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ORIGINAL PAPER

DFT study of free radical scavenging activity of erodiol

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Antioxidant activity of erodiol was examined at the M05-2X/6-311+G(d,p) level of theory in the gas and aqueous phases. The structure and energy of radicals and anions of the most stable erodiol rotamer were analyzed. To estimate antioxidant potential of erodiol, different molecular properties were examined: bond dissociation enthalpy, proton affinity together with electron transfer energy, and ionization potential followed by proton dissociation enthalpy. It was found that hydrogen atom transfer is the prevailing mechanism of erodiol behavior in gas; whereas single electron transfer followed by proton transfer and sequential proton loss electron transfer mechanisms represent the thermodynamically preferred reaction paths in water.

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Keywords: depside, erodiol, free radical scavenging mechanisms, BDE, IP, PA

Introduction

Depside is a polyphenolic compound composed of two or more aromatic rings bound by a phenolic oxygen-ester linkage. They are most often found in lichens, but have also been isolated from higher plants (Ono et al., 2002; Hillenbrand et al., 2004; Reynertson et al., 2006). It has been suggested that some depsides act as antipyretic, analgesic, antibacterial, antiviral, anti HIV-1 integrase, anticancer, and antiproliferative agents (Proksa et al., 1994; Yamamoto et al., 1995; Neamati et al., 1997; Kumar & Müller, 1999; Nielsen et al., 1999). In addition, depsides inhibit biosynthesis of prostaglandin and leukotriene B4, and they act as powerful nonsteroidal antiinflammatories (Kumar & Müller, 2000; Reynertson et al., 2006; Lv et al., 2009). A new depside, erodiol (Fig. 1), has been isolated from the aqueous extract of the dried aerial parts of *Erodium cicutarium* (Fecka & Cisowski, 2005).

Depside is an electron-rich and highly conjugated chemical system. Due to these features they easily

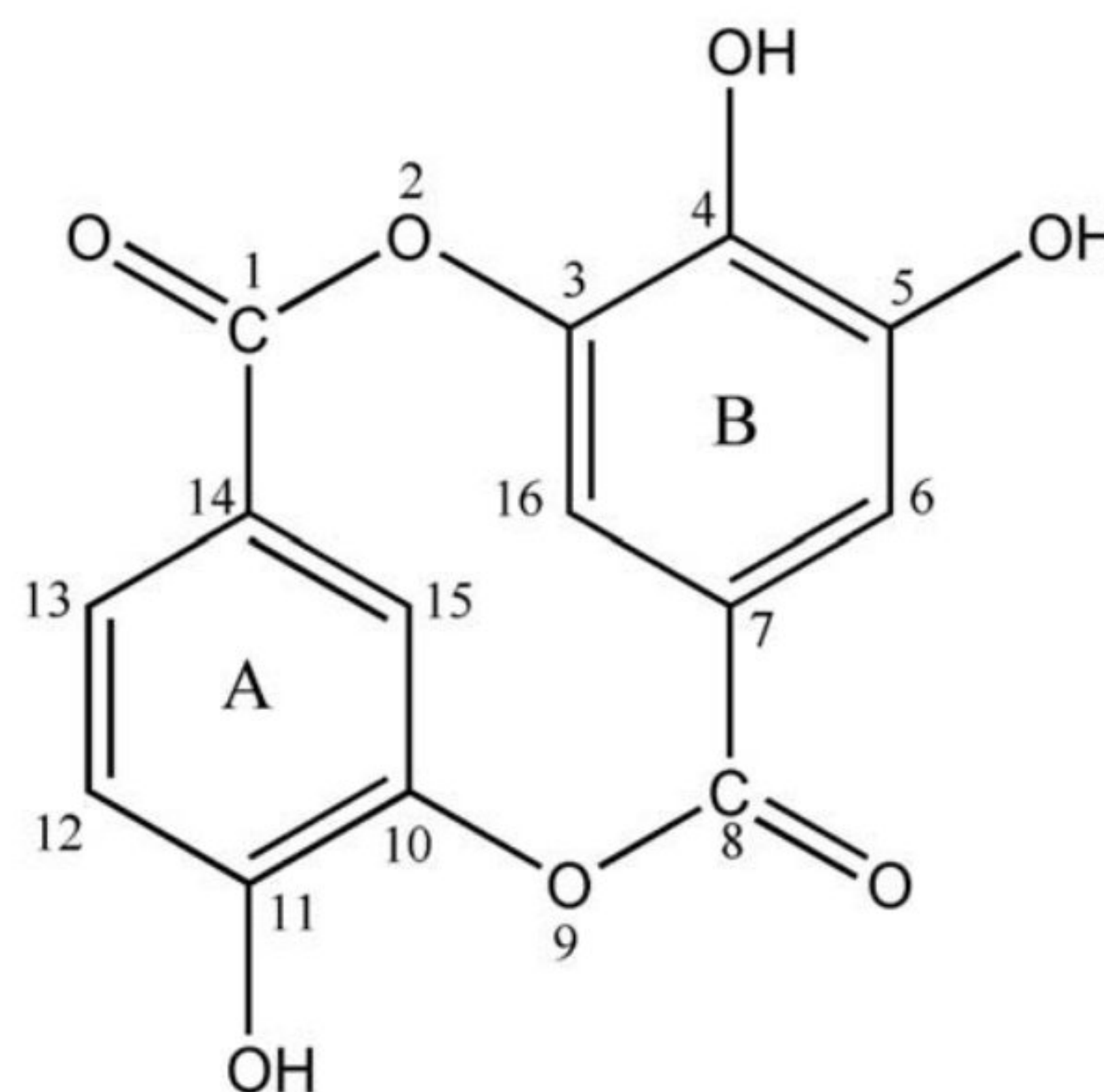


Fig. 1. Structural formula of erodiol. Labels on the atoms are used throughout the paper.

