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Quantum Chemical Modeling of Chiral Catalysis. Part 6. On the Relative Stability of Dimers of Chiral Oxazaborolidines Used in the Catalytic Enantioselective Reduction of Ketones

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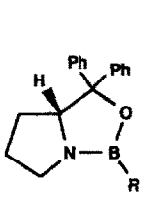
Abstract: - Dimerization of oxazaborolidines functioning as chiral catalysts was investigated by means of *ab initio* molecular orbital methods. The most stable form of the oxazaborolidine dimers studied was found to be structurally analogous to cyclodiborazane $(H_2B\text{-}NH_2)_2$. The heat of dimerization of $H_2B\text{-}NH_2$ was predicted at 298 K to be -22 kJ mol^{-1} (6-31G*//6-31G* energy corrected with respect to vibrational and temperature effects). Heats of dimerization of oxazaborolidines were predicted to be less negative than -22 kJ mol^{-1}. In a Lewis basic solvent the dimerization energy was predicted to be about 20 kJ mol^{-1} more positive than in nonpolar solvents.

INTRODUCTION

Oxazaborolidines (e.g. **1**) could be considered as one of the first and most important discoveries in the field of controlled construction of chiral molecules on the basis of catalysis. The enantioselective reduction of ketones by using THF•BH_3 as a source of hydrogen and **1** as a catalysts (CBS reduction)[1] was also one of the first catalytic enantioselective processes of which the enantioselectivity was very high and the most important features of the mechanism[1a,1e,1g] were understood. Since then, many therapeutically important molecules have been synthesized by applying the CBS reduction.[1] One of the latest achievements in this field is the efficient and general method developed for the enantioselective synthesis of α-amino acids.[2] Another area appears to be the enantioselective Diels-Alder reaction.[3]



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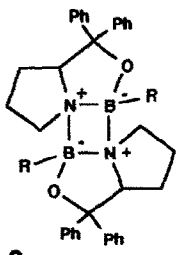

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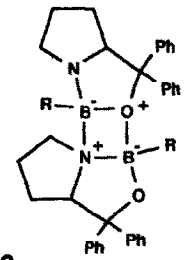

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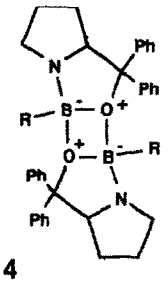

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Although oxazaborolidines and related structures containing assemblies of adjacent Lewis acidic and basic centers already form an important class of tools for establishing molecular chirality there could be still many potential catalysts which have not yet been discovered. Therefore, it would be important to know how these polar

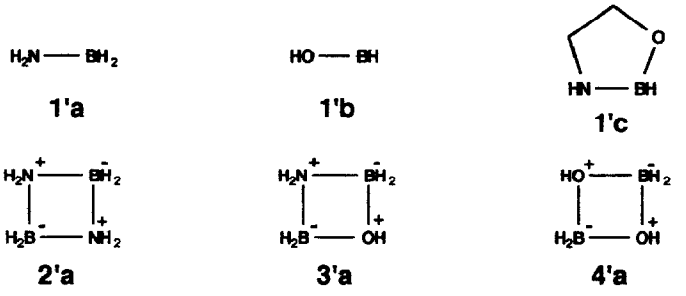
molecules behave. Furthermore, for the purpose of optimization of the performance of the catalysts it would be necessary to know the general properties of the catalysts, where the observable properties originate from, what are the properties most important for the high performance of the catalysts, and, of course, how these properties could be adjusted. After the discovery of the mechanism of CBS reduction by Corey *et al.*[1] oxazaborolidines have been studied also by using computational methods.[4] In those computational works,[4] as in other reports describing the mechanism of CBS reduction,[1] the oxazaborolidine system has been dealt with as a monomer although the catalyst (**1**) has been suggested to exist as a dimer (on the basis of NMR studies).[1a] Nevertheless, not much appears to be known about the structures of these dimers.

Dimerization of oxazaborolidines (**1**) would most probably be based on interactions between Lewis acidic and basic centers of two monomers. As the oxazaborolidine system has one Lewis acidic and two Lewis basic centers it was envisaged that three different types of dimers, i.e. **2** (*N,N*-adducts), **3** (*N,O*-adducts) and **4** (*O,O*-adducts), could be formed. Each of the dimers **2**, **3** and **4** may exist in two isomeric forms, i.e. one in which the oxazaborolidine rings are on the same side of the 4-membered ring (*syn* adducts) and the other in which they are on the opposite sides (*anti* adducts).

The parent structure of the *N,N*-adducts (**2**), cyclodiborazane $(H_2B\text{-}NH_2)_2$, appeared to be considerably well characterized[5] whereas no experimental observations on analogs of **3** and **4** seem to be reported in the literature. Several structures analogous to the *N,O*-adducts (**3**) have been discussed in the previous parts of this series.[4d] On the basis of these studies[4d,5] and an early computational study[6] on the formation of $(H_2B\text{-}OH)_2$ one could predict that *O,O*-adducts (**4**) would hardly be formed and that the formation of *N,N*-adducts (**2**) would be energetically more favorable than that of the corresponding *N,O*-adducts (**3**). On the other hand, as the cyclic systems of **2**, **3** and **4** should be more strained than those of the corresponding nonfused parent systems it is unclear how much one could rely upon conclusions drawn by examining the parent systems only. In order to understand properties and the formation of **2**, **3** and **4**, other dimer models, representing the dimeric oxazaborolidine system more closely than those derived from $H_2B\text{-}NH_2$ or $H_2B\text{-}OH$, need to be studied.

