Influence of Fluorine Atoms and Aromatic Rings on the Acidity of Ethanol

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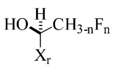
Absolute gas-phase acidities $\Delta_{acid}G^0$(OH) and $\Delta_{acid}G^0$(CH) were calculated at the B3LYP and MP2 levels using six different standard basis sets for the OH and CH heterolytic bond cleavage of ethanol and twelve derivatives of the type $CH_{3-n}F_nCHX_rOH$, where *n* ranges from zero to three and represents the number of fluorine atoms and *r* represents hydrogen and the type of aromatic ring, namely: X_0 = hydrogen, X_1 = phenyl, X_2 = 1-naphthyl, and X_3 = 9-anthryl. The similarity between calculated and experimental $\Delta_{acid}G^0$(OH) values for ethanol (**1a**), 2-fluoroethanol (**1b**), 2,2-difluoroethanol (**1c**), 2,2,2-trifluoroethanol (**1d**), and 1-phenylethanol (**2a**) was used to validate the right theoretical method for this study. Substituent partial contributions to hydroxyl−, methylene−, and methine−hydrogen acidities were evaluated by linear combination. Good parameter fittings of the primary and secondary alcohols were obtained and interpreted as additive contribution of the substituent effects. The nonlinear contributions were identified. Calculations prove that fluoroalcohols exhibit C−H acidity, which is usually lower than O−H acidity. In principle, the inversion of this acidity order is possible by the introduction of a large aromatic ring instead to increase the number of fluorine atoms.

Introduction

Fluoroethanol derivatives are gaining importance in organic chemistry. For example 2,2,2-trifluoroethanol (**1d**) is mainly used as a protic solvent of high dielectric constant,[1] and pure enantiomers of 2,2,2-trifluoro-1-phenylethanol (**2d**), 2,2,2-trifluoro-1-(1-naphthyl)ethanol (**3d**), and 2,2,2-trifluoro-1-(9-anthryl)ethanol (**4d**) are chiral solvating agents.[2] The reported pK_a values for **1d** and **2d** measured in aqueous solution (12.43 and 11.90, respectively)[3,4] and the absolute gas-phase acidity for **1d** indicate that their hydroxyl acidity resembles the phenols more than ordinary alcohols.[1] Recent calculations[5] of C−H bond strengths in 2-fluoroethanol (**1b**), 2,2-difluoroethanol (**1c**), and **1d** at the B3P86/6-311++G(2df,p) and B3P86/6-311++G-(3df,2p) level of theory showed the methylene−hydrogen to have the weakest C−H bond for homolytic bond cleavage. This finding might anticipate the possibility of abstracting the methylene−hydrogen from the structure of **1d** by the heterolytic bond cleavage. Although the methine C−H bond strength of **2d**−**4d** is unknown, experience indicates that this methine−hydrogen is acidic. In this context, the nonequivalence of chemical shifts induced by a pure enantiomer of **4d** on the ^{1}H NMR spectra of racemic organic solutes having two basic sites was explained by Pirkle and Hoover[2] on the basis of the dibasic solute model, which states that acidic carbinol function (hydroxyl−hydrogen) of the S enantiomer of **4d** interacts strongly with a hydrogen bond receptor in the enantiomeric solutes, whereas the carbinyl hydrogen (methine−hydrogen), also somewhat acidic because of the electronegative character of the trifluoromethyl substituent, seeks interaction with a secondary basic site in the solutes. The lack of information in the current chemical literature about the acidity of methylene−hydrogen in **1d** and methine−hydrogen of **2d**−**4d** as well as our interest in the acidity of phenols[6] has lead us to undertake a theoretical study of the hydroxyl−, methylene−, and methine−hydrogen acidity of the following alcohols (Scheme 1): ethanol (**1a**), **1b**−**1d**, phenylethanol (**2a**), 2-fluoro-1-phenylethanol (**2b**), 2,2-difluoro-1-phenylethanol (**2c**), **2d**, 1-naphthylethanol (**3a**), 2-fluoro-1-(1-naphthyl)ethanol (**3b**), 2,2-difluoro-1-(1-naphthyl)ethanol (**3c**), **3d**, 9-anthrylethanol (**4a**), 2-fluoro-1-(9-anthryl)ethanol (**4b**), 2,2-difluoro-1-(9-anthryl) ethanol (**4c**), and **4d**.

SCHEME 1: General Structure of Ethanol and Its Derivatives Included in This Study[a]



	X_r	X_0 = H	X_1 = Phenyl	X_2 = 1-Naphthyl	X_3 = 9-Anthryl
$CH_{3-n}F_n$	n \ r	0	1	2	3
CH_3	**0**	**1a**	**2a**	**3a**	**4a**
CH_2F	**1**	**1b**	**2b**	**3b**	**4b**
CHF_2	**2**	**1c**	**2c**	**3c**	**4c**
CF_3	**3**	**1d**	**2d**	**3d**	**4d**

[a] Study was carried out with enantiomers having the configuration shown in the drawing.

Therefore, the aim of this article is to study the influence of the aryl and fluorine substituents on the acidity of ethanol by the analysis of the absolute gas-phase acidity of the $CH_{3-n}F_n$-CHX_rOH at 298.15 K, for the heterolytic bond cleavage reactions $CH_{3-n}F_nCHX_rOH \rightarrow CH_{3-n}F_nCHX_rO^- + H^+$ and $CH_{3-n}F_nCHX_rOH \rightarrow CH_{3-n}F_nC^-\ X_rOH + H^+$ at the B3LYP and MP2 levels using six different standard basis set.

Theory and Calculations

Ethanol and Its Fluorine Derivatives. The heterolytic bond cleavage reactions in the gas phase for hydroxyl−hydrogen, methylene− and methine−hydrogen of ethanol, and its fluorine derivatives are represented by eqs 1 and 2, respectively

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$$\mathrm{CH_{3-\mathit{n}}F_{\mathit{n}}CHX_{\mathit{r}}OH \rightarrow CH_{3-\mathit{n}}F_{\mathit{n}}CHX_{\mathit{r}}O^{-} + H^{+}} \quad (1)$$

$$\mathrm{CH_{3-\mathit{n}}F_{\mathit{n}}CHX_{\mathit{r}}OH \rightarrow CH_{3-\mathit{n}}F_{\mathit{n}}C^{-}X_{\mathit{r}}OH + H^{+}} \quad (2)$$

and their corresponding absolute gas-phase acidity is represented by eqs 3 and 4

$$\Delta_{\mathrm{acid}}G^{0}(\mathrm{OH})_{n,r} = G^{\mathrm{o}}(\mathrm{CH_{3-\mathit{n}}F_{\mathit{n}}CHX_{\mathit{r}}O^{-}}) + G^{\mathrm{o}}(\mathrm{H^{+}}) - G^{\mathrm{o}}(\mathrm{CH_{3-\mathit{n}}F_{\mathit{n}}CHX_{\mathit{r}}OH}) \quad (3)$$

$$\Delta_{\mathrm{acid}}G^{0}(\mathrm{CH})_{n,r} = G^{\mathrm{o}}(\mathrm{CH_{3-\mathit{n}}F_{\mathit{n}}C^{-}X_{\mathit{r}}OH}) + G^{\mathrm{o}}(\mathrm{H^{+}}) - G^{\mathrm{o}}(\mathrm{CH_{3-\mathit{n}}F_{\mathit{n}}CHX_{\mathit{r}}OH}) \quad (4)$$

In the general formula of ethanol derivatives and anions shown in eqs 1−4, n is the number of fluorine atoms and r is the type of substituent on methylene carbon, namely, X_0 = H, X_1 = 1-phenyl, X_2 = 1-naphthyl, and X_3 = 9-anthryl.

