	+	H_2O	-44	-50	-60	-61
2'a	+	$H_2C{=}O$	->	**3'a**			-75	-33	-37	-33
2'b	+	$H_2C{=}O$	->	**3'b**			-39	-3	+4	+8
H_3B	+	$H_2C{=}O$	->	**4**			-71	-41	-34	-31
H_3B	+	H_2O	->	$H_3B{\bullet}OH_2$			-105	-60	-43	-38

[a] Complexation energies given in kJ mol^{-1}.



2'a **2'a**

<B-N-B = 102.7°

2'b **2'b**

<B-N-B = 104.5°
<N-B-O = 121.6°

2'c **2'c**

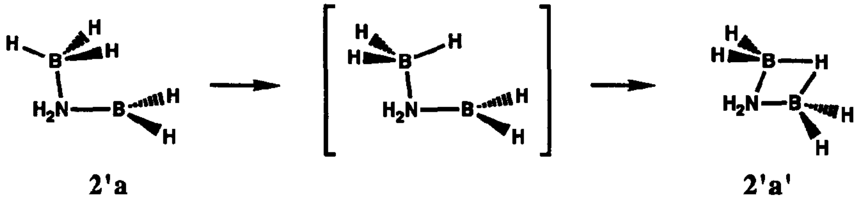
<B-N-B = 104.6°
<N-B-O = 110.2°

Scheme 1. Stereo representations of the optimized geometries of **2'a-c** calculated at the 6-31G* level. Some of the most important bond lengths and bond angles of **2'a-c** are included. The values in parenthesis are the corresponding bond lengths of the 6-31G* optimized structures of **1'a-c**.

During the formation of **2'a-c** the positive charge of the boron of **1'a-c** increases and the LUMO energy decreases (the most prominent component of the LUMO orbital of **1'a-c** is the $2p_z$ function of the ring boron which is perpendicular to the plane of the ring) which both indicate strengthening of the Lewis acidity of ring boron (see Table 2). This strengthening is inevitable for the coordination of a ketone to **2**. Interactions of $H_2C{=}O$ with **1'a-c** appeared to be repulsive even when the 3-21G basis (strongly overestimates these effects) was used.

The charge distribution of BH_3 moiety (see Table 2) undergo clear changes when a borane coordinates to the nitrogen of **1'a-c**. Polarization of the charge distribution bonds of BH_3 increases so that the hydrogens become more negative and the boron more positive. The polarization effect increases in the following order: **2'a** < **2'b** < **2'c** < $H_3B{\bullet}NH_3$. The strength of polarization correlates with the energy of formation of the adducts, with the length of the $B\text{-}NH_3$ bond of the adducts [the length of N-B bond of $H_3N\text{-}BH_3$ is 1.683 Å (6-31G*//6-31G*)], and with the HOMO energies of the adducts [the highest occupied molecular orbital (HOMO) of the adducts consist mostly of the 2p functions of the boron of BH_3 and the 1s functions of the hydrogens of BH_3]; i.e. the more negative energy of formation, or the shorter the N-B bond, or the less negative the HOMO energy, the stronger the polarization effect. If we assume that the reducing power of borane adducts correlates with the strength of polarization of the BH_3 moiety of the adducts, and compare values of **2'a-c** with the corresponding values of $H_2O\text{-}BH_3$ we may predict that **2'b-c** are stronger reducing agents than $H_2O\text{-}BH_3$. This implies that the potential reduction of a ketone by free $H_3B{\bullet}THF$ present in the reaction mixture should not seriously compete with the intramolecular reduction promoted by the BH_3-oxazaborolidine complex present only in catalytic amounts.

In the complexes **2'a-c** the both borons are adjacent to the same atom which may allow interactions similar to those present in diboranes. In the case of **2'a** the complex collapsed to a 4-membered cyclic aminodiborane structure **2'a'** when the hydrogen of BH_3 *trans* to the BH_2 moiety about the $N\text{-}BH_3$ bond was turned to a *cis* arrangement, as shown below.