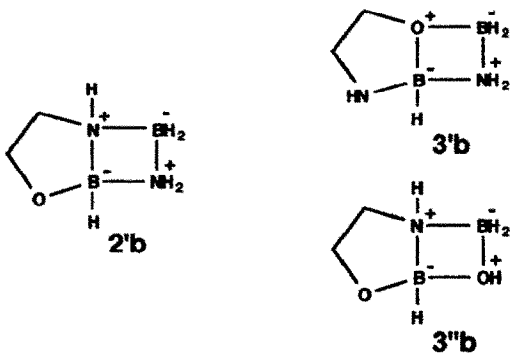
The aim of this work was to study structural properties and relative stabilities of **2**, **3** and **4** by means of *ab initio* molecular orbital calculations. Standard *ab initio* calculations were carried out by using the Gaussian 80[7] series of programs at the 3-21G, 4-31G, 6-31G, 4-31G* and 6-31G* levels. Modeling techniques similar to those applied in the case of previous studies of this series[4] were employed, i.e. simple models analogous to the actual catalytically active structures were examined.

The systems **1'a**, **1'b** and **1'c** were used as models of oxazaborolidines (**1**). The relative stability of 4-membered rings of **2** - **4** was determined by inspecting the parent structures **2'a**, **3'a**, and **4'a**. Effects of fusing an oxazaborolidine ring to the parent systems were studied by using the models **2'b**, **3'b**, **3''b** and **4'b**.



Relative stabilities of dimeric *anti* and *syn* adducts, each consisting of two molecules of **1'c**, were

inspected by using models 2'c, 3'c and 4'c (for *anti*) and 2'c', 3'c' and 4'c' (for *syn*). These adducts were best studied at the 6-31G level (polarization functions were not used because inclusion of *d*-functions would have given rise to extremely time demanding calculations). Reliability of the results provided on the *anti* and *syn* adducts was assessed by comparing properties of these adducts with those of the corresponding smaller models 2'a-b, 3'a-b and 4'a-b inspected at both the 6-31G and 6-31G* levels. No other calculations on the structures 2'b-c, 2'c', 3'b-c, 3'c', 4'b-c or 4'c' appeared to have been published. Properties of the models 1'a-c, 2'a, 3'a and 4'a have been discussed in the literature.[4-6]



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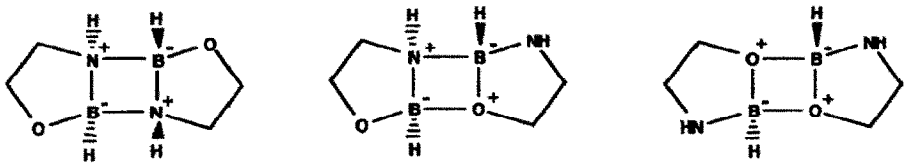

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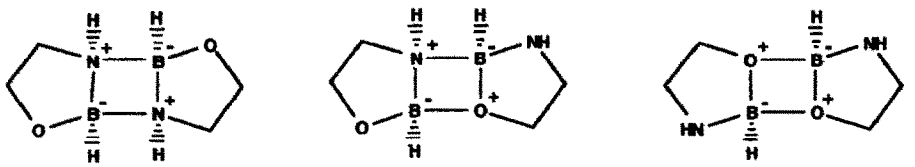


RESULTS AND DISCUSSION

Total energies and dipole moments calculated are summarized in Table 1. The optimized (6-31G*//6-31G*) structures of 2'b, 3'b, 3''b, and 4'b are shown in Scheme 1 and the optimized (6-31G//6-31G) structures of 2'c, 2'c', 3'c and 3'c' in Schemes 2 and 3.

The Parent Systems

The optimized structure of 2'a (6-31G*//6-31G*) resembles that reported by Armstrong and Perkins.[5c] In their optimized structure of 2'a the B-N bond length was 1.63 Å and the B-N-B angle 86° as the corresponding

values of this work obtained at the 6-31G*//6-31G* level were 1.608 Å and 87.7°, respectively. The dimerization energy was -43 kJ mol^{-1} (the most negative value among those of **2'a**, **3'a** and **4'a** calculated at the 6-31G*//6-31G* level, see Table 2) as the corresponding energy calculated by Armstrong and Perkins was about -11 kJ mol^{-1} (they, however, anticipated already that the dimerization energy should go down to the level of -40 kJ mol^{-1} with the improving quality of basis set).[5c]

Table 1. Total energies and dipole moments of **1'a-c**, **2'a-c**, **2'c'**, **3'a-c**, **3''c**, **3'c'**, **4'a-c** and **4'c'**.[a]

Structure	3-21G//3-21G		4-31G//4-31G		6-31G//6-31G		4-31G*//4-31G*		6-31G*//6-31G*	
	E[a]	D[a]	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	-100.76196	1.91	-101.17676	1 87	-101.27793	1.89	-101.22430	1.68	-101.32139	1.68
1'c	-232.01452	3.16	-232 95883	3.18	-233.19703	3.21	-233.07225	2.65	-233.29859	2.67
2'a	-162.12125	0	-162.77008	0	-162.93633	0	-162.83629	0	-162.99470	0
2'b	-313 09151	1.50	-314 34825	1.48	-314.66799	1.51	-314.49312	0.93	-314.79795	0.96
2'c	-464.06296	0.18	-465.92605	0.19	-466.39984	0.19	-	-	-	-
2'c'	-464.05940	1.09	-465.92167	0 76	-466.39495	0.67	-	-	-	-
3'a	-181.84477	0.82	-182.57271	1.01	-182.75550	1.07	-182.64372	1 45	-182.81873	1.48
3'b	-313.07654	2 77	-314.33241	2.65	-314.65231	2.64	-314.47255	1.86	-314.77721	1.83
3''b	-332.82019	1.57	-334 15586	1.85	-334.49239	1.90	-334.30493	1.65	-334.62681	1.75
3'c	-464 05069	3.12	-465.91389	3.30	-466 38775	3.36	-	-	-	-
3'c'	-464.04928	3.62	-465 91150	3.68	-466.38494	3.69	-	-	-	-
4'a	-201.56429	1.94	-202 37270	0	-202.57247	0	-202.45114	0.01	-202.64319	0
4'b	-332.80446	2.33	-334 13945	2.25	-334.47633	2.28	-334.28267	1.82	-334.60408	1.78
4'c	-464.03966	0.18	-465.90276	0 20	-466.37667	0.20	-	-	-	-
4'c'	-464.04013	4.27	-465.90177	4.25	-466 37543	4 24	-	-	-	-

[a] Total energies (E) given in hartrees and dipole moments (D) in debye.