The ground-state structures of alcohols **1a**−**4d** and their alcohoxide and carbon anions were optimized by the density functional theory using the B3LYP functional[7] and the second-order Møller−Plesset perturbation theory[8] with the double and triple-ζ basis set: 6-31G(d,p), 6-31+G(d,p), 6-31+G(2d,2p), 6-311G(d,p), 6-311+G(d,p), and 6-311+G(2d,2p), as implemented in the GAUSSIAN03 package.[9] Frequency calculations were carried out without any symmetry constraints to confirm that the structures obtained correspond to energy minima. The Gibbs free energy of the proton in the gas phase $G^{\mathrm{o}}(\mathrm{H^{+}},\mathrm{g}) = -6.26$ kcal mol^{-1} was obtained considering the translational energy of the proton using statistical thermodynamic relations.[10] The Gibbs free energies of the alcohols **1a**−**4d** and their anions were obtained from the calculations of the most stable conformers of each compound because studies of the conformational equilibrium effect correction for glycine and serine have shown to lead indiscernible difference.[11,12] The optimized structures of primary alcohols **1a**−**1d** used in this study almost match those found by the experimental[13] and calculated[14] data available in the literature. Good fittings were also found between the low-energy conformers calculated by us and those reported for secondary alcohols **2a** and **2d**.[15] Secondary alcohols **3a**−**3d** and **4a**−**4d** have in common the peri effect, which reduces the number of low energy conformers. The peri effect between benzylic-like hydrogen and hydrogen atoms attached to fused aromatic rings, has been well documented by dynamic NMR spectroscopy and X-ray diffraction of the enantiomers and racemic mixture of compounds **3a**[16] and **4d**.[17] In addition, we carried out the X-ray diffraction analysis of compound **4d** to support the validity of the calculated low-energy conformer used herein. (See the Supporting Information.)

Results and Discussion

Acidity of Primary Alcohols 1a−1d. To study how the absolute gas phase is sensitive to the change of basis and/or method of calculations, DFT and MP2 methods were employed with the six different standard basis sets mentioned above. Table 1 shows the calculated acidities for the hydroxyl−hydrogen $\Delta_{\mathrm{acid}}G^{0}(\mathrm{OH})_{n,0}$ and methylene−hydrogen $\Delta_{\mathrm{acid}}G^{0}(\mathrm{CH_2})_{n,0}$ of **1a**−**1d**. In general, the calculated $\Delta_{\mathrm{acid}}G^{0}(\mathrm{OH})_{n,0}$ values with 6-31G(d,p) and 6-311G(d,p) functions overestimate the experimental values[3,4,18−22] by 16 and 10 kcal mol^{-1} for B3LYP and 19 and 15 kcal mol^{-1} for MP2 levels, respectively. When diffuse functions are included, the calculated values with 6-31+G(d,p) and 6-311+G(d,p) functions underestimate the experimental values by 2.5 and 2.0 kcal mol^{-1} for B3LYP and overestimate by 2.0 and 1.9 kcal mol^{-1} for MP2 levels, respectively. When an extra polarization function is added, the calculated $\Delta_{\mathrm{acid}}G^{0}(\mathrm{OH})_{n,0}$ values approach very well to the experimental ones; the difference decreases to 2.2 and 0.9 kcal mol^{-1} for B3LYP and 0.9 and 1.5 kcal mol^{-1} for MP2 levels with 6-31+G(2d,2p) and 6-311+G(2d,2p) functions, respectively. Consequently, it is worth noticing that the B3LYP/6-311+G(2d,2p) and MP2/6-31+G(2d,2p) levels give an accurate description of acidities of alcohols **1a**−**1d**. Therefore, the B3LYP/6-311+G(2d,2p) model involving a very flexible 6-311+G(2d,2p) basis set is used to estimate the gas-phase acidities of alcohols **2a**−**4d**; it gives us a satisfactory description of the **1a**−**1d** anionic species. The use of the DFT-B3LYP approach is also justified by its good performance in calculating electron affinities,[23] acidities of thiocarbonyl derivatives,[24] azoles,[25] and phenols,[6] singlet−triplet gaps of carbenes,[26] bond dissociation energies of phenols,[27] and thermodynamic parameters of amino acids and the related ions.[11,12]

Acidity of Secondary Alcohols 2a−4d. We shall use the DFT and MP2 methods with the 6-31G(d,p), 6-31+G(d,p) and 6-311+G(2d,2p) basis function to calculate the $\Delta_{\mathrm{acid}}G^{0}(\mathrm{OH})_{n,1}$ and $\Delta_{\mathrm{acid}}G^{0}(\mathrm{CH})_{n,1}$ values for **2a**−**2d**. From Table 2, we can observe that the B3LYP calculated $\Delta_{\mathrm{acid}}G^{0}(\mathrm{OH})_{0,1}$ value with the 6-31G(d,p) function overestimates the experimental one[20] by 12.06 kcal mol^{-1}, whereas the 6-31+G(d,p) and 6-311+G(2d,2p)

TABLE 1: Absolute Gas-Phase Acidity Values for 1a−1d, in kilocalories per mole[a]

method	$\Delta_{\mathrm{acid}}G^{0}(\mathbf{1a})_{0,0}$	$\Delta_{\mathrm{acid}}G^{0}(\mathbf{1b})_{1,0}$	$\Delta_{\mathrm{acid}}G^{0}(\mathbf{1c})_{2,0}$	$\Delta_{\mathrm{acid}}G^{0}(\mathbf{1d})_{3,0}$
MP2/6-31G(d,p)	389.90[b] (431.09)[c]	384.63 (410.33)	379.53 (405.16)	371.34 (397.73)
B3LYP/6-31G(d,p)	386.59 (427.60)	381.21 (406.32)	376.45 (405.60)	369.25 (395.95)
MP2/6-31+G(d,p)	371.95 (408.78)	366.04 (d)	357.52 (385.54)	352.28 (376.31)
B3LYP/6-31+G(d,p)	369.22 (405.81)	363.32 (d)	358.53 (381.70)	350.40 (373.63)
MP2/6-31+G(2d,2p)	370.52	364.95	360.43	352.33
B3LYP/6-31+G(2d,2p)	369.95	362.95	356.63	350.98
MP2/6-311G(d,p)	384.98	380.45	376.18	368.44
B3LYP/6-311G(d,p)	379.71	374.75	370.46	362.84
MP2/6-311+G(d,p)	372.89	367.09	362.18	354.06
B3LYP/6-311+G(d,p)	369.14	363.16	358.15	350.10
MP2/6-311+G(2d,2p)	371.30 (406.20)	366.02 (d)	361.60 (384.82)	353.49 (376.54)
B3LYP/6-311+G(2d,2p)	369.95 (405.64)	364.27 (d)	359.62 (382.02)	351.82 (374.31)
experimental	370.69 ± 2.00[e] (k) 371.41 ± 2.10[f] 371.65 ± 1.09[g]	364.48 ± 2.86[h] (k) 363.52 ± 3.58[i] 364.96 ± 3.34[j]	359.22 ± 2.00[e] (k)	354.20 ± 2.00[e] (k)

