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Triadic analysis of substituent effects—gas-phase acidity of *para*-substituted phenols

Robert Vianello and Zvonimir B. Maksić*

Quantum Organic Chemistry Group, Division of Organic Chemistry and Biochemistry,
Ruđer Bošković Institute, POB 180, 10 002 Zagreb, Croatia

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Abstract—A large variety of *para*-substituted phenols was examined and their acidities in the gas-phase were rationalized by a triadic formula, which is capable of delineating the initial, intermediate and final state effects in the deprotonation process. It is shown that triadic analysis is equivalent to the homodesmotic reactions approach, while being much more informative at the same time. The applied MP2(fc)/6-311+G(d,p)//B3LYP/6-31G(d) theoretical method gives acidities in very good agreement with available measured values, meaning that calculations can safely replace the missing experimental data for compounds not easily amenable to laboratory examinations. It is found that the underlying principle leading to enhanced acidity of *para*-substituted phenols containing strong π-electron acceptor groups is the final state effect. It reflects a more pronounced ability to accommodate the excess negative charge. Particular attention has been focused on superacidifying NO_2, SO_2CF_3 and $S(O)({=}NSO_2CF_3)CF_3$ and $C(CN){=}C(CN)_2$ moieties. It is shown that their influence on acidity is strong and that the deprotonation ability increases along the sequence of substituents $NO_2 < SO_2CF_3 < S(O)({=}NSO_2CF_3)CF_3 < C(CN){=}C(CN)_2$. On the contrary, the electron releasing substituents NH_2, OCH_3, OH and CH_3 decrease acidity of phenol albeit to a small extent. Finally, it is demonstrated that pentacyano derivative of phenol is a powerful OH superacid as evidenced by ΔH_{acid} value of 287.5 kcal mol^{-1}.

1. Introduction

Substituent effects belong to the most important concepts in chemistry developed by empirical observations. They describe the influence of the spatial and electronic structural features on the chemical, physicochemical and biochemical properties of compounds. By definition, a substituent is understood as a smaller structural subunit, which affects the properties of a molecular system in a quantitative sense by preserving its general character. The latter is determined by a dominating functional group and/or by the molecular backbone itself.[1] In other words, the substituent perturbs the parent molecule in a measurable, but not dramatic way by somewhat modifying its spatial and electronic structure and consequently its behaviour. The importance of the concept can be documented by its occurrence in the literature. According to Krygowski and Stepień[2] about 20 papers daily have appeared in the period 1996–2004 involving the term substituent in the title, keywords or abstract.

Historically, the concept of substituents received a strong impetus by Hammett, who studied deprotonation of benzoic acid and its *para*-substituents in water.[3] The corresponding Hammett equation was a milestone in development of the structure–property relations, which in turn have played a crucial role in physical organic chemistry. This development triggered an explosion of papers dealing with the substituent effects in chemistry lasting for many decades, but also resulting in some reports on its applications in biology.[4] It is both surprising and gratifying that Hammett's σ-constants, deduced from the ionization of organic acids in solutions, can successfully predict equilibrium and rate constants for a wide variety of chemical reactions. It should be noted that the Hammett equation is an example par excellence of the more general linear free energy relationships. It is fair to mention that many researchers have contributed to the applications and extensions of the Hammett equation.[5–11] One of the most recent compilations of various σ-constants was published by Hansch, Leo and Taft.[12] An early attempt to rationalize the σ-constants and substituent effects in general by ab initio methods was made by Topsom[13] and Pross with coworkers.[14] An important theoretical contribution to the field was introduction of the homodesmotic reactions[15] in studying the substituent effects.[16] This topic was extensively discussed in a recent review.[2]

The original σ-constants for describing the effects of substituents placed at the *para*-position relative to the reactive site have been based upon aqueous acidities of

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* Corresponding author. Tel.: +385 1 4561117; fax: +385 1 4561118; e-mail: zmaksic@spider.irb.hr

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substituted benzoic acids.[3] The *para*-substituted phenols and the corresponding phenoxide ions provided another important test case for the concept of substituents and their effect on acidity. Concomitantly, they were the subject matter of numerous investigations.[14,17–25] Perhaps this is not surprising because of two reasons: (1) phenol is one of the simplest substituted aromatic systems capable of electron lone pair donation to the aromatic nucleus and to the possible *ortho*- and *para*-electron accepting substituents and (2) it is one of the most important organic species with appreciable biological activity.[21]

Recently, we introduced a triadic formula for interpreting the proton affinities of bases[26] and deprotonation energies of acids,[27] which was subsequently used in rationalizing substituent effects in *para*-substituted benzoic acids.[28] This approach seems to possess some advantages compared to other conventional models.[29] Hence, we felt it worthwhile to extend triadic analysis to *para*-substituted phenols and their intrinsic (gas-phase) acidities, which might throw new light onto this old problem. A wide range of different substituents is examined including some exhibiting extremely strong electron withdrawing power like NO_2, SO_2CF_3, $S(O)({=}NSO_2CF_3)CF_3$ and $C(CN){=}C(CN)_2$.

2. Theoretical approach

Acidity is defined as the change in enthalpy (ΔH_{acid}) for the reaction:

$$AH(g) \rightarrow A^{-}(g) + H^{+}(g) \tag{1}$$

leading to:

$$\Delta H_{\text{acid}} = \Delta E_{\text{acid}} + \Delta(pV) \tag{2}$$

where g denotes the gas-phase, ΔE_{acid} is the change in the total molecular energy of the species entering Eq. 1, including the zero-point vibrational energy (ZPVE) and the finite temperature thermal correction from 0 to 298.15 K. The pressure–volume work term is denoted by $\Delta(pV)$. It is useful to keep in mind that stronger acids have smaller numerical ΔH_{acid} values, which implies easier release of the acidic proton. Theoretical MP2(fc)/6-311+G(d,p)//B3LYP/6-31G(d) model (hereafter denoted as MP2) represents a good compromise between accuracy and feasibility combined with practicality. The resulting acidities compare well with experiment and considerably more demanding G2 method.[30,31] Additionally, the MP2 model offers a useful interpretation of acidities via triadic (trichotomy) formula:[27,32]

$$\begin{aligned}\mathrm{PA}(A^{-})_{\alpha} = {} & -\mathrm{IE}(A^{-})_{n}^{\mathrm{Koop}} + E(\mathrm{ei})_{\mathrm{rex}}^{(n)} + (\mathrm{BAE})_{\alpha}^{\bullet} \\ & + 313.6\ \mathrm{kcal/mol}\end{aligned} \tag{3}$$

