Conformational preferences of $R^1R^2C{=}O{\cdot}H_2BF$ complexes

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Molecular orbital calculations have quantified both the C–H hydrogen bond and the anomeric effect in $R^1R^2C{=}O{\cdot}H_2BF$ complexes.

It has recently been shown[1] that a hydrogen bond from a formyl C–H hydrogen to fluorine or oxygen is an important conformational restriction.[2] This is consistent with our calculations on $R^1R^2C{=}O{\cdot}H_2BF$ complexes, which prefer conformations with the fluoride eclipsing the carbonyl double bond (Fig. 1). We had suggested that this conformational preference may be due to a generalised anomeric effect,[3] which led to the interaction between fluorine and the adjacent group. The crystallographic results suggest that a formyl C–H to fluorine hydrogen bond is the controlling interaction. This can be used to explain the selectivity in many reactions. Here we report new *ab initio* calculations which allow us to investigate the relative importance of these two effects.

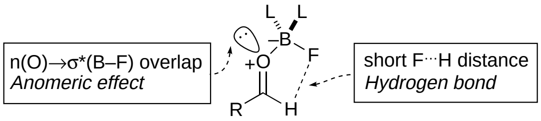

Fig. 1 Carbonyl H_2BF complexes: anomeric effect and hydrogen bond

The orientation of the coordinating Lewis acid will be affected by an anomeric effect (reinforced by a dipole–dipole interaction between the C=O and B–F bonds which we include in the anomeric effect for this analysis), a hydrogen bond and steric effects. It is not easy to separate these effects, because they will be combined in all molecules. The effect of changing from fluoride to chloride to bromide can be calculated. However, this may be expected to diminish both the anomeric effect (because the π–σ* energy match will be adversely effected) and also any H–halide interaction, because the orbital overlap will become less. This will not, therefore, help to distinguish these two effects.

We have already reported that the barrier for rotation around the O–B bond of formaldehyde complexed with H_2BF (Fig. 2, structure 1) is 14 kJ mol^{-1} at the MP2/6-31G*//3-21G level, using CADPAC.[4] We have now repeated this calculation at the MP2/6-31G**//MP2/6-31G** level and obtained a very similar figure (15 kJ mol^{-1}). In this complex, steric effects between the formyl hydrogen and the Lewis acid are likely to be small, so this should represent the sum of the anomeric effect and the hydrogen bond strength. In order to try and separate these effects, we performed calculations on the ketene complex **2** and the propynal complex **3**, reasoning that both these complexes should not have a hydrogen bond, but would show the anomeric effect. The results are summarised in Table 1.

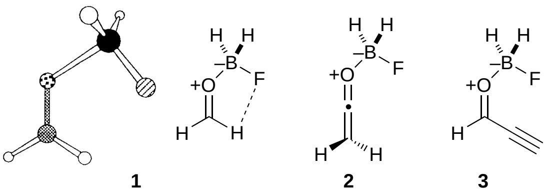

Fig. 2 Complexes with and without hydrogen bonds

Table 1 Results of calculations at the MP2/6-31G**//MP2/6-31G** level

Molecule	Barrier to rotation about O–B kJ mol^{-1}	H–F distance for lowest energy structure/Å	Strength of complexation/ kJ mol^{-1} [a]	C=O–B–F torsion angle for lowest energy structure (°)
1	15	2.20	48	0
2	1.4[b]	—	15	0
3	6	—	34	0
4	13	2.04	54	60
5	—[c]	2.26, 2.34	50	14

[a] No correction for BSSE or zero-point energy was made. [b] MP2/6-31G**//3-21G level. [c] Not determined because of the size of the system.

The ketene complex **2** shows only weak association with the Lewis acid. The barrier to rotation is less than 2 kJ mol^{-1}, but the O–B bond is 2 Å long. We may take this as a minimum value for the magnitude of the anomeric effect, which is likely to be larger in molecules, such as **1**, for which the O–B bond is shorter.

