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COMPUTATION OF O-C-F AND N-C-F SYSTEMS: AB-INITIO CALCULATIONS AND A MM2 PARAMETERIZATION STUDY. THEORY vs. EXPERIMENT[1]

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Abstract. *A parameterization scheme of Allinger's MM2 force field for the anomeric effect in O-C-F and N-C-F systems is presented. The scarcity of experimental data, in particular for the N-C-F case, dictated the use of ab-initio calculations to account for the energetic and structural manifestations of the effect. The resulting modified force field was tested against available X-ray, microwave and NMR results leading to a very good agreement between calculations and experiment. In addition, ab-initio results were used to demonstrate the role of the anomeric effect in lowering barriers to N-inversion and elevating barriers for rotation around single C-N bonds. The results for the fluoro compounds, when juxtaposed to other systems, provide a complete treatment of the anomeric effect for first row elements.*

INTRODUCTION

Within the scope of our theoretical and experimental studies of stereoelectronic effects in X-C-Y moieties[1-6], we have developed a general parameterization scheme of Allinger's MM2 force field[7] for the *anomeric effect* and applied it to O-C-O[2a], N-C-N[4] and O-C-N[1b,6] systems. In order to complete this treatment of stereoelectronic effects for first row elements, we have extended it now to the O-C-F and N-C-F moieties. This is also especially important in view of the growing interest in fluoro carbohydrates as intermediates in glycosidation processes[21] and to the use of such compounds for studying the interactions of fluoro sugars with enzymic binding sites[22].

The *anomeric effect*[8-10], which in carbohydrates means the preference of an axial (1) over the equatorial (2) conformation, is observed in X-C-Y moieties (X having non-bonding electrons and Y being an electronegative atom/group) by the fact that conformers having a lone pair (*lp*) antiperiplanar to an adjacent polar bond gain special stability (cf. 3 vs. 4). The most accepted explanation for the effect was given in MO terms[11] viz., delocalization of a *lp*

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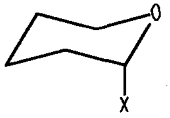
situated on X into the adjacent $\sigma^*_{C\text{-}Y}$ orbital. This interaction is proportional to the overlap (i.e., relative orientation) of the participating orbitals and inversely proportional to the energy gap between them[12]. In valence bond terms this corresponds to the double bond - no bond resonance **5** ↔ **5'** or the negative hyperconjugation concept[13]. Other, both intuitive and theoretically based hypotheses have been also put forward[8-10,14]. The existence of an *anomeric effect* in a system influences its properties *as* follows[1b,4,6,8-11]: (i) *energy:* preference of *gauche* (axial) over *anti* (equatorial) forms. (ii) *structure:* in a *lp*-X-C-Y moiety, a *lp* - C-Y antiperiplanar orientation results in shortening of X-C, elongation of C-Y and opening of X-C-Y. (iii) *reactivity:* variation of rates of attack at or around the anomeric center.



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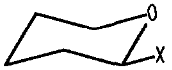

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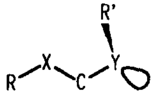

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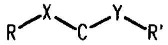

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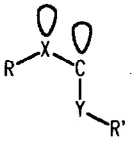

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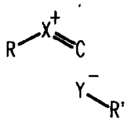

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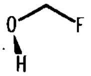

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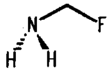

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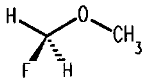
In addition, X-C-Y moieties having hydrogen atoms on either X or Y may exhibit H-bond type interactions of the forms X...H-Y, Y...H-X, X...H(C-Y) and Y...H(C-X)[4]. While these are non-classical H-bonds due to geometry constraints, they are still stabilizing.

The theoretical background for understanding the nature and role of stereoelectronic effects in O-C-F and N-C-F systems, was developed and presented in numerous papers[13,15-20]. These studies however did not go beyond the smallest model molecules namely, fluoromethanol ($HOCH_2F$, **6**), fluoromethylamine (H_2NCH_2F, **7**) and fluoromethylmethylether ($MeOCH_2F$, **8**). Based on those theoretical studies the following conclusions could be drawn: (i) Relative stabilities are governed by the *anomeric effect*. Thus a preference for *gauche*[†††] over the *anti* conformer of $HOCH_2F$ (6.44 Kcal/mol at 4-21G level)[16] and of $MeOCH_2F$, (**8**) (6.2 Kcal/mol at 4-31G level)[15] was found. However, no *gauche* conformers were found for H_2NCH_2F, where both minima involve a lp_N parallel to the C-F bond. The *anti* form was found to lie 5.08 Kcal/mol below the *syn* one at 6-31G** level[17].

(ii) Structural trends, typical for the *anomeric effect*, are well reproduced by *ab-initio* calculations ($HOCH_2F$ (4-21G)[16]: $L(C\text{-}O)_g = 1.405Å < L(C\text{-}O)_a = 1.420Å$, $L(C\text{-}F)_g = 1.404Å > L(C\text{-}F)_a = 1.387Å$, $A(O\text{-}C\text{-}F)_g = 110.8° > A(O\text{-}C\text{-}F)_a = 106.6°$; $MeOCH_2F$ (4-31G)[15]: $L(C\text{-}O)_g = 1.396Å < L(C\text{-}O)_a = 1.405Å$, $L(C\text{-}F)_g = 1.395Å > L(C\text{-}F)_a = 1.376Å$, $L(Me\text{-}O)_g = 1.447Å > L(Me\text{-}O)_a = 1.437Å$). Such an analysis was not possible for the N-C-F system (*vide supra*). Nevertheless, the expected dependence of C-N and C-F bond lengths on the *lp*-N-C-F dihedral angle (vide supra) was demonstrated by the construction of the complete torsional potential[17].

Based on this knowledge, we turn now to develop a reliable computational tool for reconstructing and predicting structures and energies of O-C-F and N-C-F containing molecules, beyond the practical limitations of *ab-initio* calculations. Semi-empirical methods are known to perform poorly for X-C-Y moieties[4,13] although some MNDO and PCILO calculations were used for the O-C-F system both in the isolated form and in solution[23]. In order to obtain an extended and uniform database, we have computed (GAUSSIAN 90)[24a] a set of X-C-F (X=O,N) containing molecules at the 3-21G[24b] and 6-31G*[24c] levels. At the same time, we have retrieved from the literature available experimental data on such systems and used all this information as described below.



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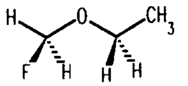

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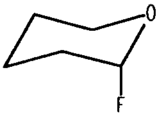

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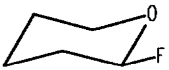

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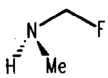

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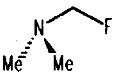

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††† Conformers of the O-C-F system are defined by the R-O-C-F dihedral angle. Those of the N-C-F system, by lp-N-C-F. *a=anti*; *g=gauche*; *s=syn*. These definitions apply to all anomeric moieties involving either oxygen and/or nitrogen. Thus, **6** is a g^+ and **7** is an *a* conformation, while **18** is an *aa* and **22** is a g^+g^+ conformation.