(1 kcal/mol = 4.184 kJ/mol). This formula describes protonation of the conjugate base (anion A^{-}), or in other words a reversed deprotonation of a neutral acid. Here, the site of protonation is denoted by α and $\mathrm{IE}(A^{-})_{n}^{\mathrm{Koop}}$ is the nth Koopmans' ionization energy of the anion A^{-} calculated in the fixed nuclei and frozen electron density approximation. The electron affinity of the proton is 313.6 kcal/mol. The reorganization of both the nuclei and electrons occurring due to the fact that ionization is not a sudden event is denoted by $E(\mathrm{ei})_{\mathrm{rex}}^{(n)}$. It is taken for granted that the relaxation in the $A^{-} + H^{+}$ protonation process is completed before the $H^{\bullet}$ and $A^{\bullet}$ radicals start to interact and form a new A–H bond. Hence, the relaxation energy is defined as:

$$E(\mathrm{ei})_{\mathrm{rex}}^{(n)} = \mathrm{IE}(A^{-})_{n}^{\mathrm{Koop}} - \mathrm{IE}(A^{-})_{1}^{\mathrm{ad}} \tag{4}$$

where $\mathrm{IE}(A^{-})_{1}^{\mathrm{ad}}$ is the first adiabatic ionization energy. Several comments are necessary here. Firstly, Koopmans' ionization energy is calculated within the one-electron Hartree–Fock (HF) picture employing the 6-311+G(d,p) basis set, which enables simple interpretation of the genuine properties of the final state (A^{-}). Since $\mathrm{IE}(A^{-})_{n}^{\mathrm{Koop}}$ describes ionization from the nth molecular orbital, it can be selected in such a way that it corresponds to MO, which is pivotal in the protonation process. For example, the nth MO in most cases belongs to the lone pair, which is attacked by the proton thus mirroring the properties of the reaction site as closely as possible. This is not possible, if the first adiabatic ionization energy $\mathrm{IE}(A^{-})_{1}^{\mathrm{ad}}$ is considered. It follows as a corollary that the relaxation energy $E(\mathrm{ei})_{\mathrm{rex}}^{(n)}$ has two components. The first is provided by $\mathrm{IE}(A^{-})_{n}^{\mathrm{Koop}} - \mathrm{IE}(A^{-})_{h}^{\mathrm{Koop}}$, where the index h stands for the highest occupied MO(HOMO). It describes stabilization by a transfer of an electron from the HOMO to a hole in the nth MO created by ionization given in the approximation of the frozen nuclear and electronic charge distributions. The second term in $E(\mathrm{ei})_{\mathrm{rex}}^{(n)}$ is the relaxation effect accompanying ionization from the HOMO yielding $E(\mathrm{ei})_{\mathrm{rex}}^{(h)} = \mathrm{IE}(A^{-})_{h}^{\mathrm{Koop}} - \mathrm{IE}(A^{-})_{1}^{\mathrm{ad}}$. We shall consider only a lump sum of these two relaxation effects in this paper defined by Eq. 4. Secondly, the formation of the new bond causes an additional relaxation effect, which is not separately considered, but it is included in the bond association energy $(\mathrm{BAE})_{\alpha}^{\bullet}$ instead.

The triadic analysis carried out here is based on the MP2 method. Koopmans' ionization energies are calculated by the restricted HF/6-311+G(d,p)//B3LYP/6-31G(d) model. Bond dissociation energies are obtained by the use of the restricted open-shell MP2 approach. All calculations were performed by using the GAUSSIAN 98 program.[33]

3. Results and discussion

3.1. Substituents effect on acidity of phenols

A large variety of substituents exhibiting widely different electron donor and acceptor abilities is examined (Fig. 1). They encompass F, Cl, Br, CH_3, $C(CH_3)_3$, $CH{=}CH_2$, $C{\equiv}CH$, CHO, COOH, CF_3, BH_2, $B(CH_3)_2$, NH_2, $N(CH_3)_2$, OH, OCH_3, SH, SCH_3, CN, NO_2, SO_2CF_3, $S(O)({=}NSO_2CF_3)CF_3$, $C(CN){=}C(CN)_2$ and $(CN)_5$. The latter system is the only multiply substituted phenol studied here in order to find out whether the pentacyano derivative acts as a superacid as was the case with polycyano substituted benzoic acid[28] and by a number of other aromatic compounds.[34–36] Perusal of the data presented in Table 1

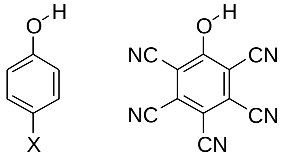

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Figure 1. Schematic representation of the studied phenols.

reveals a very good agreement between the calculated and measured proton affinities, which lends credence to the method applied. Particularly interesting is the result obtained for the parent phenol, which in turn has been explored by a number of experimental researchers and theoreticians over a large span of years.[17–24] The most recent experimental value for its acidity of Angel and Erwin[23] is 347.5 ± 1.9 kcal mol^{-1}, which is in a nice accordance with our computational result (348.3 kcal mol^{-1}). It is worth mentioning that our adopted computational procedure is useful in discriminating the experimental data. The value cited by NIST Database of 350.0 ± 2.0 kcal mol^{-1} is the average value of five measurements carried out in the time span of 26 years. Although their average is in agreement with our result, if the lower error bar is taken into account, we feel that the measured value obtained by Angel and Erwin[23] is more accurate. It appears that phenol is less acidic than the benzoic acid, where ΔH_{acid} assumes 339.5 kcal mol^{-1} ($\Delta H_{\mathrm{acid}}(\mathrm{exp}) = 340.2 \pm 2.2$ kcal mol^{-1}).[28] Triadic analysis 3 is well suited to interpret this difference. For this purpose a compact formula can be written such as:

$$\Delta \mathrm{PA}(\mathrm{A}^-) = \left[\Delta(-\mathrm{IE}_n^{\mathrm{Koop}});\ \Delta E(\mathrm{ei})_{\mathrm{rex}}^{(n)};\ \Delta(\mathrm{BAE})_{\alpha}^{\bullet}\right] \qquad (5)$$

where Δ is the difference between the corresponding entities of the examined and reference molecule or anion, while squared parentheses imply summation of the embraced three terms. We shall select phenol as a standard system for measuring variations in acidity, if not stated otherwise. It turns out that the increase in acidity of benzoic acid (PA = [−15.5; −6.7; 13.4] = −8.8 kcal mol^{-1} is a consequence of two contributions, the first being a more stabilized MO describing the in-phase combination of the lone pairs AOs of oxygen to be protonated in the σ-plane of the benzoic acid anion. The reason behind is that the corresponding MO is quite stable being HOMO-3 orbital,[28] possessing orbital energy as low as −0.22200 a.u. In the phenoxide anion, on the other hand, the molecular orbital describing the σ-distribution of the oxygen lone pairs is given by the out-of-phase combination of the oxygen AOs yielding HOMO-2 (Fig. 2). The latter is energetically higher (−0.19741 a.u.) by 15.5 kcal mol^{-1}. This means that formation of the new O–H bond upon protonation of the benzoic acid anion is more costly by that amount, since an electron has to be activated from the energetically lower MO. Consequently, benzoic acid should be more acidic. To put it in another way, one can say that deprotonation of the benzoic acid leaves the electron in a more stable HOMO-3 orbital. Hence, the excess negative charge is better

