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Insights in the radical scavenging mechanism of syringaldehyde and generation of its anion

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ABSTRACT

The ability of syringaldehyde, a naturally occurring phenolic antioxidant and medicinally important compound, to scavenge free radicals according different mechanisms was elucidated by computing the respective reaction enthalpies at DFT B3LYP/6-311++G** level. Bond dissociation enthalpy, ionization potentials and proton affinities were calculated in gas phase, benzene, water and DMSO in order to account for different environment (nonpolar lipid membranes and polar physiological liquids) where the antioxidant action in the living organism could take place and various experimental *in vitro* conditions. Molecular and electronic properties influencing the reactivity of syringaldehyde according to the different mechanisms were discussed in the light of the reported radical scavenging activities in crocin bleaching, oxidation potential of the first anodic peak and DPPH test. According to the calculated reaction enthalpies, in polar environment the syringaldehyde reacts preferably by sequential proton loss electron transfer which is related to the formation of a phenoxy anion. Such phenoxy anion was generated in DMSO solution and the changes in the force field, steric and electronic structure, resulting from the conversion, were described in detail based on the IR spectral data and DFT computations.

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1. Introduction

Syringaldehyde (4-hydroxy-3,5-dimethoxybenzaldehyde) is a phenolic aldehyde found in fruits [1–3], nuts [4] and plants that synthesize lignin-related compounds [5–9]. It is released as aroma and taste compound in liquors as a result of the lignin hydrolysis while the alcohol ages in wooden barrels [10,11]. Pyrolysis of lignin during food smoking also produces syringaldehyde together with a number of other syringol derivatives, which contribute not only to the smoke aroma [12–14], but also provide antimicrobial and antioxidant effects in the smoked foods [14–17]. Antimicrobial, antifungal and antiparasite properties of syringaldehyde have been studied in a number of publications [8 and references therein]. The antioxidant capacity of syringaldehyde has been evaluated in relation to the oxidative stability of smoked foods and alcoholic beverages by various *in vitro* assays: bleaching of carotenoid crocin [18,19], scavenging of DPPH and ABTS radicas [7,18,19], determination of the oxidation potential [18], Rancimat [19] and liposomes assays [19].

In the human organism, reactive oxygen species (ROS) and oxidative stress are associated to inflammation, aging, cancer, heart disease and other disorders [20]. By interfering with ROS production or scavenging, the antioxidants may protect against oxidative tissue damage in vital organs. In order to estimate the antioxidant effect of syringaldehyde in living cells, its ability to scavenge superoxide anion in a cell-free hypoxanthine/xanthine-oxidase system and to inhibit the ROS production by human neutrophils, induced by opsonized zymosan- or phorbol 12-myristate 13-acetate was studied [21]. The compound was not able to scavenge the superoxide anion, while significantly inhibited the ROS production by activated human neutrophils [21]. Comparison to the inhibitory effects shown by vanillin, vanillic acid and acetovanillone, lacking a second methyl group in vicinity to the phenolic function, indicated that C-5 methoxylation leads to enhancement of the ROS inhibitory activity. The antioxidant activity of syringaldehyde was further tested in HL-60 cells by 2′,7′-dichlorodihydrofluorescein diacetate method, but in contrast to the above, no activity was detected [22]. The production of prostagladines is another factor that plays a major role in the inflammation processes. It is regulated by the enzyme cyclooxigenase (COX-2) and for this reason, inhibitors of COX-2 are used in the treatment of

