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BOND DISSOCIATION ENTHALPY OF PHENOLIC ANTIOXIDANTS

Henryk Szymusiak, Ryszard Zieliński*

Department of Technology and Environmental Protection, Faculty of Commodity Science,
Poznań University of Economics, Poznań, Poland

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Homolytic bond dissociation enthalpies (BDEs) for O-H bonds in selected phenols have been theoretically calculated using density functional theory at the B3LYP/6-311G(d,p) and B3LYP/pp-cpTZ levels of theory. It was found that the B3LYP method is generally reliable for the prediction of absolute BDEs. This method works well for the prediction of substituent effects on BDEs. The deviations from experimental values are generally within 2-3 kcal/mol. The stability of phenoxyl radicals is largely affected by substituents and by internal hydrogen bonding. It was shown that, in particular, electron-donating substituents have large stabilizing effects on phenoxyl radicals. The application of the method for the prediction of the BDEs in polyhydroxyphenols is illustrated and discussed.

INTRODUCTION

Phenolic compounds are known to suppress the lipid peroxidation in living organisms, and they are also widely used as additives in food technology. Reducing the rate of such oxidative degradation process by utilizing low concentrations of substances known as ”antioxidants” is important both for all aerobic organisms as well as for many commercial products, especially for food products [Halliwell *et al*., 1995a,b; Wright *et al*., 1997]. The nutritional and medical aspects of antioxidants have been the subject of numerous reviews [Halliwell *et al*., 1995a,b; Halliwell, 2000; Aruoma, 1994] and overviews [Halliwell *et al*., 1989]. The function of antioxidants is to intercept and react with free radicals at a rate faster than the substrate. Since free radicals are able to attack lipids, fats, and proteins, it is commonly believed that they are implicated in a number of degenerative diseases and aging [Halliwell, 2000; Aruoma, 1994].

In general, two pathways are assumed for oxidation in which phenolic antioxidants can play a preventive role: the hydrogen atom transfer and electron transfer. The first pathway is H-atom transfer, for lipid (LH) peroxidation [Wright *et al*., 1997, 2001]:

$$\text{LH} \rightarrow \text{L*} \text{ (initiation)} \qquad (1)$$

$$\text{L*} + \text{O}_2 \rightarrow \text{LOO*} \text{ (addition of O}_2\text{ to carbon radical L*)} \qquad (2)$$

$$\text{LOO*} + \text{LH} \rightarrow \text{LOOH} + \text{L*} \text{ (H-atom exchange)} \qquad (3)$$

Once free radical of a lipid L* has been generated, then reaction (2) and (3) form a chain reaction. During the chain cycles through reactions (2) and (3), the lipid molecules (LH) are oxidized to lipid hydroperoxide (LOOH), which results in rancidity of fats and fatty food products. It is important to note that reaction (2) is very fast with the second kinetic order rate constant of *ca.* 10^9 M^{-1} s^{-1}, whereas reaction (3) is much slower, usually *ca.* 10^1 M^{-1} s^{-1} [Wright *et al*., 2001]. The main role of an antioxidant (ArOH) is to interrupt the chain reaction (or trap the peroxyl LOO* radical):

$$\text{LOO*} + \text{ArOH} \rightarrow \text{LOOH} + \text{ArO*} \text{ (trapping the peroxyl LOO* radical)} \qquad (4)$$

From reaction (4) it results that to be more effective the phenolic antioxidant (ArOH) should be able to easily abstract the H-atom from phenolic O-H group and the phenoxyl radical (ArO*) must be stable free radical, that very slowly reacts with substrate LH but very rapidly with peroxyl (LOO*) leading finally to non-reactive and non-radical products. The rate of reaction (3) depends on the barrier height for transfer of an H-atom from lipid LH to radical LOO* or from antioxidant (ArOH) to radical LOO* in the case of reaction (4). As the reaction (4) becomes more exothermic one can expect that the reaction barrier should decrease, and the antioxidant will react faster with peroxyl radical, in this way preventing the lipid against peroxidation more effectively. From this discussion it can be concluded that the parameter in the form of bond dissociation enthalpy (BDE) will be a representative factor in determining the efficacy of a phenolic antioxidant. The weaker the OH bond in the molecule of an antioxidant (the lower its BDE) the faster will be the reaction with free radicals such as peroxyl, alkoxyl, alkyl, superoxide, and others. For example [Wright *et al*., 2001], the free radicals such as LOO* have a much lower BDE on formation of the parent LOOH, typically about 88 kcal/mol and they will react slowly according to reaction (4) with phenol (BDE *ca.* 88 kcal/mol) but they react rapidly in more exothermic reaction with α-tocopherol (BDE

