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INFLUENCE OF INDUCTIVE EFFECTS AND POLARIZABILITY ON THE ACID–BASE PROPERTIES OF ALKYL COMPOUNDS. INVERSION OF THE ALCOHOL ACIDITY SCALE

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The inductive effects and polarizability of a series of 17 alkyl substituents were evaluated in theoretical terms from *ab initio* calculations for acid–base processes involving the corresponding alkanols. The effects allow one to account for general acid–base processes, both in the gas phase and in solution. Also, the classical inductive effect accounts for the acidity of dissolved alkanols and hence provides a straightforward explanation for the well known acidity inversion in alkanols from the gas phase to a solution. The applicability of the derived *I* and *P* values for the alkyl groups to the protonation of amines, nitriles, ethers and thiols is shown.

INTRODUCTION

Establishing relationships between structure and reactivity continues to be a central goal of physical organic chemistry and probably the best approach to developing models for rationalizing compound properties. The information most frequently used for this purpose is usually related to acid or base properties of the structures considered, mostly because of the success achieved *ca* 50 years ago with the Hammett,[1] Branch–Calvin[2] [1], and Ingold–Taft[3] techniques as applied to structural effects.

Let us concentrate on the analysis of the acid properties of unsubstituted alkanols. The fact that the acidity of these compounds in aqueous solutions decreases with increasing size and branching of their alkyl chain [pK_a(MeOH) < pK_a(EtOH) < pK_a(PrOH) < pK_a(*i*-PrOH) < pK_a(*t*-BuOH)] has traditionally been ascribed to the increase in the electron-releasing ability of an alkyl group with increase in its size and degree of branching. However, experiments on gas-phase alkanols conducted by Brauman and Blair[4,5] showed that the situation was inverted: contrary to the expectations, the larger and more branched the alkanol, the greater was its acidity. This finding was elegantly accounted for by these authors, who ascribed it to a polarizability effect. The stabilizing effect involved can be expressed in mathematical terms as

$$E = \alpha q^2/3\varepsilon r^4$$

where α denotes the polarizability, ε the dielectric constant, q the charge and r the distance between the polarizable group and the charge site. According to Taft *et al.*,[6] the situation in solution is different: the above-described polarizability effect is insignificant because the charge on the oxygen atom of the alkoxy anion disperses in the solvent via hydrogen bonds.

While specific solvation of charged forms in other compound families plays a prominent role in explanations for the changes in acid–base properties from the gas phase to solutions,[7,8] the effect in alkanols is not strong enough to account by itself for the above-mentioned acidity inversion from the gas phase to aqueous solution.

More recently, Tuñon *et al.*[9] carried out a theoretical study of the acidity inversion by using four alkanols (MeOH, EtOH; *i*-PrOH and *t*-BuOH). They developed a model based on the assumption that the charges obtained from a Mulliken population analysis for the CO group of alkoxy anions in these compounds decrease gradually with increasing size and branching of the alkyl chain. If the charge lost by the C-O group is delocalized throughout the rest of the allyl group, then the alkoxy anion will be stabilized to an extent increasing with increasing amount of delocalized charge and

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hence with the size and degree of branching of the alkyl group. The opposite situation must prevail in solution since the more charge is delocalized over the alkyl group, the less charge will be localized in the CO group and hence the less solvatable will be the compound. As a result, the stabilizing effect on alkoxy anions of interactions with the solvent will be much smaller. Based on the previous reasoning, Tuñon *et al.*[9] suggested that, because both terms are related to molecular size, their explanation could be generalized. Let us consider the following equilibrium to illustrate this point:

$$AH \rightleftharpoons A^- + H^+$$

In vacuo, because the molecular size of the compound is increased with each methyl group introduced, the equilibrium will be displaced to the right on each addition. In solution, the electrostatic stabilization decreases with increasing size, thereby favouring a displacement to the left. A balance between these two opposing trends determines the final acidity (or basicity) sequence in solution.

The above-described model does not seem appropriate here, since (a) it uses the solvated CO group as the active site given an unusual role to the carbon atom, (b) it ignores the polarizability effects of alkyl groups, which has proved vital for justifying a number of chemical facts related to acid-base properties in both the gas phase and solution, and (c) the generalization is somewhat dangerous since, for example, the equilibrium

$$RCH_2OH_{(g)} + (CH_3)_3CO^-{}_{(g)} \rightleftharpoons RCH_2O^-{}_{(g)} + (CH_3)_3COH_{(g)}$$

should be displaced to the right to an extent proportional to the molecular volume (i.e. in the R sequence *n*-butyl > *n*-pentyl > *n*-hexyl, *etc.*).