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inflammatory disorders and cancer [23,24]. Cell-based assay that utilizes the mouse macrophage cell line (RAW 264.7) shows that syringaldehyde possesses moderate inhibitory activity towards COX-2 [22]. Syringaldehyde is able to inhibited prostaglandin synthetase in a dose-dependent way, exerting half of the potency of aspirin [25]. Recently the neuroprotective effect of syrinaldehyde on cerebral ischemia injury in rats was reported [26]. It was demonstrated that the anti-oxidative and anti-apoptic properties of the compound makes it very effective in the prevention of ischemic damage to the brain [26]. Other medicinally significant property of syringaldehyde is its ability to lower plasma glucose in streptozotocin-induced diabetic rats [9]. All these reports convincingly outline the syringaldehyde as naturally-occurring anti-oxidant and medicinally important compound as well as good lead in the development of more effective anti-inflammatory and anti-diabetic agents. As a result of its suitable molecular structure and characteristics is was already used as building block in new larger antioxidant dendrimer molecules [27] and alkaloids [28]. Such modification has lead to dramatic increase of the anti-oxidant capacity of the new derivatives [27]. Having in mind, these promising features of syringaldehyde and the various, even contradicting, data on its antioxidant activity, it is worthy to throw more light on the possible mechanisms of its antioxidant action, molecular and electronic parameters that might influence its ability to scavenge free radical through to the different mechanisms and interact with enzymes involved in the redox processes in the organisms. The formation of other active forms such as phenoxy anion is essentially related to the concerned mechanisms hence the characterization of the anion species will provide helpful information. Thus the aim of the present study is to determine the preferred mechanism of antioxidant action in nonpolar and polar environment, describe the molecular geometry and electronic structure of the syringaldehyde and convert it into phenoxy in order to follow the spectral, structural, and electronic changes resulting from the conversion. For this purpose we will relay on experimental IR methods and DFT computations.

2. Materials and methods

2.1. Materials

Syringaldehyde (4-hydroxy-3,5-dimethoxybenzaldehyde, 99% putiry) was purchased from Sigma–Aldrich Co and applied without further purification. CD_3OD (99% at. Enrichment) was purchased from Merck and used to obtain CD_3ONa by reacting it with Na. Spectral quality $CDCl_3$ and DMSO-d_6 were purchased from Sigma–Aldrich Co.

2.2. Conversion of syringaldehyde into anion and IR spectra measurements

The corresponding anion was obtained by adding 0.12 mol l^{-1} DMSO-d_6 solution of the parent aldehyde to excess of dry CD_3ONa. The reaction mixture was filtered to remove the remains of solid CD_3ONa and put immediately into a spectroscopic cell to record the IR spectra. The conversion was practically complete (no bands of the parent aldehyde were seen in the spectrum after metalation). The IR spectra were recorded on a Brucker Tensor 27 FT spectrometer at a resolution of 2 cm^{-1} and 64 scans. The following sample cells were used: 0.6 mm NaCl for $CDCl_3$ and 0.129 mm CaF_2 for DMSO-d_6 solutions.

2.3. DFT computations

All theoretical calculations were performed using the Gaussian 09 package [28] of programs. Geometry and vibrational frequencies of species studied were performed by analytical gradient technique without any symmetry constraint. All the results were obtained using the density functional theory (DFT), employing the B3LYP (Becke's three-parameter non-local exchange [Becke's three-parameter non-local exchange [29] and and Lee et al. correlation [30] potentials). To establish the stability order for the neutral, radical and ionic species in solvent we used the Integral Equation Formalism Polarizable Continuum Model (IEF-PCM) [31] on the same level of theory.

In order to find the preferred geometry of the molecule of syringaldehyde, its anion, radical and radical cation, a large number of probable conformers were constructed, taking into account planar and non planar geometries with different mutual orientation of the aldehyde function, methoxy and hydroxy groups. The geometries of all constructed conformers were optimized by application of the UB3LYP functional in conjunction with the 6-311++G** basis set. For every structure, the stationary points found on the molecular potential energy hypersurfaces were characterized using standard analytical harmonic vibrational analysis. The absence of imaginary frequencies, as well as of negative eigenvalues of the second-derivative matrix, confirmed that the stationary points correspond to minima on the potential energy hypersurface. It was found that in all stable conformers the aldehyde group adopts planar conformation, while the hydroxy and methoxy groups have different possible planar and nonplanar orientations. The UB3LYP/6-311++G** optimized geometries of the conformers of syringaldehyde molecule (M1-M4), its anion (A1-A4), radical (R1-R4) and radical cation (RC1-RC4) and their relative stability are depicted in Scheme 1.

