Acta Chimica Slovaca, Vol.2, No.2, 2009, 37 - 51

DFT/B3LYP Study of the O–H Bond Dissociation Enthalpies and Proton Affinities of *para*- and *meta*-Substituted Phenols in Water and Benzene

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Abstract

For 30 *para*- and *meta*-substituted phenols in two solvents – water and benzene, the reaction enthalpies related to two mechanisms of phenolic antioxidants action, hydrogen atom transfer (HAT) and sequential proton loss electron transfer (SPLET), were calculated using IEF-PCM DFT/B3LYP/6-311++G** method. Phenolic O–H bond dissociation enthalpy (BDE) represents the reaction enthalpy of HAT. Phenoxide anion (ArO^-) proton affinity (PA) is related to the first step of SPLET – abstraction of proton from the phenol molecule. Except the comparison of calculated BDEs with available experimental and/or theoretical values, obtained BDEs and PAs were correlated with Hammett constants. We have found that electron-withdrawing groups increase BDE, while electron-donating substituents cause a rise in PA. On the contrary, electron-donating groups lower BDE and induce the increase in PA. Dependences of BDE and PA values on Hammett constants of the substituents are linear. From the thermodynamic point of view, entering SPLET mechanism represents the most probable process in water, where PAs of all studied phenols are considerably lower than BDEs. However, in benzene, BDEs are lower than PAs, i.e. HAT represents the most probable pathway. The only exception is *p*-nitrophenol – its PA is lower than BDE. In comparison to gas-phase, studied solvents attenuate the substituent effect on PA. On the other hand, substituent induced changes in BDE are larger in the solution-phase.

Keywords: integral equation formalism polarizable continuum model; phenolic antioxidant; salvation; solvent effect; substituent effect.

Introduction

Oxidation reactions are the major cause of the irreversible deterioration of biological systems and synthetic polymers. Oxidation generally corresponds to a free radical chain reaction (Gugumus 1990). The most important reactive radical intermediates formed during oxidation reactions are hydroxyl ($HO^\bullet$), alkoxyl ($RO^\bullet$) and peroxyl ($ROO^\bullet$) radicals (Gugumus 1990, Zhu 1997).

Antioxidants are chemical compounds that can quench reactive radical intermediates formed during the oxidative processes. It is well-known fact that phenolic compounds act as chain-breaking antioxidants. Phenoxyl radicals represent important intermediates in many biological and industrial applications (Gugumus 1990, Zhu 1997, Halliwell 1989). Their importance in relation to the antioxidant activity of phenols has led to an increased interest in these systems in last years. Besides the two generally accepted mechanisms of phenolic antioxidants (generally ArOH) action (Wright 2001, Vafiadis 2005, Musialik 2005), namely hydrogen atom transfer (HAT)

$$ArOH \rightarrow ArO^\bullet + H^\bullet \qquad (1)$$

and single-electron transfer followed by proton transfer (SET-PT),

$$ArOH \rightarrow ArOH^{+\bullet} + e^- \qquad (2.1)$$

$$ArOH^{+\bullet} \rightarrow ArO^\bullet + H^+ \qquad (2.2)$$

recently another mechanism has been discovered – sequential proton loss electron transfer (SPLET) mechanism (Musialik 2005, Litwinienko 2003, 2004 and 2007, Foti 2004)

$$ArOH \rightarrow ArO^- + H^+ \qquad (3.1)$$

$$ArO^- \rightarrow ArO^\bullet + e^- \qquad (3.2)$$

On the basis of the kinetic measurements, it was experimentally confirmed that α-tocopherol and other phenols can react with $DPPH^\bullet$ (2,2-diphenyl-1-picrylhydrazyl radical) and other electron deficient radicals by two different and nonexclusive mechanisms, HAT and SPLET. Addition of the water to solvent (methanol, ethanol) resulted in the considerable increase in the reaction rate between $DPPH^\bullet$ and α- tocopherol (Musialik 2005, Staško 2007).

From the antioxidant action viewpoint, the net result of the three mechanisms is the same, i.e. the formation of phenoxy radical $ArO^\bullet$. Kinetic measurements showed that the balance among these mechanisms depends on both the environment and the reactants

(Litwinienko 2007). Reaction enthalpies related to the individual steps of the above mentioned mechanisms are denoted as follows:

BDE – O–H bond dissociation enthalpy related to eq. 1
IP – ionization potential, enthalpy of electron transfer from the antioxidant, eq. 2.1
PDE – proton dissociation enthalpy, eq. 2.2
PA – proton affinity of phenoxide ion, eq. 3.1
ETE – electron transfer enthalpy, eq. 3.2.

IP and PA are reaction enthalpies related to the first step of SET-PT and SPLET, respectively. Therefore, BDE, IP and PA determine thermodynamically preferred reaction pathway.

Fu et al. (Fu 2004) studied solvation effect of H_2O and DMSO on ΔBDEs, where ΔBDE = BDE(X-PhOH) – BDE(PhOH) represents difference between substituted phenol and non-substituted phenol BDEs, of eight *para*-substituted phenols using two approaches. In the first one, an explicit complex between the phenol and solvent molecule (further denoted X–PhOH...H_2O) was constructed. In the second approach, authors used polarizable continuum model (PCM) method. Gas-phase geometries of all species were optimized employing B3LYP/6-31G(d) method, enthalpies were calculated using 6-311++G(2df,p) basis set. Guerra et al. (Guerra 2004) employed three approaches in the study of water effect on O–H BDEs of eight *para*-substituted phenols. The microsolvation approach, i.e. hydrogen-bonding (HB) model, considers the interaction of finite number (usually two) of water molecules with the studied phenol and phenoxyl radical. In the second approach, they applied PCM method for BDE computations. In the third one, they applied PCM method in addition to HB model. They used DFT/B3LYP method with 6-31G* basis set.

Singh et al. (Singh 2007) studied ΔBDEs of eight *para*-substituted phenols in DMSO using conductor-like PCM (C-PCM) method. Bakalbassis et al. (Bakalbassis 2003 and 2006) studied bond dissociation enthalpies of *ortho*-substituted phenols in various solvents using DFT/B3LYP calculations and PCM method. The polarizable continuum model presents good accuracy, reliability, adaptability, and a reduced computational effort in describing solvent effects (Miertuš 1981 and 1982, Pascual-Ahuir 1987). PCM method has been widely adopted in recent years, especially in the description of the thermodynamic characteristics of solvation (Tomasi 1994 and 2005, Cramer 1999, Böes 2006).