It should be noted that the above-mentioned inversion of alkanol acidity from the gas phase to an aqueous solution also takes place in switching to *i*-PrOH[10] and DMSO solutions.[11]

In this work, we aimed to provide a sound explanation not only for the acidity inversion in alkanols from the gas phase to solution, but also for the general acid–base properties of this type of compound. For this purpose, we started from an idea originally put forward by Taft *et al.*[6] and used alkyl substituents giving no solvated active sites but resulting in major changes in the acid–base properties of the corresponding alkanol. In this respect, alkyl groups bearing halogen substituents was the best choices. This paper analyses theoretically 17 alcohols encompassing an acidity range of 11 pK_a units in an aqueous solution, 21·5 pK_a units in DMSO solution and 44 kcal mol^{-1} in the gas phase. It also establishes theoretically the intrinsic inductive effects and polarizability of the different alkyl groups considered.

THEORETICAL CALCULATIONS

All computations were carried out by using a standard version of the program Gaussian 92[12] at the Hartree–Fock level with the 6–31G** polarization basis set. Neither diffuse functions nor electronic correlation effects were taken into account in these calculations. Geometries were fully optimized using Berny's algorithm[13] (an extended geometry was adopted for *n*-alkanols in order to avoid potential cyclization and coiling effects[14]). From the optimized geometries, the zero-point vibrational energy (ZPVE), the thermal energy ($H - H°$) and entropy contributions were calculated by using vibrational frequencies scaled by a factor of 0·89.[15]

Table 1 gives the total energies, ZPVE, $H - H°$ and S values for the 17 alcohols, alkoxy anions and alkoxy cations studied. The geometries derived for the molecular structures can be obtained from the authors on request.

RESULTS AND DISCUSSION

Table 2 shows the theoretical basicity (I) and acidity (II) $\Delta H°$ and $\Delta G°$ values of alkanols calculated from the data in Table 1 and their experimental counterparts in the gas phase and in aqueous and DMSO solution.

$$ROH_2^+ \rightleftharpoons ROH + H^+ \quad \text{(I)}$$

$$ROH \rightleftharpoons RO^- + H^+ \quad \text{(II)}$$

The theoretical data on ΔG and ΔH for processes (I) and (II) as a function of their corresponding experimental data in gas phase are shown is Figures 1–4. The agreement between this set of experimental and theoretical data is sufficiently good for supporting the reliability of the calculated values [ΔG(I) ($n = 11$, $r = 0{\cdot}984$ and s.d. = 2·6 kcal mol^{-1}), ΔH(I) ($n = 11$, $r = 0{\cdot}978$ and s.d. = 32·4 kcal mol^{-1}), ΔG(II) ($n = 14$, $r = 0{\cdot}995$ and s.d. = 1·7 kcal mol^{-1}) and ΔH(II) ($n = 14$, $r = 0{\cdot}995$ and s.d. = 1·8 kcal mol^{-1}).

Figures 5 and 6 show the theoretical ΔG (II) values for the isolated molecules (*i.e.* the gas-phase acidity) as a function of the ΔG values for the acidity in aqueous and DMSO solutions, respectively. As can be clearly seen in both figures, there is a linear correlation between the data for the gas phase and solution; also, the trend is inverted for unsubstituted alkanols.

Alcohols are among the compound families that lend themselves readily to the evaluation of the inductive and polarizability effects of an alkyl group. According to Taft *et al.*,[6] the free energy for a basic (III) and acid equilibrium (IV):

$$ROH_{(g)} + CH_3OH_{2(g)}^+ \rightleftharpoons ROH_{2(g)}^+ + CH_3OH_{(g)} \quad \text{(III)}$$

$$ROH_{(g)} + CH_3O_{(g)}^- \rightleftharpoons RO_{(g)}^- + CH_3OH_{(g)} \quad \text{(IV)}$$

reflect the fact that the polarizability effect (P) for R relative to CH_3 arises from the greater charge-induced

Table 1. Energies (E_T), zero-point vibrational energies (ZPVE), thermal correction ($H - H°$) and entropy contributions (S) for the neutral, protonated and deprotonated forms of alcohols studied

