Pergamon

Tetrahedron: Asymmetry Vol. 5, No. 4, pp. 767-772, 1994
Elsevier Science Ltd
Printed in Great Britain
0957-4166/94 $6.00+0.00

0957-4166(94)E0100-O

Quantum Chemical Modeling of Chiral Catalysis. Part 18. Conformational Studies on Chiral *N*-Sulfonylated 1,3,2-Oxazaborolidines and Related Aldehyde Complexes Potentially Involved in the Catalytic Asymmetric Diels-Alder Reactions

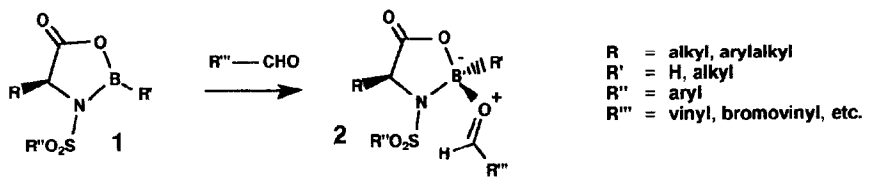
Vesa Nevalainen

Division of Organic Chemistry, P.O. Box 6, SF-00014 University of Helsinki, Finland

Abstract: - Properties of Lewis acidic oxazaborolidines **1** were investigated by means of *ab initio* MO methods (RHF, *N*-sulfonylated 1,3,2-oxazaborolidine **1'** as a model). Energies of the coordination of aldehydes to **1** were estimated by using formaldehyde and acrolein adducts of **1'** as models. Energies (MP2/6-31G//6-31G) of the coordination of formaldehyde to **1'** were -1 kJ mol^{-1} (**2'b**; axial S=O) and +26 kJ mol^{-1} (**2'a**; equatorial S=O). The corresponding energies of the formation of acrolein adducts (**3'a** and **3'b**, both *s-trans*, equatorial S=O) were higher, +43 kJ mol^{-1} (vinyl equatorial) and +54 kJ mol^{-1} (vinyl axial). An *s-cis* conformer of **3'a** was found to be unstable.

INTRODUCTION

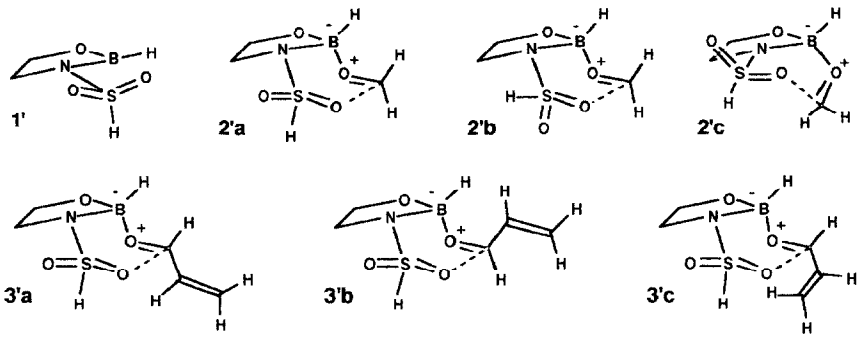
The asymmetric Diels-Alder reaction catalyzed by chiral *N*-sulfonylated oxazaborolidine derivatives (e.g. **1**) has been studied intensively[1,2] since the first examples reported by Yamamoto *et al.*[2a] and Helmchen *et al.*[2b] The first step of this reaction has been proposed to be the coordination of the carbonyl compound to the Lewis acidic boron of **1** leading to the formation of **2**.[1f-j] Probing of the structure of **2** has been attempted recently by means of *ab initio* MO (RHF) methods.[3] Those studies indicate that **1** may behave as a bidentate complexation agent [in the case of a formaldehyde adduct of *N*-sulfonylated oxazaborolidine (**1'**) the oxygen of formaldehyde was found to be bound to the boron of oxazaborolidine and the carbon to one of the oxygens of the *N*-sulfonyl group].[3]



The goal of the work described in this paper was to compare the coordination of formaldehyde and acrolein to *N*-sulfonylated oxazaborolidines and to study conformational effects related to the coordination process.