In our previous work, we found that DFT/B3LYP method with 6-311++G** basis set provides results in good accordance with available experimental or theoretical BDEs and PAs of various mono-substituted phenols, tocopherols and chromans in the gas-phase (Klein 2006 and 2007). Chosen computational approach described especially the effect of the substituents correctly. On the contrary, *ab-initio* MP2, MP3 and MP4 methods did not give reliable results, since they significantly underestimate substituent induced changes in BDE (Klein 2006). We have also found that DFT/B3LYP tends to slightly underestimate absolute values of reaction enthalpies. However, this is generally known fact (Cabral 2005). Our preliminary results – BDEs of phenol and 9 *para*-substituted phenols in water (Klein 2006) indicated that employed IEF-PCM approach gives acceptable results. Moreover, we found that in the gas-phase, HAT represents the thermodynamically favored pathway, while SPLET mechanism is the most probable process in the water. Found PA values in water were considerably lower than corresponding BDEs (Klein 2006). In both previously studied environments, i.e. in the gas-phase and water, SET-PT mechanism is not the preferred one, because ionization potentials of substituted phenols (Klein 2006), tocopherols and chromans (Klein 2007) were always significantly higher than their BDEs.

The goal of this work is to continue the work commenced in (Klein 2006) and to calculate O–H BDEs and PAs of 30 *para*- and *meta*-substituted phenols (Fig. 1) in water and benzene in order to assess the substituent and solvent effects on the two reaction enthalpies. Water and benzene were chosen as the typical polar and non-polar solvent. Substituent effects are among the most important concepts of structural effects influencing the chemical, physicochemical, and biochemical properties of chemical species (Krygowski 2005, Hansch 1991). Although in the literature it is possible to find a few experimental reports focused on the substituted phenols BDEs in water and benzene, these papers cover usually less than ten *para*-substituted phenols (Mulder 1988, Lucarini 1996, Lind 1990). Only two above mentioned theoretical studies (Fu 2004, Guerra 2004) of water solvent effect on *para*-substituted phenols are available. No paper related to the substituent and solvent effects on PA is available yet. One of the integral aims of this work is to determine thermodynamically preferred mechanism in the water and benzene.

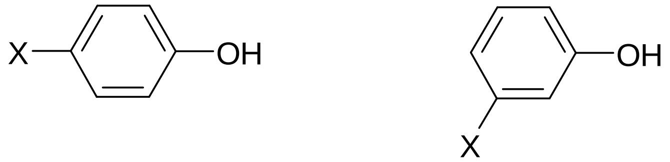

Fig. 1. Studied monosubstituted phenols, X = Br, *t*-Bu, CF_3, CN, Cl, F, Me, MeCO, MeO, $MeSO_2$, NH_2, NMe_2, NO_2, OH, Ph

Materials and Methods

Computational details

All calculations were performed using Gaussian 03 program package (Frisch 2003). The geometry of each compound, radical or anion structure was optimized using DFT method with UB3LYP functional without any constraints (energy cut-off of 10^{-5} kJ mol^{-1}, final RMS energy gradient under 0.01 kJ mol^{-1} Å^{-1}). The calculations were performed in 6-311++G** basis set (Binkley 1980). For the species having more conformers, all conformers were investigated. The conformer with the lowest electronic energy was used in this work. Solvent contribution to the total enthalpies was computed employing integral equation formalism IEF-PCM method (Cances 1997 and 1998). Since Gaussian 03 allows solution-phase geometry optimization, this approach was used for the parent molecules and their respective radicals and anions. All enthalpies were calculated for 298 K.

Accuracy of the energy evaluation in the case of systems involving open-shell species is sensitive to spin contamination. Spin contaminations of radicals were found in the 0.76–0.78 range. After the annihilation of the first spin contaminant, they dropped to correct value 0.75. Therefore, spin contamination should not bias found enthalpies.

Results and Discussion

In the case of DFT method, which does not provide enthalpies directly, the total enthalpies of the species X, H(X), at temperature T are usually estimated from the expression (Wright 2001, Bakalbassis 2003, Klein 2006, Chandra 2002)

$$H(\mathrm{X}) = E_0 + \mathrm{ZPE} + \Delta H_{\mathrm{trans}} + \Delta H_{\mathrm{rot}} + \Delta H_{\mathrm{vib}} + RT \tag{4}$$

where E_0 is the calculated total electronic energy, ZPE stands for zero-point energy, $\Delta H_{\mathrm{trans}}$, ΔH_{rot}, and ΔH_{vib} are the translational, rotational and vibrational contributions to the enthalpy. Finally, RT represents PV-work term and is added to convert the energy to enthalpy. $\Delta H_{\mathrm{trans}}$ (3/2 RT), ΔH_{rot} (3/2 RT or RT for a linear molecule), and ΔH_{vib} contributions to the enthalpy are calculated from standard formulas (Atkins 1998).

From the calculated total enthalpies we have determined the following quantities

$$\mathrm{BDE} = H(\mathrm{ArO}^{\bullet}) + H(\mathrm{H}^{\bullet}) - H(\mathrm{ArOH}) \tag{5}$$

$$\mathrm{PA} = H(\mathrm{ArO}^{-}) + H(\mathrm{H}^{+}) - H(\mathrm{ArOH}) \tag{6}$$

The calculated gas-phase enthalpy of proton, $H(\mathrm{H}^+)$, is 6.197 kJ mol^{-1}. For the enthalpies of hydrogen atom ($\mathrm{H}^\bullet$) and proton (H^+) hydration we used published experimental values: $\Delta_{\mathrm{hydr}}H(\mathrm{H}^\bullet) = -4$ kJ mol^{-1} (Bizarro 1999, Parker 1992), $\Delta_{\mathrm{hydr}}H(\mathrm{H}^+) = -1090$ kJ mol^{-1} (Atkins 1998). For the $\mathrm{H}^\bullet$ solvation in benzene, we have also employed published value $\Delta_{\mathrm{solv}}H(\mathrm{H}^\bullet) = 6$ kJ mol^{-1} (Bizarro 1999, Parker 1992). Because we have not found the enthalpy of H^+ solvation in benzene in the literature, we used the value $\Delta_{\mathrm{solv}}H(\mathrm{H}^+) = -884$ kJ mol^{-1}. This value we estimated from DFT IEF-PCM calculation and it represents the enthalpy of reaction $C_6H_6(l) + H^+(g) \rightarrow (C_6H_6)^+(solv)$ in benzene. The potential inaccuracies of determined BDE and PA values, introduced by the application of experimental or estimated enthalpies of $\mathrm{H}^\bullet$ and H^+ solvation, will cancel when the substituent effects are expressed in terms of ΔBDE and ΔPA values. On the other hand, absolute BDE and PA values enable the comparison of the solvent effect on these quantities and to find the preferred reaction pathway in the studied solvents.

