ELSEVIER

Journal of Molecular Structure 321 (1994) 205–214

Journal of
MOLECULAR
STRUCTURE

The conformation of 2-fluoroethanol – is intramolecular hydrogen bonding important?

Jan M. Bakke*, Leif H. Bjerkeseth, Tor E.C.L. Rønnow, Kjersti Steinsvoll

Organic Chemistry Laboratories, Norwegian Institute of Technology, University of Trondheim, N-7034 Trondheim, Norway

(Received 17 November 1993)

Abstract

The conformations of 2-fluoroethanol (FE) and *trans*-4-*tert*-butyl-*cis*-2-fluorocyclohexanol (**1**) have been investigated by FT-IR and ^{1}H NMR spectroscopy and the methyl ether of **1** (**3**) by ^{13}C NMR spectroscopy. The energies of the conformations of FE, its methyl ether, *cis*-2-fluorocyclohexanol (**4**) and its methyl ether (**5**) were investigated by molecular mechanics (MMPMI) calculations. FE and its methyl ether were investigated by ab initio calculations (MP2/6-31++G**//MP2/6-31++G**). The results were all consistent with a dominance (> 90%) of the gauche rotamer around the CH_2CH_2 fragment in FE. Furthermore, the gauche rotamer around the CH_2OH bond of FE with the hydroxyl proton pointing towards the fluorine atom was also a major component making the conformation Gg′ the most important one. However, from the conformations of the methyl ethers 1-fluoro-2-methoxyethane and **3** it was concluded that an intramolecular hydrogen bond was not important for this dominance. Other interactions, e.g. the repulsive forces between the lone pair electrons of the oxygen atom and the fluorine atom, were found to be more important than a hydrogen bond for the conformational composition around the C–O bond. The rotamer distribution around the CH_2CH_2 bond was found to be the result of the gauche effect.

1. Introduction

The conformation of 2-fluoroethanol (FE) and the question of intramolecular hydrogen bonding in this molecule have been the subject of research activity for a long time [1,2]. The conformation has been studied in the gas phase by electron diffraction [3] and microwave spectroscopy [4]. The results from both techniques indicated the gauche rotamer of the CH_2CH_2 fragment to be the dominant one, and also that the hydroxyl proton pointed towards the fluorine atom, making an internal hydrogen bond possible (conformation Gg′ in Fig. 1). However, both investigations found an $OH \cdots F$ distance close to the sum of the van der Waals radii, indicating only a weak intramolecular hydrogen bond to be present, or none at all.

In the liquid phase, FE has been investigated mainly by IR spectroscopy and particularly in the OH region of the spectrum. In 2-haloethanols, two bands are observed in this sector (Table 1), one for an assumed intramolecular hydrogen-bonded conformer and one at higher frequency for a "free" one. For FE, only one asymmetric band was observed which could be resolved into a low-intensity band at higher frequency and a major one at lower frequency (Table 1). From variable-temperature IR spectroscopy, the relative strength

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* Corresponding author.

0022-2860/94/$07.00
SSDI 0022-2860(93)07968-3

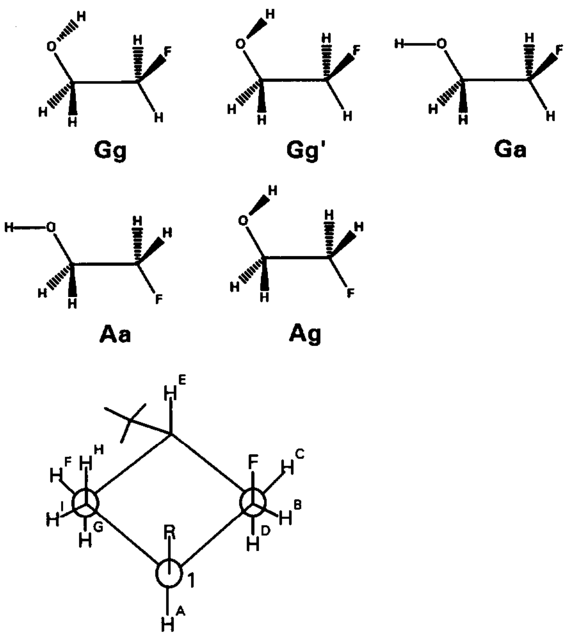


Fig. 1. Conformations of 2-fluoroethanol and a Newman projection of **1** (R = H) and **3** ($R = CH_3$) as seen from the oxygen atom towards C^1. R is in the anti conformation.

of the intramolecular hydrogen bonds was found to be F > Cl ≈ Br > $I\text{-}CH_2CH_2OH$, but the shift in the OH frequency followed the opposite order, contrary to the Badger–Bauer rule [6]. This has also been observed for intermolecular hydrogen bonding to halocyclohexanes [8].

