DOI: 10.1002/chem.200902599

Ligand Close Packing, Molecular Compactness, the Methyl Tilt, Molecular Conformations, and a New Model for the Anomeric Effect

Ronald J. Gillespie,*[a] **Edward A. Robinson,**[b] **and Julien Pilmé**[c]

Abstract: All the atoms in a molecule attract each other until they reach their equilibrium positions at which point the repulsive forces between the atoms just balance the attractive forces and there are no resultant forces acting on any of the atoms in the molecule. Thus, we can consider that in the equilibrium geometry the atoms in a molecule are arranged as compactly as possible. This is the basis of the ligand close packing (LCP) model according to which three or four monatomic ligands X, such as F, Cl or O (formally =O or O^-) pack as closely as possible around a small central atom such as a boron or carbon atom giving a truly close-packed equilateral triangular AX_3 molecule or a tetrahedral AX_4 molecules. Such monatomic ligands can, to a good approximation, be described as having a spherical shape with a single ligand radius r_X. In contrast, ligands with donor atoms with lone pairs such as the oxygen atom in an OX group have a less symmetrical electron density requiring two ligand radii, $r_{O_{lp}}$ in the lone pair direction, and r_{O_b} in the bonding direction, where $r_{O_{lp}} < r_{O_b}$ for an approximate description. On this basis we propose an explanation for the "methyl tilt", in methanol and many related molecules, and in conjunction with the concept of compactness, a model for explaining the relative energies of the conformations of molecules containing OH and OMe ligands, including molecules that exhibit the anomeric effect. We compare our model for the anomeric effect with the widely accepted "hyperconjugation" model. We also discuss the relationship between the concept of compactness and the concept of hardness.

Keywords: anomeric effect · density functional calculations · ligand close packing · molecular conformations · molecular structure

Introduction

All the atoms in a molecule attract each other by bonding forces, conventionally described as covalent, ionic, polar, or by van der Waals forces until they reach their equilibrium positions at which point the vector sum of all the forces acting on each individual atom is zero. Any small decrease in the distances between any two atoms increases the nucleus–nucleus and electron–electron repulsions and therefore the total energy of the molecule while any small increase in the distances between any two atoms increases the attraction between the electrons and the nuclei.[1] At equilibrium these two opposing forces just balance.

The attractions between the ligands X and between the central atom A and the ligands X in an AX_3 or AX_4 molecule cause these atoms to cluster as closely as possible around the central atom A giving a planar trigonal geometry for an AX_3 molecule and a tetrahedral geometry for an AX_4 molecule. In other words the X ligands are close-packed around the central atom A in the equilibrium geometry so that the molecule is as compact as possible. This statement is the basis of the LCP (ligand close packing) model.[2] The concept of compactness is discussed in more detail in the Section on Conformations, Molecular Compactness and the Generalized Anomeric Effect.

In the case of a small central atom from Period 2, such as boron and carbon, the X···X distances in AX_3 and AX_4 molecules have been found to be remarkably constant and very nearly independent of the presence of other ligands Y, and Z in molecules such as BX_2Y, $BX_2Y_2^-$, CX_3Y and CX_2YZ,

---

[a] Prof. Dr. R. J. Gillespie
Department of Chemistry, McMaster University
Hamilton, Ontario L8S 4M1 (Canada)
E-mail: ronald.gillespie@sympatico.ca

[b] Prof. Dr. E. A. Robinson
35, Beach Road West, Portishead, Bristol
BS20 7HX (UK)
and the University of Toronto (Canada)

[c] Dr. J. Pilmé
Université de Lyon, Université Lyon 1, Faculté de pharmacie
69373 Lyon, Cedex 08 (France)
and UPMC Université Paris 06
Laboratoire de Chimie Théorique, UMR-CNRS 7616
75252 Paris Cedex (France)

where X, Y and Z are monatomic ligands such as F, Cl or O (formally =O or O^-). In such molecules the ligands can be regarded as having approximately spherical shapes and as "touching" each other and the central atom A, so that a ligand radius r_X can be obtained from half the distance X···X. These radii have been shown to be additive so that in a molecule such as CX_3Y the X···Y distance can be predicted from the sum of the radii of X and Y.[2] This additivity of ligand radii is good additional evidence that the ligand atoms are indeed close packed around the central atom. Evidence for the LCP model and of its usefulness is illustrated, for example, by the difference between the bond lengths in BF_3 (130.7 pm) and BF_4^- (138.6 pm). These distances predict the same value of 226 pm for the F···F distance in both molecules and a ligand radius r_F for fluorine bonded to carbon of 113 pm.[2] This quantitative LCP explanation of the bond lengths is much simpler and more convincing than the often cited qualitative "explanation" in terms of the supposed double bond character (back-bonding) in the BF bonds in BF_3 for which there is no independent evidence.

The O and N atoms in diatomic and polyatomic ligands such as OH, OMe, NH_2, and NMe_2, cannot, however, be regarded as even approximately spherical, because the electron density is distorted from a spherical distribution by the attraction of the H atom or the C atom of the methyl ligand, while also causing the formation of one lone pair in the valence shell of nitrogen and two lone pairs in the valence shell of oxygen. Because the lone pairs are attracted only by the core they spread out as much as possible around the core while the electron density in the bonding regions is attracted, not only by the core of the central atom, but also by the ligands so that the electron density in the bonding region extends out further from the core than in the lone-pair region. We suggested previously[3] that the oxygen atom in an OH or OMe group can be satisfactorily described by two radii: $r_{O_{lp}}$ in the lone pair direction and r_{O_b} in the opposite or bonding direction, although in reality the radius of the oxygen atom must vary continuously between these two values. So the description of the oxygen atom by just these two radii $r_{O_{lp}}$ and r_{O_b} is only an approximation which is reasonably satisfactory for a given molecule. However, the values of $r_{O_{lp}}$ and r_{O_b} may vary by as much as ±3–4 pm from molecule to molecule, because the contacts made by the oxygen atom with the other atoms in a molecule are not in the same direction in all molecules.

As we have explained above, lone-pair domains take up more angular space in the valence shell of an atom in a molecule than the bond-pair domains which extend further away from the central atom towards the ligands. However, this does not imply that they also occupy more space in directions away from the valence shell. Indeed they occupy less space in these directions, so that the radius of an atom is smaller in the lone pair direction than in other directions. In reality, lone pairs are not well represented by the typical hybrid orbital shapes (sometimes called "rabbit ears")[4] that are often used to depict lone pairs. These shapes could lead to the conclusion that lone pairs have a larger radius than bond pairs, rather than a smaller radius and might therefore repel atoms that are not bonded to the central atom, rather than allowing them to come closer to the lone-pair region than to other regions of the atom. The asymmetry of the electron density around an O atom in a diatomic ligand such as OH, or OMe has several important consequences for molecular structure, which we discuss in this paper.

1) We show that the asymmetry of the oxygen atom, in conjunction with the concept of compactness, provides an explanation for the frequently observed tilt of a CX_3 group towards the oxygen atom in a CX_3OY molecule. In the case of the CH_3 group this is known as the "methyl" tilt.
2) We show that the concept of compactness enables us to predict which of the conformers of $A(OX)_3$ and $A(OX)_4$ molecules has the lowest energy.
3) We show that the lowest energy conformations of many other molecules containing one or more OX groups, including those that exhibit the anomeric effect (Section on Conformations, Molecular Compactness and the Generalized Anomeric Effects), can similarly be predicted using the concept of compactness.

The Methyl Tilt

It has been known for more than fifty years that in molecules of the type $YO\text{-}CX_3$, where X is a monatomic ligand, and Y is either a monatomic ligand or a polyatomic ligand, that the CX_3 group is tilted towards the lone pair side of the O atom, usually by approximately 2–5°. But no explanation of this phenomenon seems to have been previously proposed.[5] It is the purpose of this section to give an explanation for the tilt of the methyl group and other CX_3 groups.

Table 1 gives the experimental bond angles, bond lengths and interatomic distances for one of the simplest molecules to exhibit the methyl tilt, namely methanol CH_3OH and Table 2 and Figure 1 the calculated data and its analysis in terms of interatomic distances. Historically, in discussions of the methyl tilt, the methyl group was assumed to retain its C_{3v} symmetry because of the lack of precise data on the positions of the H atoms in the methyl group and the tilt angle was defined as the angle between the assumed C_3 axis of the CH_3 group and the direction of the C−O bond in CH_3OY molecules. However, later accurate structures, determined both experimentally and by theory, show that in general in this type of molecule the CH_3 group does not retain C_3 symmetry around the C–O axis because it tilts away from this axis and this tilt is accompanied by very small but real changes in the C−H bond lengths and OCH angles.

On the basis of the LCP model we expect the three methyl hydrogen atoms and the O atom to be close packed around the carbon atom. The Me group tilts towards the lone pair side of the oxygen atom with the smaller radius and away from the bonding side of the oxygen with a larger

Table 1. Structure, interligand distances (pm) and the methyl tilt for methanol.[a]

Method	ed	ed/mw	mw	d
C−H_c	109.6(11)	109.8(1)	109.4(3)	109.50(2)
C−H_t	110.2(11)	109.8(1)	109.4(3)	109.50(2)
C−O	142.8(1)	142.9(1)	142.1(2)	142.53
O−H^O	96.0	97.5(10)	96.3(8)	96.56
$<HCH_{av}$	108.2	109.0	109.1	108.8
$\sphericalangle COH^O$	–	107.6(9)	108.0(4)	108.37
$\sphericalangle OCH_c$	106.8	106.4	106.7	106.4
$\sphericalangle OCH_t$	112.6	111.6	111.4	112.1
$H\cdots H_{av}$	178.2	178.8	178.2	178.0
$C\cdots H^O$	–	196(2)	195(2)	195.0
$O\cdots H_c$	204	204	203	203
$O\cdots H_t$	211	210	210	210
$r_{O_{lp}}$	115	115	114	114
r_{O_b}	122	121	121	121
tilt	3.9	3.4	3.2	3.8
ref.	[b]	[c]	[c]	[d]

[a] Distances in pm and bond angles in degrees. [b] O. J. Benston, J. D. Ewbank, D. W. Paul, J. Klimkowski, L. Schäfer, *Appl. Spectrosc.* **1984**, *38*, 204. [c] T. Iijima, *J. Mol. Struct.* **1989**, *212*, 137. [c] M. C. L. Gerry, R. M. Lees, G. Winnewisser, *J. Mol. Spectrosc.* **1976**, *61*, 231. [d] L. Wang, Y.-B. Duan, Y.-B. Matsushima, K. Takagi, *Chem. Phys. Lett.* **2002**, *365*, 432, give a structure resulting from calculation of the best fit based upon published spectral data for methanol and its isotopomers (CH_3OH, $CH_3{}^{18}OH$, CH_3OD and CD_3OD). Note: References [c] and [d], give only average HCH and HCO bond angles and the Me tilt, from which we calculated the two HCO bond angles.