Properties of **3'a** have been discussed earlier.[4d] Comparison of the structures of **2'a** and **3'a** reveals that the B-N bonds shorten as one of the nitrogens of **2'a** is changed to an oxygen (by 0.012 Å, 6-31G*//6-31G*) whereas the B-N-B angle enlarges only by 0.3°. When the nitrogen of **3'a** is changed to an oxygen the B-O bond shortens from 1.596 Å of **3'a** to 1.556 Å of **4'a** and the B-O-B bond angle decreases from 90.0° to 89.5° (6-31G*//6-31G*). The optimized length of the B-O bond of **4'a** of this work is somewhat longer than that reported by Flood and Gropen[6] (1.53 Å, *ab initio* calculations, partially optimized structural parameters).

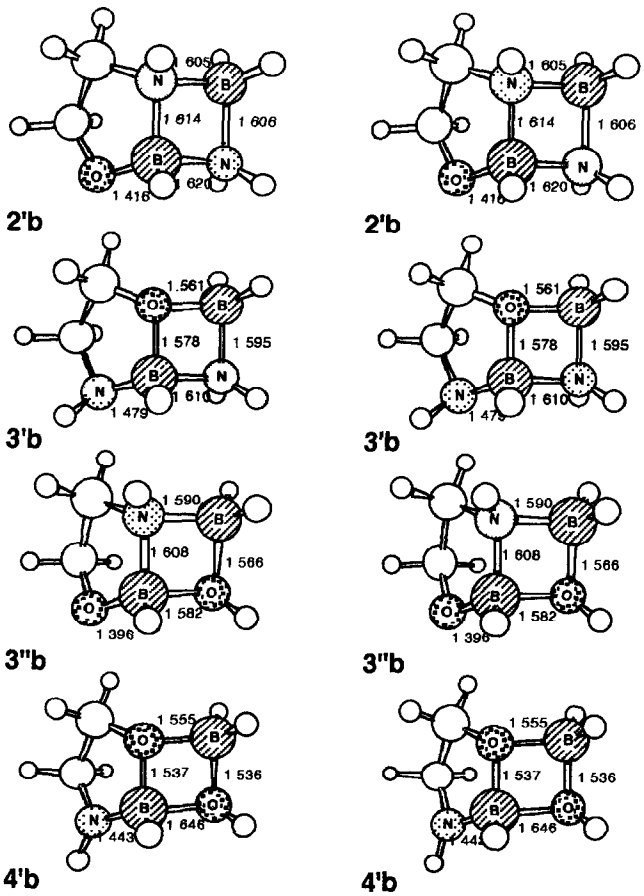
Table 2. Energies of the formation of the parent dimers **2'a**, **3'a** and **4'a**.[a]

Reaction	3-21G	4-31G	6-31G	4-31G*	6-31G*
				ΔE[a]	
H_2B-NH_2 (1'a) + H_2B-NH_2 (1'a) -> 2'a	-90	-34	-28	-46	-43
H_2B-NH_2 (1'a) + H_2B-OH (1'b) -> 3'a	-104	-46	-39	-26	-22
H_2B-OH (1'b) + H_2B-OH (1'b) -> 4'a	-106	-50	-44	-7	-1

[a] Energies (ΔE) given in kJ mol^{-1}.

Energies of the formation of the parent dimers shown in Table 2 are interesting in that on the basis of calculations done without polarization functions (e.g. at the 6-31G level) the relative order of stabilities of **2'a**, **3'a** and **4'a** is reverse to that obtained when polarization functions were included (e.g at the 6-31G* level). At the

6-31G* level the stability of the ring system appears to decrease from the most negative value of **2'a** (i.e. -43 kJ mol^{-1}, see Table 2) by steps of about 21 kJ mol^{-1} to the level of **4'a** (i.e. -1 kJ mol^{-1}, see Table 2) as nitrogen atoms are replaced by oxygens. It looks also as if the dimeric system **4'a** [i.e. $(H_2B\text{-}OH)_2$] would be hardly stabilized at all with respect to the corresponding monomers. This conclusion was drawn also by Flood and Gropen,[6] who estimated the energy of the formation of **4'a** to be somewhat higher, about +30 kJ mol^{-1}.

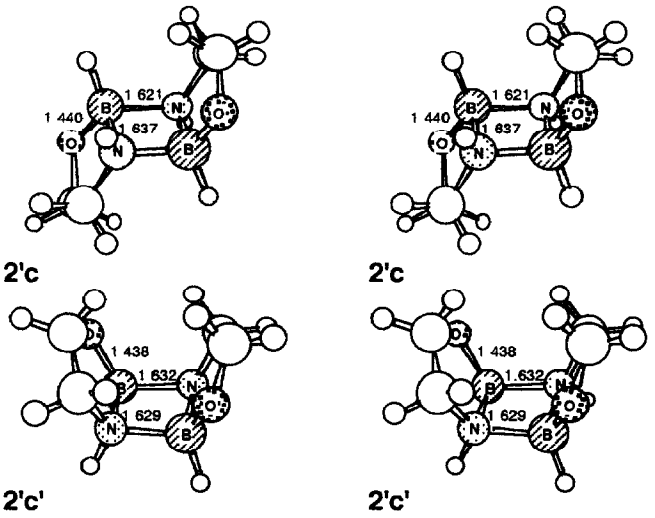


Scheme 1. Stereo representations of the optimized (6-31G*//6-31G*) structures of adducts **2'b**, **3'b**, **3"b** and **4'b** [adducts of $H_2B\text{-}NH_2$ (**1'a**) or $H_2B\text{-}OH$ (**1'b**) to 1,3,2-oxazaborolidine (**1'c**)]. Some of the most important bond lengths [in Å] are shown (the corresponding B-N and B-O bond lengths of **1'c** were 1.400 Å and 1.365 Å and those of $H_2B\text{-}NH_2$ and $H_2B\text{-}OH$ 1.389 Å and 1.345 Å).