MODELS AND COMPUTATIONAL METHODS

Modeling techniques similar to those described in the previous reports of this series[3,4] were employed. Standard *ab initio* molecular orbital calculations (RHF) were performed using the Gaussian 90 series of programs at the 3-21G and 6-31G levels.[5] All the optimizations were carried out using the BERNY method.[5,6] The effects of electron correlation were assessed on the basis of the Moller-Plesset theory. Single-point calculations were performed on the structures optimized at the 6-31G level (MP2/6-31G//6-31G). The structures **1'**, **2'a-c** (boat conf.) and **3'a-c** (boat conf.) were used as models of **1** and **2** . Properties of these models, except those of **2'a**,[3] appear to be not yet studied.



RESULTS AND DISCUSSION

In addition to **2'a** (axial H_{SO_2}) reported earlier[3] another conformer (**2'b**; equatorial H_{SO_2}) was found to be stable. The optimized structure of this adduct (**2'b**), along with that of the catalyst model **1'**, is shown in Figure 1. The optimized structures of the adducts (**3'a** and **3'b**; acrolein *s-trans*) are presented in Figure 2. The adducts (**3'c**; acrolein *s-cis*) and **2'c** turned out to be stable only at the 3-21G level. Results of conformational analyses of **1'** (energies, dipole moments, LUMO energies and the charge of the ring boron of **1'** as a function of the torsion angle H-S-N-B) are summarized in Figure 3. Energies and dipole moments of the optimized structures of **1'**, **2'a-b** and **3'a-c** are shown in Table 1 and the most important bond and torsion angle parameters in Table 2.

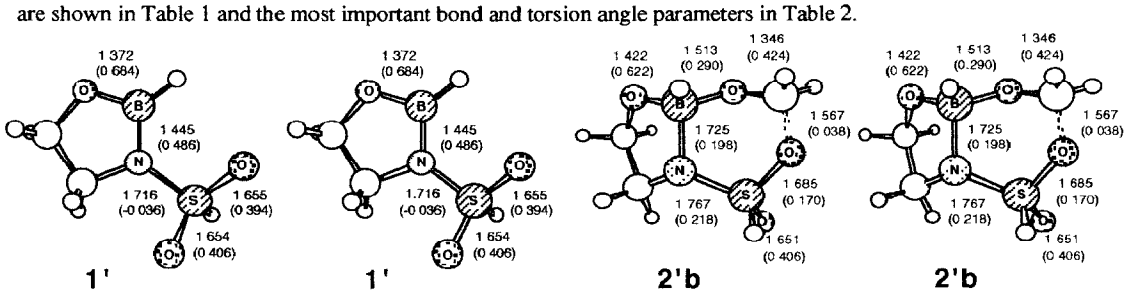


Figure 1. Optimized (6-31G//6-31G) structures of *N*-sulfonylated 1,3,2-oxazaborolidine (**1'**) and its formaldehyde complex (**2'b**) Also the most important bond lengths [in Å] and the corresponding Mulliken overlap populations (in parentheses) are shown

Compared with the values of **1'** the bond lengths and angles (Table 2) of **2'a - b** (Fig. 1) and **3'a - b** (Fig. 2) indicate that the B-O, B-N, N-S and S-O bonds of the catalyst moiety lengthen and the sulfonyl group turns out of the plane of the oxazaborolidine ring (e.g. the S-N-B-O_{catal} torsion angle increases from -172.2° of **1'** to 134.3° of **2'b**, Fig. 1) in consequence of the coordination of formaldehyde to **1'**. A comparison of the related Mulliken overlap populations (Fig. 1 and 2) implies the changes in the electron structure of **1'** to be closely similar to those observed as alkoxy- or aminoboranes coordinate[4,7] to a borane *N*-adduct of oxazaborolidine.