Table 1. Triadic analysis of proton affinities (PAs) of conjugate bases of *para*-substituted phenols obtained by applying ROMP2(fc)/6-311 + G(d,p)//B3LYP/6-31G(d) method and formula 3[a,b]

Substituent	$(\mathrm{IE})_n^{\mathrm{Koop}}$	$(\mathrm{IE})_1^{\mathrm{ad}}$	$E(\mathrm{ei})_{\mathrm{rex}}^{(n)}$	$(\mathrm{BAE})^{\bullet}$	PA(thr)	PA(exp)[c]
NH_2	$(123.5)_3$	36.5	87.0	74.5	351.6	352.5 ± 2.1
OCH_3	$(122.9)_3$	39.7	83.2	76.4	350.3	350.4 ± 2.1
OH	$(122.8)_3$	40.6	82.2	76.8	349.8	350.4 ± 2.1
CH_3	$(122.9)_3$	43.6	79.3	79.5	349.5	350.3 ± 2.1
H	$(123.9)_3$	51.9	72.0	86.6	348.3	347.5 ± 1.9[d]
$C(CH_3)_3$	$(125.1)_3$	45.5	79.6	79.7	347.8	348.5 ± 2.1
$N(CH_3)_2$	$(125.4)_3$	40.0	85.4	73.6	347.2	351.3 ± 2.1
F	$(128.0)_3$	52.5	75.5	84.4	345.5	346.8 ± 2.1
Cl	$(133.7)_3$	50.4	83.3	79.6	342.8	343.1 ± 2.1
$CH{=}CH_2$	$(136.3)_3$	51.0	85.3	79.9	342.5	
SMe	$(133.9)_3$	50.1	83.8	78.6	342.1	
SH	$(77.2)_2$	65.9	11.3	94.0	341.7	
Br	$(135.6)_3$	52.0	83.6	79.9	341.5	
$C{\equiv}CH$	$(141.1)_3$	54.3	86.8	81.0	340.3	
$B(CH_3)_2$	$(140.3)_3$	59.5	80.0	83.3	337.4	
CF_3	$(142.3)_3$	69.9	72.4	91.7	335.4	337.0 ± 2.1
COOH	$(146.4)_3$	61.2	85.2	82.7	335.1	335.9 ± 2.1
BH_2	$(143.7)_3$	65.6	78.1	85.3	333.3	
CHO	$(148.3)_3$	64.1	84.2	83.2	332.7	333.0 ± 2.1
CN	$(149.0)_3$	64.9	84.1	83.0	331.7	332.2 ± 2.1
NO_2	$(159.7)_3$	69.0	90.7	83.1	327.7	327.8 ± 2.1
SO_2CF_3	$(162.5)_3$	86.7	75.8	95.6	322.5	322.6 ± 2.1
$S(O)({=}NSO_2CF_3)CF_3$	$(176.2)_3$	118.7	57.5	118.9	313.8	
$C(CN){=}C(CN)_2$	$(185.7)_4$	86.8	98.9	85.2	312.0	
$(CN)_5$	$(211.6)_3$	114.8	96.8	88.7	287.5	

All terms are given in kcal mol^{-1}.

[a] Koopmans' ionization energies $(\mathrm{IE})_n^{\mathrm{Koop}}$ are obtained by the HF/6-311 + G(d,p)//B3LYP/6-31G(d) calculations. It should be noted that index n corresponds to HOMO-$n+1$ molecular orbital.

[b] $(\mathrm{IE})_n^{\mathrm{Koop}}$ and $(\mathrm{IE})_1^{\mathrm{ad}}$ are Koopmans' nth and the first adiabatic ionization energies, respectively.

[c] Experimental data are taken from Lias, S. G.; Liebman, J. F., *Ion Energetics Data*, in *NIST Chemistry WebBook*, NIST Standard Reference Database Number 69, Linstrom, P. J.; Mallard, W. G. (Eds.), March 2003, National Institute of Standards and Technology, Gaithersburg MD, 20899 (http://webbook.nist.gov) if not stated otherwise.

[d] Ref. 23.