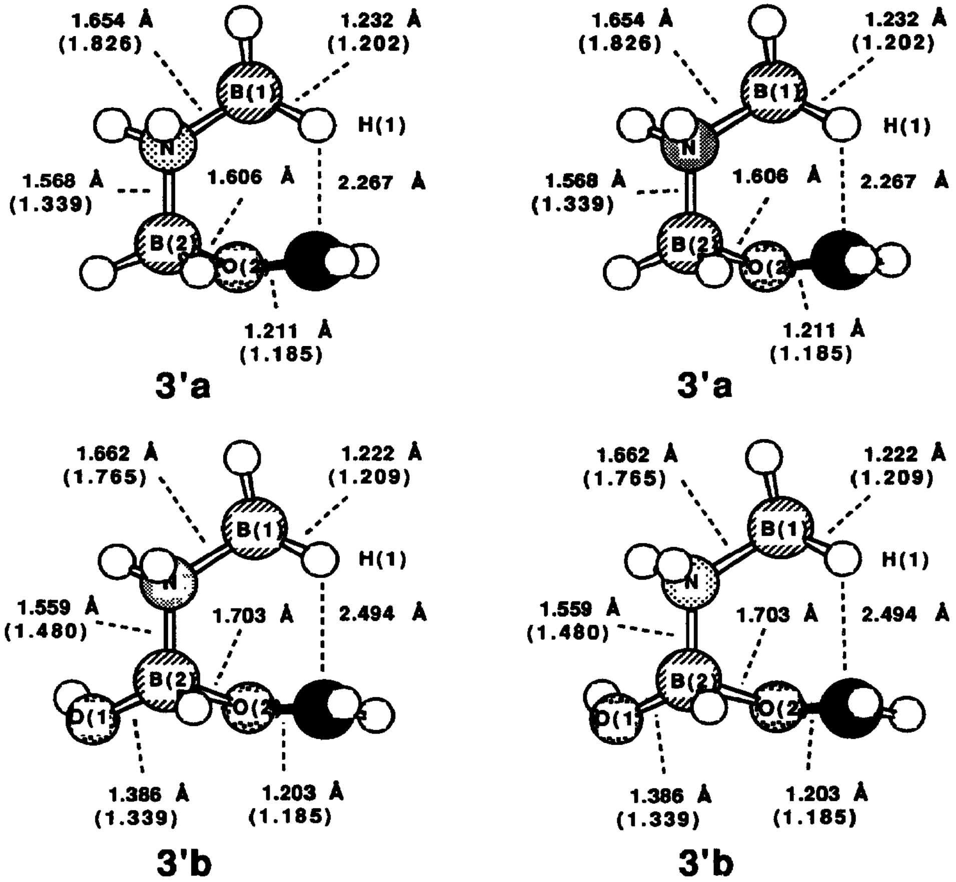
The energy of **2'a'** was 53 kJ mol^{-1} below **2'a** when calculated at the 6-31G*//6-31G* level. Similar collapses were observed neither in the case of **2'b** nor **2'c**. This type of property of **2'a** to form B-H-B bridges could be rationalized by comparing the LUMO energies of **2'a** and BH_3 with those of **2'b-c**. The LUMO value 2.94 eV of **2'a** is closer to that of BH_3 (2.41 eV) than values 4.50 eV and 4.28 eV of **2'b** and **2'c**. In order to prevent the collapse of **2'a** to **2'a'** shown above the structure **2'a** was forced to the *trans* geometry by using symmetry constraints. The structural parameters of **2'a'** calculated at the 6-31G*//6-31G* level were practically equal with the microwave structure of **2'a'** reported in the literature.[2e]

The energetic feasibility of the formation of borane adducts **2'a-c** depends on the properties of **1'a-c** (see Table 3). The energetics of the complex formation correlates with the HOMO energies of **1'a-c**; i.e. the less negative the HOMO energy of **1** the higher complexation energy in the formation of **2**. Practically the HOMO orbitals of **1'a-c** consist of the lone pairs of nitrogen accompanied with some density of the oxygen lone pairs. This is a useful result in that reliable HOMO and LUMO orbital energies may be provided by using methods which require less computational resources than ab initio calculations at the 6-31G* level. The energy of formation of borane adducts correlates with the same matters as the strength of polarization of the BH_3 moiety discussed above.

On the basis of energies shown in Table 3 we could predict that the formation of BH_3 adducts of ketones in the reaction of a ketone with $H_3B{\bullet}THF$ should not seriously compete with the borane-oxazaborolidine adduct formation (the energy of formation of **2'c** is 24 kJ mol^{-1} more negative that the energy of formation of **4**).

