Effect of fluorination: Conformation of 2,6-difluoroanisole

Yana V. Zarembo [a], Alexander V. Belyakov [a], Frank Trautner [b], Heinz Oberhammer [b],*

[a] *St. Petersburg State Technological Institute, 190013 St. Petersburg, Russia*
[b] *Institut für Physikalische und Theoretische Chemie, Universität Tübingen, 72076 Tübingen, Germany*

Abstract

The geometric structure and conformation of 2,6-difluoroanisole, $2,6\text{-}C_6H_3F_2OCH_3$, has been determined with gas electron diffraction (GED) and quantum chemical calculations (MP2 and B3LYP with 6-311++G(2df,pd) basis sets). The GED intensities have been analyzed with a static as well as with a dynamic model. The static model resulted in a structure with near-perpendicular orientation of the O–CH$_3$ bond with a thermal average dihedral angle $\tau(C2C1-OC) = 70 \pm 3°$. With the dynamic model a perpendicular equilibrium structure and a potential function for internal rotation around the C–O bond with a very flat minimum at $\tau(C2C1-OC) = 90°$ and with a barrier of 1.8 ± 0.6 kcal/mol at $\tau(C2C1-OC) = 0°$ was derived. Quantum chemical calculations predict double-minimum potential functions for the electronic energies, which become single-minimum potentials upon addition of zero-point vibrational energies. The change of conformation from planar in anisole to perpendicular in 2,6-difluoroanisole has been rationalized by orbital interactions between the oxygen electron lone pairs and benzene ring orbitals and by steric repulsion.
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1. Introduction

In a joint project between the electron diffraction laboratories at the Moscow State University, Ivanovo State University, St. Petersburg State Technological Institute and University of Tübingen, the effect of fluorination on the structure and conformational properties of anisole is investigated. In these studies gas electron diffraction (GED), microwave spectroscopy, vibrational spectroscopy and quantum chemical calculations are applied. The conformation of the parent anisole has been discussed controversially in the literature. Photoelectron spectra [1] and dynamic NMR data [2], as well as low-level ab initio calculations (HF approximation) [2–5] result in mixtures of planar and perpendicular conformers. On the other hand, gas electron diffraction [6], microwave spectroscopy [7], and high-level ab initio calculations [8] demonstrate clearly the presence of a single conformer with planar heavy atom skeleton ($\tau(C2C1-OC) = 0°$). This sterically unfavorable conformation has been rationalized by strong conjugation between the p-shaped electron lone pair of

oxygen and the π system of the ring. Fluorination of the methyl group has a strong effect on the conformation of anisole. In trifluoromethoxybenzene (α,α,α-trifluoroanisole) [9,10] and in *p*-fluoro(trifluoromethoxy)benzene ($4,\alpha,\alpha,\alpha$-tetrafluoroanisole) [11] the CF$_3$ group is oriented perpendicular to the plane of the benzene ring ($\tau(C2C1-OC) = 90°$). A small contribution of a planar conformer cannot definitely be excluded. For *o*-fluoro(trifluoromethoxy)benzene ($2,\alpha,\alpha,\alpha$-tetrafluoroanisole) a single conformer with perpendicular orientation has been observed and *m*-fluoro(trifluoromethoxy)benzene ($3,\alpha,\alpha,\alpha$-tetrafluoroanisole) exists primarily as a perpendicular conformer with a possible small contribution of a planar form [12].

The effect of fluorination of the benzene ring on the orientation of the CH$_3$ group depends on the position of fluorination. Fluorination in *para* or *para* and *meta* positions has no effect on the conformation of anisole. Both, 4-fluoroanisole and 3,4-difluoroanisole possess planar structures [13]. 2-Fluoroanisole, however, exists as a mixture of two conformers, planar ($\tau(C2C1-OC) = 180°$) and nonplanar ($\tau(C2C1-OC) = 57(8)°$) [14]. For 2,3,5,6-tetrafluoroanisole a GED study results in a nonplanar structure with $\tau(C2C1-OC) = 67(15)°$, if a static model is used in the analysis. With a dynamic model the best fit of the GED intensities is obtained for a wide single-minimum potential function for internal rotation

around the C1–O bond with its minimum at τ(C2C1–OC) = 90°, corresponding to a perpendicular equilibrium structure. However, the presence of a double minimum potential corresponding to two equivalent near-perpendicular conformers cannot be excluded. Furthermore, the potential barrier for planar orientation (2.7 ± 1.6 kcal/mol) is not well determined [15]. The results of quantum chemical calculations are ambiguous, depending strongly on the chosen method. The HF approximation with 6-311++G(3df,2pd) basis sets reproduce this potential function satisfactorily. The B3LYP method and MP2 approximation with the same basis sets fail to reproduce the experiment. These methods predict double-minimum potentials with non planar orientation of the O–C bond and barriers to internal rotation of 0.5 kcal/mol or less. MP2 calculations with pc-2 basis sets result in a single-minimum potential and a barrier to internal rotation of 0.8 kcal/mol, if zero-point vibrational corrections are included.