Adducts of Aminoborane and Hydroxyborane to 1,3,2-Oxazaborolidine

Optimized structures (6-31G*//6-31G*) of the adducts (i.e. **2'b**, **3'b**, **3"b** and **4'b**) of aminoborane (**1'a**) and hydroxyborane (**1'b**) to 1,3,2-oxazaborolidine (**1'c**) are depicted in Scheme 1. Energies of the formation of **2'b**, **3'b**, **3"b** and **4'b** are shown in Table 3.

The structure of **2'a**, described also in the literature,[5] resembles much that of **2'b** (see Scheme 1). Only one of the B-N bonds of **2'b** deviates 0.012 Å from the value 1.608 Å of **2'a**. Other bond lengths are similar withing the range of alteration of 0.006 Å. Also the B-N-B bond angles of **2'b** (87.9° and 88.2°) are close to the corresponding value of **2'a** (87.7°). In contrast to **2'a** the 4-membered ring of **2'b** is not completely planar; the torsion angle B-N-B-N of **2'b** is 1.7°. The oxazaborolidine moiety of **2'b** was not planar either as the torsion angle measured along the pathway of the bonds N-C-C-O turned out to be 29.4°.



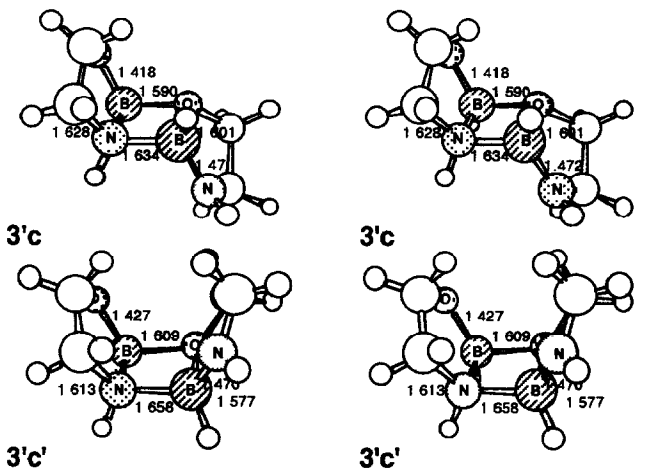
Scheme 2. Stereo representations of the optimized (6-31G//6-31G) structures of *N,N*-adducts **2'c** (*anti* configuration of monomers) and **2'c'** (*syn* configuration of monomers). The adducts are dimers of 1,3,2-oxazaborolidine (**1'c**). Some of the most important bond lengths [in Å] are shown (the corresponding B-N and B-O bond lengths of **1'c** were 1.406 Å and 1.390 Å).

As the adducts **2'a** and **2'b**, also **3'a** and **3'b** are structurally rather similar; e.g. the B-N and B-O bond lengths of **3'b** deviate from the corresponding values of **3'a**[4d] only by 0.011 Å or less, but the 4-membered oxazadiboretane ring system of **3'b** is more planar than that of **3'a** (e.g. the torsion angle B-N-B-O in the 4-membered ring of **3'b** is 2.5° whereas the corresponding value of **3'a** is 10.0 °). The small difference between structural parameters of **3'a** and **3'b** implies that fusing a five membered ring to **3'a** would not affect the B-N or B-O bonds of the oxazadiboretane ring in significant amounts. Even the configuration of nitrogen of the oxazaborolidine moiety of **3'b** is clearly tetrahedral [e.g. in the case of **3'b** the torsion angle H-N-B-H (N and B in the oxazaborolidine moiety) is 9.3° and the torsion angle H-N-B-O (N, B and O in the oxazaborolidine moiety) -118.4°; the corresponding values of the monomeric oxazaborolidine are ≈ 0° and 180°].

As properties of **3''b** (6-31G*//6-31G*) have been described in the previous parts of the series of these reports[4d] only differences of properties of **3'b** and **3''b** are mentioned here. A comparison of bond lengths of **3'b** and **3''b** (see Scheme 1) reveals that the oxazadiboretane system would not be affected much if one fuses either a C-C-N fragment or a C-C-O fragment to it (provided that the hetero atom of the fragment would be bound to a boron of the oxazadiboretane ring). Differences of bond lengths of the analogous parts of the oxazadiboretane rings of **3'b** and **3''b** are only 0.005 Å or less (see Scheme 1).