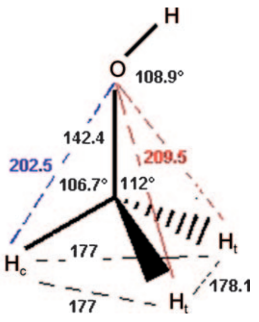


Figure 1. Optimized structure of methanol. Distances in pm and angles in degrees.

radius so as to remain as close packed as possible. There are three contacts between the H atoms of the methyl group and the O atom of which the single *cis* $H_c\cdots O$ distance has a length of 202.5 pm and the two *trans* $O\cdots H_t$ distances have equal lengths of 209.6 pm, The corresponding OCH angles are OCH_c 106.7 and OCH_t 112.0° (twice). Using the previously determined radius for the hydrogen atom bonded to carbon of 89 pm,[2] we can deduce values for the radius of the O atom in the lone pair direction and in the opposite (bonding) direction: $r_{O_{lp}} = 114$ pm and $r_{O_b} = 120$ pm. These results show clearly that the tilt of the methyl group is due to the lack of symmetry of the electron density of the oxygen and that for this molecule the oxygen atom may be assigned the two radii $r_{O_{lp}} = 114$ pm and $r_{O_b} = 120$ pm. However, these values of $r_{O_{lp}}$ and r_{O_b} give only a qualitative estimate of what can be expected for other molecules. The absolute values of $r_{O_{lp}}$ and r_{O_b} vary slightly from molecule to molecule but for most of the molecules we have studied the difference is 6–8 pm.

In general the tilt angle can be defined as

$$\text{tilt angle} = 1/3\,(2\alpha_1 - \alpha_2 - \alpha_3) \qquad (1)$$

where α_1 is the value of the largest of the OCH angles and α_2 and α_3 are the values of the two smaller angles. When $\alpha_2 = \alpha_3$, which is usually the case,

$$\text{tilt angle} = 2/3\,(\alpha_1 - \alpha_2) \qquad (2)$$

The data in Table 2 give a value of 3.5° for the tilt of the methyl group in methanol. Table 3 gives experimental bond lengths, bond angles, and interatomic distances and the methyl tilt angle for a variety of CH_3OX molecules. All these molecules exhibit a methyl tilt in the range 1.5–6.0°. We conclude that the methyl tilt is a feature of all molecules of this type, and is a consequence of the unsymmetrical nature of the electron density of the oxygen atom in an AOX group and the tendency of all molecules to adopt the most compact structure.

Table 2. Close packing of the ligands in methanol.[a]

		Interligand distances X···Y		
			Found	Predicted[a]
O−H	96.0			
C−O	142.4			
C−H_c	108.74			
C−H_t	109.35			
$<COH^O$	108.92	$C^O\cdots H^O$	196.0	117 + 76 = 193
$\sphericalangle H_cCH_t$	108.46	$H_c{}^C\cdots H_t{}^C$	177.0	89 + 89 = 178
$\sphericalangle H_tCH_t$	109.09	$H_t{}^C\cdots H_t{}^C$	178.2	89 + 89 = 178
$\sphericalangle OCH_c$	106.68	$O\cdots H_c{}^C$	202.5	***114*** + *89*
$\sphericalangle OCH_t$	112.01	$O\cdots H_t{}^C$	209.6	***121*** + *89*
tilt	3.55			

[a] Predicted from the standard radii: $r(H^C) = 89$ pm and $r(C^O) = 117$ pm as found in the majority of simple ethers with distances in pm and angles in degrees. The resulting oxygen radii, r_{lp} and r_b, shown in bold italics, are calculated from the $H^C\cdots O$ interligand distances with $r_{H^C} = 89$ pm. The structure was calculated at the B3LYP/6-311+G(2d,2p) level.

It can be seen in Table 3 that the magnitude of the tilt angle appears to depend on the electronegativity of the atom or group X; more electronegative groups such as F, Cl, NO, and NO_2 giving larger tilt angles in the range of 4–5°. With increasing electronegativity of X the oxygen atom is expected to shrink in size as its negative charge decreases. The larger tilt of the oxygen atom in the lone pair direction observed in these molecules indicates that the oxygen atom radius decreases more in the lone-pair direction than in the bonding direction. This is not surprising because lone pair electrons are expected to be more polarizable than the bonding electrons, which are under the influence of two nuclei rather than one.

A similar tilt of other CX_3 groups in CX_3OY molecules is shown by the examples of the CF_3 and CMe_3 groups in Table 4. Such group tilts are a widespread phenomenon found in a large variety of molecules in which AX_3, AX_2Y, etc., groups are bonded to oxygen such as those we discuss in the following sections.

Table 3. Oxygen ligand radii for methoxy groups in some R-OCH$_3$ molecules.[a]

R	C–H$_1$	C–H$_{2,3}$	C–O	$\sphericalangle$H$_1$CO	$\sphericalangle$H$_{2,3}$CO	H$_1$···O	H$_{2,3}$···O	Ref.
FH$_2$C-	107.8	110.6	142.4	107.5	109.8	203	208	[b]
ClH$_2$C-	107.7	111.6	142.1	107.2	109.6	202	210	[c]
H$_2$C=C(H)-	107.7	110.2	142.0	106.9	110.3	202	208	[d]
Cl	108.6	111.1	138.9	106.9	110.4	200	206	[e]
HO-(CH$_2$)$_2$-	109	109	141	107.2	110.8	202	207	[f]
C$_2$H$_5$-	108.6	109.9	141.5	107.5	111.1	203	208	[g]
Me-	108.5	109.9	141.1	107.4	111.1	202	208	[h]
n-C$_3$H$_7$-	108.6	109.9	141.3	107.4	111.1	202	208	[i]
H$_3$Si-CH$_2$-	109.2	109.4	141.6	107.0	110.9	203	208	[j]
FC(O)-	107.6	108.6	144.8	104.9	109.4	198	205	[k]
Cl(O)C-	108.8	109.2	144.8	105.1	109.9	202	209	[l]
H$_2$C=C(Me)C(O)-	110.5	110.7	143.8	104.7	109.5	202	208	[m]
p-ClC$_6$C$_4$-C(O)-	110.5	110.8	143.8	105.1	110.3	203	210	[n]
H-	109.6	110.2	142.8	106.8	112.6	204	211	[o]
O$_2$N-	108.8	109.5	143.7	103.4	110.4	199	209	[p]
ON-	109	110.2	143.7	101.8	109.9	197	209	[q]

[a] Distances in pm, angles in degrees; the oxygen ligand radii are calculated from the H···O interligand distances with $r_H = 89$ pm. [b] Fluoromethoxymethane: J. Naggawa, H. Kato, M. Hayashi, *J. Mol. Spectrosc.* **1981**, *90*, 467. [c] Chloromethoxymethane: M. Hayashi, H. Kato, *Bull. Chem. Soc. Jpn.* **1980**, *53*, 2701. [d] Methyl vinyl ether: M. Fujitake, M. Hayashi, *J. Mol. Struct.* **1985**, *127*, 21. [e] Methyl hypochlorite: J. S. Rigden, S. S. Butcher, *J. Chem. Phys.* **1971**, *6*, 395. [f] Methoxyethanol: P. Buckley, M. Brochu, *Ca. J. Chem.* **1972**, *50*, 1149. [g] Ethyl methyl ether: M. Hayashi, M. Adachi, *J. Mol. Struct.* **1982**, *78*, 5. [h] Dimethyl ether: Y. Niide, M. Hayashi, *Mol. Spectrosc.* **2003**, *220*, 65. [i] *n*-Propyl methyl ether: M. Hayashi, M. Adachi, *J. Mol. Struct.* **1982**, *78*, 53. [j] Methoxymethylsilane: Y. Shiki, N. Ibushi, M. Oyamada, J. Nakagawa, M. Hayashi, *J. Mol. Spectrosc.* **1981**, *87*. 357. [k] Methyl fluoroformate: P. Groner, C. L. Tolley, J. R. Durig, *J. Mol. Struct.* **1990**, *2231*, 471. [l] Methyl chloroformate: P. Groner, C. L. Tolley, J. R. Duriig, *Chem. Phys.* **1990**, *142*, 381. [m] H$_2$C=C(Me)C(O)-OMe: T. Tsuji, H. Ito, H. Takeuchi, S. Konaka, *J. Mol. Struct.* **1999**, *475*, 55. [n] Methoxy *p*-chlorobenzoate: H. Takashima, K. Endo, M. Ito, H. Takeuchi, T. Egawa, S. Konaka, *J. Mol. Struct.* **1999**, *478*, 13. [o] Methanol: O. J. Benston, J. D. Ewbank, D. W. Paul, J. Klimkowski, L. Schäfer, *Appl. Spectrosc.* **1984**, *38*, 204. [p] Methyl nitrate: A. P. Cox, S. Waring, *Trans. Farad Soc.* **1971**, *61*, 3441. [q] Methyl nitrite: P. H. Turner, A. P. Corkill, Cox, *J. Phys. Chem.* **1979**, *83*, 1.

Geometry of the B(OH)$_{3,4}$, B(OMe)$_{3,4}$, C(OH)$_4$,and C(OMe)$_4$ molecules

In this section, following our earlier work[3] on the geometry of B(OH)$_3$ and B(OH)$_4^-$, we discuss the geometry of B(OH)$_3$, B(OMe)$_3$, B(OH)$_4^-$, B(OMe)$_4^-$, C(OH)$_4$, and C(OMe)$_4$, and show how the relative energies of the conformations of these molecules can be predicted from their compactness. Consistent with the LCP model the oxygen atoms in these molecules are close packed around the boron atom. In the case of monatomic ligands such as F and Cl the close packing of fluorine ligands around the boron atom in the molecules BF$_3$ and BF$_4^-$, for example, has been confirmed by the equality of all the F···F distances in both molecules.[2] However, as we shall see, the O···O distances are not all equal because the angles of the contacts between the asymmetrical oxygen atoms may vary from molecule to molecule and from one conformation to another. We first consider the molecules B(OH)$_3$ and B(OMe)$_3$.