The insufficient accuracy of the GED experiment and the discrepancy between the experiment and some quantum chemical calculations, motivated us to study a similar compound with both *ortho* hydrogens substituted by fluorines, 2,6-difluoroanisole. In contrast to 2,3,5,6-tetrafluoroanisole, this compound possesses a higher number of interatomic distances between the methyl group and fluorine atoms depending on the orientation of the CH$_3$ group, relative to C$\cdots$F and F$\cdots$F distances which are independent of the conformation. Therefore, it was expected that the orientation of the O–CH$_3$ group and the shape of the potential function to internal roation can be determined more accurately for this compound. Long-range ^{13}C NMR coupling constants have been interpreted in terms of perpendicular orientation with a barrier to internal rotation of 1.3(3) kcal/mol [16]. Perpendicular orientation has also been concluded from the ^{19}F NMR coupling constant [17].

2. Quantum chemical calculations

Geometry optimizations were performed with the MP2 approximation and B3LYP method using 6-31G(d) and 6-311++G(2df,pd) basis sets. The results for the larger basis sets are listed in Table 1 together with the experimental values. A molecular model with perpendicular orientation of the O–CH$_3$ bond and atom numbering is shown in Fig. 1. The potential function for internal rotation around the C1–O bond was calculated with the same methods and basis sets by structure optimizations at fixed torsional angles in steps of 10° (Fig. 2). All methods result in double-minimum potential functions with a major barrier at planar orientation (τ(C1–O) = 0°) and a small hump at perpendicular orientation (τ(C1–O) = 90°). The predicted barrier at the planar orientation increases with increasing basis sets from 0.30 to 0.61 kcal/mol (B3LYP) and from 1.06 to 1.21 kcal/mol (MP2). On the other hand, the predicted hump at the perpendicular orientation decreases with increasing basis sets from 0.21 to 0.06 kcal/mol (B3LYP) and from 0.12 to 0.03 kcal/mol (MP2). It should be pointed out, that these

Table 1
Experimental and calculated geometric parameters

	GED (r_a)[a] static	GED (r_a/r_{h1})[a,b] dynamic	MP2[c]	B3LYP[c]
(C=C)$_{mean}$	1.390(3), p1	1.395(8), p1	1.391	1.389
(O–C)$_{mean}$	1.396(10), p2	1.391(11)[d]	1.394	1.396
C1=C2	1.395(3)[d]	1.399(8)[d]	1.396	1.396
C2=C3	1.383(3)[d]	1.390(8)[d]	1.384	1.382
C3=C4	1.391(3)[d]	1.396(8)[d]	1.392	1.390
C1–O	1.360(10)[d]	1.334(15), p2	1.358	1.359
O–C7	1.432(10)[d]	1.447(11), p3	1.430	1.433
(C–F)$_{mean}$	1.335(10), p3	1.339(6), p4	1.339	1.345
(C–H)$_{benzene}$	1.089(8), p4	1.092(17), p5	1.082	1.082
(C–H)$_{methyl}$	1.097(8)[d]	1.100(17)[d]	1.090	1.091
C2–C1–C6	116.2(10), p5	116.0(12), p6	116.9	116.4
C1–C2–C3	122.7(7)[d]	122.8(9)[d]	122.5	122.7
C2–C3–C4	119.5(7)[d]	119.4(9)[d]	118.8	118.8
C3–C4–C5	119.3(10), p6	119.6(12)[d]	120.6	120.5
C1–O–C7	115.7(19), p7	117.7(20), p7	112.8	116.2
C1–C2–F1	118.5(7), p8	118.1(7), p8	117.9	118.0
oop(C1–O)[e]	2.8[f]	3.1[f]	2.8	3.7
H–C7–H	109.0(30), p9	109.8[f]	109.8	109.7
Tilt(CH$_3$)[g]	2.8[f]	2.8[f]	2.8	3.0
τ(C1–O), V_2/V_4	70.2(25), p10	90[h], 1.75(55)/0.5	79.0	72.8

[a] Parameters in Å and °. Error limits are 3σ values and refer to the last digit. For atom numbering see Fig. 1.
[b] r_a: bond lengths; r_{h1}: angles.
[c] 6-311++G(2df,pd) basis sets.
[d] Dependent parameter.
[e] Out-of-plane angle between C1–O bond and ring plane.
[f] Not refined.
[g] Tilt angle between C_3 axis of CH$_3$ group and O–C bond direction away from C1.
[h] Equilibrium value.

potential functions include only electronic and nuclear energies. The MP2/6-31G(d) approximation predicts the zero-point vibrational energy (ZPE) at the minimum (τ(C1–O) = 73.3°) to be higher by 0.13 kcal/mol than that at the hump (τ(C1–O) = 90°). Thus, adding these ZPE to the electronic energies, all potential functions, except that derived with the B3LYP/6-31G(d) method, become single-minimum potentials with a flat minimum at τ(C1–O) = 90°. Vibrational amplitudes and corrections were derived from a calculated (MP2/6-31G(d) or B3LYP/6-31G(d)) force field, using the method of Sipachev [18]. All quantum chemical calculations were performed with the Gaussian 03 program set [19].
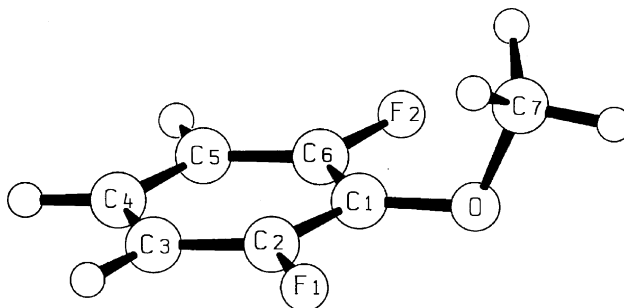

Fig. 1. Molecular model with perpendicular O–CH$_3$ bond and atom numbering.