A ^1H NMR investigation of FE in several solvents concluded that the gauche rotamer of the CH_2CH_2 fragment dominated. The spectra were recorded with high-concentration solutions and no $^3J_{CH\text{-}OH}$ coupling constants were reported [9]. Another ^1H NMR investigation of FE in $CDCl_3$ again concluded that the gauche rotamer dominated (> 90%) and also, from a correlation of δ_{OH} with c_{FE}, that intramolecular hydrogen bonding was not important for this dominance [10]. From these investigations, the rotamer composition around the $CH_2\text{–}OH$ bond could not be determined.

An important result had been reported earlier. ^{19}F and ^1H NMR studies of 2-fluoroethyl acetate and trichloroacetate showed that these molecules, with no possibility for intramolecular hydrogen bonding, also adopted the gauche conformation [11]. A photoelectron spectroscopy investigation of 1-fluoro-2-methoxyethane gave an analogous result; the gauche conformation was also the dominant conformation for the methyl ether of FE. The rotamer composition around the $CH_2\text{–}OCH_3$ bond was not available from that study [12].

From a theoretical investigation (ab initio MP2/TZ + P//HF/TZ + P) it was concluded that the Gg′ (Fig. 1) conformation of FE was 1.9 kcal mol^{-1} more stable than the Ga one, indicating the hydrogen bond to be more important for the dominance of the gauche conformation around the C–C bond than the gauche effect which contributed only 0.1 kcal mol^{-1} [13].

Table 1

IR spectroscopic data for 4-*tert*-butyl-2-halocyclohexanols and other relevant alcohols in the OH stretch region. All spectra recorded at $c < 5$ mM in CCl_4 or $CFCl_3$. All frequencies in cm^{-1}

Compound	ν_{high}	ν_{low}	A_{high}/A_{low}	$\Delta\nu$	Ref.
1-OH-eq	3625				5
1-OH-ax	3620				5
1-OH-eq-2-F-ax (**1**)	3595				5
1-OH-eq-2-F-ax (**1**)	3605				This work
1-OH-ax-2-F-ax	3620				5
2-Fluoroethanol	3640	3624	10/90	16	6
2-Fluoroethanol	3638	3621	20/80	17	This work
1-OH-eq-2-Br-ax (**2**)		3550			5
1-OH-eq-2-Br-ax (**2**)	3610	3567	16/84	43	This work
1-OH-ax-2-Br-ax	3620				5
2-Bromoethanol	3632	3593	40/60	39	6
Ethanol	3637	3627	64/36	10	7

There is, therefore, conflicting evidence as to the degree of internal hydrogen bonding in FE and thereby to the importance of the gauche effect [14]. We have used NMR and IR spectroscopy in investigations of other intramolecular hydrogen-bonded compounds and these techniques in combination might give new evidence as to the extent of hydrogen bonding in FE [15].

2. Experimental

The NMR spectra were recorded on a JEOL JNM-EX400 spectrometer. Chemical shifts are reported as ppm from TMS. The IR spectra were recorded on a Nicolet 20 SXC FT-IR spectrometer equipped with a Nicolet 620 Data Station. Overlapping bands were resolved by the FOCAS 2.1 program from Nicolet. The GC analyses were performed on a Carlo Erba 6000 Vega GC equipped with a DB-1 column (J & W Scientific, non-polar). FE and starting materials for the syntheses were commercially available. The high-dilution solutions were prepared in a dry box (N_2). The solvents were kept over molecular sieves and the solutions for IR and NMR were kept over molecular sieves for 24 h in the dry box before use. A capillary with d_6-benzene or d_4-methanol was placed in the NMR tubes for locking purposes.

2.1. Theoretical calculations

Molecular mechanics calculations were performed with the program MMPMI 1.0 [16] on a PC using the default dipole–dipole electrostatic mode. MMPMI consists of MM2 (N.L. Allinger, QCPE Program no. 395) and MMPI (N.L. Allinger, QCPE Program no. 318) as implemented by Serena Software, Bloomington, Indiana, USA. Input files for MMPMI were made by PCMODEL version 1.0 or 4.0 from Serena Software. Input files for the ab initio calculations were made by the same program based on the MMPMI optimized geometries as MOPAC input files. MOPAC 6.00 [17] on a Digital Vaxstation 3100 M38 without geometry optimization was used to transform the MOPAC *Z*-matrixes to GAUSSIAN-style *Z*-matrixes.