B(OH)$_3$ and B(OMe)$_3$: Our calculations show that B(OH)$_3$ and B(OMe)$_3$ have two low energy conformers with C_{3h} and C_s symmetry, respectively, as shown in Figure 2. The C_{3h} conformer has the lower energy and is the stable observed conformer. The calculated geometric parameters for these conformers are given in Table 5 and the O···O distances are given in Table 6. For B(OH)$_3$ they are in good agreement with the values obtained very recently by Stefani et al. at the B3LYP(6-311G**) level.[6]

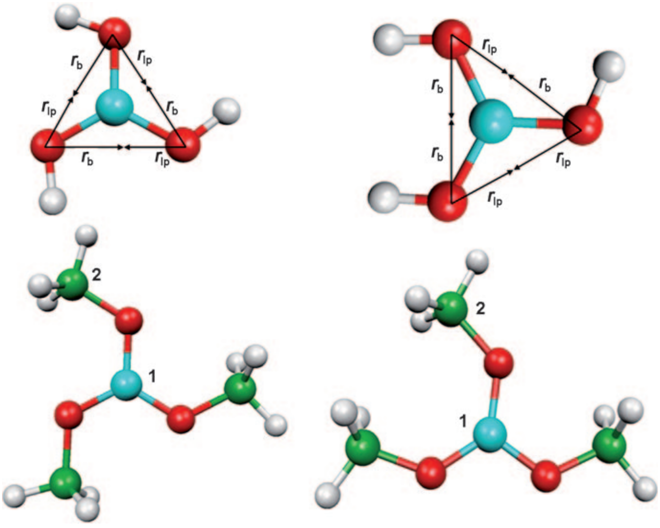


Figure 2. Ball-and-stick models of B(OH)$_3$ (top) and B(OMe)$_3$ (bottom). C_{3h} conformers (left) and C_s conformers (right).

In principle each OH or OMe group is free to rotate around the B–O bond. But there are just two arrangements of the three OH or OMe groups for which the energy of the molecule is a local minimum and which correspond to the C_{3h} and C_s conformers. The C_{3h} conformer has three equal O···O distances of 237 pm but in the C_s conformer there are three O···O distances of 232, 236 and 244 pm. Because the bond angles, bond lengths and O···O distances in the C_s conformer are significantly different from those in the C_{3h} conformer it might appear that the O atoms are not close packed in the C_s conformer even though according to the LCP model they might be expected to be close packed. However, the average of the three O···O distances in the C_s conformer (237 pm) is equal to the single value of 237 pm for the C_{3h} conformation which is consistent with the O atoms in both conformers being close-packed around the central B atom

Table 4. Oxygen ligand radii for OCF_3 and $OC(CH_3)_3$ groups.[a]

Molecule	C–F$_1$	C–F$_{2,3}$	C–O	$\sphericalangle F_1CO$	$\sphericalangle F_{2,3}CO$	$F_1\cdots O$	$F_{2,3}\cdots O$	Tilt [°]	Ref.
H_3C-OCF_3	131.8	133.6	134.7	109.0	112.3	217	223	2.2	[b]
HF_2C-OCF_3	131.5	133.5	135.6	108.3	112.4	217	224	2.7	[c]
$C_6H_5-OCF_3$	132.7	134.2	133.4	108.3	113.2	216	223	3.2	[d]
O_2N-OCF_3	132	132.2	137.8	105.5	112.5	215	225	3.6	[e]
$F-OCF_3$	131.9	131.9	139.5	105.4	111.3	216	224	3.7	[f]
$FC(O)-OCF_3$	132.3	137.9	134.7	106.3	111.9	217	224	3.7	[g]
$FO-OCF_3$	132.2	132.2	141.9	106.1	111.7	219	227	3.7	[h]
$ClSO_2-OCF_3$	131.8	131.8	142.0	105.2	110.9	218	226	3.8	[i]
$Cl-OCF_3$	131.8	132.5	136.5	105.8	111.7	215	223	3.9	[j]
F_3C-OCF_3	132.7	133.7	136.9	106.2	112.3	216	224	4.0	[k]
$OC(OCF_3)_2$	131.5	131.5	136.5	104.1	111.1	211	221	4.6	[g]
$HO-OCF_3$	132.4	132.4	137.6	105.0	112.0	214	224	4.8	[h]
$ClO-OCF_3$	132.3	132.3	137.2	106.1	113.7	215	226	5.1	[h]
Molecule	C–C$_1$	C–C$_{2,3}$	C–O	$\sphericalangle C_1CO$	$\sphericalangle C_{2,3}CO$	$C_1\cdots O$	$C_{2,3}\cdots O$	Tilt [°]	Ref.
Et–O*t*Bu	149.5	156.5	141.7	105.9	110.5	233	245	3.0	[m]
H–O*t*Bu	152.9	152.9	144.6	104.9	109.6	236	243	3.1	[m]
Me–O*t*Bu	153.2	153.2	144.8	103.2	110.2	233	244	4.6	[l]
RO–*t*Bu	152.9	152.9	144.5	102.2	109.9	232	244	5.1	[n]
R′–*t*OBu	152.9	152.9	145.6	102.5	111.0	233	246	5.7	[o]

[a] Distances in pm, angles in degrees; the oxygen ligand radii are calculated from the H–O interligand distances with $r_H = 89$ pm and $r_C = 128$ pm. References: [b] Perfluoromethyl methyl ether: R. Kuhn, D. Christen, H.-G. Mack, D. Konikowski, R. Minkwitz, H. Oberhammer, *J. Mol. Struct.* **1971**, *8*, 395. [c] Perfluoromethyl difluoromethyl ether: S. E. Ulic, H. Oberhammer, *J. Phys. Chem. A.* **2004**, *108*, 1844. [d] Perfluoromethoxybenzene: D. Federsel, A. Herrmann, D. Christen, S. Sander, H. Willner, H. Oberhammer, *J. Mol. Struct.* **2001**, *567-568*, 127. [e] Perfluoromethyl peroxynitrate: R. Kopitzky, H. Willner, H.-G. Mack, A. Pfeiffer, H. Oberhammer, *Inorg. Chem.* **1998**, *37*, 6208. [f] Trifluoromethyl hypofluorite: F. P. Diodati, L. S. Bartell, *J. Mol. Struct.* **1971**, *8*, 395. [g] Perfluoromethyl fluoroformate perfluorodimethyl carbonate: A. Hermann, F. Trautner, K. Gholivand, S. von Ahsen, E. L. Varetti, C. O. Della Vedova, H. Willner, H. Oberhammer, *Inorg. Chem.* **2001**, *40*, 3979. [h] Trifluromethyl hydroperoxide, fluoroperoxide, and chloroperoxide: C. J. Marsden, D. D. DesMarteau, L. S. Bartell, *Inorg. Chem.* **1977**, *16*, 2359. [i] M. F. Erben, C. O. Della Vévoda, R. Boese, H. Willner, C. Leibold, H. Oberhammer, *Inorg. Chem.* **2003**, *322*, 7297. [j] Trifluoromethyl hypochlorite: H. Oberhammer, T. Mahmood, J. M. Shreeve, *J. Mol. Struct.* **1984**, *117*, 311. [k] Diperfluoromethyl ether: A. H. Lowrey, C. George, P. D′Antonio, J. Karle, *J. Mol. Struct.* **1980**, *63*, 243. [l] Methyl and ethyl tertiary butyl ethers: R. D. Suenram, F. J. Lovas, W. Pereyra, J. T. Fraser, A. R. H. Walker, *J. Mol. Spectrosc.* **1999**, *181*, 67. [m] Tertiary-butanol and tertiarybutyl methyl ether: A. Suwa, H. Ohta, Konaka, *J. Mol. Struct.* **1988**, *172*, 275. [n] *tert*-Butyl formate: H. Takeuchi, T. Matsuoaka, T. Tsuji, H. Takashima, M. Ito, S. Konaka, *J. Mol. Struct.* **1998**, *471*, 275. [o] Tertiary butyl vinyl ether. C. Leibold, H. Oberhammer, *J. Am. Chem. Soc.* **1998**, *120*, 1533.

(Table 6). The differences in the O···O distances in the C_s conformer simply reflect the three different possible types of contact between the oxygen atoms.

If we assume that the oxygen atom can be described by the two radii $r_{O_{lp}}$ and r_{O_b}, the O···O distance of 239.1 pm in $B(OH)_3$ can be identified as $r_{O_b} + r_{O_{lp}}$ as shown in Figure 2 and the three O···O distances of 232, 236 and 244 pm in the C_s conformer can be identified as $r_{O_{lp}} + r_{O_{lp}}$, $r_{O_{lp}} + r_{O_b}$ and $r_{O_b} + r_{O_b}$ (Figure 3). Of these, the values of 232 and 244 pm suggest r_{lp} and r_b values close to 116 and 122 pm, respectively, in which case $r_{lp} + r_b$ should be 238 pm compared to the 237 pm in the C_{3h} conformer and 236 pm in the C_s conformer in good agreement.

For $B(OCH_3)_3$ the situation is quite similar, with average O···O distances close to 237 pm in both the C_{3h} and C_s conformers, an $r_{O_{lp}} + r_{O_b}$ value of 237 pm in the C_{3h} conformer, and $r_{O_{lp}} + r_{O_{lp}}$, $r_{O_{lp}} + r_{O_b}$ and $r_{O_b} + r_{O_b}$ values of 230, 235, and 245 pm in the C_s conformer, giving values of $r_{O_{lp}}$ and r_{O_b} close to 115 pm and 123 pm, respectively. The values of the oxygen r_{lp} and r_b radii calculated from the respective 1,3-$H_c\cdots O$ and $H_t\cdots O$ distances are 114 and 119 pm (C_{3h}), and 114 and 120 pm (C_s) for $r_{O_{lp}}$ and r_{O_b}, respectively. Although there are small differences between the various values from the different methods, the difference between the $r_{O_{lp}}$ and r_{O_b} values is always characteristically close to 6 pm in all these boron molecules. Although not perfect, the two radii model seems to work as well as might expected for such a simple model. The methyl groups in both of the $B(OCH_3)_3$ conformers have the characteristic methyl tilt expected due to the asymmetry of the electron density of the oxygen atoms in the OCH_3 groups.