Alcohol	E_T (kcal mol^{-1})	ZPVE (kcal mol^{-1})	$H - H°$ (kcal mol^{-1})	S (cal mol^{-1} K^{-1})
MeOH	−72193·0	34·6	36·6	56·6
$MeOH_2^+$	−72386·9	41·8	44·2	59·7
MeO^-	−71780·6	23·9	25·7	54·8
EtOH	−96693·0	53·8	56·3	63·8
$EtOH_2^+$	−96892·9	61·8	64·7	65·9
EtO^-	−96283·7	43·3	45·6	62·0
n-PrOH	−121189·7	72·9	76·2	71·2
n-$PrOH_2^+$	−121391·0	81·0	84·7	73·4
n-PrO^-	−120781·4	62·3	65·4	69·6
n-BuOH	−145686·2	91·9	96·0	78·5
n-$BuOH_2^-$	−145888·4	100·1	104·5	80·8
n-BuO^-	−145278·2	81·3	85·2	77·0
n-PentOH	−170182·8	111·0	115·9	85·8
n-$PentOH_2^+$	−170385·4	119·1	124·4	88·1
n-$PentO^-$	−169775·0	100·3	105·0	84·3
n-HexOH	−194679·4	130·0	135·7	93·1
n-$HexOH_2^+$	−194882·2	138·2	144·2	95·4
n-$HexO^-$	−194271·7	119·3	124·8	91·6
n-HeptOH	−219175·9	149·0	155·5	100·4
n-$HeptOH_2^+$	−219378·9	157·2	164·0	102·8
n-$HeptO^-$	−218768·3	138·3	144·6	98·9
i-PrOH	−121192·9	72·5	75·7	70·1
i-$PrOH_2^+$	−121396·8	80·2	83·9	72·9
i-PrO^-	−120785·5	62·0	65·1	68·6
t-BuOH	−145691·6	90·9	94·9	75·6
t-$BuOH_2^+$	−145899·8	98·2	102·8	79·5
t-BuO^-	−145285·7	80·5	84·3	74·5
2FEtOH	−158718·3	49·5	52·4	68·8
$2FEtOH_2^+$	−158916·0	58·1	61·0	68·7
$2FEtO^-$	−158317·0	39·1	41·7	67·0
2ClEtOH	−384655·8	48·4	51·4	71·2
$2ClEtOH_2^+$	−384850·7	56·8	59·9	71·6
$2ClEtO^-$	−384259·8	38·1	40·8	69·9
2,2FEtOH	−220756·7	44·7	47·9	72·9
$2,2FEtOH_2^+$	−220944·6	53·1	56·4	73·2
$2,2FEtO^-$	−220363·9	34·7	37·6	70·9
2,2ClEtOH	−672616·2	42·6	46·1	76·9
$2,2ClEtOH_2^+$	−672802·8	50·5	54·2	78·5
$2,2ClEtO^-$	−672230·6	32·3	35·7	76·5
2,2,2FEtOH	−282801·9	39·5	42·9	75·4
$2,2,2FEtOH_2^+$	−282981·3	47·4	51·2	77·2
$2,2,2FEtO^-$	−282412·7	29·4	32·6	74·0
2,2,2ClEtOH	−960570·2	35·9	40·0	82·3
$2,2,2ClEtOH_2^+$	−960751·5	43·7	48·1	84·4
$2,2,2,ClEtO^-$	−960189·5	25·7	29·7	82·1
$(CF_3)_2CHOH$	−493402·2	43·1	48·5	93·1
$(CF_3)_2CH0H_2^+$	−493572·4	51·2	56·8	94·3
$(CF_3)_2CHO^-$	−493032·6	33·6	38·7	92·0
$(CF_3)_3COH$	−703996·5	46·5	53·8	107·2
$(CF_3)_3COH_2^+$	−704157·8	54·3	61·9	109·2
$(CF_3)_3CO^-$	−703642·8	37·1	44·3	106·6

Table 2. ΔH(I), ΔG(I), ΔH(II) and ΔG(II) (calculated)[a] and experimental phase-gas[b] and $\Delta G^{exp}{}_{(water)}$(II) and $\Delta G^{exp}{}_{(DMSO)}$ (experimental) for processes I (basic) and II (acid) of the alcohols studied (all values in kcal mol^{-1})

	$ROH_2^+ \rightleftharpoons ROH + MH^+$				$ROH \rightleftharpoons RO^- + H^+$					
Alcohol	ΔH^{theor}	ΔG^{theor}	$\Delta H^{exp}{}_{(gas)}$	$\Delta G^{exp}{}_{(gas)}$	ΔH^{theor}	ΔG^{theor}	$\Delta H^{exp}{}_{(gas)}$	$\Delta G^{exp}{}_{(gas)}$	$\Delta G^{exp}{}_{(W)}$	$\Delta G^{exp}{}_{(DMSO)}$[h]
MeOH	186·4	179·5	181·9	174·1	401·4	394·2	380·5	374·0	20·84[c]	−20·82
EtOH	191·5	184·4	188·3	180·2	398·7	391·5	377·4	370·7	21·71[c]	−22·33
n-PrOH	192·8	185·7	190·8	183·0	397·5	390·2	375·9	369·5	22·06[d]	
n-BuOH	193·8	186·8	191·1	183·3	397·1	389·8	375·5	368·4	22·06[d]	
n-PentOH	194·1	187·0			396·9	389·6	373·8	367·3		
n-HexOH	194·3	187·2			396·8	389·5	373·1	366·4		
n-HepOH	194·5	187·5			396·7	389·4	37Z·6	365·9		
i-PrOH	195·7	188·8	191·2	183·4	396·8	389·4	375·4	368·8	22·58[c]	−23·02
t-BuOH	200·3	193·7	193·7	185·9	395·3	387·8	374·5	368·0	22·66[c]	−26·44
2FEtOH	189·1	181·3			390·6	383·4	370·0	363·5		
2ClEtOH	185·6	178·0			385·4	378·0			19·59[e]	
2,2FEtOH	179·4	171·7	176·2	168·4	382·5	375·3	366·4	359·2	18·2[f]	
2,2ClEtOH	178·5	171·2			375·2	376·6			17·66[e]	
*t*FEtOH	171·1	163·9	169·0	161·2	378·9	371·6	361·8	354·2	16·99[d]	−9·18
*t*ClEtOH	173·2	166·1	177·4	169·6	370·4	362·7			16·67[d]	
*h*F*i*PrOH	161·9	154·5	165·0	157·2	359·8	352·4	344·9	338·2	12·74[g]	
*p*F*t*BuOH	153·2	146·0	163·1	155·3	344·2	336·6	331·7	324·1	7·12[g]	13·29
H_2O		165·5[i]				403·3[i]				