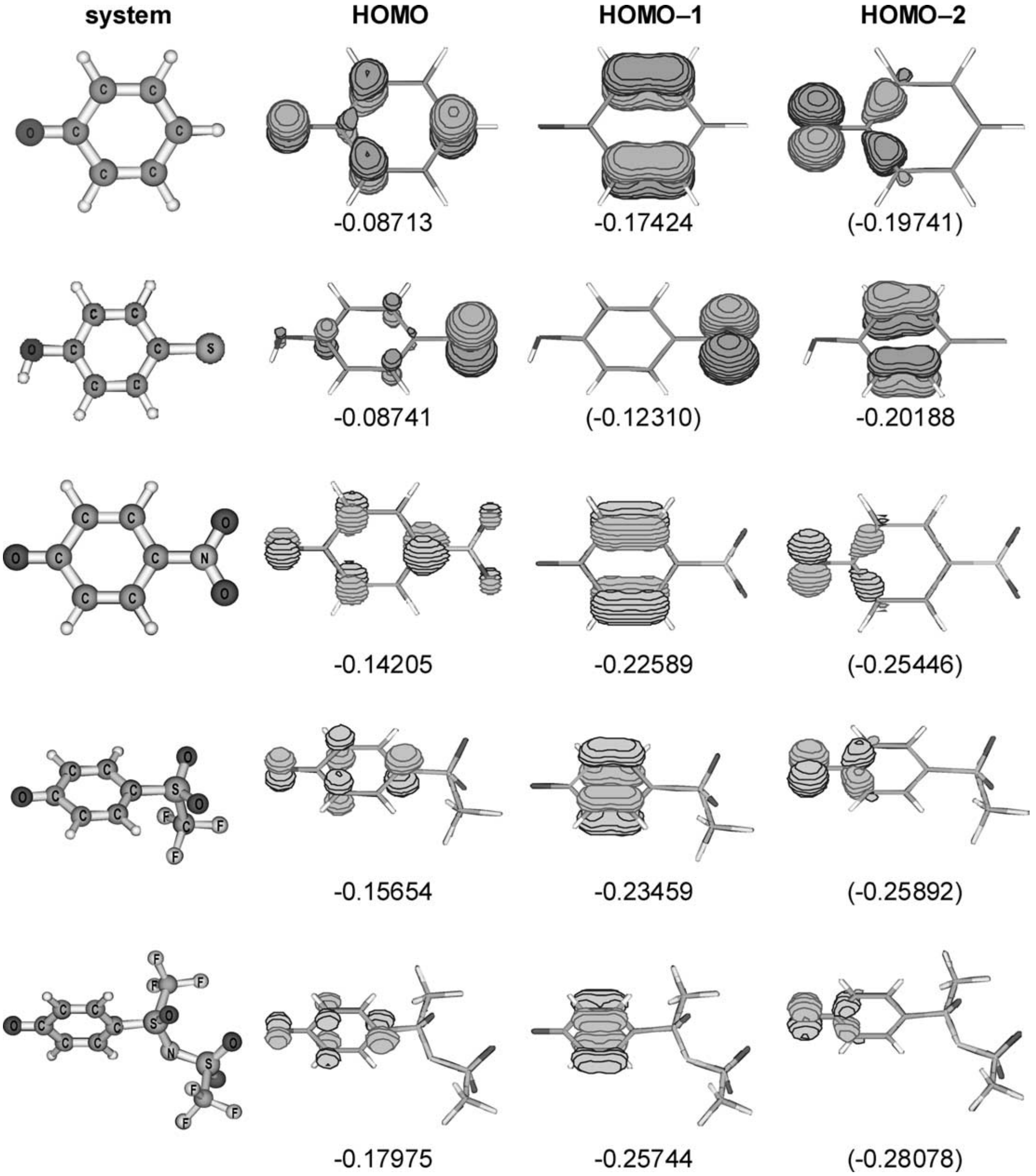


Figure 2. Schematic representation of the three highest occupied molecular orbitals for some characteristic conjugated bases under consideration together with their orbital energies (in a.u.) obtained by HF/6-311+G(d,p)//B3LYP/6-31G(d) level of theory in Koopmans' approximation. The orbital energies of MOs participating in protonation of anions most frequently are given within parentheses.

accommodated in benzoic acid anion than in phenoxide thus contributing to greater acidity of the former compound. This is a typical final state effect, which will play an increasingly important role in systems possessing the *para*-substituted electron accepting group (vide infra). Secondly, the relaxation energy is 6.7 kcal mol^{-1} higher in phenoxide, which decreases acidity of phenol. On the other hand, the homolytic O–H bond dissociation energy in phenol is 13.4 kcal mol^{-1} lower than that in benzoic acid, which diminishes the difference in acidity between these two species. We note in passing that the calculated O–H bond energy of phenol is 86.6, being in a very good agreement with the recent experimental estimate of 85.8 ± 1.9 (in mol^{-1}).[23] It follows that benzoic acid is more acidic in spite of the fact that its O–H bond is considerably stronger than that in phenol. This is in harmony with a common knowledge that acidity cannot be reduced to the strength of the X–H bond energy only, as conclusively illustrated by the triadic analysis here and elsewhere.[26–28] We shall comment on the difference in acidities between some substituted benzoic acids and phenols later on.

Let us focus now on the variation in acidity of phenols upon *para*-substitution taking the parent phenol as a reference system. The relevant data are presented in Table 2. It appears that the strongest acidifying moiety is tricyanovinyl $C(CN){=}C(CN)_2$ as evidenced by the most negative ΔPA value of -36.3 kcal mol^{-1}, which is followed by so called superacidifiers $S(O)({=}NSO_2CF_3)CF_3$ ($\Delta PA = -34.5$ kcal mol^{-1}) and SO_2CF_3 ($\Delta PA = -25.8$ kcal mol^{-1}). On the other hand, NO_2 increases the acidity of phenol by 'only' 20.6 kcal mol^{-1}. This is interesting in view of a long-standing discussion in the literature whether SO_2CF_3 is a stronger electron withdrawing group than NO_2 or not.

Table 2. Relative contributions to proton affinities (PA) of the investigated molecules obtained by triadic formula 3 taking phenol as a gauge molecule[a]

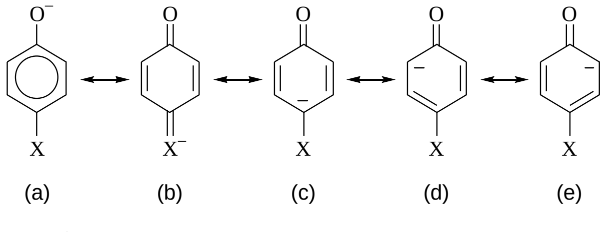
Substituent	$\Delta(\mathrm{IE})_n^{\mathrm{Koop}}$	$\Delta E(\mathrm{ei})_{\mathrm{rex}}^{(n)}$	$\Delta(\mathrm{BAE})^{\bullet}$	ΔPA (thr)	σ_p	σ_p^-
NH_2	0.4	15.0	−12.1	3.3	−0.66	−0.15
OCH_3	1.0	11.2	−10.2	2.0	−0.27	−0.26
OH	1.1	10.2	−9.8	1.5	−0.37	−0.37
CH_3	1.0	7.3	−7.1	1.2	−0.17	−0.17
H	0.0	0.0	0.0	0.0	0.00	0.00
$C(CH_3)_3$	−1.2	7.6	−6.9	−0.5	−0.20	−0.13
$N(CH_3)_2$	−1.5	13.4	−13.0	−1.1	−0.83	−0.12
F	−4.1	3.5	−2.2	−2.8	0.06	−0.03
Cl	−9.8	11.3	−7.0	−5.5	0.23	0.19
$CH{=}CH_2$	−12.4	13.3	−6.7	−5.8	−0.04	
SMe	−10.0	11.8	−8.0	−6.2	0.00	0.06
SH	46.7	−60.7	7.4	−6.6	0.15	
Br	−11.7	11.6	−6.7	−6.8	0.23	0.25
$C{\equiv}CH$	−17.2	14.8	−5.6	−8.0	0.23	0.53
$B(CH_3)_2$	−16.4	8.8	−3.3	−10.9		
CF_3	−18.4	0.4	5.1	−12.9	0.54	0.65
COOH	−22.5	13.2	−3.9	−13.2	0.45	0.77
BH_2	−19.8	6.1	−1.3	−15.0		
CHO	−24.4	12.2	−3.4	−15.6	0.42	1.03
CN	−25.1	12.1	−3.6	−16.6	0.66	1.00
NO_2	−35.8	18.7	−3.5	−20.6	0.78	1.27
SO_2CF_3	−38.6	3.8	9.0	−25.8	0.96	1.63
$S(O)({=}NSO_2CF_3)CF_3$	−52.3	−14.5	32.3	−34.5	1.35	2.30
$C(CN){=}C(CN)_2$	−61.8	26.9	−1.4	−36.3	0.98	1.70
$(CN)_5$	−87.7	24.8	2.1	−60.8		

All values are in kcal mol^{-1}.

[a] Hammett's σ-constants are taken from Ref. 12 except for $S(O)({=}NSO_2CF_3)CF_3$, which originate from Ref. 46. It should be noted that index *n* corresponds to HOMO-*n*+1 molecular orbital.