PCM method developed by Tomasi and co-workers (Miertuš 1981 and 1982, Tomasi 1994, Barone 1997) provides the solvation free energy corresponding to the 1 mol l^{-1} standard state and 298 K. Although correcting gas-phase enthalpies with PCM solvation free energies does not represent correct approach, calculated enthalpies can be considered as a reasonable approximation (Klein 2006 and 2007). Moreover, reaction entropies related to the phenolic O–H bond splitting-off or proton abstraction from the phenol molecule can be assumed almost identical for the non-substituted and substituted phenols (Fu 2004, Klein 2006) and the contribution stemming from the different standard states for the gas-phase and the solvent effect calculations will also cancel in the case of ΔBDE and ΔPA values. Therefore, all these contributions do not affect ΔBDEs and ΔPAs or the line slopes of corresponding Hammett dependences describing the substituent effect in the studied solvents.

Comparison of calculated BDE and ΔBDE values with available experimental and theoretical results

Calculated BDEs of *para*- and *meta*-substituted phenols are summarized in the Tables 1 and 2, respectively. These tables also contain gas-phase values from (Klein 2006) and Hammett constants σ_p and σ_m taken from (Hansch 1991). Only $\sigma_p(\mathrm{NMe_2}) = -0.63$ was used from (Pytela 1994), because in the previous papers (Klein 2006 and 2007) we found that employed

$\sigma_p(NMe_2) = -0.83$ (Hansch 1991) caused that reaction enthalpies related to *p*-NMe_2 group clearly did not followed the overall trends in BDE = $f(\sigma_p)$ or PA = $f(\sigma_p)$ dependences. Besides, $\sigma_p(NMe_2) = -0.63$ is close to $\sigma_p(NMe_2)$ published in (Šterba 1985), where –0.57 and –0.61 values can be found.

Lind et al. (Lind 1990) carried out pulse radiolysis (PR) experiments in water. Obtained BDEs of phenol and 11 *para*-substituted phenols are summarized in the Table 3 together with DFT calculated BDEs, further denoted DFT(1), from (Guerra 2004). Mulder et al. (Mulder 1988) estimated the BDEs of phenol and four *para*-substituted phenols from photoacoustic calorimetry (PAC) measurements in benzene. Lucarini et al. (Lucarini 1996) determined BDEs of phenol and three *para*-substituted phenols in benzene employing EPR spectroscopy. Experimental PAC and EPR BDEs in benzene are compiled in the Table 4 together with corresponding ΔBDEs.

Comparison of PR BDEs (Table 3) with calculated values (Table 1) indicates that employed IEF-PCM approach may lead to underestimation of *para*-substituted phenols O–H BDEs. Differences between experimental and calculated values are in the range from 8 kJ mol^{-1} to 20 kJ mol^{-1}. Largest discrepancies between calculated and experimental BDEs can be found for electron-donating groups *p*-NH_2 (19 kJ mol^{-1}) and *p*-MeO (20 kJ mol^{-1}). The average difference reached 14.9 kJ mol^{-1}.

In order to evaluate the reliability of employed computational approach for substituent effect description, it is inevitable to compare calculated and experimental ΔBDE values. Calculated ΔBDEs are shown in Tables 5 and 6 for *para*- and *meta*-substituted phenols, respectively. Experimental PR ΔBDEs are shown in Table 7 together with DFT(1) (Guerra 2004) and DFT(2) (Fu 2004) results of the two available theoretical works. Calculated results show that used IEF-PCM method describes substituent effect in very good agreement with experimental range of BDE changes in water. Experimental ΔBDEs of *para*-substituted phenols in water lie in 78 kJ mol^{-1} wide range, while calculated values are in 87 kJ mol^{-1} range. Largest deviations between experimental and calculated ΔBDEs were found for *p*-MeCO (8 kJ mol^{-1}) and *p*-NO_2 groups (7 kJ mol^{-1}). Deviations between the remaining calculated and experimental ΔBDE values lie within 4 kJ mol^{-1}. Average deviation between 11 experimental and calculated ΔBDEs reached 3.4 kJ mol^{-1}. This indicates that chosen IEF-PCM approach provides reliable ΔBDEs results for *para*-substituted phenols. It can be therefore assumed that ΔBDEs obtained for *meta*-substituted phenols represent reliable predicted values.

Table 5. DFT/B3LYP/6-311++G** ΔBDEs in kJ mol^{-1} of *para*-substituted phenols in water, benzene and gas-phase.

Substituent	Water	Benzene	Gas-phase[a]
p-NH_2	–55	–43	–39
p–NMe_2	–56	–46	–41
p–OH	–29	–23	–22
p–MeO	–26	–24	–24
p–*t*–Bu	–8	–8	–8
p–Me	–10	–9	–10
p–Ph	–12	–10	–10
p–F	–3	–5	–7
p–Cl	0	–2	–5
p–Br	1	–1	–4
p–MeCO	17	7	2
p–CF_3	20	11	9
p–CN	21	14	8
p–$MeSO_2$	27	20	14
p–NO_2	32	24	17

[a] From Ref. (Klein 2006).

Table 6. DFT/B3LYP/6-311++G** ΔBDEs in kJ mol^{-1} of *meta*-substituted phenols in water, benzene and gas-phase.

Substituent	Water	Benzene	Gas-phase[a]
m-NH_2	–11	–6	–5
m–NMe_2	–10	–6	–4
m–*t*–Bu	–4	–3	–4
m–Me	–3	–2	0
m–Ph	1	1	0
m–OH	–3	–2	–2
m–MeO	–4	–5	–5
m–F	8	6	4
m–Cl	8	6	3
m–MeCO	9	5	2
m–Br	8	6	3
m–CF_3	13	11	9
m–CN	17	14	10
m–$MeSO_2$	17	13	8

m–NO_2	20	16	11

[a] From Ref. (Klein 2006).

