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The applicability of AM1 and PM3 semi-empirical methods for the study of N–H bond dissociation enthalpies and ionisation potentials of amine type antioxidants

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Abstract

A study of 40 *para*-substituted anilines is presented. These serve as model structures of amine type antioxidants. Molecules and their radical structures were studied using the AM1 and PM3 quantum chemical methods in order to calculate the N–H bond dissociation enthalpies (BDEs) and ionisation potentials (IPs) which are among the most important characteristics of antioxidants. Calculated BDEs were compared with available experimental values and the results of DFT calculations to ascertain the suitability of AM1 and PM3 methods for amine BDEs calculation. The results show that both methods reproduce experimental BDEs and DFT data satisfactorily. Comparison with experimental data shows that AM1 and PM3 methods overestimate the IP values. The results also indicate that dependences of N–H bond BDEs and IPs on Hammett constants of the substituents are linear.

Keywords: Bond dissociation enthalpy; BDE; Ionisation potential; AM1 quantum chemical method; PM3 quantum chemical method; Amine; Aniline

1. Introduction

The reactions of organic compounds with oxygen are the major cause of the irreversible deterioration of biological systems and synthetic polymers. Thermal oxidation of polymers generally corresponds to a free radical chain reaction [1]. The most important reactive radical intermediates formed during oxidation reactions are hydroxyl (HO$^•$), alkoxyl (RO$^•$) and peroxyl (ROO$^•$) radicals [1,2]. These radicals are so reactive that they can readily abstract hydrogen atoms from polymer molecular backbone, ultimately breaking down the polymer molecules. Degradation results in the change of the molecular weight distribution together with changes in chemical properties and mechanical behaviour.

Antioxidants are chemical compounds that can quench the reactive radical intermediates formed during the oxidative reactions. The primary antioxidants comprise essentially sterically hindered phenols and secondary aromatic amines [1,3]. These antioxidants act usually both through chain transfer and chain termination [1]. The first step of the reactive radicals termination by this type of antioxidants is hydrogen atom transfer from the antioxidant molecule to the reactive radical intermediate [1,2]. Small amounts of antioxidants are added into most synthetic polymers to prevent or retard oxidation and to increase the service lifetimes of the products [1,2,4,5].

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Antioxidant potency is enhanced by relatively low bond dissociation energy [6,7] (in fact more correct is the term "bond dissociation enthalpy") of relevant O−H and N−H bonds in phenols and amines, respectively. Another important feature of the effective antioxidant is the ionisation potential (IP). Low IP values are favourable to raise the electron-transfer reactivity; they enhance the danger of generating a superoxide anion radical through the transfer of the electron directly to surrounding O_2 [6,8−10]. High IP decreases the electron-transfer rate between antioxidant and the oxygen molecule.

Knowledge of the BDEs has been accumulating substantially for the past 10 years owing to the recent development of both experimental and quantum chemical techniques [2,7,8,11−20]. Semi-empirical quantum chemical methods AM1 and PM3 can be suitable tool especially for the study of large antioxidant molecules, where more conformations have to be investigated. Therefore one of the aims of this work is to test the suitability of PM3 and AM1 methods for the calculation of BDEs and IPs of amine type of antioxidants. We will compare calculated BDE values of various aniline derivatives with available experimental data and with the results obtained by DFT calculations (two different approaches). Since DFT with large basis sets and ab initio calculations are extremely time-consuming and require high-performance computational resources in the case of large systems, semi-empirical methods can often represent successful alternative. From this point of view it is important to compare the results provided by semi-empirical methods also with DFT results. Up to the present no similar study is available.

The studied model compounds can be divided into the three series according Fig. 1, which represents *para*-substituted anilines. In series **2** (*N*-acetyl anilines) one of the aniline amino group hydrogen is substituted by acetyl −COMe group and in series **3** (phenylhydrazines) is the hydrogen atom replaced by another amino $-NH_2$ group. Except the comparison of PM3 and AM1 BDE and IP values with available DFT and/or experimental data, we will correlate calculated BDEs and IPs with Hammett constants published in [21].

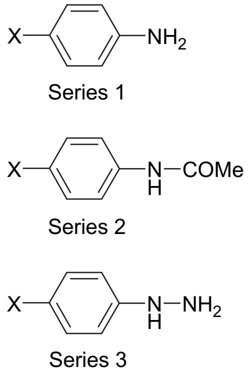

Fig. 1. Studied molecules. X = H, NMe_2, NH_2, OMe, OH, Me, F, Cl, Br, CHO, COMe, CN, CF_3, and NO_2.

2. Quantum chemical methods

Semi-empirical theoretical methods (PM3, AM1, and MNDO) are specially designed to obtain enthalpy of formation of chemical systems. Dewar's MNDO [22] and AM1 [23] methods have been widely employed in enthalpy of formation calculations and represent a standard tool for both theoretical and experimental organic chemists. Later, Stewart proposed a mathematical reparameterisation of the MNDO method called PM3 method [24,25]. In this method single-atom parameters were obtained for C, N, H, O, F, S, P, Si, Cl, Al, I and Br simultaneously, by fitting 400−500 experimental references. Generally, PM3 gives better results than the AM1 method.