Dissociation enthalpy (BDE), ionization potential (IP), proton dissociation enthalpy (PDE), proton affinity (PA), and electron transfer enthalpy (ETE) of the most stable conformers were calculated according the equations given by Klein et al. [32].

$$BDE = H(A^{\cdot}) + H((H^{\cdot}) - H(A{-}H)$$

$$IP = H\left(A^{+\cdot}\right) + H(e^{-}) - H(A{-}H)$$

$$PDE = H(A^{\cdot}) + H\left(H^{+}\right) - H\left(A^{+\cdot}\right)$$

$$PA = H(A^{\cdot}) + H(\left(H^{+}\right) - H(A{-}H)$$

$$ETE = H(A^{\cdot}) + H\left(e^{-}\right) - H\left(A^{-}\right)$$

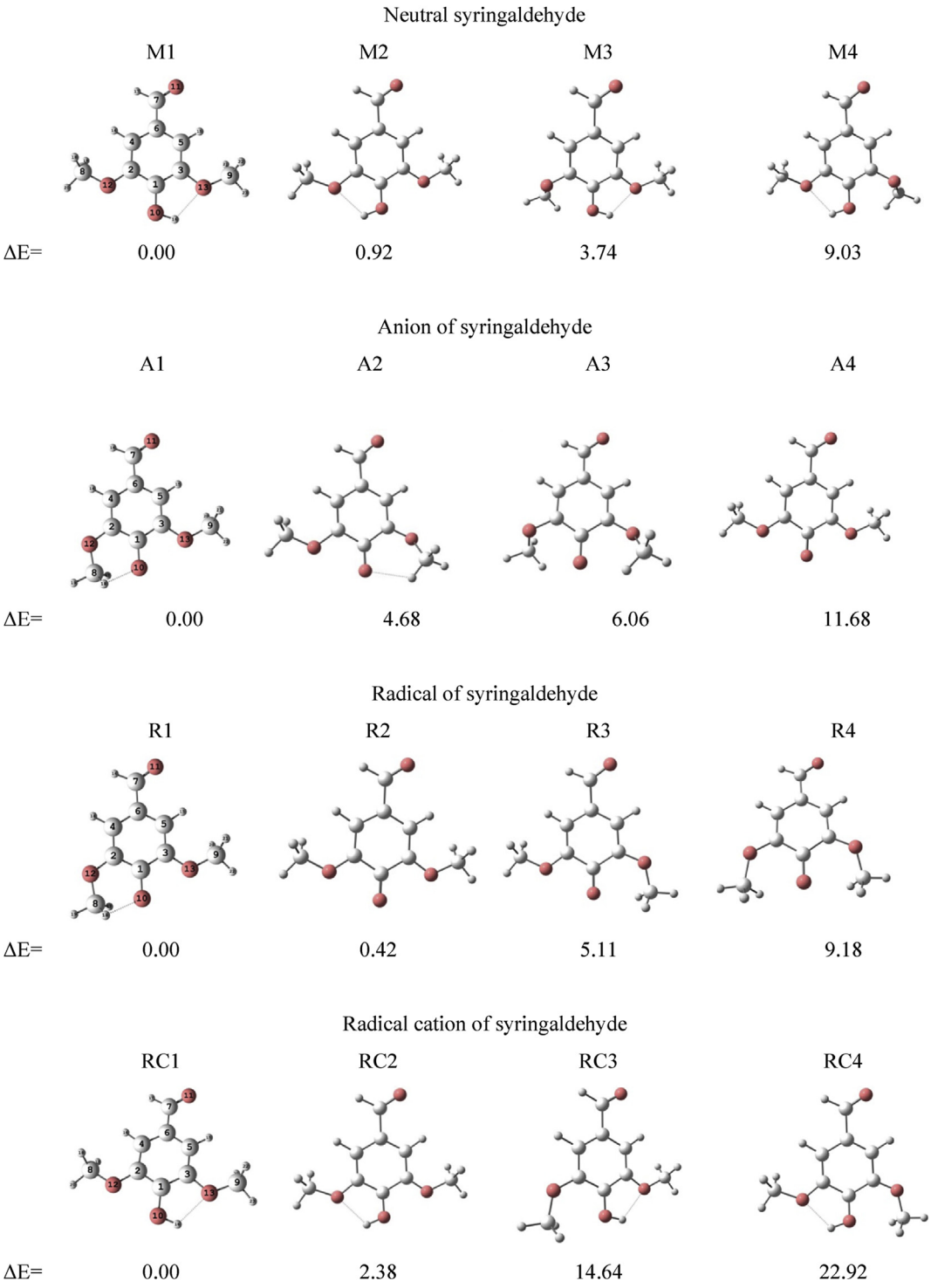
The enthalpy of hydrogen atom, *H*(H), for each solvent were obtained by the same method and basis set. All reaction enthalpies were calculated for 298 K. Solvation enthalpies of proton $H(H^{+})$ and electron $H(e^{-})$, in organic solvents, determined using IEF-PCM DFT/B3LYP/6–311++G** calculations, were taken from the literature [33].