[a] The ΔG^{theor} evaluation included the entropy term for a free proton from the Sakur–Tetrode equation.
[b] Values taken from Ref 16.
[c] Values taken from Ref. 17.
[d] Values taken from Ref 18.
[e] Value taken from Ref. 19.
[f] Values taken from Ref. 20.
[g] Values taken from Ref. 21.
[h] Values taken from Ref. 11.

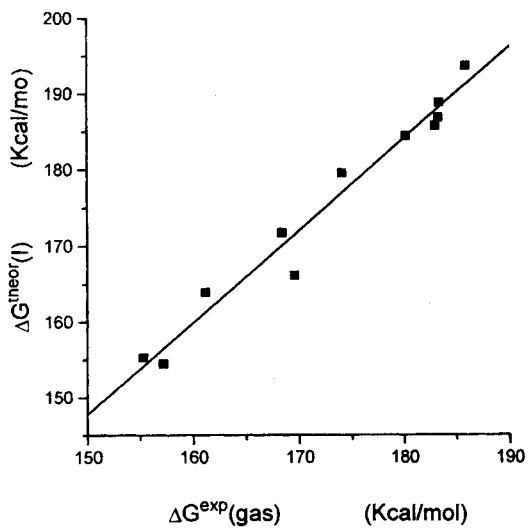

Figure 1. Plot of the theoretical free energy of acid dissociation of the protonated form against its gas-phase counterpart

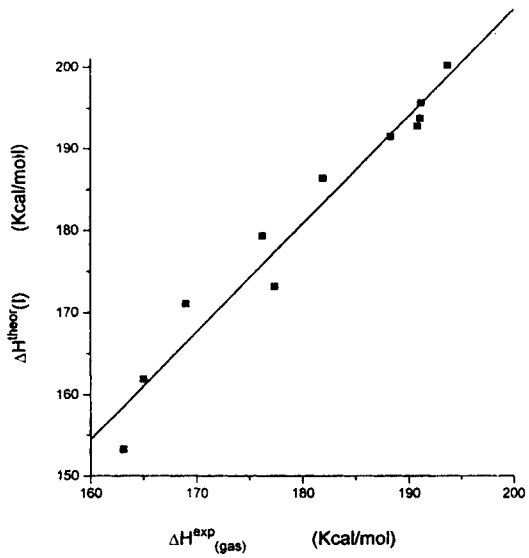

Figure 2. Plot of the theoretical enthalpy of acid dissociation of the protonated form against its gas phase counterpart

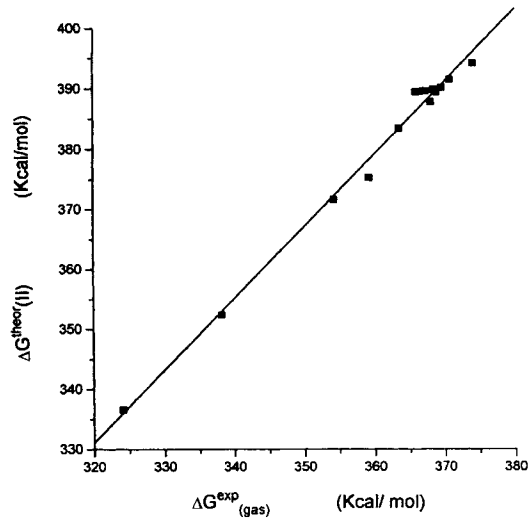

Figure 3. Plot of the theoretical free energy of acid dissociation against its gas phase counter part

