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A Hypothesis For Conformational Restriction in Complexes of Formyl Compounds With Boron Lewis Acids. Experimental Evidence for Formyl CH--O and CH--F Hydrogen Bonds.

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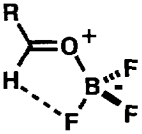
Summary: *X-Ray crystallographic analysis of six complexes of formyl compounds with B–F or B–O containing boron Lewis acids reveals in every case a geometric preference for a conformation in which the formyl group and the B–F or B–O bond are coplanar, or nearly so.*

The X-ray crystal structures of the complexes $C_6H_5CHO{\bullet}BF_3$[1] and $H_2C{=}C(CH_3)CHO{\bullet}BF_3$[2] reveal that the BF_3 is coordinated to the oxygen lone pair which is *syn* to the formyl proton and, further, that the formyl proton and one B–F bond are in plane (eclipsed) with respect to the C–O–B triad, as shown in **1**. A preference for the coplanar/eclipsed conformer **1** also has emerged from MO calculations.[3,4] It has been proposed[4] that this preference for eclipsed B–F and formyl C–H may be due to stabilization of this conformer by delocalization of the noncomplexed lone pair on oxygen into the σ^* orbital of the eclipsed B–F. Such stabilization need be only weak (1-2 kcal/mole), and even though this type of anomeric effect may seem unprecedented (the energy of the lone pair on oxygen is considerably lowered because of its positive charge), it cannot easily be ruled out. However, an alternative explanation for the stability of conformer **1** derives from the possibility of an attractive interaction between the formyl proton (which is greatly acidified by coordination to the Lewis acid in **1**) and the eclipsed coplanar fluorine (which is made more electron rich because of the negative charge on boron). Since the distance between the formyl proton and the eclipsed fluorine in the complex $H_2C{=}C(CH_3)CHO{\bullet}BF_3$[2] is 2.35 Å, which is less than the sum of the van der Waals radii of H (1.20 Å) and F (1.47 Å), 2.67 Å, such an attractive interaction or weak hydrogen bond is not unreasonable.[5]

We believe that the conformational preference for the eclipsed geometry in chiral Lewis acid-aldehyde complexes may be a significant factor in determining the absolute stereochemical pathway of their transformations. For this reason an X-ray crystallographic study was undertaken to determine the molecular geometry of a number of complexes of Lewis acids with formyl containing substrates.



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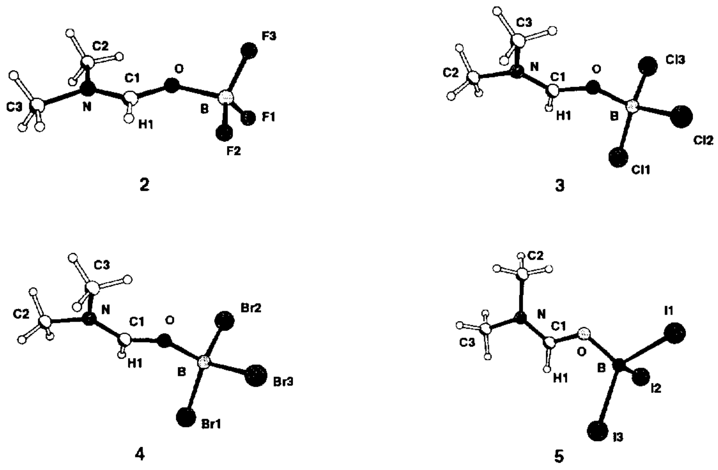


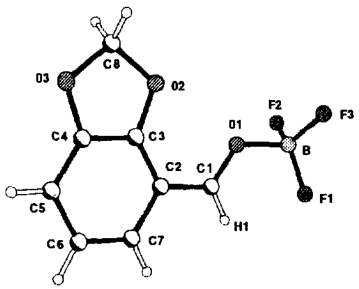
2 3 4 5

Figure 1. X-ray crystal structures of DMF•BX$_3$, X = F, Cl, Br, I (**2**, **3**, **4**, **5**).

Crystalline complexes **2** - **5** of dimethylformamide (DMF) with BF$_3$, BCl$_3$, BBr$_3$ and BI$_3$ were prepared and analyzed by single crystal X-ray diffraction. The results are summarized in Figure 1.[6] The complex DMF•BF$_3$ prefers the eclipsed-coplaner B–F/formyl arrangement, but the complexes DMF•BCl$_3$, DMF•BBr$_3$ and DMF•BI$_3$ do not. These results are understandable in terms of the formyl hydrogen bond to B–Hal, since hydrogen bonding to halide (e.g. X^-) can be expected to decrease in strength in the order F>Cl>Br>I. The distance in complex **2** between the eclipsed H (formyl) and F (boron) of 2.35 Å,[7] is considerably less than the sum of the van der Waals radii, 2.67 Å, and consistent with an attractive interaction between H and F. In contrast, it is difficult to explain the preferred molecular geometries in Figure 1 on the basis of an anomeric type oxygen lone pair delocalization into the B–Hal σ^* orbital. This delocalization would be expected to decrease in the order B–I>B–Br>B–Cl>B–F, so that DMF•BF$_3$ (**2**) would be the *least* likely complex to exhibit the eclipsed formyl C–H and B–F geometry, contrary to the experimental data.

