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Quantum Chemical Modeling of Chiral Catalysis. Part 10. On the Complexes of Carbonyl Compounds with Chiral *N*-Sulfonylated 1,3,2-Oxazaborolidines Used as Catalysts in the Enantioselective Diels-Alder Reactions

Vesa Nevalainen

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

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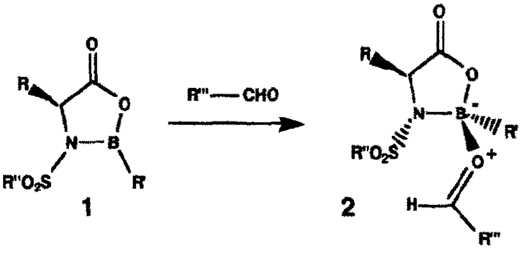
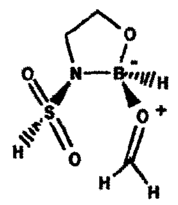
Abstract: - Formation of complexes of carbonyl compounds with *N*-sulfonylated 1,3,2-oxazaborolidines **1** was investigated by means of *ab initio* molecular orbital methods. An unusual mode of coordination leading to the formation of a six-membered ring (boat conformation) was observed as formaldehyde was used as a model of carbonyl compounds and an adduct of formaldehyde to *N*-sulfonyl-1,3,2-oxazaborolidine (**2'**) as a model of **2**. In this six-ring system the oxygen of formaldehyde was bound to the boron of oxazaborolidine and the carbon to one of oxygens of the *N*-sulfonyl-group. In consequence of this unusual complexation the C=O double bond of formaldehyde lengthened substantially, the planar shape of the carbonyl was distorted and the positive charge of the carbonyl carbon increased about 100 %.

The asymmetric catalytic Diels-Alder reaction has been a topic of interest to many involved in the development of catalytic processes in synthetic organic chemistry since the later 1970's.[1-2] One of the most interesting classes of these catalysts consists of chiral *N*-sulfonylated oxazaborolidine derivatives of amino acids (e.g. **1**).[3-5] A recent review article of Wallbaum and Martens[6] summarizes asymmetric syntheses of which the technics of transferring chirality to the target of synthesis are based on the use of chiral oxazaborolidines. The first step of the pathway of asymmetric Diels-Alder 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**.[3-6]



1 **2**



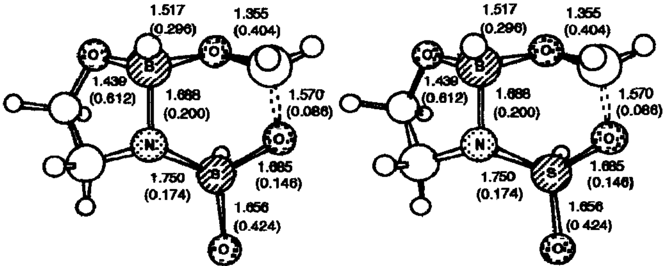
2'

R = alkyl, aryl; R' = H, alkyl; R" = aryl; R'" = vinyl, bromovinyl, etc.

A number of different mechanistic features related to the function of **1** as a catalyst in asymmetric Diels-Alder reactions have been described in the literature.[3-6] Even though the *N*-sulfonyl group of **1** has been understood to increase Lewis acidity of the boron of oxazaborolidine direct interactions between the *N*-sulfonyl group and the dienophile or diene have not been taken into account in the mechanism of the catalysis. This is somewhat surprising. As the *N*-sulfonyl group consists of highly polarized atoms it would actually be peculiar if the polar oxygens of the *N*-sulfonyl group would not participate as the carbonyl compound coordinates to the catalyst.

Moreover, the positively charged end of the carbonyl would be brought near to one of the oxygens of the sulfonyl group.

Altogether, on the basis of information in the literature it looks as if one could not predict whether the *N*-sulfonyl group would participate or not as carbonyl compounds coordinate to **1**. Consequently, the aim of this work was to probe potential interactions between the coordinating carbonyl compound and the *N*-sulfonyl group of **1**. Modeling techniques similar to those described in the previous reports of this series[7d] were employed. Standard *ab initio* molecular orbital calculations (RHF) were carried out by using the Gaussian 90 series of programs at the 3-21G, 4-31G and 6-31G levels.[9] No polarization functions were employed.[10] A simple analog (**2'**) was used as a model of **2**. The optimized structure of **2'** (6-31G//6-31G) is shown in the Figure. Energies and dipole moments and the most important structural parameters of **2'** are summarized in Table.