Ab initio calculations were performed with GAUSSIAN 90, Revision I [18], on a Cray Y-MP4D/464 using the standard GAUSSIAN 90 basis set 6-31++G** (with a set of 6 d-polarization functions on heavy atoms, a set of p-polarization functions on light atoms, a set of diffuse s- and p-functions on heavy atoms and a set of diffuse s-functions on light atoms) at the restricted MP2 level using direct and in-core methods and more than 40 Mw memory. Geometries were gradient optimized without symmetry restrictions using the Berny optimizer while including both the valence and core orbitals. No correction for zero-point energy was done. Numeric evaluation of MP2 frequencies with this basis would have been too time consuming with GAUSSIAN 90 (no analytical second derivatives for MP2).

2.2. Materials

trans-*4-*tert-*Butyl-2-fluorocyclohexanone*

To 4-*tert*-butyl-1-cyclohexenyl trimethylsilyl ether [19] (0.98 g, 4.3 mmol) in CH_2Cl_2 (distilled from P_2O_5, 10 ml) was added *N*-fluoropyridinium triflate (1.03 g, 4.2 mmol). The mixture was stirred under N_2 at 25°C for 1 h and then refluxed for 2.5 h. To the reaction mixture were added CH_2Cl_2 (50 ml), water (50 ml) and HCl (36%, 1 ml). After thorough mixing, the organic phase was washed with $NaHCO_3$ (5%, 50 ml), water (2×50 ml), dried (Na_2SO_4) and evaporated to yield a mixture of white crystals and a brown oil (1.08 g). The mixture was dissolved in ethyl ether/hexane (1 : 1) and purified by filtering through a 10 cm silica column. The filtrate (0.47 g, 36% *cis*-, 39% *trans*-4-*tert*-butyl-2-fluorocyclohexanone, the trans isomer as the hydrate (see below) and 25% 4-*tert*-butylcyclohexanone from GC analysis) was separated into its components by HPLC chromatography on a 2.12×25 cm Du Pont ZORBAX SIL column, 5% ethyl ether/hexane. The pumping system was Chrompack ISOS and the detector a Chrompack RI detector. From several injections, 92.3 mg of a compound was obtained. IR (KBr): 3366 (s), 2970 (s), 1735 (vw) cm^{-1}. IR (5% $CHCl_3$): 2964(m/s), 1730 cm^{-1}. Only relevant bands are reported. ^1H NMR ($CDCl_3$): 4.66 (d,m, J_d 5, 1 Hz, 1 H), 2.80 (t,t J 12.6, 6.3 Hz 1 H), 2.45–2.35

(m, 2 H), 2.12 (m, 1 H), 1.88 (t,t J 4.2, 12.6 Hz, 1 H), 1.70–1.51 (m, 1 H), 1.50–1.40 (m 1H), 0.91 (s, 9 H).

trans-*4*-tert-*Butyl*-cis-*2-fluorocyclohexanol* (**1**)

The hydrate of *trans*-4-*tert*-butyl-2-fluorocyclohexanone (92.3 mg, 0.49 mmol) was dissolved in methanol (10 ml) and $NaBH_4$ (67.7 mg, 1.8 mmol) was added. After stirring at room temperature for 1 h, the reaction was refluxed for 4 h, cooled and ethyl ether (30 ml) and water (30 ml) added. After separation, the water phase was extracted once with ethyl ether (30 ml), the combined organic phase washed with water (4 x 20 ml), dried (Na_2SO_4) and evaporated to yield yellow/white crystals (86.8 mg). GC indicated two products (min (% relative areas)): 5.4 (81), 5.8 (19). By crystallization (hexane) and sublimation of the crystals, 10.8 mg was obtained of a compound with > 99% of the GC area, m.p. 76.4–76.7°C, litt. 76.5°C [5]. For ^{1}H NMR data, see Table 2.

trans-*4*-tert-*Butyl*-cis-*2-fluoro-1-cyclohexyl methyl ether* (**3**)