[a] Hydroxyl−hydrogen $\Delta_{\mathrm{acid}}G^{0}(\mathrm{OH})_{n,0}$ values are given without parentheses and methylene−hydrogen $\Delta_{\mathrm{acid}}G^{0}(\mathrm{CH_2})_{n,0}$ values are given in parentheses. [b] $\Delta_{\mathrm{acid}}G^{0}(\mathrm{OH})_{n,0}$ values obtained through eq 3. [c] $\Delta_{\mathrm{acid}}G^{0}(\mathrm{CH_2})_{n,0}$ values obtained through eq 4. [d] Not obtained. The experimental values of $\Delta_{\mathrm{acid}}G^{0}(\mathrm{OH})_{n,0}$ were obtained from http://webbook.nist.gov/chemistry/. [e] From ref 3. [f] From ref 18. [g] From ref 19. [h] From ref 20. [i] From ref 21. [j] From ref 22. [k] We have not found any $\Delta_{\mathrm{acid}}G^{0}(\mathrm{CH_2})_{n,0}$ experimental data in the literature.

TABLE 2: Absolute Gas-Phase Acidity Values for 2a−2d in kilocalories per mole[a]

method	$\Delta_{\mathrm{acid}}G^0(\mathbf{2a})_{0,1}$	$\Delta_{\mathrm{acid}}G^0(\mathbf{2b})_{1,1}$	$\Delta_{\mathrm{acid}}G^0(\mathbf{2c})_{2,1}$	$\Delta_{\mathrm{acid}}G^0(\mathbf{2d})_{3,1}$
B3LYP/6-31G(d,p)	373.43[b] (385.75)[c]	369.79 (374.87)	365.01 (369.68)	359.24 (367.27)
B3LYP/6-31+G(d,p)	359.12 (373.84)	355.05 (d)	349.92 (353.99)	343.75 (349.72)
B3LYP/6-311+G(2d,2p)	359.79 (372.69)	353.05 (d)	348.18 (355.98)	344.98 (353.58)
MP2/6-31+G(d,p)	359.81 (378.90)	357.93 (d)	352.62 (362.10)	345.99 (359.43)
experimental	361.37 ± 2.86[e] (f)	f (f)	f (f)	f (f)

[a] Hydroxyl−hydrogen $\Delta_{\mathrm{acid}}G^0(\mathrm{OH})_{n,1}$ values are given without parentheses and methine−hydrogen $\Delta_{\mathrm{acid}}G^0(\mathrm{CH})_{n,1}$ values given in parentheses. [b] $\Delta_{\mathrm{acid}}G^0(\mathrm{OH})_{n,1}$ values obtained through eq 3. [c] $\Delta_{\mathrm{acid}}G^0(\mathrm{CH})_{n,1}$values obtained through eq 4. [d] Not obtained. [e] From ref 20. [f] We have not found any $\Delta_{\mathrm{acid}}G^0(\mathrm{CH})_{n,1}$ or $\Delta_{\mathrm{acid}}G^0(\mathrm{OH})_{n,1}$ experimental data.

TABLE 3: Absolute Gas-Phase Acidity Values for 3a−3d in kilocalories per mole[a]

method	$\Delta_{\mathrm{acid}}G^0(\mathbf{3a})_{0,2}$	$\Delta_{\mathrm{acid}}G^0(\mathbf{3b})_{1,2}$	$\Delta_{\mathrm{acid}}G^0(\mathbf{3c})_{2,2}$	$\Delta_{\mathrm{acid}}G^0(\mathbf{3d})_{3,2}$
MP2/6-31+G(d,p)	359.71[b] (370.80)[c]	352.72 (d)	346.31 (361.91)	343.61 (358.10)
B3LYP/6-311+G(2d,2p)	357.74 (364.85)	355.12 (d)	347.10 (357.72)	343.66 (352.65)
experimental	(e)	(e)	(e)	(e)

[a] Hydroxyl−hydrogen $\Delta_{\mathrm{acid}}G^0(\mathrm{OH})_{n,2}$ values are given without parentheses and methine−hydrogen $\Delta_{\mathrm{acid}}G^0(\mathrm{CH})_{n,2}$ are given in parentheses. [b] $\Delta_{\mathrm{acid}}G^0(\mathrm{OH})_{n,2}$ values obtained through eq 3. [c] $\Delta_{\mathrm{acid}}G^0(\mathrm{OH})_{n,2}$ values obtained through eq 4. [d] Not obtained. [e] We have not found any $\Delta_{\mathrm{acid}}G^0(\mathrm{OH})_{n,2}$ or $\Delta_{\mathrm{acid}}G^0(\mathrm{CH})_{n,2}$ experimental data in the literature.

TABLE 4: Absolute Gas-Phase Acidity Values for 4a−4d in kilocalories per mole[a]

method	$\Delta_{\mathrm{acid}}G^0(\mathbf{4a})_{0,3}$	$\Delta_{\mathrm{acid}}G^0(\mathbf{4b})_{1,3}$	$\Delta_{\mathrm{acid}}G^0(\mathbf{4c})_{2,3}$	$\Delta_{\mathrm{acid}}G^0(\mathbf{4d})_{3,3}$
B3LYP/6-31G(d,p)	365.44[b] (364.24)[c]	361.97 (361.18)	358.17 (360.69)	352.74 (355.99)
B3LYP/6-31+G(d,p)	353.57 (352.61)	346.82 (d)	344.18 (349.07)	338.83 (344.74)
B3LYP/6-311+G(2d,2p)	354.37 (353.23)	351.53 (d)	343.77 (348.79)	340.20 (345.08)
experimental	(e)	(e)	(e)	(e)

[a] Hydroxyl−hydrogen $\Delta_{\mathrm{acid}}G^0(\mathrm{OH})_{n,3}$ values are given without parentheses, and methine−hydrogen $\Delta_{\mathrm{acid}}G^0(\mathrm{CH})_{n,3}$ values are given in parentheses. [b] $\Delta_{\mathrm{acid}}G^0(\mathrm{OH})_{n,3}$ values obtained through eq 3. [c] $\Delta_{\mathrm{acid}}G^0(\mathrm{CH})_{n,3}$ values obtained through eq 4. [d] Not obtained. [e] We have not found any $\Delta_{\mathrm{acid}}G^0(\mathrm{OH})_{n,3}$ or $\Delta_{\mathrm{acid}}G^0(\mathrm{CH})_{n,3}$ experimental data in the literature.