The structure of **4'b** is interesting in that, in contrast to the nitrogen of the oxazaborolidine moiety of the

corresponding aminoborane adduct (**3'b**), the configuration of nitrogen of the oxazaborolidine moiety of **4'b** is clearly planar (see Scheme 1). This means, however, that the same π-binding interaction as that observed in a free oxazaborolidine (e.g. **1**) between the nitrogen and boron must still partially exist also in the oxazaborolidine moiety of **4'b**. The same is implied by the bond lengths of the 4-membered dioxadiboretane ring of **4'b**. Namely, as the empty π-orbital of the boron of the oxazaborolidine moiety interacts already with the adjacent nitrogen it would be less Lewis acidic and consequently it would form a weaker bond to the oxygen of the dioxadiboretane ring. This is indeed what can be seen having taken place when the B-O bond lengths of **4'b** are inspected (see Scheme 1). The B-O bond from the boron of the oxazaborolidine moiety to the oxygen of the hydroxyborane (1.646 Å, see Scheme 1) is longer than any other B-O bond in **4'b** or in any other structure of this class of dimers studied at the 6-31G* level. Conclusions drawn from Mulliken overlap populations of **4'b** are consistent with the above ones; e.g. the B-O overlap in the long bond is only 66 % of that of the next most low B-O overlap (the bond from the boron of the hydroxyborane moiety to the oxygen of the oxazaborolidine) in the dioxadiboretane ring system of **4'b**. The highest B-O overlap populations of **4'b** were in the B-O bonds of the oxazaborolidine and hydroxyborane moieties.



Scheme 3. Stereo representations of the optimized (6-31G//6-31G) structures of *N,O*-adducts **3'c** (*anti* configuration of monomers) and **3'c'** (*syn* configuration of monomers). The adducts are dimers of 1,3,2-oxazaborolidine (**1'c**). Some of the most important bond lengths [in Å] are shown (the corresponding B-N and B-O bond lengths of **1'c** were 1.406 Å and 1.390 Å).

Table 3. Energies[a] of the formation of fused dimer models **2'b**, **3'b**, **3''b**, and **4'b**.[b]

Reaction					3-21G	4-31G	6-31G	4-31G*	6-31G*
							ΔE[a]		
1'c	+	H_2B-NH_2 (**1'a**)	->	**2'b**	-88	-29	-22	-30	-27
1'c	+	H_2B-NH_2 (**1'b**)	->	**3'b**	-49	+13	+20	+24	+28
1'c	+	H_2B-OH (**1'b**)	->	**3''b**	-115	-53	-46	-22	-18
1'c	+	H_2B-OH (**1'b**)	->	**4'b**	-74	-10	-4	+36	+42

[a] Energies (ΔE) given in kJ mol^{-1}. [b] See Scheme 1.

Energies of the formation of fused dimer models **2'b**, **3'b**, **3''b**, and **4'b** are shown in Table 3. The primary conclusion drawn on the basis of a comparison of the energies shown in Table 2 and 3 is that changing one of the hydrogens adjacent to a boron of either **2'a**, **3'a** or **4'a** to an oxygen or a nitrogen together with the formation of the fused 4,5-ring system clearly destabilizes the dimer. All energies of the formation of **2'b**, **3'b**, **3''b** and **4'b** (see Table 3) are less negative than those of the corresponding parent systems **2'a**, **3'a** and **4'a** (see Table 2). In contrast to the relative order of energies of the formation of parent systems **2'a**, **3'a** and **4'a** based on the total energies calculated at the 6-31G and 6-31G* levels (see Table 2), the relative order of the 6-31G energies of the fused systems **2'b**, **3'b**, **3''b** and **4'b** (see Table 3) appears to be the same as that of the corresponding values provided at the 6-31G* level.

When the energies of the formation of **2'b** and **3'b** are compared we see that the coordination of **1'a** to the B-N side of the oxazaborolidine ring of **1'c** is favoured by 55 kJ mol^{-1} (6-31G*//6-31G*) over that to the B-O side. Surprisingly, about the same difference can be seen in the case of **3''b** and **4'b** where the coordination of **1'b** to the B-N side of **1'c** is favoured by 50 kJ mol^{-1} over that to the B-O side. Furthermore, as the energy of formation of **4'b** is already as positive as +42 kJ mol^{-1} one could predict that related fused dioxadiboretane systems would hardly be formed in the case of actual working catalysts.

Dimers of 1,3,2-Oxazaborolidine

Energies of the formation of all dimeric forms of 1,3,2-oxazaborolidine studied are shown in Table 4. The optimized structures (6-31G//6-31G) of oxazaborolidine dimers **2'c** and **2'c'** are shown in Scheme 2 and those of **3'c** and **3'c'** in Scheme 3 (the first four most stable forms).

Table 4. Energies of the formation of dimeric forms **2'c**, **2'c'**, **3'c**, **3'c'**, **4'c** and **4'c'** of 1,3,2-oxazaborolidine (**1'c**).[a]

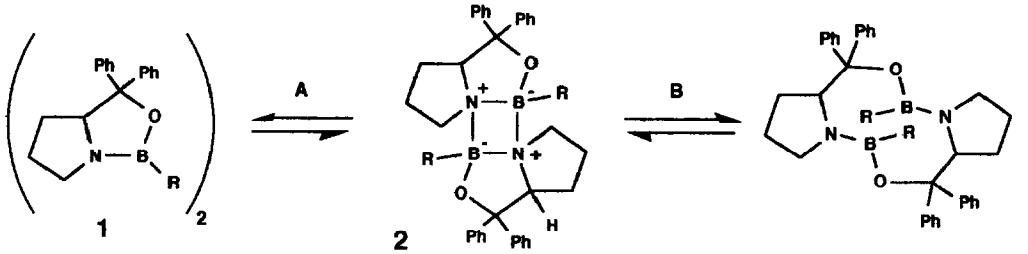
Reaction					3-21G	4-31G	6-31G
						ΔE^a	
1'c	+	1'c	->	2'c	-89	-22	-15
1'c	+	1'c	->	2'c'	-80	-11	-2
1'c	+	1'c	->	3'c	-57	+10	+17
1'c	+	1'c	->	3'c'	-53	+16	+24
1'c	+	1'c	->	4'c	-28	+39	+46
1'c	+	1'c	->	4'c'	-29	+42	+49