Recently, DFT (B3LYP) method with large basis sets has become a suitable approach for the study of various medium−large organic compounds. However, the applicability of this approach is restricted in case of many antioxidants, because their molecules often contain more than 50 atoms. Besides, the majority of large antioxidant molecules are not symmetric and often up to 20 conformations for individual molecule have to be taken into account.

We have selected PM3 and AM1 methods to compute the bond dissociation enthalpies and ionisation potentials, because these methods are fast enough to obtain results of the calculation in minute scales using an ordinary PC. Our previous work [26] indicates that PM3 method is suitable for BDE calculations of *N*,*N′*-substituted *para*-phenylenediamine antioxidants − the results were in good agreement with results of the experimental (DSC) study of the antioxidants effectiveness in polyisoprene rubber.

The ground-state geometry of studied molecules was optimised at restricted Hartree−Fock level and the geometry of the corresponding radicals was optimised at the restricted Hartree−Fock open shell (half electron) level using the standard semi-empirical PM3 and AM1 methods [27] of the Hyperchem program package [28] (energy cut-off of 10^{-5} kJ mol^{-1}, final RMS energy gradient under 0.01 kJ mol^{-1} $Å^{-1}$).

3. Results and discussion

3.1. Agreement between theoretical and experimental N−H BDEs and ΔBDEs − series 1

Bond dissociation enthalpies, BDEs, are calculated as

$$\mathrm{BDE} = \Delta_f H(\mathrm{R}^\bullet) + \Delta_f H(H^\bullet) - \Delta_f H(\mathrm{R{-}H})$$

where $\Delta_f H(R^\bullet)$ is the enthalpy of formation of the radical, $\Delta_f H(H^\bullet)$ is the enthalpy of formation of the abstracted hydrogen atom, and $\Delta_f H(R-H)$ is the enthalpy of formation of the molecule.

Table 1
Experimental and theoretical BDEs in kcal mol^{-1} of substituted anilines (series **1**)

Substituent	EC[a]	PR[b]	PAC[c]	TDC[d]	DFT[e]	DFT-LLM[f]	PM3	AM1
–	92.3	89.1	89.7	92.3	90.7	91.5	91.8	94.5
NMe_2					83.7	85.4	89.7	91.0
NH_2		86.0			84.5	85.9	89.4	91.0
OMe	90.4	87.2			86.6	87.4	90.1	92.8
OH					86.7	87.7	89.9	92.8
Me	92.0	88.7	87.5		89.2	89.6	91.2	94.6
F			88.8		89.5	91.8	91.2	94.0
Cl	92.4			92.6	90.3	91.6	91.8	95.3
Br	92.3			92.3	90.5	92.0	92.3	96.1
CHO					93.3	94.4	93.1	97.4
COMe	94.2	90.6		94.3	92.6	94.2	93.0	97.4
CN	95.2	91.8		95.2	93.3	94.6	93.1	97.2
CF_3	96.5	92.0		96.7	93.3	94.6	93.6	98.0
NO_2	96.7			96.9	94.8	96.2	94.8	99.2

[a] Data taken from Ref. [15].
[b] Data taken from Ref. [16].
[c] Data taken from Ref. [17].
[d] Data taken from Ref. [2].
[e] Data taken from Ref. [11].
[f] Data taken from Ref. [13].

Calculated and experimental N–H BDEs for series **1** molecules are compiled in Table 1. Experimental data were obtained using four methods. Bordwell and Cheng's electrochemical (EC) method uses the equilibrium acidity (pK_a) and oxidation potential (E_{ox}) values of the conjugated anion for BDE calculation [15]. Jonsson et al. used pulse radiolysis (PR) [16] and MacFaul et al. employed photoacoustic calorimetry (PAC) [17] for BDEs determination. BDEs obtained from thermodynamic cycle (TDC) method [2] are close to EC method results because this method uses pK_a values and oxidation potentials, E_{ox}, of the conjugated anions, too. PR and PAC provide BDEs lower than EC and TDC method, the difference is ca 2.5–4.5 kcal mol^{-1}. Standard deviations of the experimentally determined BDEs are in 1–2 kcal mol^{-1} range.

Li et al. [11] employed DFT (B3LYP, 6-311+G(2d,2p) basis set) for BDE calculations for species from series **1**, whereas for molecules from series **2** to **3** (RO)B3LYP was used. Tables 1, 2, 4, and 5 present their results in the column denoted "DFT". Pratt et al. [13] performed DFT calculations, too. All calculations were done with the low-level model (LLM) [12] which calls for geometries to be optimised and vibration frequencies calculated using the semi-empirical AM1 approach. This is followed by a single-point calculation at the AM1 minimum energy geometry with the (RO)B3LYP exchange-correlation functional and a 6-311+G(2d,2p) basis set. Table 1 shows obtained BDEs in the "DFT-LLM" column.