RESULTS AND DISCUSSION

Experimental data

Most of the available structural data for O-C-F systems have been obtained from X-ray analysis. It should be noted, however, that these data are to be considered according to the criteria used for parameterizing force fields of the MM2 series, originally based on gas phase electron diffraction results[7,41]. We have exhaustively searched the Cambridge Structural Database (CSD, January 1990 edition)[25] for X-ray structures containing the O-C-F and N-C-F sequences starting by retrieving all such compounds and then eliminating perturbed cases. Thus, molecules having at least one of the following features were removed: (i) R factor > 0.1; (ii) double bond/triple bond/carbonyl/heteroatom attached to the anomeric unit; (iii) charged quaternary nitrogen in the anomeric unit; (iv) presence of a coordinated metal ion in the molecule. Finally, molecules having their fluorine atom as part of a CF_3 group were also removed leaving no N-C-F cases and four examples with suitable O-C-F moieties[26-29]. These are compounds **14-18**, the relevant structural parameters of which are listed in Table 7, to be consulted in the parameterization process of MM2 and compared with the corresponding calculated data after parameterization (*vide infra*).

Microwave spectral analysis had been performed on fluoromethylmethylether[30-31] and fluoromethylethylether ($CH_3CH_2OCH_2F$)[31]. Only the *gauche* conformer (**8**) of the former and the *gauche anti* conformer (**9**) of the latter were observed, suggesting a prevalence of these conformers by at least 1.8 Kcal/mol[32]. Moments of inertia and r_s structures for both molecules, are given in Table 8 to be compared with the corresponding calculated data after parameterization of MM2 (*vide infra*).

NMR spectrometry has provided some experimental data for O-C-F containing molecules. In solution, ^{19}F-NMR, ^{1}H-NMR and ^{13}C-NMR spectra have been used to determine the favored conformation for some fluorinated carbohydrates and dioxanes[32-37]. Selected examples are gathered in Table 9, for use in the parameterization of MM2 and to be compared with the corresponding calculated data after parameterization (*vide infra*).

Ab-initio calculations

O-C-F: HF/3-21G//3-21G and HF/6-31G*//6-31G* calculations were performed on all viable conformers of $HOCH_2F$ (**6**), $MeOCH_2F$ (**8**) and $EtOCH_2F$ (**9**). Cyclic molecules i.e., 2-fluoro-tetrahydropyran (**10a,b**) were calculated at the 3-21G level. Relative energies and structural parameters of interest are presented in Table 1.

Table 1. Comparison of relative energies and structural parameters of interest as obtained from *ab-initio* (3-21G and 6-31G* levels) and the modified MMP2-87 force field for O-C-F containing molecules. Bond lengths (L) in Å, bond angles (A) and dihedral angles (D) in degrees, relative energies (Erel) in Kcal/mol.

		L			A		D	
		O-C^a	C-F	C-O^b	O-C-F	C-O-C	R-O-C-F^c	Erel
fluoromethanol (**6**)								
a	3-21G^d	1.410	1.378		106.8		180.0	6.42
		(1.390)	(1.366)					
	6-31G*	1.376	1.344		106.8		180.0	4.92
	MMP2	1.390	1.364		107.0		-175.5	4.89
g	3-21G	1.397	1.394		111.1		59.5	0.00
		(1.377)	(1.382)					
	6-31G*	1.364	1.361		110.8		63.7	0.00
	MMP2	1.375	1.385		110.5		67.3	0.00
fluoromethylmethylether (**8**)								
a	3-21G	1.404	1.378	1.438	107.9	114.4	180.0	5.63
		(1.384)	(1.366)	(1.418)				
	6-31G*	1.370	1.345	1.397	107.5	114.0	180.0	3.98
	MMP2	1.384	1.368	1.420	107.6	113.4	-179.9	4.05
g	3-21G	1.391	1.396	1.445	110.8	115.4	59.4	0.00
		(1.371)	(1.384)	(1.425)				
	6-31G*	1.358	1.363	1.404	111.1	115.3	65.4	0.00
	MMP2	1.370	1.387	1.427	111.2	115.7	67.3	0.00
fluoromethylethylether (**9**)								
a	3-21G	1.403	1.379	1.443	107.9	115.2	180.0	5.51
		(1.383)	(1.367)	(1.423)				
	6-31G*	1.369	1.346	1.403	107.5	114.5	180.0	3.98
	MMP2	1.384	1.368	1.422	107.6	113.7	179.9	4.13
g	3-21G	1.390	1.397	1.451	110.8	116.0	59.4	0.00
		(1.370)	(1.385)	(1.431)				
	6-31G*	1.357	1.363	1.411	111.1	115.7	66.3	0.00
	MMP2	1.369	1.387	1.429	111.2	115.8	67.0	0.00
2-fluoro-tetrahydropyran (**10**)								
ax	3-21G	1.399	1.405	1.454	109.5	114.6	59.0	0.00
		(1.379)	(1.393)	(1.434)				
	MMP2	1.378	1.387	1.434	109.8	115.4	63.1	0.00
eq	3-21G	1.411	1.382	1.447	107.0	113.7	179.6	4.94
		(1.391)	(1.370)	(1.427)				
	MMP2	1.392	1.369	1.427	106.8	113.0	179.9	3.72

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[a] "Inner" C-O bond. [b] "Outer" C-O bond. [c] R=H or C. [d] Bond lengths in parenthesis are corrected 3-21G values (see text).

N-C-F: HF/3-21G//3-21G and HF/6-31G*//6-31G* calculations were performed on fluoromethylamine (H_2NCH_2F, **7**), N-methylaminofluoromethane ($MeHNCH_2F$, **11**) and N,N-dimethylaminofluoromethane ($(Me_2)NCH_2F$, **12**) (Table 2). Minimum energy conformers were located with both basis sets. In addition, transition states for N-inversion and rotation around the central C-N bonds were located, for all three molecules, at the 6-31G* level. Each

Table 2. Comparison of relative energies and structural parameters of interest as obtained from *ab-initio* (3-21G and 6-31G* levels) and the modified MMP2-87 force field for N-C-F containing molecules. Bond lengths (L) in Å, bond angles (A) and dihedral angles (D) in degrees, relative energies (Erel) in Kcal/mol.