The adducts **2'a** and **2'b** are topologically equal. Also bond lengths and angles of these adducts are closely similar (Fig. 1, Table 2). The deviation of lengths of the S-O, O_{SO2}-C_{CO} and B-O_{CO} bonds of **2'a** and **2'b** is only 0.005 Å or less whereas the B-N and S-N bonds of **2'b** are 0.037, 0.017 Å longer and the C=O and B-O_{catal} bonds 0.009 and 0.017 Å shorter than those of **2'a**. In despite of these similarities, the torsion angles of **2'a** and **2'b** (Table 2) vary considerably (apart from the angles related to the orientation of the formaldehyde moiety).

The structural parameters of **3'a** (bond lengths, Fig. 2; bond angles and torsion angles, Table 2) are very closely similar to those[3] of **2'a**. Basically the related parameters of **3'b** are also rather similar to those[3] of **2'a** but the B-O_{CO} and C_{CO}-O_{SO2} bonds of **3'b** are shorter that those[3] of **2'a** or **3'a** (i.e. the aldehyde moiety of **3'b** resides closer to the catalyst than that of **2'a** or **3'a**) and the N-S bond of **3'b** is almost perpendicular (e.g. the S-N-B-O_{catal} torsion angle of **3'b** is 85°, Table 2) to the plane of N-B-O atoms of the catalyst.

The charge transfer values of **2'a**, **2'b**, **3'a** and **3'b** are as follows: -0.043 , -0.025, -0.047, -0.016 (6-31G//6-31G). These values indicate that both formaldehyde and acrolein receive a small amount of negative charge as they coordinate to **1'**. This does not mean that the π-system of acrolein would be inactivated with respect to Diels-Alder reactions. However, if the change of the charge of the vinyl moiety of acrolein is calculated it turns out that the vinyl group gains a positive charge of 0.127 as acrolein coordinates to **1'** to form **3'a** (Fig. 2). The corresponding change related to the formation of **3'b** (Fig. 2) is slightly higher, 0.134. This indicates that the C=C bond of the acrolein moiety of **3'a** would be considerably more polarized than that of free acrolein. Furthermore, in consequence of the formation of **3'a** the energy of the lowest unoccupied molecular orbital decreases by 0.07 eV (free acrolein v. **3'a**) and the negative charges of C_α and C_β of the acrolein decrease by 0.044 and 0.004. In the case of **3'b** the charges also decrease (both by 0.025) but the orbital energy slightly increases (by 0.03 eV). Altogether, in this light one could predict that the C=C bond of acrolein moiety of **3'a** and **3'b** could be more reactive (i.e. hardly less reactive) than that of free acrolein.

Table 1. Total energies (E), dipole moments (D) and complexation energies (ΔE).[a]

Structure	3-21G//3-21G			6-31G//6-31G			MP2//6-31G//6-31G	
	E^a	D^a	ΔE^b	E^a	D^a	ΔE^b	E^a	ΔE^b
1'	-776.22526	5 13	-	-780.07042	5.67	-	-780.84950	-
2'a	-889.47060	2.48	-62	-893.86877	2.32	26	-894 86460	26
2'b	-889.47817	4 54	-81	-893.87650	4.14	6	-894.87500	-1
2'c	889.46106	5 01	-37	-	-[c]	-	-	-
3'a	-965.92834	4.09	-35	-970.72546	3.52	60	-971 89665	43
3'b	-965 92580	0 76	-28	-970 72161	0 60	70	-971 89262	54
3'c	-965.93199	4 19	-44	-	-[c]	-	-	-
$H_2C{=}O$	-113.22182	2 65	-	-113.80837	3 04	-	-114.02501	-
trans-Acrolein	-189 68988	3 47	-	-190.67776	3 97	-	-191 06348	-
cis-Acrolein	-189.68989	2 88	-	-190.67577	3 35	-	-191 06159	-

[a] Total energies (E) given in hartrees, dipole moments (D) in debyes and complexation energies (ΔE) in kJ mol^{-1} [b] ΔE of **2'a-c** relative to **1'** plus $H_2C{=}O$; ΔE of **3'a-c** relative to **1'** plus *trans*-acrolein [c] The complex was found to be unstable.