TABLE 5: Absolute Gas-Phase Hydroxyl-Acidity Values $\Delta_{\mathrm{acid}}G^0(\mathrm{OH})_{n,r}$, $\delta\Delta_{\mathrm{acid}}G^0(\mathrm{OH})^{\mathrm{F}}_{n,r}$, $\delta\Delta_{\mathrm{acid}}G^0(\mathrm{OH})^{\Phi}_{n,r}$, and $\delta\Delta_{\mathrm{acid}}G^0(\mathrm{OH})^{\mathrm{F},\Phi}_{n,r}$ for 1a−4d[a]

$\Delta_{\mathrm{acid}}G^0(\mathrm{OH})_{n,r}$	$\Delta_{\mathrm{acid}}G^0(\mathrm{OH})_{n,0}$	$\Delta_{\mathrm{acid}}G^0(\mathrm{OH})_{n,1}$	$\Delta_{\mathrm{acid}}G^0(\mathrm{OH})_{n,2}$	$\Delta_{\mathrm{acid}}G^0(\mathrm{OH})_{n,3}$
n/r	$r = 0$	$r = 1$	$r = 2$	$r = 3$
$\Delta_{\mathrm{acid}}G^0(\mathrm{OH})_{0,r}$ $n = 0$	369.95[b] (0)[d] (0)[c] (0)[e]	359.79 (−10.16) (0) (0)	357.74 (−12.21) (0) (0)	354.37 (−15.58) (0) (0)
$\Delta_{\mathrm{acid}}G^0(\mathrm{OH})_{1,r}$ $n = 1$	364.27 (0) (−5.68) (0)	353.05 (−11.22) (−6.74) (1.06)	355.12 (−9.15) (−2.62) (−3.06)	351.53 (−12.74) (−2.84) (−2.84)
$\Delta_{\mathrm{acid}}G^0(\mathrm{OH})_{2,r}$ $n = 2$	359.62 (0) (−10.33) (0)	348.18 (−11.44) (−11.61) (1.28)	347.1 (−12.52) (−10.64) (0.31)	343.77 (−15.85) (−10.60) (0.27)
$\Delta_{\mathrm{acid}}G^0(\mathrm{OH})_{3,r}$ $n = 3$	351.82 (0) (−18.13) (0)	344.98 (−6.84) (−14.81) (−3.32)	343.66 (−8.16) (−14.08) (−4.05)	340.20 (−11.62) (−14.17) (−3.96)

[a] See the text. All values are in kilocalories per mole. [b] $\Delta_{\mathrm{acid}}G^0(\mathrm{OH})_{n,r}$ values obtained through eq 3. [c] $\delta\Delta_{\mathrm{acid}}G^0(\mathrm{OH})^{\mathrm{F}}_{n,r}$ values obtained through eq 5. [d] $\delta\Delta_{\mathrm{acid}}G^0(\mathrm{OH})^{\Phi}_{n,r}$ values obtained through eq 6. [e] $\delta\Delta_{\mathrm{acid}}G^0(\mathrm{OH})^{\mathrm{F},\Phi}_{n,r}$ values obtained through eq 7.

functions underestimate the experimental one by 2.25 and 1.88 kcal mol^{-1}, respectively. The MP2/6-31+G(d,p) level underestimates the experimental one by 1.58 kcal mol^{-1}. Comparison with the available experimental data reveals a good agreement among B3LYP/6-31+G(d,p), B3LYP/6-311+G(2d,2p), MP2/6-31+G(d,p), and the measured value. Table 3 shows the $\Delta_{\mathrm{acid}}G^0(\mathrm{OH})_{n,2}$ and $\Delta_{\mathrm{acid}}G^0(\mathrm{CH})_{n,2}$ values for **3a−3d** calculated at the MP2/6-31+G(d,p) and B3LYP/6-311+G(2d,2p) levels. Both of these methods gave quite similar calculated values, although we have not found any $\Delta_{\mathrm{acid}}G^0(\mathrm{OH})_{n,2}$ experimental data for comparison.

Considering that the B3LYP method gives accurate results compared with MP2 calculations and uses less cost and computer time, the $\Delta_{\mathrm{acid}}G^0(\mathrm{OH})_{n,3}$ and $\Delta_{\mathrm{acid}}G^0(\mathrm{CH})_{n,3}$ values for **4a−4d** were obtained at the B3LYP level using the 6-31G(d,p), 6-31+G(d,p), and 6-311+G(2d,2p) basis functions. Table 4 shows the results. Although we have not found any $\Delta_{\mathrm{acid}}G^0(\mathrm{OH})_{n,3}$ experimental data, the calculated values with the 6-31+G(d,p) and 6-311+G(2d,2p) basis functions are quite similar.

Influence of the Substituents in Hydroxyl Acidity. From Tables 1−4 it can be observed that the acidity of **1a** increases when the number of fluorine atoms and aromatic rings increases. If we assign $\delta\Delta_{\mathrm{acid}}G^0(\mathrm{OH})^{\mathrm{F}}_{n,r}$ and $\delta\Delta_{\mathrm{acid}}G^0(\mathrm{OH})^{\Phi}_{n,r}$ to hydroxyl acidity contributions because of fluorine and aromatic rings, respectively, then each contribution could be calculated by eqs 5 and 6 for any of the studied fluoroalcohols

$$\delta\Delta_{\mathrm{acid}}G^0(\mathrm{OH})^{\mathrm{F}}_{n,r} = \Delta_{\mathrm{acid}}G^0(\mathrm{OH})_{n,r} - \Delta_{\mathrm{acid}}G^0(\mathrm{OH})_{0,r} \qquad n,r = 0-3 \quad (5)$$

$$\delta\Delta_{\mathrm{acid}}G^0(\mathrm{OH})^{\Phi}_{n,r} = \Delta_{\mathrm{acid}}G^0(\mathrm{OH})_{n,r} - \Delta_{\mathrm{acid}}G^0(\mathrm{OH})_{n,0} \qquad n,r = 0-3 \quad (6)$$

Because the DFT method gives accurate results, the $\Delta_{\mathrm{acid}}G^0(\mathrm{OH})_{n,r}$ and $\Delta_{\mathrm{acid}}G^0(\mathrm{CH})_{n,r}$ values for **1a−4d** obtained at the B3LYP/6-311+G(2d,2p) level were used to evaluate $\delta\Delta_{\mathrm{acid}}G^0(\mathrm{OH})^{\mathrm{F}}_{n,r}$ and $\delta\Delta_{\mathrm{acid}}G^0(\mathrm{OH})^{\Phi}_{n,r}$. The corresponding values are shown in Table 5. In primary alcohols **1b**, **1c**, and **1d**, $\delta\Delta_{\mathrm{acid}}G^0(\mathrm{OH})^{\mathrm{F}}_{n,r}$ decreases 5.68, 10.33, and 18.13 kcal mol^{-1}, respectively. The latter values correlate fairly well with the fluorine electron-withdrawal property and are close to reported experimental data.[3,18−22] On the other hand, $\delta\Delta_{\mathrm{acid}}G^0(\mathrm{OH})^{\Phi}_{n,r}$

TABLE 6: Absolute Gas-Phase CH Acidity Values for Methylene and Methine of 1a−4d and Calculated Fluorine $\delta\Delta_{\mathrm{acid}}G^0(\mathrm{CH})^{\mathrm{F}}_{n,r}$, Aromatic Rings $\delta\Delta_{\mathrm{acid}}G^0(\mathrm{CH})^{\Phi}_{n,r}$, and Mixed $\delta\Delta_{\mathrm{acid}}G^0(\mathrm{CH})^{\mathrm{F},\Phi}_{n,r}$ Contributions[a]