		L				A			D		
		N-C^a	C-F	C-N^b	C-N^b	N-C-F	C-N-C	C-N-C	R-N-C-F^c	R'-N-C-F^c	Erel
						fluoromethylamine (7)					
a	3-21G^d	1.414	1.417 (1.405)			114.1			69.2	-69.2	0.00
	6-31G*	1.412	1.379			113.1			60.8	-60.8	0.00
	MMP2	1.411	1.407			113.5			58.3	-58.3	0.00
g	3-21G	Converged to *a* via N-inversion.									
	6-31G*	Converged to *a* via N-inversion.									
s	3-21G	Converged to *a* via N-inversion.									
	6-31G*	1.413	1.371			111.4			113.0	-113.0	5.35
	MMP2	1.413	1.410			115.2			120.8	-120.8	5.42
						N-methylaminofluoromethane (11)					
a	3-21G	1.413	1.418 (1.406)	1.469		113.2	116.8		-74.2	62.5	0.00
	6-31G*	1.408	1.382	1.452		113.0	115.6		-61.0	66.4	0.00
	MMP2	1.419	1.408	1.472		113.0	115.1		-55.2	65.2	0.00
g$^+$	3-21G	Converged to *a* via N-inversion.									
	6-31G*	1.426	1.360	1.449		109.0	113.8		173.6	-61.5	5.40
	MMP2	1.440	1.390	1.471		110.3	114.9		173.6	-64.6	5.63
g$^-$	3-21G	Converged to *a* via N-inversion.									
	6-31G*	1.419	1.366	1.449		109.7	115.4		75.9	-154.8	4.68
	MMP2	1.447	1.383	1.469		108.6	110.5		53.3	175.4	4.67
s	3-21G	Converged to *a* via N-inversion.									
	6-31G*	Converged to *g* via rotation.									
						N,N-dimethylaminofluoromethane (12)					
a	3-21G	1.415	1.419 (1.407)	1.468	1.468	112.5	115.1	115.1	67.4	-67.4	0.00
	6-31G*	1.407	1.383	1.450	1.450	112.8	114.1	114.1	65.7	-65.7	0.00
	MMP2	1.419	1.409	1.471	1.471	112.7	115.1	115.1	63.1	-63.1	0.00
g	3-21G	1.434	1.400 (1.388)	1.464	1.461	109.6	114.0	114.6	59.0	-165.2	5.07
	6-31G*	1.425	1.362	1.449	1.447	109.7	112.7	112.2	64.8	-166.6	4.26
	MMP2	1.443	1.385	1.462	1.463	109.7	109.9	113.4	53.4	178.6	3.59
						2-fluoro-piperidine (13)					
13a	3-21G	Converged to **13b** via N-inversion.									
13b	3-21G	1.421	1.427 (1.415)	1.476		111.2	115.4		59.7	-73.9	0.00
	6-31G*	1.416	1.394	1.459		111.2	115.2		63.4	-63.4	0.00
	MMP2	1.421	1.410	1.473		111.3	114.9		61.3	-59.9	0.00
13c	3-21G	1.448	1.398 (1.386)	1.474		108.4	112.8		-177.1	-47.3	7.14
	MMP2	1.445	1.386	1.472		107.9	113.2		-178.0	-57.1	5.69
13d	3-21G	1.444	1.400 (1.388)	1.472		108.2	114.4		-179.2	47.9	6.22
	MMP2	1.441	1.391	1.472		108.8	114.4		-174.7	63.4	5.21

[a] "inner" C-N bond. [b] "outer" C-N bond. [c] R=H or C.
[d] bond lengths in parenthesis are corrected 3-21G values (see text).

transition state was verified by having one imaginary frequency and by distortions towards both stable conformers. For comparison, corresponding transition states for ethylamine were calculated as well. In order to complete the data set for the N-C-F system, four conformers of 2-fluoro- piperidine (**13a-d**) were also computed (3-21G level). These are F=ax; H(N)=ax (**13a**), F=ax; H(N)=eq (**13b**), F=eq; H(N)=ax (**13c**), and F=eq; H(N)=eq (**13d**). Only three distinct minima were found, F=ax;H(N)=ax converged to F=ax;H(N)=eq via N-inversion. Relative energies and structural parameters of interest are given in Table 2.

Rotation/Inversion Potentials

The role of the *anomeric effect* in lowering barriers to N-inversion was demonstrated in the past[4b,13,38]. In order to further pursue the subject and extend it to rotational barriers around single C-N bonds in anomeric moieties[18], selected compounds were subjected to a detailed analysis.

3-21G calculations: The C-N rotational potential of fluoromethylamine (**7**) is characterized by a single minimum at lp-N-C-F=180.0° and a transition state (TS) at

Table 3. 6-31G* *ab-initio* results for minimum energy conformers and transition states of compounds **7**, **11-12** and of ethylamine ($EtNH_2$).

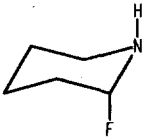
Molecule	Conformer[a]	ϕ[b]	Σ_A[c]	Erel[d]
fluoromethylamine (7)	*a*	180.0	346.7	0.00
	s	0.0	343.4	5.35
	RTS	-102.5	328.1	7.76
	ITS	0.0	356.6	5.60
N-methylaminofluoromethane (11)	*a*	-175.2	337.4	0.00
	g^-	-37.5	338.9	4.68
	g^+	57.6	334.4	5.40
	RTS *a* -> g^-	-100.8	336.0	9.61
	RTS *a* -> g^+	112.5	334.8	7.62
	ITS *a* -> g^-	-6.01	358.0	5.60
N,N-dimethylaminofluoromethane (12)	*a*	180.0	340.8	0.00
	g	-50.4	337.8	4.26
	RTS	108.1	341.3	9.44
	ITS	0.0	349.0	6.09
ethylamine	*a*	180.0	328.1	0.08
	g	56.0	328.2	0.00
	RTS	118.7	330.7	2.82
	ITS	16.3	359.9	5.88

[a] RTS = Rotational transition state, ITS = N-inversion transition state.

[b] ϕ = lp-N-C-F. The location of the N_{lp} is determined according to the following procedure: 3 unit vectors are drawn from the nitrogen along its 3 bonds. The lp is located along the negative direction of the vector sum of these 3 vectors.

[c] Σ_A = sum of bond angles around the nitrogen atom.

[d] In Kcal/mol.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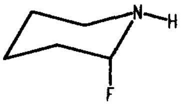
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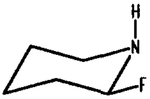
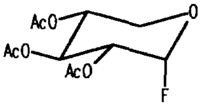

13c


13d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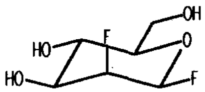
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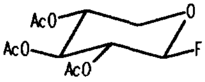
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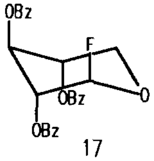
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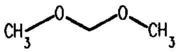
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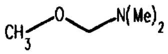
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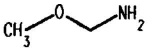
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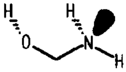
22

lp-N-C-F=95.0° (9.33 Kcal/mol), in accord with the work of Schleyer and Kos[46]. Further rotation results in conformers not stable towards N-inversion to the *anti* form[47]. This instability is carried on to the mono-methylated case (**11**) where both g^- and g^+ conformers go over to the *anti* one via this route and is hampered only in the di-methylated compound (**12**). This suggests that the barrier to N-inversion in **12** is higher than in **7** and **11** as supported by 6-31G* calculations (*vide infra*).