The theoretical vibrational spectra were interpreted by means of potential energy distributions (PEDs) using VEDA 4 program [34]. For a better correspondence between experimental and calculated wave values, we modified the results using the empirical scaling factors, reported by Merrick et al. [35].

3. Results and discussion

3.1. Antioxidant properties of syringaldehyde

It has been found that phenolic compounds inhibit the lipid



Scheme 1. Conformers of syringaldehyde molecule (M1-M4) and of its anion (A1-A4), radical (R1-R4) and radical cation (RC1-RC4). The relative energies ΔE are given in kJ.mol^{-1} with respect to the most stable conformers.

peroxidation by direct hydrogen atom transfer to the lipid radicals [32,36–38]:

$$R{-}H + LOO^{\bullet} \rightarrow R^{\bullet} + LOOH \quad (1)$$

In this reaction they form a phenoxyl radical less reactive and more stable than the attacked LOO·. This is the first mechanism that we considered in our study of the antioxidant action of syringaldehyde. In the living organism it is connected to the lipid peroxidation at the biological membranes. The measure used to quantify the hydrogen atom transfer (HAT) is the bond dissociation enthalpy (BDE) of the cleaved bond i.e. the O–H of syringaldehyde. The antioxidant mechanism in the living organism would differ depending on where it takes place – on the nonpolar cell membranes or in the polar physiological liquids whose main constituent is water. The different antioxidant assays also present different

reaction conditions. For this reason, we considered in our study also two antioxidant mechanisms involving ionization steps: single electron transfer (SET mechanism, see Eqs. (2a–2b)) [32,39–41], and sequential proton loss electron transfer (SPLET mechanism, see Eqs. (3a–3b)) [32,42]:

$$R{-}H + LOO^{\bullet} \rightarrow R^{+\bullet} + LOO^{-} \quad (2a)$$

$$R^{+\bullet} + LOO^{-} \rightarrow R^{\bullet} + LOOH \quad (2b)$$

$$R{-}H \rightarrow R^{-} + H^{+} \quad (3a)$$

$$R^{-} + LOO^{\bullet} \rightarrow R^{\bullet} + LOO^{-} \quad (3b)$$

These two mechanisms could be characterized by ionization potential (IP) of the radical cation formed in the course of SET and proton affinity (PA) of the anion formed in the course of SPLET reaction. The probably certain compound to react via HAT, SET or SPLET could be judged based on the calculated reaction enthalpies for each of the mechanisms [32]. We performed calculations of the respective values in nonpolar conditions (gas phase and benzene) and in polar media (water and DMSO). The following section presents the obtained reaction enthalpies of syringaldehyde and those of vanillin, which is included in the study as a reference compound, in effort to find molecular and electronic characteristics accounting for the differences in their relative activity. The calculated reaction enthalpies will be compared to the available literature data from several *in vitro* antioxidant assays and critically discussed. Table 1 summarizes the BDE, IP, PDE, PA and ETE values for both compounds in gas phase, benzene, DMSO and water.