2' **2'**

Figure. Optimized (6-31G//6-31G) structure of the complex **2'** of formaldehyde with *N*-sulfonylated 1,3,2-oxazaborolidine. The most important bond lengths are given in ångströms. Below the bond lengths are shown the corresponding Mulliken overlap populations in parentheses.

Inspection of the optimized structure of **2'** (the Figure and the Table) reveals several new features related to the way by which complexation of carbonyl compounds to *N*-sulfonylated oxazaborolidines can take place. For instance, in **2'** the both ends of C=O are clearly bound to the catalyst model (oxygen to boron and carbon to one of the oxygens of SO_2). In consequence of this unusual coordination the planar geometry of the carbonyl group has been distorted (e.g. in **2'** the $C_{C=O}$ atom was found to be 0.277 Å out of the plane of its adjacent oxygen and hydrogen atoms; 6-31G//6-31G) and the C=O bond has lengthened (e.g. the C=O bond of formaldehyde has lengthened by 0.145 Å as **2'** formed; 6-31G//6-31G, the Table). Comparison of Mulliken overlap populations of free formaldehyde (0.974; 6-31G//6-31G) and the formaldehyde moiety of **2'** (0.404; 6-31G//6-31G, the Figure) reveals that the C=O overlap has decreased almost 60 % as the formaldehyde has been bound to the *N*-sulfonylated oxazaborolidine system of **2'**. As the sum of the three angles of the trigonal system[11] formed by the distorted formaldehyde moiety of **2'** was calculated the relative amount of the sp^2 - sp^3 nature of the hybridization of the carbonyl carbon of **2'** turned out to be about 1:1 [e.g. the sum of $\partial(H_a\text{-}C\text{-}O_{C=O})$, $\partial(H_e\text{-}C\text{-}O_{C=O})$ and $\partial(H_a\text{-}C_{C=O}\text{-}H_e)$ was 343.1° (6-31G//6-31G) which corresponds to the degree of 46 % of sp^3-hybridization]. Indeed, these unusual structural changes (together with those related to the hybridization of the ring nitrogen being described below) allow the most polar parts of **2'** to form a six-membered cyclic system which consists of the carbon and oxygen atoms of the formaldehyde moiety and the boron, nitrogen, sulfur and oxygen (of SO_2, residing below the carbonyl carbon of **2'**, the Figure) atoms of the catalyst model (the Figure). Conformation of the cyclic system is clearly boat.

Not only the structural parameters of formaldehyde change as the adduct **2'** forms but also the charge distribution. The charge of carbonyl oxygen of **2'** is -0.810 (6-31G//6-31G) whereas the corresponding value of free formaldehyde (-0.454) is only about 56 % of that. As the negative charge of $O_{C=O}$ appears to increase it would not be surprising if the positive charge of $C_{C=O}$ would increase too. Indeed, the positive charge of $C_{C=O}$ of **2'** (+0.315; 6-31G//6-31G) is about two times as high as that of free formaldehyde (+0.159; 6-31G//6-31G). Analysis of charges of the atoms of formaldehyde moity of **2'** reveals that formaldehyde has received electrons from the *N*-sulfonylated oxazaborolidine system. The amount of additional charge was -0.043 (6-31G//6-31G). At a glance this may look as a deactivating factor with respect to the Diels-Alder reaction. Nevertheless, this result implies only that the negative charge of $O_{C=O}$ bound to the *N*-sulfonylated oxazaborolidine system would increase more than the positive charge of the $C_{C=O}$ end of the carbonyl interacting with the sulfonyl oxygen. In the case of α,β-enals the enhanced positive charge of $C_{C=O}$ would be delocalized to the adjacent olefine moiety [on the basis of this study about one half of the *sp*^{2}-nature of the carbonyl carbon could be predicted to be left allowing delocalization of the positive charge] enhancing its dienophilicity. Also calculated low dipole moments of **2'** (e.g. 2.32 D; 6-31G//6-31G, the Table) reflect unusual advantageousness of this type of coordination of carbonyl compounds to *N*-sulfonylated oxazaborolidines. Namely, the moments are considerably lower than those of free formaldehyde (e.g. 0.72 D lower at the 6-31G level).