PM3 calculations provided the bond dissociation enthalpies in very good agreement with experimental EC and TDC values. In comparison with DFT [11] PM3 method gives worse result only in the case of –CN substituent, the rest of the values corresponds to the EC and TDC data better than DFT results. DFT data are in better agreement with PR and PAC methods. DFT-LLM [13] provides better results than PM3 method in four cases – for the strongest electron withdrawing groups –COMe, –CN, $-CF_3$, $-NO_2$. DFT-LLM results are in better agreement with EC and TDC than DFT method used by Li et al. [11]. Both DFT approaches tend to underestimate the BDE values.

AM1 method provided higher BDE values than PM3 for all studied molecules (increase in BDEs 1.3–4.4 kcal mol^{-1}). The larger electron withdrawing effect of the substituent is, the larger the difference between PM3 and AM1 methods is. For series **1** PM3 gives better results than AM1, which overestimates BDE values. Since BDE represents the difference between the enthalpies of the molecule and its radical formed by hydrogen atom splitting-off, this indicates that AM1 method may give worse results for radicals in the case of electron withdrawing groups in *para* position – these groups stabilize the formed radical [11]. AM1 overestimation of the BDEs correlates with the rise of Hammett σ_p constants.

It is relatively difficult to decide which theoretical approach is the best when we compare ΔBDE values, Table 2. ΔBDE represents the difference between BDEs of the *para*-substituted aniline and the aniline itself, i. e. $\Delta BDE = BDE(X-C_6H_4NH_2) - BDE(C_6H_5NH_2)$. The largest differences between experimental and DFT values are 3.2 kcal mol^{-1} in the case of $-NH_2$ substituent and 2.2 kcal mol^{-1} for –OMe group. The values

Table 2
ΔBDE values in kcal mol^{-1} of series **1** and Hammett constants of substituents σ_p[a]

Substituent	EC	PR	PAC	TDC	DFT	DFT-LLM	PM3	AM1	σ_p
NMe_2					−7	−6.1	−2.1	−3.5	−0.83
NH_2		−3.1			−6.3	−5.6	−2.4	−3.5	−0.66
OMe	−1.9	−1.9			−4.1	−4.1	−1.7	−1.7	−0.27
OH					−4	−3.8	−1.9	−1.7	−0.37
Me	−0.3	−0.4	−2.2		−1.5	−1.9	−0.6	0.1	−0.17
F			−0.9		−1.3	0.3	−0.6	−0.5	0.06
Cl	0.1			0.3	−0.4	0.1	0	0.8	0.23
Br	0.0			0.0	−0.2	0.5	0.5	1.6	0.23
CHO					2.6	2.9	1.3	2.9	0.42
COMe	1.9	1.5		2.0	1.9	2.7	1.2	2.9	0.50
CN	2.9	2.7		2.9	2.6	3.1	1.3	2.7	0.66
CF_3	4.2	2.9		4.4	2.6	3.1	1.8	3.5	0.54
NO_2	4.4			4.6	4.1	4.7	3	4.7	0.78

[a] Data taken from Ref. [21].

calculated using DFT-LLM are most different from experimentally determined BDEs for the same two substituents. Differences are 2.5 kcal mol^{-1} (–NH$_2$) and 2.2 kcal mol^{-1} (–OMe). The largest differences between experimental (TDC) and PM3 values we found were 2.6 kcal mol^{-1} for –CF$_3$ group and 1.6 kcal mol^{-1} for –CN group. AM1 gives the worst results for –Me group (2.3 kcal mol^{-1}) in comparison with PAC value. On the other hand, PAC provided ΔBDE value substantially different from EC and PR values which are very close to each other and in much better agreement with AM1 calculation result. For –Br substituent AM1 found value 1.6 kcal mol^{-1} while EC and TDC give 0 kcal mol^{-1}. If we compare ΔBDE values determined from EC data with the theoretical methods, AM1 shows the lowest average deviation (0.64 kcal mol^{-1}), followed by DFT (0.79 kcal mol^{-1}), DFT-LLM (0.84 kcal mol^{-1}) and PM3 (0.90 kcal mol^{-1}). These deviations from experimental data are lower than standard deviation of experimentally determined BDEs. We can therefore consider that all four theoretical methods represent suitable approach for the *para*-substituted anilines BDE and ΔBDE calculations. Results of the two semi-empirical methods cannot be considered less reliable than DFT results. Moreover, both semi-empirical methods work significantly faster than DFT. PM3 method is better for BDEs calculation, while AM1 provides ΔBDE values closer to the experimental data.

*3.2. Agreement between theoretical and experimental IPs – series **1***

Table 3 summarizes experimental and calculated IP values of series **1** molecules. IPs are calculated as

$$\mathrm{IP}=\Delta_f H(\mathrm{R{-}H}^{+\bullet})-\Delta_f H(\mathrm{R{-}H})$$

where $\Delta_f H(\mathrm{R{-}H}^{+\bullet})$ is the enthalpy of formation of the cation radical, and $\Delta_f H(\mathrm{R{-}H})$ is the enthalpy of formation of the compound. Calculated IPs between 8.06 and 9.42 eV (PM3) or 7.92 and 9.27 eV (AM1) represent typical values for most organic molecules. Both semi-empirical methods give analogous values – differences between them do not exceed 0.21 eV (2.6%). For all compounds PM3 calculations provide slightly higher values.