Compactness and the relative energies of the conformers of $B(OH)_3$, and $B(OMe)_3$: The difference in the energies of the two conformers might in principle be attributed to the differences in their bond lengths and angles. However, because the three oxygen atoms are close packed around the boron atom the BO_3 portion of these molecules is as compact as possible and has the same energy in both conformers. Why then do the two conformations have different energies? The answer is that the H or C atoms of the

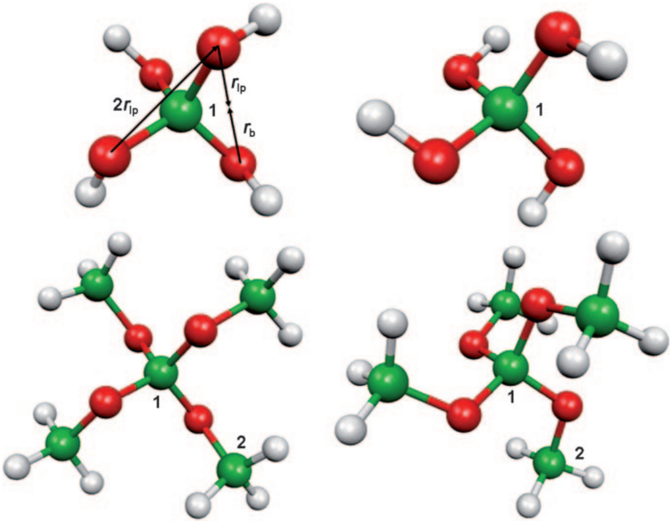


Figure 3. Ball-and-stick models of $A(OH)_4$ (left) and $A(OMe)_4$ (right). D_{2d} conformations (left) and S_4 conformations (right).

Table 5. Optimized B3LYP/6-311+G(2d,2p) geometries for $B(OH)_3$, $B(OCH)_3$, $B(OH)_4^-$, $B(OCH_3)_4^-$, $C(OH)_4$ and $C(OCH_3)_4$.[a]

	$B(OH)_3$		$B(OCH_3)_3$		$B(OH)_4^-$		$B(OCH_3)_4^-$	
	C_{3h}	C_s	C_{3h}	C_s	S_4	D_{2d}	S_4	D_{2d}
B−O	136.9(3)	137.9(1) 137.0(1) 136.3(1)	136.7(3)	136.8(3)	148.4(4)	148.5(4)	147.5(4)	147.7(4)
O−CH$_3$			142.7(3)	141.8(1) 142.3(1) 142.1(1)			139.8(4)	139.6(4)
O−H	96.0(3)	96.0(1) 95.7(1) 95.3(1)			96.9(4)	95.9(4)		
C−H$_c$			108.7(3)	108.8(3)			109.7(4)	109.9(4)
C−H$_t$			109.0(6)	109.1(6)			109.9(8)	110.0(8)
∢OBO	120.0(3)	116.43(1) 118.39(1) 125.18(1)	120.0(3)	113.6(1) 117.3(1) 129.1(1)	114.1(2) 107.2(4)	104.4(2) 112.1(4)	112.4(2) 107.9(4)	103.6(2) 112.4(4)
∢BOH	112.9(3)	112.2(1) 115.7(1) 116.2(1)			106.9(4)	105.8(4)		
∢BOC			120.7(3)	121.3(1) 128.8(1) 129.3(1)			116.9(4)	116.0(4)
∢H$_c$CH$_t$			108.7(6)	108.8(6)			107.3(4)	106.2(4)
∢H$_t$CH$_t$			109.4(3)	108.8(6)			108.2(8)	108.2(8)
∢OCH$_c$			107.2(3)	107.4(3)			108.8(4)	108.9(4)
∢OCH$_t$			111.0(6)	111.9(6)			112.1(8)	112.5(8)

	$C(OH)_4$		$C(OCH_3)_4$	
	S_4	D_{2d}	S_4	D_{2d}
C−O	139.2(4)	139.3(2)	139.1(4)	139.4(4)
O−CH$_3$			143.0(4)	142.9(4)
O-H	96.4(4)	96.3(4)		
C−H$_c$			108.7(4)	108.8(4)
C−H$_t$			108.8(8)	109.2(4)
∢OCO	113.7(2) 107.4(4)	103.5(2) 112.5(4)	113.0(2) 107.8(4)	102.6(2) 113.0(4)
∢COH	107.6(4)	106.5(4)		
∢COC			115.8(4)	114.8(4)
∢H$_c$CH$_t$			109.9(8)	110.4(8)
∢H$_t$CH$_t$			109.5(4)	107.6(4)
∢OCH$_c$			105.7(4)	106.0(4)
∢OCH$_t$			110.0(8)	110.0(8)

[a] Bond lengths in pm, bond angles in degrees. Note that the C−H$_c$, C−H$_t$, ∢HCH, and ∢OCH data for the C_s conformer of $B(OCH_3)_3$ are averaged over all three OCH$_3$ groups.

Table 6. Optimized individual and average O···O 1,3 interligand distances in $B(OH)_3$, $B(OCH_3)_3$, $B(OH)_4^-$, $B(OCH_3)_4^-$, $C(OH)_4$, and $C(OCH_3)_4$.[a]

	$B(OH)_3$		$B(OCH_3)_3$		$B(OH)_4^-$		$B(OCH_3)_4^-$	
	C_{3h}	C_s	C_{3h}	C_s	S_4	D_{2d}	S_4	D_{2d}
O···O	237.1(3)	232.3(1) 235.5(1) 244.0(1)	236.6(3)	230.3(1) 234.6(1) 245.4(1)	238.8(4) 249.1(2)	234.7(2) 246.3(4)	238.8(4) 245.5(2)	232.3(2) 245.6(4)
Av**	237.1	237.3	236.6	236.8	242.2	242.4	241.0	241.2

	$C(OH)_4$		$C(OCH_3)_4$	
	S_4	D_{2d}	S_4	D_{2d}
O···O	224.5(4) 233.3(2)	218.6(2) 231.5(4)	224.8(4) 232.1(2)	217.6(2) 232.5(4)
Av[b]	227.4	227.2	227.2	227.5

[a] O···O distances in pm. [b] Weighted averages.

OH or OMe group are not close packed with the neighboring oxygen atoms in either conformer because the two bonds formed by the oxygen atom have directions that are determined by the presence of the two lone pairs in the valence shell of the oxygen atom. In the case of $B(OH)_3$ the O···H and O···C distances (Table 7) are much longer than they would be if the oxygen and hydrogen atoms were close packed. The hydrogen atoms would nevertheless be expected to take those positions in which they are as closely packed as possible with the oxygen atoms. So the relative compactness of the two conformations can be predicted from the 1,4 O···H and 1,4 O···C distances. (The description 1,4 is used for the distance from one atom in a molecule to the fourth atom along a chain of bonds. This follows from the terminology 1,3-distance first introduced by Glidewell[7] to describe the distance between the first and third, or vicinal, atoms along a chain of atoms.) The shorter the 1,4 O···H or O···C distances, the more closely packed are the H or C atoms with their oxygen neighbors, and therefore the more compact is the molecule. In the C_{3h} conformer of $B(OH)_3$ the three 1,4 H···O distances each have a length of 244.5 pm. In the C_s conformer there are three different 1,4 H···O distances with lengths of 260.5, 259.4, and 240.4 pm with an average value of 253.1 pm. This is larger than the 1,4 O···H distance in the C_3 conformer, showing that that the C_s conformer is the less compact and therefore higher energy conformer in agreement with its calculated relative energy of 18.5 kJ mol^{-1} (Table 7).

The O···C distances in the C_{3h} conformer of B(OMe)$_3$ all have the same length of 277.7 pm while the C_s conformer has three 1,4 O···C distances of 274.8, 305.1, and 306.1 pm with a larger average value of 285.5 pm showing that the C_s conformation is the less com-

Table 7. 1,4-Non-bonding O···H distances in conformers of $B(OH)_3$, $B(OH)_4^-$,$C(OH)_4$; and 1,4-non-bonding O···C distances in conformers of $B(OMe)_3$, $B(OCH_3)_4^-$ $C(OCH_3)_4$, with their relative energies [kJ mol^{-1}].

Molecule		Nonbonding 1,4 distances			
		1,4		Average	ΔE
$B(OH)_3$	C_{3h}	O···H	244.5(3)[a]	244.5	0.00
	C_s	O···H	240.4(1), 260.5(1), 259.4(1)	253.4	18.5
$B(OH)_4^-$	S_4	O···H	237.5(1), 238.4(1), 239.9(1), 250.6(1)		6.6
			266.5(1), 277.7(1), 279.6(1), 280.7(1)	258.8	0.00
	D_{2d}	O···H	259.4(8)	259.4	5.0
$C(OH)_4$	S_4	O···H	229.1(1), 230.5(1), 231.0(1), 238.6(1)		
			252.1(1), 260.2(1), 260.7(1), 262.3(1)	245.6	0.00
	D_{2d}	O···H	247.0(8)	247.0	7.5
$B(OMe)_3$	C_{3h}	O···C	277.7(3)	277.7	0.00
	C_s	O···C	274.8(1), 305.1(1), 306.1(1)	295.3	33.5
$B(OMe)_4^-$	S_4	O···C	283.5(1), 284.0(1), 284.2(1), 284.4(1)		
			301.1(1), 301.1(1), 301.5(1), 301.8(1)	292.7	0.00
	D_{2d}	O···C	294.6(8)	294.6	6.6
$C(OMe)_4$	S_4	O···C	271.4(1), 271.8(1), 271.9(1), 272.0(1)		
			289.8(1), 289.9(1), 290.0(1), 290.0(1)	280.9	0.00
	D_{2d}	O···C	282.9(8)	282.9	10.8

[a] Number of distances of the same value.

pact in agreement with its higher energy of 33.5 kJ mol^{-1}, and with experiment.

Experimental studies have shown that the gaseous molecules $B(OH)_3$ and $B(OMe)_3$ both have a C_{3h} geometry[8,9] In the crystalline state $B(OH)_3$ has C_{3h} symmetry but the bond lengths differ from the calculated values because of intermolecular interactions including hydrogen bonding.[10]

Compactness and the relative energies of the conformers of $B(OH_4)^-$, $B(OMe)_4^-$, $C(OH)_4$ and $C(OMe)_4$: The calculated minimum energy structures of these molecules have S_4 symmetry but each also has a slightly higher energy conformation with D_{2d} geometry (Table 5). Figure 4 shows the structures of each conformation. The O···O distances in Table 6 show that the average O···O distance in the S_4 conformer (242.2 pm) is equal to that in the D_{2d} conformer (242.6 pm), consistent with the close-packing of the O atoms in both conformations. But, as is the case for $B(OH)_3$ and $B(OMe)_3$ the hydrogen atoms of the OH groups and the carbon atoms of the OMe groups are not close packed with the neighboring oxygen atoms to which they are not directly bonded. In principle the OH and OC bonds are able to rotate freely about the central C–O or B–O bonds taking up those positions that locally minimize the energy of the molecule. There are two such positions which correspond to the two conformations D_{2d} and S_4. In these conformations the hydrogen or C atoms are in positions in which they are as close as possible to the three oxygen atoms to which they are not directly bonded thereby reducing the 1,4 O···H or 1,4 O···C distances as much as possible (Table 7). In each case it is found that the average O···H or O···C distance is smaller in the S_4 conformer than in the D_{2d} conformer, which is therefore the minimum energy most compact conformer and has the lower energy in agreement with the calculated energy difference (Table 7).

