Fluorescence was viewed through an interference filter (Corion), 300 nm for the exciplex and 287 nm for the amine fluorescence band-pass 12 nm). Because of the low optical density of the sample, and thus low fluorescence intensity, measurements were carried out by using a cylindrical cell, entirely constructed of Suprasil, 10 cm × 3.0 cm. This arrangement helped decrease the scattered light. Typical acquisition times were ca. 1-2 h. Fluorescence excitation spectra were obtained by using the time-correlated photon-counting apparatus in the multichannel scaling mode; in this way, it essentially functioned as a counting gated integrator. The excitation resolution was 1.6 nm. Because of the very low intensities encountered, three or four scans, each with a duration of 20 min, were obtained and cumulatively stored in the multichannel analyzer. Spectra were corrected by using a sodium salicylate screen as quantum counter. Absorption spectra were obtained by using a Varian 2300 spectrophotometer. The fluorescence standards used were toluene vapor (for the exciplex) and N,N-dimethyloctylamine (for the amine emission). The former was assigned an efficiency of 0.25 for 265-nm excitation at a pressure of 0.6 torr. This value was scaled from the value of 0.30 as reported by Burton and Noyes, Jr.,[35] for an ca. 14-torr pressure by the ratio of the measured lifetimes (i.e., 64.3 ns for 0.6 torr and 54.5 ns for 14.5 torr). The fluorescence quantum efficiency from *N,N*-dimethyloctylamine vapor (0.18 torr) was assigned a value of 1.0 between λ_{exc} = 250 and 230 nm.

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Quantitative Models of Gas-Phase Proton-Transfer Reactions Involving Alcohols, Ethers, and Their Thio Analogues. Correlation Analyses Based on Residual Electronegativity and Effective Polarizability

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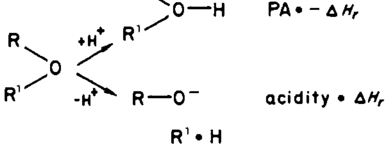
Abstract: The enthalpy of reaction for the gas-phase addition of a proton to an alcohol or ether (proton affinity) can be quantitatively modeled by a two-parameter expression. The two empirical parameters, residual electronegativity and effective polarizability, are both dependent on atomic composition, molecular structure, and reaction site and can be rapidly calculated by previously published procedures. Residual electronegativity reflects the electron-attracting ability of an atom in a particular molecular environment. Effective polarizability is related to conventional polarizability while allowing for attenuation of influence of more remote atoms and bonds. The same model applies to thiol and thioether proton affinity. Gas-phase acidity of alcohols is also described by these parameters, especially if allowance is made for the particularly high O-H bond-dissociation energy of water. The influence of polarizability is found to be less in determining the acidity values compared to proton affinity. It is concluded that the electronegativity and polarizability parameters offer novel access to quantitative reactivity data.

In discussing chemical reactivity, the organic chemist uses traditional concepts such as partial atomic charges, electronegativity, polarizability, hard and soft character, hyperconjugation, etc. However, these notions are frequently applied in a qualitative manner only. The synthesis and reaction design computer program EROS[1] is founded on just such descriptions of chemical reactivity, but in developing EROS, we are devising appropriate quantitative models for the above effects. In order to demonstrate their general applicability and suitability, we are first testing them against well-defined experimental data which have become available through recent developments in experimental technique. In particular, high-pressure mass spectrometry and ion cyclotron resonance spectroscopy have given accurate quantitative data on gas-phase reactions. Such data are of particular significance in that they have forced revision of some long-accepted concepts in chemical reactivity dealing as they do with isolated molecules uncorrupted by the influence of solvent.

Gas-phase protonation of alcohols is favored by alkyl groups in the order of increasing *positive* charge stabilization Me < Et < *i*-Pr < *t*-Bu.[2] This result is consistent with the traditional concept of such alkyl groups being electron releasing, as also implied by the aqueous-phase acidity of the alcohols (pK_a(MeOH) < pK_a(EtOH) < pK_a(*i*-PrOH) < pK_a(*t*-BuOH)). However, *gas*-phase studies of alcohol acidity show the opposite order to solution,[3] and they indicate that alkyl groups stabilize *negative* charge in the same sequence as they stabilize positive charge: Me < Et < *i*-Pr < *t*-Bu. This dichotomy was resolved by consideration of additional effects over and above the traditional inductive mechanism. Stabilization due to substituent polarizability was suggested by Brauman et al.[3] Thus, in any quantitative analysis of protonation reactions in the gas phase, we can expect to have to use multiparameter models and that measures of inductive effect alone will be insufficient. The two reaction types, protonation (eq 1) and deprotonation (eq 2), thus comprise fundamental test cases both in the context of our model development as well as in physical organic chemistry in general.



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(2)

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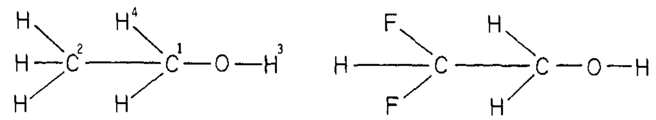

Iteration 0													
q	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
x	7.17	7.976	7.170	7.976	14.188	7.170	7.170	14.660	7.976	7.170	7.976	14.188	7.170
Iteration 1													
q	0.020	-0.060	0.020	-0.123	-0.338	0.175	0.020	-0.176	0.331	0.020	0.123	-0.338	0.175
x	7.295	7.428	7.295	9.133	9.973	8.247	7.295	12.990	11.220	7.195	9.133	9.973	8.247
Iteration 6													
q	0.025	-0.041	0.055	0.042	-0.396	0.210	0.104	-0.207	0.262	0.106	0.105	-0.390	0.210
x	7.326	7.599	7.514	8.363	9.290	8.453	7.813	11.893	10.512	7.550	8.960	9.359	8.455