In gas phase and benzene the BDEs of both syringaldehyde and vanillin are considerably lower that the respective IPs and PAs which indicates the HAT mechanism as the most favorable one in nonpolar medium. BDEs of syringaldehyde are smaller than those of vanillin outlining it as a better radical scavenger than vanillin via HAT.

To be able to prevent the lipid peroxidation, the radical of syringaldehyde should be more stable than the attacked lipid radical i.e. to have lower BDE value. Experimental estimations based on radical kinetics, gas-phase acidity cycles, and photoionization mass spectrometry measurements report that LOO radicals typically display a BDE of about 367 kJ mol^{-1} [44]. However, a lipid BDE value, representative for the chosen level of theory is needed to enable an accurate comparison. For this reason, we calculated the respective BDE value of methanol to methoxy radical at the same level of theory according to the following equation:

$$BDE(CH_3OH) = H(CH_3O^{\bullet}) + H(H^{\bullet}) - H(CH_3OH) = 413\ kJ.mol^{-1}$$

Effective chain-breaking antioxidants such as α-tocopherol show substantially lower BDE − 327 kJ mol^{-1} calculated in gas-phase and 293 kJ mol^{-1} in water using the same computational scheme [32]. In the present case, the calculated BDE values of syringaldehyde are also significantly lower than that of methanol so a good capacity for syringaldehyde to prevent lipid peroxidation could be expected.

Bartolomeazzi et al. studied the capacity of syringaldehyde to scavenge peroxyl radicals in crocin bleaching assay [18]. The authors found that syringaldehyde shows better capacity than the vanillin and that both of them are more effective than the respective phenols. This behavior is opposite to the expected based on the electron-withdrawing properties of the aldehyde group and its anticipated destabilizing effect on the phenoxyl radicals of the aldehydes. It was therefore assumed that it is due to their partial ionization in the reaction conditions (pH ~ 7, in water/ethanol solution) leading to the formation of phenoxy anions which are more active species than the neutral molecules [18]. Crocin bleaching at pH 3 showed reduction of the antiradical capacity of both aldehydes and supported the above assumption [18].

The radical scavenging capacity of the studied species is connected to the stability of the respective radicals. The latter could be characterized by the odd electron delocalization through the conjugated system i.e. the spin density distribution. The spin density over the fragments in syringaldehyde and vanillin in benzene, representing the nonpolar conditions, are illustrated in Fig. 1.

The spin density at the phenoxyl oxygen in the syringaldehyde radical is smaller by 0.034 than the one at the corresponding atom in the vanillin radical. It indicates its higher stability compared to vanillin radical and supports its experimentally observed higher radical scavenging capacity via HAT.

In polar environment, the syringaldehyde could undergo ionization and the formed ionic species are stabilized by the polar solvent. Thus the SET and SPLET mechanisms might became more favorable than the HAT mechanism.

The ability of the antioxidants to donate an electron (and act as radical scavengers via SET) is expressed by their IPs. Experimentally it could be estimated by measuring the oxidation potential of the first anodic peak of the studied compounds. The syringaldehyde is characterized by lower calculated IPs than the vanillin in accordance with the experimentally determined higher ability of syringaldehyde to donate an electron [18]. The calculated IP values in liquid phase are substantially reduced compared to gas phase due to the fact that the electron and the radical cations of

Table 1
DFT bond dissociation enthalpy (BDE), ionization potential (IP), proton dissociation enthalpy (PDE), proton affinity (PA), and electron transfer enthalpy (ETE) values of syringaldehyde and vanillin in kJ.mol^{-1}.