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* Author’s address for correspondence: Henryk Szymusiak, Department of Technology and Environmental Protection, Faculty of Commodity Science, Poznań University of Economics, Aleja Niepodległości 10, 60-967 Poznań, Poland; e-mail: ktos@ae.poznan.pl

ca. 77 kcal/mol). Tocopherols are effective chain-breaking antioxidants that prevent lipid peroxidation, in contrast to phenol. In some cases other factors may also play a role in determining what makes an effective antioxidant. These include the presence of bulky groups near the OH group [De Heer *et al*., 1999, 2000], hydrogen bonding characteristics of the solvent [Valgimigli *et al*., 1995, 1996], or biological context, solubility, inter-phase phenomena. Hovever, as far as specific molecular properties are concerned, the BDE is of particular importance to experimentalists and theoreticians.

To perform a systematic study of antioxidants from a theoretical perspective one needs to determine accurately the BDE. A number of theoretical studies have addressed this point, many of them have been QSAR studies which attempted to correlate antioxidant activity with various molecular properties, especially with BDE [Wright *et al*., 1997, 2001; De Heer *et al*., 1999, 2000; Van Acker *et al*., 1996; Brinck *et al*., 1997; Da Silva *et al*., 1999; Migliavacca *et al*., 1997; Szymusiak *et al*., 2000; Tyrakowska *et al*., 1999].

In recent years, quantum chemical calculations have become an increasingly used tool for determination of gas phase thermochemistry. The development of the Gaussian 2 (G2) [Curtiss *et al*., 1991] and Complete Basis Set (CBS) [Ochterski *et al*., 1996] approaches has provided the chemists with efficient techniques for calculating thermochemical data with experimental accuracy. Unfortunately, these methods use high-level *ab initio* methods, which limits the sizes of systems that can be studied to only small systems consisted of several atoms [Brinck *et al*., 1999]. Density functional theory (DFT) methods have in recent years evolved as an important complement to advanced *ab initio* methods. The advantage of DFT methods is that they allow studing considerably larger systems with only limited loss in accuracy [Brinck *et al*., 1999].

In the present study, we have employed a DFT method to analyze the substituent effects on antioxidant activity of selected phenolic compounds in the sense of their O-H bond dissociation enthalpies, BDEs. The computed data is critically evaluated against available experimental values. The results obtained are analyzed and discussed in relation to the possibility of using the proposed methods for the prediction of BDE values and other useful data for more complex compounds such as polyphenols.

METHODS

We have used B3LYP functional in two combinations of basis set: in the first combination geometries of phenols and their phenoxy radicals were optimized in 6-31G(d,p) basis set and the single-point calculations were performed in higher 6-311G(d,p) basis set. In the second combination, the Dunnings correlation consistent basis sets were used: cc-pVDZ (double-zeta) in optimization step and then cc-pVTZ (triple-zeta) in single-point calculation. We have used B3LYP functional because this functional has been shown to provide reliable geometries, frequencies, and bond energies [Brinck *et al*., 1999]. Harmonic frequencies for all neutral and radical molecules have been computed at (U)HF/3-21G(d) level due to too large size of most molecules studied. All calculations refer to the gas phase.

The value of BDE is calculated as the enthalpy difference at 298 K for the reaction:

$$\mathrm{ArOH} \rightarrow \mathrm{ArO^*} + \mathrm{H^*} \qquad (5)$$

where ArOH is the parent phenol and ArO* is the corresponding phenoxyl radical. Calculated at HF/3-21G(d) level thermal correction to enthalpy was done without scaling the zero-point energy and vibrational contribution to this enthalpy. The total enthalpy at 298 K for given species is the sum of the thermal correction to the enthalpy and the B3LYP electronic energy from the final step. The Gaussian 98 suite of programs has been used for the *ab initio* and DFT calculations reported in this study.

