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Quantum Chemical Modeling of Chiral Catalysis. Part 12. On the Influence of the Nature of the Ring System on Binding in Ketone - Borane Complexes of Chiral Oxazaborolidines Used as Catalysts in the Enantioselective Reduction of Ketones

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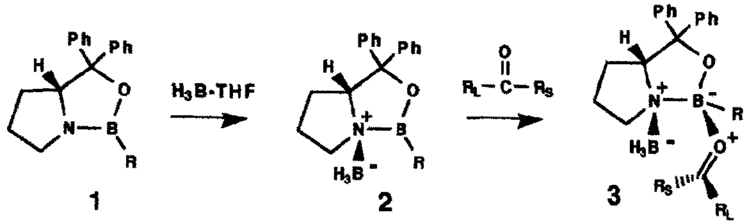
Abstract: - Coordination of ketones (formaldehyde as a model) to borane *N*-adducts of 1-aza-2-bora-3-oxa-bicyclo[3.3.0]octane **1'** and 1,3,2-oxazaborolidine was investigated by means of *ab initio* molecular orbital methods. Coordination energies were more positive in the case of the more strained and rigid bicyclic 1-aza-2-bora-3-oxa-bicyclo[3.3.0]octane **1'**. Why 1-aza-2-bora-3-oxa-bicyclo[3.3.0]octane **1'** derivatives can perform better as catalysts than the corresponding simple 1,3,2-oxazaborolidines is discussed.

INTRODUCTION

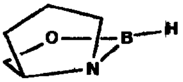
Chiral oxazaborolidines **1** are known to induce highly enantioselective catalytic reduction of ketones in the presence of Lewis acidic borane derivatives able to donate a hydride. The history, present results and most important applications of 1,3,2-oxazaborolidines in enantioselective syntheses have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



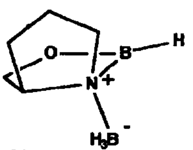
Mechanism of the reduction has been suggested to involve formation of the borane adduct **2**.[1,2] Coordination of the ketone to be reduced to **2** would lead to the formation of **3**.[1,2] Formation of **2** (R=CH_3) has been confirmed by Corey *et al.* (an X-ray crystallographic study)[3] and the mechanism of the catalysis has been studied also by means of *ab initio* MO methods.[4,5] In previous parts of this series of *ab initio* studies two types of oxazaborolidine catalysts and their borane *N*-adducts have been described.[5c] Simple models were used:[5c] 1-aza-2-bora-3-oxa-bicyclo[3.3.0]octane as a model of 4,4-diphenyl-1-aza-2-bora-3-oxa-bicyclo[3.3.0]octane type of catalysts **1** devised by Corey *et al.*[2] and 4-methyl-1,3,2-oxazaborolidine as a model of 4-alkyl-5,5-diphenyl-1,3,2-oxazaborolidines invented by Itsuno *et al.*[6] The better performance of catalysts of Corey *et al.*[1,2] was proposed[5c] to be attributable to the higher rigidity and more advantageous shape of the ring systems of the catalysts. The present report summarizes results provided as probing of the formation of **3** was attempted by means of *ab initio* MO methods.

MODELS AND COMPUTATIONAL METHODS

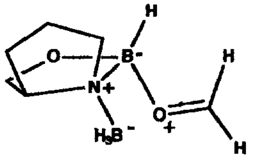
The models used in this study were as follows: 1-aza-2-bora-3-oxa-bicyclo[3.3.0]octane **1'** (a model of **1**);[5c] borane *N*-adduct **2'** (a model of **2**)[5c] and the borane - formaldehyde complex **3'** (a model of **3**). Also the other possible way of coordination[5d] of formaldehyde to **2'** was evaluated by using **3"** as a model [a related study on the coordination of formaldehyde to a borane *N*-adduct of 1,3,2-oxazaborolidine (by using **4'** and **4"** as models) has been described in part VIII of this series[5d]]. Modeling techniques applied were similar to those of previous studies of this series.[4d] Standard *ab initio* calculations were carried out by using the Gaussian 80[7] series of programs at the 3-21G, 4-31G and 6-31G levels. No other calculations on the structures **3'** or **3"** appeared to have been published. Results of MNDO studies on plausible transition states related to hydride transfer occurring in complexes **3** has been lately reported by Liotta *et al.*[8] Liotta *et al.* propose the hydride transfer to occur *via* a chair transition state whereas *ab initio* studies of this series indicate the complex **3**, of which the formation precedes the hydride transfer, to stay in a conformation which could be described best as twisted boat.[4d,5d]



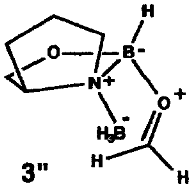
1'