6-31G calculations* (Table 3): Four stationary points were located on the potential surface of fluoromethylamine (**7**), in accord with the work of Dunitz[17]. The two minima (*anti* = 0.00 Kcal/mol, *syn* = 5.35 Kcal/mol) are separated by two transition states (TS's) lying on the rotational (7.76 Kcal/mol) and N-inversion (5.60 Kcal/mol) interconversion pathways. Minimum energy conformers located for N-methylaminofluoromethane (**11**) correspond to *a* (0.00 Kcal/mol), g^+ (5.40 Kcal/mol) and g^- (4.68 Kcal/mol). Rotational TS's were located for *a* -> g^- and *a* -> g^+ pathways (9.61 and 7.62 Kcal/mol respectively). Interconversion by N-inversion is possible only between the *a* and g^- conformers via a TS located at 5.60 Kcal/mol. Similar calculations for N,N-dimethylaminofluoromethane (**12**) led to two minima (*anti* = 0.00 Kcal/mol, *gauche* = 4.26 Kcal/mol) separated by a symmetric N-inversion TS (6.09 Kcal/mol) and a rotational TS (9.44 Kcal/mol). The latter number is in very good agreement with experimental values of 10 Kcal/mol for two N,N-dialkyl-substituted derivatives[48]. The corresponding relative energies for the stationary points of ethylamine ($EtNH_2$), calculated for comparison are: 0.00 Kcal/mol (*gauche* - global minimum), 0.08 Kcal/mol (*anti* - minimum), 2.82 Kcal/mol (rotational TS) and 5.88 Kcal/mol (N-inversion TS).

Table 4. 3-21G relative energies (Erel in Kcal/mol) for different conformers of X-C-Y moieties (X=O,N; Y=O,N,F)†††.

Molecule	Conformer	Erel	Reference
Dimethoxymethane (**18**)	*aa*	9.39	2a
	ag	3.91	
	g^+g^+	0.00	
Methylenediamine (**19**)	*aa*	0.00	4
	ag	1.62	
	g^+g^+	2.70	
Fluoromethylmethylether (**8**)	*a*	0.00	This work
	g	5.63	
N,N-dimethylaminofluoromethane (**12**)	*a*	0.00	This work
	g	5.07	
1-methoxy-N,N-dimethylmethylamine (**20**)	*aa*	0.00	6b
	ag^-	4.56	
	g^-g^+	0.34	
1-methoxymethylamine (**21**)	g^-a	0.00	6b
	aa	0.95	

According to the dihedral angle ϕ = F-C-N-lp (Table 3), all rotational TS's for molecules **7**, **11-12** have nearly orthogonal lp_N and σ^*_{C-F} orbitals (i.e., no *anomeric effect* per its definition). In particular, the *a* -> g^- ($\phi = -100.8^\circ$, E = 9.6 Kcal/mol) and *a* -> g^+ ($\phi = 112.5^\circ$, E = 7.62 Kcal/mol) TS's of **11** indicate that the greater the deviation from orthogonality, the lower is the TS. For comparison, in $EtNH_2$ (no anomeric interaction), the *a* -> *g* interconversion goes through a nearly eclipsed TS ($\phi = 118.7^\circ$).

Rotation-inversion coupling in the various TS's can be estimated from ϕ and nitrogen's pyramidality (Σ_A = sum of bond angles around the nitrogen). In all cases (save $EtNH_2$ where $\phi = 16.3^\circ$), ϕ values for N-inversion TS's correspond to a nearly parallel, rotational free, lp_N- σ^*_{C-F} orientation thus maximizing the anomeric interaction while Σ_A approaches 360°, representing a planar nitrogen. Since nitrogen pyramidality in the Me substituted cases (**11** and **12**) is mainly governed by steric hindrance (i.e., Σ_A is roughly constant along the rotational pathway) the unsubstituted case (**7**) should be considered a better probe for the anomeric influence. Indeed, Σ_A value for the rotational TS is much smaller than those in the minimum energy conformers (Table 3). As the anomeric interaction is switched off, the energy cost of flattening the nitrogen atom is not compensated by increasing its lp's P-character to obtain a better overlap with the σ^*_{C-F} orbital.

Contrary to the situation in $EtNH_2$ where the rotational TS (2.82 Kcal/mol) is lower than that of N-inversion (TS = 5.88 Kcal/mol), in **7**, **11** and **12**, the order is inverted. The role of the anomeric effect in lowering TS's for N-inversion (nitrogen's flattening to obtain a better anomeric interaction) and rising rotational TS's (a partly double character of the C-N bond) is thus once more demonstrated[4b,13,18,38].

The 3-21G *ab-initio* results on the fluorinated compounds complete a series of similarly calculated X-C-Y systems (X=O,N; Y=O,N,F)[1b,2a,4] from which anomeric interactions involving first row elements can be deduced (Table 4). A relatively pure lp_O- σ^*_{C-O} interaction (i.e., free from severe steric and H-bond interactions) can be estimated from the energy differences between *aa*, *ag* and g^+g^+conformers†††of dimethoxymethane (DMM, **18**; 0, 1 and 2 anomeric interactions respectively)[2a]. Taking the average between the first (E_{aa}- E_{ag}= 5.5 Kcal/mol) and the second (E_{ag} - E_{g+g+} = 3.9 Kcal/mol) interactions, we obtain a value of 4.7 Kcal/mol. similarly[4], 1.35 Kcal/mol are estimated for lp_N- σ^*_{C-N} from methylenediamine (MDA, **19**) data. Only *anti* and *gauche* (non eclipsed) forms of X-C-F moieties are considered, leading to 5.07 and 5.63 Kcal/mol for lp_N- σ^*_{C-F} (**12**) and lp_O- σ^*_{C-F} (**8**) respectively, the former perhaps slightly underestimated due to destabilization of **12**-*anti* by steric interactions. Two different anomeric interactions exist in the O-C-N system[6]: 4.56 Kcal/mol are obtained for lp_N- σ^*_{C-O} based on a comparison between *aa* and ag^- conformers†††of 1-methoxy-N,N-dimethylmethylamine (**20**) while ambiguous results are found for lp_O- σ^*_{C-N} (0.95 Kcal/mol from g^-a and *aa* conformers of 1-methoxymethylamine (**21**) and 4.22 Kcal/mol from ag^-

and g^-g^+ conformers of 1-methoxy- N,N-dimethylmethylamine (**20**)). An attempt to quantify this interaction by comparing the g^-g^+, g^+g^+ and ag^+ conformers of 1-methoxymethylamine (**21**) failed due to convergence to g^-a, g^+a and aa forms respectively. Similarly, the g^+g^+ conformer of aminomethanol (**22**; 1 lp_O- σ^*_{C-N} anomeric interaction) is not a minimum energy point at the 3-21G level[6]. Thus, this interaction seems to be too weak to stabilize, by itself, the respective conformers. A comparison between lp_O- σ^*_{C-O} (4.7 Kcal/mol) vs. lp_O- σ^*_{C-N} (unknown but small value, see above) and lp_N- σ^*_{C-O} (4.6 Kcal/mol) vs. lp_N- σ^*_{C-N} (1.3 Kcal/mol) indicates that a C-O bond is, as expected, a better σ-acceptor than a C-N bond. However, a comparison between the π-donor ability of oxygen and nitrogen which is now available from lp_O- σ^*_{C-F} vs. lp_N- σ^*_{C-F} and lp_O- σ^*_{C-O} vs. lp_N- σ^*_{C-O}, viz., 5.6, 5.1, 4.7 and 4.6 Kcal/mol for the four anomeric interactions, respectively, indicates resemblance between the two in this respect.

Force Field Calculations

The modification of and calculations with the MMP2-87 force field were performed following our previous approach[1b,2a,4]. The starting geometries of compounds **14-17** (Table 7) were used as retrieved from the CSD[25]. A multitude of conformers is available for the substituted tetrahydropyrans listed in entries 3-5 of Table 9. The driver option incorporated in MM2 was used to obtain a set of starting points by varying the substituents' dihedral angles. This was followed by a full optimization of the low lying conformers and finally, the equilibrium mixture composition was evaluated through Boltzmann distribution.