RESULTS AND DISSCUSION

A number of theoretical as well as experimental investigations of varying degrees of sophistication have been reported with the aim to understand the structural factors that determine the strength of O-H phenolic bonds [Wright *et al*., 1997, 2001; De Heer *et al*., 1999, 2000; Van Acker *et al*., 1996; Brinck *et al*., 1997; Da Silva *et al*., 1999; Migliavacca *et al*., 1997; Szymusiak *et al*., 2000; Tyrakowska *et al*., 1999; Bordwell *et al*., 1994; Laarhoven et al., 1999, Lucarini *et al*., 1994, 1996, 2001, 2002; Wayner *et al*., 1996; Brigati *et al*., 2002]. It has been already well empirically established that electron-withdrawing substituent causes an enhancement of the O-H BDE value and thus a worsening of antioxidant actvity of phenols. From the molecular point of view, it can be also said that such substituent reduces their persistence due to the increased reactivity of the related phenoxyl radicals. The electron-releasing substituents reveal quite opposite effect. The experimental data provided by Brigati *et al.* [2002] on substituents scarcely investigated so far in relation to their effects on the O-H BDE give an excellent opportunity to check how modern theoretical methods of quantum chemistry deal with this problem. The reported experimental BDE for phenols containing different substituents in the para position of 2,6-di-tert-butylphenol were measured by using the EPR radical equilibration technique, which seems to guarantee at the present the best accuracy for the determination of realistic experimental data. The 4-substituted 2,6-di-tert-butylphenols are candidates for good antioxidants because of large persistence that characterizes their phenoxyl radicals related to sterical protection of radical oxygen center by large tert-butyl substituents in ortho positions. These data as well as those calculated theoretically by using four various protocols connected with computing time are collected in Table 1.

Another factor to be checked is the influence of thermal correction to enthalpy used in order to better fit the experimental data which refer to enthalpies measured under normal conditions and not to strictly electronic energies. Calculation of this thermal correction is related to additional step calculation and it is interesting to consider whether it would be possible to skip this step without lowering the quality of final results. It should be noted that although the absolute values of BDE with no corrections are typically only sligtly lower than experimental values, the corrections change the BDEs in direction to lower values by *ca*. 7-10 kcal/mol.

Figure 1 illustrates the relationship between the calculated values of BDE and their experimental partners showing good linear correlation. The linear regression correlation coefficients are as follows: 0.9904, 0.9888, 0.9806 and 0.9891 for method I, II, III and IV, respectively. Since in EPR experiments a number of additional parametrs is obtained as by-product when measuring radical concentration, Brigati *et al.* [2002] give some of these parameters which are collected in Table 2 together with computed data. It is seen that the computed values of hyperfine splittings are a bit higher than the observed ones but they are in good linear correlation as shown in Figure 2.

Brigati *et al.* [2002] reported also the existence of linear correlation between bond dissociation enthalpy values of 4-substituted 2,6-di-tert-butylphenols and the room-temperature hyperfine splittings at the meta protons measured in benzene solution of the corresponding phenoxyl radicals. Similar plot (data not shown) can be obtained from calculated results given in Tables 1 and 2. Existence of such linear relationships suggests the importance of the ground-state and of the radical determines the O-H BDE values. The decrease in observed and calculated meta proton splitings, when reducing the electron-acceptor character of the para substituents, can be understood in terms of an increasing weight of some resonance structures that induce opposite spin densities at the meta position. A relatively good correlation between BDE values and the hyperfine constants that characterize radical state of a phenol seems to suggest that magnitude of the O-H bond dissociation depends mainly on radical effect. In conclusion, it can be stated that when considering 4-substituted phenols, relatively not expensive theoretical methods based on B3LYP functional are able to predict both the values of BDE with using correlation line parameters shown in Figure 1 as well as parameters characterizing the radical state of phenolic antioxidants observed in the EPR experiments.

As another validation of the proposed wider use of theoretical methods for the calculation of BDE and hyperfine constants we demonstate the results for three compounds with

TABLE 1. Absolute and relative O-H bond dissociation energies calculated by B3LYP/6-311G(d,p)//B3LYP/6-31G(d,p) assigned as "Method I", B3LYP/6-31G(d,p)//B3LYP/6-31G(d,p) assigned by "Method II", B3LYP/cc-pVTZ//B3LYP/cc-pVDZ assigned by "Method III", and B3LYP/cc-pVDZ//B3LYP/cc-pVDZ assigned as "Method IV", and experimental data[a]. BDE calculated from electronic energies are in the upper row. The values given in the lower row correspond to BDE with thermal correction to enthalpy.