[a] Energies (ΔE) given in kJ mol^{-1}

As in the case of the adducts **2'a-b**, **3'a-b** and **4'a-b** (see Tables 2 and 3), also the formation of *N,N*-adducts of 1,3,2-oxazaborolidines (**2'c** and **2'c'**) turned out to be clearly more favoured (see Table 4) than that of the corresponding *N,O*-adducts (**3'c** and **3'c'**) or *O,O*-adducts (**4'c** and **4'c'**). Purely on the basis of energies of the formation of **2'c** and **2'c'** the formation of dimeric *anti*-adducts could be predicted to be generally somewhat favoured over the corresponding *syn*-adducts ($\Delta E_{2'c\text{-}2'c'}$ = 13 kJ mol^{-1}, see Table 4). However, the formation of *N,N-syn*-adducts of actual working catalysts (e.g. **1**) would be hampered by repulsive, almost overlapping, interactions between two of the four *C*-5 phenyl groups of the oxazaborolidine rings of the dimers. The overlap can be seen clearly if one imagines all the hydrogens of carbons adjacent to the oxazaborolidine oxygens of the *syn*-adduct (**2'c'**, see Scheme 2) to be replaced by phenyl groups. The same operation in the case

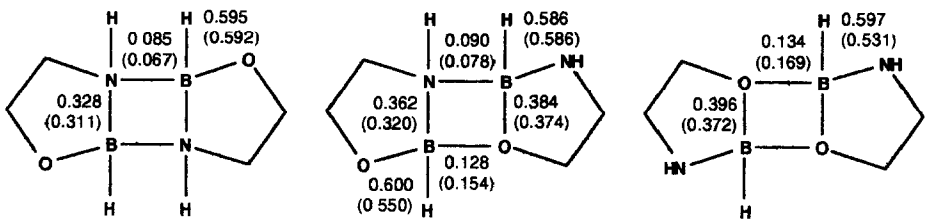
of the corresponding *anti*-adduct **2'c** reveals that no similar overlap would exists. Namely, in the corresponding derivative of **2'c** the phenyl groups would reside on opposite sides of the 4-membered ring of **2'c**.

Comparison of bond lengths of the *N,N*-adducts **2'c** and **2'c'** (see Scheme 2) reveals that lengths of all the B-N bonds are rather similar (the largest difference ≈ 0.016 Å). Furthermore, in the case of the more stable one of the dimers (i.e. **2'c**) the B-N bonds between the monomeric units are even slightly shorter than those of the oxazaborolidine moieties. Consequently, one could envisage that as a dimer of an oxazaborolidine decomposes, rupture of the B-N bonds of the 4-membered ring could occur equally to both directions of the two theoretically possible 2+2 cleavages (corresponding to the equilibriums **A** and **B**, see Scheme 4); one leading back to the monomers (equilibrium **A**) and the other to a 10-membered ring system (equilibrium **B**).



Scheme 4. Two theoretically possible 2+2 cleavages of the dimeric *N,N*-adducts (**2**) of oxazaborolidine (**1**).

The hypothetical reactions illustrated in Scheme 4 lead, however, to a conflict with results of early NMR-studies of Corey *et al.*[1a] The species representing dimeric oxazaborolidine has been observed to be in equilibrium with the corresponding monomer; formation of any other species (e.g. the 10-membered ring system arising from the proposed equilibrium **B**, see Scheme 4) was not mentioned.[1a] Therefore, on the basis of bond lengths of these dimers it would be difficult to explain why only the monomer - dimer equilibrium (**A**) would be seen and the other process (**B**) not. Inspection of Mulliken overlaps between adjacent B, N and O atoms of **2'c**, **2'c'**, **3'c**, **3'c'**, **4'c** and **4'c'** shown in Scheme 5 would be highly helpful for solving this problem.



Scheme 5. Mulliken overlaps of adjacent B, N and O atoms of dimeric *anti*-adducts **2'c**, **3'c** and **4'c** of 1,3,2-oxazaborolidine (on the basis of 6-31G//6-31G). The values in parentheses are the corresponding overlaps of the *syn*-adducts (**2'c'**, **3'c'** and **4'c'**). Formal charges are not included for purposes of clarity.

In the case of both the B-N and B-O overlaps those holding the monomers together are substantially lower than others between atoms belonging to the same oxazaborolidine moieties (e.g. in the case of **2'c** the B-N overlaps between different oxazaborolidine moieties are only about 22 - 26 % of the B-N overlaps of the fusion bonds, see Scheme 5). As so much less electron density appears to be involved in the binding responsible for holding the oxazaborolidine moieties together than in the fusion bonds dimers of oxazaborolidines could be best described as two molecules which can adopt a configuration in which the most Lewis acidic and Lewis basic centers of the molecules can favorably interact with not much formation of bonds based on sharing electron density between the interacting atoms. As an obvious solution to the problem illustrated in Scheme 4 one observes that cleaving the bonds holding the oxazaborolidine moieties together (weak interactions, see Scheme 5) would be much easier than cleaving the B-N fusion bonds preventing the 5-membered oxazaborolidine ring from opening (strong interactions, see Scheme 5); i.e. the equilibrium **B** indeed should not play any significant role in the dimerization of oxazaborolidines.

The above deduction of the high preference for the equilibrium **A** over the **B** one (see Scheme 4) could be confirmed further by inspecting the B-N overlaps of the *N,O*-adducts **3'c** and **3'c'** (see Scheme 5) where the B-N overlap holding the monomers together is only 25 % of the B-N bond preventing the 5-membered oxazaborolidine ring from opening. A similar relationship can be found also in the case of B-O bonds of the 4-membered rings of **3'c** and **3'c'**; the B-O overlap holding the monomers together is 33 % of that of the B-O bond maintaining the oxazaborolidine ring system. Even in the case of the energetically least advantageous *O,O*-adducts (**4'c** and **4'c'**) the same applies, the B-O overlaps between different oxazaborolidines are only 34 % of those of the B-O fusion bonds.