$\Delta_{\mathrm{acid}}G^0(\mathrm{CH})_{n,r}$	$\Delta_{\mathrm{acid}}G^0(\mathrm{CH})_{n,0}$	$\Delta_{\mathrm{acid}}G^0(\mathrm{CH})_{n,1}$	$\Delta_{\mathrm{acid}}G^0(\mathrm{CH})_{n,2}$	$\Delta_{\mathrm{acid}}G^0(\mathrm{CH})_{n,3}$
n/r	$r = 0$	$r = 1$	$r = 2$	$r = 3$
$\Delta_{\mathrm{acid}}G^0(\mathrm{CH})_{0,r}$ $n = 0$	405.64[b] (0)[d] (0)[c] (0)[e]	372.69 (−32.95) (0) (0)	364.85 (−40.79) (0) (0)	353.23 (−52.41) (0) (0)
$\Delta_{\mathrm{acid}}G^0(\mathrm{CH})_{1,r}$ $n = 1$	f (f) (f) (f)	f (f) (f) (f)	f (f) (f) (f)	f (f) (f) (f)
$\Delta_{\mathrm{acid}}G^0(\mathrm{CH})_{2,r}$ $n = 2$	382.02 (0) (−23.62) (0)	355.98 (−26.04) (−16.71) (−6.91)	357.72 (−24.30) (−7.13) (−16.49)	348.79 (−33.23) (−4.44) (−19.18)
$\Delta_{\mathrm{acid}}G^0(\mathrm{CH})_{3,r}$ $n = 3$	374.31 (0) (−31.33) (0)	353.58 (−20.73) (−19.11) (−12.22)	352.65 (−21.66) (−12.20) (−19.13)	345.08 (−29.23) (−8.15) (−23.18)

[a] All values are in kilocalories per mole. [b] $\delta\Delta_{\mathrm{acid}}G^0(\mathrm{CH})_{n,r}$ values obtained through eq 4. [c] $\delta\Delta_{\mathrm{acid}}G^0(\mathrm{CH})^{\mathrm{F}}_{n,r}$ values obtained through eq 8. [d] $\delta\Delta_{\mathrm{acid}}G^0(\mathrm{CH})^{\Phi}_{n,r}$ values obtained through eq 9. [e] $\delta\Delta_{\mathrm{acid}}G^0(\mathrm{CH})^{\mathrm{F},\Phi}_{n,r}$ obtained through eq 10. [f] Not calculated.

values for secondary alcohols **2a**, **3a**, and **4a** decrease 10.16, 12.21, and 15.58 kcal mol^{-1}, respectively. It must be noticed that the acidity decrement in the above-mentioned secondary alcohols is proportional to the size and resonance effect of the aromatic rings. The comparison of $\delta\Delta_{\mathrm{acid}}G^0(\mathrm{OH})^{\mathrm{F}}_{n,r}$ for **1b**, **1c**, and **1d**, and $\delta\Delta_{\mathrm{acid}}G^0(\mathrm{OH})^{\Phi}_{n,r}$ for **2a**, **3a**, and **4a** makes evident the fact that substitution of one hydrogen of **1a** by one fluorine atom causes a smaller effect than the substitution by one phenyl group; the substitution of two hydrogens of **1a** by two fluorine atoms causes almost the same effect as one naphthyl group, and the substitution of three hydrogen atoms of **1a** by three fluorine atoms has a larger effect than one anthryl group. The absolute gas-phase acidity of secondary fluoroalcohols **2b**−**4b**, **2c**−**4c**, and **2d**−**4d** would have an extra term $\delta\Delta_{\mathrm{acid}}G^0(\mathrm{OH})^{\mathrm{F},\Phi}_{n,r}$ that can be characterized as the nonlinear combination of the effects of fluorine and aromatic rings, as is shown in eq 7

$$\Delta_{\mathrm{acid}}G^0(\mathrm{OH})_{n,r} - \Delta_{\mathrm{acid}}G^0(\mathrm{OH})_{0,0} = \delta\Delta_{\mathrm{acid}}G^0(\mathrm{OH})^{\mathrm{F}}_{n,r} + \delta\Delta_{\mathrm{acid}}G^0(\mathrm{OH})^{\Phi}_{n,r} + \delta\Delta_{\mathrm{acid}}G^0(\mathrm{OH})^{\mathrm{F},\Phi}_{n,r} \quad n,r = 0{-}3 \qquad (7)$$

The introduction of known hydroxyl acidity values in eq 7 gave the $\delta\Delta_{\mathrm{acid}}G^0(\mathrm{OH})^{\mathrm{F},\Phi}_{n,r}$ values for secondary alcohols **2b**−**4d** contained in Table 5. $\delta\Delta_{\mathrm{acid}}G^0(\mathrm{OH})^{\mathrm{F},\Phi}_{n,r}$ values calculated in this way range from 1.06 (**2b**) to −3.96 (**4d**) kcal mol^{-1}.

Influence of the Substituents in the Acidity of Methylene and Methine Hydrogen Atoms. The procedure described above for the calculation of fluorine and aromatic rings contribution to hydroxyl acidity can be extended to analyze methylene and methine CH acidity of the studied fluoroalcohols. Therefore, fluorine $\delta\Delta_{\mathrm{acid}}G^0(\mathrm{CH})^{\mathrm{F}}_{n,r}$, aromatic rings $\delta\Delta_{\mathrm{acid}}G^0(\mathrm{CH})^{\Phi}_{n,r}$, and $\delta\Delta_{\mathrm{acid}}G^0(\mathrm{CH})^{\mathrm{F},\Phi}_{n,r}$ mixed contributions to CH acidity can be calculated from eqs 8, 9, and 10, respectively

$$\delta\Delta_{\mathrm{acid}}G^0(\mathrm{CH})^{\mathrm{F}}_{n,r} = \Delta_{\mathrm{acid}}G^0(\mathrm{CH})_{n,r} - \Delta_{\mathrm{acid}}G^0(\mathrm{CH})_{0,r} \quad n,r = 0{-}3 \qquad (8)$$

$$\delta\Delta_{\mathrm{acid}}G^0(\mathrm{CH})^{\Phi}_{n,r} = \Delta_{\mathrm{acid}}G^0(\mathrm{CH})_{n,r} - \Delta_{\mathrm{acid}}G^0(\mathrm{CH})_{n,0} \quad n,r = 0{-}3 \qquad (9)$$

$$\Delta_{\mathrm{acid}}G^0(\mathrm{CH})_{n,r} - \Delta_{\mathrm{acid}}G^0(\mathrm{CH})_{0,0} = \delta\Delta_{\mathrm{acid}}G^0(\mathrm{CH})^{\mathrm{F}}_{n,r} + \delta\Delta_{\mathrm{acid}}G^0(\mathrm{CH})^{\Phi}_{n,r} + \delta\Delta_{\mathrm{acid}}G^0(\mathrm{CH})^{\mathrm{F},\Phi}_{n,r} \quad n,r = 0{-}3 \qquad (10)$$

Using the acidity values obtained from the B3LYP/6-311G+(2d,2p) level (Tables 1−4), we obtained the data shown in Table 6. In primary alcohols **1c** and **1d**, $\delta\Delta_{\mathrm{acid}}G^0(\mathrm{CH})^{\mathrm{F}}_{n,r}$ contributions decrease 23.62 and 31.13 kcal mol^{-1}, whereas the $\delta\Delta_{\mathrm{acid}}G^0(\mathrm{CH})^{\Phi}_{n,r}$ contribution for secondary alcohols **2a**, **3a**, and **4a** decreases 32.95, 40.79, and 52.41 kcal/mol, respectively. In this case, the substitution of two and three hydrogen atoms of **1a** by two and three fluorine atoms causes a lower effect than the substitution of one hydrogen atom of **1a** by 1-naphthyl and 9-anthryl group, respectively; for example, the resonance effect contribution in **4a** is 21.08 kcal mol^{-1} stronger than the fluorine electron-withdrawal effect in **1d**. The mixed $\delta\Delta_{\mathrm{acid}}G^0(\mathrm{CH})^{\mathrm{F},\Phi}_{n,r}$ contribution calculated for secondary fluoroalcohols **2c**, **2d**, **3c**, **3d**, **4c**, and **4d** ranges from −6.91 to −23.18 kcal mol^{-1}.