Substituent	Method I		Method II		Method III		Method IV		Experiment[c]	
	BDE	ΔBDE[b]	BDE	ΔBDE[b]	BDE	ΔBDE[b]	BDE	ΔBDE[b]	BDE	ΔBDE[b]
4-H	81.77[d] 73.89[e]	0 0	81.56 73.68	0 0	82.70 74.82	0 0	80.73 72.85	0 0	82.80	0
4-NO_2	85.82[d] 77.30[e]	4.05 3.41	85.75 77.23	4.19 3.48	86.75 78.23	4.05 4.41	84.67 76.15	3.94 3.30	84.94	2.14
4-CN	83.83 74.81	2.06 0.92	83.68 74.66	2.12 0.98	84.84 75.82	2.14 1.00	82.76 73.74	2.03 0.89	84.24	1.44
4-CHO	83.70 74.51	1.93 0.62	83.58 74.39	2.02 0.71	84.77 75.58	2.07 0.76	82.65 73.46	1.92 0.61	84.23	1.43
4-COOH	84.14 75.47	2.37 1.58	84.01 75.34	2.45 1.66	85.34 76.67	2.64 1.85	83.05 74.38	2.32 1.53	84.27	1.47
4-COOMe	83.81 75.80	2.04 1.91	83.65 75.64	2.09 1.96	85.01 77.00	2.31 2.18	82.56 74.54	1.83 1.69	84.10	1.30
4-Cl	80.97 73.20	-0.80 -0.69	80.85 73.08	-0.71 -0.60	81.98 74.21	-0.72 -0.61	79.81 72.04	-0.92 -0.81	82.41	-0.39
4-Me	79.84 72.71	-1.93 -1.18	79.72 72.60	-1.84 -1.08	80.79 73.66	-1.91 -1.16	78.87 71.74	-1.86 -1.11	81.02	-1.78
4-t-But	80.20 72.51	-1.57 -1.38	80.07 72.38	-1.49 -1.30	28.28 71.59	3.42 3.23			81.24	-1.56
4-MeO	76.12 68.56	-5.65 -5.33	76.11 68.55	-5.45 -5.13	76.96 69.40	-5.74 -5.42	75.21 67.65	-5.52 -5.20	78.31	-4.49
4-NH_2	72.86 65.08	-8.91 -8.81	73.10 65.32	-8.46 -8.36	73.84 66.06	-8.86 -8.76	72.01 64.23	-8.72 -8.62		
4-ph	83.24 74.35	1.47 0.46	83.60 74.72	2.04 1.04	31.31 72.42	1.39 2.40			81.24	-1.56
4-vin-ph	76.42	-5.35	76.49	-5.07					78.90	-3.90

[a] all values (in kcal/mol) correspond to 298 K and 1 atm; [b] DBDE = BDE(R = H) - BDE(R = X); [c] experimental data are from Brigati *et al.* [2002].

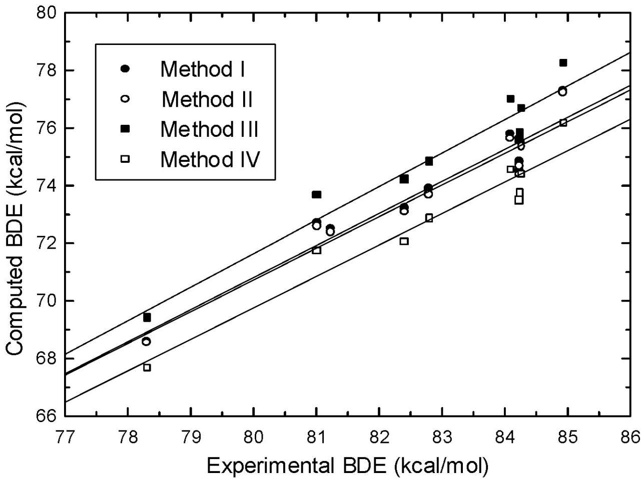


FIGURE 1. Relationship between experimental BDE values and those computed by different methods.

