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Anomeric effect in the N–C–F moiety

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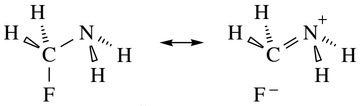
Experimental geometric structures and natural bond orbital (NBO) analyses demonstrate that anomeric effects may play an important role for structural and conformational properties of compounds containing the N–C–F moiety.

The anomeric effect has originally been formulated to rationalise the structures, conformational properties and reactivities of cyclic oxygen-containing carbohydrates, especially, sugars.[1] Such donor-acceptor interactions between electron lone pairs and vicinal σ* orbitals operate equally effectively in acyclic compounds, which contain atoms with lone pairs, such as N, O and F. These interactions have been termed a generalised anomeric effect.[2] Fluoromethylamine, FCH_2NH_2, became the most prominent model compound for theoretical studies and one of the strongest anomeric effects has been predicted for this compound.[3] This effect favours antiperiplanar (ap) orientation of the C–F bond relative to the nitrogen lone pair lp(N). Furthermore, the classic interpretation, which involves a double-bond-no-bond resonance structure (Scheme 1), indicates the expected structural consequences of the anomeric effect: shortening of the N–C bond, lengthening of the C–F bond and an increase of the angles around carbon and nitrogen. The natural bond orbital (NBO) analysis derived by Weinhold and Brunck allows a quantitative description of this effect.[4] The interaction energy between donor and acceptor orbitals is inversely proportional to the energy difference between the two orbitals and proportional to the square of the off-diagonal Fock matrix element. This element behaves similarly to the overlap matrix element. Here, we discuss the anomeric effect lp(N) → σ*(C–F) and its structural consequences in some compounds containing the N–C–F moiety. The experimental bond lengths and conformational properties of these compounds are compared with calculated results (MP2/6-31G*) and the strength of the anomeric effect is derived from NBO analyses. All quantum-chemical calculations were performed with the GAUSSIAN98 program.[5]



Scheme 1

Since the prominent model compound FCH_2NH_2 is unstable and cannot be investigated experimentally, (fluoromethyl)dimethylamine (FCH_2NMe_2) **1**, is considered instead. Gas electron diffraction (GED) results in a single conformer with the ap orientation of the C–F bond (Figure 1).[6] This is in agreement with the calculated potential function for internal rotation around the N–C bond (Figure 2). The second conformer with the C–F bond in the synclinal (sc) orientation is predicted to be higher in energy by 4.8 kcal mol^{-1}, and the barrier to internal rotation to be 10.5 kcal mol^{-1}. The lp(N) → σ*(C–F_{ap}) interaction energy (28.2 kcal mol^{-1}), which is even slightly higher than that in the model compound FCH_2NH_2 (27.1 kcal mol^{-1}), is to a large extent responsible for this high barrier. This interaction energy decreases to zero for a perpendicular orientation of the C–F bond relative to the lone pair [ϕ(lp–N–C–F) = 90°] and increases again to 26.4 kcal mol^{-1} for the sterically unfavourable staggered orientation [ϕ(lp–N–C–F) = 0°]. This anomeric effect also implies a large contribution of the double-bond-no-bond resonance structure, leading to a short bond from nitrogen to the fluorinated carbon atom [N–C_F = 1.408(13) Å] compared to the distance to the methyl group [N–C_{Me} = 1.466(9) Å] and to an extremely long C–F bond of 1.410(5) Å (Table 1). Furthermore, the NCF angle [115.9(24)°] and the mean NCN angle [111.6(11)°] are larger than tetrahedral values expected for *sp*^{3} hybridization.

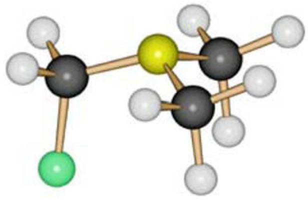


Figure 1 Molecular model for FCH_2NMe_2.

Table 1 Experimental and calculated relevant bond lengths in some fluorinated methylamines and lp(N) → σ*(C–F_{ap}) orbital interaction energies in kcal mol^{-1}.