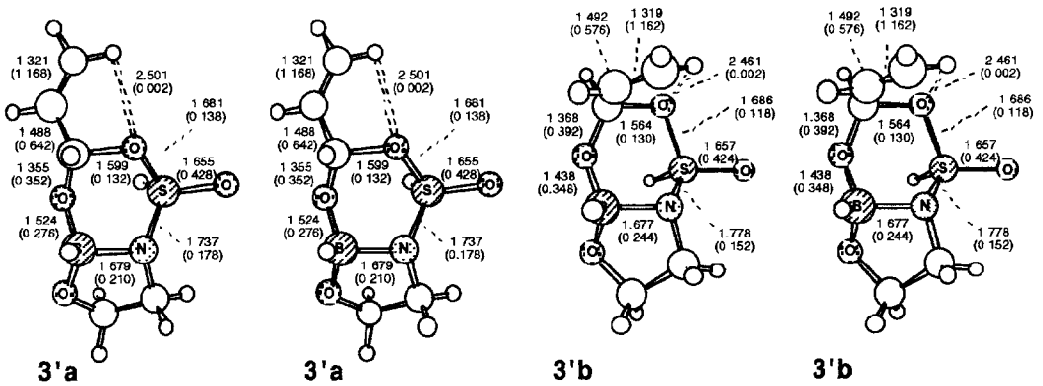


Figure 2. Optimized (6-31G//6-31G) structures of the acrolein adducts (**3'a** and **3'b**) of *N*-sulfonylated 1,3,2-oxazaborolidine (**1'**). Also the most important bond lengths [in Å] and the corresponding Mulliken overlap populations (in parentheses) are shown

Results of the conformational analyses of **1'** (Fig. 3) indicate that one conformer of *N*-sulfonylated oxazaborolidines would be favoured over the others [only one minimum (**B**, Fig. 3) was found in the case of **1'**]. In this conformer the hydrogen adjacent to the sulfur is almost perpendicular to the plane of the ring (e.g. the torsion angle H-S-N-B of **1'** is -99.0°, 6-31G//6-31G, Table 2) and both the sulfonyl oxygens reside on the same side of the ring. However, the orientation of the sulfonyl group of **1'** (Fig. 1) does not correspond to that of the most acidic / reactive conformer of **A** (Fig. 3). Both the dipole moment and the positive charge of the ring boron increase with the increasing value of the torsion angle H-S-N-B of **1'** until 180° where they have a maximum (corresponding to **A**, Fig. 3). Also

one of the two minima of LUMO of **1'** resides near 180°. Unfortunately, it looks as if the catalytic performance of systems conformationally analogous to **A** had not yet been studied. The adduct **2'b** (Fig. 1) could be, however, considered as a formaldehyde adduct of **A** (Fig. 3).

Table 2. Optimized (6-31G//6-31G) bond and torsion angles of *N*-sulfonylated oxazaborolidine (**1'**) and its formaldehyde and acrolein adducts (**2'a-b** and **3'a-b**).