Briefly, the SO_2CF_3 group was introduced as a strong acidifying factor by Yagupolskii[37,38] and Sheppard.[39,40] More recently, new superacceptor electron groups were discussed by replacing one or two oxygen atom(s) in SO_2CF_3 by intrinsically even stronger electron withdrawing moieties like, for example, $=NSO_2CF_3$.[41–44] Goumont et al.[45] provided convincing experimental evidence of the unusually strong electron transmission ability of the highly acidifying SO_2CF_3 group, which was considered to be a consequence of its high polarizability. Finally, an extremely strong electron withdrawing power of the $S(O)({=}NSO_2CF_3)CF_3$ moiety has been established experimentally by Terrier et al.[46] Triadic analysis provides a penetrating insight into the *para*-NO_2 acidifying effect in phenol compared to that exerted by SO_2CF_3, $S(O)({=}NSO_2CF_3)CF_3$ and $C(CN){=}C(CN)_2$ groups. Let us start with the former group. The triadic formula yields a change caused by *para*-NO_2 relative to the parent phenol: $\Delta PA(NO_2) = [-35.8;\ 18.7;\ -3.5] = -20.6$ kcal mol^{-1} implying that the better distribution of the negative charge in the anion (final state effect) is of paramount importance in increasing the acidity by 20.6 kcal mol^{-1}. Analogously, $\Delta PA(SO_2CF_3) = [-38.6;\ 3.8;\ 9.0] = -25.8$ kcal mol^{-1} indicating that the final state effect is decisive again, but the influence of the relaxation and bond association energy (BAE) is different to that in *para*-NO_2 phenol. This is evident by calculating $PA(SO_2CF_3)$ relative to $PA(NO_2)$: $PA(SO_2CF_3) - PA(NO_2) = [-2.8;\ -14.9;\ 12.5] = -5.2$ kcal mol^{-1}. Thus, it appears that the relaxation energy is by 14.9 kcal mol^{-1} smaller in SO_2CF_3 *para*-derivative of phenol. This finding is in accordance with a generally accepted idea that the NO_2 group is stabilized by substantial resonance $^{-}O{-}N^{+}{=}O \leftrightarrow O{=}N^{+}{-}O^{-}$, which is particularly pronounced in the anionic state. In contrast, the SO_2CF_3 seems to stabilize the excess negative charge via polarizability effect,[45,46] while the resonance effect is very modest. Finally, the bond association energy is by 12.5 kcal mol^{-1} larger in *para*-SO_2CF_3 phenol. The combined effect of the bond association O–H energy and the relaxation energy contributes 2.4 kcal mol^{-1} to the increased acidifying effect of the SO_2CF_3 group. The rest (2.8 kcal mol^{-1}) is due to a better accommodation of the negative charge in the *para*-SO_2CF_3 phenol anion as reflected by a more stable HOMO-2 orbital. Hence, the physical origin of the stronger acidifying ability of SO_2CF_3 group is perfectly clear. Similar analysis related to *para*-$S(O)({=}NSO_2CF_3)CF_3$ phenol gives $\Delta PA[S(O)({=}NSO_2CF_3)CF_3] = [-52.3;\ -14.5;\ 32.3] = -34.5$ kcal mol^{-1} relative to the parent phenol. The dramatic increase in acidity is primarily due to a strong stabilization of the HOMO-2 orbital, which hosts the two electrons of the lone pair created upon deprotonation of the OH group. Additional contribution to acidity originates from a decreased relaxation energy in *para*-$S(O)({=}NSO_2CF_3)CF_3$ substituted phenol. These two synergistic effects are somewhat diminished by the strongly increased O–H bond energy by 32.3 kcal mol^{-1}. As a final comment let us compare the acidity of the $C(CN){=}C(CN)_2$ *para*-substituted phenol against acidity of the parent molecule: $\Delta PA[C(CN){=}C(CN)_2] = [-61.8;\ 26.9;\ -1.4] = -36.3$ kcal mol^{-1}. The influence of the final state is dramatic indeed due to the fact that deprotonation leaves the lone pair placed in a low energy HOMO-3 orbital. The present analysis provides conclusive evidence that the intrinsic acidifying power in the gas-phase decreases along the series $C(CN){=}C(CN)_2 > S(O)({=}NSO_2CF_3)CF_3 > SO_2CF_3 > NO_2$ in *para*-substituted phenols, which resolves a longstanding dilemma. It is somewhat surprising that tricyanovinyl is a stronger acidifier than superacidifiers[45,46] SO_2CF_3 and $S(O)({=}NSO_2CF_3)CF_3$.

In order to get a big picture on the acidity of substituted phenols let us consider the data presented in Table 2. Their perusal leads to a conclusion that there are two widely different types of *para*-substituents, namely, very strong π-electron acceptors and π-electron donors. The first group is rather large yielding considerable enhancement in acidity. It is comprised of CHO, COOH, CF_3, BH_2 and CN groups apart from the already discussed NO_2, SO_2CF_3, $S(O)(=NSO_2CF_3)CF_3$ and $C(CN)=C(CN)_2$ strongly acidifying moieties. It is easy to see that these groups stabilize the resulting conjugate bases as illustrated by Scheme 1, where Pauling's resonance structures are sequenced according to decreasing importance. The first resonance structure (a) describes the most stable pattern of the π-electron spin coupling. The second structure (b) corresponds to the long range π-electron density transfer to a strongly electron withdrawing group X. The third resonance structure (c) should considerably contribute to the stability of the anion too as a rule, since the negative charge is placed at the nearest neighbour of the group X. The latter is attached to the *para*-carbon by an atom, which carries appreciable positive charge. Terrier et al.[46] provided some evidence that the resonance structure (b) is only moderately important for SO_2CF_3 and $S(O)(=NSO_2CF_3)CF_3$ moieties. It should be noticed that similar resonance structures can be written for the initial neutral acids too, but they contain a bipolar (zwitterionic) distribution of the charge. These structures are less stabilizing than the corresponding ones in the conjugate bases (Scheme 1) implying that the anions are better stabilized. Consequently, it is intuitively clear that deprotonation should be more favourable for the electron captive substituents. This qualitative conjecture is in accordance with the increased acidity in phenols substituted by the group 1 substituents (Table 2). Triadic analysis offers a more detailed description of this phenomenon. It turns out that the excess negative charge produced by deprotonation is placed in very stable HOMO-2 orbitals in CHO, COOH, CF_3, BH_2, CN, NO_2, SO_2CF_3 and $S(O)(=NSO_2CF_3)CF_3$ (Table 2) thus contributing considerably to the stability of anions. A subset of this group of compounds is given by substituents with less pronounced π-electron withdrawing power. Typical representatives are halogens F, Cl and Br. The stabilization contributions of their HOMO-2 orbitals in anions are small to modest being −4.1, −9.8 and −11.7 (in kcal mol^{-1}), respectively. The second distinctly different group of substituents is provided by the π-electron releasing atoms like nitrogen and oxygen in NH_2, OH and OCH_3. It is obvious that two π-electron donors placed at *para*-positions will interfere in a way to destabilize the initial acid and somewhat more so the corresponding anion. Hence, the substituted phenols should be less acidic. The actual numbers given in Table 2 show that this effect takes place indeed, but that it is rather small at the same time. Survey of the data in Table 2 indicates that there are two opposing effects in these systems: the relaxation energy and the bond association energy. The former diminishes the acidity of phenols and prevails over a decrease in the $(\mathrm{BAE})^{\bullet}$ term, which contributes towards an increase in acidity.



Scheme 1.