$\bar{x}_{12}$ for the PA of ethanol:

$$\bar{x}_1 = \frac{1}{2}(x_{C-1} + x_{H-3}) = \frac{1}{2}(8.363 + 8.453) = 8.408$$
$$\bar{x}_2 = \frac{1}{3}(x_{C-2} + 2x_{H-4}) = \frac{1}{3}(7.599 + (2)(7.514)) = 7.542$$
$$\bar{x}_{12} = \frac{1}{2}(\bar{x}_1 + \frac{\bar{x}_2}{4}) = 5.147$$

$\bar{x}_{12}$ for the acidity of ethanol:

$$\bar{x}_1 = x_{C-1} = 8.363$$
$$\bar{x}_2 = \frac{1}{3}(x_{C-2} + 2x_{H-4}) = 7.542$$
$$\bar{x}_{12} = \frac{1}{2}(\bar{x}_1 + \frac{\bar{x}_2}{4}) = 5.124$$

Figure 1. Calculation of the residual electronegativity parameter $\bar{\chi}_{12}$ from values obtained through iterative partial equalization of orbital electronegativity[8] illustrated with ethanol and 2,2-difluoroethanol as examples.

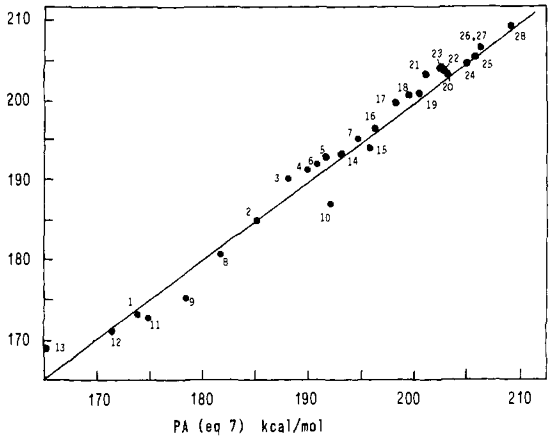

Figure 2. Experimental proton affinities of water, alcohols, and ethers plotted against values calculated by eq 7. The numbers refer to the entries in Table I ($n = 28$, $r = 0.989$, $s = 1.8$ kcal/mol).

Conventionally, proton affinity (PA) is quoted as the negative of the enthalpy of reaction 1. Thus increasing PA implies increasing exothermicity, whereas gas-phase acidity is an endothermic process; both quantities therefore assume positive values.

Several quantum mechanical calculations of PA of alcohols and ethers as well as acidities of alcohols have been analyzed,[4] and linear relationships between PA and O-1s ESCA shifts enabled the development of charge potential models for estimating PA's.[5] However, in all these studies the data sets discussed have been limited in scope. Additionally, in attempting to quantify the earlier suggestions[3,6] that polarizability is in part responsible for stabilization of charge in the gas phase, Taft and co-workers[7] analyzed the PA and acidity data of alcohols, and they were thus able to derive polarizability-effect contributions for various alkyl substituents.

In contrast, our aim has been to develop more general models which are applicable to the entire sets of available data on alcohol and ether PA, as well as alcohol acidity, and which can be used directly and conveniently to predict data for unknown derivatives. For this purpose we have based our analyses on *residual electronegativity*[8,9] and *effective polarizability* values,[10] both of which are now outlined.

Methods

PA[11] and acidity[12] data were taken from the literature. Linear models were constructed by multilinear regression analysis with independent variable values calculated from the following empirical models.

Residual Electronegativity. The conventional view of covalent bond formation between two atoms is that charge is transferred from the electropositive atom (i.e., that with lower electronegativity) to the more electronegative atom (higher electronegativity). As charge is transferred, the electronegativities of the two atoms assume more equal values, until on completion of bond formation the electronegativities are exactly equal. This concept leads to unfortunate consequences, such as all atoms of the same element in a particular molecule carry the same charge (e.g., H atoms in CH_3OH) and that isomeric groups are bound to have equal electronegativities (e.g., $FCH_2CH_2CH_2$–, cf. CH_3CH_2CHF–).[13]

A new quantitative model was therefore devised which was aimed at overcoming these difficulties and which was based on the concept of partial equalization of orbital electronegativity (PEOE).[8] By an iterative procedure this model enables calculation of unique charge values for each atom in a molecule, and furthermore gives each atom, i, a residual electronegativity value, χ_i, characteristic of its molecular environment. As an example, the atomic charges and residual electronegativities of C_2H_5OH and F_2CHCH_2OH are shown in Figure 1, for the initial state,

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after one iteration, and on completion of partial equalization (6th iteration).

The χ_i value reflects the remaining potential of atom i to attract further electron density toward itself. It is just this property that should be of importance in deciding how a particular substituent will exert a polar influence over charge development on a neighboring atom, as for instance on protonation of an ether. In fact, we have consistently found that a combination term ($\bar{\chi}_{12}$), derived from values for both first (χ_1) and second (χ_2) sphere neighbors (Figure 1), performs somewhat better than either of the individual terms.

Two points are to be noted. Firstly, the final $\bar{\chi}_{12}$ values derived reflect the influence of more remote atoms, e.g., the fluorine atoms in 2,2-difluoroethanol, despite the fact that their own χ-values are not explicitly included in the $\bar{\chi}_{12}$ expression. Secondly, we distinguish between the value to be used in PA studies and that for acidity by inclusion of the hydroxylic hydrogen in the former, but not in the latter. This reflects the situation pertaining in acid ionization where this hydrogen is no longer present to exert an influence on anion stabilization.