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participate in proton and electron transfers. These fundamental chemical and biological processes play a significant role in the determination of their antioxidant activity. In the radical scavenging mechanisms, a reactive radical accepts a hydrogen atom from a hydroxyl group of an antioxidant and thus becomes inactivated. There are three major mechanisms through which phenolic compounds, in this particular case depsides (DOH), scavenge free radicals: hydrogen atom transfer (HAT, Eq. (1)), single electron transfer followed by proton transfer (SET-PT, Eq. (2)), and sequential proton loss electron transfer (SPLET, Eqs. (3a)–(3c)) (Wright et al., 2001; Klein & Lukeš, 2006; Litwinienko & Ingold, 2007).



In the HAT mechanism, homolytic cleavage of the O—H bond occurs, i.e. hydrogen atom is rapidly transferred from depside to a radical. A significant feature of the HAT mechanism is that the proton and electron are transferred together. It is worth pointing out that some important biochemical processes occur via the proton coupled electron transfer mechanism (PCET). The coupling of proton and electron provides reaction paths where these species are transferred simultaneously in the same direction (Bors et al., 1990; Rice-Evans & Miller, 1996; Cao et al., 1997; Huynh & Meyer, 2007; Meyer et al., 2007).

In the SET-PT mechanism, a depside is transformed into the radical cation by donating an electron to the free radical present in the system (e.g. lipid). This mechanism leads to indirect H-abstraction. The SPLET mechanism takes place once the depside anion, DO^- , is formed (Eqs. (3a)–(3c)). Further electron transfer from the depside anion to a radical leads to the formation of the depside radical, DO^\bullet , and the corresponding anion R^- , which is then protonated.

In all three mechanisms, the formed DO^\bullet radical has to be relatively stable, providing that the reactions shown in Eqs. (1)–(3) are thermodynamically favorable, i.e. that it is easier to abstract a hydrogen atom from DOH than from RH. This implies that the reaction of an antioxidant molecule with the radical has to be faster than that of the radical with the substrate. In this way, toxic effects of radicals (such as the oxidative stress) are prevented or postponed. In addition, both the antioxidant molecule and the corresponding products need to be non-toxic and should not induce pro-oxidant effects (Hertog & Hollman, 1996).

These mechanisms, which all have the same net result, are governed by different thermodynamic properties: bond dissociation enthalpy (BDE) of erodiol in the HAT mechanism, proton affinity (PA) of erodiol together with the electron transfer energy (ETE) of the erodiol anion in the SPLET mechanism, and ionization potential (IP) of erodiol and proton dissociation enthalpy (PDE) of the erodiol radical cation in the SET-PT mechanism. This paper uses these thermodynamic properties in the assessment of possible radical scavenging potential of erodiol.

Theoretical

It is well-known that polyphenols can dissociate in basic media. Previous investigations of the antioxidant activity of morin (Marković et al., 2012a) and the morin anion (Marković et al., 2012b) showed that both species exhibit similar behavior, except for the PA value which is significantly higher in case of the anion. Taking this fact into account, we focused our attention on the undissociated form of the compound.

Density functional theory calculations were carried out with the Gaussian 09 program package (Frisch et al., 2009). The minima were fully optimized using the hybrid meta exchange-correlation M05-2X functional (Zhao et al., 2006) and 6-311+G(d,p) basis set (McLean & Chandler, 1980; Raghavachari et al., 1980). All radicals were evaluated using an unrestricted scheme in order to take spin polarization into account, which is required in such DFT calculations.

To determine the nature of the stationary points, and the zero point energies (ZPE) and thermal corrections to enthalpies at 298.15 K, harmonic frequencies were calculated using the rigid rotor harmonic oscillator approximation (McQuarrie, 2000). The obtained zero imaginary frequencies confirmed that all stationary points correspond to the equilibrium geometries. The M05-2X/6-311+G(d,p) thermal corrections to the enthalpy were scaled using the recommended scaling factor of 0.9467 (Merrick et al., 2007). The spin and charge densities were estimated using the natural bond orbital (NBO) analysis (Glendening et al., 2001; Weinhold & Landis, 2005).

To calculate the thermodynamic properties in solvent environment (water), the Solvation Model Density (SMD) (Marenich et al., 2009), as implemented in Gaussian 09, was used in combination with the DFT calculation at the M05-2X/6-311+G(d,p) level of theory.

The bond dissociation enthalpy (BDE) was calculated using the following equation:

$$\text{BDE} = H_{\text{EO}^\bullet} + H_{\text{H}} - H_{\text{EOH}} \quad (4)$$

where H_{EOH} , H_{EO^\bullet} , and H_{H} represent the enthalpies of erodiol, erodiol radical, and hydrogen atom, respectively.