To a solution of **1** (5 mg) in dry THF (5 ml) cooled to 0°C were added methyl iodide (0.1 ml) and NaH (5 mg). The reaction was left at 5°C for three days and worked up as described for **1**, yield 3 mg of an oil which contained 83% (GC, area %) of **3**. ^{1}H NMR data are given in Table 2. GC/MS of the reaction product (HP 5985A, 25 m BP-1 fused silica column) gave m/z 188 (0.7%), 168 (0.7%), 132 (11.5%), 131 (10%), 71 (100%) for the peak with 83% of the area. ^{13}C (J_{C-F}) {^{1}H}: 88.79 (C^2, 172.8 Hz), 79.98 (C^1, 18.40 Hz), 56.08 (CH_3–O, $^3J_{C\text{-}O\text{-}C\text{-}H^A} = 4.0 \pm 0.2$ Hz, $^1J_{C-H} = 140.9 \pm 0.1$ Hz, from a gated decoupling experiment), 40.37 (C^4), 30.93 (C^3, 20.18 Hz), 27.42 ($(CH_3)_3C$), 25.59 (C^6, 3.71 Hz), 24.84 (C^5).

cis- *and* trans-*2-Bromo-4*-tert-*butylcyclohexanone*

Bromination of 4-*tert*-butylcyclohexanone by the method of Bedoukian [20] gave a 5 : 1 mixture of *trans*-:*cis*-2-bromo-4-*tert*-butylcyclohexanone from which the *trans* isomer was separated by preparative HPLC (see above).

cis-*2-Bromo*-trans-*4*-tert-*butylcyclohexanol* (**2**)

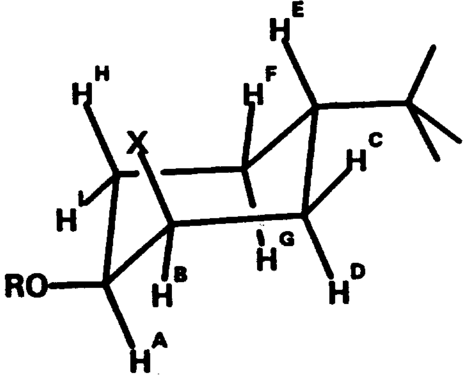
This was made by $NaBH_4$ reduction of the bromoketone. The product had the same physical characteristics as those reported in ref. 5. ^{1}H NMR data are given in Table 2.

3. Results and discussion

One of the problems in the determination of the conformational composition of FE is the rotamer composition around the C–OH bond. ^{1}H NMR spectroscopy of alcohols at high dilution in non-polar solvents gives information on this from the $^3J_{CH\text{-}OH}$ coupling constant. In FE, however, the equivalence of the $^3J_{CH\text{-}OH}$ coupling constant for the Gg and Gg′ conformers (Fig. 1) makes it impossible to estimate the relative proportions of these two from the ^{1}H NMR spectra. If, however, the gauche F–C–C–O fragment of FE was built into a conformationally stable and unstrained system it would be possible to obtain a unique coupling constant for the CH–OH rotamer which had a possibility for intramolecular hydrogen bonding. These conditions would be fulfilled if the fluorine atom occupied an axial position and the hydroxyl group an equatorial one in a conformationally locked cyclohexane system. In this configuration, the conformation with the hydroxyl hydrogen pointing towards the fluorine atom would have a dihedral angle for H–O–C–H^A (Fig. 1) of about 180° with a ^3J of about 12 Hz, and the other two rotamers would have dihedral angles of +60° and −60° with a ^3J of about 2 Hz [15]. Such systems have been studied by IR and CW NMR spectroscopy. However, the ^{1}H NMR spectra were obtained at concentrations where intermolecular hydrogen bonds were important [5,21]. The C–OH rotamer composition under conditions where weak intramolecular hydrogen bonds would be important is therefore not known.

We have synthesized *trans*-4-*tert*-butyl-*cis*-2-fluorocyclohexanol (**1**) by a three-step route, applying preparative HPLC to separate the stereoisomers at each stage. We preferred this procedure to the eleven-step stereospecific route already reported [5]. For the preparation of **1** we used the electrophilic 1-fluoropyridinium

Table 2
^1H NMR data for the cyclohexyl derivatives **1**, **2** and **3**. Shifts downfield from TMS in ppm; coupling constants in Hz[a]