Coordination of Formaldehyde to Borane Adducts

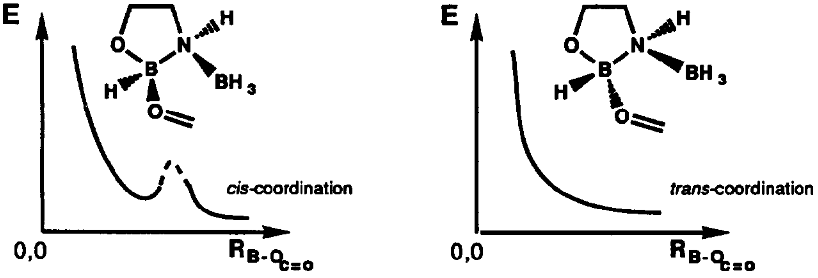
One of the main result of these calculations is that the formation of complexes similar to **3'a-b** is possible and it may be considered as an additional evidence for the validity of the previously suggested mechanism of the catalysis.[1]



Scheme 2. Stereo representations of the optimized geometries of **3'a-b** calculated at the 6-31G* level. Some of the most important bond lengths of **3'a-b** are included. The values in parenthesis are the corresponding bond lengths of the 6-31G* optimized structures of **2'a-b**.

The results imply that the hydride transfer from the N-BH_3 moiety to the carbonyl is not a spontaneous reaction and neither is the back elimination of the ketone. Thus there must be an energy barrier, first for the formation of 3, and then another barrier for the hydride transfer. We do not know yet how high the barriers are but the energy of formation of **3'b** (+8 kJ mol^{-1}) implies the minimum between these barriers to be just above the level of free **2'b** and formaldehyde. Since the energy needed for the formation of **3'b** is low and the structural changes occurring during the coordination process are minimal [the substituent on the boron of oxazaborolidine moiety (e.g. H, Me, *n*-Bu) moves slightly out of the O-B-N plane], we may predict the first barrier to be low enough not to prevent the addition of the ketone to **2** which means also that systems similar to **2** would be in equilibrium with their ketone complex until the ketone will be trapped by the hydride transfer.

These results prove only that complexes similar to **3** may exist but do not say how "narrow" the pathway from **2** to **3** would be. However, a curious observation was made when the site selectivity of the coordination of $H_2C=O$ to **2'b-c** was inspected. Namely, the *cis* configuration of the ketone and BH_3 appeared to be stable, but the $B\text{-}O_{C=O}$ interaction in the case of *trans*-coordinated complexes was repulsive even when calculated at the 3-21G level which strongly overestimates the $B\text{-}O_{C=O}$ interaction, as illustrated in Scheme 3.



Scheme 3. Comparison of energetics of the coordination of $H_2C=O$ to a borane complex in the case in which the C=O and BH_3 groups would be *cis* or *trans* about the ring of the oxazaborolidine.

Although the energy of formation of **3'a** (-33 kJ mol^{-1}) is somewhat higher than that of **3'b** (+8 kJ mol^{-1}) their structural parameters are surprisingly similar (see Scheme 2). The major structural difference between **3'a** and **3'b** appears in the length of the $B\text{-}O_{C=O}$ bond which is 0.097 Å shorter in the former.

The structural changes occurring in the formaldehyde moiety of **3'a-b** imply that formaldehyde is bound more tightly in **3'a** than in **3'b** (the C=O bond has lengthened more and the $B\text{-}O_{C=O}$ bond is considerably shorter in **3'a**). When formaldehyde adds to **2'a-b** the B(1)-N bond shortens and the B(2)-N bond lengthens. In the case of **2'a/3'a** the B(1)-N bond shortens by 0.172 Å and the B(2)-N bond lengthens by 0.169 Å whereas in the case of **2'b/3'b** the corresponding changes are 0.103 Å and 0.079 Å. These changes are related to the decreased electron demand of B(2) which is sp^3 hybridized in **3'a-b**. The consequently increasing electron density of the adjacent nitrogen strengthens the N-BH_3 bond, and what most important, it increases further the polarization of the BH_3 moiety (the negative charge of H(1) increases about 100% and the positive charge of the boron B(1) increases about 50% from the values of **2'a-b**).