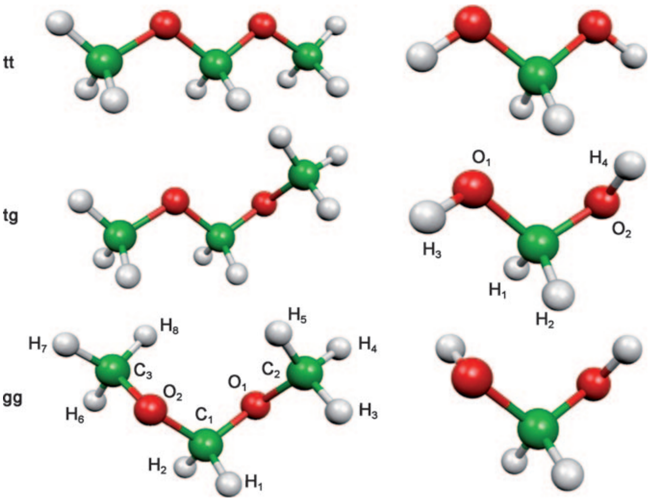


Figure 4. Ball-and-stick models of the tt (top), tg (middle), and gg (bottom) conformers of methanediol (right) and dimethoxymethane (left).

All the OMe molecules in Table 6 exhibit the typical tilt of the methyl group consistent with the asymmetrical electron density of the oxygen atom as discussed in the Section on The Methyl Tilt. The tilt angles for these molecules are given in Table 8.

Table 8. Tilt angles for $B(OMe)_3$, $B(OMe)_4^-$ and $C(OMe)_4$.

Molecule		$\sphericalangle OCH_s$	$\sphericalangle OCH_t$	Tilt [°]
$B(OMe)_3$	C_{3h}	107.2	111.4	2.8
	C_s	107.3	111.3, 111.9	3.7
$B(OMe)_4^-$	S_4	108.8	112.1	2.2
	D_{2d}	108.9	112.5	2.4
$C(OMe)_4$	S_4	105.7	111.0	3.5
	D_{2d}	106.0	111.3	3.5

The differences between the average lengths of the O···H or O···C contacts in all four molecules are rather small, and might possibly be considered to be within the error limits of the calculated structures. However, the conclusions reached from this data are consistent among all four molecules. The rather small differences between the average O···H and O···C distances are not unexpected because the BO_4 and CO_4 portions of both molecules are close packed and very nearly spherical so that the difference in the compactness produced by the two alternative positions of the H atom or Me group makes only a rather small, but nevertheless important, difference in the compactness of the two conformers. Indeed it is interesting to note that the differences between the average 1,4-interatomic distances of the two conformations of the molecules in Table 9, are roughly proportional to the energy differences ΔE between the two conformations of the four molecules. This data provides further evidence that the 1,4 O···H and O···C distances in these molecules, and therefore their relative compactness do indeed determine the energy differences between the conformers. We will find a similar correlation for the molecules discussed in the Section on Conformations, Molecular Compactness and Generalized Anomeric Effects.

Table 9. Differences, Δd, in the 1,4 O···H and O···C distances, and the relative energies, ΔE, for the pairs of conformers of $B(OH)_3$, $B(OH)_4^-$, $C(OH)_4$ and $B(OMe)_3$, $B(OMe)_4^-$, and $C(OH)_4$.

Molecule	ΔE [kJ mol^{-1}]	Δd [pm]
$B(OH)_3$	18.5	8.9
$B(OH)_4^-$	5.0	0.6
$C(OH)_4$	7.5	1.4
$B(OCH_3)_3$	33.5	15.2
$B(OCH_3)_4^-$	6.6	1.7
$C(OCH_3)_4$	10.8	2.2

There have been several experimental determinations of the structure of $B(OH)_4^-$ which show that in the solid state it has D_{2d} symmetry, presumably because of solid-state effects.[11] These structures agree reasonably well with our calculated D_{2d} conformation. There have been no experimental studies of $C(OH)_4$ which is not a known stable molecule. The gas-phase structure of $C(OMe)_4$ has been found to have S_4 symmetry[12] while in the solid state $B(OMe)_4^-$ has D_{2d} symmetry presumably because of solid state effects, including perhaps hydrogen bonding.[13]

The molecules we have discussed in this section all have structures that provide examples of the anomeric effect. In the following section we discuss this much studied and controversial effect, with some more, and better known, examples of the effect which we will show is related to the concept of compactness.

Conformations, Molecular Compactness and the Generalized Anomeric Effect

In this Section we show that the relation between compactness and the relative energies of the possible conformations of a molecule can be extended to many other molecules with OH and OMe groups. We have included some typical anomeric molecules in our investigation. The generalized anomeric effect is the preference for *synclinal* (*sc*, *gauche*) over *antiperiplanar* (*ap*, *trans*) conformations in a molecular fragment R-X-C-Y, where X possesses one or more lone pairs of electrons, (e.g., N, or O) and Y is an electronegative atom or group (e.g., F, Cl, OH, OMe). We show that the relative energies of anomeric molecules can be predicted from their compactness and their 1,4 O···H and O···C distances thus providing a simple explanation for the anomeric effect.

Several different explanations for this effect have been proposed. It has been the subject of several books, many symposia, innumerable papers and much discussion over a period of more than fifty years[14] and yet there is no generally agreed explanation. Among the various explanation that have been proposed the negative hyperconjugation model has become the most widely accepted.[15] This model considers that the delocalization of a lone pairs on Y into the low energy C–O antibonding orbital, denoted by $n_Y \rightarrow \sigma^*_{CO}$, is maximized when the lp-X-C-Y unit has the *antiperiplanar* or *trans* conformation so that the atom Y is then in the *synclinal* or *cis* conformation. However, natural bond order (NBO) studies[16] have shown that although the $n_Y \rightarrow \sigma^*_{CO}$ orbital interactions often appear to make the dominant contribution to determining the conformational preference, other steric and electrostatic effects should also be taken into account. Criticism and doubts about the negative hyperconjugation explanation contimue to be made, such as those expressed in two recent papers.[17] The authors of these papers used QTAIM[18] to study differences in the electron density between the conformations of anomeric molecules of the type R-O-C-O-R′ and R-*N*-C-*N*-R′. They claim that the electron density differences and the corresponding changes in the atomic charges between the different conformations are not compatible with the negative hyperconjugation model but are compatible with an explanation based on the differences in the interatomic attractions and repulsions between the atoms as a consequence of the differences in the atomic charges in different conformations. Another recent paper[19] has discussed the anomeric effect in terms of a generalized VB study of 2-methoxyhydropyran. This paper shows that the conformational changes in bond lengths and angles are well-represented by the GVB-PP calculations. The authors concluded that the use of the electronic hyperconjugation concept may not be appropriate.

We now discuss how the principle of maximum compactness that we have used to understand the relative energies of the different conformations of the molecules discussed in the previous Section can be used to understand the relative energies of the conformations of many other molecules, including those that have been discussed in terms of the anomeric effect without recourse to orbital interactions.

Methanediol and dimethoxymethane: There have been many experimental and theoretical studies of these molecules because they provide simple examples of the generalized anomeric effect[14] and have structures related to the pyranose molecules which provided the first example of the anomeric effect.[20]

Dimethoxymethane has been shown by theoretical and experimental studies to exist only in the *gauche*,*gauche* (gg) conformation.[21] The structure of methanediol has not been studied experimentally because it is unstable in the gas phase but theoretical studies have shown that for this molecule the gg conformer is also the most stable.[22] However, calculations show that the *gauche*,*trans* (gt), and *trans*,*trans* (tt) conformations of both molecules have only slightly higher energies. The structures of these conformations are shown in Figure 4.

Some 1,3- and 1,4-distances of the methanediol conformers are given in Table 10. The 1,3-data show that the O···O distances in each conformer are consistent with oxygen radii of 112 pm (r_{lp}) and 118 pm (r_b) and the $H_1\cdots H_2$ and $H_{1,2}\cdots O$ distances close to 178, 200 and 207 pm, respectively, in each conformer are consistent with these oxygen radii and the standard H^C radius of 89 pm, showing that the C−H hydrogen atoms and oxygen atoms are close packed around the carbon atom. However, the O−H hydrogen atoms are not close packed and the $OH_3\cdots O_2$ and $OH_4\cdots O_1$ 1,4-distances have average distances of gg 256 < tg 276 < tt 307 pm, showing that the compactness decreases in this series and that the gg conformation should be the most compact, in agreement with their relative energies (see Table 12).

In the dimethoxymethane conformers, the O···O distances are very similar to those in methanediol and consistent with the same oxygen radii of 112 p, (r_{lp}) and 118 pm (r_b). the other 1,3-distances show that O_1, O_2, C_1 and C_2 are all closely packed around the central C_1 atom, as are the hydrogen atoms in the methyl groups with their carbon atoms, which is also the case in the methoxy groups of all the molecules we have studied. However, the C_2 and C_3 atoms are not close packed. The 1,4 $C_{2,3}\cdots H$ distances gg, 294, 294, gt 357 286 (average 322), tt 353, 353 pm are given in Table 10. They increase in the order gg 294 < tg 322 < tt 353 pm, showing that the compactness of these conformers decreases in this series and that the gg conformation should be the most compact in agreement with their relative energies (see Table 12), and with experiment.