Compound	Proton								
	A	B	C	D	E	F	G	H	I
R = H X = F $CFCl_3$ (**1**)	3.35 d,m 29.9 (H,F)	4.71 brd. d 51.4 (H,F)	2.11 m	1.25 d,d,d 44.4 (H,F) 13.1 2.1	1.36 t,t 12.5 3.2	1.78 d,quint. 13.2 3.2	1.01 d,quart. 2.1 13.1	1.48 d,quart. 3.3 13.2	1.84 m
R = H X = Br $CDCl_3$ (**2**)	3.33 t,t 3.5 11.2	4.76 m	2.23 d,t 12.3 3.1	1.6–1.7 m	1.7 m	1.8 m	1.10 d,quart. 4.3 12.8	1.6–1.7 m	1.8 m
R = CH_3 X = F $CDCl_3$ (**3**)	3.08 d,d,d,d 29.1 (H,F) 11.8 ± 0.1 4.8 ± 0.1 2.2 ± 0.1	4.95 d,quart. 51.5 (H,F) 2.0 ± 0.2	2.13 m	1.20 d,t,d 43.6 (H,F) 12.8 ± 0.05 2.1 ± 0.1	1.47 t,t 12.6 ± 0.2 3.3 ± 0.2	1.84 d,quint. 13.2 ± 0.1 3.2 ± 0.1	1.04 m	1.64 d,quart. 3.6 12.4	1.92 m

[a] d, doublet; t, triplet; m, multiplet; quart., quartet; quint., quintet.

triflate as fluorinating reagent. This is reported to react with enol acetates, enol ethers and enol silyl ethers [22]. We tried the reaction with all three derivatives of 4-*tert*-butylcyclohexanone, but only the silyl ether gave the desired result. From the vicinal coupling constants of **1** and its methyl ether (**3**) (Table 2), it was apparent that **1** and **3** had a chair conformation of the cyclohexane ring and also had the fluorine atom in an axial position and the hydroxyl/methoxyl group in an equatorial one. We therefore have a model for the gauche CH_2CH_2 rotamer of FE (i.e. Gg, Gg′ and Ga).

3.1. ^1H NMR spectroscopy

In Table 3, the ^1H NMR data for the CH–OH fragments of **1** and FE are given together with the CH_2CH_2 vicinal coupling constant for FE. For FE the rotational composition around the CH_2CH_2 fragment can be calculated by use of the average ^3J for the gauche and anti conformations of the

Table 3
^1H NMR data for *trans*-4-*tert*-butyl-*cis*-2-fluorocyclohexanol (1) and 2-fluoroethanol. All spectra recorded at $c < 5$ mM in $CFCl_3$ or CCl_4

Compound	δ_{OH} (ppm)	$^3J_{CH\text{-}OH}$ (Hz)
(1)	1.37	11.7 (5)
2-Fluoroethanol	1.45[a]	6.69 (2)

[a] $^3J_{CH\text{-}OH} = 4.24(5)$ Hz.

F–CH_2–CH_2–O fragment of 2-fluoroethyl trichloroacetate [11]. From these values and the observed coupling constant, a rotational composition around the C–C bond of 93% of the gauche rotamer was obtained, in agreement with earlier reports [1–4,9,10]. From $^3J_{anti} = 12$ Hz and $^3J_{gauche} = 2$ Hz for $^3J_{CH\text{-}OH}$ [15,23] and the observed coupling constant, a rotational composition of 94% gauche and 6% anti around the CH–OH bond in FE was obtained. From these results it was clear that the two conformations Gg and/or Gg′ were the major ones for FE in solution at high dilution. It was, however, not possible to discriminate between Gg and Gg′ due to their equivalence in $^3J_{CH\text{-}OH}$.

This ambiguity was removed in **1**. The observed value for $^3J_{CH\text{-}OH}$ (11.7 ± 0.5 Hz, Table 3) showed that the anti rotamer with the hydroxyl proton pointing towards the fluorine atom, that is, the dihedral angle H–O–C–$H^A \approx 180°$ (Fig. 1), was the dominant one (97%). As the F–C–C–O fragment in **1** was locked into the conformation equivalent to the gauche rotamer of FE, the F–C–C–O–H fragment of **1** was in the equivalent conformation of Gg′ for FE (Fig. 1). As Gg and/or Gg′ was dominant in FE (from ^1H NMR), it therefore follows that of these two, the Gg′ conformation with the hydroxyl proton near the fluorine atom was dominant (> 90%) in FE at low concentration in non-polar solvents. This is in accordance with the ED and MW results in the gas phase [3,4].