Experimental values were obtained on the basis of several techniques: mass spectrometry [29,30], photoelectron spectroscopy [31–33], and from charge transfer spectra [34]. If we compare calculated values with those experimentally determined, we can see that PM3 and AM1 methods overestimate ionisation potential values. The differences are in 0.2–1.2 eV range. Average deviations from experimental values are 0.82 and 0.70 eV in the case of PM3 and AM1, respectively.

Table 3
IP values in eV of series **1**

Substituent	Experiment	PM3	AM1
–	7.73[a]	8.61	8.52
NMe$_2$		8.60	8.52
NH$_2$	6.89[b]	8.06	7.92
OMe		8.31	8.20
OH		8.35	8.27
Me	7.85[c]	8.47	8.36
F	7.9[d]	8.74	8.55
Cl	7.8[d]	8.58	8.56
Br	7.7[d]	8.78	8.63
CHO		8.89	8.82
COCH$_3$	8.27[e]	8.86	8.78
CN	8.64[f]	8.98	8.86
CF$_3$		9.15	9.06
NO$_2$	8.34[b]	9.42	9.27

[a] Data taken from Ref. [33].
[b] Data taken from Ref. [29].
[c] Data taken from Ref. [31].
[d] Data taken from Ref. [34].
[e] Data taken from Ref. [32].
[f] Data taken from Ref. [30].

*3.3. Dependence of ΔBDE and ΔIP values on Hammett constants – series **1***

The Hammett equation (and its extended forms) has been one of the most widely used means for the study and interpretation of organic reactions and their mechanisms. Hammett constants σ_m (for substituent in *meta* position) and σ_p (for substituent in *para* position) obtained from ionisation of organic acids in solutions can frequently successfully predict equilibrium and rate constants for a variety of families of reactions [21]. Pratt et al. [8,20] and DiLabio et al. [12] found that ΔBDE values of *para*-substituted phenols, 6-substituted-3-pyridinols, 2-substituted-5-pyrimidinols, and anilines are linearly dependent on Hammett constants σ_p. Using PM3 data, we obtain linear plot (Fig. 2) with regression

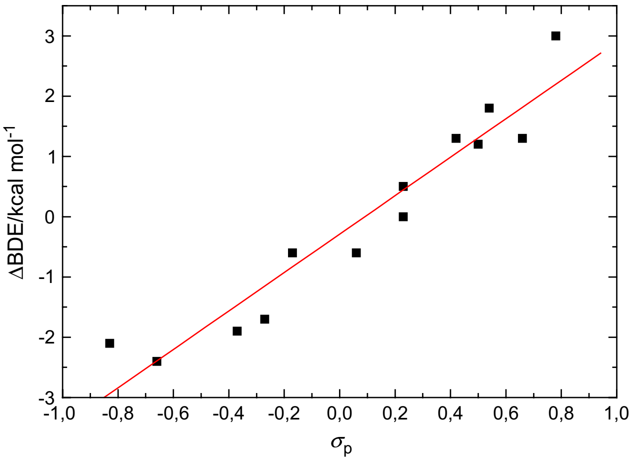

Fig. 2. Dependence of ΔBDE vs. σ_p for PM3 data – series **1**.

coefficient $R = 0.959$. Dependence of AM1 ΔBDE values on Hammett σ_p constants is shown in Fig. 3 ($R = 0.975$). DFT and DFT-LLM methods give linear dependence with $R = 0.987$. ΔBDE vs σ_p dependences for all four theoretical methods describe following equations

$$\Delta BDE/\mathrm{kcal\,mol^{-1}} = -0.290 + 3.188\sigma_p\ (\mathrm{PM3})$$

$$\Delta BDE/\mathrm{kcal\,mol^{-1}} = 0.196 + 5.130\sigma_p\ (\mathrm{AM1})$$

$$\Delta BDE/\mathrm{kcal\,mol^{-1}} = -1.447 + 6.979\sigma_p\ (\mathrm{DFT})$$

$$\Delta BDE/\mathrm{kcal\,mol^{-1}} = -0.921 + 7.029\sigma_p\ (\mathrm{DFT-LLM})$$

Experimental EC ΔBDEs also show linear dependence on Hammett constants with $R = 0.921$.

Pratt et al. [8] found that ionisation potential (IP) values of *para*-substituted phenols, 6-substituted-3-pyridinols and 2-substituted-5-pyrimidinols linearly depend on Hammett constants, too. Studied anilines show linear dependence of ΔIP values, $\Delta IP = IP(X{-}C_6H_4NH_2) - IP(C_6H_5NH_2)$, on Hammett constants. Correlation coefficients are 0.962 and 0.976 for PM3 and AM1, respectively.