Table 1. Relative energies (kJ mol^{-1}) for isolated and solvated (SMD) erodiol rotamers. ΔE , ΔH , and ΔG denote differences in the total energy, enthalpy, and free energy, with respect to the most stable conformer, whereas ΔE_{solv} and ΔG_{solv} stand for the solvation total energy and the solvation free energy

Rotamer	ΔE	ΔH	ΔG	ΔE^{SMD}	ΔH^{SMD}	ΔG^{SMD}	ΔE_{solv}	ΔG_{solv}
E	0	0	0	0	0	0	-82.84	-83.09
Ea	17.36	17.36	17.49	2.51	2.09	2.93	-97.65	-97.65
Eb	20.13	20.42	19.71	2.72	2.55	2.80	-100.21	-100.00
Ec	21.55	21.97	21.05	2.72	2.93	2.30	-101.63	-101.80
Ed	38.33	38.66	37.95	5.73	5.36	6.02	-115.39	-115.02
Ee	40.29	40.96	39.50	5.86	5.73	5.90	-117.28	-116.69

The ionization potential (IP) and proton dissociation enthalpy (PDE) were calculated using the following equations:

$$\text{IP} = H_{\text{EOH}^{\bullet+}} + H_{e^-} - H_{\text{EOH}} \quad (5)$$

$$\text{PDE} = H_{\text{EO}^{\bullet}} + H_{\text{H}^+} - H_{\text{EOH}^{\bullet+}} \quad (6)$$

where $H_{\text{EOH}^{\bullet+}}$ represent the enthalpy of the erodiol radical cation, H_{H^+} is the enthalpy of the proton, and $\text{PDE} = H_{\text{EO}^{\bullet}} + H_{\text{H}^+} - H_{\text{EOH}^{\bullet+}} + H_{e^-}$ is the enthalpy of the electron.

The proton affinity (PA) and electron transfer enthalpy (ETE) were defined as:

$$\text{PA} = H_{\text{EO}^-} + H_{\text{H}^+} - H_{\text{EOH}} \quad (7)$$

$$\text{ETE} = H_{\text{EOH}^{\bullet}} + H_{e^-} - H_{\text{EOH}^-} \quad (8)$$

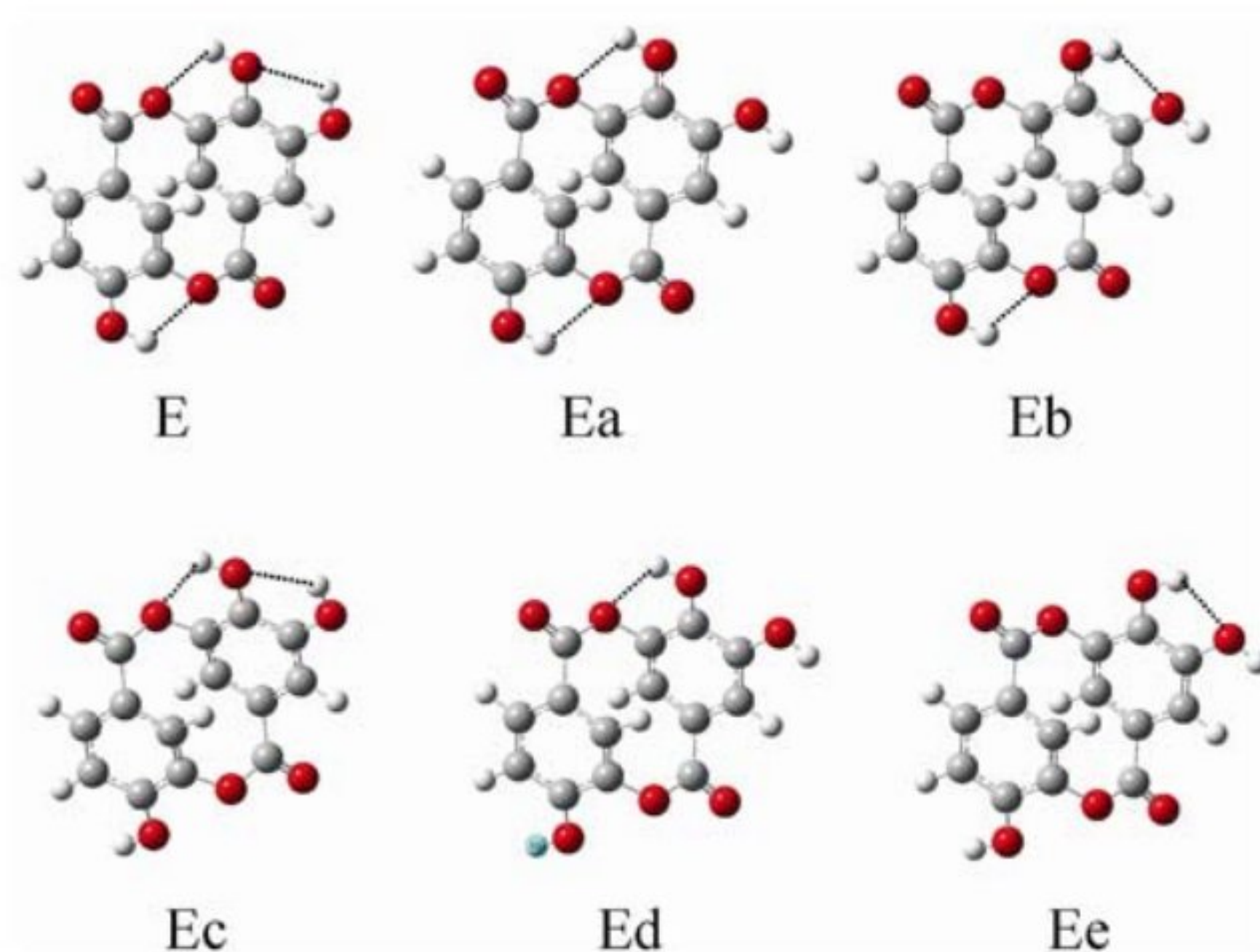
where H_{EO^-} is the enthalpy of the erodiol anion.