Bond angles	1'	2'a	2'b	3'a	3'b	Torsion angles	1'	2'a	2'b	3'a	3'b
B-N-S	126 7°	112 0°	112.0°	112.4°	105.5°	S-N-B-O_{catal}	-172.2°	112 9°	134 3°	121.3°	85 0°
N-S-O_{ring}	108.8°	103 0°	106.0°	102.4°	101.4°	S-N-B-O_{CO}	-	-4.5°	18.7°	4.5°	-27.6°
N-S-$O_{off\text{-}ring}$	107 8°	117.0°	120 9°	117.6°	117.9°	H-S-N-B	-99.0°	-57.0°	132.0°	-61.3°	-41 4°
S-O-C_{CO}	-	113.6°	116.4°	113.2°	113.6°	B-N-S-$O_{off\text{-}ring}$	148.8°	177.5°	-104.6°	173.5°	-168.6°
O-C_{CO}-O	-	107 4°	108.2°	106.3°	106.5°	B-N-S-O_{ring}	14.0°	51 5°	30.0°	47.2°	66.2°
B-O-C_{CO}	-	118 2°	120.9°	119.4°	124.2°	B-O-C-O_{ring}	-	76.6°	63.6°	68.4°	73 4°
N-B-O_{CO}	-	102 0°	102 0°	101 6°	105.0°	S-O-C-O_{CO}	-	-7.0°	9 4°	6.6°	-13.8°
N-B-O_{catal}	106.9°	99 7°	98.0°	99.4°	97.9°	C-C-C-O_{CO}	-	-	-	-140.6°	129 8°
C-C-O_{CO}	-	-	-	112.6°	117.0°	C-C-C_{CO}-H	-	-	-	84.9°	-101 2°
C-C-C_{CO}	-	-	-	125.8°	126.4°	C-C-C-O_{SO2}	-	-	-	-23.9°	9 3°
H-C-O_{CO}	-	-	-	114.6°	109.5°						

The energy (ΔE) of formation of **2'b** (-1 kJ mol^{-1}, MP2/6-31G//6-31G, Table 1) is more advantageous than that of **2'a** (+26 kJ mol^{-1}). The relative order of these energies could be rationalized on the basis the relative acidities of two conformers (**A** and **B**, Fig 3) of **1'**. As pointed out above, **2'b** (Fig. 1) represents a formaldehyde adduct of **A** whereas **2'a**[3] represents that of **B**. Expecting that the coordination of formaldehyde to the more acidic conformer (**A**) would be energetically more advantageous one could predicts that the energy of formation of **2'b** should be more favorable than that of **2'a**, as indeed it is (Table 1). Nevertheless, this does not mean that the formation of aldehyde adducts of actual working catalysts (e.g. **1**) conformationally analogous to **2'b** would be favoured over that of those analogous to **2'a** because the substituents of the oxazaborolidine ring would control the coordination process.

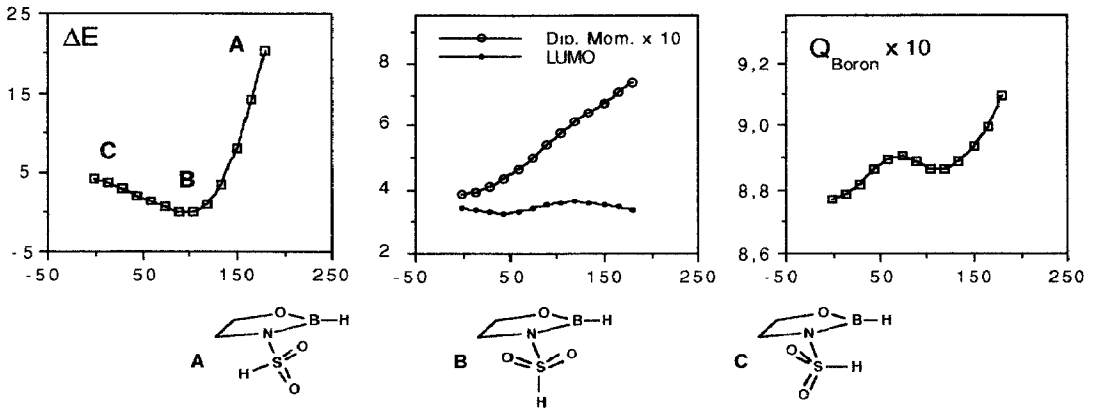


Figure 3. The relative energies (ΔE, kJ mol^{-1}), dipole moments (Dip Mom x 10, debyes), LUMO-energies (eV) and the charge of the ring boron (Q_{Boron} x 10) of *N*-sulfonylated 1,3,2-oxazaborolidine (**1'**) calculated at the 6-31G level as a function of the torsion angle H-S-N-B (other parameters reoptimized in each point)