Table 7. Published experimental and DFT ΔBDEs in kJ mol^{-1} of *para*-substituted phenols in water.

	Experimental[a]	DFT(1)[b]			DFT(2)[c]	
Substituent	PR	PCM	HB	HB+PCM	PCM	X–PhOH...H_2O
p-NH_2	–53				–46	–52
p-NMe_2	–59	–52	–54	–63		
p-OH	–33	–29	–33	–30	–27	–27
p-MeO	–23	–24	–20	–23	–29	–33
p-Me	–9	–8	–10	–10	–15	–21
p-F	–4					
p-Cl	–3	2	–1	4	–5	4
p-Br	–1					
p-MeCO	9	16	17	24		
p-CF_3					12	19
p-CN	20	21	25	30	15	19
p-NO_2	25	31	36	41	19	29

[a] From Ref. (Lind 1990).
[b] DFT/B3LYP/6-31G*, from Ref. (Guerra 2004).
[c] DFT/B3LYP/6-311++G(2df,p)//B3LYP/6-31G(d), from Ref. (Fu 2004).

Unfortunately, just few experimental BDEs of *para*-substituted phenols were determined in benzene (Table 4). Moreover, EPR and PAC BDEs and ΔBDEs are quite distinct. PAC experiments provided lower BDEs closer to calculated values (Table 1). Due to the lack of experimental results, the reliability of calculated BDEs and ΔBDEs in benzene cannot be verified. Obtained results may serve as predicted values.

Although there are two studies of the bond dissociation enthalpies of *para*-substituted phenols, Fu et al. (Fu 2004) published only ΔBDEs. As we already mentioned, Guerra et al. (Guerra 2004) employed three approaches: hydrogen-bonding (HB) model, PCM method and PCM method in addition to HB model (HB+PCM). They used DFT/B3LYP method with 6-31G* basis set. Obtained BDEs of phenol and 8 *para*-substituted phenols are compiled in Table 3 – in the three columns (HB, PCM, HB+PCM) with common heading DFT(1). Comparison with experimental PR results shows that PCM method overestimates experimental values. Obtained BDEs are higher than experimental ones by 8–17 kJ mol^{-1}; the average deviation reached 13.6 kJ mol^{-1}. This indicates that PCM calculations carried out at the gas-phase optimum geometries (B3LYP/6-31G*) overestimate BDEs in water. HB+PCM led to even higher BDEs and the average deviation was 21.5 kJ mol^{-1}. HB approach gave values in very good accordance with experimental BDEs, since the average deviation reached only 3.2 kJ mol^{-1}. However, HB approach tends to overestimates experimentally found ΔBDE values for groups with strong electron-withdrawing effect (*p*-MeCO, *p*-CN and *p*-NO_2). The average deviation between experimental and computed ΔBDEs reached 3.9 kJ mol^{-1} for PCM method, 4.3 kJ mol^{-1} for HB model and 7.1 kJ mol^{-1} for HB+PCM method. When we compared our IEF-PCM and experimental PR ΔBDE values for the same 8 phenols, the average deviation reached 3.8 kJ mol^{-1}. The comparison with all 11 available experimental PR ΔBDEs confirms that IEF-PCM method describes substituent effect in the best agreement with experimental data, since the average deviation is only 3.4 kJ mol^{-1}. Table 7 contains also the results obtained by Fu et al. (Fu 2004) in two columns under common DFT(2) heading. In the first approach (X–PhOH...H_2O column), an explicit complex between the phenol and solvent molecule was constructed. Column denoted PCM contains results of PCM method calculations based on optimum gas-phase geometries. Average deviations of calculated ΔBDEs with 7 available experimental PR values reached 5.4 kJ mol^{-1} and 5.9 kJ mol^{-1} in the case of X–PhOH...H_2O approach and PCM method, respectively.

On the basis of available experimental values, we can sum up that IEF-PCM approach may underestimate phenolic O–H bond dissociation enthalpies in water. However, it describes the substituent effect correctly.

Table 1. DFT/B3LYP/6-311++G** BDEs of *para*-substituted phenols in water, benzene and gas-phase in kJ mol^{-1}, and Hammett constants σ_p.

Substituent	Water	Benzene	Gas-phase^a	$\sigma_p{}^b$
—	352^d	355	347	
p-NH_2	297^d	312	308	–0.66^c
p-NMe_2	296	309	306	–0.63
p-OH	323^d	332	325	–0.37
p-MeO	326^d	331	323	–0.27
p-*t*-Bu	344	347	339	–0.20
p-Me	342^d	346	337	–0.17
p-Ph	340	345	337	–0.01
p-F	349	350	340	0.06
p-Cl	352^d	353	342	0.23
p-Br	353^d	354	343	0.23
p-MeCO	369^d	366	354	0.50
p-CF_3	372	371	358	0.54
p-CN	373^d	369	355	0.66
p-$MeSO_2$	379	375	361	0.72
p-NO_2	384^d	379	364	0.78

[a] From Ref. (Klein 2006).
[b] From Ref. (Hansch 1991).
[c] From Ref. (Pytela 1994).
[d] From Ref. (Klein 2006).

Table 2. DFT/B3LYP/6-311++G** BDEs of *meta*-substituted phenols in water, benzene and gas-phase in kJ mol^{-1}, and Hammett constants σ_m.

Substituent	Water	Benzene	Gas-phase[a]	σ_m[b]
m-NH_2	341	349	342	–0.16
m-NMe_2	342	349	343	–0.16
m-*t*-Bu	348	352	343	–0.10
m-Me	349	353	347	–0.07
m-Ph	353	356	347	0.06
m-OH	349	353	345	0.12
m-MeO	348	350	342	0.12
m-F	360	361	351	0.34
m-Cl	360	361	350	0.37
m-MeCO	361	360	349	0.38
m-Br	360	361	350	0.39
m-CF_3	365	366	356	0.43
m-CN	369	369	357	0.56
m-$MeSO_2$	369	368	355	0.60
m-NO_2	372	371	358	0.71

[a] From Ref. (Klein 2006).
[b] From Ref. (Hansch 1991).

Table 3. Published experimental and DFT BDEs in kJ mol^{-1} of *para*-substituted phenols in water.