On the basis of results of this computational study it looks as if the most stable form of dimeric oxazaborolidine would be analogous to the *N,N-anti*-adduct **2'c** (see Scheme 2). As the energy of formation of **2'c** was found to be -15 kJ mol^{-1} (i.e. rather low but clearly negative, see Table 4) and the energies of the formation of *N,N*-adducts appeared to become more negative with improving quality of basis sets (e.g. the energy of formation of **2'a** was -28 kJ mol^{-1} at the 6-31G level and -43 kJ mol^{-1} at the 6-31G* level, see Table 2; in the same way the energy of formation of **2'b** was -22 kJ mol^{-1} at the 6-31G level and -27 kJ mol^{-1} at the 6-31G* level, see Table 3) the energy of the formation of **2'c** if calculated at the 6-31G* level would be probably slightly more negative than -15 kJ mol^{-1} obtained without polarization functions. Therefore, a reasonable estimate for the 6-31G*//6-31G* energy of the formation of **2'c** could be -20 ± 5 kJ mol^{-1}. This energy could be corrected with respect to the basis set superposition error by using the counterpoise method[8] but as the correction has been reported to be unreliable[9] at the polarization level it was not attempted (the quality of basis sets should be improved instead of applying the counterpoise method).[9] Furthermore, this error would have a smaller effect on the relative energies of different coordination geometries than on the absolute coordination energies.

As an energy estimated on the basis of *ab initio* calculations represents only the electronic contribution of the actual enthalpy of the dimerization the difference in vibrational energy between the monomer and dimer together with temperature effects should be taken into account. Estimation of vibrational energies would, however, require a complete vibrational analysis of the monomer and dimer. As vibrational analysis of neither dimeric oxazaborolidines nor monomers has been published [so far even the structure of the dimer(s) has been almost a matter of speculation only] and calculating the vibrational frequencies followed by a normal coordinate analysis would have been a major project on its own, no vibrational correction of the energies of **1'c** or **2'c** was attempted. On the other hand, as vibrational analyses of both the monomer **1'a** and the parent model of *N,N*-adducts (**2'a**) have been published[5b] the dimerization energy of **1'a** (the energy of formation of **2'a**) obtained at the 6-31G* level was corrected with respect to both the zero-point energy [$H_{vib}(0)$] and the vibrational energy at 298 K [$H_{vib}(298)$] by using the frequencies shown in Table 5. Temperature effects (ΔH_T) were estimated by assuming

classical equipartition of energy among the rotational and translational degrees of freedom (1/2 *RT* for degree of freedom) and assuming the *PV* work term of $(\Delta n)RT$ as shown below:

$$\Delta H_R^{298} = \Delta E_{elec} + \Delta H_T + \Delta H_{vib}(0) + \Delta H_{vib}(298)$$

$$\Delta H_T = \Delta E_{trans} + \Delta E_{rot} + (\Delta n)RT$$

$$E_{trans} = 3/2\ RT \qquad E_{rot} = 3/2\ RT$$

$$H_{vib}(0) = 1/2\ Nh\sum \nu_i \qquad H_{vib}(T) = N\sum h\nu_i/(e^{h\nu_i/kT} - 1)$$

The zero-point energies $[H_{vib}(0)]$ calculated by using the above formulae and the vibrational frequencies shown in Table 5 were 121.1 kJ mol^{-1} for **1'a** and 271.7 kJ mol^{-1} for **2'a**. The vibrational contribution at 298 K was only 1.2 kJ mol^{-1} for **1'a** and 3.8 kJ mol^{-1} for **2'a**. As the temperature effects summarize to -9.9 kJ mol^{-1} and the electronic contribution was -43 kJ mol^{-1} (see Table 2) we obtain the dimerization energy of **1'a** as ΔH_R^{298} = (-43 + 29.5 + 1.4 - 9.9) kJ mol^{-1} = -22 kJ mol^{-1}. This energy could be considered also as an estimate of the energy of dimerization of **1'a** in a nonpolar solvent. All the other dimerization energies calculated (see Tables 2 - 4) are clearly less negative than that of **1'a** (see Table 2). Therefore, it could be reasonable to predict the value -22 kJ mol^{-1} of **1'a** to be a limit of dimerization energies of related molecules; i.e. the heat of dimerization of any oxazaborolidine would hardly be more negative than -22 kJ mol^{-1}.

Table 5. Vibrational frequencies[a] of aminoborane $H_2B\text{-}NH_2$ (**1'a**) and cyclodiborazane $(H_2B\text{-}NH_2)_2$ (**2'a**).[b]

$(H_2B\text{-}NH_2)_2$				$H_2B\text{-}NH_2$	
3338	(A_{1g})	1140	(A_{1g})	3416	(A_1)
3338	(B_{3u})	1120	(B_{1g})	3399	(B_2)
3287	(B_{1u})	1102	(A_u)	2583	(B_2)
3286	(B_{2g})	990	(B_{3g})	2530	(A_1)
2395	(B_{1u})	943	(B_{3u})	1663	(A_1)
2393	(B_{3g})	942	(B_{1u})	1345	(A_1)
2368	(A_{1g})	920	(A_u)	1192	(A_1)
2367	(B_{2u})	916	(B_{2u})	1061	(B_2)
1666	(A_{1g})	893	(B_{1g})	936	(B_1)
1656	(B_{3u})	875	(B_{2g})	789	(A_2)
1416	(B_{2u})	806	(B_{2g})	704	(B_2)
1313	(B_{1g})	801	(B_{3g})	621	(B_1)
1242	(A_{1g})	693	(B_{1u})		
1185	(B_{2u})	657	(A_{1g})		
1161	(B_{3u})	214	(B_{1u})		

[a] Frequencies are in wavenumbers. [b] From ref. 5b.