Parameterization

The parameterization of MM2[7] for X-C-F systems was done essentially along the lines described for the O-C-N,[1b] O-C-O[2a] and N-C-N[4] ones.

In view of the small size of the molecules under consideration and the known deficiencies of both basis sets[††††], a combined approach was used, viz., parameterization for relative energies and geometries was based on 6-31G* and 3-21G results respectively. C-O and C-N bond lengths were corrected according to microwave data (vide infra). In order to minimize interference with the normal operation of the program, changes concern only anomeric units.

[††††] Nitrogen's pyramidality is underestimated by the 3-21G basis set resulting in a more "planar" nitrogen atom[6,13]. Thus, the magnitude of the lp_N- σ^*_{C-X} anomeric interaction is overestimated. The improved anomeric interaction resulting from the use of a pure *p* orbital on nitrogen, was already noted for both N-C-F[13,17] and N-C-N[4b] systems. At the same time, this basis set provides geometrical parameters in accord with experimental as well as with post HF methods, in contrast to the 6-31G* one which causes severe bond shortening[4,6,42].

Options may be selected at will via the input. The structural and energetic features we aimed at reproducing are the following:

1. Relative energies of *gauche* (axial) vs. *anti* (equatorial) conformers.
2. Structural changes induced by anomeric interactions: (i) "inner" C-X (X=O,N) and C-F and "outer" C-X bond lengths (ii) X-C-F and C-X-C bond angles (iii) C-N bond lengths in tertiary amines within an N-C-F anomeric unit.

Below, the criteria for parameterization are elaborated on, and the resulting parameters are listed in Table 5.

The energy criterion:

Determination of torsional parameters. Following the well established approach[2,4,6], conformational preferences were introduced mainly via the torsional potentials. Three double sets of such parameters containing the X-C-F moieties namely, F-C-X-lp, F-C-X-H and F-C-X-C had to be adjusted. Starting from the smallest model molecules **6** and **7** we have established a reasonable fit between *ab-initio* and MMP2-87 results using the first two. We then moved to the larger molecules **8**, **9**, **11** and **12** taking care of the third F-C-X-C term. Finally, we have used the resulting potentials to treat the cyclic molecules **10** and **13**, bearing in mind that these molecules were calculated with the 3-21G basis set only. The MMP2 energy differences between the conformers should therefore be set smaller than the *ab-initio* ones[††††].

Introduction of H-bond type interactions. It stands to reason that R-X-C-F systems may exhibit H-bond type interactions of the forms F...H-X and F...H-C(X) which are bound to influence the relative energies as well as the structural features of the various conformers. Indeed, a growing volume of evidence for the existence of such interactions is found in the literature, and their importance with regards to biological systems was discussed[22,28].

In the original MMP2-87 force field[7] F...H-X H-bonds were taken care of via special VDW parameters for the F...H(O) and F...H(N) atom pairs. We extended this to similar vicinal interactions and included F...H-C(X) interactions.

The geometry criterion:

The basis for the structural parameterization consisted of the calculated (3-21G) results, along with experimental gas phase data, when available. To correlate between the two methods we compared 3-21G and microwave analysis results for a set of molecules (Table 6)[40,42-45] and, following the work of Schäfer et al.[40], derived correction terms for 3-21G C-O and C-F bond lengths. These consisted essentially in bond shortening by 0.020Å and 0.012Å, respectively. Corrections for other structural parameters were either found to be insignificant or could not be evaluated due to insufficient data.

Table 5. Modified MMP2-87 force field parameters.

Torsional parameters

Angle	V1	V2	V3
F-C-O-lp	0.00	2.70	0.30
F-C-O-H	0.70	0.00	0.30
F-C-O-C	1.70	0.00	0.30
F-C-N-lp	1.45	3.00	0.00
F-C-N-H	-0.35	-0.30	0.40
F-C-N-C	-0.30	-0.40	0.30

"VDW" parameters

Type	r	ε
F...H-(C-O)	2.050	0.600
F...H-(C-N)	2.050	2.300

Bending parameters

Type	θ_0 XCH$_2$F	θ_0 XCHF	k$_{bend}$	k$_{O/N}$	k'$_{O/N}$
O-C-F	111.7	110.7	0.90	4.00	3.40[a]
C-O-C	Original MMP2-87 values			4.30	
N-C-F	115.0	113.5	1.10	7.40	5.60[b]
C-N-C	Original MMP2-87 values			8.00	13.00[b]

anomeric bond lengths correction terms

Inner bonds

Type	k	d	d'
C-F[c]	0.017	0.035	
C-O exocyclic	0.011	0.020	0.039[d]
C-O endocyclic	0.011	0.012	0.031[d]
C-F[e]	0.033	0.017	
C-N	0.034	-0.009	

Outer bonds

Type	a	b
C-O exocyclic	0.700	-0.040
C-O endocyclic	0.700	-0.028
C-N	0.125	0.008

C-N bond shortening in tertiary amines - 0.013Å

[a] A different correction term is applied to O-C-F bond angles when O is substituted by a carbon atom (see text).
[b] A different correction term is applied to N-C-F/C-N-C bond angles for tertiary amines (see text).
[c] Parameters for C-F bonds in O-C-F anomeric moiety. A distinction is made between endo and exocyclic bonds (see text).
[d] O substituted by a carbon atom (see text).
[e] Parameters for C-F bonds in N-C-F anomeric moiety.

Table 6. 3-21G (r_e) and microwave (r_s) C-O and C-F bond lengths (Å). The first and second references cited refer to r_e and r_s values respectively.

Molecule	C-O		C-F		Reference
	r_e	r_s	r_e	r_s	
Methanol	1.441	1.421			42, 40
Diethylether	1.433	1.410			42, 40
Methylethylether (*trans*)	1.437	1.404			This work, 40
	1.432	1.415			
Ethanol (*trans*)	1.444	1.431			42, 40
2-fluoropropane			1.416	1.398[a]	43
Fluoropropane (*trans*)			1.409	1.401	This work, 44
Fluoropropane (*gauche*)			1.412	1.390	This work, 44
Fluoroethane			1.410	1.398	42, 45
Fluoromethylmethylether (*gauche*)	1.391	1.362	1.396	1.385	This work, 30, 31
	1.445	1.424			
Fluoromethylethylether	1.390	1.359	1.397	1.385	This work, 31
(*gauche trans*)	1.451	1.437			

[a] r_O structure

All available conformers of compounds **6**, **8-10** and **7**, **11-13** were included in the parameterization process for O-C-F and N-C-F systems respectively. Structural parameters in the anomeric unit were treated in a manner similar to the O-C-O[2] and N-C-N[4] systems. However, since the lp_F- σ^*_{C-X} anomeric interaction is independent of rotation around the C-F bond, parameters depend only on the lp_X- σ^*_{C-F} interaction.