If we compare the properties of BH_3 and **2'a-c** which correlate with Lewis acidity of the sp^2 hybridized boron we find out that BH_3 resembles closely **2'a**. The energy released in the coordination of formaldehyde to **2'a** is -33 kJ mol^{-1} and in the case of BH_3 the coordination energy is -31 kJ mol^{-1} (formation of **4**). Nevertheless, the $B\text{-}O_{C=O}$ bond of **4** appears to be substantially longer than the corresponding bond of **3'a-b** [length of the $B\text{-}O_{C=O}$ bond of **4** was 1.756 Å whereas that of **3'a** was 1.606 Å (6-31G*//6-31G* level)].

Inspection of the charge distributions of **2'a-b** and **3'a-b** is also revealing. Polarization of the BH_3 and

C=O moieties occur so that the hydrogen of BH_3 pointing towards the carbonyl group in **3'a-b** has almost two times more negative charge than the corresponding atom of **2'a-b**, whereas the boron atom of the BH_3 moiety has become more positive. In the carbonyl moiety the carbon has become more positive and the oxygen more negative, which is reasonable in that the electrons needed for the coordination of the carbonyl oxygen to the Lewis acid moiety must come from the formaldehyde. As we observed the *cis* configuration of the ketone and BH_3 moieties to be favored (see Scheme 3) we may further rationalize that observation in the light of the charge distribution and molecular orbitals calculated for **3'a-b**. Namely, in the case of the *cis* arrangement the negatively charged hydride moiety of BH_3 is spatially close to the positively polarized carbonyl which also adopts a conformation in which the plane of the polarized carbonyl of **3'a-b** is right below the hydride moiety. Around that conformation electrostatic interactions are favorable and also the dipole moment values of **3'a-b** are low.

On the basis of the net atomic charges shown in Table 2 one could expect **2'b** to be a stronger Lewis acid because the positive charge of B(2) of **2'b** is much higher than that of **2'a**. However, the LUMO values of **2'a-b** imply that **2'a** should react more readily with nucleophiles than **2'b** which is a contradictory conclusion to that we get on the basis of charges. If we accept the energies of formation of **3'a-b** to mirror the feasibility of formation of complexes similar to **3** in general we conclude that one should rely more on the LUMO energies of the corresponding Lewis acids (**2**) than the charges when trying to predict the ease of formation of the complexes analogous to **3**. Of course, more studies are needed to confirm this relation and also the effect of the solvent (THF) should be taken into account.

Conformational Analysis of the Ketone Complexes of Borane Adducts

Since we know the optimum structure of **3'b** it could be interesting to determine the conformational freedom of the carbonyl moiety in order to find the all directions from which the ketone may easily approach the Lewis acidic boron of the oxazaborolidine moiety of **3**. Because the structure of **3'b** is flexible in contrast to the cyclic arrangement of **3** we can study also the conformational effects of the $B\text{-}O_{OH}$ moiety and determined the rotation barrier of the $N\text{-}BH_3$ bond.

The conformational energies, dipole moments, and electron densities of the B-H(1) (for numbering of atoms see Scheme 2) and $B\text{-}O_{C=O}$ bonds were calculated as a function of the dihedral angle N-B-O=C of **3'b** as depicted in Diagram 1. The corresponding values of the dihedral angles B-N-B-H(1) and N-B-O-H are shown in Diagrams 2 and 3.

Diagram 1 shows that the formaldehyde ligand of **3'b** is at the optimum conformation when the torsion angle N-B-O=C is around 83°. In this conformation the most negatively charged hydrogen of the BH_3 group, i.e. H(1) (see Scheme 2), is located 2.5 Å above the carbonyl carbon in which case also the dipole moment of the system is close to its minimum. When the bond $B\text{-}O_{C=O}$ is rotated so that the positively charged carbon moves away from the BH_3 group both the energy and dipole moment of the system increase.

There are two shallow energy minima around angles -160° and -70°. In the former the positive moiety of formaldehyde points away from the BH_3 group and the dipole moment is at the maximum (all oppositely charged groups are as far from each other as possible). When we tried to perform a normal unlimited geometry optimization of that conformation in order to refine it further the catalyst moiety started to repel the formaldehyde and no energetic minima were found until the formaldehyde and catalyst moieties appeared at a distance longer than 3 Å. This observation reveals that electrostatic interactions between the BH_3 and carbonyl moieties are important for the stability of these ketone complexes. The second slightly stabilized conformation, in which the carbonyl group resides above the $N\text{-}B\text{-}O_{OH}$ plane of **3'b** is not possible in the case of 3, because the carbonyl group would collide with the phenyl substituent on the carbon adjacent to the oxygen of the oxazaborolidine moiety revealing the clever design of the catalyst 3. Thus we did not try to refine that conformation.