As the 6-31G*//6-31G* energy of the formation of **2'c** was predicted above (by comparing the 6-31G energy of **2'c** with 6-31G and 6-31G* energies of structural analogs of **2'c**) to be about -20 ± 5 kJ mol^{-1} one could evisage the actual heat of dimerization of **1'c** to be close to zero; even though it would be difficult to say whether the value would be negative or positive. As the heat of dimerization would anyway be low the monomer -

dimer equilibrium in a solution of an oxazaborolidine would be sensitive to the chemical nature of the solvent and temperature. On the other hand, in contrast to the monomeric form of an oxazaborolidine free to interact with both surrounding Lewis basic and Lewis acidic molecules (e.g. solvents), in a dimer of an oxazaborolidine the polar parts of the molecule would be buried deep to the nonpolar framework surrounding the active center of the catalyst; i.e. polar parts of the dimer would not be exposed to the solvent. Furthermore, dipole moments of all the dimer models are low (see Table 1) and in the case of *N,N*-adducts (**2'c** and **2'c'**) the dipole moments are even ≈ 0 D (should be zero because symmetry reasons, see Scheme 2). Consequently, the dimer should be more stable in nonpolar solvents; as indeed has been observed to be the case.[1a]

The dimerization energy deduced above for oxazaborolidines in nonpolar solvents could be corrected with respect to the presence of a Lewis basic solvent (e.g. THF). As it has been shown in the previous parts of the reports of this series[4c] one could estimate how much energy would be needed for the decomposition of an oxazaborolidine - solvent complex. The energy of decomposition of a water - 1,3,2-oxazaborolidine complex (water used as a model of THF)[4c] was determined to be ≈ 10 kJ mol^{-1} (6-31G//6-31G). As two molecules of the water - 1,3,2-oxazaborolidine complex would be needed for the formation of one dimer molecule the dimerization energy of an oxazaborolidine in a Lewis basic solvent (e.g. THF) could be estimated to be about 20 kJ mol^{-1} less than in a nonpolar solvent. Also this result is consistent with earlier experimental observations of Corey *et al.*[1a] who found that the monomeric forms would be present in significant amounts in THF solutions of oxazaborolidines whereas in nonpolar solvents (e.g. in C_6H_6) the dimer dominates.[1a]

As the models used in this work do not take into account effects arising from the presence of the pyrrolidine ring fused to the oxazaborolidine system of the actual catalysts (e.g. **1** derived from diphenylprolinol) it would be more difficult to estimate the dimerization energy of **1** than it was in the case of **1'c**. In the dimer of **1** the pyrrolidine rings would be in spiro positions with respect to the 4-membered ring formed in the dimerization process. Therefore, as the pyrrolidine rings would "point away" from other parts of the dimer (e.g. see Scheme 2, the structure of **2'c**) there should be no important repulsive interactions arising from the presence of the pyrrolidine rings. Actually effects of the presence of the pyrrolidine rings could even make the dimerization energy more negative because the angle strain arising from the partial B-N double bond of the 5,5 ring fusion of the monomeric oxazaborolidine would disappear as the dimeric *N,N*-adduct is formed. Although the direction of the effects of strain to the dimerization process of **1** can be predicted, its relative importance with respect to the other effects discussed here cannot be estimated on the basis of results of this work. Computational studies on these exciting catalysts continue.

CONCLUSIONS

Among the most probable processes leading to dimeric oxazaborolidines the formation of *N,N*-adducts containing a 4-membered ring analogous to that of cyclodiborazane $(H_2B\text{-}NH_2)_2$ was found to be energetically the most advantageous one. Energies of the formation of the *N,N*-adducts based only on the calculated total energies (*ab initio*) were low but clearly negative. The dimerization energy -43 kJ mol^{-1} (6-31G*//6-31G*) of aminoborane $H_2B\text{-}NH_2$ (**1'a**) was found to reduce to the level of -22 kJ mol^{-1} when corrected with respect to vibrational and temperature effects. By comparing uncorrected dimerization energies of different dimer models one can draw a conclusion that the heat of dimerization of any oxazaborolidine would hardly be more negative than that of **1'a** (i.e. -22 kJ mol^{-1}); most probably the actual heat of dimerization of oxazaborolidines would be close to zero. Therefore, in a solution of an oxazaborolidine the monomer - dimer equilibrium would be sensitive to the chemical nature of the solvent and temperature.

In the presence of a Lewis basic solvent dimerization energies of oxazaborolidines were predicted to be

about 20 kJ mol^{-1} more positive than in a nonpolar solvent. Results of this work imply also that in the case of oxazaborolidine catalysts derived from diphenylprolinol the formation of dimers in which the oxazaborolidine moieties fused to the cyclodiborazane system reside on the opposite sides of the cyclodiborazane ring (*anti*-adducts) would be greatly favoured over those ones in which the oxazaborolidine moieties reside on the same side of the cyclodiborazane ring (*syn*-adducts).

Energies of the formation of *N,O*-adducts turned out to be positive (e.g. +17 kJ mol^{-1} at the 6-31G//6-31G level for the most stable *N,O*-adduct derived from 1,3,2-oxazaborolidine). The formation of *O,O*-adducts was found to be energetically clearly disadvantageous (e.g. +46 kJ mol^{-1} at the 6-31G//6-31G level for the most stable *O,O*-adduct derived from 1,3,2-oxazaborolidine). Therefore, most probably the *O,O*-adducts, and perhaps also the *N,O*-adduct, would not play any role in the dimerization of oxazaborolidines.

On the basis of all the evidences represented in this report it looks obvious that the dimeric forms of oxazaborolidines would be structurally analogous to the *N,N*-adducts.

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