All the chiral *N*-sulfonylated oxazaborolidines known as efficient catalysts of Diels - Alder reactions are 4-substituted.[1,2] Because of this substitution the formation of analogs of **2'b** could be predicted to be less advantageous than expected on the basis of the relative energies of **2'a** and **2'b**. This prediction could be best rationalized by inspecting the structure of **2'b** (Fig. 1). If the 4-position of **2'b** would be bearing a bulky group the orientation of the group should be *trans* to the adjacent sulfonyl group (the corresponding *cis* configuration would be much more hindered). On the other hand, in the *trans* configuration the substituent of the sulfur (in the best catalysts a bulky aryl, e.g. 2,4,6-triisopropylphenyl)[1,2] would be brought (causing hindrance) close to the bulky substituent on the 4-position

of the oxazaborolidine ring. In contrast to that, in the case of adducts analogous to **2'a** the substituent of the sulfonyl group and the 4-substituent would reside on the opposite sides of the oxazaborolidine ring system. Furthermore, in the case of α,β-enal analogs of **2'a** the bulky aryl group would reside below the π-face of the enal coordinated to the catalysts. Therefore, the bulky aryl would also *block one face of the vinyl moiety involved in the Diels - Alder reaction and stabilize the α,β-enal coordinated to the catalyst by intramolecular π-stacking interactions.* This proposal is supported by two experimentally proven facts. The enantioselectivity of *N*-sulfonylated oxazaborolidines practically disappears[2b] if the *N*-aryl is replaced by a group not capable of π-stacking (e.g. trifluoromethyl) and the enantioselectivity of these catalysts increases with the increasing number of electron donating (negative Hammet σ constants, not Lewis basic) substituents (e.g. alkyls) on the aryl.[2a] Geometric relations of the groups involved in this type of π-stacking could be assessed also in the light of a rough model built by substituting the 4-position of **3'a** by *i*-propyl and the hydrogen of sulfur by 4-methylphenyl (model **A**, Fig. 4).