All reaction enthalpies defined in Eqs. (4)–(8) were calculated at 298 K. The recommended values for the enthalpy of the proton ($6.197 \text{ kJ mol}^{-1}$ in gas and $-1090 \text{ kJ mol}^{-1}$ in water), and the electron ($3.145 \text{ kJ mol}^{-1}$ in gas and -236 kJ mol^{-1} in water) were used (Bartmess, 1994; Klein et al., 2007; Rimarčik et al., 2010).

Results and discussion

Conformation of a molecule plays a crucial role in the evaluation of the radical scavenging activity of polyphenolic compounds; erodiol in this case. This consideration is based on the fact that the behavior of phenol groups is strongly influenced by electronic effects of the adjacent functional groups and the overall geometry of the molecule.

A detailed conformational analysis of erodiol in the gas phase was performed by combining synperiplanar and antiperiplanar orientations of hydrogen atoms for dihedral angles ω_1 (C3–C4–O4–H4), ω_2 (C4–C5–O5–H5), and ω_3 (C10–C11–O11–H11). Six different conformations of erodiol were revealed (Fig. 2). Analysis of the energies of erodiol conformers (Table 1) showed that E is the most stable rotamer.

**Fig. 2.** Conformations of the erodiol molecule, E is the most stable, Ea–Ee are less stable rotamers.

In the most stable structure of erodiol (E in Fig. 2) there are three internal hydrogen bonds (IHBs): O4–H4···O2 (2.227 Å), O5–H5···O4 (2.194 Å), and O11–H11···O9 (2.177 Å). All IHBs have a stabilizing effect on the molecule structure, especially those between H4 and O2, and those between H11 and O9. Conformations that lack these IHBs (rotamers Ea–Ee in Fig. 2) are less stable with respect to the absolute minimum (Table 1). On basis of the values in Table 1 it is clear that IHBs between hydrogens from phenolic groups and oxygens from ester groups have stronger stabilizing effect than between two phenolic groups. The NBO analysis of E revealed that the lone pair–antibonding orbital interactions between the ester oxygens and the adjacent O–H bonds are responsible for the IHBs formation. Namely, it was found that the charge transfer from the lone pair on O9 (2p orbital) to the σ^* antibonding O11–H11 orbital is a favorable donor–acceptor interaction. There is a similar charge transfer from the 2p orbital on O2 to the σ^* antibonding O4–H4 orbital. Negligible charge transfer was observed from the 1p orbital on O4 to the σ^* antibonding O5–H5 orbital. These findings are in accordance with the IHB lengths (see Table S1 in Supplementary data).

All six gas-phase minima were examined by simulating aqueous solution with the SMD model. The

Table 2. Relative energies (kJ mol^{-1}) for erodiol radicals rotamers in the gas and aqueous (SMD) phases. ΔE and ΔH denote differences in the total energy and enthalpy with respect to the most stable rotamer, ΔE_{solv} and ΔG_{solv} stand for the solvation total energy and the solvation free energy, whereas BDE and PDE denote the bond dissociation enthalpy and the proton dissociation enthalpy

Rotamer	ΔE	ΔH	ΔE^{SMD}	ΔH^{SMD}	ΔE_{solv}	ΔG_{solv}	BDE	BDE^{SMD}	PDE	PDE^{SMD}
O4R1	0.33	0.38	0.92	0.79	-88.45	-87.36	352.42	342.25	931.78	49.87
O4R2	19.20	19.50	3.01	2.97	-105.23	-104.01	371.54	344.43	950.90	52.05
O4R3	35.61	36.23	8.33	8.37	-116.32	-114.93	388.28	349.82	967.63	57.45
O4R4	52.63	53.56	10.50	10.63	-131.17	-129.49	405.60	352.04	984.96	59.71
O5R1	14.43	14.60	4.60	4.69	-98.87	-98.53	366.60	346.10	946.00	53.76
O5R2	34.98	35.40	7.36	7.49	-116.61	-115.94	387.44	348.90	966.80	56.57
O5R3	0.00	0.00	0.00	0.00	-89.04	-88.66	352.04	341.41	931.40	49.08
O5R4	19.62	19.92	2.89	2.85	-105.77	-104.93	371.96	344.30	951.32	51.92
O11R1	34.10	35.10	26.90	28.03	-96.23	-95.98	387.10	369.49	966.50	77.11
O11R2	50.29	51.38	29.79	30.42	-109.50	-108.37	403.38	371.83	982.74	79.50
O11R3	50.04	51.25	29.00	30.04	-110.08	-109.29	403.30	371.46	982.65	79.12