	Experimental[a]	DFT(1)[b]		
Substituent	PR	PCM	HB	HB+PCM
—	369	379	366	385
p-NH_2	316			
p-NMe_2	310	326	311	321
p-OH	336	350	332	354
p-MeO	346	354	345	361
p-*t*-Bu				
p-Me	360	370	356	375
p-Ph				
p-F	365			
p-Cl	366	381	365	388
p-Br	368			
p-MeCO	377	395	383	408
p-CF_3				
p-CN	388	400	391	415
p-$MeSO_2$				

p-NO_2	394		409	401	426

[a] From Ref. (Lind 1990).
[b] DFT/B3LYP/6-31G*, data taken from Ref. (Guerra 2004).

Table 4. Published experimental BDE and ΔBDE values in kJ mol^{-1} of *para*-substituted phenols in benzene.

	BDE		ΔBDE	
Substituent	EPR[a]	PAC[b]	EPR	PAC
—	369	351		
p-MeO	346	326	–23	–35
p-*t*-Bu	357	343	–12	–8
p-Me	360		–9	
p-Cl		353		2
p-CF_3		364		13

[a] From Ref. (Lucarini 1996).
[b] From Ref. (Mulder 1988).

O–H Bond dissociation enthalpies: effect of solvents and substituents

In comparison to gas-phase, only BDEs of phenols with strongest electron-donating groups (NH_2, NMe_2 and OH) in *para* position are lower in water. Water causes negligible decrease (1 kJ mol^{-1}) of BDE of phenols with NH_2 and NMe_2 groups in *meta* position. BDEs of the rest of studied substituted phenols are higher. The largest rise in BDE can be found for strong electron-withdrawing groups, especially in the *para*-position.

In the benzene, all BDEs are higher than corresponding gas-phase values. Differences in BDEs are growing with the increase in the electron-withdrawing character of substituents. Again, the differences are more pronounced for groups located in *para* position. When we compare BDEs in the water and benzene mutually, we can see that BDEs in water are larger only in the case of strong electron-withdrawing groups (*p*-MeCO, *p*-CF_3, *p*-CN, *p*-$MeSO_2$, *p*-NO_2, *m*-MeCO, *m*-$MeSO_2$ and *m*-NO_2). However, the differences do not exceed 5 kJ mol^{-1}. Compared to benzene, water induces larger, more than 10 kJ mol^{-1}, drop in BDEs of phenols with strongest electron-donating groups NH_2 and NMe_2 in *para* position (Table 1).

We can conclude that there is no substantial difference between found BDEs in the three environments. Differences between individual BDE values in the gas-phase, benzene and water lie in relatively narrow range, from –15 kJ mol^{-1} (*p*-NH_2 in water and benzene) to +20 kJ mol^{-1} (*p*-NO_2 in water and gas-phase). In all studied environments, electron-donating groups decrease of O–H BDE, whereas electron-withdrawing groups cause its increase. However, environment affects the extent of the substituent induced changes.

The Hammett equation (and its extended forms) has been one of the most widely used tools for the study and interpretation of organic reactions and their mechanisms. Hammett constants σ_p (for substituent in *para* position) and σ_m (for substituent in *meta* position) obtained from ionization of organic acids in solutions can frequently successfully predict equilibrium and rate constants for a variety of families of reactions (Krygowski 2005, Hansch 1991). Hammett constants correlate very well with the changes in phenolic O–H bond dissociation enthalpies and proton affinities (Zhu 1997, Fu 2004, Guerra 2004, Klein 2006, Chandra 2002, Pratt 2004). Here, dependences of obtained reaction enthalpies on the Hammett constants enable the investigation of substituent effects in relation to studied solvents.

Figures 2 and 3 present the correlation between Hammett constants (σ_m and σ_p, shortly denoted as $\sigma_{m,p}$) and BDEs in water and benzene, respectively. The equations obtained from the linear regression are as follows

$$\mathrm{BDE/kJ\ mol^{-1}} = 341 + 56\sigma_p \qquad \text{(water)} \qquad (7)$$

$$\mathrm{BDE/kJ\ mol^{-1}} = 348 + 34\sigma_m \qquad \text{(water)} \qquad (8)$$

$$\mathrm{BDE/kJ\ mol^{-1}} = 345 + 44\sigma_p \qquad \text{(benzene)} \qquad (9)$$

$$\mathrm{BDE/kJ\ mol^{-1}} = 353 + 25\sigma_m \qquad \text{(benzene)} \qquad (10)$$

In the gas-phase (g), we obtained these dependences (Klein 2006)

$$\mathrm{BDE/kJ\ mol^{-1}} = 337 + 38\sigma_p \qquad \text{(g)} \qquad (11)$$

$$\mathrm{BDE/kJ\ mol^{-1}} = 345 + 19\sigma_m \qquad \text{(g)} \qquad (12)$$

For the sake of compatibility, we used $\sigma_p(NMe_2) = -0.63$ in the case of gas-phase BDE = $f(\sigma_p)$ dependence (eq. 11). Table 8 summarizes found line slopes, ρ, with their errors and correlation coefficients, *R*. Analogous results we obtain from ΔBDE = $f(\sigma_{m,p})$ dependences, since ΔBDE represents the difference between BDEs of substituted and non-substituted phenol. The values are only shifted on *y*-axis (the intercept would be lower by BDE of non-substituted phenol).

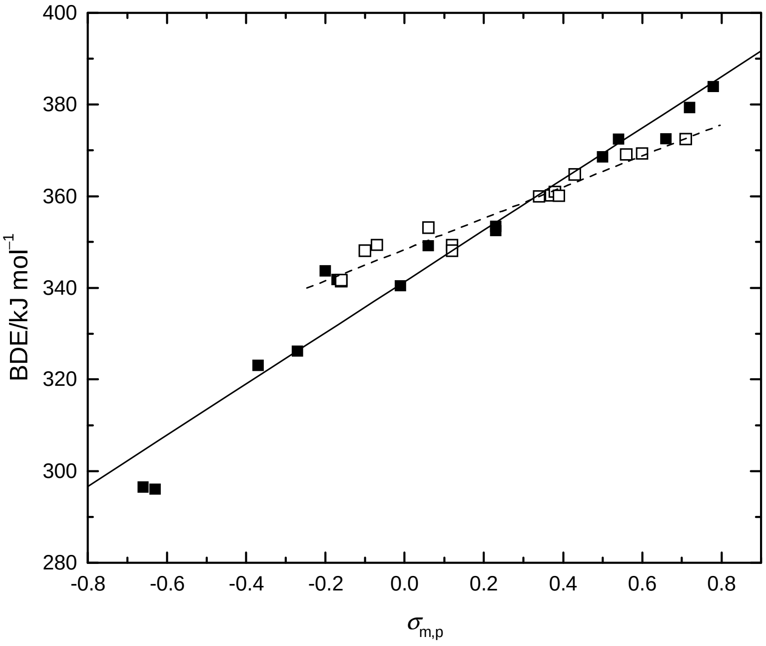

Fig. 2. Dependence of BDE *vs*. σ_p (solid squares, solid line) and σ_m (open squares, dashed line) in water.