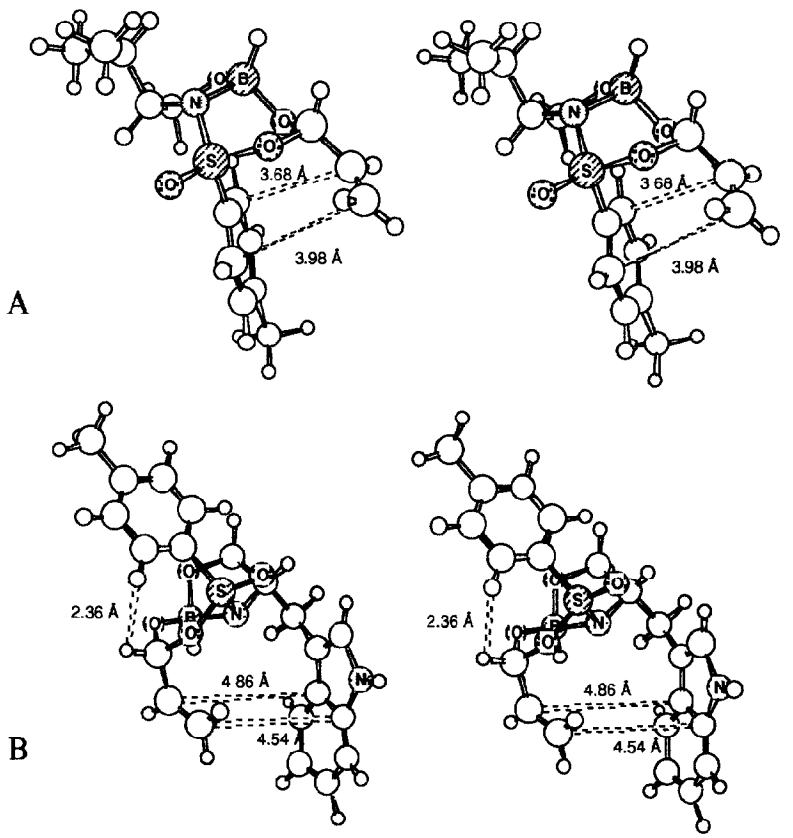


Figure 4. Models of α,β-enal (acrolein as a model) adducts of *N*-tosyl-4-isopropyl-1,3,2-oxazaborolidines (**A**) and *N*-tosyl-4-β-indolylmethylene-1,3,2-oxazaborolidines (**B**) In the case of the adduct (**A**) one of the hydrogens of *C*-4 of **3'a** was replaced by isopropyl whereas in the case of **B** the corresponding hydrogen of **3'b** was replaced by indolylmethylene. The hydrogen adjacent to the sulfur was replaced by 4-methylphenyl. Standard bond lengths and angles were used to construct the indolylmethylene, 4-methylphenyl and isopropyl moieties. The models (**A** and **B**) are not optimized.

Another relation between π-stacking and the catalytic function of *N*-sulfonylated oxazaborolidines has been introduced earlier by Corey *et al.*[1f] who proposed π-stacking to be responsible for the change of the absolute stereochemistry of the product of Diels - Alder reaction observed as the bulky 4-substituent of **1** (R=alkyl) was changed to a β-indolylmethylene group.[1f] This type of π-stacking would not be possible in the case of systems analogous to **3'a**

(the vinyl moiety in an equatorial position, Fig. 2). However, if the vinyl group of an α,β-enal adduct of **1** (R=β-indolylmethylene) would be in an axial conformation [as in analogs of **3'b** (Fig. 2)] it could form a π-stack with the 4-β-indolylmethylene group. Geometric relations of the groups involved in this type of π-stacking could be roughly estimated on the basis of the model **B** (Fig. 4) built by substituting the 4-position of **3'b** by a β-indolylmethylene group and the hydrogen of sulfur by 4-methylphenyl.

Mezrhab *et al.*[8] have recently determined a crystal structure of a π-stacked system, the structure of *trans*-2-[1-(2-naphthyl)-1-methylethyl]-cyclohexyl crotonate, of which the π-planes were found to be parallel (distances between the neighboring carbons of the crotonate and naphthyl groups were within the range of 3.41 - 3.99 Å).[8] However, the distances between the carbons of the aromatic and vinyl π-systems in **A** and **B** (Fig. 4) appear to be similar to those reported by Mezrhab *et al.*[8] Therefore, even though **A** (Fig. 4) is only a rough model it can be used to demonstrate the nature of the role which the aryl substituent of the *N*-sulfonyl group could play in processes potentially responsible for the high enantioselectivities observed in Diels - Alder reactions catalyzed by chiral **1**. Although it is difficult to draw any conclusions on the relative stabilities of **A** and **B** (Fig. 4) on the basis of the present work π-staking related to the model **B** could be predicted to be more advantageous than that of **A**. Namely, if the isopropyl group of **A** is changed to β-indolylmethylene the catalysts would produce a Diels - Alder adduct which is an enantiomer of that produced by the corresponding 4-isopropyl substituted system.[1f] This change of the configuration of the product could be rationalized on the basis of the relative energies of **3'a** and **3'b** (ΔE of **3'b** is 11 kJ mol^{-1} higher than that of **3'a**; MP2/6-31G//6-31G, Table 1). Formation of adducts analogous to **A** (the vinyl group in an equatorial position) would be normally (e.g. in the case of 4-alkyl substituted systems) favoured but if a significantly more electron rich π-system is placed on the other side of the oxazaborolidine ring (e.g. the 4-substituent replaced by indolyl) the electron rich π-system could stabilize the otherwise less stable axial orientation of the vinyl moiety (as in the case of **B**, Fig. 4). Consequently, in systems analogous to **B** the π-face of the vinyl encountered by the reacting diene would be opposite to that of systems analogous to **A**. Computational studies on the properties of catalytically active chiral oxazaborolidines continue.