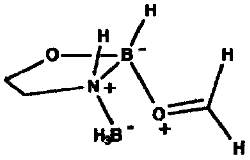
2'



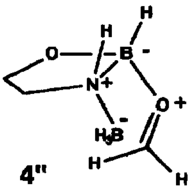
3'



3"



4'



4"

RESULTS AND DISCUSSION

Optimized structures of **3'** and **3"** (6-31G//6-31G) are shown in the Figure. Total energies and dipole moments of **1'**, **2'**, **3'** and **3"** are shown in Table 1. Energies and charge transfer values of the formation of **3'** and **3"** are shown in Table 2. The most important Mulliken overlap population values of **3'**, **3"**, **4'** and **4"** are summarized in Table 3.

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

Structure	3-21G//3-21G		4-31G//4-31G		6-31G//6-31G	
	E[a]	D[a]	E	D	E	D
1'	-347.30477	3.36	-348.71702	3.44	-349.07697	3.49
2'	-373.58165	6.06	-375.09120	5.84	375.47586	5.80
3'	-486.81667	2.60	-488.78291	2.43	-489.28150	2.40
3"	-486.81820	3.92	-488.78512	2.93	-489.28383	2.86
H_3B	-26.23730	0	-26.34927	0	-26.37679	0
$H_2C{=}O$	-113.22182	2.66	-113.69261	3.02	-113.80836	3.04

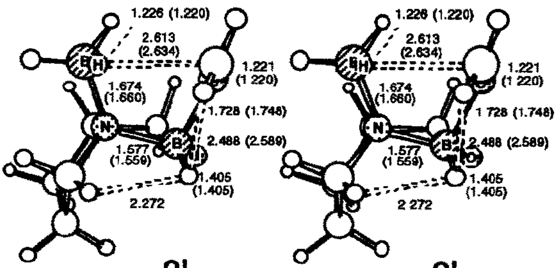
[a] Total energies (E) given in hartrees and dipole moments (D) in debyes.

Table 2. Energies (ΔE)[a] and charge transfer values (ΔQ)[b] of the formation of borane - formaldehyde complexes 3', 3'', 4' and 4''.[c]

Complex	3-21G	4-31G	6-31G	ΔQ (6-31G)[b]		
		ΔE[a]		$H_2C{=}O$	H_3B	Catalyst
3'	-35	+2	+7	+0.124	-0.225	+0.101
3''	-39	-3	+1	+0.141	-0.222	+0.081
4'[d]	-38	-3	+1	+0.122	-0.232	+0.110
4''[d]	-51	-10	-5	+0.156	-0.230	+0.074

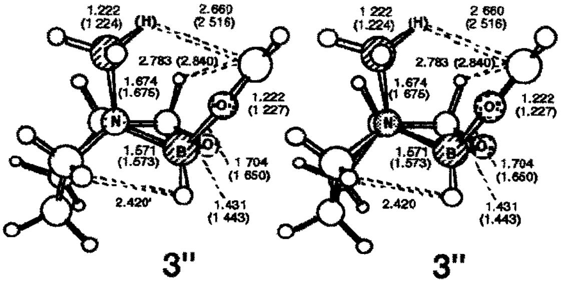
[a] Energies (ΔE) given in kJ mol^{-1}. [b] With respect to the neutral counterparts. [c] See the Figure.
[d] From ref. 5d.

As the energy of coordination of borane to 1-aza-2-bora-3-oxa-bicyclo[3.3.0]octane (formation of 2') was 14 kJ mol^{-1} (6-31G//6-31G) more negative than that of 1,3,2-oxazaborolidine[5c] one could have expected also the energy of formation of 3' to be more advantageous than that of 4'. However, the energy of formation of 3' turned out to be 6 kJ mol^{-1} more positive than that of 4' (6-31G//6-31G, Table 2). Also the energy of formation of 3'' was 6 kJ mol^{-1} more positive than that of 4'' (6-31G//6-31G, Table 2). Therefore, even though the relief of angle strain at the partial B=N double bond [due to the resonance B-N <-> $B^-{=}N^+$] of the ring system of 1' facilitates the coordination of borane to the ring nitrogen,[2a] the next step of the mechanism of the catalysis appears to involve nothing related. As the difference of energies of formation of 3' and 4' is small (as is that of 3'' and 4'') one could predict properties related to the Lewis acidity of the ring boron of borane adducts of both the strained bicyclic oxazaborolidine catalysts (e.g. 2) and less-strained, non-fused, non-bridged oxazaborolidines to be closely similar.