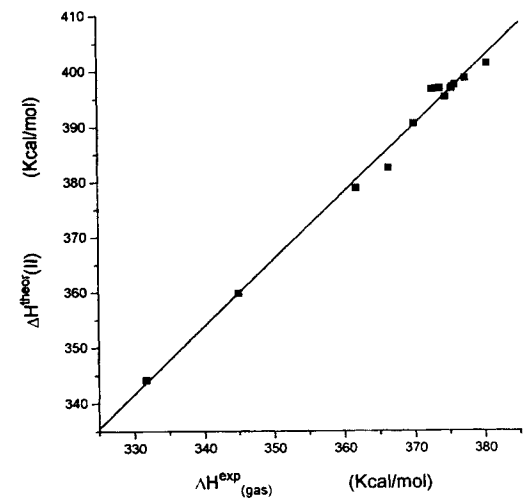

Figure 4. Plot of the theoretical enthalpy of acid dissociation against its gas phase counterpart

dipole stabilization of either the cation or the anion (i.e. ROH_2^+ relative to $CH_3OH_2^+$ and RO^- relative to CH_3O^-). An inductive electron-releasing effect of R (I) will stabilize ROH_2^+ relative to $CH_3OH_2^+$, but will destabilize RO^- relative to CH_3O^-. Therefore, one can initially write $-\Delta G(\mathrm{III}) \approx I + P$ and $-\Delta G(\mathrm{IV}) \approx -I + P$. Consequently, I can be evaluated from $[-\Delta G(\mathrm{III}) + \Delta G(\mathrm{IV})]/2$, and then P can be calculated from the free energies of process (III) or (IV).

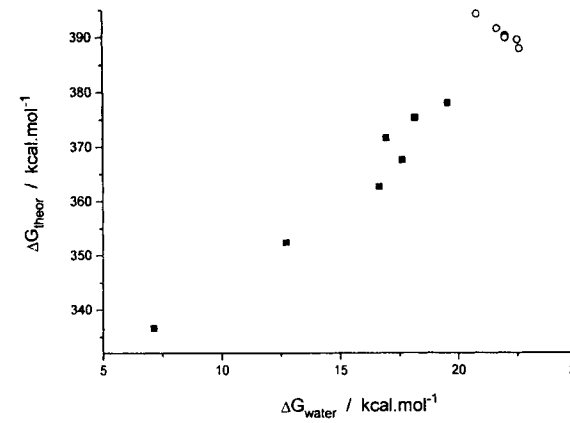

Figure 5. Plot of the theoretical free energy of acid dissociation against its aqueous solution counterpart. (■) Haloalkanols; (○) alkanols

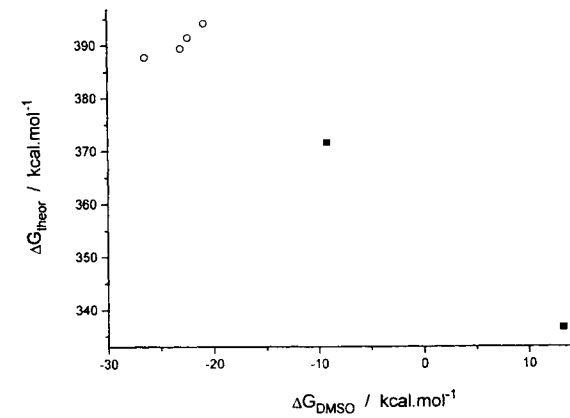

Figure 6. Plot of the theoretical free energy of acid dissociation against its DMSO solution counterpart. (■) Haloalkanols; (○) alkanols

Table 3 gives the inductive effects (I) and polarizability effects (P) for the 17 alkyl groups studied. As can be seen, the unsubstituted alkyl compounds studied have positive inductive effects (typical of electron-releasing groups), whereas the halogen-containing alkyl compounds possess negative inductive effects (typical of electron-withdrawing groups). The results allow one to draw three additional interesting conclusions;

(a) Both I and P increase with increasing length of the alkyl chain in n-alkyl compounds; the effect, however, decreases with more than five carbon atoms in the chain. Both I and P are strongly correlated in the unsubstituted compounds studied, which may allow the substituent effect to be described in terms of a single parameter.

Table 3. Inductive (I) and polarizability (P) effects referred to methyl group (all values in kcal mol^{-1})

R	I(Me)	P(Me)
Me	0·0	0·0
Et	1·1	3·8
n-Pr	1·1	5·1
n-Bu	1·4	5·8
n-Pent	1·4	6·1
n-Hex	1·5	6·2
n-Hep	1·6	6·4
i-Pr	2·2	7·1
t-Bu	3·9	10·3
2FEt	−4·5	6·3
2ClEt	−8·9	7·3
2,2FEt	−13·3	5·6
2,2ClEt	−17·5	9·2
*t*FEt	−19·1	3·5
*t*ClEt	−22·4	9·1
*h*FiPr	−33·2	8·2
*p*FtBu	−45·5	12·1

(b) Branching increases I and P to a greater extent than does increasing chain length. Thus, $I(\text{Pr}) = 1{\cdot}1$ whereas $I(i\text{-Pr}) = 2{\cdot}2$, and $P(\text{Pr}) = 5{\cdot}1$ whereas $P(i\text{-Pr}) = 7{\cdot}1$; also, $I(\text{Bu}) = 1{\cdot}4$ whereas $I(t\text{-Bu}) = 3{\cdot}9$ and $P(\text{Bu}) = 5{\cdot}8$ whereas $P(t\text{-Bu}) = 10{\cdot}3$ (all values in kcal mol^{-1}).