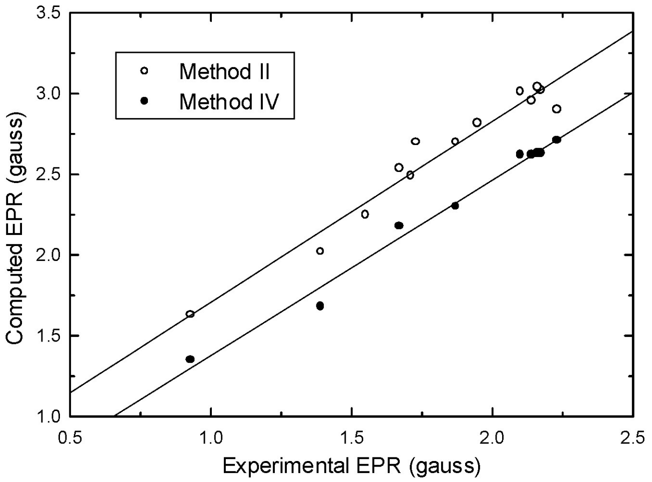


FIGURE 2. Relationship between experimental values of hyper-fine splittings ($a_{3,5}$) and those computed by methods II and IV.

more than one O-H groups. The advantage of theoretical methods over experimental ones is that the theoretical methods can estimate at least relative BDE values for all O-H groups present in the molecule of a given phenolic antioxidant, whereas in experimental techniques only the weakest O-H bond in the molecule is measured with some effect from other weak O-H bonds. The results of calculation for O-H BDE that can be compared to recently published data are shown in Table 3.

Figure 3 shows the structures studied together with explicite shown BDEs and hyperfine splittings.

It should be noted that the data reported by Lucarini *et al.* [2002] for the first time include experimental results for O-H BDEs for naturally occurring phenolic antioxidants which have catechol and pyrogallol moiety in their structure. Those data are of particular importance to us bacause we can investigate performance of commonly used theoretical methods in hydrogen bonded systems. As it can be seen from Table 3 and Figure 3, the value of O-H BDE for 2,5-di-tert-pentylhydroquinone can be very accurately predicted by the proposed method. In the case of 3,5-di-tert-butylcatechol and propyl gallate the values

TABLE 2. Experimental and calculated EPR spectral parameters of 4-substituted 2,6-di-tert-butylphenoxyl radicals: B3LYP/6-31G(d,p)//B3LYP/6-31G(d,p) assigned by "Method II", and B3LYP/cc-pVDZ//B3LYP/cc-pVDZ assigned as "Method IV". Hyperfine splittings (a) are given in gauss. Experimental data are from Brigati *et al.* [2002].

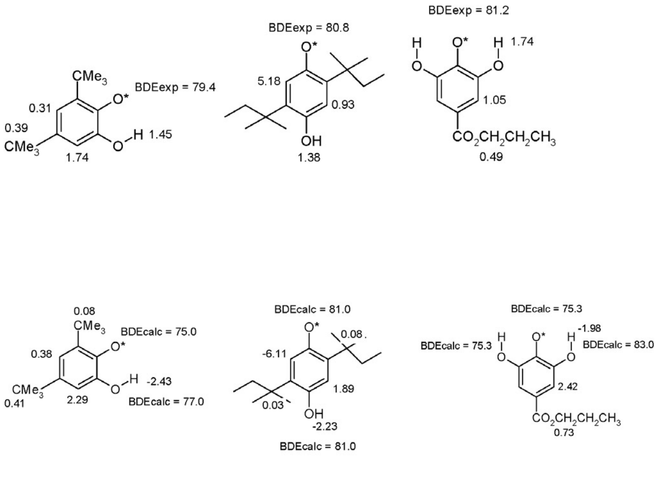
Substituent	Method II		Method IV		Experiment	
	$a_{3.5}$	a_{other}	$a_{3.5}$	a_{other}	$a_{3.5}$	a_{other}
4-H	2.82	-9.40 (1H)	2.45	-8.49	1.95	9.72 (1H)
4-NO_2	2.90	-1.67 (1N)	2.71	-1.90 (1N)	2.23	2.23 (1N)
4-CN	3.02	1.85 (1N)	2.63	2.65 (1N)	2.17	1.37 (1N)
4-CHO	3.01	-0.14 (1H)	262	-0.13 (1H)	2.10	0.45 (1H)
4-COOH	3.04		2.63		2.16	
4-COOMe	2.96	0.62 (3H)	2.62	0.55 (3H)	2.14	0.53 (3H)
4-Cl	2.70	1.58 (^{35}Cl)	2.30	1.97 (^{35}Cl)	1.87	1.47 (^{35}Cl)
4-Me	2.54	10.20 (3H)	2.18	9.32 (3H)	1.67	11.20 (3H)
4-t-But	2.49	0.35 (9H)			1.71	0.38 (9H)
4-MeO	1.63	1.74 (3H)	1.35	1.65 (3H)	0.93	1.53 (3H)
4-NH_2	0.38	4.31 (1N)	0.74	4.31 (1N)	-	-
4-ph	2.70	0.42 (2H)			1.73	1.73 (3H) 0.67 (2H)
4-vin-ph	25.25	-0.706 (1H) 3.08 (1H)			1.55	6.39 (1H) 2.85 (1H) 1.55 (3H) 0.57 (2H)