Table 3. Relative energies (kJ mol^{-1}) for erodiol anions rotamers in the gas and aqueous (SMD) phases. ΔE and ΔH denote differences in the total energy and enthalpy with respect to the most stable rotamer, ΔE_{solv} and ΔG_{solv} stand for the solvation total energy and the solvation free energy, whereas PA denotes the proton affinity

Rotamer	ΔE	ΔH	ΔE^{SMD}	ΔH^{SMD}	ΔE_{solv}	ΔG_{solv}	PA	PA^{SMD}
O4A1	0.00	0.00	0.00	0.00	-241.63	-242.50	1329.55	80.21
O4A2	31.17	31.76	3.51	3.56	-269.83	-269.32	1361.26	83.76
O4A3	48.41	49.50	11.51	11.63	-279.49	-278.11	1379.05	91.84
O4A4	80.08	81.63	14.77	14.98	-308.32	-306.06	1411.14	95.14
O5A1	40.67	41.38	20.29	20.63	-262.38	-262.88	1370.93	100.83
O5A2	71.92	73.18	23.47	23.93	-290.91	-290.62	1402.73	104.10
O5A3	6.5	6.65	10.9	11.05	-237.27	-238.49	1336.20	91.21
O5A4	36.99	37.70	14.35	14.52	-264.81	-264.76	1367.21	94.73
O11A1	27.5	28.62	11.8	12.34	-257.90	-257.69	1358.13	92.55
O11A2	44.64	45.73	14.27	14.56	-272.80	-272.13	1375.24	94.77
O11A3	58.03	59.37	15.02	15.52	-285.47	-284.76	1388.88	95.73

lowest energy was found for rotamer E. The order of energies of the remaining five rotamers (Ea–Ee) was found to be the same as in the gas phase (Table 1). The relative energies are decreased by SMD with regard to the gas phase, which is the usual consequence of the interactions of every phenolic and ester group with the solvent. Three IHBs present at the gas-phase minimum are shorter by about 0.03 Å than the corresponding bonds in solution (Table S1).

Since structure E is the most stable conformation of erodiol in both phases, the further discussion will be addressed to this rotamer which will be called erodiol.

Homolytic and heterolytic O—H bond cleavage in erodiol

Reasoning based on the energies of homolytic and heterolytic O—H bond cleavage can point to the possible antioxidant mechanisms of erodiol. The obtained O—H bond cleavage energies are presented as the BDE and PA values in Tables 2 and 3.

Homolytic O—H bond cleavage in erodiol can provide three different radicals: O4R, O5R, and O11R. Each radical can adopt several conformations (4, 4,

and 3, respectively). In case of O4R, these rotamers are: O4R1, O4R2, O4R3, and O4R4. Similar notation is used for the other two radicals. In Fig. 3, each radical is presented by its most stable rotamer form, whereas all possible rotamers are depicted in Fig. S1. The order of stability for the radical species obtained from erodiol in the gas phase is (decreasing to the left): O5R, O4R, O11R; which implies that homolytic cleavage of the 5-OH bond is slightly favored. The most stable radical, O5R3, is stabilized by two IHBs (O4—H···O5 and O11—H···O9). As for O4R and O11R radicals, the most stable rotamers are O4R1 and O11R1, whose energies are by 0.33 kJ mol^{-1} and 34.10 kJ mol^{-1} higher than that of O5R3 (Table 2). It is obvious that the probability of O4 and O5 radicals formation is equal, whereas the formation of O11 radical is very unlikely. For this reason, the O11 radical was excluded from further discussion.

The order of stability for the radical forms computed in the aqueous phase is basically the same as that in the gas phase (Table 2). The ΔE_{solv} and ΔG_{solv} values show that all radicals are more stable in a solution. This stabilization is more pronounced in cases of radicals with fewer IHBs, as hydrogen bonds