Effective Polarizability. Mean molecular polarizability (MMP) is a quantification of the ease with which a dipolar system undergoes electronic distortion in the presence of an external field, to give an induced dipole moment.[14] It is these induced dipole moments in unsubstituted alkyl groups which are believed to be the main source of stabilization of charges in gaseous ions formed by protonation or deprotonation (e.g., eq 1 and 2). Classical electrostatics yields eq 3 for the energy of stabilization (E) due to charge (q)-induced dipole interaction where $\bar{\alpha}$ is the MMP, r the separation of charge and induced dipole, and ϵ the dielectric constant.

$$E = -\frac{q^2\bar{\alpha}}{2\epsilon r^4} \tag{3}$$

It can be seen from this equation that the stabilization is highly distance dependent. Moreover, there exist additional complicating features in the case of systems where the interacting charge and induced dipole are part of the same molecule. These include structural variations, particularly conformational effects which can further influence the local dielectric constant, ϵ; uncertainty of exact charge distribution, since the charge will be delocalized to a lesser or greater extent; and undefined mechanisms of interaction, especially in view of the large field strengths in the close neighborhood of the charge center.[3,6] Therefore, a general and rigorously theoretical quantification of the polarizability effect is an intractable problem. In order to cut through this Gordian knot, we have introduced an empirical formula (eq 4) which enables calculation of effective polarizability values (α_d),[10] and which is a modification of a literature formula[15] for MMP.

$$\alpha_d = \frac{4}{N}(\sum_i d^{n_i-1}\tau_i)^2 \tag{4}$$

N is the total number of electrons in the system. τ_i is a polarizability contribution for each atom, i, characteristic for each element in a particular hybridization state,[15] and thus the formula allows for heteroatom influences. The all-important attenuation of substituent influence is accounted for by the damping factor, d^{n_i-1}, where d is given a value of 0.75, and n_i is the number of bonds between atom i and the charged reaction center. The value of $d = 0.75$ has been arrived at by systematic investigation of several series of experimental data besides those discussed here, where in most cases values differing from 0.75 led to statistically inferior models.[10]

The α_d values have been shown to be useful in studies of relaxation phenomena during charge development due to core electron ionization processes,[10] as well as amine protonation.[9,10]

A consequence of eq 4 is that α_d values are dependent on reaction site. Thus, for $CH_3OCH_2CH_2OH$ protonation at the ether oxygen, $\alpha_d = 4(2\tau_C + 0.75(\tau_C + 5\tau_H) + 0.75^2(\tau_O + 2\tau_H) + 0.75^3\tau_H)^2/36 = 4.161$. Protonation at the hydroxyl oxygen implies $\alpha_d = 2.909$, corresponding to decreased polarizability-derived stabilization at this site. Again, as before for $\bar{\chi}_{12}$, a distinct mechanistic picture was imposed onto the calculation of α_d: for protonation of alcohols the hydroxyl hydrogen was included, whereas for the acidity studies it was disregarded: $\alpha_d(CH_3OC_2H_4OH) = 2.63$.

We have also introduced a simple bond-counting model for effective polarizability to give a connectivity number, N_c (eq 5), which was originally designed to be applicable to unsubstituted alkyl groups.[10]

$$N_c = \sum_n b_n(0.5)^{n-1} \tag{5}$$

Here, b_n is the number of bonds in the n'th neighbor sphere; and the attenuation factor of 0.5 was determined empirically from studies of several systems (see ref 10 for worked examples). However, polarizability values for fluorocarbons are very similar to the corresponding unsubstituted alkanes, implying that connectivity numbers could also be used for fluoro derivatives. In fact, α_d values for an arbitrary series of fluoroalkyl derivatives as calculated by eq 4, which takes explicit account of the heteroatoms, correlate closely with the connectivity numbers from eq 5, which makes no attempt to distinguish between C–C, C–H, and C–F bonds (number of compounds $n = 17$; correlation coefficient $r = 0.97$; standard deviation $s = 0.35$ N_c units). In those series where only such bonds are present, the α_d and N_c effective polarizability values have both been used in the multilinear regression (MLR) analyses.

Results and Discussion

Proton Affinity of Alcohols and Ethers. Calculated input data for the regression analyses are recorded in Table I, along with the experimental values. In the first instance, the PA data on alcohols and ethers were regressed jointly against either a single parameter or combinations of two, and the more relevant results are collected in Table II. It is readily seen that no single parameter correlates directly with PA, within the desired error limits. The parameters studied include the charge on oxygen, q_O, alone, thus indicating that ground-state charge distribution does not reflect PA. However, it is equally clear that PA for the combined alcohol/ether data set is satisfactorily reproduced by two-parameter models—those based on $\bar{\chi}_{12}$, along with either α_d or N_c (eq 6 and 7; Table II, entries 7 and 8), being most acceptable. However, use of mean molecular polarizability, $\bar{\alpha}$, with $\bar{\chi}_{12}$ is much inferior, illustrating clearly that the effective polarizability models are superior to MMP in the context of chemical reactivity. Analogous dual-parameter regressions substituting charge, q_O, for $\bar{\chi}_{12}$ were not as satisfactory.

$$\mathrm{PA(calcd)} = 272.8 - 19.29\bar{\chi}_{12} + 5.22\alpha_d \tag{6}$$

$$\mathrm{PA(calcd)} = 283.6 - 22.73\bar{\chi}_{12} + 5.05N_c \tag{7}$$

The values calculated from eq 6 are also recorded in Table I, and those from eq 7 are plotted against experimental values in Figure 2. The regression expressions are entirely consistent with intuition and experience, in that the positive signs of the α_d and N_c coefficients indicate that an increase in polarizability increases the cation stabilization and results in higher PA. In contrast, the negative sign of the $\bar{\chi}_{12}$ coefficient reflects the fact that increased residual electronegativity is commensurate with decrease of stabilization of the positive charge. The polar effects in this series are accounted for perfectly satisfactorily by the PEOE procedure without any prior decision as to whether a through-bond inductive or a through-space field effect is the predominating mechanism.

The regression models reproduce the observed differences in PA between isomeric molecules (e.g., EtOH/Me_2O; THP/2-methyltetrahydrofuran; n-BuOH/t-BuOH/Et_2O). In each case the differences are due mainly to polarizability influences. The difference in experimental PA of about 1 kcal/mol between Et_2O and THF has been commented upon before in terms of "internal inductive effects".[16] This difference is reflected by the regression of eq 6, the higher PA of the former ether being due almost entirely to polarizability effects (1.29 kcal/mol), and is little effected by electronegativity (0.13 kcal/mol). In other words, the two extra β-hydrogens are responsible through their contribution to polarizability for the increased PA.