To obtain information on the energies of the conformations of FE, we performed a variable-temperature ^1H NMR study. Owing to the relatively small variations in the vicinal couplings for both the CH_2–CH_2 and the CH_2–OH fragments, the precision of the measurements was low: for CH_2CH_2, $\Delta H = -0.97 \pm 0.16$ kcal mol^{-1}, $\Delta S = 1.9 \pm 0.6$ e.u. ($K = c_{gauche}/c_{anti}$); for CH_2OH, $\Delta H = -1.72 \pm 0.47$ kcal mol^{-1}, $\Delta S = -0.5 \pm 1.6$ e.u. ($K = c_{gauche}/c_{anti}$). The entropies were small and, with the large uncertainties, insignificant. The precision of the enthalpies was better and the sum of the two was within the limits of error of the value reported from an IR spectroscopy investigation ($\Delta H = -2.07 \pm 0.53$ kcal mol^{-1}, $\Delta S = -3.6$ e.u. for $K = [OH]_{bonded}/[OH]_{free}$) [6]. Our results showed that the conformational change took place by rotations of both the C–OH bond and the CH_2CH_2 bond. The result from the variable-temperature IR study therefore included the energy of both these rotations and not only the formation of the gauche rotamer around the C–O bond (assumed stabilized by a hydrogen bond).

The dominant Gg′ conformation of FE has a possibility of intramolecular hydrogen bonding. However, the question of the importance of such a bond for the conformational composition remains to be answered. We have earlier argued for the view that in certain molecules there will be a repulsive force between the lone pair electrons of the hydroxyl oxygen and the hydrogen bond acceptor, especially for certain olefinic and benzylic alcohols [24]. This might also be the case for FE and for **1**. A repulsion between the lone pair electrons of the oxygen atom and the electronegative fluorine atom would turn the lone pair electrons away from the fluorine atom and at the same time move the hydroxyl proton towards it. A dominance of a rotamer with the hydroxyl hydrogen pointing towards a hydrogen acceptor may therefore not always be caused by an intramolecular hydrogen bond.

We have used several techniques to assess these two effects, namely IR spectroscopy of the hydroxyl group at high dilution in non-polar solvents, theoretical calculations and determination of the rotamer composition of the methyl ether of the alcohol [24,25]. In the latter case, no hydrogen bonding is possible and only the repulsive forces remain.

3.2. *IR spectroscopy*

In Table 1, the IR data for FE and a series of related compounds are given. FE showed two overlapping bands in the OH stretch region, at 3621 cm^{-1} (80%) and 3638 cm^{-1} (20%) with $\Delta\nu$ of 17 cm^{-1}. For 2-bromoethanol this figure was 39 cm^{-1} and for ethanol 10 cm^{-1}. The results from ^{1}H NMR spectroscopy showed the Gg′ conformation to be the major one for FE. Accordingly, we assigned the major band at 3621 cm^{-1} to this conformation. In Table 1 there are also data for analogues of 2-bromo- and 2-fluoroethanol together with the unsubstituted alcohols. In all cases, the bromine-substituted alcohols with a possibility for intramolecular hydrogen bonding showed a large $\Delta\nu$ compared to the unsubstituted ones. The corresponding fluorine-substituted ones showed only small shifts.

In many cases there is a linear relationship between the enthalpy of a hydrogen bond and the shift towards lower frequency for the hydroxyl band in the IR spectrum, the Badger–Bauer rule. It has been reported, however, that there is an inverse relationship for the 2-haloethanols [6,8]. However, from the study of 2-halophenols it was argued that the reported enthalpies contained both the attractive force of the hydrogen bond and the repulsive force between the lone pairs and the halogen atoms [26]. The results from the variable-temperature ^{1}H NMR study of FE showed that the measured energies by variable-temperature IR spectroscopy included both the gauche effect and the energy of the rotation around the CH$_2$–OH bond. The Badger–Bauer rule may, therefore, apply for the 2-haloethanols and, accordingly, the small observed shift for FE would indicate only a weak intramolecular hydrogen bond for this compound.

3.3. Conformation of the methyl ether of the alcohol 1

In the methyl ether of **1** (**3**), the possibility of a hydrogen bond to the fluorine atom is removed, but any repulsive forces between the oxygen lone pair electrons and the fluorine atom will still be present. A determination of the rotamer composition around the $CH_3O{-}CH^A$ bond would therefore give an indication of the importance of these forces. The conformation of **3** corresponding to the "hydrogen-bonded" conformer of **1** would have $H^A{-}C{-}O{-}CH_3 \approx 180°$ (the anti rotamer). From inspection of space filling models it was evident that this rotamer was considerably more sterically crowded than the corresponding conformation of the alcohol **1**. This was confirmed by MMPMI [16] calculations on *cis*-2-fluorocyclohexanol (**4**) and its methyl ether **5**. The calculations were performed with the hydroxyl/methoxyl groups in the equatorial and the fluorine atom in the axial positions. The results are given in Table 4. The anti rotamer of **5** ($CH_3{-}O{-}C{-}H = 180°$) had a steric energy 1.8 kcal mol^{-1} higher than the one with the angle close to −60°. Of this, 1.5 kcal mol^{-1} was an increase in the bending energy located to the CH$_3$–O–CH system. For *cis*-2-fluorocyclohexanol (**4**) in the same conformation, the MMPMI calculation indicated the "bonded" rotamer ($H{-}O{-}C{-}H \approx 180°$) to be lowest in energy with the bending energy equal for all three conformations (Table 4). From these results, one would expect the anti rotamer of the methyl ether **3** to have a very low population. Any appreciable population of this rotamer would therefore