3.4. Agreement between theoretical and experimental ΔBDEs — series **2** and **3**

For series **2** and **3** (Tables 4 and 5) fewer experimental values [18,19] are available at present. The comparison of the experimental and calculated BDE values of non-substituted compound **2** indicates that AM1 calculated value is in significantly better agreement with experimentally determined value than PM3 value. PM3 method underestimates BDE value, about 10 kcal mol^{-1}. DFT method [11] underestimates the BDE value (4 kcal mol^{-1} difference), too. AM1 calculated ΔBDEs are in the best agreement with experimental data — average deviation reached 0.47 kcal mol^{-1}. The average deviation of PM3 results from experimental data is 0.71 kcal mol^{-1}. This is caused especially by large (2.8 kcal mol^{-1}) difference in values determined for —OMe substituent; the average deviation of the rest of PM3 values from those experimentally obtained is only 0.36 kcal mol^{-1}. In the case of DFT [11], the average deviation from experimental ΔBDEs reached 0.56 kcal mol^{-1}. All three theoretical methods provide ΔBDEs in good agreement with experiments.

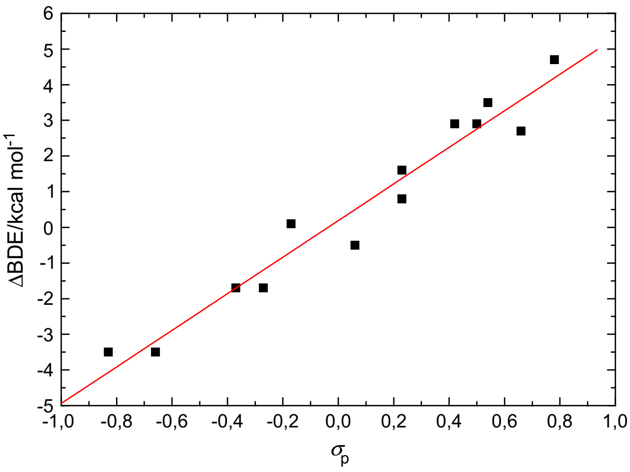

Fig. 3. Dependence of ΔBDE vs. σ_p for AM1 data — series **1**.

Table 4
ΔBDE values in kcal mol^{-1} of series **2**

Substituent	Experiment[a]	DFT[b]	PM3[c]	AM1[d]
NMe_2		−7.9	−2.3	−6.5
NH_2			−1.8	−6.3
OMe	−3.6	−4.3	−0.8	−3.9
OH			−1.9	−3.8
Me	−1.8	−1.5	−1.3	−1.7
F		−1.2	−0.2	−3.0
Cl	−0.2	−0.6	0.1	−0.9
Br	0.2	−0.4	0.7	−0.9
CHO			1.0	−0.9
$COCH_3$	1.1	1.9	1.1	1.4
CN	2.2	2.6	1	1.2
CF_3	2.7	2.6	1.9	2.0
NO_2	3.1	4.1	3	3.2

[a] Data taken from Ref. [18], BDE of non-substituted compound **2**: 98.9 kcal mol^{-1}.

[b] Data taken from Ref. [11], BDE of non-substituted compound **2**: 94.8 kcal mol^{-1}.

[c] BDE of non-substituted compound **2**: 88.6 kcal mol^{-1}.

[d] BDE of non-substituted compound **2**: 98.1 kcal mol^{-1}.

Table 5
ΔBDE values in kcal mol^{-1} of series **3**

Substituent	Experiment[a]	DFT[b]	PM3[c]	AM1[d]
NMe_2		−2.8	−0.7	−1.4
NH_2			−0.8	−1.5
OMe		−1.9	−0.7	−1.1
OH			−0.6	−1.1
Me	−0.7	−0.6	−0.3	−0.4
F		−0.1	−0.5	−1.3
Cl	0.1	−0.4	−0.4	−0.6
Br		−0.2	0.2	−0.3
CHO		0.4	0.3	0.3
$COCH_3$		0.5	0.2	0.2
CN	5.0	0.7	−0.3	−0.1
CF_3	5.0	0.8	0.1	0.4
NO_2		1.1	1.2	0.5

[a] Data taken from Ref. [19], BDE of non-substituted compound **3**: 72.9 kcal mol^{-1}.

[b] Data taken from Ref. [11], BDE of non-substituted compound **3**: 74.0 kcal mol^{-1}.

[c] BDE of non-substituted compound **3**: 74.3 kcal mol^{-1}.

[d] BDE of non-substituted compound **3**: 75.8 kcal mol^{-1}.

Since for series **3** molecules (Table 5) we have found only four experimental values [19], no relevant conclusions can be drawn from the comparison of the experimentally and theoretically determined BDEs or ΔBDEs. All theoretical methods appear to significantly underestimate ΔBDEs in the case of electron withdrawing groups.

*3.5. Agreement between theoretical and experimental IPs — series **2** and **3***

Table 6 summarizes IP values of substances from series **2**. In comparison with available experimental values (electron impact technique) [35,36], PM3 and AM1 methods overestimate IPs. Differences between the two methods do not exceed 0.36 eV (3.9%). For all compounds (except −Cl substituent) PM3 calculations give slightly higher values. The differences between theoretical and experimental values are in 0.4–0.9 eV range. Average deviations from experimental values are 0.68 and 0.57 eV in the case of PM3 and AM1, respectively. These are lower than deviations found for series **1**.