The calculated (eq 6) and experimental (in parentheses) PA values (in kcal/mol) of THP 200.2 (200.7) and its oxa analogues 1,4-dioxane 195.3 (194.1) and 1,3-dioxane 191.6 (199.2)[17] provide further insights. We note that the PA of THP and 1,4-dioxane are satisfactorily reproduced by our model. In 1,4-dioxane, the increased electronegativity due to the nonprotonated oxygen, as well as a decrease in polarizability resulting from replacement of CH_2 by O (cf. entries 15 and 19, Table I), leads to the observed decrease in PA compared with THP. Thus, we find no need to

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Table I. Experimental and Calculated Proton Affinity and *Acidity* Values and Molecular Parameters[a]

	molecule	q_0	$\bar{\chi}_{12}$	α_d	N_c	proton affinity/ *acidity*	
						exptl[b]	calcd[c]
1	H_2O	−0.411	5.267	0.789	2.000	173.0	175.4
			5.267	*0.394*	*1.000*	*390.8*	
2	MeOH	−0.398	5.120	2.143	3.500	184.9	185.3
			5.079	*1.779*	*2.500*	*379.2*	*378.3*
3	EtOH	−0.395	5.147	2.847	4.250	190.3	188.4
			5.124	*2.509*	*3.250*	*376.1*	*376.1*
4	*n*-Pr*OH*	−0.395	5.156	3.154	4.625	191.4	189.9
			5.140	*2.841*	*3.625*	*374.7*	*375.2*
5	*i*-Pr*OH*	−0.392	5.173	3.610	5.000	192.7	191.9
			5.169	*3.284*	*4.000*	*374.1*	*373.8*
6	*n*-BuOH	−0.395	5.158	3.230	4.813	192.0	190.2
			5.143	*2.941*		*373.7*	*374.9*
7	*t*-BuOH	−0.389	5.200	4.391	5.750	195.0	195.5
			5.214	*4.071*	*4.750*	*373.3*	*371.4*
8	CHF_2CH_2OH	−0.389	5.421	2.281	4.250	180.6	180.2
			5.548	*2.027*	*3.250*	*367.0*	*368.3*
9	CF_3CH_2OH	−0.386	5.572	2.208	4.250	174.9	176.9
			5.781	*1.976*	*3.250*	*364.4*	*363.6*
10	CF_3CH_2OEt	−0.371	5.470	4.159	6.500	187.6	189.0
11	$(CF_3)_2MeCOH$	−0.374	6.065	3.591	5.750	172.9	174.6
12	$(CF_3)_2CHOH$	−0.377	6.039	2.892	5.000	170.9	171.5
13	$(CF_3)_3COH$	−0.367	6.514	3.635	5.750	169.0	166.2
			7.256	*3.439*		*329 ± 5*	*330.9*
14	Me_2O	−0.386	5.094	3.557	5.000	193.1	193.2
15	1,4-dioxane	−0.375	5.309	4.765	6.500	194.1	195.3
16	EtOMe	−0.383	5.117	4.266	5.750	196.5	196.4
17	THF	−0.380	5.147	4.770	6.250	199.6	198.5
18	Et_2O	−0.380	5.141	5.018	6.500	200.4	199.9
19	THP	−0.380	5.159	5.141	6.750	200.7	200.2
20	*n*-Pr_2O	−0.380	5.156	5.683	7.250	202.9	203.0
21	2-MeTHF	−0.377	5.183	5.539	7.000	203.0	201.8
22	*i*-PrOEt	−0.377	5.164	5.788	7.250	203.4	203.4
23	*t*-BuOMe	−0.377	5.164	5.788	7.250	203.8	203.4
24	*n*-Bu_2O	−0.380	5.159	5.881	7.625	203.9	204.0
25	*n*-Pn_2O	−0.380	5.159	5.815	7.813	205.2	203.7
26	*i*-Pr_2O	−0.374	5.187	6.567	8.000	206.0	207.1
27	*t*-BuOEt	−0.374	5.187	6.567	8.000	206.0	207.1
28	*t*-BuO-*i*-Pr	−0.372	5.211	7.353	8.750	208.8	210.7
29	$MeOCH_2CH_2OH$	−0.393[d]	5.253	2.909		189.1	186.7
		−0.381[e]	5.200	4.161			194.3
			5.292	*2.630*		*372.5*	*372.4*
30	neo-PhOH	−0.395	5.175	3.932	5.375	194.0	193.5
			5.171	*3.644*	*4.375*	*371.8*	*373.1*
31	$PhCH_2OH$	−0.391	5.254	3.866	5.219	189.7	191.7
			5.261	*3.596*		*369.6*	*371.3*
32	*i*-BuOH	−0.395	5.166	3.529	5.000	192.9	191.6
			5.156	*3.231*	*4.000*	*373.4*	*374.1*
33	oxepane	−0.380	5.158	5.553		202.4	202.3
34	1,3-dioxane	−0.355	5.466	4.643		199.2	191.6
35	$MeOCH_2CH_2OMe$	−0.381	5.202	4.223		205.1	194.5
36	*t*-BuCH(Me)OH		*5.216*	*4.442*	*5.125*	*370.7*	*370.7*
37	*t*-BuCH(Et)OH		*5.232*	*4.863*	*5.500*	*369.6*	*369.6*
38	*t*-BuCH(*i*-Pr)OH		*5.247*	*5.292*	*5.875*	*368.5*	*368.5*
39	$(t\text{-}Bu)_2CHOH$		*5.263*	*5.726*	*6.250*	*367.3*	*367.4*
40	2-BuOH		*5.181*	*3.231*		*372.9*	*373.6*
41	1-PhOH		*5.143*	*2.908*		*372.8*	*375.0*
42	$(Me)_2CHC_2H_4OH$		*5.144*	*3.100*		*372.5*	*374.6*
43	1-$C_6H_{13}OH$		*5.143*	*2.803*		*372.2*	*375.2*
44	*i*-PrC_3H_6OH		*5.143*	*2.932*		*372.1*	*374.9*
45	$EtC(Me)_2OH$		*5.230*	*4.437*		*372.0*	*370.4*
46	*i*-PrCH(Me)OH		*5.201*	*4.031*		*372.0*	*371.8*
47	Et_2CHOH		*5.201*	*4.031*		*371.8*	*371.8*
48	1-$C_7H_{15}OH$		*5.143*	*2.662*		*371.6*	*375.4*
49	*t*-BuC_2H_4OH		*5.145*	*3.290*		*371.6*	*374.2*
50	*n*-$PrC(Me)_2OH$		*5.230*	*4.537*		*371.4*	*370.3*
51	$Et_2C(Me)OH$		*5.243*	*4.831*		*371.2*	*369.5*
52	1-$C_8H_{17}OH$		*5.143*	*2.509*		*371.1*	*375.7*
53	*n*-$BuC(Me)_2OH$		*5.230*	*4.479*		*370.9*	*370.4*
54	*i*-PrCH(Et)OH		*5.215*	*4.442*		*370.8*	*370.7*
55	1-$C_9H_{19}OH$		*5.143*	*2.353*		*370.6*	*376.0*
56	Et_3COH		*5.261*	*5.240*		*370.3*	*368.2*
57	$(i\text{-}Pr)_2CHOH$		*5.234*	*4.863*		*370.2*	*369.6*
58	CH_2FCH_2OH		*5.329*	*2.163*		*371 ± 2*	*372.5*
59	$(CH_2F)_2CHOH$		*5.583*	*2.796*		*366 ± 2*	*366.2*