Table 4

Relative steric energies (kcal mol^{-1}) and rotational composition (%) of 2-ax-fluoro-1-eq-cyclohexanol (**4**) and 2-ax-fluoro-1-eq-methoxycyclohexane (**5**) from MMPMI calculations and experimental rotational composition (%) of the corresponding alcohol **1** and methyl ether **3**

Dihedral angle H–O–C–H or H$_3$C–O–C–H (deg)	**4** (MMPMI)	**1** (NMR)	**5** (MMPMI)	**3** (NMR)
60	1.69 (4)	(3)	0.53 (28)	(62)
−60	0.86 (18)		0.00 (68)	
180	0.00 (78)	(97)	1.79 (3)	(38)

Table 5
Relative energies (kcal mol^{-1}) and conformational composition (%), for 2-fluoroethanol and 1-fluoro-2-methoxyethane from calculations (MMPMI [16] and ab initio [18], MP2/6-31++G**//MP2/6-31++G**)

Conformation	2-Fluoroethanol		1-Fluoro-2-methoxyethane	
	Ab initio	MMPMI	Ab initio	MMPMI
Gg	3.03 (1)	2.14 (2)	1.61 (3)	2.52 (1)
Gg′	0.00 (95)[a]	0.00 (64)	0.21 (30)	1.36 (7)
Ga	2.37 (2)	0.63 (22)	0.01 (42)	0.00 (67)
Aa	2.25 (1)	0.64 (11)	0.00 (22)[b]	0.19 (24)
Ag	2.56 (1)	2.03 (2)	1.58 (3)	2.47 (1)

[a] The zero of energy was −253.618 583 8 Hartrees.
[b] The zero of energy was −292.789 378 9 Hartrees.

strongly suggest that the repulsive forces discussed above were indeed important for the rotamer composition around the C–O bond of the methyl ether **3**, of the alcohol **1** and by implication, of FE itself.

The rotamer composition of **3** was assessed by the $^{3}J_{\mathrm{C-O-C-H}}$A coupling constant. This was obtained from a ^{13}C NMR spectrum recorded under gated decoupling conditions and was found to be 4.0 ± 0.2 Hz. We have earlier used the values 8–9 Hz for the anti rotamer and 1–1.5 Hz for the gauche rotamer for the $^{3}J_{\mathrm{C-H}}$ coupling constant [25]. From these figures a rotational composition around the $\mathrm{CH_3O{-}CH^A}$ bond of about 40% anti (corresponding to Gg′ for the methyl ether of FE) and about 60% gauche was obtained (Table 4), close to the statistical distribution around the $\mathrm{C_1{-}O}$ bond. There is therefore no appreciable energy difference between the anti and the two gauche rotamers of the methyl ether **3**. However, the MMPMI calculations on **5** indicated the anti rotamer to be 1.5 kcal mol^{-1} higher in bending energy than the two gauche rotamers. To obtain an equal population of all three rotamers, this repulsion must have been counteracted, e.g. by repulsion between the oxygen lone pair electrons and the fluorine atom. This repulsion

Table 6
Ab initio MP2/6-31++G** geometries for FE and its methyl ether[a]

Conformer	F–C–C–O (deg)	C–C–O–H (deg)	O–H (Å)	$\mathrm{CH_2{-}O}$ (Å)	$\mathrm{CH_3{-}O}$ (Å)	C–O–H (deg)	F···H(O) (Å)
2-Fluoroethanol (FE)							
Gg	64.5	62.5	0.965	1.422		108.90	
Gg′	63.3	−59.3	0.967	1.423		107.38	2.46
Ga	72.3	−162.7	0.964	1.425		109.03	
Aa	180.0	180.0	0.964	1.429		108.89	
Ag	181.2	−75.9	0.965	1.428		108.79	
1-Fluoro-2-methoxyethane							
Gg	64.4	73.8		1.417	1.421		
Gg′	74.8	−79.8		1.417	1.428		
Ga	72.1	−174.3		1.415	1.420		
Aa	−179.9	180.0		1.418	1.421		
Ag	179.1	−88.6		1.423	1.424		

[a] Detailed geometries are available from the authors by request.

must have been of the order of 1 kcal mol^{-1}. Therefore, the dominance of the anti rotamer for the alcohol **1** was not caused by a hydrogen bond alone but to a significant extent by this repulsion.