TABLE 3. Absolute and relative O-H bond dissociation energies calculated by B3LYP/6-311G(d,p)// B3LYP/6-31G(d,p) assigned as “Method I”, B3LYP/6-31G(d,p)// B3LYP/6-31G(d,p) assigned as “Method II”, B3LYP/cc-pVTZ//B3LYP/cc-pVDZ designed by “Method III”, and B3LYP/cc-pVDZ//B3LYP/cc-pVDZ assigned as “Method IV”, and experimental data[a]. BDE values calculated from electronic energies are in the upper row. Numbers given in the lower row correspond to BDE with subtracted thermal correction to enthalpy.

Compound	Method I	Method II	Method III	Method IV	Experiment[a]
	BDE	BDE	BDE	BDE	BDE
3,5-di-tert-butylcatechol (for C2-OH)	75.23 67.41	74.95 67.13	76.16 68.34	73.57 65.75	79.4
3,5-di-tert-butylcatechol (for C1-OH)	77.23 69.27	77.01 69.05	78.04 70.08	75.50 67.54	-
2,5-di-tert-pentylhydroquinone	80.84	80.98	81.66	79.59	80.8
propyl gallate (for C3-OH)	83.26 75.00	82.97 74.71	84.03 75.77	81.34 73.08	-
propyl gallate (for C4-OH)	75.77 67.71	75.33 67.27	76.79 68.73	73.54 65.48	81.2

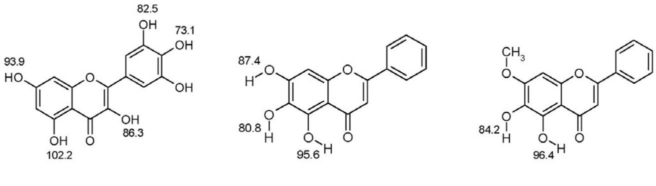
[a] all values (in kcal/mol) correspond to 298 K and 1 atm; [b] DBDE = BDE(R = H) - BDE(R = X); [c] experimental data are from Lucarini *et al*. [1996].

of O-H BDE are systematically lower by about 4-5 kcal/mol. As noted by Lucarini *et al*. [2002], the BDE value for catechol group can not be estimated from additivity rule which works well for monophenolic compounds, the value calculated this way is 83.7 kcal/mol and 88.7 kcal/mol for 3,5-di-tert-butyl-catechol and for propyl galate, respectively. The additional contribution arising from intramolecular hydrogen bonding involving the second hydroxyl group is not taken into account in additivity rule and is slightly overestimated in theoretically derived values. In fact, the intramolecular hydrogen bonding in the semiquinone radical from catechols has been suggested to be responsible for the good antioxidant activity of catechol containing derivatives [Van Acker *et al*., 1996; Lucarini *et al*., 2002]. Catechols are known to experience strong kinetic solvent effects on the hydrogen atom abstraction reaction by oxygen- and nitrogen-centered radicals [Lucarini *et al*., 2002] and theoretical calculations refer to gas phase environment. The above remarks refer also to pyrogallol-containing molecules, where two hydrogen bonds are shared by the central oxygen atom. So, taking into account that gas phase DFT methods have trends to underestimate the O-H BDEs in catechol or pyrogallol- moiety containing molecules, as is the case in this study, we can propose using these methods to carefull estimation of O-H bond strength of other molecules such as flavonoids. There is also an opportunity to compare calculated hyperfine splittings to those observed experimentally, which are a bit higher but correlated with experimental data. It is important to mention that theoretical calculations are able to predict the sign of the splitting that experimentally are not observed, which was shown in Figure 3. At last but not least, in Figure 4 the computed BDE values for few naturally occurring flavonoids are reported. It is worth emphasising that the predicted difference in BDE for py-



