

Theoretical Study of Additivity of the Deprotonation Energies in Aromatics. I. Disubstituted Benzenes[†]

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Introduction

According to Brønsted, acidity is the capability of a molecule to give up a proton.¹ More specifically, acidity may be expressed either by the equilibrium constant, the pK_a value, or by the Gibbs energy change (ΔG°_T) for the reaction



Theoretical estimates of acidity involve a difference in energy for the optimized structures of RH and R⁻ corrected by a difference in the vibrational zero-point energy (ZPE). Recently, excellent agreement with experiment for intrinsic acidities was obtained by the G2 method.^{2,3} Unfortunately, this approach is too intricate to be practical in medium-sized molecules like benzene and its numerous derivatives, becoming unfeasible if even larger molecular systems are investigated. It is the aim of the present work to find a more economical theoretical model that is applicable to large compounds and yet capable of providing reliable information on acidity. Moreover, we shall offer convincing evidence that acidities of polysubstituted benzenes follow a simple additivity rule, implying that acidity is straightforwardly obtained once the increments for monosubstituents are known. This feature parallels additivity in the proton affinities (PAs) of aromatics established recently.^{4,5}

Theoretical Model and Results

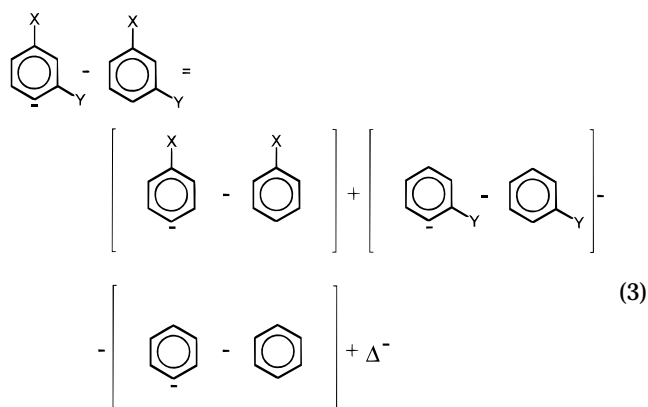
Deprotonation energies (DPEs) are estimated by using a general equation:

$$\text{DPE}(\text{RH}_\alpha) = E(\text{R}_\alpha^-) + \text{ZPE}(\text{R}_\alpha^-) - [E(\text{RH}) + \text{ZPE}(\text{RH})] \quad (2)$$

where E signifies the total molecular energy, RH and R⁻ stand for the acid in question and its conjugated base, respectively, while α denotes the site of deprotonation. Since the latter leads to molecular anions by forming a

lone pair, a flexible basis set is necessary since diffuse distribution of the lone pair density requires use of the diffuse functions. Concomitantly, molecular geometries were optimized by utilizing the HF/6-31+G* model which was employed for calculations of the ZPEs, too. However, aromatic systems possess mobile and highly delocalized π -electrons, implying that their correlation should be explicitly taken into account. This was achieved by the Møller–Plesset perturbation theory of the second order (MP2)⁶ by using single point calculations. Specifically, we employed three models: HF/6-31+G*, MP2(fc)/6-31+G**//HF/6-31+G*, and MP2(fc)/6-311+G**//HF/6-31+G* denoted by I, II and III, respectively. Calculations have been carried out by using Gaussian 94 and GAMESS program packages.^{7,8} The ZPEs were multiplied by a common weighting factor 0.89 as usual.⁶

In discussing the additivity hypothesis for deprotonation energies we made use of the idea of homodesmotic chemical reactions⁹ in which the number of structural groups of the specific types of covalent bonds, classified according to the hybridization states of participating atoms, is kept constant. Homodesmotic reactions proved very useful in considering a number of molecular properties like the strain energy and electron delocalization,⁹ intramolecular interactions between molecular fragments,⁶ electrophilic substitution reactivity in fused planar systems,¹⁰ and the additivity of the PAs.^{4,5} To illustrate their application here let us consider the deprotonation of a 1,3-disubstituted benzene as a typical example. After some rearrangements the corresponding homodesmotic reaction reads:



By adding and subtracting the DPE of benzene on the right-hand side of eq 3 one obtains