Species	BDE	IP	PDE	PA	ETE
syringaldehyde	333	7 50	905	1394	261
vanillin	354	789	886	1391	285
Benzene (2.28)[a]					
syringaldehyde	341	647	108	395	360
vanillin	361	674	101	396	379
DMSO (47.24)[a]					
syringaldehyde	340	501	−43	90	368
vanillin	360	520	−42	94	384
Water (80.10)[a]					
syringaldehyde	332	478	52	181	349
vanillin	351	497	53	185	365
Gas phase					

[a] Relative dielectric permittivity [43] and references therein.

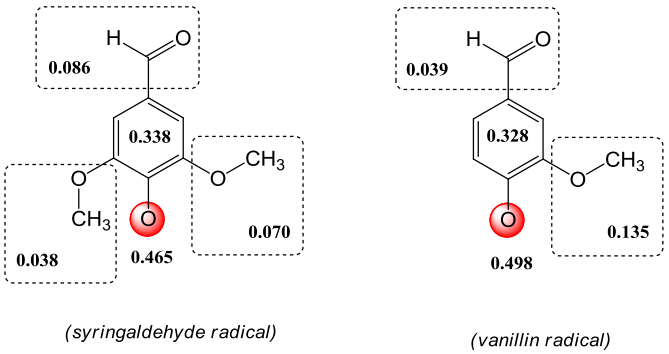


Fig. 1. Calculated spin density over fragments of the radicals of syringaldehyde and vanillin in benzene.

syringaldehyde and vanillin are solvated and stabilized even by nonpolar solvents such as benzene. The greater stabilisation in polar medium leads to further reduction of the corresponding IPs in water and DMSO. However, they are still higher than the BDE values in all studied media, and also higher than the IP of phenol (807 kJ mol^{-1} in gas phase and 346 kJ mol^{-1} in water solution calculated at the same theoretical level [32]). Comparison to the latter was suggested by Wright et al. [39] as effective approach to estimate the probability certain compounds to react via SET mechanism. When IPs of the studied antioxidants drop to ca. 167 kJ mol^{-1} below phenol, the SET mechanism would gain importance in solution [39]. As could be seen in Table 1, neither in gas-phase, nor in water, the IPs of syringaldehyde and vanillin are below that of phenol, hence the SET mechanism should be excluded as possible mechanism of action for both compounds.

As the SPLET mechanism also involves charged species, the respective reaction enthalpies are also affected by the solvation and the medium polarity. Mainly due to the large enthalpy of H^+ solvation, the PAs in benzene are considerably lower from those in gas-phase and they are further lowered in polar medium. The PA values in Table 1 show lower energy requirements for the SPLET mechanism than HAT in polar medium. On the other hand, in some cases the HAT mechanism could be competitive to the SPLET one, because in spite of the low values of PA, the second step of the SPLET mechanism, i.e. the electron transfer, might require higher energy than the corresponding hydrogen atom abstraction [42]. This concerns also the present case, as the ETE values of syringaldehyde and vanillin are higher than the BDE values in DMSO and water. The PAs in DMSO are slightly lower than in water due to the greater solvation enthalpy of the proton [32]. Unlike the substantially different BDE values, the PAs of both compounds differ only slightly. However, according to the calculated ETE values of syringaldehyde and vanillin, the phenoxy anion of the former is more prone to donate its electron the free radical (in the second step of the SPLET mechanism). This, combined with the better radical stability of the resulting radical, outlines the syringaldehyde as better radical scavenger via SPLET as well.