3' 3'

Bond angles	3'(4')	3''(4'')
B-N-B	117.4° (119.7°)	114.8° (117.3°)
N-B-O_{ring}	106.8° (106.3°)	105.3° (103.5°)
N-B-O_{CO}	105.8° (104.8°)	109.2° (106.8°)
O-B-O	105.5° (104.4°)	104.3° (105.9°)
B-O-C_{CO}	123.7° (126.2°)	124.7° (123.9°)
H-C_{CO}-H	119.3° (119.0°)	120.0° (120.5°)
B-H_{BH3}-C_{CO}	102.0° (105.4°)	107.2° (106.8°)
H_{BH3}-C_{CO}-O_{CO}	87.6° (85.7°)	81.3° (88.3°)



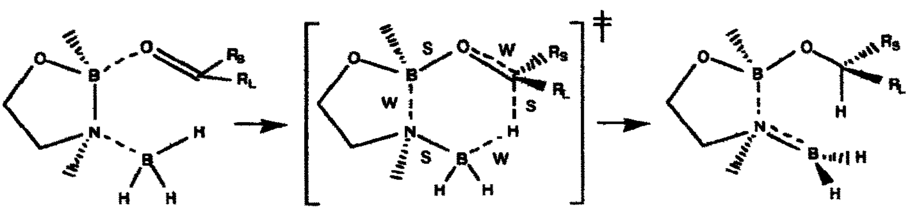
3'' 3''

Torsion angles	3'(4')	3''(4'')
B_{BH3}-N-B-O_{CO}	-14.4° (-22.0°)	10.7° (18.4°)
B_{BH3}-N-B-O_{ring}	-126.5° (-132.3°)	-100.7° (-93.0°)
C_{CO}-O_{CO}-B-O	-162.6° (-161.3°)	22.3° (24.8°)
C_{CO}-O_{CO}-B-N	84.8° (87.0°)	-89.9° (-85.0°)
N-C-C-O	28.0° (25.5°)	21.2° (31.3°)
N-B-O-C_{ring}	22.7° (20.9°)	-5.5° (-10.0°)
B-O_{ring} -C-C	-32.3° (-29.4°)	-9.7° (-12.8°)
H_{BH3}-B-N-B	-57.5° (-47.2°)	55.9° (49.0°)
C-N-B-O_{ring}	-3.9° (-3.6°)	18.6° (18.6°)

Figure. Stereo representations of the optimized (6-31G//6-31G) structures of formaldehyde-borane complexes (3' and 3'') of 1-aza-2-bora-3-oxa-bicyclo[3.3.0]octane (1'). The most important bond lengths and non-bonded distances (indicated by dashed bonds) [in Å], bond angles and torsion angles are shown. The corresponding values of the analogs 4' / 4'' (from ref. 5d) are given in parentheses.

Although the energetic effects related to the enhanced performance of the strained bicyclic oxazaborolidine catalysts are not clearly distinguishable (energetic effects behind changes of *ee* by a few percentages are very small) inspection of relative differences of structural parameters of 3', 3'', 4' and 4'' can be revealing. By comparing properties of the pairs 3'/4' and 3''/4'' one could determine what type of relative changes fusing another 5-membered ring to the parent oxazaborolidine system (corresponding to the hypothetical transformation of catalysts of Itsuno^6 to those of Corey^2) would give rise to. The structures of 3', 3'', 4' and 4'' were compared with respect to the relative changes of lengths and Mulliken overlap populations of bonds (the Figure and Table 3) involved in the transition state of the hydride transfer depicted in the Scheme. A related analysis of 4' and 4'' has been described in part VIII of this series.^{5d} Results of the comparison are summarized in Table 4.

Scheme



W = bond weakened
S = bond strengthened

Inspection of the patterns of changes shown in Table 4 reveals that the complexes 4' and 4'' do not behave in the same way as a 5-membered ring is fused to their N-C bonds. In the case of 4' the bonds which are supposed to weaken as the hydride transfer occurs (the Scheme) have weakened further as the 5-ring has been added (the hypothetical conversion 4' -> 3'; bonds of which the length increases and the Mulliken overlap decreases are predicted to weaken). In the analogous manner, bonds which are supposed to strengthen in consequence of the hydride transfer (the Scheme) appeared to strengthen further as the 5-ring was added (bonds of which the length decreases and the Mulliken overlap increases are predicted to strengthen). Also the positive charge of the formaldehyde moiety of 3' (Table 2) is somewhat higher than that of 4' indicating the carbonyl carbon of 3' to have a higher propensity to accepting a hydride than the carbonyl of 4' would have. Furthermore, the $B\text{-}O_{CO}\text{-}C_{CO}$ bond angle (the Figure) of 4' is larger than that of 3'. All these results clearly imply fusing a 5-ring to the N-C bond of 4' to turn the configuration of 4' closer to that of the hydride transfer. However, opposite conclusions can be drawn in the case of 4''/3''.