Table 11. 1,3- and 1,4-interatomic distances for some fluoro alcohols and ethers that exhibit the anomeric effect.[a]

			g	t
HO−CFH$_2$	1,3	$H\cdots H$	181	181
		$H\cdots F$	200, 201	199(2)
		$C\cdots H^O$	193	194
		$H\cdots O$	200, 207	207(2)
		$F\cdots O$	229	222
	1,4	$H\cdots H^O$	227	235, 306
		$F\cdots H^O$	257	306
HO−CF$_2$H	1,3	$F\cdots F$	218	220
		$H\cdots F$	201(2)	199, 201
		$F\cdots O$	225(2)	218, 225
		$H\cdots O$	200	191
		$C\cdots H^O$	190	191
	1.4	$H\cdots H^O$	281	235
		$F\cdots H^O$	244(2)	247, 302
MeO−CFH$_2$	1,3	$H\cdots H$	178(3)	178(3)
		$H\cdots O$	208(2), 203	209(2), 202
		$O\cdots F$	223	222
		$O\cdots H$	205	206(2)
		$F\cdots H$	200, 201	200(2)
	1,4	$C\cdots F$	289	351 (no contact)
Me−OCF$_2$H	1,3	$H\cdots H$	178(2), 179	179(2), 177
		$H\cdots O$	209(2), 202	209(2), 202
		$O\cdots F$	223, 226.	218, 226
		$O\cdots H$	199	206
		$F\cdots H$	201(2)	200, 199
		$F\cdots F$	218	219
	1,4	$C\cdots F$	280(2)	286, 349 (no contact)
		$H\cdots C$	253, 323, 330	260(2), 267

[a] H^O is the -OH hydrogen.

Table 10. 1,3- and 1,4-interatomic distances in molecules exhibiting the anomeric effect with OH and OMe ligands.

			gg	tg	tt
$H'_2C(OH)_2$	1,3	$H_1\cdots H_2$	179	179	179
		$O_1\cdots O_2$	235	229	222
		$H_{1,2}\cdots O_1$	208(2), 200(2)	207(4)	199(2), 208
	1,4	$H_3\cdots O_2$	256(2)	241, 311	307(2)
		$H_1\cdots H_{3,4}$	230(2), 280(2)	236, 280, 311, 324	232(4)
$H'_2C(OMe)_2$	1,3	$H_1\cdots H_2$	180	181	180
		$H_3\cdots H_{4,5}$	179(6)	179(6)	179(6)
		$O_1\cdots O_2$	236	230	224
		$H_{1,2}\cdots O_1$	200(2), 207(2)	208, 207(2), 200	207(4)
		$H_{3,4}\cdots O_1$	203(2), 209(4)	203(2), 209(4)	202(2), 209(4)
		$O_2\cdot\cdot H_{1,2}$	200(2), 207(2)	207(2), 200, 208	207(4)
	1,4	$H_1\cdots C_{2,3}$	259(2), 327(2)	254, 260, 327, 266	262(4)
$H'_2C{=}C(OMe)_2$	1,3	$H_1\cdots H_2$	186	185	184
		$H_3\cdots H_{4,5}$	178(4), 178(2)	178.(6)	178.(6)
		$C_2\cdots C_{3,4}$	237	237	237
		$C^*\cdots O_{2,3}$	236(2)	234, 241	241(2)
		$O_1\cdots O_2$	231	224	216
		$H_{1,2}\cdots C_1$	209(2)	208, 212	211(2)
		$H_{3,4}\cdots O_1$	203(2), 208(4)	201(2), 208(2), 209(2)	201(2), 208(4)
	1,4	$H_{1,2}\cdots O_{2,3}$	261(2), 333(2)	256, 274, 333, 335	271(2), 336(2)
		$O_{1,2}\cdots C_{3,2}$	284(2)	264, 356	350(2)
$O{=}C(OMe)_2$	1,3	$H_1\cdot\cdot H_{3,4}$	179(4), 178(2)	178(2), 179(4)	176(3), 178(4)
		$C_1\cdot\cdot C_2$	239, 242	235, 241	234(2)
		$O_1\cdot\cdot O_2$	230, 224, 222	223, 223, 226	217, 227(2)
		$H_{3,4}\cdots O_1$	202(2), 209(4)	202(2), 209.(2), 208(2)	203(3), 207(3), 210(2)
	1,4	$O_2\cdots C_1$	291, 276	257, 354	349(2)
		$O_3\cdots C_{1,2}$	330, 345	266, 352	267(2)

Dimethyl carbonate and 1,1-dimethoxyethene: Dimethyl carbonate has been studied extensively in both the gas and liquid phases, by IR and Raman spectroscopy, by gas phase electron diffraction, and by ab initio and molecular mechanics calculations, as discussed in a paper by Bohets and van der Veken.[23] The main conclusion from all the previous work is that the gas phase consists of a mixture of the *cis*,*cis* and *cis*,*trans* conformers in which the *cis*,*cis* predominates. Ab initio calculations show that there is also a slightly higher energy near *trans*,*trans* conformer with the methyl groups slightly above and below the molecular plane. The cc, ct, and tt conformations of this molecule are shown in Figure 5.

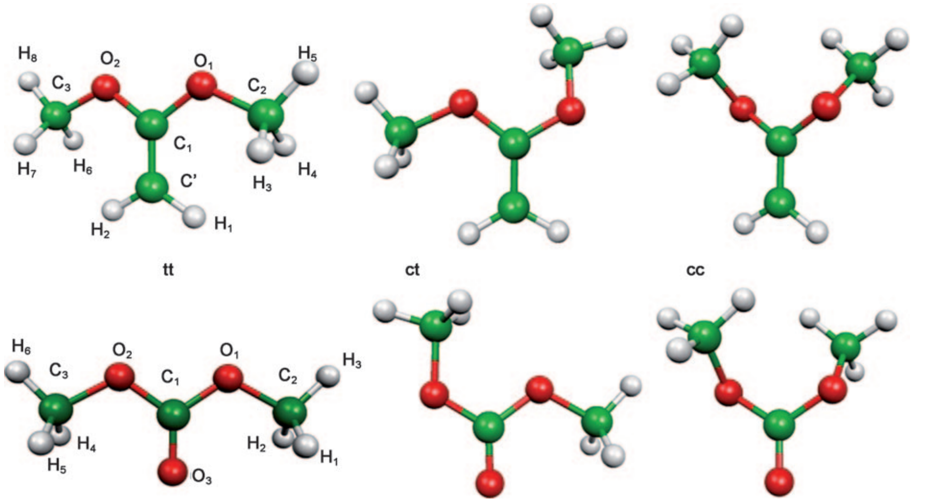


Figure 5. Ball-and-stick models of the conformers of dimethoxyethene $CH_2{=}C(OMe)_2$ (top) and dimethyl carbonate $(MeOC)_2C{=}O$ (bottom).

Dimethoxyethene has been studied both theoretically and experimentally and it has been found that the *cis*,*cis* conformer is the lowest energy experimentally observed conformer.[24] The 1,3- and 1,4-distances for both molecules are given in Table 10. The 1,3-distances show that the O_1, O_2, and O_3 atoms are close-packed around C_1 in both molecules The relative compactness of the three conformations of both molecules is determined by the 1,4 $C_3{\cdots}O_1$, $C_2{\cdots}O_2$, distances which show that the compactness of these molecules increases in the order tt < tg < gg in agreement with the calculated relative energies (Table 12).

In all molecules we have studied the lowest energy conformer has the shortest 1,4 H···O or H···C contacts with the H or atom directed toward the lone pair side of the oxygen atom. This means that we can predict which conformer of any of the molecules we have studied has the lowest energy simply by looking at the structures of the conformers to see which of the conformers has the H or C atom of the 1,4 O···H or O···C contact pointing toward the lone-pair side of the oxygen atom and is therefore shorter than the 1,4-distance between the 1,4-H atom and the bonding side of the oxygen atom. For example, we can predict by simply looking at the structures of vinyl alcohol and vinyl methyl ether (Figure 6), as determined by Eskandar and Mosquera[17] that for both the alcohol and the ether, the *syn* conformers have a lower energy than the *anti* conformers. Our calculations show that the *syn* conformers are 5.06 and 7.68 kJ mol^{-1}, respectively, lower in energy than the *anti* conformers. Moreover the *syn* conformers are the experimentally observed structures.

Fluoromethanol and the molecules CH_2FOMe, CHF_2OH,and CHF_2OMe: There has been considerable discussion about the reason why fluoromethanol and related fluroalcohols and ethers have a *gauche* conformation rather than a *trans* conformation (Figure 7) and these molecules have been quoted as further examples of the anomeric effect. Extensive ab intio calculations are available for fluoromethanol[24] and methoxymethylfluoride.[25] In these cases the *gauche* conformation has been shown to be more stable than the trans conformation. The gauche structure of methoxymethylfluoride has also been confirmed by microwave spectroscopy.[26]

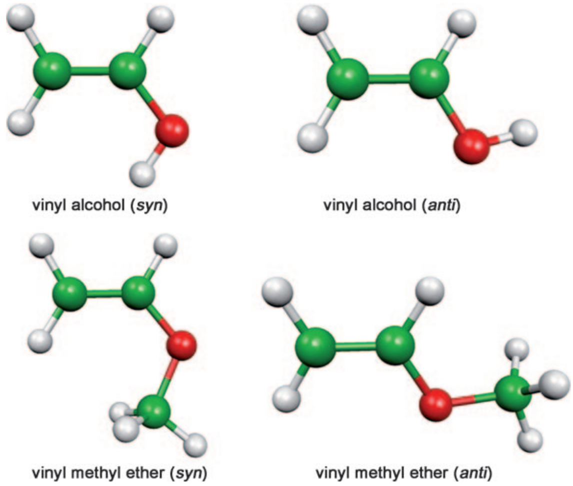

vinyl alcohol (*syn*) vinyl alcohol (*anti*)
vinyl methyl ether (*syn*) vinyl methyl ether (*anti*)

Figure 6. Ball-and-stick the conformers of vinyl alcohol (top) and vinyl methyl ether (bottom).