Parameter	CH_2FNMe_2		CF_3NMe_2		CF_3NF_2	
	GED^{a,b}	MP2^e	GED^{a,c}	MP2^e	GED^{a,d}	MP2^e
N–C_F	1.408(13)	1.412	1.383(16)	1.401	1.476(5)	1.480
N–C_{Me}	1.466(9)	1.460	1.481(10)	1.465		
C–F_{ap}	1.410(5)	1.419	1.351(4)	1.372	1.322(2)	1.330
C–F_{sc}				1.349		1.331
lp(N) → σ*(C–F_{ap})		28.2		27.4		7.6

$^a r_a$ values, experimental error limits are 3σ values. ^{b}Ref. 5. ^{c}Ref. 6. ^{d}Ref. 7. ^{e}6-31G* basis sets.

A similarly strong anomeric effect also occurred in (trifluoromethyl)dimethylamine (CF_3NMe_2) **2**, with a lp(N) → σ*(C–F_{ap}) interaction energy of 27.4 kcal mol^{-1}. In this compound internal rotation around the N–C_F bond is governed by a threefold potential, and the barrier (4.7 kcal mol^{-1}) is much lower than that in the monofluorinated derivative. In addition to the anomeric effect, which shortens the N–C bond and lengthens the C–F_{ap} bond, electrostatic interactions N^-–C^+ and C^+–F^- shorten all bonds around carbon. These interactions are expected to be stronger in the trifluoromethyl compound than in the monofluoromethyl derivative. This is reflected in a shorter N–C_F bond in **2** [1.383(16) Å][7] compared to that in **1** [1.408(13) Å]. In the GED experiment, only a mean value of the C–F bond lengths [1.351(4) Å] could be derived, but quantum-chemical calculations predict the C–F_{ap} bond (1.372 Å) to be longer by more than 0.02 Å than the C–F_{sc} bonds (1.349 Å).

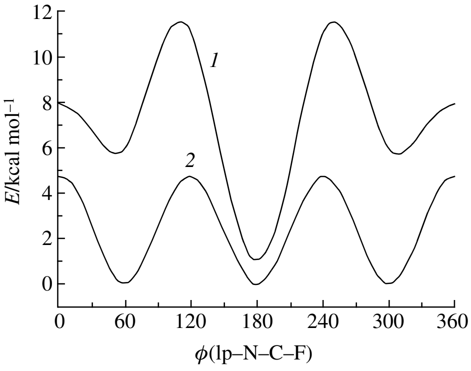


Figure 2 Potential functions to internal rotation around the N–C_F bond in (*1*) FCH_2NMe_2 and (*2*) CF_3NMe_2. (The upper curve is shifted by 1 kcal mol^{-}

Table 2 Experimental and calculated relevant geometric parameters of *trans* and *cis* hexafluoroazomethane and orbital interaction energies in kcal mol^{-1}.

Parameter	*trans*-$CF_3N{=}NCF_3$		*cis*-$CF_3N{=}NCF_3$	
	GED^{a,b}	MP2^{d}	GED^{a,c}	MP2^{d}
N=N	1.235(10)	1.255	1.229(8)	1.254
N–C	1.460(6)	1.469	1.494(5)	1.484
N=N–C	113.4(16)	111.4	122.1(8)	123.7
lp(N) → $\sigma^*(C–F_{ap})$		8.9		
lp(N) → σ^*(N–C)		0.7		18.3

[a] r_a values, experimental error limits are 3σ values. [b] Ref. 10. [c] Ref. 11. [d] 6-31G* basis sets.

A much longer N–C_F bond [1.476(5) Å] and a small mean value for the C–F bonds [1.322(2) Å] were determined for (trifluoromethyl)difluoroamine (CF_3NF_2) **3** in a joint analysis of GED intensities and rotational constants derived from microwave spectra.[8] Quantum-chemical calculations demonstrate that ap and sc oriented C–F bonds possess equal lengths (Table 1). These structural properties suggest that the anomeric effect plays no major role in this compound. This is confirmed by the NBO analysis, which reveals that the effect in this trifluoromethylamine with an interaction energy of only 7.6 kcal mol^{-1}, is much smaller than that in **1** or **2**. Furthermore, the electrostatic interaction in the N–C bond is expected to be slightly repulsive in **3** (N^+–C^+), causing a lengthening of the N–C_F bond. The NBO analysis can rationalise the big change in anomeric interaction between CF_3NMe_2 and CF_3NF_2. The two fluorine atoms bonded to nitrogen contract the lone pair orbital and thus lower its energy. This increases the energy difference between donor and acceptor orbitals from 0.93 a.u. in **2** to 1.21 a.u. in **3** and decreases the value of the Fock matrix element from 0.143 to 0.087 a.u. Both effects lower the interaction energy strongly. Despite the weak anomeric effect in CF_3NF_2, the calculated barrier to internal rotation around the N–C bond (6.4 kcal mol^{-1}) is higher than that in CF_3NMe_2. Long N–C_F bonds have also been observed for CF_3NCl_2 [1.470(6) Å][9] and CF_3NBr_2 [1.481(13) Å].[10]