(c) Replacing hydrogen atoms at C-2 in the ethyl group by halogen atoms increases the inductive effect of the alkyl chain. Obviously, the increase is larger for chlorine atoms than for fluorine atoms: $I(Cl_3CH_2) - I(CH_3CH_2) = 21$ kcal mol^{-1} and $I(CF_3CH_2) - I(CH_3CH_2) = 18$ kcal mol^{-1}). The effect is also greater for branched chains relative to straight chains: $I[(CF_3)_2CH] - I[(CH_3)_2CH] = 31$ kcal mol^{-1} and $I[(CF_3)_3C] - I[(CH_3)_3C] = 42$ kcal mol^{-1}.

Figure 7 shows the acidity values for the alcohols in the aqueous solution as a function of the inductive effect of the substituents. As can be seen, the two parameters are proportional (even for the unsubstituted alkanols), so the above-mentioned acidity inversion can only arise from the gas-phase polarizability of these compounds. This polarizability effect is lost on going to an aqueous solution.

Figure 8 shows the acidity values for the alcohols in DMSO as a function of the inductive effects of the substituents. Again, the two parameters are fully proportional. In principle, the fact that the inductive effect is such a faithful reflection of the acidity of the alcohols studied in DMSO is surprising since it must involve a mechanism by which the charge of alkoxy anions is dispersed in a solvent considered non-protic such as DMSO. Measurements recently recorded in our laboratory show that DMSO behaves like a slightly acidic solvent.[22]

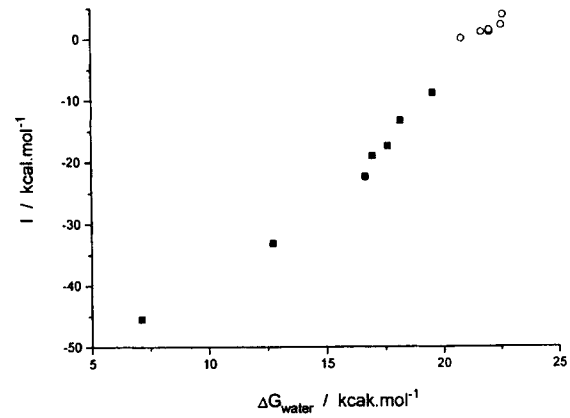

Figure 7. Plot of the inductive effect of the substituent against the free energy of acid dissociation of the alcohols in aqueous solution. (■) Haloalkanols; (o) alkanols

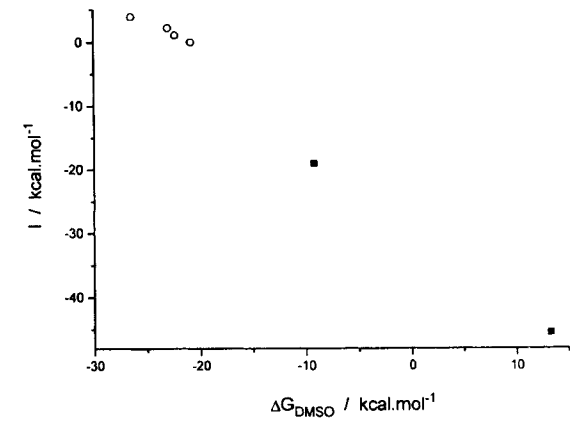

Figure 8. Plot of the inductive effect of the substituent against the free energy of acid dissociation of the alcohols in DMSO solution. (■) Haloalkanols; (o) alkanols

Table 4 gives the charges of the most relevant atoms for the molecular structures used as examples to illustrate the effects of alkyl groups in these compounds. The charge on the hydroxyl hydrogen atom tends to be slightly less positive as the $+I$ effect of the substituent increases and its $-I$ effect decreases. The charge on the acid hydrogen in the protonated forms of the alkanols studied also reflects the influence of the inductive effect of the substituent. It should be noted that, while the charges on the CO group of the four compounds previously studied by Tuñon *et al.*[9] are consistent with the above-described trends, the real significance of this finding is that the solvated active site in these compounds (i.e. the oxygen atom) is also influenced by the inductive effect of the substituent, also, the charge provides no explanation for the acidity inversion.