The calculated 1,3- and 1,4-distances for the *gauche* and *trans* conformations of all four molecules are given in Table 11. The 1,3-distances show that in all four molecules the ligands are close packed around the central C atom. Fluoromethanol is closely related to methanediol in that one of the OH groups in $H_2C(OH)_2$ is replaced by a fluorine atom so that one of its two 1,4 HO···H distances is replaced by a 1,4 F···H distance and it is this distance that determines the relative stabilities of the gauche and trans conformations of all four molecules. The 1,4 $F{\cdots}H_1$ distance in fluoromethanol has a length of 257 pm in the gauche conformation and the considerably longer distance of 306 pm in the trans conformation showing that the gauche conformer is the more compact and therefore has the lower energy, in agreement with the calculated energies (Table 12) and with experiment. It should be noted that in the *trans* conformation the F and H atoms are not in direct contact. The 1,4 F···H distances in the *gauche* and *trans* conformations of CH_2FOMe, CF_2HOH and CF_2HOMe are in each case smaller in the *gauche* conformation also leading to

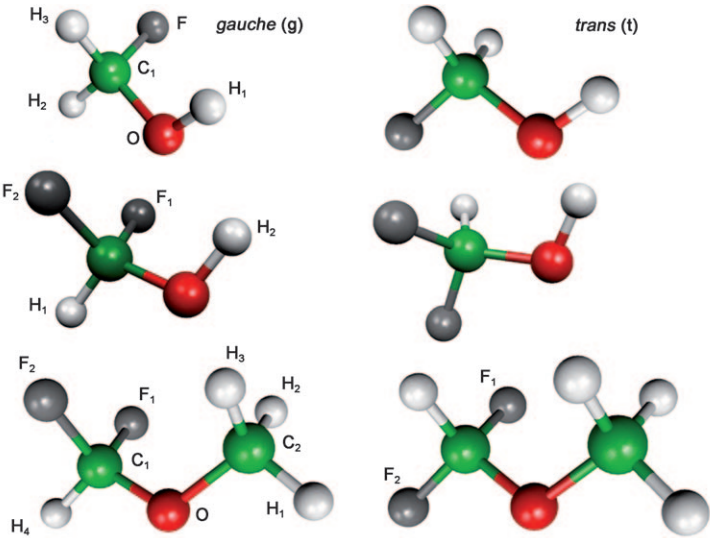


Figure 7. Ball-and-stick models of the conformers of CH_2FOH (top), CF_2HOH (middle), CF_2HOCH_3 (bottom).

the same conclusion that in every case the gauche conformation has a lower energy than the *trans* conformation.

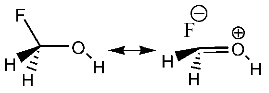
Molecular volume and molecular compactness: Table 12 gives the molecular volume determined by QTAIM[18] of each of the conformers of the molecules discussed in this Section. The data shows that the most compact and therefore lowest energy conformer has the smaller volume. This is not unreasonable, in that the more the atoms are crowded together the more compact the molecule becomes and its volume decreases correspondingly. In principle the most compact shape for a molecule is spherical which would be the shape of a molecule held together by only non-directional forces. For example, a large number of mercury atoms, held together by metallic bonding, can be regarded as a giant molecule, that spontaneously forms a spherical drop. But in the vast majority of molecules the atoms are held together by a variety of both directional and non-directional and forces and so they adopt the most compact but not necessarily the closest packed structure, and the smallest possible volume consistent with the directional nature of some of the interatomic forces.

Table 12. QTAIM molecular volumes ($Bohr^3$)[a] and relative energies ΔE [$kJ\,mol^{-1}$].

Molecule		ΔE	Molecular volume
$CH_2(OH)_2$	gg	0.0	411.9
	tg	14.4	412.1
	tt	32.1	414.0
$CH_2(OCH_3)_2$	gg	0.0	740.8
	tg	10.0	744.0
	tt	22.3	747.3
$CH_2{=}C(OCH_3)_2$	tt	0.0	830.5
	ct	5.0	832.6
	cc	17.0	838.1
$O{=}C(OCH_3)_2$	tt	0.0	738.8
	tg	12.8	739.1
	gg	69.3	739.4
$HO{-}CFH_2$	g	0.0	370.0
	t	20.7	372.0
$HO{-}CF_2H$	g	0.0	557.6
	t	10.5	561.7
$H_3CO{-}CFH_2$	g	0.0	535.1
	t	18.0	538.8
$H_3CO{-}CF_2H$	g	0.0	557.6
	t	7.8	561.7

[a] Calculated for the 0.001 pm isosurface.

C−O and C−F bond lengths: There has been considerable discussion of the bond lengths in these and similar molecules because it has been claimed that they are in agreement with the negative hyperconjugation orbital model according to which the C−F bond in the *gauche* conformer should be longer than a "normal" C−F bond and in particular longer than the C−F bond in the *trans* conformation. This prediction is based on the resonance structure description of the molecule in which the C−F bond has single-bond–no-bond character and is therefore claimed to be longer than normal while the C_1−O bond should be shorter than normal because it has some double bond character as shown by the resonance structures in Scheme 1.



Scheme 1. Resonance structures for fluoromethanol.

The supposed no-bond covalent bond character of the C−F bond is not a good description of the bond because in reality it is a highly ionic bond and it would be reasonable to expect that with increasing ionic character the C−F bond would decrease in length. The C−F bond is indeed longer in the *gauche* conformer than in the *trans* conformer but the C−F bonds in CF_2HOH are both still longer than in CFH_2OH. What then causes the difference in the C−F bond lengths between these two molecules? The C−F bond lengths in these two molecules vary over the range 139.9 to 134.6 pm. These C−F bond lengths and those in some related molecules together are given in Table 13 together with some C−O bond lengths. So the question immediately arises as to what is a "normal" bond length. It can be justifiably argued that there are no "normal" bond lengths. The length of a given bond depends on the nature of the molecule in which it is located and may vary very considerably from molecule to molecule for a number of reasons including packing considerations and the atomic charges of the bonded atoms. The large variation of these bond lengths shows that at least for C−F and C−O bonds there are no "normal" lengths for these bonds. Arguably the concept of a normal bond length and the related concept of a covalent radius for each atom[28] have become increasingly less useful, as more and more bond lengths have been accurately determined. Consequently it is no longer very useful to compare bond lengths with a standard normal bond length and

Table 13. Selection of CO and CF bond lengths.

Molecule	C–F [pm]	C–O [pm]
CF_4	131.9	
$F_3C{-}CF_3$	132.6	
$F_2C{=}CF_2$	132.4	
$CF_3{}^+$	124.4	
HCF_3	133.2	
H_2CF_2	135.7	
H_3CF	139.1	
$F_3C\text{-}OO\text{-}C(O)F$	131.9 (all)	139.3 ($O\text{-}CF_3$)
		137.6 ($O\text{-}C(O)F$)
		118.6 ($C{=}O$)
$F_3C{-}OF$	131.9	139.5
$F_3C{-}OH$	132.8	134.6
$F_3C{-}O^-$	139.2	122.7
$F_2C{=}O$	131.7	117.0
$F_2C(OF)_2$	131.7	138.7
$FCO_2{}^-$	150.5	122.5
$F_3C\text{-}O\text{-}CF_3$	132.7	136.9 ($O\text{-}CF_3$)
$F_3C\text{-}O\text{-}CH_3$	131.8	134.7 ($O\text{-}CF_3$)
	133.6	142.6 ($O\text{-}CH_3$)
$H_2FC\text{-}O\text{-}CH_2F$	137.4	139.6 ($O\text{-}CH_2F$)
$H_3C\text{-}O\text{-}CH_2F$	138.5	136.2 ($O\text{-}CH_2F$)
$H_3C\text{-}O\text{-}CH_3$		142.1 ($O\text{-}CH_3$)
$O[C(O)CF_3]_2$	133.6	120.3 ($C{=}O$)
		136.0 ($C\text{-}O$)
$CO_3{}^{2-}$		131.8

the interpretation of the C-O and C–F bond lengths in the molecules as providing support for the negative hyperconjugation model of anomeric molecules is no longer very convincing.

It is not the purpose of this paper to discuss the variations of the lengths of C–F and C–O bonds in any detail. But it is noticeable that an important factor determining the length of a C–F bond appears to be the number of fluorine atoms bonded to the carbon atom. The C–F bond length decreases as the number of fluorine atoms bonded to the same carbon atom increases as can be seen by the data in Table 13. The QTAIM atomic charges[18] for some relevant molecules are given in Table 14. They show, as expected, that the charge on a carbon atom in these molecules increases with the increased number of F atoms and it is reasonable to suppose that the corresponding decrease in length is due to the increased electrostatic attraction between the C and F atoms.

Table 14. Calculated C–F bond lengths and QTAIM charges on carbon and fluorine in the fluoromethanes, fluoromethanols and the fluoromethyl groups in fluoromethyl methyl ethers.

	C–F [pm]	q(F)	q(C)	$-q$(Me)
H_3CF	139.5	−0.62	+0.47	
H_2CF_2	136.5	−0.61	+1.09	
HCF_3	134.2	−0.60	+1.71	
CF_4	132.7	−0.59	+2.39	
$FH_2C{-}OH$	139.9	−0.62	+1.03	
$F_2HC{-}OH$	136.9	−0.61	+1.61	
$F_3C{-}OH$	135.1	−0.60	+2.28	
	132.8			
$FH_2C{-}OMe$	140.6	−0.62	+1.03	+0.58
$F_2HC{-}OMe$	137.3	−0.61	+1.61	+0.58
$F_3C{-}Me$	135.4	−0.60	+2.27	+0.58
	133.2			

The interpretation of C–O bond lengths in terms of their supposed double bond character as in the negative hyperconjugation model for anomeric molecules is also not very convincing as it ignores other factors such as polarity and packing, as we have demonstrated for C–F bonds.

Compactness and Hardness

We have shown that for alcohols and ethers of the type X-C-OH and X-C-OMe in which X is an electronegative atom or group, in particular F, OH or OMe, that the experimentally observed and lowest energy conformation is that which is the most compact. It seems reasonable to propose that there is a general rule which states that molecules arrange themselves to be as compact as possible. The tendency of molecules to adopt a compact form is exemplified in many other cases, for example: 1) The formation of carbon nanotubes and fullerenes which are more compact than the corresponding graphite sheet with the same number of atoms; 2) the tendency of many large biomolecules to adopt a roughly spherical shape; 3) the tendency of long chain molecules to form the helical structures of many proteins and DNA; 4) the tendency of long chain perflurohydrocarbons to form helical structures that are more compact than straight chain molecules.[28]

It seems reasonable to generalize our conclusion about the compactness of the molecules studied in this paper by stating that "there appears to be a rule of nature that molecules arrange themselves to be as compact as possible". This statement is reminiscent of the statement made by Pearson[29] in 1987 that: "there appears to be a rule of nature that molecules arrange themselves to be as hard as possible", alternatively "at equilibrium a molecule is as hard as possible." Similarly we may say that "When a molecule is in its equilibrium structure it is as compact as possible."

Hardness is a measure of compressibility[30] while compactness is a measure of how closely packed the atoms are in a molecule. It is reasonable to think that the more compact a molecule is the harder it will be to compress. Clearly compactness and hardness are closely related and both are important properties of a molecule.