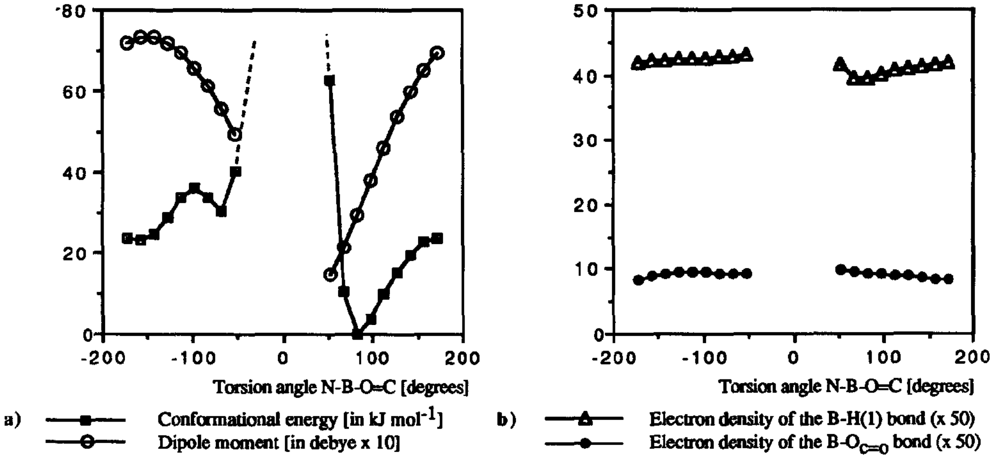


Diagram 1. Dependence of energies, dipole moments and electron densities of the B-H(1) and B-O$_{C=O}$ bonds on the torsion angle N-B-O=C of **3'b** calculated at the 6-31G* level.

On the basis of the part b of Diagram 1 we conclude that electron densities of the B-O$_{C=O}$ or B-H(1) bonds are practically independent of the conformational changes (remembering that bond lengths were kept fixed during the rotations), although it appears that the only recognizable minimum of the electron density of the B-H(1) bond overlaps with the minimum conformational energy (consequently the closer H(1) is to the carbonyl carbon the weaker B-H(1) bond). On the basis of the conformational analysis of the carbonyl moiety of **3'b** we may conclude in general that the geometry favorable for the hydride transfer appears also to be the global energy minimum for the coordination of a ketone to the catalyst, i.e. there is only one conformation clearly favored which happens to be the desired one.

Diagram 2 suggests that the orientation of the hydride moiety of **3'b** is also important. The conformational energy has a minimum when the torsion angle B-N-B-H(1) is -47° and hydride H(1) - carbonyl (C$_{C=O}$) distance is 2.5 Å whereas the H(1) - C$_{C=O}$ distance has the minimum at 2.1 Å when the angle B-N-B-H(1) is 0° and the energy of the system is about 24 kJ mol^{-1} above the minimum.

As the part a of Diagram 2 shows, the rotation barrier of the B(1)-N bond is about 30 kJ mol^{-1}. It is substantially higher than the corresponding barrier of BH_3-NH_3 which has been calculated to be 7.7 kJ mol^{-1} at the 6-31G* level[5c] (the experimental value 8.6 kJ mol^{-1}, microwave study).[6] This high rotation barrier may be related to electrostatic interactions present in **3'b** but not in BH_3-NH_3, e.g. there is a positively charged formaldehyde moiety right below the BH_3 group of **3'b** which likely attracts the negatively charged hydrogens of the BH_3 group.

On the basis of the conformational analysis of **3'b** shown in the part b of Diagram 2 one could conclude that the electron density of B-H(1) bond has the minimum (where the hydride would be so loose as it can be) value between the conformational energy optimum of the torsion angle B-N-B-H(1) (-47°) and minimum distance of H(1) and $C_{C=O}$ [the B-N-B-H(1) torsion angle is 0°]. As in the case of the torsion angle N-B-O=C the binding of formaldehyde to B(2) (i.e. the $B\text{-}O_{C=O}$ bond) is not significantly affected by these conformational changes and neither is the dipole moment of **3'b**.