Table 4. Charges on the most relevent atomic sites in the molecular forms studied as determined from Mulliken analysis

	Neutral form		Anion form		Cation form
Alcohol	q_H	q_O	q_C	q_O	q_{H^+}
MeOH	0·33	−0·63	0·23	−0·91	0·46
EtOH	0·33	−0·64	0·32	−0·91	0·44
n-PrOH	0·33	−0·65	0·33	−0·92	0·45
n-BuOH	0·33	−0·65	0·33	−0·92	0·44
n-PentOH	0·33	−0·65	0·33	−0·92	0·44
n-HexOH	0·33	−0·65	0·33	−0·92	0·44
n-HepOH	0·33	−0·65	0·33	−0·92	0·44
i-PrOH	0·33	−0·64	0·39	−0·92	0·44
t-BuOH	0·33	−0·65	0·45	−0·93	0·43
2FEtOH	0·33	−0·63	0·21	−0·90	0·46
2ClEtOH	0·34	−0·62	0·31	−0·88	0·45
2,2FEtOH	0·34	−0·63	0·22	−0·91	0·46
2,2ClEtOH	0·35	−0·62	0·31	−0·87	0·46
*f*FEtOH	0·35	−0·63	0·20	−0·89	0·46
*f*ClEtOH	0·36	−0·62	0·33	−0·83	0·46
$(CF_3)_2CHOH$	0·37	−0·62	0·14	−0·88	0·47
$(CF_3)_3COH$	0·38	−0·62	0·03	−0·87	0·48

In summary, the acidity inversion in alkanols found on going from the gas phase to solution is caused by the following fact: in gas phase, the size and branching of the alkylated chain produced a net increase in acidity, because its polarizability clearly overcomes the decrease in acidity produced by the inductive effect. However, in solution some mechanism of charge dispersion makes the contribution of the polarizability become negligible, and the acidity of alkanols decreases because of the inductive effect of the alkyl group.

In view of the results, it seemed logical to examine the potential use of I and P data for alkyl groups with compound families other than alcohols. To this end, however, it is preferable to refer the effects to the hydrogen atom (usually considered the null substituent) rather than to the methyl group as before.

Because the computational level previously used, 6–31G**, was inappropriate for describing the anion resulting from the deprotonation of water, we thought it more correct to derive the protonation and deprotonation ΔG values that would correspond to 6–31G** calculations from linear relationships between the 6–31G** data for processes (I) and (II) and their experimental counterparts for the gas phase for *n*-alkanols.[16,23] In this way, we obtained 165·5 and 403·3 kcal mol^{-1} for water, so the inductive effects relative to H would be 2·5 kcal mol^{-1} greater than those relative to the methyl group and the polarizability values would be 11·6 kcal mol^{-1} greater than those relative to Me.

Let us analyse the data for a gas-phase protonation equilibrium such as that of a primary amine,

$$RNH_2 + H^+ \rightleftharpoons RNH_3^+ \quad \text{(V)}$$

where R denotes H, Me, Et, Pr, Bu, Pent, Hept, *i*-Pr, *t*-Bu, FCH_2CH_2, F_2CHCH_2, F_3CCH_2 or $(CF_3)_3C$. The substituents cause a basicity change of 30 kcal mol^{-1} in the primary amine.[16] These data are accurately described by I and P effects through the following equation:

$$\Delta G = (0{\cdot}644 \pm 0{\cdot}020)I + (0{\cdot}644 \pm 0{\cdot}049)P + 196{\cdot}0 \quad (1)$$

with $n = 13$, $r = 0{\cdot}995$ and s.d. = 0·9 kcal mol^{-1}.

Similarly, in the gas-phase protonation equilibrium of a nitrile,

$$RCN + H^+ \rightleftharpoons RCNH^+ \quad \text{(VI)}$$

where R denotes H, Me, Et, Pr, Bu, *i*-Pr, *t*-Bu or $ClCH_2CH_2$, the substituents cause a basicity change of 14 kcal mol^{-1} in the cyano group[16] that is accurately described by I and P through the following equation:

$$\Delta G = (0{\cdot}604 \pm 0{\cdot}205)I + (0{\cdot}988 \pm 0{\cdot}119)P + 165{\cdot}5 \quad (2)$$

with $n = 8$, $r = 0{\cdot}974$ and s.d. = 2·0 kcal mol^{-1}.

Also, for symmetric ethers,

$$R_2O + H^+ \rightleftharpoons R_2OH^+ \quad \text{(VII)}$$

where R denotes H, Me, Et, Pr, Bu, Pent, *i*-Pr or CF_3CH_2, the substituents induce a change of 39 kcal mol^{-1} in the ether basicity that, again, can be expressed through I and P:

$$\Delta G = (1{\cdot}492 \pm 0{\cdot}041)I + (1{\cdot}791 \pm 0{\cdot}048)P + 159{\cdot}2 \quad (3)$$

with $n = 8$, $r = 0{\cdot}999$ and s.d. = 0·77 kcal mol^{-1}.