CH versus Hydroxyl Acidities. In the structure of studied compounds, aromatic groups are located one bond closer than fluorine atoms to the atom that undergoes deprotonation. Despite the large distance between substituents and the hydroxyl−hydrogen, calculations show that, in general, the hydroxyl acidity is bigger than the CH acidity of methylene− or methine−hydrogen. This global acidity difference $\Delta_{\mathrm{acid}}G^0(\mathrm{CH{-}OH})_{n,r}$ and fluorine $\delta\Delta_{\mathrm{acid}}G^0(\mathrm{CH{-}OH})^{\mathrm{F}}_{n,r}$, aromatic ring $\delta\Delta_{\mathrm{acid}}G^0(\mathrm{CH{-}OH})^{\Phi}_{n,r}$, and mixed $\delta\Delta_{\mathrm{acid}}G^0(\mathrm{CH{-}OH})^{\mathrm{F},\Phi}_{n,r}$ contributions can be estimated from eqs 11, 12, 13, and 14, respectively. The corresponding data are given in Table 7.

$$\delta\Delta_{\mathrm{acid}}G^0(\mathrm{CH{-}OH})_{n,r} = \Delta_{\mathrm{acid}}G^0(\mathrm{CH})_{n,r} - \Delta_{\mathrm{acid}}G^0(\mathrm{OH})_{n,r} \quad n,r = 0{-}3 \qquad (11)$$

$$\delta\Delta_{\mathrm{acid}}G^0(\mathrm{CH{-}OH})^{\mathrm{F}}_{n,r} = \Delta_{\mathrm{acid}}G^0(\mathrm{CH{-}OH})_{n,r} - \Delta_{\mathrm{acid}}G^0(\mathrm{CH{-}OH})_{0,r} \quad n,r = 0{-}3 \qquad (12)$$

$$\delta\Delta_{\mathrm{acid}}G^0(\mathrm{CH{-}OH})^{\Phi}_{n,r} = \Delta_{\mathrm{acid}}G^0(\mathrm{CH{-}OH})_{n,r} - \Delta_{\mathrm{acid}}G^0(\mathrm{CH{-}OH})_{n,0} \quad n,r = 0{-}3 \qquad (13)$$

$$\Delta_{\mathrm{acid}}G^0(\mathrm{CH{-}OH})_{n,r} - \Delta_{\mathrm{acid}}G^0(\mathrm{CH{-}OH})_{0,0} = \delta\Delta_{\mathrm{acid}}G^0(\mathrm{CH{-}OH})^{\mathrm{F}}_{n,r} + \delta\Delta_{\mathrm{acid}}G^0(\mathrm{CH{-}OH})^{\Phi}_{n,r} + \delta\Delta_{\mathrm{acid}}G^0(\mathrm{CH{-}OH})^{\mathrm{F},\Phi}_{n,r} \quad n,r = 0{-}3 \qquad (14)$$

Positive $\Delta_{\mathrm{acid}}G^0(\mathrm{CH{-}OH})_{n,r}$ values mean that hydroxyl hydrogen is more acidic than the methylene or methine−hydrogen, and the negative values mean the opposite. Positive $\Delta_{\mathrm{acid}}G^0(\mathrm{CH{-}OH})_{n,r}$ values decrease from 35.69 kcal mol^{-1} for primary alcohol **1a** to 4.88 kcal mol^{-1} for the secondary fluoroalcohol **4d**. The magnitude of $\delta\Delta_{\mathrm{acid}}G^0(\mathrm{CH{-}OH})^{\mathrm{F}}_{n,0}$ values for primary fluoroalcohols **1c** (−12.29 kcal mol^{-1}) and **1d** (−13.20 kcal mol^{-1}) show the electron-withdrawing property

TABLE 7: Absolute Gas-Phase Acidity Values for Methylene− or Methine−Hydrogen $\Delta_{\mathrm{acid}}G^0(\mathrm{CH{-}OH})_{n,r}$ of Reaction 2 for 1a−4d[a]

$\Delta_{\mathrm{acid}}G^0(\mathrm{CH{-}OH})_{n,r}$	$\Delta_{\mathrm{acid}}G^0(\mathrm{CH{-}OH})_{n,0}$	$\Delta_{\mathrm{acid}}G^0(\mathrm{CH{-}OH})_{n,1}$	$\Delta_{\mathrm{acid}}G^0(\mathrm{CH{-}OH})_{n,2}$	$\Delta_{\mathrm{acid}}G^0(\mathrm{CH{-}OH})_{n,3}$
n/r	$r = 0$	$r = 1$	$r = 2$	$r = 3$
$\Delta_{\mathrm{acid}}G^0(\mathrm{CH{-}OH})_{0,r}$ $n = 0$	35.69[b] (0)[d] (0)[c] (0)[e]	12.90 (−22.79) (0) (0)	7.11 (−28.58) (0) (0)	−1.14 (−36.83) (0) (0)
$\Delta_{\mathrm{acid}}G^0(\mathrm{CH{-}OH})_{1,r}$ $n = 1$	f (f) (f) (f)	f (f) (f) (f)	f (f) (f) (f)	f (f) (f) (f)
$\Delta_{\mathrm{acid}}G^0(\mathrm{CH{-}OH})_{2,r}$ $n = 2$	22.40 (0) (−13.29 (0)	7.80 (−14.60) (−5.10) (−8.19)	10.62 (−11.78) (3.51) (−16.80)	5.02 (−17.38) (6.16) (−19.45)
$\Delta_{\mathrm{acid}}G^0(\mathrm{CH{-}OH})_{3,r}$ $n = 3$	22.49 (0) (−13.20) (0)	8.60 (−13.89) (−4.30) (−8.90)	8.99 (−13.5) (1.88) (−15.08)	4.88 (−17.61) (6.02) (−19.22)

[a] The $\delta\Delta_{\mathrm{acid}}G^0(\mathrm{CH{-}OH})^{\mathrm{F}}_{n,r}$, $\delta\Delta_{\mathrm{acid}}G^0(\mathrm{OH{-}CH})^{\Phi}_{n,r}$, and $\delta\Delta_{\mathrm{acid}}G^0(\mathrm{CH{-}OH})^{\mathrm{F},\Phi}_{n,r}$ values achieve the fluorine, aromatic ring, and fluorine-ring contributions to the acidity of $\mathrm{CH}_{3-n}\mathrm{F}_n\mathrm{CHX}_r\mathrm{OH}$. All values are in kilocalories per mole. [b] $\delta\Delta_{\mathrm{acid}}G^0(\mathrm{CH{-}OH})$ values obtained from eq 11. [c] $\delta\Delta_{\mathrm{acid}}G^0(\mathrm{CH{-}OH})^{\mathrm{F}}_{n,r}$ values obtained from eq 12. [d] $\delta\Delta_{\mathrm{acid}}G^0(\mathrm{CH{-}OH})^{\Phi}_{n,r}$ values obtained through eq 13. [e] $\delta\Delta_{\mathrm{acid}}G^0(\mathrm{CH{-}OH})^{\mathrm{F},\Phi}_{n,r}$ values obtained through eq 14. [f] Not calculated.