[a] Entries 1–28 were included in the PA correlation analyses. Entries 29–35 were used for PA predictions (see text). Entries 2–5, 7–9, 30, 32, and 36–39 were included in the gas-phase acidity correlation analyses, with 1 as an additional point in the alkoxyl electron affinity correlation. Entries 6, 13, 29, 31, and 40–59 were predicted by eq 11. [b] Data taken from ref 7, 11, 12, 16–18, 24, and 25. [c] Proton affinity calculated from eq 6 and acidity calculated from eq 11. [d] Protonation at hydroxyl O atom. [e] Protonation at ether O atom.

Table II. Results of Correlation Analyses

entry	parameters	r^a	s^b
Proton Affinity of Alcohols and Ethers ($n^c = 28$)			
1	q_0	0.271	11.8
2	$\bar{\chi}_{12}$	0.745	8.2
3	α_d	0.846	6.5
4	N_c	0.759	8.0
5	$\bar{\alpha}$	0.671	9.1
6	q_0, α_d	0.958	3.6
7	$\bar{\chi}_{12}$, α_d	0.994	1.4
8	$\bar{\chi}_{12}$, N_c	0.989	1.8
9	$\bar{\chi}_{12}$, $\bar{\alpha}$	0.941	4.2
Proton Affinity of Thiols and Thioethers ($n = 12$)			
10	α_d	0.947	3.4
11	N_c	0.956	3.1
12	$\bar{\chi}_{12}$, α_d	0.993	1.1
13	$\bar{\chi}_{12}$, N_c	0.994	1.1
Gas-Phase Acidity of Alcohols ($n = 13$)			
14	q_H	0.602	3.3
15	$\bar{\chi}_{12}$	0.805	2.5
16	α_d	0.324	3.9
17	N_c	0.443	3.4
18	$\bar{\chi}_{12}$, α_d	0.978	0.9
19	$\bar{\chi}_{12}$, N_c	0.981	0.9
Gas-Phase Acidity of Alcohols Including H_2O ($n = 14$) (Electron Affinity of RO· Radicals)			
20	$\bar{\chi}_{12}$	0.734	2.9
21	α_d	0.469	3.8
22	N_c	0.556	3.5
23	$\bar{\chi}_{12}$, α_d	0.981	0.8
24	$\bar{\chi}_{12}$, N_c	0.978	0.9

[a] (Multiple) regression coefficient. [b] Standard deviation in kcal/mol. [c] Number of compounds in data set.

invoke "special factors"[17] or conformational effects[18] to explain this difference. However, we do believe that there is an additional feature present in 1,3-dioxane which is not accounted for by our topological model and which is responsible for the anomalously high PA of this molecule. Intuitively, one would expect that the increased electronegativity due to the nonprotonated oxygen atom (one bond closer to the formal positive charge than in 1,4-dioxane), as well as the decreased effective polarizability, would both lead to decreased PA, as is in fact suggested by eq 6. Dipole interactions between the O^+–H bond and the free electron pair on the other oxygen, when both are axially oriented, could be responsible for the increased stabilization of the protonated form of 1,3-dioxane as against that of 1,4-dioxane.

The PA's of the sequence EtOH, F_2CHCH_2OH, F_3CCH_2OH are well reproduced, the observed decrease in this case being mostly due to increased residual electronegativities.[19] Table III gives a quantitative analysis of the changes in the electronegativity and polarizability contributions in going from EtOH to F_2CHCH_2OH and F_3CCH_2OH (negative values correspond to decreased PA, i.e., destabilization of the protonated form). The two formulas for calculating effective polarizabilities (eq 4 and 5) give different amounts of polarizability contributions for the two fluoroalcohols. While *mean molecular polarizabilities* change little when substituting F for H, the *polarizability effect* of fluorine in situations such as that discussed here is less clear. The only comparable study of which we are aware is that of ref 7. The polarizability effect contributions, *P*, derived by Taft and co-workers[7b] are 3.9 for CH_3CH_2, 4.1 for F_2CHCH_2, and 2.6 for F_3CCH_2. Thus the effect of substitution of F for H is somewhat erratic, leading in F_3CCH_2 to an apparent decrease in the polarizability effect contribution, as also obtained, in our case, with eq 4. In the absence of further experimental data on the PA of fluorinated alcohols and ethers, a final decision between the two models for calculating effective polarizabilities for compounds containing fluorine has to be postponed. In any case the differences are rather small.