Finally, for thiols,

$$RSH \rightleftharpoons RS^- + H^+ \quad \text{(VIII)}$$

where R denotes H, Me, Et, Pr, *i*-Pr and *t*-Bu, the substituents studied induce a change of 26 kcal mol^{-1} in the thiol acidity[16] that is accurately described by

$$\Delta G = (-1{\cdot}296 \pm 0{\cdot}750)I + (1{\cdot}570 + 0{\cdot}211)P + 163{\cdot}1 \quad (4)$$

with $n = 6$, $r = 0{\cdot}998$ and s.d. = 0·85 kcal mol^{-1}.

In the four processes above, the independent term of the fitting accurately reproduces the acid or basic behaviour of the parent compound, viz. ammonia (ΔG = 195·6 kcal mol^{-1}), hydrogen cyanide (ΔG = 163 kcal mol^{-1}), water (ΔG = 159·0 kcal mol^{-1}) and SH_2 (ΔG = 162·8 kcal mol^{-1}).

One alternative treatment of alcohol acidity was recently developed by Taft *et al.*[23] on the basis of their model for intrinsic effects (polarizability, field/inductive and resonance) of the substituent. Although the treatment is good, it is inappropriate for analysing the acidity inversion in alkanols because the field/inductive effects of alkyl groups are assumed to be zero in this methodology. It was obviously of interest to compare our I and P effects with the σ_F and σ_α values for alkyl

groups. Figure 9 shows a plot of the intrinsic effect σ_α against our P values for the alkyl groups. As can be seen, the two data sets are acceptably correlated by the following equation

$$\sigma_\alpha = (-0{\cdot}0308 \pm 0{\cdot}0023)P + 0{\cdot}0015 \qquad (5)$$

($n = 15$, $r = 0{\cdot}966$ and s.d. $= 0{\cdot}04$ in σ_α units) since the substituents studied encompass 75% of the σ_α, polarizability scale.

Figure 10 shows a plot of the intrinsic effect σ_F against our I values. As can be seen, the two data sets are well correlated taking into account the zero σ_F value assumed for unsubstituted alkyl groups:

$$\sigma_F = (-0{\cdot}0124 \pm 0{\cdot}0005)I + 0{\cdot}046 \qquad (6)$$

with $n = 15$, $r = 0{\cdot}988$ and s.d. $= 0{\cdot}03$ in σ_F units.

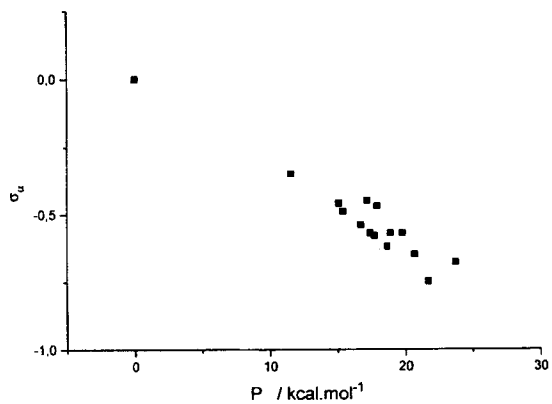

Figure 9. Plot of the intrinsic polarizability effect (σ_α) against the polarizability effect (P)

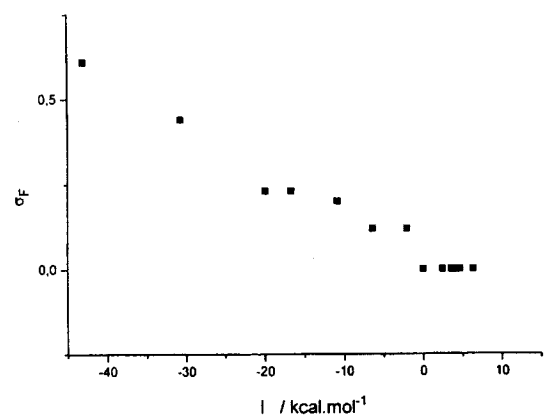

Figure 10. Plot of the intrinsic field/inductive effect (σ_F) against the inductive effect (I)

CONCLUSIONS

The proposed treatment allows one not only to account for the acidity of alcohols and other compound families (based on conventional chemical properties such as inductive and polarizability effects of substituents), but also to evaluate I and P theoretically for any substituent by use of an affordable computational procedure. Our I and P values can also be used to estimate intrinsic polarizability (σ_α) and field/inductive (σ_F) effects with a precision better than 0·05 units, thereby providing an alternative method for their determination.

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