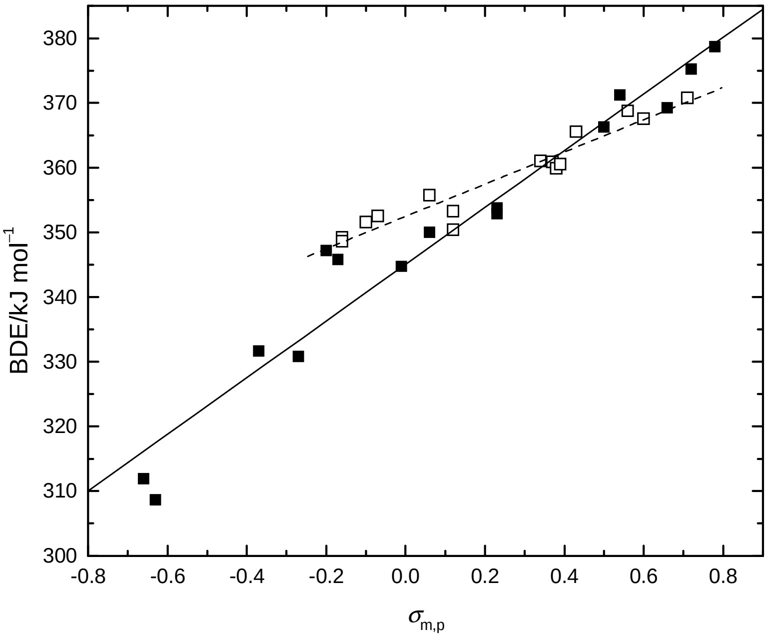

Fig. 3. Dependence of BDE *vs*. σ_p (solid squares, solid line) and σ_m (open squares, dashed line) in benzene.

The line slopes, ρ, obtained from the data presented in (Fu 2004, Guerra 2004, Lind 1990) are summarized, together with their errors, number of available substituted phenols, n, and correlation coefficients, R, in the Table 9. With respect to errors of obtained ρ values, we can say that IEF-PCM method provides the results in accordance with the majority of available experimental and theoretical results. Only HB+PCM approach tends to overestimate the substituent effect in water. Line slope values in eqs. 7–10 indicate that the two studied solvents increase the substituent effect of groups located both in *para* and *meta* positions on BDE. Obtained line slopes are higher than those found for gas-phase, eqs. 11 and 12.

Equations 7–12 show that substituent effect is the largest in water. In the gas-phase, studied substituents cause the lowest changes in BDE, i.e. BDE = $f(\sigma_{\mathrm{m,p}})$ dependences found in (Klein 2006) are less steep than those for water and benzene. Therefore, we can conclude that studied solvents induce considerable changes in the substituent effect in comparison to gas-phase. However, if the errors of the line slopes are taken into consideration, the substituent effect of groups in *para* position in the benzene and gas-phase is similar (Table 8).

Table 8. Line slopes of BDE = $f(\sigma_{\mathrm{m,p}})$ dependences, ρ, and correlation coefficients, R.

Environment	ρ/kJ mol^{-1}	R	substituent position
water	56±4	0.975	*para*
	34±2	0.975	*meta*
benzene	44±3	0.973	*para*
	25±2	0.961	*meta*
gas-phase*	38±3	0.970	*para*
	19±2	0.931	*meta*

* From Ref. (Klein 2006).

Calculated PA values in water and benzene

Our previous study (Klein 2006) confirmed that applied DFT/B3LYP method gives reliable gas-phase PA values of *para*- and *meta*- substituted phenols (calculated values were confronted with two experimental data sets and with computational results of other authors – Table 3 in (Klein 2006)). The substituent induced changes in PA were also correctly described (Klein 2006).

Since no experimental or theoretical results in the solution-phase are available yet, calculated proton affinities (Tables 10 and 11) can serve as predicted values. Mainly due to

the large enthalpy of H^+ hydration (–1090 kJ mol^{-1} (Atkins 1998)), in the water, PAs are significantly lower than gas-phase values. In benzene, calculated PAs are noticeably higher – the differences between PAs in water and benzene reached ca 300 kJ mol^{-1} for all investigated phenols. Less negative H^+ solvation enthalpy represents the major reason of higher PAs in benzene. On the other hand, PA values in benzene are by ca 1000 kJ mol^{-1} lower in comparison to the gas-phase values.
In the studied environments, proton affinities grow in this order:

water < benzene << gas-phase

In water, PAs are significantly lower than corresponding BDEs. This indicates that from the thermodynamic point of view, entering SPLET mechanism represents the more probable process in water. In non-polar benzene, HAT represents preferred reaction pathway, though the differences between PAs and BDEs are not so pronounced as in the gas-phase (Klein 2006). The only exception is *p*-nitrophenol – its PA is lower than its BDE (by 8 kJ mol^{-1}). Here, we should point out that PAs in benzene were determined using solvation enthalpy of H^+, $\Delta_{solv}H(H^+)$, obtained from IEF-PCM DFT/B3LYP/6-311++G** calculation of the enthalpy change related to $C_6H_6(l) + H^+(g) \rightarrow (C_6H_6)^+(solv)$ process. On the basis of this model of H^+ solvation, we found $\Delta_{solv}H(H^+) = –884$ kJ mol^{-1}. The same approach provided enthalpy of H^+ hydration $\Delta_{hydr}H(H^+) = –1020$ kJ mol^{-1}, while the experimental value is –1090 kJ mol^{-1} (the difference is 6 %). Mejías and Lago also calculated hydration enthalpy of proton by means of PCM DFT method (Mejías 2000). For H_3O^+ hydration they obtained –999 kJ mol^{-1}. Therefore, it can be expected that real solvation enthalpy of H^+ in benzene may reach more negative value. Consequently, proton affinities in benzene, compiled in Tables 10 and 11, can be overestimated by several tens of kJ mol^{-1}. This implies that proton affinities of greater number of studied phenols may actually reach lower values than corresponding BDEs in benzene. Obtained results indicate that strong electron-withdrawing substituents are able to alter thermodynamically preferred reaction pathway in benzene.