Table 7 shows calculated values of IPs for series **3** compounds. Differences in the values are small and they do not exceed 0.29 eV (3.1%). Contrary to previous series, in this series AM1 method provides higher values of IP than PM3 for the majority of the substituents. Unfortunately, no experimental IP values are available for this series.

Table 6
IP values in eV of series **2**

Substituent	Experiment	PM3	AM1
–		9.03	8.77
NMe_2		8.25	7.91
NH_2	7.12[a]	8.20	8.07
OMe		8.52	8.38
OH	7.57[a]	8.75	8.47
Me	7.75[a]	8.67	8.58
F	8.20[b]	9.13	8.77
Cl	8.07[b]	8.76	8.81
Br	8.17[b]	8.98	8.87
CHO		9.26	9.11
$COCH_3$		9.26	9.05
CN		9.17	9.13
CF_3		9.36	9.35
NO_2		9.61	9.60

[a] Data taken from Ref. [35].
[b] Data taken from Ref. [36].

Table 7
IP values in eV of series **3**

Substituent	PM3	AM1
–	8.67	8.81
NMe_2	8.18	8.01
NH_2	8.26	8.17
OMe	8.49	8.48
OH	8.53	8.55
Me	8.58	8.64
F	8.81	8.84
Cl	8.60	8.86
Br	8.75	8.86
CHO	9.00	9.11
$COCH_3$	8.79	9.06
CN	8.93	9.15
CF_3	9.05	9.34
NO_2	9.29	9.56

*3.6. Dependence of ΔBDE and ΔIP values on Hammett constants — series **2** and **3***

PM3 provides ΔBDE values for various substituents in the case of series **2** in significantly narrower range, while AM1 calculations give ΔBDEs in wider range that corresponds to experimental and DFT results better. PM3 gives significantly lower ΔBDEs for electron donor substituents. Using linear regression we have found these dependences

$$\Delta\mathrm{BDE/kcal\,mol^{-1}} = -0.219 + 2.983\sigma_\mathrm{p}\ (\mathrm{PM3})$$

$$\Delta\mathrm{BDE/kcal\,mol^{-1}} = -2.044 + 5.777\sigma_\mathrm{p}\ (\mathrm{AM1})$$

$$\Delta\mathrm{BDE/kcal\,mol^{-1}} = -1.867 + 6.631\sigma_\mathrm{p}\ (\mathrm{DFT})$$

Correlation coefficients of these regressions reached following values: 0.952 (PM3, Fig. 4), 0.965 (AM1, Fig. 5), and 0.981 (DFT). Although DFT data show the best correlation, it is important to keep in mind that regression analysis was carried out only for 10 available substituents instead of all 13 substituents used in PM3 and AM1 regressions. If we compare found dependences with series **1** regression analysis results, we can see that

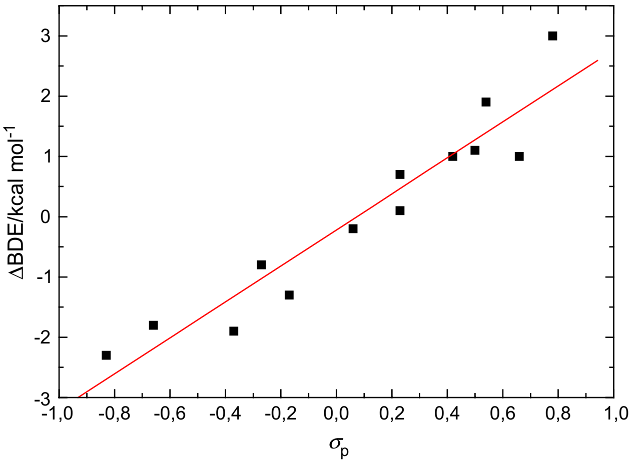

Fig. 4. Dependence of ΔBDE vs. σ_p for PM3 data — series **2**.

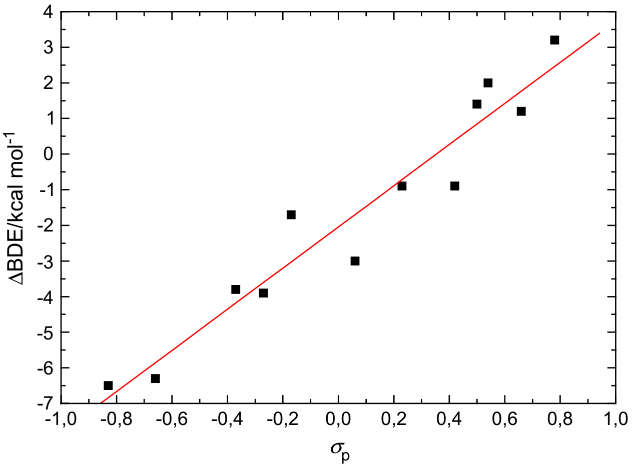

Fig. 5. Dependence of ΔBDE vs. σ_p for AM1 data – series **2**.

the line slopes reach similar values for the individual methods. This indicates that substitution of one aniline $-NH_2$ group hydrogen with electron withdrawing acetyl −COMe group does not affect the effect of the substituents in *para* position on N−H bond dissociation enthalpy.