The propynal complex **3** shows much stronger complexation. The barrier to rotation around the O–B bond is now 6 kJ mol^{-1}, which is a typical magnitude for an anomeric effect.[5] There is likely to be some steric repulsion between the triple bond and the fluorine, which suggests that this value may be slightly too low. However, if we accept the value of 6 kJ mol^{-1} for the anomeric effect, we are left with 9 kJ mol^{-1} to attribute to the hydrogen bonding interaction, for complex **1**. We may conclude, therefore, that both effects are important, but the hydrogen bonding interaction is probably larger.

Our calculations also suggested that there may be hydrogen bonding interactions to hydrogens further from the carbonyl group (Fig. 3). The barrier to rotation for the acetone complex **4** is 19 kJ mol^{-1} (RHF/3-21G level). If we assume that the anomeric effect has a similar magnitude to the formaldehyde case, this gives a value of 13 kJ mol^{-1} for the hydrogen bond. At a higher level of theory (MP2/6-31G**//MP2/6-31G**) the geometry of the global minimum structure changes. Instead of a C=O–B–F dihedral angle of about 0° (as found at the RHF/3-21G level and illustrated in Fig. 3), the preferred geometry has a dihedral angle of about 60°. The barrier to rotation falls to 14 kJ mol^{-1}. If, following Allinger,[6] we assume that the anomeric effect falls off as the square of the consine of the C=O–B–F angle, then the anomeric contribution at 60° rotation is about 1.5 kJ mol^{-1}. We may, therefore, suggest a strength of about 12

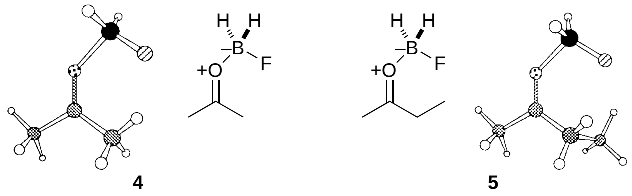

Fig. 3 Acetone and butanone complexes (RHF/3-21G geometries)

kJ mol^{-1} for the F–H hydrogen bond to the methyl group of acetone, which is similar to that estimated at the lower level of theory. This is stronger than the hydrogen bond for the formyl C–H, presumably because the geometry is better. The F–H distance in the formaldehyde complex is 2.20 Å, compared with 2.04 Å for the acetone complex. For comparison, the sum of the van der Waals radii for hydrogen and fluorine is 2.55 Å. The C–H–F angle is 100° for formaldehyde, and a more favourable 130° for acetone.

The structure of the (*Z*)-butanone complex **5**, in which the Lewis acid is complexed to the side of the ethyl group, appears to show hydrogen bonds both to the methylene adjacent to the carbonyl and also to the remote methyl group. Such an interaction is unusual, as the C–H bond is not activated by an adjacent group.[7] The geometries obtained at the low and high levels of theory are rather similar. If the energy is monitored as the O=C–C–C dihedral angle is rotated, there is a sudden change as the hydrogen bond to the methyl group breaks. This energy jump is about 4 kJ mol^{-1} at the MP2/6-31G** level. The complexation energy is similar for complexation on the methyl side and the ethyl side of the ketone (there is a preference for complexation on the methyl side at the RHF/3-21G level, which diminishes at higher levels of theory), and so the energy of the interaction with the methylene hydrogen must be at about 8 kJ mol^{-1}, to balance the overall energy. In fact, the strength of the hydrogen bond is likely to be greater than this, because this figure does not take adverse steric effects into account.

A summary of the different effects controlling the preferred conformations of the Lewis acid complexes is given in Table 2. This should help with the further analysis of the many systems for which these effects are important.[8]

In conclusion, hydrogen bonds and anomeric effects are both important in determining the preferred conformations of carbonyl–Lewis acid complexes of this type. These calculations have allowed us to approximately quantify these effects, and this should be a useful guide in designing systems which take advantage of this interaction.

Table 2 Quantification of anomeric and hydrogen bonding effects

Parameter		Energy/kJ mol^{-1}
Anomeric effect:	(for eclipsing geometries)	6
Hydrogen bonds:	Formyl C–H	9
	α-Methyl C–H	12
	β-Methyl C–H	4
	α-Methylene C–H	8

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Footnote and References

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