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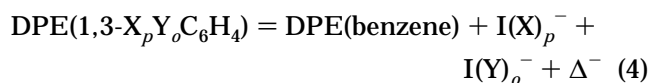
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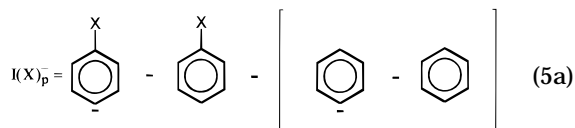
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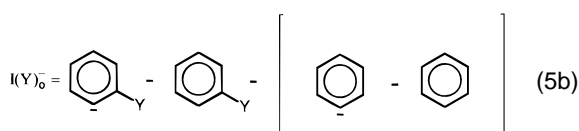
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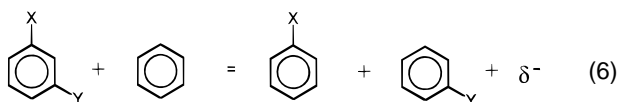
where $\text{I}(\text{X})_p^-$ and $\text{I}(\text{Y})_o^-$ denote increments of deprotonation due to para- and ortho-monosubstitutions:



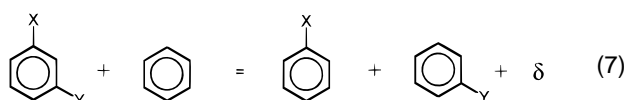
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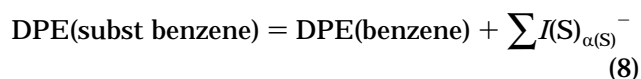
Here the superscript minus denotes a loss of a proton. It should be kept in mind that the deprotonation site is specified relative to both substituents as in eq 4, where proton abstraction takes place para to X and ortho to Y. It is clear from eqs 5a and 5b that increments describe the change in DPE of the parent molecule (benzene) caused by the substituent at the particular position in the ring. In other words, each substituent behaves as if the other was nonexistent, thus providing a basis for the independent substituent approximation (ISA). Apparently, the deprotonation energy of a disubstituted benzene will be given in a simple additive fashion (4) if Δ^- is relatively small. In order to see that Δ^- is small indeed, let us examine the following homodesmic reactions:



and



Subtracting eqs 6 and 7 we find out that $\Delta^- = \delta^- - \delta$. Since δ^- and δ are expected to be reasonably small in view of the close matching of the bonding features in the homodesmic reactions 6 and 7, one concludes that Δ^- should be small enough to ensure additivity in the DPEs. It follows that the additivity formula (4) will give satisfactory results if (a) either the interference energies between substituents X and Y, mediated by the benzene ring, are small in the initial and final states or (b) they are appreciable but comparable in disubstituted benzene and its deprotonated forms. Calculations show that condition a is satisfied in most cases and that b holds if δ and δ^- cannot be abandoned. Finally, one can straightforwardly generalize eq 4 to include polysubstituted benzenes:



where the summation goes over all substituents S and $\alpha(\text{S})$ signifies the position of the substituent relative to the deprotonation site ($\alpha = o, m, p$). It should be reiterated that formula 8 is given within the ISA model,

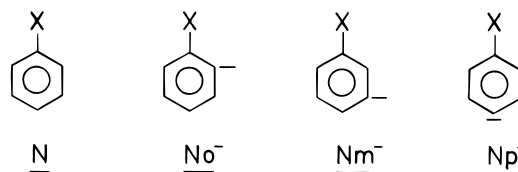


Figure 1. Monosubstituted benzenes and some of their deprotonated forms. N denotes substituents X = CH₃, OH, F, and CN assuming values 1, 2, 3 and 4, respectively.

Table 1. Deprotonation Energy Increments for Various Substituent X and Positions α in Benzene Ring As Estimated by Several Theoretical Models (in kcal/mol)

theoretical models ^{a,b} increments $\text{I}(\text{X})_a^-$	I	II	III
$\text{I}(\text{CH}_3)_o^-$	0.0	-1.2	-1.2
$\text{I}(\text{CH}_3)_m^-$	0.5	0.5	0.4
$\text{I}(\text{CH}_3)_p^-$	1.1	0.4	0.3
$(\text{OH})_o^-$	-12.0	-15.0	-14.6
$\text{I}(\text{OH})_m^-$	-3.8	-3.0	-2.9
$\text{I}(\text{OH})_p^-$	0.3	-1.3	-1.0
$\text{I}(\text{F})_o^-$	-11.9	-13.8	-13.0
$\text{I}(\text{F})_m^-$	-7.5	-6.7	-6.3
$\text{I}(\text{F})_p^-$	-4.7	-5.5	-5.0
$\text{I}(\text{CN})_o^-$	-20.1	-17.4	-17.1
$\text{I}(\text{CN})_m^-$	-16.1	-15.8	-15.7
$\text{I}(\text{CN})_p^-$	-17.5	-15.0	-15.0

^a Theoretical models HF/6-31+G*, MP2(fc)/6-31+G**//HF/6-31+G* and MP2(fc)/6-311+G**//HF/6-31+G* are denoted by I, II, and III, respectively. ^b Deprotonation energies of benzene calculated by models I, II, and III are 405.7, 400.7, and 398.7, respectively (in kcal/mol).




which performs very well in spite of its utmost simplicity, as evidenced by present results.

