The intramolecular C-F hydrogen bond of 2-fluorophenyldiphenylmethanol

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doi: 10.1039/b902203a(http://dx.doi.org/10.1039/b902203a)
The intramolecular C–F···HO hydrogen bond of 2-fluorophenyldiphenylmethanol†

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Received (in Gainesville, FL, USA) 3rd February 2009, Accepted 25th August 2009
First published as an Advance Article on the web 7th September 2009
DOI: 10.1039/b902203a

The intramolecular C–F···HO hydrogen bond of 2-fluorophenyldiphenylmethanol was observed by X-ray crystallographic analysis and NMR spectroscopy. The features of the spectra were compared to triphenylmethanol (a fluorine-free analog) and 2-fluorophenyldiphenylmethane.

In a previous report, we discussed the C–F···HO hydrogen bond of 9-fluoro-18-hydroxy[3.3]metacyclophane,1 and its stabilization energy was estimated to be 0.84–3.7 kJ mol−1.

C–F···HO or C–F···HN hydrogen bonds occur very rarely because they are weak,2 and other stronger interactions predominate under typical circumstances. However, several attempts have continued in order to observe and estimate these hydrogen bonds under particular conditions (mainly in the gas phase) using various modern spectroscopic methods or ab initio calculations.3 In both solution and the solid phase, there are controversies about the existence of this hydrogen bond. Shimonoi and Glusker concluded that “C–F···H–X (X = C, N, O) interactions cannot be ignored in predictions of modes of molecular packing in complexes and in crystals” based on crystallographic analyses and a CSD (Cambridge Structural Database) database analysis.4 On the contrary, Dunitz and Taylor took a negative view about the interaction after their analysis of the CSD.5 In a recent study, Hulliger et al. pointed out that X···H···F contacts are caused not only by hydrogen bonds but also by crystal packing, and that the number of O···H···F and N···H···F contacts is significantly lower because O···H and N···H act rather as proton acceptors than proton donors.6 Another group, however, support the positive role of the F atom in crystal engineering.7 In bio-organic chemistry, the isosteric and isoelectronic nature of the F atom to the OH group were noted, and Hagan and Rzepa mentioned that the F atom is an OH mimic hydrogen bond acceptor in desolvated enzyme cavities, although rare.8 However, there are a few observations of O···H···F and N···H···F interactions in solution. Recently, experimental O···H···F evidence by Strauss et al.9 was denied by Esninet et al.10 On the other hand, N···H···F hydrogen bonding-driven foldamers were found by Li et al.11 Other examples have been found by our group1 and by Vasella et al. (described below).12 In such a situation, the role of the C–F···HO hydrogen bond is somewhat subtle, and thus we must accumulate examples. In our opinion, because the interaction is very weak, the C–F···HO hydrogen bond is influenced by the subtle conditions of molecular structure; in some cases being visible and in others invisible.

The aim of this study is to observe a C–F···HO interaction by some of the most common and familiar tools to organic chemists, X-ray crystallographic analysis, and NMR and IR spectroscopy. For this purpose, the molecular design of the target molecule becomes very important. Similar approaches were attempted by Vasella et al. using fluorinated saccharides, and they succeeded in observing the C–F···HO hydrogen bond by 1H NMR and IR spectroscopy.12 However, their X-ray crystallographic analyses revealed that the OH proton in each compound was not directed toward the F atom.

In our current approach to detect such a weak hydrogen bond, we chose 2-fluorophenyldiphenylmethanol (1)13 as a touchstone because it is a simple molecule and its reference compound analogues are accessible. Furthermore, as shown in Fig. 1, the F and H(O) atoms of 1 would form a six-membered ring through C–C bonds. This is very important and a preferable condition for the formation of a hydrogen bond. Triphenylmethanol (2) and 2-fluorophenyldiphenylmethane (3) were used as reference compounds, and were purchased or prepared according to the literature.14,15 A single crystal of 1 suitable for an X-ray crystallographic analysis was obtained from n-hexane, and its molecular structure is shown in Fig. 2. An analysis shows that H(15) and F are adjacent to each other and that the distance between them (223 pm) is much shorter than the sum of the van der Waals radii of the two atoms (267 pm), although rotating C–OH and C(OH)–Ar bonds is very easy. In this report, the values of the van der Waals radii used are those reported by Bondi.16 The O(1)–F distance (283 pm) is also shorter than the sum of the van der Waals radii of the F (147 pm) and O (152 pm) atoms. Accordingly, these values are definitive evidence of a C–F···HO hydrogen bond in 1. The F···H–O angle is somewhat acute (118.7 °) for a hydrogen bond, but this is due to the very nature of the molecular structure.