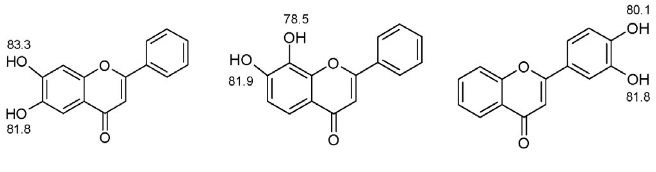
3.5-di-tert-butylcatechol

FIGURE 3. Experimental (top row) and calculated (by method II, bottom row) hyperfine splittings (gauss) and bond dissociation enthalpies (theoretical values not corrected).



Myricetin Baicalein Baicalin

FIGURE 4. Calculated bond dissociation energies, BDE (kcal/mol), (not corrected) for each O-H group of myricetin, baicalein and baicalin.



6.7-dihydroxyflavone 7.8-dihydroxyflavone 3’.4’-dihydroxyflavone

FIGURE 5. Calculated bond dissociation energies, BDE (kcal/mol), (not corrected) for each O-H group of selected katechol-containing compounds.

rogallol moiety in baicalein and in myricetin depends highly on its location in flavone structure. Very similar conclusions refer to di-hydroxyflavones shown in Figure 5.

CONCLUSIONS

Theoretically computed parameters characterizing the effectiveness of phenolic antioxidants, designed for food industry, such as bond dissociation enthalpy can be used in the case when experimental data are not determined, which is the case for most of polyphenolic compounds. The computed bond dissociation energies are usually lower in absolute values when compared to the experimentally derived ones but they are linearly correlated with available so far experimental data determined using the same experimental EPR radical equilibration technique, and can be simply improved by using the correlation equation parameters.

The computed bond dissociation enthalpies although still a little less acurate for simple substituted phenols than those estimated on the basis of the group additivity rule in polysubstituted phenols can be used in screening the antioxidant activity of more complex polyphenolic antioxidants such as flavonols, flavanes, catechins, and anthocyanines, abundant in foods of plant origin.