Energetic properties of benzene, phenyl anion, and substituted benzenes $\text{C}_6\text{H}_5\text{X}$ (X = CH₃, OH, F and CN) and their ortho-, meta-, and para-deprotonated forms (Figure 1) are given in tables.¹¹ The selected substituents exhibit widely different modes of interaction with the phenyl ring. It is well-known that CH₃ is a weak σ - and π -donor, CN is a strong σ - and π -withdrawing group, whereas OH and F are σ -acceptors and π -donors. We shall use the deprotonation energy of benzene as a gauge, which assumes the values 405.7, 400.7, and 398.7 (in kcal/mol) for models I, II, and III, respectively. Since the corresponding experimental energy is 398.8 kcal/mol,¹² it follows that model III is very well suited for studying deprotonation energies in substituted benzenes at the ring sites. This conjecture is corroborated by the calculated DPE of phenol (347.7 kcal/mol), which compares well with the measured value of 349.8 kcal/mol.¹² The estimated increments for CH₃, OH, F, and CN calculated according to eq 5 by models I, II, and III are presented in Table 1. Perusal of the data shows that increments are not very sensitive to the choice of basis set, if theory at the MP2 level is employed. One observes that the Hartree-Fock values are not unreasonable, but could deviate by ~ 3 kcal/mol compared to the MP2 values, which is not satisfactory. If the increments are low, then the HF estimates might assume a wrong sign occasionally. Negative increments imply that substitution lowers deprotonation energies, thus leading to increased acidity. It is interesting to note that ortho-positions are the most acidic ones even in the case of the electron-donating CH₃ group. Another point of interest is provided by σ -accept-

(11) Tables involving computed energies are deposited as supporting information.

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Table 2. Comparison of Deprotonation Energies of Some Disubstituted Benzenes (in kcal/mol) As Estimated by Theoretical Models I, II, and III with the Corresponding Additivity Values^{a,b}

X	Y	I	A (I)	II	A (II)	III	A (III)
							
F	F						
(F) _o	(F) _m	386.5	386.3	380.2	380.2	379.3	379.4
(F) _m	(F) _p	394.0	393.5	389.3	388.5	388.2	387.4
F	CH ₃						
(F) _o	(CH ₃) _m	394.8	394.3	387.9	387.4	386.7	386.1
(F) _m	(CH ₃) _p	400.0	399.3	395.3	394.4	393.6	392.7
(F) _p	(CH ₃) _m	402.0	401.5	396.3	395.7	394.8	394.1
(F) _m	(CH ₃) _o	399.1	398.2	393.5	392.8	391.9	391.2
F	OH						
(F) _o	(OH) _m	389.5	390.0	383.1	383.9	382.2	382.8
(F) _m	(OH) _p	399.1	398.5	393.6	392.7	392.2	391.4
(F) _p	(OH) _m	399.7	397.2	395.0	392.2	393.6	390.8
(F) _m	(OH) _o	389.8	386.2	382.6	379.0	381.0	377.8
F	CN						
(F) _o	(CN) _m	378.4	377.7	372.0	371.1	370.9	370.0
(F) _m	(CN) _p	381.5	380.7	380.0	379.0	378.4	377.4
(F) _p	(CN) _m	385.5	384.9	380.2	379.4	378.8	378.0
(F) _m	(CN) _o	379.3	378.1	377.7	376.6	376.5	375.3
							