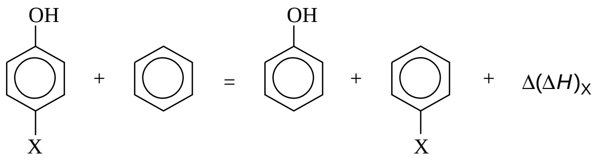
The substituent, which represents a notable exception is the SH group, since the site of deprotonation in *para*-substituted phenol is not the OH but the SH group instead just like in the benzoic acid.[28] This has a profound influence on the values of contributions entering triadic formula. Firstly, the lone pair molecular orbital created by deprotonation belongs to the sulfur atom. It is the HOMO-1 orbital of σ-symmetry (Fig. 2) and not the HOMO-2 orbital like in all other compounds. The corresponding ionization energy within Koopmans' approximation assumes 77.2 kcal mol^{-1}, which is dramatically lower than in the parent phenol. Taking into account other terms entering Eq. 3 one obtains $\Delta PA(SH)=[46.7;\ -60.7;\ 7.4]=-6.6$ kcal mol^{-1} relative to free phenol indicating that the dominating effect leading to the higher acidity of *para*-SH derivative is given by the very small relaxation energy (11.3 kcal mol^{-1}). The contribution of relaxation energy to proton affinity of anion is negative being as low as −60.7 kcal mol^{-1}, thus exerting a predominating effect leading to increased acidity. This overwhelms the combined positive contributions of the Koopmans' term and the higher bond association energy. Methylation at the SH group completely changes this picture, since in this case we are left without the acidic proton at the sulfur atom. Concomitantly, *para*-SCH_3 phenol is deprotonated at the hydroxyl group. Hence, the triadic terms related to SCH_3 substituent are more compatible with those of other substituents. Specifically: $\Delta PA(SMe)=[-10.0;\ 11.8;\ -8.0]=-6.2$ kcal mol^{-1}. It appears that a synergistic effect of Koopmans' ionization potential and bond association energy leads to an enhancement of acidity by 6.2 kcal mol^{-1}. This is practically the same as that of the SH group. It is important to realize, however, that both the site of deprotonation and the underlying physical picture are completely different in these two cases.

A point of considerable importance is the pentacyano derivative of phenol, which is highly acidic as evidenced by PA of 287.5 kcal mol^{-1}. This is comparable in its strength to some strong mineral acids like HNO_3, H_2SO_4 and $HClO_4$. Their experimental gas-phase ΔH_{acid} values are 324.5, 306.3 and 288.0 kcal mol^{-1}, respectively. The reason behind such a high acidity of pentacyanophenol is the large stabilization of the HOMO-2 orbital in the conjugate base, which contributes −87.7 kcal mol^{-1} to acidity of this simple superacid. It is also noteworthy that pentacyano derivative of phenol, where the cyano groups are attached to the aromatic nucleus is considerably stronger acid than the corresponding pentacyano benzoic acid (PA = 303.0 kcal mol^{-1}) although the effect of the single cyanation at the *para*-position is very close in both systems. One of the main reasons is that the O–H bond association energy in benzoic acid is 17 kcal mol^{-1} larger than that in phenol.[28]

It is of some interest to compare and comment on the effects of single *para*-substitutions in phenol and benzoic acid. One can distinguish two distinctly different sets. The first set of substituents is embodied by Cl, CH_3, NH_2, OH, OCH_3 and SH. They do not change the difference in acidity of the parent systems to a large extent. In other words, the derivatives of benzoic acid are more acidic by approximately 9 kcal mol^{-1}, which corresponds to a difference in acidity between unsubstituted benzoic acid and phenol. The second group of substituents is given by CHO, COOH, BH_2, $B(CH_3)_2$, NO_2 and CN, which increase the acidity of the substituted phenols in such a way that they become practically the same as the corresponding substituted benzoic acids. Since these substituents exhibit appreciable electron withdrawing power, which strongly stabilizes the corresponding anions, it follows that their π-electrons resonance effect with O^- in phenoxide is more pronounced than with carboxyl COO^- group in benzoic acid anions. This has some important consequences. It means that Hammett's σ-constants do not depend only on the nature of the substituent and its position on the (aromatic) perimeter, but also on the intrinsic properties of the reaction center. It should be noted that the differences in acidities between derivatives of benzoic acid and phenol (not given here) can be easily analyzed by using the earlier data[28] and present results employing triadic formula.

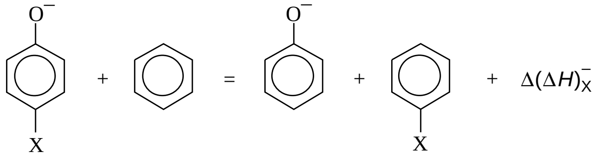
3.2. Homodesmotic reactions and triadic analysis

Let us describe the influence of *para*-substituents on the acidity of phenol by homodesmotic reactions. Consider for this purpose the enthalpies of the following reactions:



(6)

and



(7)

The difference of relations 7 and 6 gives:

$$\Delta H_{\mathrm{acid}}(\mathrm{ph})_{\mathrm{X}} = \Delta H_{\mathrm{acid}}(\mathrm{ph}) + \left[\Delta(\Delta H)^{-}_{\mathrm{X}} - \Delta(\Delta H)_{\mathrm{X}}\right] \quad (8)$$

where $\Delta(\Delta H)_X$ and $\Delta(\Delta H)^-_X$ yield the enthalpies of interactions between the *para* situated groups in phenol and phenoxide, respectively. It appears that the change in deprotonation energy of phenol upon *para*-substitution by X—the increment $I(X)_p$—is determined by $\Delta(\Delta H)^-_X - \Delta(\Delta H)_X$. However, the same magnitude is obtained by Eq. 5. Hence, it follows:

$$I(\mathrm{X})_p = \Delta(\Delta H)^{-}_{\mathrm{X}} - \Delta(\Delta H)_{\mathrm{X}} = \left[\Delta(-\mathrm{IE}^{\mathrm{Koop}}_{n});\ \Delta E(\mathrm{ei})^{(n)}_{\mathrm{rex}};\ \Delta(\mathrm{BAE})^{\cdot}_{\alpha}\right] \quad (9)$$

where Δ in the triadic formula denotes a change occurring in phenol derivative imposed by substituent X relative to the parent phenol. It follows that triadic analysis is equivalent to the homodesmotic reactions approach, but provides more information on the effect of substituents on the acidity of the initial acid. It enables dissection of the deprotonation process into the initial, intermediate and final state effects at the global level, which is conceptually advantageous. Notice that the homodesmotic reactions approach describes the influence of the initial and final states (relative to the parent phenol) by $\Delta(\Delta H)_X$ and $\Delta(\Delta H)^-_X$, respectively. It does not provide, for example, information on the site of deprotonation reflected in the $(\mathrm{IE})^{\mathrm{Koop}}_n$ term included in the trichotomy analysis.