REFERENCES

1. Aruoma O.I., Nutrition and health aspects of free radicals and antioxidants. Food Chem. Toxicol., 1994, 32, 671-683.
2. Bordwell F.G., Zhang X.M., Satish A.V., Cheng J.-P., Assessment of the importance of changes in ground-state energies on the bond dissociation enthalpies of the O-H bonds in phenols and S-H bonds in thiophenols. J. Am. Chem. Soc., 1994, 116, 6605-6610.
3. Brigati G., Lucarini M., Mugnaini V., Pedulli G.F., Determination of the substituent effects on the O-H bond dissociation enthalpies of phenolic antioxidants by the EPR radical equilibration technique. J. Org. Chem., 2002, 67, 4828-4832.
4. Brinck T., Haeberlein M., Jonsson M., A computational analysis of substituent effects on the O-H bond dissociation energy in phenols: polar versus radical effects. J. Phys. Chem., 1997, 119, 4239-4244.
5. Brinck T., Lee H.N., Jonsson M., Quantum chemical studies on the thermochemistry of alkyl and peroxyl radicals. J. Phys. Chem. A , 1999, 103, 7094-7104.
6. Curtiss L.A., Raghavachari K., Trucks G.W., Pople J.A., Gaussian-2 theory for molecular energies of first- and second-row compounds. J. Chem. Phys., 1991, 94, 7221.
7. Da Silva M.A.V.R.,.Matos M.A,R, Morais V.M.F., Miranda M.S., Thermochemical and theoretical study of tert-butyl and di-tert-butylphenol isomers. J. Org. Chem., 1999, 64, 8816-8820.
8. Halliwell B., Gutteridge J.M.C., 1989, Free Radicals in Biology and Medicine. 2nd ed., Clarendon Press, Oxford.
9. Halliwell B., Asechbach R., Iloliger J., Aruoma O.I., The characterization of antioxidants. Food Chem. Toxicol., 1995a, 33, 601-617.
10. Halliwell B., Murcia A.M., Butler J., Chiroco S., Aruoma O.I., Free radicals and antioxidants in food and *in vivo*: what they do and how they work. Crit. Rev. Food Sci. Nutr., 1995b, 35, 7-20.
11. Halliwell B., Lipid peroxidation, antioxidants and cardiovascular desease: how should we move forward? Cardiovasc. Res., 2000, 47, 410-418.
12. De Heer M.I, Korth H.-G., Mulder P., Polymethoxy phenols in solution: O-H bond dissociation enthalpies, structures, and hydrogen bonding. J. Org. Chem., 1999, 64, 6969-6975.
13. De Heer M.I., Mulder P., Korth H.-G., Ingold K.U., Lusztyk J., Hydrogen atom abstraction kinetics from intramolecularly hydrogen bonded ubiquinol-O and other (poly)methoxy phenols. J. Am. Chem. Soc., 2000, 122, 2355-2360.
14. Laarhoven L.J.J., Mulder P., Wayner D.D.M., Determination of bond dissociation enthalpies in solution by photoacoustic calorimetry. Acc. Chem. Res., 1999, 32, 342-349.
15. Lucarini M., Pedulli G.F., Cipollone M., Bond dissociation enthalpy of α-tocopherol and other phenolic antioxidants. J. Org. Chem., 1994, 59, 5063-5070.
16. Lucarini M., Pedrielli P., Pedulli G.G., Bond dissociation energies of O-H bonds in substituted phenols from equilibrium studies. J. Org. Chem., 1996, 61, 9259-9263.
17. Lucarini M., Pedulli G.F., Valgimigli L., Amorati R., Minisci F., Thermochemical and kinetic studies of a bisphenol antioxidant. J. Org. Chem., 2001, 66, 5456-5462.
18. Lucarini M.,.Mugnaini V, Pedulli G.F., Bond dissociation enthalpies of polyphenols: the importance of cooperative effects. J. Org. Chem., 2002, 67, 928-931.
19. Migliavacca E., Carrupt P.-A., Test B., Theoretical parametrs to characterize antioxidants. Part 1. The case of vitamin E and analogs. Helv. Chim. Acta, 1997, 80, 1613-1626.
20. Ochterski J., Petersson G.A., Montgomery Jr. J.A., A complete basis set model chemistry. V. Extensions to six or more heavy atoms. J. Chem. Phys., 1996, 104, 2598.
21. Szymusiak H., Lemańska K., Zieliński R., Tyrakowska B., Experimental and theoretical study on antioxidant activity of structurally related 4-hydroxycinnamic and 4-hydroxybenzoic acids. Curr. Topics Biophys., 2000, 24, 209-218.
22. Tyrakowska B., A.E.M.F. Soffers A.E.M.F., Szymusiak H., Boeren S., Boersma M.B., Lemańska K., Vervoort J., Rietjens I.M.C.M., The TEAC antioxidant activity of 4-hydroxybenzoates. Free Rad. Biol. Med., 1999, 27, 1427-1436.
23. Valgimigli L., Banks J.T., Ingold K.U., Lusztyk J., Kinetic solvent effects on hydroxylic hydrogen atom abstraction are independent of the nature of the abstracting radical. Two extreme tests using vitamin E and phenol. J. Am. Chem. Soc., 1995, 117, 9966-9971.
24. Valgimigli L., Ingold K.U., Lusztyk J., Antioxidant activities of vitamin E analogues in water and a Kamlet-Taft β-value for water. J. Am. Chem. Soc., 1996, 118, 3545-3549.
25. Van Acker S.A.B.E., van den Berg D.J., Tromp M.N.J.L., Griffoen D.H., van Bennekom W.P., van der Vogh W.J.F., Bast A., Structural aspects of antioxidant activity of flavonoids. Free Rad. Biol. Med., 1996, 20, 331.

26. Wayner D.D.M., Lusztyk E., Ingold K.U., Mulder P., Application of photoacoustic calorimetry to the measurements of the O-H bond strength in vitamin E (α- and δ-tocopherol) and related phenolic antioxidants. J. Org. Chem., 1996, 61, 6430-6433.
27. Wright J.S., Carpenter D.J.,.McKay D.J, Ingold K.U., Theoretical calculation of substituent effects on the O-H bond strength of phenolic antioxidants related to vitamin E. J. Am.Chem Soc., 1997, 119, 4245-4252.
28. Wright J.S, Johnson E.R., Di Labio G.A., Predicting the activity of phenolic antioxidants: theoretical method, analysis of substituent effects, and application to major families of antioxidants. J. Am. Chem. Soc., 2001, 123, 1173-1183.