TABLE 8: Correlation Equations for 1a−4d Involving the Aromatic Ring and Fluorine Contributions to the Absolute Gas-Phase Acidity for Hydroxyl−, Methylene−, or Methine−Hydrogen, $\Delta_{\mathrm{acid}}G^0 = A_0 + A_1Z_1 + A_2Z_2 + A_3Z_1Z_2$[a]

$\Delta_{\mathrm{acid}}G^0$	Z_1	Z_2	A_0	A_1	A_2	A_3	R^2	S
$\Delta_{\mathrm{acid}}G^0(\mathrm{OH})_{n,r}$	$\delta\Delta_{\mathrm{acid}}G^0(\mathrm{OH})^{\Phi}_{0,r}$	$\delta\Delta_{\mathrm{acid}}G^0(\mathrm{OH})^{\mathrm{F}}_{n,0}$	369.65	0.991	0.982	0.011	0.97	1.55
$\Delta_{\mathrm{acid}}G^0(\mathrm{CH})_{n,r}$	$\delta\Delta_{\mathrm{acid}}G^0(\mathrm{CH})^{\Phi}_{0,r}$	$\delta\Delta_{\mathrm{acid}}G^0(\mathrm{CH})^{\mathrm{F}}_{n,0}$	405.53	0.994	1.021	0.014	0.99	2.04
$\Delta_{\mathrm{acid}}G^0(\mathrm{CH{-}OH})_{n,r}$	$\delta\Delta_{\mathrm{acid}}G^0(\mathrm{CH{-}OH})^{\Phi}_{0,r}$	$\delta\Delta_{\mathrm{acid}}G^0(\mathrm{CH{-}OH})^{\mathrm{F}}_{n,0}$	35.69	1.000	1.054	0.0400	0.97	1.71

[a] $\Delta_{\mathrm{acid}}G^0$ values are in kilocalories per mole.

of the fluorine atom that stabilize the negative charge of the resulting carbanions. In a similar way, $\delta\Delta_{\mathrm{acid}}G^0(\mathrm{CH{-}OH})^{\Phi}_{0,r}$ values of secondary alcohols **2a**, **3a**, and **4a** decrease from 22.79 to 28.58 to 36.83 kcal mol^{-1}, respectively. It must be noticed that these values are proportional to the size of the aromatic groups, and they lead to anticipate the stability order of the benzylic carbanions produced by heterolytic methine−hydrogen cleavage. As we can observe, the substitution of the second and third hydrogen atoms in **1a** by fluorine atoms has a lower effect than the introduction of 1-naphthyl or 9-anthryl groups. The differences $[\delta\Delta_{\mathrm{acid}}G^0(\mathrm{CH{-}OH})^{\Phi}_{0,2} - \delta\Delta_{\mathrm{acid}}G^0(\mathrm{CH{-}OH})^{\mathrm{F}}_{2,0}]$ and $[\delta\Delta_{\mathrm{acid}}G^0(\mathrm{CH{-}OH})^{\Phi}_{0,3} - \delta\Delta_{\mathrm{acid}}G^0(\mathrm{CH{-}OH})^{\mathrm{F}}_{3,0}]$ are 15.29 and 23.66 kcal mol^{-1}, respectively. These results suggest that, in principle, the inversion of the acidity order is possible by the introduction of a large aromatic group instead to increase the number of fluorine atoms. For example, alcohol **4a** has an anthryl group and no fluorine atoms; the methine−hydrogen is 1.14 kcal mol^{-1} more acidic than the hydroxyl−hydrogen. The mixed $\delta\Delta_{\mathrm{acid}}G^0(\mathrm{CH{-}OH})^{\mathrm{F},\Phi}_{n,r}$ contribution calculated for secondary fluoroalcohols **2c**, **2d**, **3c**, **3d**, **4c**, and **4d** ranges from −8.19 to −19.22 kcal mol^{-1}.

Linear and Nonlinear Substituent Contributions to Hydroxyl−, Methylene−, and Methine−Hydrogen Acidities. Linear regression analysis of $\Delta_{\mathrm{acid}}G^0$ in terms of the aromatic ring (Z_1) and fluorine (Z_2) contributions help us to obtain the linear ($Z_1 + Z_2$), and nonlinear (Z_1Z_2, Z_1^2, Z_2^2) substituent contributions to hydroxyl−, methylene−, and methine−hydrogen acidity. The regression equation $\Delta_{\mathrm{acid}}G^0 = A_0 + A_1Z_1 + A_2Z_2 + A_3Z_1Z_2 + A_4Z_1^2 + A_5Z_2^2$ was tested involving single-, double-, triple-, and quadruple-parameters. The statistical significance of the regression equations was obtained, and the best-fitting values were achieved for the triple-parameter equation $\Delta_{\mathrm{acid}}G^0 = A_0 + A_1Z_1 + A_2Z_2 + A_3Z_1Z_2$. Table 8 shows that, in general, the fitted constants A_1 and A_2 values are close to one and the A_3 value is lower than one, suggesting that the linear contribution term is higher than the nonlinear term. The correlation coefficients (R^2) are 0.99, 0.99, and 0.97, and the standard deviations (S) are 0.42, 2.04, and 1.71. To analyze the nature of the Z_1Z_2 term, the hydroxyl acidity of $\mathrm{CH}_{3-n}\mathrm{F}_n\mathrm{CHX}_r\mathrm{OH}$ ($\Delta_{\mathrm{acid}}G^0(\mathrm{OH})_{n,r}$) can be obtained as a linear combination of the acidities of the base fragment $\mathrm{CH_3CH_2OH}$ ($\Delta_{\mathrm{acid}}G^0(\mathrm{OH})_{0,0} \cong A_0$), the aromatic ring $\mathrm{CH_3CHX}_r\mathrm{OH}$($\delta\Delta_{\mathrm{acid}}G^0(\mathrm{OH})^{\Phi}_{0,r} = A_1Z_1$), and the fluorine $\mathrm{CH}_{3-n}\mathrm{F}_n\mathrm{CH_2OH}$($\delta\Delta_{\mathrm{acid}}G^0(\mathrm{OH})^{\mathrm{F}}_{n,0} \cong A_2Z_2$) contributions; the small extra acidity term is added to include the nonlinear contributions ($0.011(\delta\Delta_{\mathrm{acid}}G^0(\mathrm{OH})^{\Phi}_{0,r}\delta\Delta_{\mathrm{acid}}G^0(\mathrm{OH})^{\mathrm{F}}_{n,0}) \cong A_3Z_1Z_2$). After algebraic manipulations, it was found that the extra term $\delta\Delta_{\mathrm{acid}}G^0(\mathrm{OH})^{\mathrm{F},\Phi}_{n,r}$ from eq 7, equals the $A_3Z_1Z_2$ term

$$\delta\Delta_{\mathrm{acid}}G^0(\mathrm{OH})^{\mathrm{F},\Phi}_{n,r} \cong -0.011(\delta\Delta_{\mathrm{acid}}G^0(\mathrm{OH})^{\Phi}_{0,r})(\delta\Delta_{\mathrm{acid}}G^0(\mathrm{OH})^{\mathrm{F}}_{n,0}) \qquad n,r = 0{-}3 \quad (15)$$