Table. Total energies,[a] dipole moments[b] and the most important bond lengths[c] of **2'**.

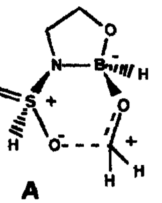
Property	**3-21G//3-21G**	**4-31G//4-31G**	**6-31G//6-31G**
E	-889.47060	-892.93992	-893.86877
D	2.48	2.61	2.32
$B\text{-}N_{ring}$	1.671	1.674	1.688
$S\text{-}N_{ring}$	1.686	1.702	1.750
$S\text{-}O_{ring}$	1.642	1.659	1.685
$O_{SO2}\text{-}C_{CO}$	1.556	1.574	1.570
$C_{CO}\text{-}O_{CO}$	1.368	1.351	1.355
$B\text{-}O_{CO}$	1.514	1.517	1.517
$B\text{-}O_{ring}$	1.445	1 433	1.439
$S\text{-}O_{off\text{-}ring}$	1.584	1.621	1.656
$C{=}O_{free\ formaldehyde}$	1.207	1.206	1.210

[a] Total energies (E) given in hartrees. [b] Dipole moments (D) given in debyes. [c] bond lengths given in ångströms [Å].

Support on the proposed importance of *N*-sulfonyl group in the stabilization of the formaldehyde moiety of **2'** can be found also as the structure of the *N*-sulfonyl group is inspected **2'**. For example, at the 6-31G level the bond between sulfur and the oxygen coordinated to the carbonyl carbon is about 0.029 Å longer than the other S-O bond (the Figure). Furthermore, the Mulliken overlap population of the former is only about one third of that of the latter (the Figure) and the negative charge of the sulfonyl oxygen coordinated to the carbonyl is -0.756 (6-31G//6-31G) whereas that of the other is lower (-0.631; 6-31G//6-31G). Nevertheless, the former oxygen is not very tightly bound to the carbonyl carbon. Namely, the Mulliken overlap population of $C\text{-}O_{SO_2}$ is only 0.086 (6-31G//6-31G) whereas that of C=O is about 4.5 times higher (0.404, the Figure). Therefore, the $C\text{-}O_{SO_2}$ binding could be best described with ionic interactions; two oppositely charged atoms brought close together, as illustrated below (config. A).

Although it might be attractive to consider **A** to resonate with **B** geometry of the ring nitrogen of **2'** would not alow that; the nitrogen resides 0.503 Å (6-31G//6-31G) above the plane formed by its adjacent boron, carbon and sulphur atoms. By using the sum of the three angles[11] formed by the nitrogen and atoms adjacent to it as a measure of pyramidality one observes the nitrogen to be almost completely *sp*^{3} hybridized (e.g. at the 6-31G level the sum of the angles was calculated to be 332.8° which implies the degree of *sp*^{3} hybridization of the nitrogen to be about 86 %). Nevertheless, these results indicate only that the **A** - **B** resonance would not play any significant role in systems of which the conformation would be analogous to that of 2' (the Figure; one must also note that 2' may have many other conformations).

Altogether, it looks as if *N*-sulfonylated oxazaborolidines could clearly have some properties of bidentate complexation agents; the ring boron behaves as a Lewis acid and one of the oxygens of the adjacent sulfonyl group as a Lewis base. Although the results of this work do not prove that the mechanism of catalytic asymmetric Diels-Alder reaction would involve the formation of chelates analogous to 2' the results indicate that formation of these chelates could be possible; i.e. the main goal of this work, to demonstrate that the formation of 2 could be possible in some cases has been achieved. There results may help development of new and better catalysts for the asymmetric Diels-Alder reaction and other related reactions involving the use of bidentate composite Lewis acid - base systems as catalysts.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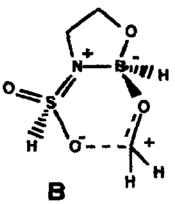
B

The complex 2' has a number of conformers which need to be studied before more advanced conclusions could be drawn with respect to the role of these type of complexes in the asymmetric Diels-Alder reaction. Further computational studies on the structure and formation of 2' and its conformers are in progress.

ACKNOWLEDGEMENTS

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10. Iclusion of polarization functions would have given a more realistic describtion of properties of 2' but, on the other hand, the size of 2' would also have gone far beyound limits of resources available for routine computational chemistry.
11. The sum of the three angles would be 360° in the case of planar systems and 328.4° in the case of tetrahedral ones.