On the contrary, four molecules of 2 form an intermolecularly hydrogen-bonded tetrahedron with each four OH groups.17 This is a distinct difference between 1 and 2 caused by the presence of the F atom at an appropriate position.
In addition to the crystallographic information, the hydrogen bond was also observed in solution. In the $^1$H NMR spectra, the OH signal of 1 appeared as a doublet ($^2J_{HF} = 9.2$ Hz) at 3.51 ppm in CD$_2$Cl$_2$ (1 × 10$^{-2}$ mol dm$^{-3}$). The coupling constant was too large for long-range coupling through five bonds, because the OH signal of 2-fluorobenzyl alcohol (when considered to be a partial structure of 1) appears as a singlet at 2.8 ppm. Bernet and Vasella have described that the OH signal of 2-fluorobenzyl alcohol appeared in a rather lower field region (3.51 ppm; 2-fluorobenzyl alcohol, 3.88 ppm), together with the spin coupling, ten times larger than O–H rotation ($\sim$ 470 J mol$^{-1}$). However, the spin coupling between the OH and F atoms in this strain-free system is definitive evidence of a redistribution of electrons between the OH and F orbitals. Therefore, the electrostatic term in this hydrogen bond should be evaluated too. Furthermore, the proximity of the F and H atoms is also evidence of a bond, because molecule 1 has no steric crowding and the rotation of each bond is free. If there is no interaction between F and HO, compound 1 would form an intramolecular OH⋯OH hydrogen bond, just as for 2.

Therefore, the observed phenomena in this report appropriately indicate the presence of C–F⋯HO hydrogen bond.

In conclusion, another example of a C–F⋯HO hydrogen bond system has been confirmed by crystallographic analysis and $^1$H NMR spectroscopy. As mentioned above, the C–F⋯HO hydrogen bond is very weak; thus, careful molecular design is very important in order to observe the interaction using the typical techniques available to organic chemists.

This work was supported by a Grant-in-Aid for Scientific Research (no. 19550052) from the Japan Society for the Promotion of Science (JSPS).
Experimental

Melting points: Yanaco MP-500D apparatus in Ar sealed tubes; values are uncorrected.

NMR: JEOL AL-300 (300.4 MHz for 1H, 75.6 MHz for 13C) and 283.0 MHz for 19F, with TMS and CFCl3 as internal references, respectively.

IR: JASCO IR-FT/IR 4200 (CCl4, in NaCl cells (0.1 and 0.5 mm) at 25 °C).

FAB MS: JEOL JMS-SX/SX102A.

Elemental analysis: the Service Centre of the Elementary Analysis of Organic Compounds affiliated with the Faculty of Science, Kyushu University.

Crystallography was performed using the YAMAZEN YFLC-254-GR1I medium-pressure liquid chromatography system.

2-Fluorophenylidiphenylmethanol (1)

This compound was obtained by the reaction of methyl 2-fluorobenzoate and phenyl magnesium iodide, and its physical and spectral properties were consistent with those in the literature.13

2-Fluorophenylidiphenylmethane (3)

This compound was prepared by the reduction of 1 by Et3SiH in CH2Cl2.14 Compound 1 (100.2 mg, 0.36 mmol) was dissolved in 1.8 mL of AcOH, and 0.4 mL of Et3SiH was added. The mixture was heated under reflux for 40 h. The mixture was then evaporated in vacuo and the resultant brown oil was chromatographed on silica gel using hexane–CH2Cl2 (50 : 50 volume) as the eluent. Colorless crystals, 28.0 mg (29.6%), m.p. 84.3–84.7 °C, Rf = 0.45 (n-hexane), size 0.53 × 0.37 mm, monoclinic, space group C2/c. The mixture was heated under reflux for 40 h. The mixture

r = 2.83 × 10−10 m. From these data, we obtained E ≈ 5.6 kJ mol−1. The resultant energy is close to our previously reported value, and thus it is shown that the interaction is reproducible by simple estimation of the dipole–dipole interaction. Furthermore, the rotational energy of the O–H group was estimated to be 467 J (E = h2/8π2I J2 + 1, I = m × r2 × cos 14.5° (CH2OC ≈ 90°)). Thus, the dipole–dipole interaction is enough to stop the OH rotation.

References

† Based on the crystallographic analysis data, the dipole–dipole interaction energy of the O–H and C–F groups in compound 1 was roughly estimated (Fig. 3). Here, θ1 = 70.3°, θ2 = 109.1°, φ = 9.7°, μ1 = 4.7 × 10−30 C m, μ2 = 5.0 × 10−30 C m, ε0 = 8.85 × 10−12 C2 J−1 m−1 and

20 An example in which the reduction of JC= and a high field shift of the 19F NMR signal by a hydrogen bond was found in recent research: H. Takemura, R. Ueda and T. Iwanaga, J. Fluorine Chem., 2009, 130, 684–688.