Substituting eq 15 in eq 7, we obtain the linear and nonlinear substituent contributions to hydroxyl−hydrogen acidity

$$\delta\Delta_{\mathrm{acid}}G^0(\mathrm{OH})_{n,r} - \Delta_{\mathrm{acid}}G^0(\mathrm{OH})_{0,0} \cong \delta\Delta_{\mathrm{acid}}G^0(\mathrm{OH})^{\mathrm{F}}_{n,r} + \delta\Delta_{\mathrm{acid}}G^0(\mathrm{OH})^{\Phi}_{n,r} - 0.011(\delta\Delta_{\mathrm{acid}}G^0(\mathrm{OH})^{\Phi}_{0,r}\delta\Delta_{\mathrm{acid}}G^0(\mathrm{OH})^{\mathrm{F}}_{n,0}) \qquad n,r = 0{-}3 \quad (16)$$

Similar linear regression analysis can be applied to $\Delta_{\mathrm{acid}}G^0(\mathrm{CH})_{n,r}$ and $\Delta_{\mathrm{acid}}G^0(\mathrm{CH{-}OH})_{n,r}$ so that the best fitting values were obtained for $\Delta_{\mathrm{acid}}G^0 = A_0 + A_1Z_1 + A_2Z_2 + A_3Z_1Z_2$. The extra terms $\delta\Delta_{\mathrm{acid}}G^0(\mathrm{CH})^{\mathrm{F},\Phi}_{n,r}$ and $\delta\Delta_{\mathrm{acid}}G^0(\mathrm{CH{-}OH})^{\mathrm{F},\Phi}_{n,r}$ from eqs 10 and 14 respectively, are

$$\delta\Delta_{\mathrm{acid}}G^0(\mathrm{CH})^{\mathrm{F},\Phi}_{n,r} \cong -0.014(\delta\Delta_{\mathrm{acid}}G^0(\mathrm{CH})^{\Phi}_{0,r})(\delta\Delta_{\mathrm{acid}}G^0(\mathrm{CH})^{\mathrm{F}}_{n,0}) \qquad n,r = 0{-}3 \quad (17)$$

and

$$\delta\Delta_{\mathrm{acid}}G^0(\mathrm{OH{-}CH})^{\mathrm{F},\Phi}_{n,r} \cong -0.040(\delta\Delta_{\mathrm{acid}}G^0(\mathrm{OH{-}CH})^{\Phi}_{0,r})(\delta\Delta_{\mathrm{acid}}G^0(\mathrm{OH{-}CH})^{\mathrm{F}}_{n,0}) \qquad n,r = 0{-}3 \quad (18)$$

Substituting eqs 17 and 18 in eqs 10 and 14, we obtain the linear and nonlinear substituent contributions to $\Delta_{\mathrm{acid}}G^0(\mathrm{CH})_{n,r}$ and $\Delta_{\mathrm{acid}}G^0(\mathrm{CH{-}OH})_{n,r}$

$$\delta\Delta_{\mathrm{acid}}G^0(\mathrm{CH})_{n,r} - \Delta_{\mathrm{acid}}G^0(\mathrm{CH})_{0,0} \cong \delta\Delta_{\mathrm{acid}}G^0(\mathrm{CH})^{\mathrm{F}}_{n,r} + \delta\Delta_{\mathrm{acid}}G^0(\mathrm{CH})^{\Phi}_{n,r} - 0.014(\delta\Delta_{\mathrm{acid}}G^0(\mathrm{CH})^{\Phi}_{0,r}\delta\Delta_{\mathrm{acid}}G^0(\mathrm{CH})^{\mathrm{F}}_{n,0}) \quad n,r = 0,3 \qquad (19)$$

$$\delta\Delta_{\mathrm{acid}}G^0(\mathrm{CH{-}OH})_{n,r} - \Delta_{\mathrm{acid}}G^0(\mathrm{CH{-}OH})_{0,0} \cong \delta\Delta_{\mathrm{acid}}G^0(\mathrm{CH{-}OH})^{\mathrm{F}}_{n,r} + \delta\Delta_{\mathrm{acid}}G^0(\mathrm{CH{-}OH})^{\Phi}_{n,r} - 0.040(\delta\Delta_{\mathrm{acid}}G^0(\mathrm{CH{-}OH})^{\Phi}_{0,r}\delta\Delta_{\mathrm{acid}}G^0(\mathrm{CH{-}OH})^{\mathrm{F}}_{n,0}) \quad n,r = 0,3 \qquad (20)$$

From the linear regression analysis, we can assume that the effects of the fluorine atoms and aromatic rings on the acidity of ethanol are linearly additive.

Conclusions

The influence of the aryl and fluorine substituents on the acidity of ethanol was analyzed by the absolute gas-phase acidity of $CH_{3-n}F_nCHX_rOH$ at $T = 298.15$ K for the heterolytic bond cleavage reactions $CH_{3-n}F_nCHX_rOH \rightarrow CH_{3-n}F_nCHX_rO^- + H^+$ and $CH_{3-n}F_nCHX_rOH \rightarrow CH_{3-n}F_nC^- X_rOH + H^+$, where n and r are the number of fluorine atoms and aromatic rings, respectively ($n,r = 0-3$), and X_0 = hydrogen, X_1 = phenyl, X_2 = 1-naphthyl, and X_3 = 9-anthryl. The absolute gas-phase acidities $\Delta_{\mathrm{acid}}G^0(\mathrm{OH})$ and $\Delta_{\mathrm{acid}}G^0(\mathrm{CH})$ were calculated at the B3LYP and MP2 levels using six different standard basis sets. The $\Delta_{\mathrm{acid}}G^0(\mathrm{OH})$ values showed a good approach with the experimental values reported in the literature for ethanol and its fluorine derivatives. Fluorine and aromatic ring contributions to the absolute hydroxyl−, methylene−, and methine−hydrogen acidity for ethanol and 12 fluorinated derivatives were evaluated by the linear regression analysis. Good parameter fittings of the primary and secondary alcohols were obtained and interpreted as the additive contribution of the substituent effects. The nonlinear contributions were identified. Calculations prove that fluoroalcohols exhibit C−H acidity, which is usually lower than O−H acidity. In principle, the inversion of this acidity order is possible by the introduction of a large aromatic ring instead to increase the number of fluorine atoms. Current research to explore this fact is in progress.

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Supporting Information Available: Cartesian coordinates, electronic and zero-point energies, and thermochemical data for fully optimized geometries as well as the X-ray structure of compound **4d** are included. The complete crystallographic data of compound **4d** has been deposited at the Cambridge Crystallographic Data Centre with deposition number CCDC 722576. This material is available free of charge via the Internet at http://pubs.acs.org.

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