A widely used method for evaluation of radical scavenging activity is the DPPH assay where the experiment is conducted in polar methanol medium and the ionization of the studied compounds through SPLET contribute to their radical scavenging activity [45]. The activity of syringaldehyde and vanillin was tested according to this assay by several authors [7,18,19,45]. The relative activity of syringaldehyde as compared to vanillin is slightly higher according to Bartolomeazzi et al. [18]. In contradiction to this, Bountagkidou et al. [19] found both compounds inactive towards DPPH. However, more recent studies on syringaldehyde and isovanillin, isolated from Hainanian cassava [7], report superior activity of syringaldehyde in the DPPH assay to isovanillin, a positional isomer of vanillin known as more effective scavenger than vanillin itself [46]. On the other hand, in the course of the reaction with DPPH radical, the initial antioxidant could be converted in other chemical species such as dimers possessing antiradical activity [47–49] or other free radicals resulting from chemical reaction with DPPH [50]. Then these products would contribute to the DPPH reduction along with the initial antioxidant, which limits the usefulness of DPPH assay to draw conclusions on the structure-activity relationship. Complex mechanism of the antiradical reactions was demonstrated also for the $ABTS^{\cdot+}$ scavenging assay making it unreliable as method to study of the structure-activity relationship as well [19,51,52]. Despite these limitations, synthetic dendrimers of vanillin and syringaldehyde containing four phenolic units were tested in DPPH method and showed same relationship in the activities as the monomeric aldehydes i.e. syringaldehyde-based dendrimer was more active than the vanillin-based one [27].

Having in mind the importance of the anionic form in the SPLET mechanism, we focussed our efforts to study the ability of syringaldehyde to form an anion and characterize it in more details. For this purpose we converted the syringaldehyde into phenoxy anion by treating it with excess of dry CD_3ONa in DMSO-d_6 solution and followed the spectral, structural, and electronic changes resulting from the conversion by experimental IR methods and DFT computations.

3.2. IR spectra of syringaldehyde and its anion

The IR spectra for syringaldehyde and its anion will be considered first one by one, and then the spectral changes, caused by the conversion, will be summarized based on the observed frequency shifting. The IR spectra (1800 - 1100 cm^{-1}) of both species in DMSO-d_6 are shown in Fig. 2.

The numerical values of experimental vibrational characteristic are listed together with the theoretical ones in Table 2. The agreement between the experimental and calculated values is very good – the mean absolute deviation between observed and calculated frequencies is 10.5 cm^{-1}, which is not away from the low border of the 10–20 cm^{-1} interval of deviations, typical for the DFT calculations for molecules containing carbonyl or cyano groups [53–56].

According to the calculations the ν(OH) vibration is pure i.e. it is not mixed with any other mode. The ν(OH) band of syringaldehyde cannot be measured in DMSO/DMSO-d_6 because a broad band is present in the 3400-2700 cm^{-1} region of the spectrum, due to the formation of hydrogen bonds of syringamdehyde mainly with the solvent. In $CDCl_3$ solution a sharp band for ν(OH) appears at 3530 cm^{-1}, downshifted by 62 cm^{-1} in comparison to 3-hydroxybenzaldehyde in the same solution [57]. This shift indicates that the OH group in syringaldehyde participates in an intramolecular hydrogen bond with the oxygen atom of the methoxy group as in the case of vanillin [55].

The Fermi-doublet, typical for ν(C–H) bands of the formyl groups - CHO in aldehydes, was found at 2841 and 2732 cm^{-1} (unperturbed frequency: 2786 cm^{-1}) for the molecule studied. The normal vibrations of predominantly ring C–C stretching character have been predicted correctly by the theoretical method used as

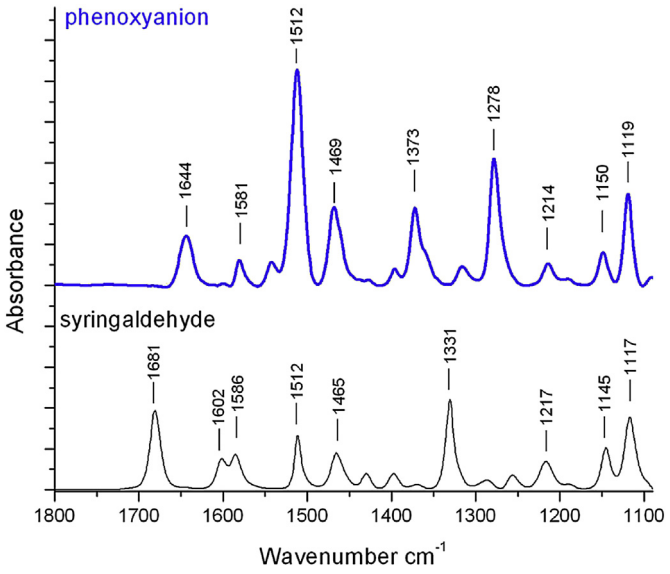


Fig. 2. Infrared spectra of syringaldehyde and of its anion (with counter ion Na^+) in DMSO-d_6 (0.12 mol l^{-1}).