3.4. *Ab initio calculations*

The rotational composition around the CH_3O–CH_2 bond of 1-fluoro-2-methoxyethane was not available from NMR spectroscopy due to the spectroscopic equivalence of the conformations corresponding to Gg and Gg′ as discussed for FE. We have therefore performed ab initio calculations on FE and 1-fluoro-2-methoxyethane at the MP2/6-31++G**//MP2/6-31++G** level and basis.

For 1-fluoro-2-methoxyethane, the ab initio calculations (Tables 5 and 6) indicated the gauche CH_2CH_2 conformations to be the important ones (75%) and thereby showed the gauche effect [14] to be more important for the conformation around the CH_2–CH_2 bond than an intramolecular hydrogen bond. Furthermore, the ab initio calculations indicated the conformation corresponding to the Gg′ of FE to be populated to 30% despite the obvious steric crowding of this conformation. This was in contrast to the result from a molecular mechanics calculation (MMPMI, Table 5) which gave conformation Gg′ of 1-fluoro-2-methoxyethane at 1.36 kcal mol^{-1} higher energy (7% populated) than the Ga conformation.

FE geometry has not been optimized at the MP2 level before. The results for FE (Tables 5 and 6) were close to those reported by ab initio [13], ED [3] and MW [4] studies and were also close to our results from the NMR experiments (95% Gg′). The O–H bond length was about 0.002 Å longer and the angle C–O–H about 1.5° smaller for Gg′ than for the other conformers. The same tendencies were observed in the earlier ab initio work [13]. The F · H · O angle in the Gg′ conformation was calculated to be 102.6° and the F · HO distance to be 2.46 Å. In earlier work, this distance was found to be 2.52 Å (ab initio [13]), 2.49 Å (ED [3]) and 2.42 Å (MW [4]). This is close to the sum of the van der Waals radii for hydrogen and fluorine [3,4] and an intramolecular hydrogen bond, if present, must be weak.

From a comparison of the energies of the two conformations Ga and Gg′ of FE by ab initio calculations it was concluded that the intramolecular hydrogen bond was important for the stabilization of the conformation Gg′ [13]. However, other reasons for the stabilization of this conformation, e.g. repulsion, were not discussed. From the results of the present investigation, these effects cannot be ignored.

4. Conclusions

All investigations, experimental and theoretical, agree that in the dominant conformation of FE, the hydroxyl group and the fluorine atom were gauche to each other [1–4,6,9,10,13]. The present investigation has shown that in non-polar solvents at high dilution the hydroxyl hydrogen was directed towards the fluorine atom (conformation Gg′ dominant, > 90%). We have assessed the importance of hydrogen bonding for this dominance.

The results from the photoelectron spectroscopy investigation of 1-fluoro-2-methoxyethane [12], the NMR investigation of 2-fluoroethyl acetate and trichloroacetate [11] and the ab initio calculations on 1-fluoro-2-methoxyethane in this work all show that the gauche rotamer around the CH_2–CH_2 bond is dominant for these compounds as well. This means that it is not necessary to invoke an intramolecular hydrogen bond to explain the dominance of this rotamer in FE, but rather that the dominance was caused by the gauche effect [14]. Furthermore, both the results from the NMR investigation of the methyl ether **3** and the ab initio calculations on 1-fluoro-2-methoxyethane showed that the existence of a hydrogen bond was not necessary to explain the rotational composition around the C–O bond. Instead, other interactions such as the repulsion between the lone pair electrons of the hydroxyl oxygen and the fluorine atom were important for this composition. These points, together with the rather long OH–F distance found in both experimental [3,4] and theoretical investigations (this work and ref. 13), show that a hydrogen bond would be so weak that it could not be important for the conformational composition of FE or its analogues such as **1**.

This conclusion also has a consequence for the interpretation of the IR spectrum of FE. With a weak intramolecular hydrogen bond in FE, the small frequency shift between the two bands in the OH region is in accordance with the Badger–Bauer rule.

5. Acknowledgements

This work was supported by the Norwegian Research Council for Science and the Humanities who also supported the use of the Cray Y-MP4D/464 in Trondheim.

6. References

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