Values in Tables 10 and 11 show that electron-donating groups cause increase in PA, while electron-withdrawing groups lower substituted phenols PA. This trend is opposite to that observed in the case of BDEs. We can conclude that balance among HAT and SPLET mechanisms depends on both the solvent and the substituent present in the phenol molecule.

Effect of substituents – dependence of PAs on Hammett constants

Figures 4 and 5 show PA = $f(\sigma_{m,p})$ dependences for water and benzene, respectively. Linear regression provided these equations

$$\mathrm{PA/kJ\ mol^{-1}} = 146 - 37\sigma_p \quad \text{(water)} \quad (13)$$

$$\mathrm{PA/kJ\ mol^{-1}} = 152 - 34\sigma_m \quad \text{(water)} \quad (14)$$

$$\mathrm{PA/kJ\ mol^{-1}} = 436 - 56\sigma_p \quad \text{(benzene)} \quad (15)$$

$$\mathrm{PA/kJ\ mol^{-1}} = 451 - 66\sigma_m \quad \text{(benzene)} \quad (16)$$

In the gas-phase (Klein 2006), we found following linear dependences

$$\mathrm{PA/kJ\ mol^{-1}} = 1427 - 76\sigma_p \quad \text{(g)} \quad (17)$$

$$\mathrm{PA/kJ\ mol^{-1}} = 1445 - 88\sigma_m \quad \text{(g)} \quad (18)$$

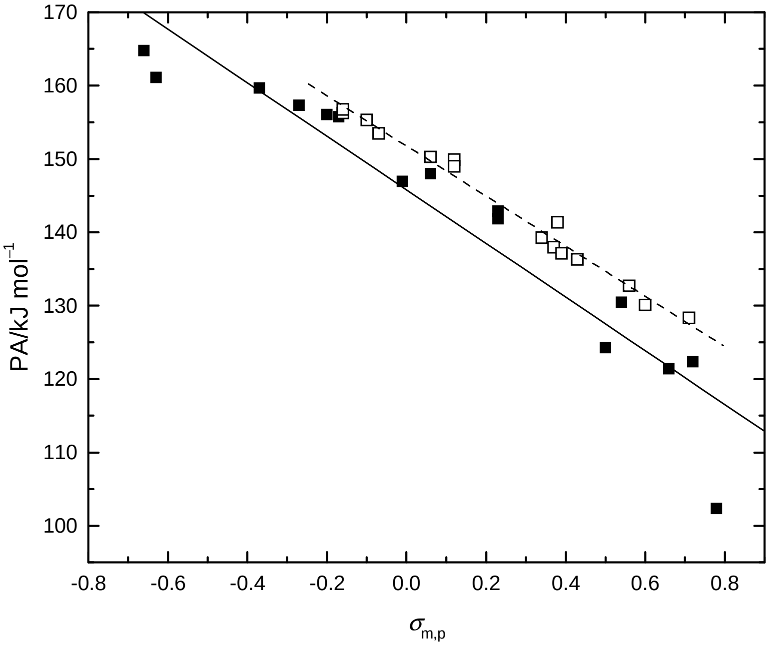

Fig. 4. Dependence of PA *vs.* σ_p (solid squares, solid line) and σ_m (open squares, dashed line) in water

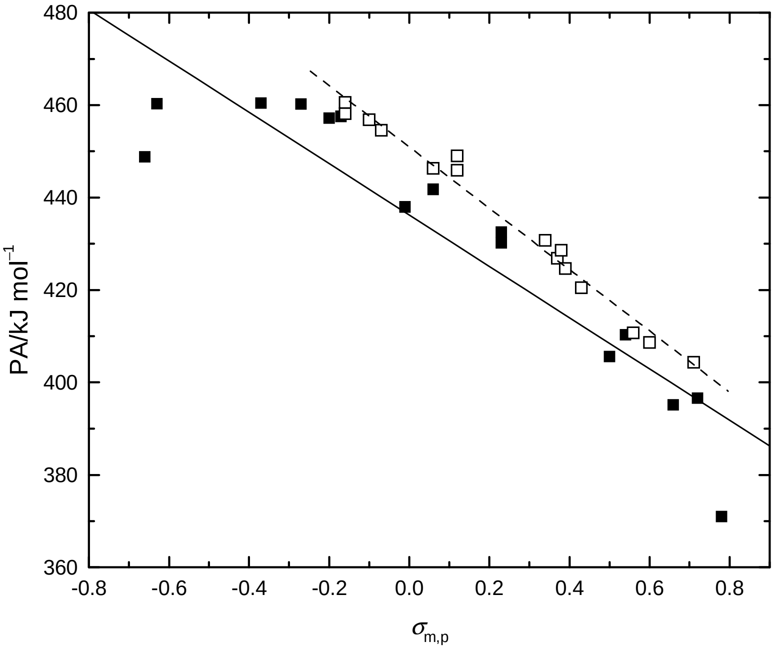

Fig. 5. Dependence of PA *vs.* σ_p (solid squares, solid line) and σ_m (open squares, dashed line) in benzene

In this work, for PA = $f(\sigma_p)$ dependence in the gas-phase, $\sigma_p(NMe_2) = -0.63$ was used in order to assure the compatibility with eqs. 13 and 15. Correlation coefficients, line slopes and their errors are summarized in the Table 12. Found correlation coefficients confirm excellent linearity of obtained PA = $f(\sigma_m)$ dependences which is also apparent from Figs. 4 and 5. In the case of substituents in *para* position, PA values can be successfully correlated with σ_p^- constants, too. These are used for phenols and anilines if the permanent negative charge on the reaction site can be resonance stabilized by a substituent (Krygowski 2005, Chandra 2002). Linear fit confirmed that PA values correlate with σ_p^- constants better than σ_p constants. We obtained following equations

$$\text{PA/kJ mol}^{-1} = 151 - 32\sigma_p^- \qquad \text{(water)} \qquad (19)$$

$$\text{PA/kJ mol}^{-1} = 445 - 51\sigma_p^- \qquad \text{(benzene)} \qquad (20)$$

The error of the line slope reached 2 kJ mol^{-1} in the case of water and 3 kJ mol^{-1} for benzene. For gas-phase, in (Klein 2006) we obtained

$$\text{PA/kJ mol}^{-1} = 1438 - 67\sigma_p^- \qquad \text{(g)} \qquad (21)$$

with 4 kJ mol^{-1} error of the line slope. Correlation coefficients of PA = $f(\sigma_p^-)$ dependences (eqs. 19–21) are in the range from –0.983 to –0.968.