After discussing anomeric effects in fluorinated methylamines with *sp*^{3}-hybridised nitrogen atoms, we consider orbital interactions in hexafluoroazomethane ($CF_3N{=}NCF_3$), which contains *sp*^{2}-hybridised nitrogen atoms. This compound exists as *trans* and *cis* isomers, which are stable at room temperature. Their molecular structures have been determined by GED (Figure 3) and relevant geometric parameters[11,12] and results of NBO analyses are listed in Table 2. In the *trans* isomer, both CF_3 groups eclipse the N=N bond. This implies that one C–F bond is oriented ap to the nitrogen lone pair, but the lp(N) → $\sigma^*(C–F_{ap})$ interaction energy (8.9 kcal mol^{-1}) is low. Interaction with the two C–F_{sc} bonds is negligible (1.4 kcal mol^{-1}). The consequences of this weak anomeric effect are long N–C bonds [1.460(6) Å] and nearly equal C–F_{ap} and C–F_{sc} bond lengths (not given in Table 2). In the *cis* isomer, which is predicted (MP2) to be higher in energy by 12.6 kcal mol^{-1}, both CF_3 groups nearly stagger the N=N bond with one bond oriented synperiplanar (sp) and two bonds oriented anticlynal (ac) to the lone pair. Nevertheless, the lp(N) → $\sigma^*(C–F_{ac})$ interaction energy (7.0 kcal mol^{-1}) is almost as high as the lp(N) → $\sigma^*(C–F_{ap})$ energy in the *trans* isomer (8.9 kcal mol^{-1}). In addition to this, a strong lp(N) → → σ^*(N–C) anomeric effect between the lone pair and the vicinal N–C bond occurs in the *cis* isomer with an interaction energy of 18.2 kcal mol^{-1}. This effect corresponds to a triple-bond-no-bond resonance structure $N^+{\equiv}N\ C^-$, and shortening of the N=N bond and lengthening of the N–C bond is expected. Indeed, the experimental N=N bond length in the *cis* isomer [1.229(8) Å] is slightly shorter than that in the *trans* form [1.235(10) Å] despite the much larger steric strain in the *cis* form. The experimental N–C bond length shows the expected lengthening from 1.460(6) Å in the *trans* isomer to 1.494(8) Å in the *cis* form. The rather different sizes of anomeric effects in *trans* and *cis* isomers are primarily a consequence of different N=N–C angles, which increase from 113.4(16)° in the *trans* form to 122.1(8)° in the *cis* form. According to NBO analyses, an increase of the bond angle causes a higher *p*-character and a higher energy of the nitrogen lone pair in the *cis* isomer. Additionally, larger Fock matrix elements are calculated for this form.

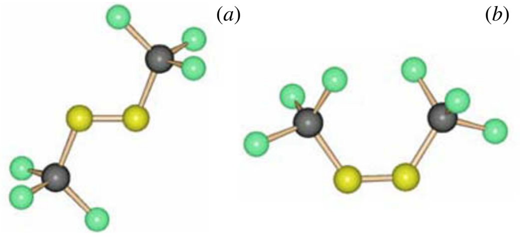


Figure 3 Molecular models for (*a*) *trans* and (*b*) *cis* conformers of $CF_3N{=}NCF_3$.

The above examples demonstrate that experimental structures and conformational properties of compounds containing the N–C–F moiety reflect clearly the influence of anomeric effects. The strength of this effect depends strongly on the energy and shape of the nitrogen lone pair.

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