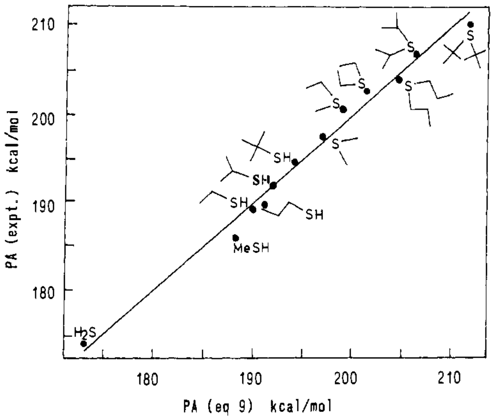

Figure 3. Experimental proton affinities of hydrogen sulfide, thiols, and thioethers plotted against values calculated by eq 9 ($n = 12$, $r = 0.993$, $s = 1.1$ kcal/mol).

On the other hand, the electronegativity and polarizability effects' contributions to PA on successive replacement of H by CH_3 in the β-position of EtOH for the two different models expressed with eq 6 and 7 are in good agreement (see Table III; note that the PA's for isobutyl alcohol and neopentyl alcohol are predicted values). The electronegativity contribution to PA is relatively minor in unsubstituted alkyl derivatives (i.e., where heteroatoms are absent), implying that α_d or N_c alone should correlate with PA in this restricted series. In fact, such a correlation is observed to hold for alcohols and ethers ($r = 0.990$; $s = 0.94$ kcal/mol for α_d; $r = 0.994$, $s = 0.71$ kcal/mol for N_c). Inclusion of the $\bar{\chi}_{12}$ electronegativity term with either the α_d or the N_c polarizability parameter for this restricted series of unsubstituted alcohols and ethers gave no statistical improvement in the correlation, as judged by Ehrenson's $\mathscr{f}$-statistic test.[21]

The usefulness of the expressions can be further tested through their ability to predict PA's of molecules. Several such examples not included in the compilations of data originally used for the MLR analyses are available.[7a,17,18] Thus the PA value calculated from eq 6 (experimental value), for isobutyl alcohol is 191.6 kcal/mol (192.9)[7a], that for neopentyl alcohol is 193.5 (194.0),[7a] that for benzyl alcohol is 191.7 (189.7),[7a] and that for oxepane is 202.3 (202.4).[17] Values for other molecules are less well reproduced, but for clearly understood reasons. Thus, the PA of 1,2-dimethoxyethane is calculated to be only 194.5 kcal/mol compared with the experimental value of 205.1 kcal/mol.[17,18] The difference of about 10.5 kcal/mol is undoubtedly due to increased stabilization originating from an intramolecular hydrogen bond, and this value is situated between previous estimates for H bond stabilization of 7 and 12.7 kcal/mol.[17,18] Similarly, the calculated PA value for hydroxyl protonation of 2-methoxyethanol (186.7

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(18) Sharma, R. B.; Blades, A. T.; Kebarle, P. *J. Am. Chem. Soc.* **1984**, *106*, 510–516.

(19) There could be also some form of weak intramolecular interaction between OH and remote fluorine atoms in the fluoro alcohols. It is more likely electrostatic in nature (dipole–dipole), rather than a formal H bond. Since its value is very low,[20] and since moreover protonation should only slightly increase its value, we have made no allowance for its effect in developing the models.

(20) (a) Krueger, R. J.; Mettee, H. D. *Can. J. Chem.* **1964**, *42*, 340–346. (b) Perttilä, M. *Spectrochim. Acta, Part A* **1979**, *35A*, 585–592 and previous papers from this author. (c) Kalasinsky, V. F.; Anjaria, H. V. *J. Phys. Chem.* **1980**, *84*, 1940–1944.

(21) Ehrenson, S. *J. Org. Chem.* **1979**, *44*, 1793–1797.

Table III. Electronegativity and Polarizability Effects' Contributions to Proton Affinity and Acidity of Alcohols Derived from Ethanol[a]

	proton affinity				acidity			
	$\Delta PA(\bar{\chi}_{12})$		$\Delta PA(\alpha_d)$	$\Delta PA(N_c)$	$\Delta\Delta H_r(\bar{\chi}_{12})$		$\Delta\Delta H_r(\alpha_d)$	$\Delta\Delta H_r(N_c)$
alcohol	eq 6	eq 7	eq 6	eq 7	eq 11	eq 12	eq 11	eq 12
F_2CHCH_2OH	-5.3	-6.2	-3.0	0.0	-8.7	-8.0	0.9	0.0
F_3CCH_2OH	-8.2	-9.7	-3.3	0.0	-13.4	-12.4	1.0	0.0
$CH_3CH_2CH_2OH$	-0.2	-0.2	1.6	1.9	-0.3	-0.3	-0.6	-0.8
$(CH_3)_2CHCH_2OH$	-0.4	-0.4	3.6	3.8	-0.7	-0.6	-1.3	-1.5
$(CH_3)_3CCH_2OH$	-0.5	-0.6	5.7	5.7	-1.0	-0.9	-2.0	-2.3

[a] In kcal/mol; values give the difference of the product of the regression coefficient with the appropriate parameter for the alcohol under consideration and that of ethanol, e.g., $\Delta PA(\bar{\chi}_{12})(\text{eq } 6)(F_2CHCH_2OH - CH_3CH_2OH) = -19.29(5.421 - 5.147)$.