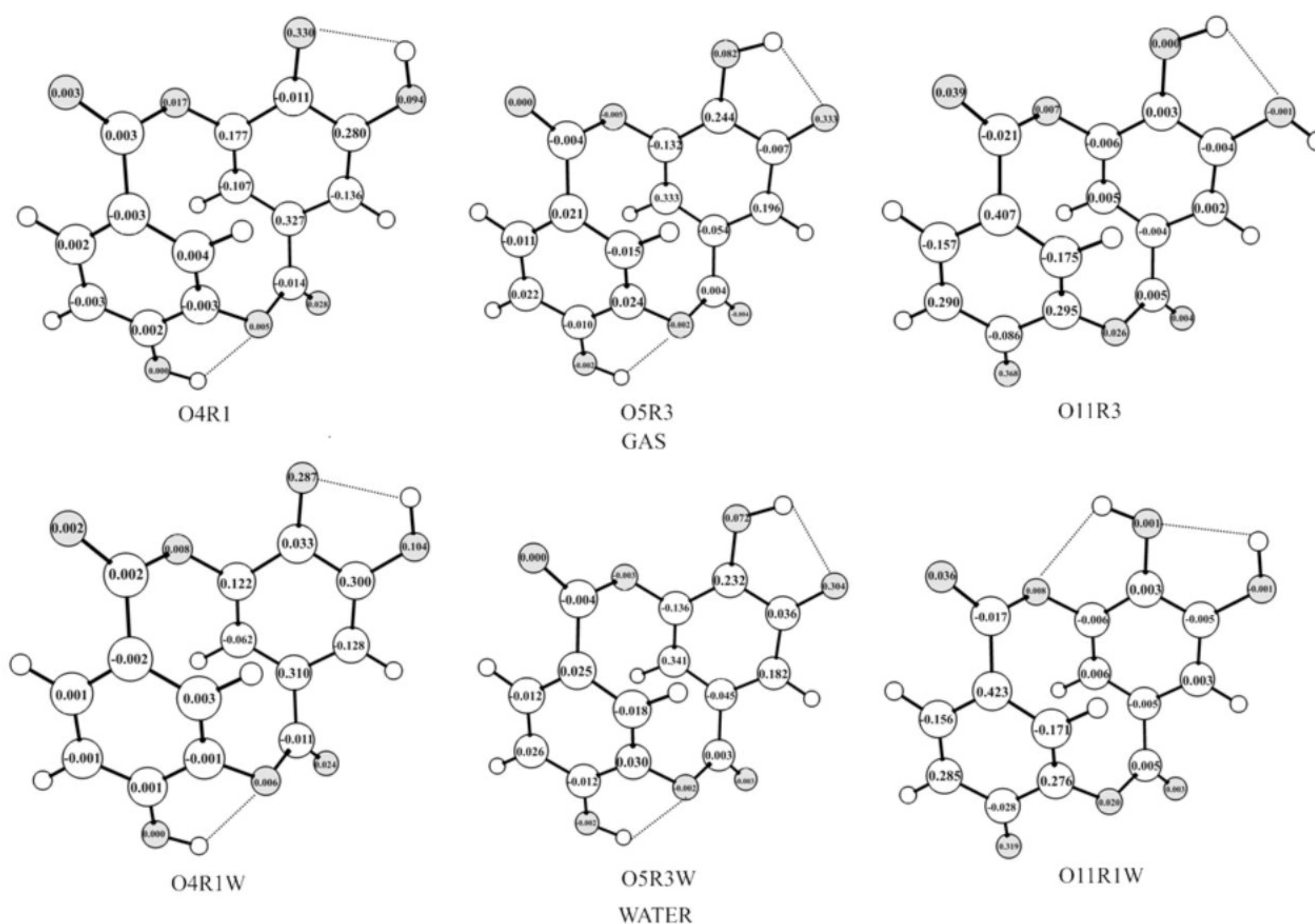


Fig. 3. Optimized structures of the erodiol radicals. Numbers represent the spin density values.

with water molecules compensate for the lack of IHBs.

As already emphasized (Leopoldini et al., 2004a, 2004b; Trouillas et al., 2006; Marković & Manojlović, 2010), spin density can be used to determine the potential for delocalization and, thus, the stability of polyphenol radicals. The spin distribution obtained by the NBO analysis of the O5R3 and O4R1 radicals in both media revealed that the unpaired electron is delocalized over O5 (O4) and it corresponds to *ortho* and *para* carbon atoms.

Heterolytic cleavage of the O—H bonds of erodiol leads to the formation of three anions: O4A, O5A, and O11A. Each of these anions is able to adopt several conformers. The eleven anionic rotamers are denoted in a similar way as the radical rotamers: R (radical) is replaced by A (anion). In Fig. 4, each anion is presented by its most stable rotamer, whereas all possible rotamers are depicted in Fig. S2.

The order of stability for the anionic species in the gas and aqueous phases is (decreasing to the left): O4, O5, O11 (Table 3); which implies that the heterolytic cleavage of the 4-OH bond is favored. Obviously, the stability sequence for the anion species is somewhat different from that calculated for the species formed by the homolytic cleavage of O—H bonds. In addition to hydrogen bonding, ion–dipole interactions play a significant role in case of ionic species dissolved in water. As a consequence of the interactions of the anionic

and hydroxyl groups of erodiol anions with water, the ΔE_{solv} and ΔG_{solv} (Table 3) are significantly lower in comparison to those obtained for the radical species (Table 2).

The most stable anion, O4A1, is stabilized by two IHBs (O5—H···O4 and O11—H···O9). The enthalpies of O5A3 and O11A1 are by 6.5 kJ mol⁻¹ and 27.5 kJ mol⁻¹ higher than that of O4R1 in the gas phase, and by 10.9 kJ mol⁻¹ and 11.8 kJ mol⁻¹ higher in the aqueous phase (Table 3). For this reason, O5 and O11 anions were excluded from further discussion. Distribution of the natural charge indicates that O4 bears the highest negative charge (−0.76 in the gas phase, and −0.89 in water). In comparison to neutral erodiol, the negative charge is increased on the anionic oxygen O4 and on carbon C7 (Fig. 4).

Bond dissociation enthalpy, ionization potential, and proton affinity of erodiol

BDE, IP, and PA values of erodiol (Table 4) are discussed here. These values play an important role in the study of the antioxidant mechanisms of erodiol. The BDE value for each OH group corresponds to the most stable radical rotamer and they are similar to, or lower than those of hydroxybenzoic acid (256.5–374.9 kJ mol⁻¹), cinnamic acid (350.2–441.8 kJ mol⁻¹) (Leopoldini et al., 2004c; Mandado et