CONCLUSIONS

Adducts of acrolein to *N*-sulfonylated 1,3,2-oxazaborolidine were found to be structurally similar to those of the related adducts of formaldehyde. The double bond of an α,β-enal coordinated to an *N*-sulfonylated oxazaborolidine could be predicted to be more reactive than that of the corresponding free α,β-enal. The results of this work compared with experimental findings reported in the literature indicate that the process determining the absolute stereochemistry of the product may involve π-stacking of the reacting α,β-enal and one of the aryl substituent(s) of the catalyst.

ACKNOWLEDGEMENTS

The University of Helsinki and the TEKES foundation are acknowledged for providing computational resources needed to carry out this study. The author thanks Dr. T. A. Hase for valuable comments.

REFERENCES AND NOTES

1 (a) Pindur, U.; Lutz, G., Otto, C. *Chem. Rev.* **1993**, *93*, 741, (b) Deloux, L.; Srebnik, M *Chem. Rev.* **1993**, *93*, 763, (c) Kagan, H. B , Riant, O *Chem. Rev.* **1992**, *92*, 1007; (d) Wallbaum, S., Martens, J *Tetrahedron Asymmetry* **1992**, *3*, 1475; (e) Corey, E. J., Loh, T.-P. *Tetrahedron Letters* **1993**, *34*, 3979, (f) Corey, E. J , Loh, T.-P.; Roper, T D ; Azimiora, M. D ; Noe, M C *J. Am. Chem. Soc.* **1992**, *114*, 8290, (g) Corey, E. J., Sarshar, S *J. Am. Chem. Soc.* **1992**, *114*, 7938, (h) Corey, E. J.; Ishihara, K. *Tetrahedron Letters* **1992**, *33*, 6807; (i) Corey, E. J.; Loh, T -P *J. Am. Chem. Soc.* **1991**, *113*, 8966, (j) Sartor, D ; Saffrich, J.; Helmchen, G , Richards, C. J.; Lambert, H *Tetrahedron Asymmetry* **1991**, *2*, 639

2 (a) Takasu, M ; Yamamoto, H *SYNLETT* **1990**, 194; (b) Sartor, D.; Saffrich, J; Helmchen, G. *SYNLETT* **1990**, 197.

3. Nevalainen, V *Tetrahedron Asymmetry* **1993**, *4*, 1565

4 Nevalainen, V *Tetrahedron Asymmetry* **1991**, *2*, 1133

5 Gaussian 90, Revision I, Frisch, M. J., Head-Gordon, M.; Trucks, G. W., Foresman, J. B.; Schlegel, H. B.; Raghavachari, K.; Robb, M.; Binkley, J S , Gonzalez, C , Defrees, D J , Fox, D. J.; Whiteside, R A ; Seeger, R ; Melius, C F , Baker, J.; Martin, R L ; Kahn, L. R ; Stewart, J J P ; Topiol, S ; Pople, J. A , Gaussian, Inc., Pittsburgh PA, 1990.

6. A structure is stated to be stable if a stationary point corresponding to the structure was found by using the BERNY method of Gaussian 90 (ref. 5) For a structure stated to be unstable the stationary point was not found

7. Nevalainen, V *Tetrahedron Asymmetry* **1993**, *4*, 2001 and references therein

8 Mezrhab, B , Dumas, F., d'Angelo, J., Riche, C *J. Org. Chem.* **1994**, *59*, 500.

(*Received in UK* 2 *March* 1994)