F	F						
(F) _o	(F) _o	381.8	381.9	373.2	373.2	372.7	372.7
(F) _o	(F) _p	389.2	389.1	381.7	381.4	381.0	380.7
(F) _m	(F) _m	391.1	390.7	387.6	387.3	386.4	386.1
F	CH ₃						
(F) _o	(CH ₃) _o	394.2	393.8	386.1	385.7	384.9	384.5
(F) _o	(CH ₃) _p	395.2	394.9	387.7	387.3	386.4	386.0
(F) _m	(CH ₃) _m	399.1	398.7	394.8	394.5	393.1	392.8
(F) _p	(CH ₃) _o	401.3	401.0	394.4	394.0	392.8	392.5
F	OH						
(F) _o	(OH) _o	382.5	381.8	373.0	371.9	372.2	371.1
(F) _o	(OH) _p	394.5	394.1	386.2	385.6	385.1	384.7
(F) _m	(OH) _m	394.8	394.4	391.3	391.0	390.0	389.5
(F) _p	(OH) _o	389.1	389.0	380.7	380.2	379.6	379.1
F	CN						
(F) _o	(CN) _o	374.2	373.7	370.1	369.5	369.2	368.6
(F) _o	(CN) _p	377.0	376.3	372.5	371.9	371.3	370.7
(F) _m	(CN) _m	382.6	382.1	378.8	378.2	377.3	376.7
(F) _p	(CN) _o	381.1	380.9	378.1	377.8	377.0	376.6
							
F	F						
(F) _o	(F) _m	386.5	386.3	380.6	380.2	379.7	379.4
F	CH ₃						
(F) _o	(CH ₃) _m	394.5	394.3	387.7	387.4	386.4	386.1
(F) _m	(CH ₃) _o	398.5	398.3	393.3	392.8	391.6	391.2
F	OH						
(F) _o	(OH) _m	390.1	390.0	384.4	384.0	383.2	382.8
(F) _m	(OH) _o	386.7	386.2	379.8	379.0	378.6	377.8
F	CN						
(F) _o	(CN) _m	377.9	377.7	371.4	371.1	370.2	370.0
(F) _m	(CN) _o	378.5	378.1	376.8	376.6	375.6	375.3

^a Additivity estimates of the deprotonation energies obtained within the framework of the model *N* are denoted by A(*N*), where *N* = I, II, and III. ^b Site of the cleaved proton is determined by its position relative to both substituents (X)_α and (Y)_β, where α, β = *o*, *m*, *p*.

ing and π -donating OH and F substituents, which introduce a strong discrimination between the ortho-position on one side and the meta- and para-positions on the other. In contrast, the CN group activates almost uniformly all ring positions as far as the heterolytic

proton cleavage is concerned. Actual values of the DPE increments are of some interest, particularly in conjunction with the corresponding proton affinity (PA) increments. The point is that the proton abstraction is determined predominantly by the σ -skeleton orbitals, whereas the ring protonation "measures" mostly the π -electron distribution.^{4,5,13} Concomitantly, acidity and basicity parameters provide complementary information on the role of σ - and π -electrons in specifying properties of aromatic systems. We defer, however, a detailed discussion to a later full paper.

Ring deprotonation energies of ortho-, meta- and para-disubstituted benzenes are surveyed in Table 2. Perusal of the presented data shows that all three methods reflect a remarkable additivity in the ring proton DPEs as evidenced by the average absolute deviations from the full calculations. They read 0.6, 0.7 and 0.7 (in kcal/mol) for models I, II, and III, respectively. The fact that the simple Hartree–Fock model reproduces the additivity in DPEs relatively well indicates that it is an intrinsic feature that does not strongly depend on finer details of the electron density distribution. It should be stressed, however, that model I yields deprotonation energies in somewhat worse accordance with the available experimental values as compared to models II and III (viz. benzene and toluene), thus being less satisfactory. Generally speaking, however, one can safely state that the additivity formula (8) works very well for deprotonation energies of the aromatic protons in disubstituted benzenes. Our predictions can be easily tested by experimental techniques in the systems involving F and CN substituents. We feel also that the increments introduced in this work will give a new insight into the Hammett and Taft relations commonly used in predicting acidity of polysubstituted aromatics.¹⁴

Conclusion

To summarize, it appears that both ab initio models II and III represent a good compromise between accuracy and practicability in predicting intrinsic acidity of substituted benzenes. The independent substituent approximation (ISA) leads to a simple, intuitively appealing and transparent additivity formula, offering an elementary rule of thumb capable of reproducing and rationalizing DPEs in multiply substituted benzenes. Its performance is remarkable as evidenced by comparison with the full ab initio calculations based on the models II and III. We are confident that the same additivity formula—mutatis mutandis—will work in other aromatic systems and for other substituents.

Acknowledgment. This work was supported in part by Ministry of Science and Technology of the Republic of Croatia. We thank The University of Zagreb Computation Centre and the IBM project "Academic Initiative for Croatia" for computation time and excellent service.

Supporting Information Available: Total molecular energies and zero-point vibrational energies of the considered molecules and anions (4 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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