3.3. Acidity and Hammett's σ_p^- constants

A relation between the proton affinities of the conjugate bases and Hammett's σ-constants is of general importance. A correlation between $\Delta PAs(A^-)$ relative to phenoxide anions and σ_p constants for 'neutral' substituents is plotted in Figure 3a. It is poor as reflected in R^2 coefficient 0.839. The average absolute deviations AAD for $\Delta PA(A^-)$ is rather high (2.5 kcal mol^{-1}). This is not surprising because the acidity of substituted phenols is predominantly determined by the final conjugate base anionic states. Consequently, a correlation against the σ_p^- constants should be more adequate. Indeed, much better correlativity is obtained by σ_p^- constants ($R^2 = 0.971$) as illustrated by Figure 3b. The AAD dropped to 1.0 kcal mol^{-1}. It should be mentioned that the SH group is not considered in these calculations, because it deprotonates at sulfur atom. A decisive influence of the final state in determining acidity is mirrored by Koopmans' ionization energies $\Delta(\mathrm{IE})^{\mathrm{Koop}}_n$ and ΔPAs, which is pictorially represented by Figure 4a. The corresponding correlation coefficient is $R^2 = 0.973$ with AAD of 1.0 kcal mol^{-1}. Finally, a high correlativity between $\Delta(\mathrm{IE})^{\mathrm{Koop}}_n$ and σ_p^- constants ($R^2 = 0.979$) is evident from Figure 4b, which is of considerable interest, because $\Delta(\mathrm{IE})^{\mathrm{Koop}}_n$ is a gas-phase parameter, whereas σ_p^- constants are developed by studying reactivity in (aqueous) solutions. A high degree of their compatibility indicates that intrinsic properties of substituted phenols are greatly preserved in solutions.

It is of interest to use these correlations in order to estimate σ_p^- constants for superacidifiers $C(CN){=}C(CN)_2$ and $S(O)({=}NSO_2CF_3)CF_3$. The former moiety should have σ_p^- constants of 2.39 and 2.65 using correlations given Figures 3b and 4b, respectively. It appears that these values are appreciably higher than $\sigma_p^- = 1.70$ deduced from experiments in solution.[12] Similarly, the σ_p^- constant for $S(O)({=}NSO_2CF_3)CF_3$ deduced from Figures 3b and 4b should be 2.27 and 2.20, respectively. The former value is close to $\sigma_p^- \cong 2.30$ estimated by Terrier et al.[46] by experiments in aqueous solution. Hence, it is possible that $S(O)({=}NSO_2CF_3)CF_3$ is a stronger acidifier than

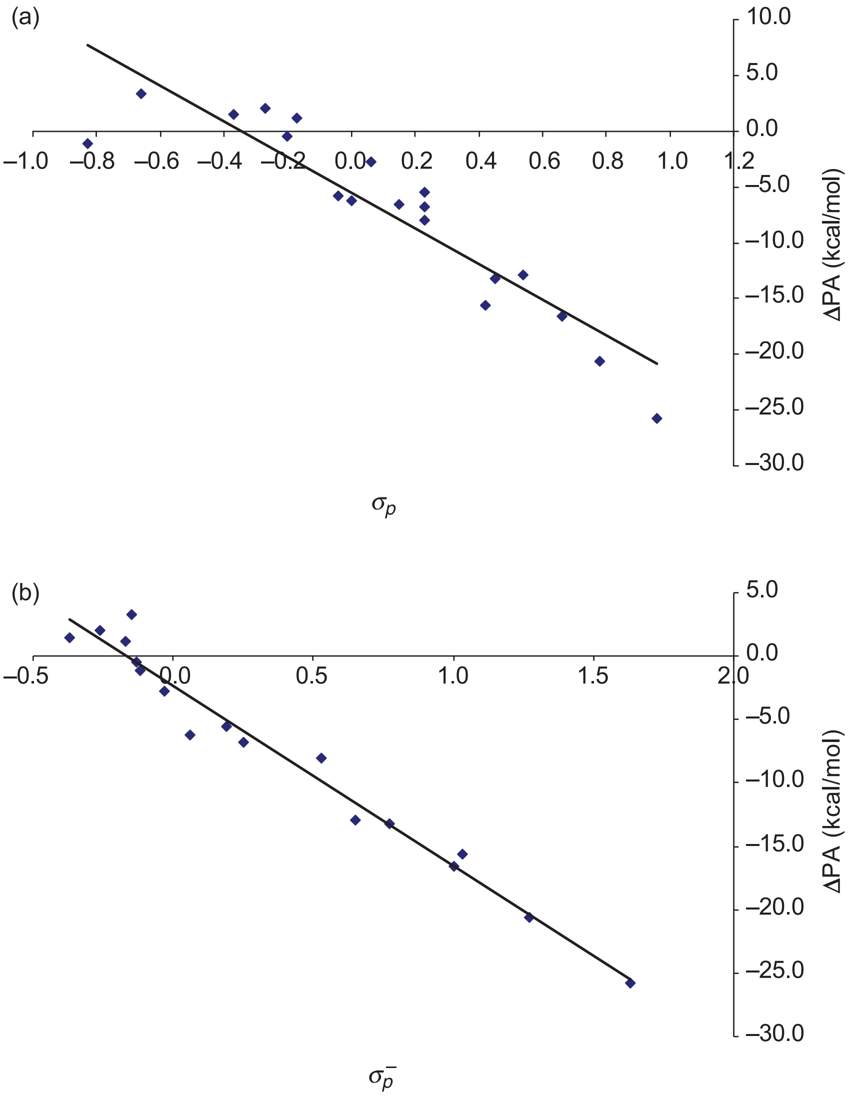


Figure 3. (a) A plot of proton affinities of anions relative to phenoxide ΔPA against Hammett's σ_p constants ($\Delta PA(A^-) = -15.92\sigma_p - 5.55$). (b) Approximate linear relationship between $\Delta PA(A^-)$ and Hammett's σ_p^- constants ($\Delta PA(A^-) = -14.18\sigma_p^- - 2.38$).

C(CN)=C(CN)$_2$ in H_2O implying that the hydrogen bonding of S(O)(=NSO$_2$CF$_3$)CF$_3$ with water molecules is much more effective than is the case with the cyano groups in the *para*-tricyanovinyl phenol. As a final remark it should be noted that σ_p^- values for the NO$_2$ group developed from correlations depicted in Figures 3b and 4b are 1.29 and 1.43 thus being in good accordance with the experimental $\sigma_p^-(\exp) = 1.27$.[12] It is fair to conclude that theoretical (gas-phase) results correlate well with experiment even in the case of extremely strong acidifiers, C(CN)=C(CN)$_2$ being a notable exception.