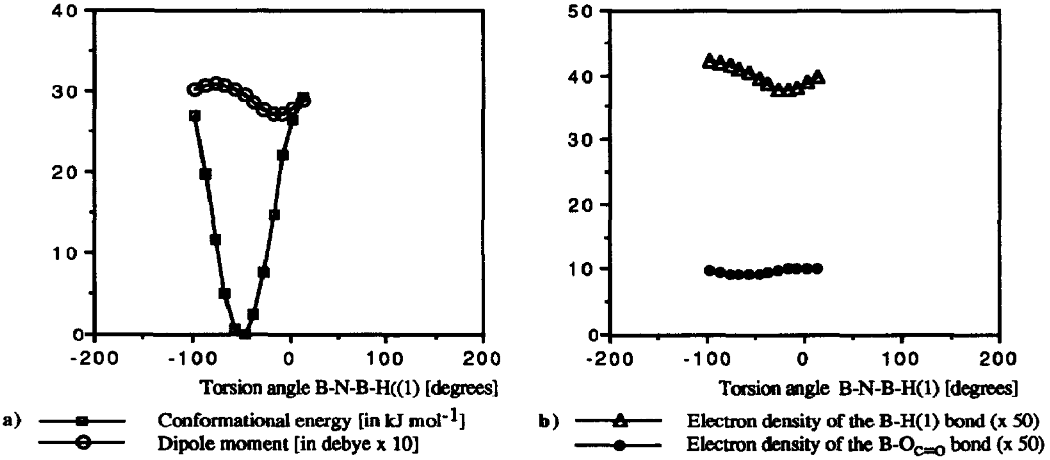


Diagram 2. Dependence of energies, dipole moments and electron densities of the B-H(1) and $B\text{-}O_{C=O}$ bonds on the torsion angle B-N-B-H(1) of **3'b** calculated at the 6-31G* level.

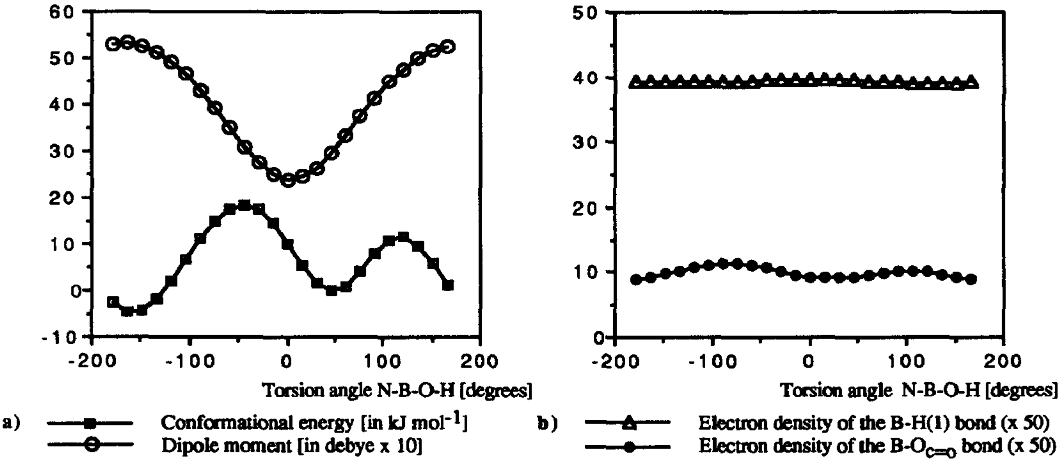
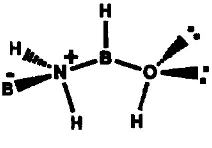
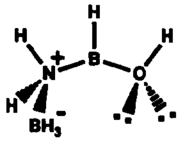


Diagram 3. Dependence of energies, dipole moments and electron densities of the B-H(1) and $B\text{-}O_{C=O}$ bonds on the torsion angle N-B-O-H of **3'b** calculated at the 6-31G* level.