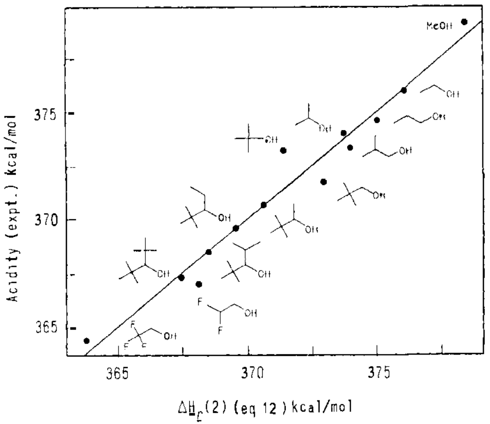
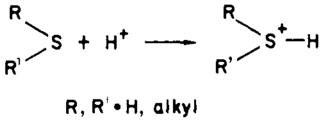


Figure 4. Experimental gas-phase acidity data (enthalpies of eq 2) of alcohols plotted against values calculated by eq 12 ($n = 13$, $r = 0.978$, $s = 0.9$ kcal/mol).

kcal/mol) is 2.4 kcal/mol less than that which can be derived by extrapolation from experimental results.[7a,22] Here, protonation only serves to increase the strength of the H bond already present in the neutral molecule.

Proton Affinity of Thiols and Thioethers. The generality of the models and parameters outlined above is extended by their application to the PA of a series of 12 sulfur analogues (eq 8).



(8)

Again, the best results were obtained with a two-parameter equation based on $\bar{\chi}_{12}$ and either α_d or N_c (eq 9 and 10 and Figure 3). The data for thiols, thioethers, and H_2S are all included in

$$PA = 802.1 - 130.62\bar{\chi}_{12} + 7.21\alpha_d \tag{9}$$

$$PA = 701.4 - 111.51\bar{\chi}_{12} + 6.74N_c \tag{10}$$

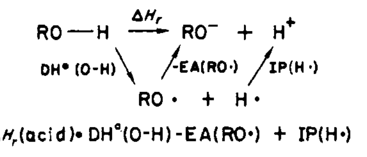
the same model, again establishing the well-balanced nature of our approach.

Gas-Phase Acidity of Alcohols. Since increased alkyl substitution leads to both higher PA and increased gas-phase acidity, it was of interest to investigate the applicability of our empirical models to the latter (eq 2). In the first instance, data for 13 alcohols were analyzed by MLR with use of various parameters (Table I). Statistical results are recorded in Table II. The best correlations found are given by eq 11 and 12 (Table II, entries 18 and 19; Figure 4).

$$\Delta H_r(2)(\text{calcd}) = 485.2 - 20.41\bar{\chi}_{12} - 1.80\alpha_d \tag{11}$$

$$\Delta H_r(2)(\text{calcd}) = 479.4 - 18.87\bar{\chi}_{12} - 2.01N_c \tag{12}$$

Scheme I



The same parameters are involved here as in the PA studies. However, the picture which now emerges is that both increased residual electronegativity and increased effective polarizability act to stabilize the negative alkoxide charge, consistent with the physical interpretation. (Recall, increased acidity implies decreased $\Delta H_r(2)$ values, hence the negative signs of the coefficients in eq 11 and 12.) Depending on the types of compounds, either of these sources of stabilization can predominate. For instance, the difference between *i*-PrOH and di-*t*-butylcarbinol ($\Delta\Delta H_r(12) = 6.4$ kcal/mol, $\Delta\Delta H_r(\text{exptl}) = 6.8$ kcal/mol) is due in the main to the polarizability contribution of the six additional β-methyl groups (4.4 kcal/mol). Table III gives the changes in the electronegativity and polarizability contributions to the acidities in replacing H by F or CH_3 in ethanol (negative values correspond to decreased values of $\Delta H_r(2)$, i.e., stabilization of the anion). Clearly, fluorine drastically increases the acidity through its electronegativity effect.[23] Compared with ethanol, extra stabilization of 8.7 kcal/mol is calculated from this source for F_2CHCH_2OH as against an overall experimental increment of 9.1 kcal/mol. For the fluorine compounds the two models (eq 11 and 12) give different polarizability contributions to the acidity (as is the case with PA), but the differences are only small even in the presence of three fluorine atoms. Substitution of CH_3 for H increases the acidity and electronegativity and polarizability effects, both leading to increased anion stabilization.

Since the completion of the acidity study new data have been published for 19 unsubstituted alcohols.[24] The empirical models are able to reproduce these values satisfactorily, with the exception of derivatives containing longer alkyl chains (Table I). It appears that in these cases the calculated substituent polarizability contributions are underestimated, and thus are failing to account for the continuing increase in PA as the chain length increases. It has been suggested[11a,c] that this phenomenon is due to the alkyl chain undergoing coiling, bringing potentially remote parts of the group nearer to the charge center, and thus increasing polarizability-derived stabilization. Our models make no allowance for this effect.

Additional, less precise data are available for some substituted alcohols.[25] With use of eq 11, the $\Delta H_r(2)$ value for 2-fluoroethanol was calculated to be 372.5 kcal/mol (compared with an experimental value of 371 ± 2 kcal/mol), for 1,3-difluoro-2-propanol 366.2 (366 ± 2), and for perfluoro-*tert*-butyl alcohol 330.9 (329 ± 5). Agreement with experiment is good, notably so for the latter molecule which involves an appreciable extrap-

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[22] The experimental PA value for 2-methoxyethanol is derived from the corresponding ΔG value assuming $T\Delta S$ typical for such intramolecularly H bonded systems. However, the ΔG term itself was derived by extrapolation,[7a] and it is not clear which system was used for the extrapolation and what allowance was made for intramolecular H bonding. Therefore, the value of 2.4 kcal/mol for the extra stabilization may not be quantitatively precise.

[23] Again we have made no allowance for the low intramolecular interaction between the OH bond and the remote fluorine atoms which might be present in the fluoro alcohols (cf. ref 19 and 20).

[24] Boand, G.; Houriet, R.; Gäumann, T. *J. Am. Chem. Soc.* **1983**, *105*, 2203–2206.

[25] Clair, R. L.; McMahon, T. B. *Int. J. Mass Spectrom. Ion Phys.* **1980**, *33*, 21–36.

olation beyond the data used to derive the model represented by eq 11.