2,3-Methylenedioxybenzaldehyde and BF$_3$ formed a crystalline 1 : 1 complex, the structure of which was shown by X-ray diffraction studies to be **6**. In this structure the formyl hydrogen and proximate B–F are nearly eclipsed (HCBF dihedral angle 10°) with an H–F distance of 2.36 Å, indicating a closer than van der Waals contact.

B-Bromocatecholborane did not yield crystalline complexes with aldehydes, probably because of insufficient Lewis acidity. However, a crystalline complex was obtained with the more basic DMF. The structure of this complex (**7**) was determined by X-ray diffraction to be that shown in Figure 2 as a stereopair representation. Two molecules of DMF are coordinated to boron in complex **7**. One DMF is arranged with a nearly coplanar arrangement of the formyl group and the nearby B–O bond (14° dihedral angle) and a formyl H to oxygen distance of 2.45 Å well within the value of 2.72 Å, which represents the sum of the H and O van der Waals radii.[5] The proximity of the formyl CH and the nearby oxygen is consistent with a weak attractive



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interaction, i.e. H bond between them. Evidence for many other examples of the C–H--O hydrogen bond in crystalline solids has been summarized in recent papers.[8]

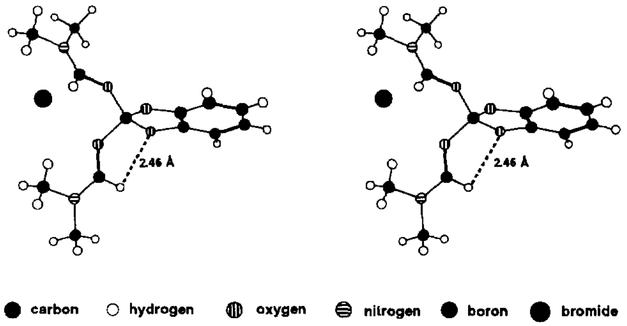

Figure 2. Stereopair representation of the DMF complex **7**.

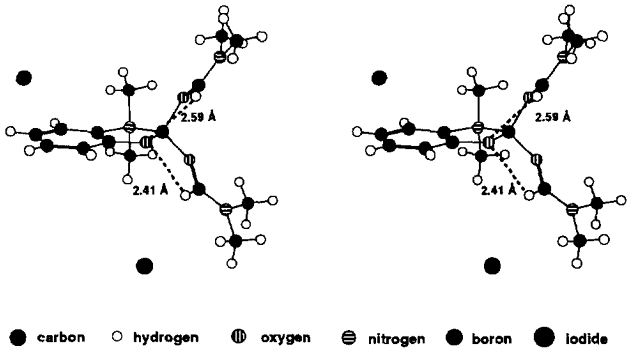

Figure 3. Stereopair representation of the DMF complex **8**.

A crystalline 2 : 1 complex was also prepared of DMF with 2-(*N*,*N*-dimethylamino)phenoxyboron diiodide. Treatment of a methylene chloride solution of 2-(*N*,*N*-dimethylamino)trimethylsilyloxybenzene with BI_3 in methylcyclohexane at -78 °C initially, and then at 23 °C for 45 min gave, after removal of solvent, a nearly colorless powder which was dissolved in dry CH_2Cl_2 and treated with DMF in CH_2Cl_2. X-Ray quality crystals of the 2 : 1 complex **8** were obtained within 24 h. The structure of **8** was determined by X-ray diffraction analysis to be that shown in Figure 3 as a stereopair representation. In structure **8** both formyl C–H hydrogens are oriented towards the oxygen of the oxazaborolidine ring with CH--O distances of 2.41 and 2.59 Å. It seems reasonable that the closer of these CH--O contacts represents another instance of CH--O hydrogen bonding. Intramolecular steric effects and crystal structure packing effects also may contribute to the conformational preference observed for **8** in the solid state.

The working hypothesis for conformational restriction in complexes of formyl compounds with boron Lewis acids which is presented herein is supported by the X-ray crystallographic results for complexes **1**, **2**, **6**, **7** and **8**. The formyl CH--X hydrogen bond, where X = F or O, in these structures is a reasonable (but not proven) concept which is attractive not only because it provides an explanation of the observed molecular geometry for these complexes in the solid state, but also because it leads to simple and straightforward rationalization of the enantioselectivity in a number of important chiral Lewis acid-catalyzed reactions of aldehydes. The following paper describes several examples of such enantioselective transformations and the possible role of CH--O hydrogen bonding in determining transition-state geometry.[9] The concept of CH--O hydrogen bonding in Lewis acid-catalyzed reactions of aldehydes has definite heuristic value in the design of new enantioselective catalysts and reactions. The merit of the hypothesis will be determined by the success of the predictions which follow from it.[10]

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