Results obtained for series **3** follow the trend found for the two previous series. Here the dependence of ΔBDE values (Table 5) on Hammett constants shows that AM1 method gives better results – individual points are significantly less scattered along the regression line; the values of correlation coefficients are: 0.792 (PM3), 0.898 (AM1) and 0.966 (DFT). We found following dependences

$$\Delta\text{BDE/kcal mol}^{-1} = -0.236 + 0.886\sigma_p\ (\text{PM3})$$

$$\Delta\text{BDE/kcal mol}^{-1} = -0.611 + 1.286\sigma_p\ (\text{AM1})$$

$$\Delta\text{BDE/kcal mol}^{-1} = -0.709 + 2.423\sigma_p\ (\text{DFT})$$

Again, regression analysis in the case of PM3 and AM1 methods was carried out for 13 different substituents, while in the case of DFT we used only 10 available ΔBDE values. Contrary to series **1** and **2**, the differences in the found ΔBDEs are significantly lower. In series **1** and **2** ΔBDEs obtained using DFT method are in 11–12 kcal mol^{-1} range, while in series **3** the difference between the lowest and the highest value reached only 4 kcal mol^{-1}. PM3 and AM1 in all three series give even narrower intervals of ΔBDEs. Of course, close ΔBDE values contribute to worse correlation of the calculated ΔBDEs with Hammett constants. Besides, similar ΔBDEs indicate that strong electron donor $-NH_2$ substituent, located on aniline amino group, partly eliminates the effect of substituents in *para* position.

Potential inaccuracy of the two semi-empirical methods can be unambiguously ascribed to problems with calculation of radical species. The optimum geometry may not correspond to the geometry with the minimum energy due to the half-electron approximation typically used in many semi-empirical program packages [25,28]. The application of the two tested semi-empirical methods may be limited in case of the series of compounds with weakened substituent effect on N−H bond BDE.

Regression analysis showed that $\Delta\text{IP} = f(\sigma_p)$ dependence is in the case of series **2** molecules linear, correlation coefficients are 0.936 and 0.977 for PM3 and AM1, respectively. The linearity of $\Delta\text{IP} = f(\sigma_p)$ dependence found for series **3** molecules is analogous to series **1** and **2**, correlation coefficient for AM1 method results ($R = 0.976$) is again closer to 1 than correlation coefficient for PM3 data ($R = 0.937$).

3.7. Correlation of ΔBDE with ΔIP values

Since for an effective antioxidant, a low BDE of hydrogen atom splitting-off and high IP are important features, it is interesting to correlate ΔIP and ΔBDE values. As can be supposed from the linearity of $\Delta\text{BDE} = f(\sigma_p)$ and $\Delta\text{IP} = f(\sigma_p)$ dependences, $\Delta\text{IP} = f(\Delta\text{BDE})$ dependence is linear, too. Figs. 6–8 present $\Delta\text{IP} = f(\Delta\text{BDE})$ dependences obtained using AM1 method results, since this method provides ΔBDEs in better agreement with experimental and/or DFT results and obtained ΔIPs correlate with Hammett constants better. The correlation coefficient reached the following values: 0.976 for series **1**, 0.965 for series **2** and 0.900 for series **3**. In the case of the first two series the value of the line slope is practically identical: 0.157 for series **1** and 0.154 for series **2**. For series **3** regression analysis gives the value 0.547 which is approximately 3.5-times higher than slopes obtained for series **1** and **2**.

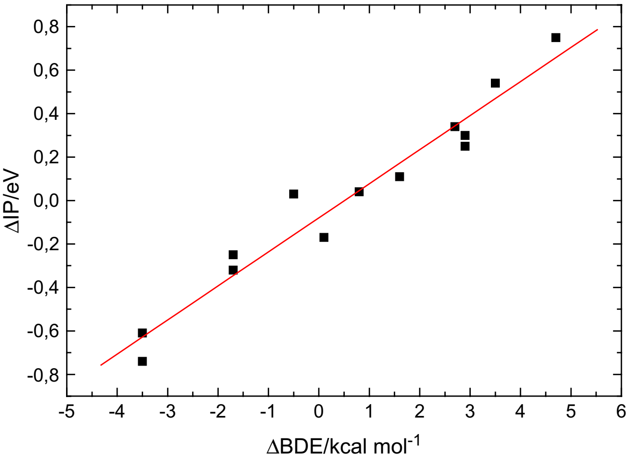

Fig. 6. Dependence of ΔBDE vs. ΔIP for AM1 data – series **1**.