"Inner" anomeric X-C and C-F bond lengths. The function that determines l_0 for all "inner" anomeric bond lengths is[7c]:

(1) $l_0' = l_0 - \delta l$

where (in MM2 bicoordinate oxygen has two equivalent *sp*³ lone pairs):

(2) $\delta l(C\text{-}O)_{O\text{-}C\text{-}F} = k/2[(1+\cos 2\omega_{O1})+(1+\cos 2\omega_{O2})]+d$

(3) $\delta l(C\text{-}F)_{O\text{-}C\text{-}F} = -k/2[(1+\cos 2\omega_{O1})+(1+\cos 2\omega_{O2})]+d$

(4) $\delta l(C\text{-}N)_{N\text{-}C\text{-}F} = k/2[1+\cos 2\omega_N]+d$

(5) $\delta l(C\text{-}F)_{N\text{-}C\text{-}F} = -k/2[1+\cos 2\omega_N]+d$ and:

ω_{O1} = lp1-O-C-F; ω_{O2} = lp2-O-C-F; ω_N = lp-N-C-F

A positive term shortens l_0, while a negative one lengthens it; *d* induces a constant shift, accounting for the interplay between anomeric interactions and C-X bond shortening known to occur when several electronegative atoms are connected to the same carbon[3,39].

Changes in the C-F bond lengths ($(C\text{-}F)_g - (C\text{-}F)_a$) for the O-C-F system, gradually increase from 0.016Å to 0.018Å and to 0.023Å when going from fluoromethanol (**6**) to fluoromethylmethylether (**8**) and to 2-fluoro-THP (**10**) (see Table 1). This may be attributed to changes in the oxygen's electrons donating power when substituted by methyl groups. In the original MMP2-87 scheme, electronegativity corrections elongate C-X (X=O,N) bonds when X is substituted by hydrogen atoms. To avoid duplicate corrections, these were circumvented when C-X is included in an anomeric unit. The electronegativity effect is added to the *d* and tertiary amine terms. Consequently, we have correlated *d* with the substitution pattern on O/N (see Table 5).

C-X bonds adjacent to an X-C-F unit. Following our studies on the C-O-C-O-C and C-N-C-N-C units[2,4], we introduced a weak dependence between the change in the "inner" X-C bond length and the "outer" one. This is expressed by:

(6) $l_0' = l_0 + D$

where:

(7) $D = a\delta l + b$

A better agreement with *ab-initio* results for "inner" and "outer" C-X bonds was obtained by differentiating between exo- and endocyclic cases and assigning different parameters for each. This is done automatically by the program and is justified by increased steric interactions experienced by a lp-X-C-F moiety when C-X is constrained to a ring.

C-N bond lengths in tertiary amines. Ab-initio calculations have demonstrated the gradual decrease in C-N bond lengths when going from primary to secondary and to tertiary amines[7d]. However, an analysis of suitable X-ray structures discovered only negligible differences[4b]. The inclusion of a tertiary amine within an anomeric unit leads to ambiguous results (Table 2). For example, "inner" C-N bonds of the anti conformers of **7** (primary amine), **11**, **13b** (secondary amines) and **12** (tertiary amine) are roughly the same ranging from 1.413Å to 1.421Å. Similar resemblance is found in the "outer" C-N bond lengths (1.469Å vs. 1.468Å for the anti conformers of **11** and **12** respectively). It seems that in this case, the interplay between anomeric interactions, steric interactions and C-X bond shortening (vide supra) mask the trends observed in the CH_3NH_2, $(CH_3)_2NH$, $(CH_3)_3N$ series[43]. A good reproduction of *ab-initio* results was obtained by applying a shortening factor of 0.013Å to "inner" anomeric C-N bonds alone.

X-C-F and C-X-C bond angles. The equation that expresses θ_0(X-C-F) as a function of the lp_X- $\sigma^*_{C\text{-}F}$ interaction is[1b]:

(9) $\theta_0' = \theta_0 + \delta\theta$

where:

(10) $\delta\theta(\text{O-C-F}) = k_O/2[(\cos2\omega_{O1}-1)+(\cos2\omega_{O2}-1)]$

(11) $\delta\theta(\text{N-C-F}) = k_N/2[\cos2\omega_N-1]$

In addition, θ_0 and K_{bend} for the O-C-F and N-C-F bond angles had to be established. Equations 12-14 describe the parameterization scheme for the C-O-C and C-N-C bond angles. Here, only k_O and k_N had to be established, while θ_0(C-O-C) and θ_0(C-N-C) maintained their original MMP2-87 values.

(12) $\theta_0' = \theta_0 + \delta\theta$

(13) $\delta\theta(\text{C-O-C}) = k_O/2[(1+\cos 2\omega_{O1})+(1+\cos 2\omega_{O2})]$

(14) $\delta\theta(\text{C-N-C}) = k_N/2[1+\cos 2\omega_N]$

For the X-C-F cases we followed the central atom substitutions dependence of θ_0 as implemented in MMP2. The distinction was extended to the k_N and k_O correction terms in equations 10,11 and 14 (see Table 5).

The results for the O-C-F and N-C-F systems are displayed in Tables 1 and 2 respectively, next to the *ab-initio* calculated results.

As evident from the results (*ab-initio* and experimental) and noted by others[13,15-20], the *anomeric effect* is fully operative in both systems. The O-C-F moiety is characterized by prevalence of *gauche* (axial) over *anti* (equatorial) forms, the former having shorter C-O and longer C-F bond lengths and larger C-O-C and O-C-F bond angles. For N-C-F (**7**), the energy gain from a parallel *lp* - C-F bond orientation is large enough to overcome two H/H eclipsed interactions making the *syn* form the second lowest minimum[17], while the expected *gauche* conformer goes over to the *anti* one via nitrogen inversion. Increasing steric interactions by replacing either one (**11**) or two (**12**) hydrogen atoms by a methyl group, provides rotational barriers high enough to hold the *gauche* forms while eliminating the *syn* ones. Geometrical features observed in this system (Table 2) are in accord with theory.

At this point, the reparameterized force field had to be tested on large molecules, both in the crystal and in the gas phase. In the former case, this was done on compounds **14-17**, the crystal structures of which had been retrieved from the CSD *(vide supra)* and the results, i.e., structural parameters, are compared in Table 7. For the gas phase, the MW analytical results of **8** and **9** are compared with the newly computed data in Table 8. As to the conformational preferences, the calculated results are compared with the NMR data in Table 9.

Table 7 Comparison of selected structural parameters between X-ray and modified MMP2-87 results for molecules **14-17**[26-29]. Bond lengths (L) in Å, bond angles (A) and dihedral angles (D) in degrees (carbohydrate atom numbering).

		14		**15**		**16**		**17**	
		X-ray	MMP2	X-ray	MMP2	X-ray	MMP2	X-ray	MMP2
	C5-O1	1.445	1.432	1.441	1.430	1.428	1.425	1.450	1.432
L	O1-C2	1.380	1.378	1.402	1.390	1.406	1.390	1.362	1.377
	C2-F	1.397	1.385	1.368	1.370	1.366	1.368	1.389	1.385
A	C-O-C	113.7	114.4	111.5	113.8	109.9	112.9	112.6	115.3
	O-C-F	109.9	108.9	104.9	107.5	105.7	106.2	110.7	109.9
D	C-O-C-F	64.2	58.2	178.6	179.7	174.4	182.9	-64.6	-61.8

Table 8. Comparison of moments of inertia and structural parameters of interest as obtained from microwave analysis (MW, references 30 and 31), *ab-initio* (3-21G, 6-31G*) calculations and the modified MMP2-87 force field for the *gauche* conformer of fluoromethylmethylether (**8**) and the *gauche*-trans conformer of fluoromethylethylether (**9**). Bond lengths (L) in Å, bond angles (A) and dihedral angles (D) in degrees, moments of inertia (I) in amu × Å^2.