Conclusion

We have shown the oxygen atom in an OX group cannot be assigned a single ligand radius, as in the case of monatomic ligands such as F, Cl, or O (formally O^- or =O), because of its nonsymmetrical electron density, and we have seen that the unsymmetrical density around the oxygen atom has some very important consequences. In particular it provides an explanation for the "methyl tilt", and it is important factor for understanding the relative energies of the conformers of molecules containing OH and OMe groups. Although the unsymmetrical form of the electron density of an oxygen atom in an OX group cannot be quantitatively described by assigning the oxygen atom just the two radii $r_{O_{lp}}$ and r_{O_b} for many purposes this is nevertheless a very useful approximation.

Another important concept introduced in this paper is that of compactness which enables us to predict which of the various conformations of the molecules discussed in this paper has the lowest energy. We have shown that the relative compactness of two conformations of a molecule can be determined from a consideration of the 1,4-interatomic distances or from the relative volumes of the conformations as calculated by the QTAIM.[15] The success of this idea with the molecules we have studied gives us confidence to suggest that it is a rule of nature that the lowest energy conformation of a molecule is in general the most compact conformation.

Computational Details

Calculations were performed at the density functional B3LYP level[30] using the Gaussian 2003 program.[31] The all-electron basis set 6-311+G-(2d,2p) was employed for all the atoms in the molecules. All the geometries have been fully optimized. Ball-and-stick models were visualized with the Molekel software.[32] Molecular volumes were calculated in the framework of the QTAIM theory[18] with the TopMod program.[33]

---

[1] J. Hernández-Trujillo, F. Cortés-Guzmán, D.-C. Fung, R. F. W. Bader, *Faraday Discuss.* **2006**, *135*, 79.

[2] R. J. Gillespie, E. A. Robinson, *Adv. Mol. Struct. Res.* **1998**, *4*, 1; R. J. Gillespie, G. L. Heard, E. A. Robinson, *J. Mol. Struct.* **1999**, *485*, 305; R. J. Gillespie, *Coord. Chem. Rev.* **2000**, *197*, 51; R. J. Gillespie, E. A. Robinson, *C. R. Chim.* **2005**, *8*, 1631; R. J. Gillespie, P. L. A. Popellier, *Chemical Bonding and Molecular Structure*, Oxford University Press, New York, **2001**; R. J. Gillespie, *J. Chem. Educ.* **1963**, *40*, 295.

[3] G. L. Heard, R. J. Gillespie, D. W. H. Rankin, *J. Mol. Struct.* **2000**, *520*, 237.

[4] K. I. Gobbato, H.-G. Mack, H. Oberhammer, C. O. D. Védova, *J. Am. Chem. Soc.* **1997**, *119*, 803.

[5] See, for example: Y. Niide, M. Hayashi, *J. Mol. Spectrosc.* **2003**, *220*, 65.

[6] D. Stefani, I. Pashalidis, A. V. Nicolaidea, *J. Mol. Struct.* **2008**, *871–892*, 33.

[7] C. Glidewell, *Inorg. Chim. Acta* **1975**, *12*, 219.

[8] T. R. Gilson, *J. Chem. Soc. Dalton Trans.* **1991**, 2463.

[9] G. Gundersen, T. Jonvik, R. Seip, *Acta Chem. Scand. Ser. A* **1981**, *35*, 325; M. A. Hartl, D. J. Williams, A. I. Acatrinei, A. Stowe, L. L. Daemen, *Z. Anorg. Allg. Chem.* **2007**, *633*, 120.

[10] R. R. Shuvalov, P. C. Burns, *Acta. Crystallogr. Sect. C* **2003**, *59*, 147, and references therein)

[11] N. Narasimhamurthy, H. Manohar, A. Samuelson, J. Chandrasekhar, *J. Am. Chem. Soc.* **1990**, *112*, 2937; J. M. Burke, J. A. K. Howard, T. B. Marder, C. Wilson, *Acta. Crystallogr. Sect. C* **2000**, *56*, 1354; H. Effenberger, *Acta Crystallogr. Sect. B* **1993**, *8*, 82; L. J. Csetenyi, F. P. Glasser, R. Howie, *Acta Crystallogr. Sect. C* **1982**, *49*, 1039.

[12] F. C. Mijlhoff, H. J. Geise, E. J. M. van Schaik, *J. Mol. Struct.* **1974**, *20*, 393.

[13] N. W. Alcock, R. M. Hagger, W. D. Harrison, M. G. H. Wallbridge, *Acta. Crystallogr. Sect. B* **1982**, *38*, 676; G. J. Gainsford, T. Kemmitt, *Acta Crystallogr. Sect. C* **2005**, *61*, 206.

[14] A. J. Kirby, *The Anomeric Effect and Related Stereoelectronic Effects at Oxygen*. Springer, Berlin, **1983**; P. Deslongchamps, *Stereoelectronic Effects in Organic Chemistry*, Pergamon, Oxford, **1983**; G. R. J. Thatcher, *The Anomeric Effect and Associated Stereoelectronic Effects*, ACS, Washington, **1993**; L. Carballeira, I. J. Pérez-Juste, *Comput. Chem.* **2000**, *21*, 462.

[15] P. von R. Schleyer, A. J. Kos, *Tetrahedron* **1983**, *39*, 1141.

[16] U. Salzner, P. von R. Schleyer, *J. Am. Chem. Soc.* **1993**, *115*, 10231; U. Salzner, P. von R. Schleyer, *J. Org. Chem.* **1994**, *59*, 2138.

[17] A. Vila, R. A. Mosquera, *J. Comput. Chem.* **2007**, *28*, 1516; K. Eskandari, R. A. Mosquera, *J. Phys. Chem. A* **2007**, *111*, 8491.

[18] R. F. W. Bader, *Atoms in Molecules: A Quantum Theory*, Oxford University Press, Oxford, **1990**; P. L. A. Popellier, *Atoms in Molecules: An Introduction*, Pearson Education, Harlow, **2000**.

[19] R. S. Bitzer, A. G. H. Barbosa, C. O. da Silva, M. A. C. Nascimento, *Carbohydr. Res.* **2005**, *340*, 2171.

[20] J. T. Edward, *Chem. Ind.* **1955**, 1102; R. U. Lemieux, P. Chu, *J. Am. Chem. Soc.* **1958**, *80*, 31; N. R. U. Lemieux In *Molecular Rearrangements* (Ed.: P. de Mayo), Interscience Publishers, New York, **1964**, p. 709.

[21] L. B. Favero, W. Caminati, B. Velino, *Phys. Chem. Chem. Phys.* **2003**, *5*, 4776; J.-H. Lii, K.-S. Chen, K. A. Durkin, N. L. Allinger, *J. Comput. Chem.* **2003**, *24*, 1473; Y. Yokoyama, Y. Ohashi, *Bull. Chem. Soc. Jpn.* **1999**, *72*, 2183.

[22] Y.-P. Chang, T. M. Su, *J. Mol. Struct.* **1996**, *365*, 183.

[23] H. Bohets, B. J. van der Veken, *Phys. Chem. Chem. Phys.* **1999**, *1*, 1817.

[24] C. Reibold, H. J. Oberhammer, *J. Am. Chem. Soc.* **1999**, *121*, 4852; B. M. Pinto, B. M. Schlegel, S. Wolfe, *Can. J. Chem.* **1987**, *65*, 1658.

[25] G. F. Smits, M. C. Krool, C. Altona, *Mol. Phys.* **1988**, *615*, 813; J. R. Duri, J. Lin, Guirgis, B. van der Veken, *J. Struct. Chem.* **1993**, *34*, 103; H. Roohi, A. Ebrahmi, *J. Mol. Struct.* **2005**, *733–779*, 14; G. A. Jeffrey, J. H. Yates, *J. Am. Chem. Soc.* **1979**, *101*, 820.

[26] J. Nakagawa, H. Kato, M. Hayashi, *J. Mol. Spectrosc.* **1981**, *90*, 467.

[27] L. Pauling, *Nature of the Chemical Bond*, 3rd ed., Cornell University Press, Ithaca, **1960**, pp. 218, 221–228.

[28] W. G. Golden, E. M. Brown, S. E. Solem, R. W. Zoeliner, *J. Mol. Struct.* **2008**, *867*, 22.

[29] R. G. Pearson, *J. Chem. Educ.* **1987**, *64*, 561; R. G. Pearson, *Acc. Chem. Res.* **1993**, *26*, 250; R. G. Pearson, *J. Chem. Educ.* **1999**, *76*, 2; P. W. Ayers, R. G. Parr, *J. Am. Chem. Soc.* **2000**, *122*, 2010.

[30] C. Lee, W. Yang, R. G. Parr, *Phys. Rev. B* **1988**, *37*, 785; A. D. Becke, *J. Chem. Phys.* **1993**, *98*, 5648.

[31] Gaussian 03, Revision B.02, M. J. Frisch, G. W. Trucks, H. B. Schlegel, E. Scuseria, M. A. Robb, J. R. Cheeseman, J. A. Montgomery, Jr., T. Vreven, K. N. Kudin, J. C. Burant, J. M. Millam, S. S. Iyengar, J. Tomasi, V. Barone, B. Mennucci, M. Cossi, G. Scalmani, N. Rega, G. A. Petersson, H. Nakatsuji, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, M. Klene, X. Li, J. E. Knox, H. P. Hratchian, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, P. Y. Ayala, K. Morokuma, G. A. Voth, P. Salvador, J. J. Dannenberg, V. G. Zakrzewski, S. Dapprich, A. D. Daniels, M. C. Strain, O. Farkas, D. K. Malick, A. D. Rabuck, K. Raghavachari, J. B. Foresman, J. V. Ortiz, Q. Cui, A. G. Baboul, Clifford, S. J. Cioslowski, B. B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R. L. Martin, D. J. Fox, T. Keith, M. A. Al-Laham, C. Y. Peng, A. Nanayakkara, M. Challacombe, P. M. W. Gill, B. Johnson, W. Chen, M. W. Wong, C. Gonzalez, J. A. Pople, Gaussian, Inc., Pittsburgh PA, **2004**.

[32] Molekel, P. Flukiner, H. P. Luthi, S. Portman, J. Weber, Swiss Center for Scientific Computing (Switzerland), **2000–2002**.

[33] S. Noury, X. Krokidis, F. Fuster, B. Silvi, *Comput. Chem.* **1999**, *23*, 597; J. Pilmé, J.-P. Piquemal, *J. Comput. Chem.* **2008**, *29*, 1440.

Received: September 22, 2009