PA = $f(\sigma_{m,p})$ dependences and PA = $f(\sigma_p^-)$ clearly indicate that solvents attenuate the substituent effect. Water attenuates the effect of substituents more than benzene. With the respect to the found errors of the line slopes (3 and 1 kJ mol^{-1} for groups in *para* and *meta* positions, respectively) in water, significant difference between line slopes of PA = $f(\sigma_p)$ and PA = $f(\sigma_m)$ dependences cannot be observed. However PA = $f(\sigma_p)$ dependence is steeper. On the other hand, in the benzene and gas-phase, groups in *meta* position affect the proton affinity stronger than groups in *para* position.

Table 9. Line slopes of BDE = $f(\sigma_p)$ dependences, ρ, number of BDE values used in linear fit, n, and correlation coefficients, R, in water for various methods of BDE determination.

Method	ρ/kJ mol^{-1}	n	R	Reference
IEF-PCM	56±4	15	0.975	this work
PR experiments	49±6	11	0.942	(Lind 1990)
DFT(1)/PCM	53±4	8	0.982	(Guerra 2004)
DFT(1)/HB	58±4	8	0.982	(Guerra 2004)
DFT(1)/HB+PCM	66±5	8	0.983	(Guerra 2004)
DFT(2)/PCM	46±3	8	0.985	(Fu 2004)
DFT(2)/X–PhOH...H_2O	57±4	8	0.989	(Fu 2004)

Table 10. DFT/B3LYP/6-311++G** calculated PAs in kJ mol^{-1} of *para*-substituted phenols in water, benzene and gas-phase, and Hammett constants σ_p^-.

Substituent	Water	Benzene	Gas-phase[a]	σ_p^{-} [b]
—	152[a]	451	1449	
p-NH_2	165[a]	449	1466	–0.15
p-NMe_2	161	460	1453	–0.12
p-OH	160[a]	460	1455	–0.37
p-MeO	157[a]	460	1456	–0.26
p-*t*-Bu	156	457	1449	–0.13
p-Me	156[a]	458	1454	–0.17
p-Ph	147	438	1419	0.02
p-F	148	442	1436	–0.03
p-Cl	143[a]	432	1422	0.19
p-Br	142[a]	430	1417	0.25

continued

Substituent	Water	Benzene	Gas-phase[a]	$\sigma_p^{-\,b}$
p-MeCO	124[a]	406	1387	0.84
p-CF_3	130	410	1390	0.65
p-CN	121[a]	395	1372	1.00
p-$MeSO_2$	122	397	1371	1.13
p-NO_2	102[a]	371	1346	1.27

[a] From Ref. (Klein 2006).
[b] From Ref. (Hansch 1991).

Table 11. DFT/B3LYP/6-311++G** calculated PAs in kJ mol^{-1} of *meta*-substituted phenols in water, benzene and gas-phase in kJ mol^{-1}.

Substituent	Water	Benzene	Gas-phase[a]
m-NH_2	156	458	1455
m-NMe_2	157	461	1457
m-*t*-Bu	155	457	1449
m-Me	153	455	1452
m-Ph	150	446	1434
m-OH	150	446	1440
m-MeO	149	449	1446
m-F	139	431	1423
m-Cl	138	427	1415
m-MeCO	141	429	1415
m-Br	137	425	1411
m-CF_3	136	420	1403
m-CN	133	411	1390
m-$MeSO_2$	130	409	1386
m-NO_2	128	404	1383

[a] From Ref. (Klein 2006).

Table 12. Line slopes of PA = $f(\sigma_{m,p})$ dependences, ρ, and correlation coefficients, R.

Environment	ρ/kJ mol^{-1}	R	substituent position
water	–37±3	–0.952	*para*
	–34±1	–0.992	*meta*
benzene	–56±7	–0.921	*para*
	–66±3	–0.991	*meta*
gas-phase	–76±7	–0.952	*para*
	–88±5[a]	–0.978[a]	*meta*

[a] From Ref. (Klein 2006).

Conclusion

In this article, the phenolic O–H bond dissociation enthalpies and proton affinities, related to HAT and SPLET mechanisms of phenols antioxidant action for *meta*- and *para*-substituted phenols were studied. DFT/B3LYP IEF-PCM method with 6-311++G** basis set provides BDE and especially ΔBDE values are in very good agreement with experimental data obtained from pulse radiolysis measurements in water. We have found that electron donating substituents induce the rise in PA, while electron-withdrawing groups cause the increase in BDE. The linearity of BDE = $f(\sigma_{\mathrm{m,p}})$ and PA = $f(\sigma_{\mathrm{m,p}})$ dependences can be considered satisfactory and obtained equations may be used to predict O–H BDEs and PAs or ΔBDEs and ΔPAs for *para*- and *meta*-substituted phenols from their Hammett constants or vice versa.

Entering SPLET mechanism represents thermodynamically preferred reaction pathway in water, where PAs of all studied phenols are considerably lower than BDEs. In benzene, BDEs of all but one studied phenols are lower than PAs, i.e. HAT represents the most probable pathway. Only PA of *p*-nitrophenol is lower than its BDE. Generally, obtained results indicate that various solvents and substituents are able to alter the thermodynamically favored pathway. In comparison to gas-phase, studied solvents attenuate the substituent effect on PA. On the other hand, substituent induced changes in BDE are larger in solution-phase.

Acknowledgement

This work has been supported by Science and Technology Assistance Agency under the contracts No APVT-20-005004. The work has been also supported by Slovak Grant Agency (VEGA 1/0137/09 and VEGA 1/0774/08).

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