In order to put the present results into a proper perspective, we shall briefly comment on some local descriptors used in interpreting acidities of phenols. The simplest descriptor is the formal atomic charge of the oxygen and hydrogen atoms pertaining the reaction OH center. Gross and Seybold[21] examined Mulliken charges,[47] the electrostatic atomic charges of Merz, Singh and Kollman[48] and the natural population charges of Weinhold et al.[49] of H atom in neutral phenols and O$^-$ atom in the corresponding phenoxide anions. Both descriptors correlated very poorly with the experimental pK_a values. Romero and Méndez[22] used the hydrogen atomic charge in *para*-substituted phenols in combination with the electronegativity of the X–C6H4O$^{\cdot}$ fragment and concluded that Mulliken q(H) was pivotal in rationalizing acidities of phenols. This finding should be taken with caution, because q(H) reflects properties of the initial state, thus being in contradiction with evidence that acidities of *para*-substituted phenols containing electron accepting groups are determined by the final state. More sophisticated local descriptors are provided by the minima of the electrostatic potential in the vicinity of the reactive center $V_{\min}$[50] and the average local ionization energy I(r).[51] The latter is calculated on molecular surface of constant density, where I(r) has its lowest value $I_{s,\min}$, which in turn corresponds to a site expected to be the most reactive towards electrophiles. Haeberlein and Brinck[19] found an excellent correlation between $I_{s,\min}$ and selection of σ_p^- constants for 11 *para*-substituted phenols ($R^2 = 0.994$) by using HF/6-31+G(d) model. Furthermore, they found very good correlations between the B3LYP/6-31+G(d) acidities and $V_{\min}$ calculated near the hydroxyl oxygen in both phenoxide anions and phenols. Based on these results, they reached a somewhat conflicting conclusion that it is sufficient

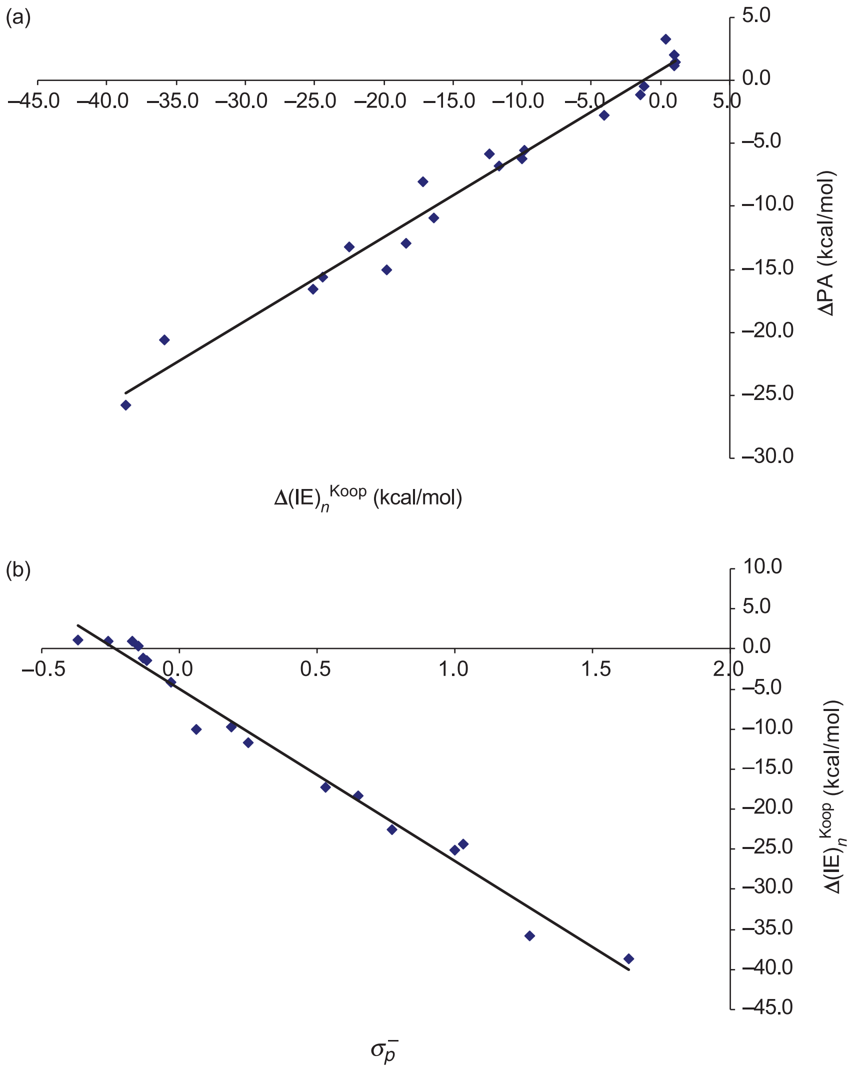


Figure 4. (a) Correlation between $\Delta PA(A^-)$ and relative Koppmans' ionization energies $\Delta(IE)_n^{Koop}$ reflecting the final state effect ($\Delta PA(A^-) = 0.66\Delta(IE)_n^{Koop} + 0.85$). (b) Linear relation between $\Delta(IE)_n^{Koop}$ and Hammett's σ_p^- constants ($\Delta(IE)_n^{Koop} = -21.48\sigma_p^- - 4.98$).

to do calculations on either substituted phenols or the corresponding phenoxide ions. The point is that it cannot be true both ways since properties of phenols correspond to the initial state, whereas features of phenoxides reflect the final state effects. We have shown that in phenols substituted by electron releasing groups the intermediate relaxation energy plays a decisive role in decreasing acidity (vide supra), while in phenols possessing very strong electron accepting substituents the final state is a governing factor. It follows that local descriptors of acidity should be taken with due caution.

4. Conclusion

Triadic analysis provides a global description of the deprotonation process, which can be dissected in three stages: the initial, intermediate and final step. The corresponding energy contributions provide useful insight into the phenomenon, which includes properties of the initial acid reflected in the homolytic dissociation energy, ability of the final anion to accommodate excess negative charge in the molecular orbital undergoing a drastic change in deprotonation and the intermediate relaxation of the electron charge density and the nuclei in the anion. An important result of the present analysis is that substituents can be clearly distinguished by their electron donor and electron acceptor capability. The former decrease the acidity of phenol, whereas the latter increase its acidity albeit to a small extent. The electron accepting substituents influence acidity via the final state mirrored by Koopmans' ionization energy of the MO hosting the excess electron. The strongest acidifying effect is exerted by SO_2CF_3, $S(O)({=}NSO_2CF_3)CF_3$ and $C(CN){=}C(CN)_2$ groups, which surpass that of the NO_2 group. Finally, it is demonstrated that pentacyano derivative of phenol offers itself as a powerful OH superacid as evidenced by ΔH_{acid} value of 287.5 kcal mol^{-1}.

As to Hammett's 'experimental' σ_p^- constants, they correlated well with $\Delta PA(A^-)$ and Koopmans' ionization $\Delta(IE)_n^{Koop}$ energies of the conjugate bases, where Δ denotes values relative to the parent phenol. This is remarkable, since σ_p^- constants are derived from the experimental values in solutions, whereas calculations refer to the gas-phase. It is our strong belief that σ-constants should be developed by careful ab initio calculations on single molecules in the future, to be subsequently supplemented by experiments and computations including solvent effects.

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