		8				9			
		MW	3-21G	6-31G*	MMP2	MW	3-21G	6-31G*	MMP2
I	Ix	28.555	29.949	27.891	28.584	33.785	35.175	32.653	35.338
	Iy	90.176	88.790	87.534	91.023	197.820	195.979	194.632	197.667
	Iz	105.473	107.014	103.178	106.770	211.821	213.000	209.028	212.300
L	C-F[a]	1.385	1.396 (1.384)	1.363	1.387	1.385	1.397 (1.385)	1.363	1.387
	C-O(i)[b]	1.362	1.391 (1.371)	1.358	1.370	1.359	1.390 (1.370)	1.357	1.369
	C-O(o)[c]	1.424	1.445 (1.425)	1.404	1.427	1.437	1.451 (1.431)	1.411	1.429
A	O-C-F	111.3	110.8	111.1	111.2	110.3	110.8	111.1	111.2
	C-O-C	113.5	115.4	115.3	115.7	114.1	116.0	115.7	115.8
D	F-C-O-C	69.2	59.4	65.4	67.3	70.4	59.4	66.3	67.0

[a] Bond lengths in parenthesis are corrected 3-21G values (see text). [b] "inner" C-O bond.
[c] "outer" C-O bond.

The differences between structural parameters obtained by theoretical (*ab-initio*) and experimental (X-ray, microwave) methods should be noted[40,41]. *Ab-initio* calculations (at the level used in this paper) treat a single molecule in the gas phase at 0 K to produce equilibrium structure, r_e, with no vibrational corrections. This is not the case for microwave analysis which provides vibrationally dependent r_s structures. X-ray diffraction treats the solid phase and gives distances between centers of electron distributions. A precise reconstruction of data from all sources with a single force field parameters set is therefore both theoretically and practically not warranted. The scarcity of the data until now, did not justify the development of several sets but the flexibility of the parameterization procedure renders it possible as more data accumulate. With this in mind, a survey of the results (Tables 7-9) reveals the very good performances of the modified force field. All energetic and structural features are reconstructed to similar accuracies, C-X-C bond angles being perhaps an exception due to the restrictions imposed by maintaining MMP2-87's original θ_0 and k_{bend} values. The comparison with NMR data is of interest, in particular as a rough probe of conformational space by MM2 (Table 9). In all cases, calculated axial/diaxial F-substituent(s) are preferred over equatorial ones, in full agreement with experiment.

CONCLUSIONS

Ab-initio calculations on O-C-F and N-C-F systems were extended to include larger model molecules and cyclic compounds. Anomeric interactions dominate both structure and energy of these systems as is evident from theory and experiments. The magnitude of the different *anomeric effects* suggests that while oxygen and nitrogen largely differ in their σ-acceptor ability, they are π-donors of roughly the same magnitude.

A computational tool for large O-C-F and N-C-F systems was developed by parameterizing Allinger's MMP2-87 force field complementing the previous one developed for the O-C-O[2a], N-C-N[4] and O-C-N[1b,6] systems, to complete this treatment of stereoelectronic effects for first row elements. Its ability to reproduce both energetic and structural manifestations of the *anomeric effect* makes it a valuable tool in studying the field of fluorinated sugars.

The entire parameterization scheme is available on request from the authors.

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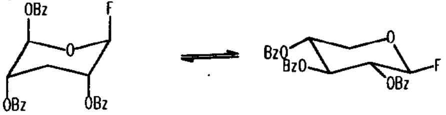
Table 9. Comparison of relative energies as obtained from NMR spectroscopy and the modified MMP2-87 calculations. In all cases, an axial fluorine atom is preferred (see text). Relative energies (Erel) are given in Kcal/mol. MMP2 energies take all possible rotamers into account (see text).

		Eax - Eeq (Kcal/mol)		Ref
		MMP2-87	Exp	
1		-7.05	Axial Favored	36
2		-7.71	<-2; >96%	32, 33
3		-0.41	Axial Favored	28
4		-0.13	Axial Favored -0.98; 86%	35, 37
5		-1.36	Axial Favored -1.3; 92%	35, 37