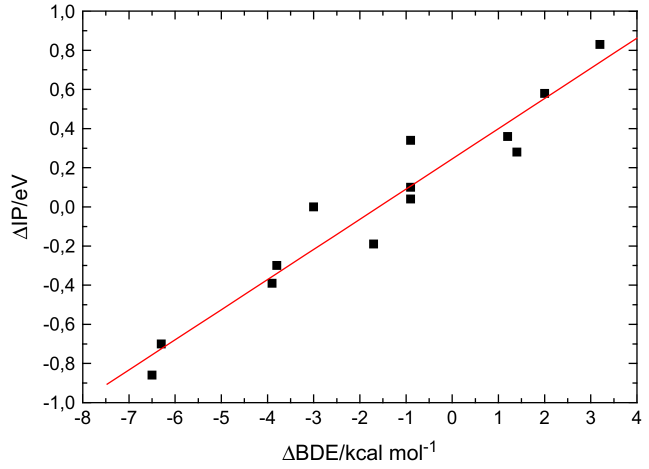

Fig. 7. Dependence of ΔBDE vs. ΔIP for AM1 data – series **2**.

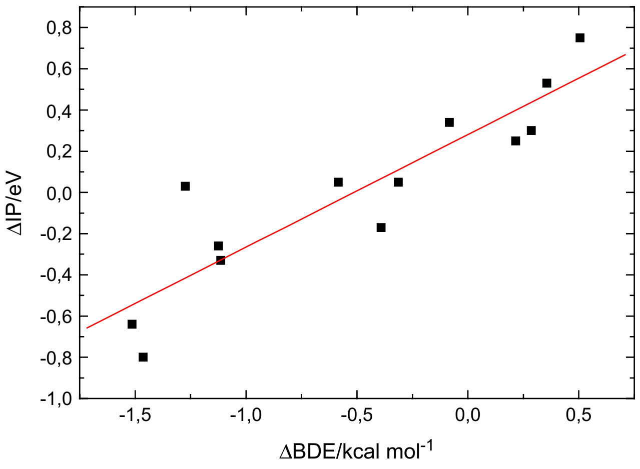

Fig. 8. Dependence of ΔBDE vs. ΔIP for AM1 data – series **3**.

While ΔIPs of series **2** and **3** are similar, ΔBDEs of the series **3** lie in approximately three times narrower range and thus they are responsible for steeper slope. In all three series the drop in ΔIP values accompanies the drop in ΔBDE values. This is unfavourable for the antioxidant effectiveness. The optimal substituent should simultaneously cause a decrease in N–H bond BDE and an increase in IP. Generally, the lower slope of ΔIP = *f*(ΔBDE) dependence found for series **1** and **2** is more favourable than that of series **3**.

4. Conclusion

We can conclude that for series **1** AM1 method provides ΔBDE values closer to experimental (mainly EC and TDC) data – the values correspond to experimental results even better than ΔBDE values obtained from two DFT approaches with large basis set. On the other hand, PM3 method BDEs agree with experimental EC and TDC data better. AM1 method tends to overestimate individual BDE values.

For series **2** calculated AM1 ΔBDE values correspond to experimental and DFT data better than PM3 values which lie in significantly narrower range. For series **3** both semi-empirical methods provide slightly less reliable values, since the substituent effect on BDE is significantly lower and BDEs reached values in relatively narrow range. AM1 results still correspond to the expected linear dependence of ΔBDE values on Hammett constants better.

Calculated IPs are higher than experimental values found for molecules from series **1** to **2**. The differences are in 0.2–1.2 eV range. Both methods describe the trend in substituent effect on IP satisfactorily.

Obtained results show that PM3 and AM1 semi-empirical quantum chemical methods can be successfully applied for BDE and ΔBDE calculations. These methods can be applied not only for compounds studied in this paper, but also for *N*,*N*′-substituted *p*-phenylenediamine antioxidants BDE calculation [26] or various *para*- and *meta*-substituted phenols [37] (data available on request). Moreover, these methods work fast enough to obtain results of calculation in minute scale while the application of DFT (B3LYP) with large basis sets remains restricted for large antioxidant molecules consisting of 50 or more atoms due to high computational costs.

The results also indicate that Hammett constants describe the substituent effect on N–H bond strength (BDE) and ionisation potential satisfactorily. It means that BDEs and IPs of various *para*- and *meta*-substituted compounds can be successfully predicted when the BDE and IP values of the non-substituted compound and linear ΔBDE = $f(\sigma_p, \sigma_m)$ and ΔIP = $f(\sigma_p, \sigma_m)$ dependences are known. This approach may be utilized in development of new antioxidants. Linear correlation of ΔBDEs and ΔIPs with Hammett constants can be successfully employed in the judgment of the results of quantum chemical method reliability in the case of molecules with various substituents in *para* and *meta* positions. Moreover, linear BDE = *f*(IP) dependence of a series of molecules allows assessment of BDE on the basis of calculated IP. This can be advantageous, since direct BDE determination needs the calculation of enthalpies of formation of two species – molecule and the corresponding radical. Furthermore, estimation of BDE from calculated IP value enables to get around the problems with inaccuracy of the calculations of radical species.

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