Inspection of the relative changes of bond lengths and Mulliken overlap populations of 4'' and 3'' (Table 4) reveals that, adding a 5-ring to 4'' (the hypothetical conversion 4'' -> 3'') causes the bonds which are supposed to strengthen as the hydride transfer occurs (the Scheme) not to strengthen, but weaken. In the same way, the bonds which are supposed to weaken (the Scheme) actually strengthen as the second ring is added to 4''. Also the positive charge of the formaldehyde moiety of 3'' (Table 2) is considerably lower than that of 4'' indicating the carbonyl carbon of 3'' to have a lower propensity to accepting a hydride than the carbon of 4'' would have. Furthermore, the $B\text{-}O_{CO}\text{-}C_{CO}$ bond angle (the Figure) of 3'' is larger than that of 4''. All these results clearly imply fusing a 5-ring to the N-C bond of 4'' to turn the configuration of 4'' away from that of the hydride transfer.

On the basis of the comparison above one could draw a conclusion that the bicyclic strained oxazaborolidine catalysts devised by Corey^{2} can work better than the corresponding less strained simple oxazaborolidine analogs invented by Itsuno^{6} because the second ring of the catalysts of Corey enhances possibilities of the desired hydride transfer (through analogs of 3') to occur. On the other hand, the second ring also decreases the possibilities of the competing undesired hydride transfer (through analogs of 3"). This conclusion is interesting in the light of results of recent works of Berenguer, Garcia, Gonzalez and Villarrasa^{9} as they proposed, on the basis of experimental studies on a group of catalyst models, the formation of the minor enantiomer in the oxazaborolidine catalyzed reductions of ketones to originate form hydride transfers taking place in the ketone - borane complexes structurally analogous to 3" or 4" as the major enantiomer would be produced through complexes structurally analogous to 3' or 4'.^{9} Computational studies of these exciting catalysts continue.

Table 3. Selected Mulliken overlap populations[a] of the borane - formaldehyde complexes 3', 3", 4' and 4".

Bond	3'	3''	4'[b]	4''[b]	$H_2C{=}O$
$N\text{-}B_{ring}$	0.334	0.328	0.338	0.324	-
$N\text{-}B_{BH3}$	0.104	0.104	0.078	0.118	-
$B\text{-}O_{ring}$	0.630	0.580	0.660	0.566	-
$B\text{-}O_{CO}$	0.070	0.122	0.070	0.144	-
$B\text{-}H_{BH3}$	0.776	0.772	0.784	0.774	-
C=O	0.682	0.670	0.694	0.646	0.862
$H_{BH3}\text{-}C_{CO}$	0.008	0.008	0.004	0.014	-

[a] On the basis of calculations carried out at the 6-31G level. [b] From ref. 5d.

Table 4. Comparison of structural changes[a,b] observed in the borane - formaldehyde complexes 4' and 4" as a 5-membered ring was fused to the N-C bonds of their oxazaborolidine rings (hypothetical reactions 4' -> 3' and 4" -> 3").

	4' -> 3'			4" -> 3"		
Parameter	Bond length	Overlap popul.	Prediction	Bond length	Overlap popul.	Prediction
$N\text{-}B_{ring}$	W	W	W	S	S	S
$B\text{-}O_{CO}$	S	-	S[c]	W	W	W
C=O	W	W	W	S	S	S
$H_{BH3}\text{-}C_{CO}$	S	S	S	W	W	W
$B\text{-}H_{BH3}$	W	W	W	S	W	?[d]
$N\text{-}B_{BH3}$	W	S	S[e]	S	W	W[e]

[a] "W" indicates weakening of the bond; "S" indicates strengthening of the bond. [b] Changes of bond lengths and Mulliken overlap populations; on the basis of calculations carried out at the 6-31G level. [c] Change of the bond lengths was significant, overlap populations did not change. [d] Changes of both the overlap populations and bond lengths were small. [e] Change of the overlap populations was more significant than that of the bond lengths.

CONCLUSIONS

The results of this work imply strained and rigid bicyclic oxazaborolidine catalysts to be able to better guide the hydride transfer to occur through the desired configuration of the ketone - borane complex of the catalyst (analogous to that of 3') than the corresponding non-fused, less-strained, and less-rigid parent oxazaborolidines. Although it was not expected, results of this work also indicate that more energy can be needed as ketones coordinate to borane adducts of the former class of catalysts than in the case of the corresponding reaction with borane adducts of the latter class. Difference between these coordination energies should be considerably smaller than that of the energies of coordination of borane to these catalysts (most of the ring strain of the bicyclic catalysts 1 would be relieved as their borane adducts are formed).

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