REFERENCES

1. a. Structure and Conformation of Heterocycles. Part 24. For part 23 see 1b.
   b. H. Senderowitz, P. Aped, B. Fuchs *J. Comput. Chem.* in press.
2. a. P. Aped, Y. Apeloig, A. Ellencweig, B. Fuchs, I. Goldberg, M. Karni, E. Tartakovsky *J. Am. Chem. Soc.* **1987** *109*, 1486.
   b. B. Fuchs, A. Ellencweig, E. Tartakovsky, P. Aped *Angew. Chem. Int. Ed. Engl.* **1986** *25*, 287.
3. a. L. Schleifer, H. Senderowitz, P. Aped, E. Tartakovsky, B. Fuchs *Carbohyd. Res.* **1990** *206*, 21.
   b. B. Fuchs, L. Schleifer, E. Tartakovski *Nouv. J. Chim.* **1984** *8*, 275.
4. a. P. Aped, B. Fuchs, L. Schleifer, S. Wolfe *J. Comput. Chem.* **1989** *10*, 265.
   b. H. Senderowitz, P. Aped, B. Fuchs *Tetrahedron* **1992** *48*, 1131..
5. a. B. Fuchs, A. Ellencweig *Recl. Trav. Chim. Pays-Bas* **1979** *98*, 326.
   b. B. Fuchs, S. Weinman, U. Shmueli, A. R. Katritzky, R. C. Patel *Tetrahedron Lett.* **1981** *22*, 3541.
   c. R. Müller, W. von. Philipsborn, L. Schleifer, P. Aped, B. Fuchs *Tetrahedron* **1991** *47*, 1013.
6. H. Senderowitz, P. Aped, B. Fuchs *Helv. Chim. Acta* **1990** *73*, 2113.
7. a. MM2, N. L. Allinger, Y. H. Yuh, S. Profeta, Program No. 406 Quantum Chemistry Program Exchange, Indiana University, Bloomington, Ind.
   b. N. L. Allinger *J. Am. Chem. Soc.* **1977** *99*, 8127; N. L. Allinger, S. H. M. Chang, D. H. Glaser, H. Honig *Isr. J. Chem* **1980** *20*, 5.
   c. L. Nørskov-Lauritsen, N. L. Allinger *J. Comput. Chem* **1984** *5*, 326.
   d. S. Profeta, N. L. Allinger *J. Am. Chem. Soc.* **1985** *107*, 1907, and references cited therein.
8. A. J. Kirby, "*The Anomeric Effect and Related Stereoelectronic Effects at Oxygen*"; Springer verlag: Berlin, 1983.
9. P. Deslongchamps, "*Stereoelectronic Effects in Organic Chemistry*"; Wiley; New-York, 1983.
10. W. A. Szarek, D. Horton Eds., "*Anomeric Effect, Origin and Consequences*", ACS Monograph, Washington, D.C., 1979, Vol 87.
11. a. C. Altona, Ph.D. Thesis, University of Leiden, 1964.
    b. C. Romers, C. Altona, H.R. Buys, E. Havinga *Top. Stereochem.* **1969** *4*, 39.
12. S. David, O. Eisenstein, W. J. Hehre, L. Salem, R. Hoffmann *J. Am. Chem. Soc.* **1973** *95*, 3806.
13. A. E. Reed, P. v. R. Schleyer *Inorg. Chem.* **1988** *27*, 3969.
14. G. F. Smits, M. C. Krol, C. Altona *Mol. Phys.* **1988** *65*, 513.
15. G. A. Jeffrey, J. H. Yates *J. Am. Chem. Soc.* **1979** *101*, 820.
16. L. Schäfer, C. Van Alsenoy, J. O. Williams, J. N. Scarsdale *J. Molec. Struct. THEOCHEM* **1981** *76*, 349.
17. J. J. Irwin, Tae-Kyu Ha, J. D. Dunitz *Helv. Chim. Acta* **1990** *73*, 1805.
18. L. Radom, W. J. Hehre, J. A. Pople *J. Am. Chem. Soc.* **1972** *94*, 2371.
19. a. S. Wolfe, M-H Whangbo, D J. Mitchell *Carbohyd. Res.* **1979** *69*, 1.
    b. S. Wolfe, A. Rauk, L. M. Tel, I. G. Csizmadia *J. Chem. Soc. B* **1971**, 136.
    c. S. Wolfe, L. M. Tel, W. J. Haines, M. A. Robb, I. G. Csizmadia *J. Am. Chem. Soc.* **1973** *95*, 4863.
20. J. E. Boggs, M. Altman, F. R. Cordell, Y. Dai *J. Molec. Struct. THEOCHEM* **1983** *94*, 373.
21. a. K. C. Nicolaou, R. E. Dolle, D. P. Papahatjis, J. L. Randall *J. Am. Chem. Soc.* **1984** *106*, 4189.
    b. S. Hashimoto, M. Hayashi, R. Noyori *Tett. Lett.* **1984** *25*, 1379.
    c. M. Kreuzer, J. Thiem *Carbohyd. Res.* **1986** *149*, 347 and references cited therein.
22. I. P. Street, C. R. Armstrong, S. G. Withers *Biochemistry* **1986** *25*, 6021 and references cited therein.

23. I. Tvaroška, T. Bleha, *Advances in Carbohydrate Chemistry and Biochemistry*, vol. **47** p. 45 (1989).
24. a. *Gaussian 90* M. J. Frisch, M. Head-Gordon, G. W. Trucks, J. B. Foresman, H. B. Schlegel, K. Raghavachari, M. A. Robb, J. S. Binkley, C. Gonzalez, D. J. Defrees, D. J. Fox, R. A. Whiteside, R. Seeger, C. F. Melius, J. Baker, R. L. Martin, L. R. Kahn, J. J. P. Stewart, S. Topiol, J. A. Pople. Gaussian, Inc., Pittsburgh PA, 1990.
    b. J. S. Binkley, J. A. Pople, W. J. Hehre *J. Am. Chem. Soc.* **1980** *102*, 939.
    c. P. C. Hariharan, J. A. Pople *Theor. Chim. Acta* **1973** *28*, 213.
25. F. H. Allen, S. Bellard, M. D. Brice, B. A. Cartwright, A. Higgs, T. Hummelink, B. G. Hummelink-Peters, O. Kennard, W. D. S. Motherwell J. R. Rodgers, D. G. Waston *Acta Crystallogr., Sect. B, Struct. Sci.* **1979** *B35*, 2331.
26. V. G. Kothe, P. Luger *Acta. Cryst.* **1979** *B35*, 2079.
27. V. P. Luger, J. Buschmann, H-J Schmidt *Acta. Cryst.* **1982** *B38*, 2732.
28. S. G. Withers, I. P. Street, S. J. Rettig *Can. J. Chem.* **1986** *64*, 232 and references cited therein.
29. M. Imoto, N. Kusunose, Y. Matsuura, S. Kusumoto, T. Shiba *Tetrahedron Lett.* **1987** *28*, 6277.
30. a. J. Nakagawa, M. Hayashi *Chemistry letters* **1976**, 349.
    b. J. Nakagawa, H. Kato, M. Hayashi *J. Molec. Spectroscopy* **1981** *90*, 467.
31. a. M. Hayashi, H. Kato, M. Oyamada *J. Molec. Spectroscopy* **1980** *83*, 408.
    b. M. Hayashi, H. Kato *Bull. Chem. Soc. Jpn.* **1980** *53*, 2701.
32. B. Fuchs, A. Ellencweig *J. Org. Chem.* **1979** *44*, 2274.
33. B. Fuchs, A. Ellencweig *Nouv. J. Chim.* **1979** *3*, 145.
34. L. D. Hall, J. F. Manville *Can. J. Chem.* **1969** *47*, 1.
35. L. D. Hall, J. F. Manville *Can. J. Chem.* **1969** *47*, 19 and refrences cited therein.
36. J. Burdon, I. W. Parsons *Tetrahedron* **1971** *27*, 4553.
37. P. Luger, P. L. Durette, H. Paulsen *Chem. Ber.* **1974** *107*, 2615.
38. D. Kost, M. Raban *J. Am. Chem. Soc.* **1982** *104*, 2960.
39. N. L. Allinger, M. R. Iman, M. R. Frierson, Y. Yuh, L. Schäfer, Mathematics and Computational Concepts in Chemistry, N. Trinajstic, Ed., E. Horwood, Ltd., London, **1986**, p. 8.
40. a. L. Schäfer, C. Van Alsenoy, J. N. Scarsdale *J. Mol. Struct.* **1982** *86*, 349.
    b. W. J. Hehre, J. A. Pople *J. Am. Chem. Soc.* **1970** *92*, 2191.
41. U. Burkert, N. L. Allinger, *"Molecular Mechanics"*, ASC Monograph 177, American Chemical Society, Washington D.C., 1982.
42. W. J. Hehre, L. Radom, P. v. R. Schleyer, J. A. Pople, *"Ab initio Molecular Orbital Theory"*, John Wiley & Sons. New York, **1986**.
43. G. A. Guirgis, H. Nanaie, J. R. Durig *J. Chem. Phys.* **1990** *93*, 3837.
44. M. Hayashi, M. Fujitake *J. Mol. Struct.* **1986** *146*, 9.
45. L. Nygaard *Spectrochemica* Acta **1966** *22*, 1261.
46. P. v. R. Schleyer, A. J. Kos *Tetrahedron* **1983** *39*, 1141.
47. H.-B. Bürgi, K. C. Dubler-Steuble *J. Am. Chem. Soc.* **1988** *110*, 4957.
48. M. M. Rahman, D. M. Lemal *J. Am. Chem. Soc.* **1988** *110*, 1964.