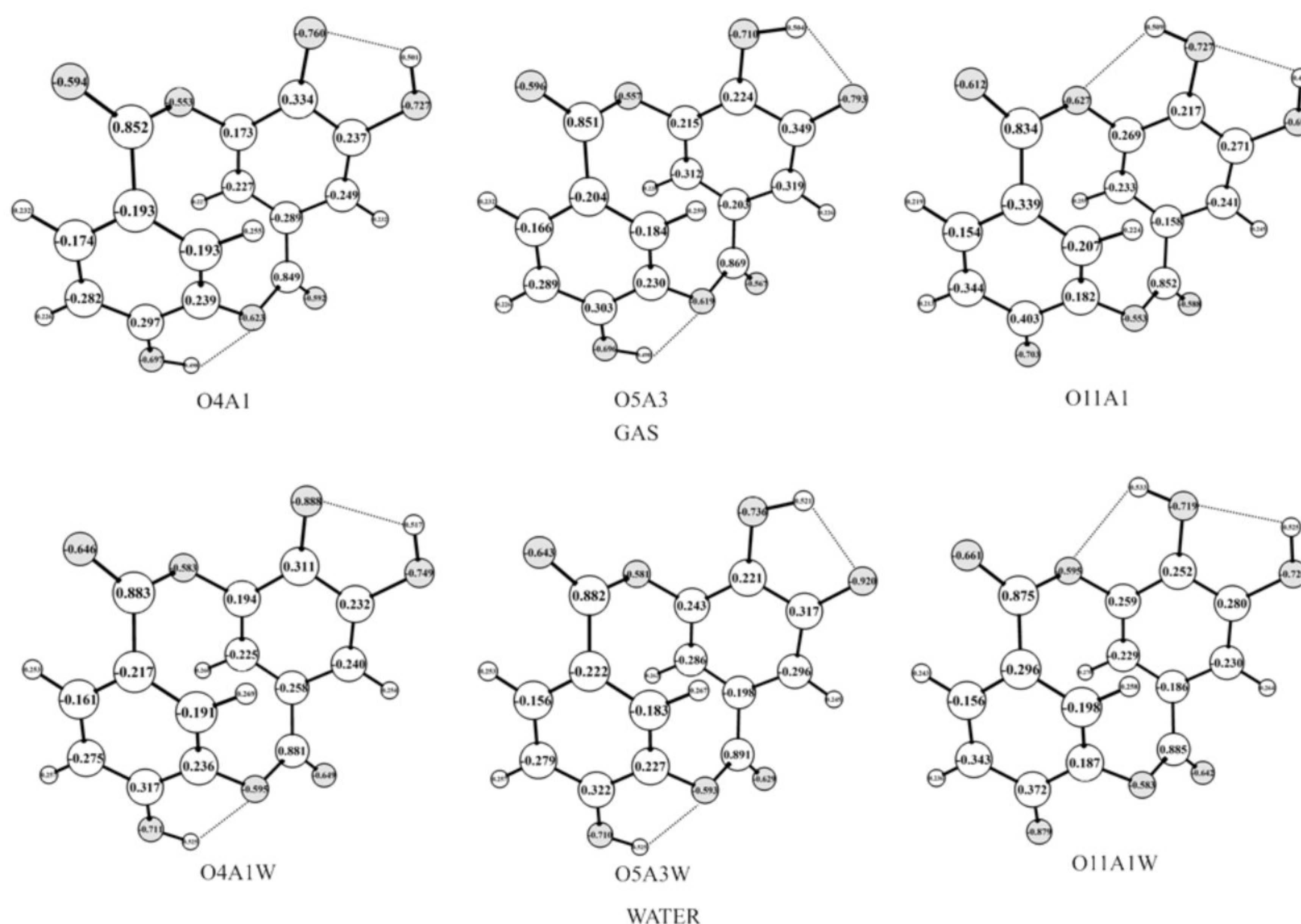


Fig. 4. Optimized structures of the erodiol anions. Values of corresponding charges are represented by numbers.

Table 4. Calculated parameters for free radical scavenging activity of erodiol and phenol (in kJ mol^{-1})

Position	Gas phase					Water solution				
	HAT	SET-PT		SPLET		HAT	SET-PT		SPLET	
	BDE	IP	PDE	PA	ETE	BDE	IP	PDE	PA	ETE
Erodiol		742.5					292.2			
4-OH	352.4		931.8	1329.5	344.7	342.3		49.9	80.2	261.9
5-OH	351.9		931.4	1336.2	337.6	341.4		49.1	91.2	250.0
11-OH	403.3		982.7	1358.1	367.0	369.5		77.1	92.6	276.8
Phenol	360.3	822.0	860.1	1456.0	226.2	85.54	362.1	-4.4	125.1	232.7

al., 2004), or phenol (346.0–366.5 kJ mol^{-1}) (Wayner et al., 1996; de Heer et al., 1999; Moa et al., 2006). It should be emphasized that these BDE values were mostly obtained using the B3LYP functional with different basis sets. Table 4 shows that the BDE values for 4-OH and 5-OH groups are very similar, and significantly lower than that for 11-OH. Therefore, it can be supposed that 5-OH and 4-OH groups undergo the HAT mechanism with almost the same probability.

The order of the BDE values calculated for the aqueous phase is the same as that for the gas phase. As a consequence of the interactions of the radicals with the solvent molecules, these BDE values are reduced by at least 10 kJ mol^{-1} in com-

parison to those obtained for the gas phase.