The acidity of 2-methoxyethanol is calculated from eq 11 to be 372.4 kcal/mol, in remarkably good agreement with the experimental value of 372.5 kcal/mol,[12] despite the fact that no allowance has been made for the additional stabilization undoubtedly present in this molecule resulting from an intramolecular H bond.[26]

Water itself is anomalous in that it deviates markedly from the correlation defined by alcohols. This probably results from the exceptionally high O–H bond-dissociation energy of water (119 kcal/mol compared with about 104 kcal/mol for alcohols). The energy associated with the ionization can be viewed as a composite of terms, as shown in the thermochemical cycle of Scheme I. Allowance was made for this value, as well as for the slightly different DH° values of the other alcohols in so far as they are known,[12] by studying the term ΔH_r(acid) – DH°(O–H) (=IP(H·) – EA(RO·)).

It was now found that a perfectly satisfactory correlation could be derived ($r = 0.982$, $s = 0.83$ kcal/mol). This not only included water but also brought other alcohols which previously deviated slightly from the correlation into better alignment (e.g., *t*-BuOH, neopentyl alcohol). Since the ionization potential of the hydrogen atom, IP(H·), is constant for the molecules in the series, the implication is that residual electronegativity and effective polarizability are together describing alkoxyl electron affinity rather better than acidity itself.[30]

PA can also be factored into an analogous thermochemical cycle, but in this case it appears that the DH°(OH) values are sufficiently constant throughout the series (or at least show a sufficiently regular trend) that no allowance for them is necessary in the analyses.

Comparison of the values for the changes in polarizability effect contributions to PA and acidity in Table III reveals an interesting point: proton affinity is more than two and a half times as sensitive to a given change in polarizability as acidity. Naive application of the classical electrostatic eq 3 would suggest equal contributions in each system. However, as we have already outlined, there are several complicating features to the quantification of polarizability influences when the charged center and polarizable moiety are part of the same molecule, and there is no reason to believe the situations in cation and anion stabilization should be the same.

Taft and co-workers had previously made the simplifying assumption that the polarizability effect would be approximately equal for gas-phase protonation and deprotonation of alcohols.[7a] More recent work by this group has led them to the same conclusions as above: PA is more sensitive than acidity to polarizability.[7b,31] By a fundamentally different approach from our own, new polarizability effect contributions (analogous to substituent constants) were derived.[7] These values correlate reasonably well with the calculated α_d and N_c contributions ($n = 11$, $r = 0.91$, $s = 1.17\alpha_d$ units; $n = 11$; $r = 0.97$; $s = 0.65N_c$ units). However, the ease with which α_d (or N_c) may be calculated and the fact that it is not derived from previously available experimental data renders it suitable for prediction of unknown data.

Conclusion

Starting from atomic properties (valence-state orbital electronegativities or hybridization-state polarizability contributions), the procedures for calculating residual electronegativities and effective polarizability both work through the topology of a molecule, the network of bonds. Thus, values are obtained that reflect both the atomic composition and molecular structure. It has been shown here that these values can be used to quantify reactivity data on fundamental heterolytic processes: the uptake of a proton and the loss of a proton. The present approach raises the attractive proposition of deriving directly thermodynamic and reactivity data without recourse to substituent constants, using quantitative data related to concepts familiar to the organic chemist which can now be calculated rapidly and easily for each individual species.

Acknowledgment. Financial support by ICI Plc, England, and computation time by Leibniz Rechenzentrum, Munich, are gratefully acknowledged. We thank Prof. R. W. Taft for communicating results prior to publication and a referee for illuminating comments.

Registry No. 1, 7732-18-5; **2**, 67-56-1; **3**, 64-17-5; **4**, 71-23-8; **5**, 67-63-0; **6**, 71-36-3; **7**, 75-65-0; **8**, 359-13-7; **9**, 75-89-8; **10**, 461-24-5; **11**, 1515-14-6; **12**, 920-66-1; **13**, 2378-02-1; **14**, 115-10-6; **15**, 123-91-1; **16**, 540-67-0; **17**, 109-99-9; **18**, 60-29-7; **19**, 142-68-7; **20**, 111-43-3; **21**, 96-47-9; **22**, 625-54-7; **23**, 1634-04-4; **24**, 142-96-1; **25**, 693-65-2; **26**, 108-20-3; **27**, 637-92-3; **28**, 17348-59-3; **29**, 109-86-4; **30**, 75-84-3; **31**, 100-51-6; **32**, 78-83-1; **33**, 592-90-5; **34**, 505-22-6; **35**, 110-71-4; **36**, 464-07-3; **37**, 3970-62-5; **38**, 5162-48-1; **39**, 14609-79-1; **40**, 78-92-2; **41**, 71-41-0; **42**, 123-51-3; **43**, 111-27-3; **44**, 626-89-1; 45, 75-85-4; **46**, 598-75-4; **47**, 584-02-1; **48**, 111-70-6; **49**, 624-95-3; **50**, 590-36-3; **51**, 77-74-7; **52**, 111-87-5; **53**, 625-23-0; **54**, 565-67-3; **55**, 143-08-8; **56**, 597-49-9; **57**, 600-36-2; **58**, 371-62-0; **59**, 453-13-4; H^+, 12408-02-5.

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(26) It is not clear if any allowance has been made for intramolecular H bonding in calculating the $\Delta H_r(2)$ acidity value for $MeOCH_2CH_2OH$ from the corresponding measured ΔG value.[12] Intramolecularly H bonded $MeOCH_2CH_2OH$ is favored over other conformations by quantities variously estimated at 1,[27] 1.8,[28] and 3 kcal/mol.[29]

(27) Caminati, W.; Wilson, E. B. *J. Mol. Spectrosc.* **1980**, *81*, 356–372.

(28) Buckley, P.; Brochu, M. *Can. J. Chem.* **1972**, *50*, 1149–1156.

(29) Prabhumirashi, L. S. *J. Chem. Soc., Faraday Trans. 2* **1978**, *74*, 1567–1572.

(30) The correlation with alkoxyl electron affinity circumvents any interference of H bonding, as these effects cancel in the term ΔH_r(acid) – DH°(O–H).

(31) Taft, R. W., personal communication.