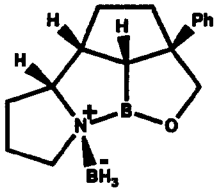
As shown in Diagram 3 the third part of the conformational analysis (rotation of the $B\text{-}O_{OH}$ bond) revealed two energetic minima, one around 46° and the other around -165° of the torsion angle N-B-O-H from which the latter was about 5 kJ mol^{-1} lower in energy. These two advantageous conformers are presumably formaldehyde complexes of borane adducts **2'b** and **2'b'** shown below. We performed a full geometry optimization also for **2'b'** at the 6-31G* level. It was found to be about 10 kJ mol^{-1} lower in energy than **2'b**.



2'b

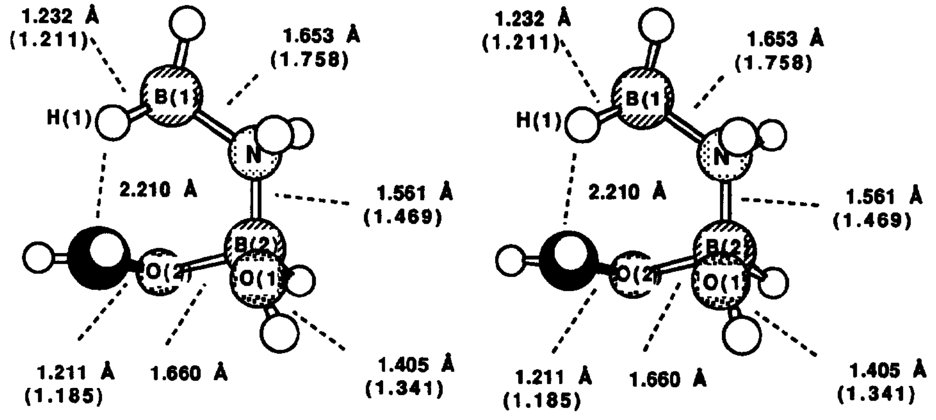


2'b'



2'd

The advantageousness of these conformations can be rationalized by inspecting orientations of the lone pairs (denoted above as "◀ :" and "⋯◀ :") of the O_{OH} moiety that have the best conjugation with the electron deficient boron of the O-B-N moiety (the boron is adjacent to the positively charged nitrogen) in these two systems. Actually the electron demand of that boron appears to increase when the hydrogen of the N-B-O-H moiety is rotated out of plane as implied by the electron density of the B-$O_{C=O}$ bond (the electron density increases) shown in the part b of Diagram 3. The electron density of the B-$O_{C=O}$ bond has two maxima, first one around 90° and the other around -90°. The minimum of dipole moment value appears to reside in the middle of those maxima, i.e. at 0°. In fact, on the basis of the results of the conformational analysis of the B-O_{OH} bond we conclude that analogs of **2'b'**, e.g. the molecule **2'd**, should work as catalysts in the same way as **2** does. A full geometry optimization at the 6-31G* level was eventually performed also for the other advantageous conformer of molecule **3'b**, in which the torsion angle N-B-O-H was about -165°, i.e. for **3'b'**. The structure **3'b'** appeared to be 13.4 kJ mol^{-1} more stable than **3'b**. The stereo representation of the optimized geometry of **3'b'** is shown in Scheme 4.



3'b' **3'b'**

Scheme 4. Stereo representation of the 6-31G* optimized geometry of the conformer of **3'b** (denoted as **3'b'**) in which the free electron pairs of the oxygen O(1) atom of the catalyst model are *cis* to the B(2)-N moiety [about the B(2)-O(1) bond] of the catalyst model. Some of the most important bond lengths are included. The values in parenthesis are the corresponding bond lengths of the 6-31G* optimized structure of **2'b'**.

When we compare the structures and the energies of formation of **3'b** and **3'b'** we see that in **3'b'** the carbonyl oxygen is more tightly bound to the catalysts that in the case of **3'b** (the B-$O_{C=O}$ bond is shorter and the C=O double bond is longer in **3'b'** than in **3'b**). The hydride of the BH_3 moiety is closer to the carbonyl group and the B-H(1) bond has lengthened considerably more in **3'b'** than in **3'b**. On the basis of all these evidences we may become convinced further that analogs of **3'b'** (i.e. systems similar to **2'd**) could be potential catalysts. Nevertheless, **2'd** and similar compounds would have less practical importance because they are more difficult to synthesize than **2** and analogs of it. Our computational studies on these exciting catalysts continue.

Acknowledgements

The University of Helsinki and the TEKES foundation are acknowledged for providing computational resources needed to carry out this study.

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