The IP value of erodiol obtained from SMD calculations is significantly lower than that calculated for the gas phase (Table 4). This is due to the stabilization of charged systems in polar solvents. The calculated IP value of erodiol in gas is somewhat higher than those of common synthetic food additives, such as propyl gallate, dihydroguaiaretic acid, and butylated hydroxyanisole (702.1 kJ mol^{-1} , 672.0 kJ mol^{-1} , and 638.9 kJ mol^{-1} , respectively) (Mandado et al., 2004), or of the powerful antioxidant epigallocatechin-3-gallate (618.0 kJ mol^{-1}) which is a constituent of green tea (Rice-Evans et al., 1996; Mandado et al., 2004).

The PA value for each OH group of erodiol corresponds to the most stable anion rotamer. The PA values calculated for the gas phase are higher by about 300 kJ mol⁻¹ than those computed for the water solution, which is a consequence of the interactions of the anionic and hydroxyl groups with the solvent molecules. Tables 3 and 4 show the sequence of the calculated PA values for both gas and aqueous phases (increasing to the left): O4, O5, O11; which indicates that the proton transfer from the 4-OH group is easier than that from the 5-OH and 11-OH groups.

Antioxidant mechanisms of erodiol

Δ IP and Δ BDE values of a certain phenolic compound can be used to determine the main mechanism governing its antioxidant activity. These values were calculated as the difference between the BDE and IP values of a phenolic compound (erodiol in this case) and phenol as a reference compound (Wright et al., 2001). The IP, O-H BDE, and O-H PDE values for phenol computed at the M05-2X/6-311+G(d,p) level of theory for gas and aqueous phases are presented in Table 4. According to the Wright's rules (Wright et al., 2001), for Δ IP \geq -151 kJ mol⁻¹ and Δ BDE of around -188 kJ mol⁻¹, HAT is considered to be the dominant mechanism, whereas for Δ IP < -188 kJ mol⁻¹, the predominant mechanism is SET-PT.

The results for the gas phase, i.e. the Δ IP and Δ BDE values of about -80 kJ mol⁻¹ and -8 kJ mol⁻¹ (Tables 4 and S3), indicate that HAT is a potential antioxidant mechanism for erodiol in gas or nonpolar solvents. The SET-PT and SPLET mechanisms, employed by several authors (Wright et al., 2001; Foti et al., 2004; Musialik & Litwinienko, 2005; Litwinienko & Ingold, 2007; Rimarčík et al., 2010), cannot be discarded as possible mechanisms of erodiol behavior in water due to the relatively low IP and PA values.

Further inspection of the data in Table 4 revealed that the IP, PDE, and PA values are significantly lower in water than in the gas phase. Obviously, this is a consequence of the stabilization of charged species in polar solvents. On the other hand, there is no such pronounced difference between the BDE values in the studied environments. On basis of these facts, it can be concluded that the HAT mechanism is dominant in the gas phase, as the BDE values of all OH groups of erodiol are significantly lower than their corresponding IP and PA values. On the other hand, both SET-PT and SPLET mechanisms are probable reaction pathways in water, since the IP and PA values are lower than the corresponding BDE ones.

In both studied media, the most abstractable hydrogen atoms of the erodiol molecule are those from 5-OH and 4-OH groups. It is reasonable to expect that the HAT and SET-PT mechanisms proceed in these groups and result in the formation of the 5-O[•] and 4-O[•] phenoxyl radicals. The SPLET mechanism starts

with the deprotonation of the 4-OH group, due to its lowest PA value and it results in the formation of the 4-O[•] phenoxyl radical.

Conclusions

In this paper, the HAT, SPLET, and SET-PT mechanisms of erodiol behavior were investigated on the basis of the corresponding thermodynamic properties. Positions 5-OH and 4-OH are the most favored sites for homolytic and heterolytic O—H cleavage in the gas and aqueous phases. The 11-OH site does not occur in the antioxidant mechanisms of erodiol due to the fact that the hydrogen atom of the 11-OH group forms a strong hydrogen bond with the O9 atom in the parent molecule. Our results indicate that one-step HAT is the mechanism that best explains the radical-scavenging activity of erodiol in the gas phase. On the other hand, the SET-PT and SPLET mechanisms represent thermodynamically preferred reaction paths in water due to the stabilization of the charged species in aqueous solutions.

It is worth emphasizing that the findings of this work are in accordance with the experimental results (Cai et al., 2006) on the free radical scavenging ability of phenolic compounds, as well as with the DFT predictions based on the thermodynamic quantities (Leopoldini et al., 2004b; Klein & Lukeš, 2006; Marković et al., 2009; Marković & Manojlović, 2010; Rimarčík et al., 2010). When comparing the BDE and the IP values of erodiol in gas/water with those of some other phenolic compounds (epicatechin: BDE = 308.4/325.1, IP = 714.6 kJ mol⁻¹/541.0 kJ mol⁻¹; gallic acid: BDE = 302.1/344.3, IP = 791.2 kJ mol⁻¹/580.3 kJ mol⁻¹; cyanidin: BDE = 332.2/376.6, IP = 1030.1 kJ mol⁻¹/583.7 kJ mol⁻¹; kaempferol: BDE = 338.5/364.0, IP = 702.9 kJ mol⁻¹/551.9 kJ mol⁻¹, Leopoldini et al., 2004b), it can be concluded that erodiol is a moderately strong antioxidant.

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Supplementary data

Supplementary data associated with this article can be found in the online version of this paper (DOI: 10.2478/s11696-013-0402-0).

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