Table 2
Theoretical (IEF-PCM B3LYP/6–311++G**) and experimental (solvent DMSO-d_6) vibrational frequencies (ν in cm^{-1}) and IR integrated intensities (A in km mol^{-1}) of syringaldehyde.

ν_{calc}[a]	A	Assignments with PED[b]	$\nu_{exp.}$
3614	273.7	100 ν(OH)	3530[c]
3117	3.3	99 ν(Ph-H)	
3107	1.9	100 ν(Ph-H)	
3056	20.1	88 $\nu^{as}(CH_3)$	3055
3049	23.9	89 $\nu^{as}(CH_3)$	
3002	38.0	100 $\nu^{as}(CH_3)$	3007
2992	44.6	100 $\nu^{as}(CH_3)$	2967
2935	56.1	100 ν^{s} (CH_3)	2943
2928	67.5	100 ν^{s} (CH_3)	
2837	165.2	100 ν(C–H)	2786[d]
1679	657.7	78 ν(C=O)	1681
1601	242.4	51 ν^{Ph} (CC),10 δ(COH)	1602
1574	216.0	48 ν^{Ph}(CC), 22δ^{Ph}(CCH)	1586
1498	188.4	21 δ^{Ph}(CCC), 18δ^{Ph}(CCH), 14ν(C–OH)	1512
1464	54.8	98 $\delta(CH_3)$	1465
1460	51.2	95 $\delta(CH_3)$	
1455	128.8	56 $\delta(CH_3)$, 17δ^{Ph}(CCH)	1430
1454	14.6	93 $\delta(CH_3)$	
1450	15.9	92 $\delta(CH_3)$	
1449	1.6	71 $\delta(CH_3)$	
1423	159.8	33 δ(HOC), 19 δ(HCO)	
1399	161.2	38 δ(HCO), 29 ν^{Ph} (CC)	1397
1370	124.3	45 δ(HCO), 20 δ(HOC)	1369
1314	776.0	44 ν(C–OCH_3), 13 ν(C–CHO)	1331
1268	128.8	30 δ^{Ph}(CCH),14 δ(HOC)	1286
1236	70.7	61 ν(C–OH), 20δ^{Ph}(CCH)	1256
1204	410.5	38 ν(C–OCH_3),19 δ(HOC)	1217
1184	41.0	74 $\delta(CH_3)$	
1179	5.5	76 $\delta(CH_3)$	
1144	17.0	69 $\delta(CH_3)$	1145
1143	1.5	28 δ^{Ph}(CCH), 22δ^{Ph}(CCH)	
1132	445.4	38 ν(C–CHO)	1117
1103	602.4	44 ν(O–CH_3), 18 ν(C–OCH_3)	

[a] Scaled by 0.9686 [35].
[b] Vibrational modes: ν, stretching; δ, bending. The numbers before the mode symbols indicate % contribution (10 or more) of a given mode to the corresponding normal vibration, according to the potential energy distribution matrix.
[c] Solvent $CDCl_3$.
[d] Unperturbed frequency.

Table 3
Theoretical (IEF-PCM B3LYP/6–311++G**) and experimental (solvent DMSO-d_6) vibrational frequencies (ν in cm^{-1}) and IR integrated intensities (A in km mol^{-1}) of syringaldehyde anion.

	ν_{calc}[a]	A	Assignments with PED[b]	$\nu_{exp.}$
1.	3160	8.8	99ν(Ph-H)	
2.	3116	19.0	100ν(Ph-H)	
3.	3092	37.2	88ν^{as} (CH_3)	
4.	3080	44.8	89ν^{as} (CH_3)	3081
5.	3043	54.3	100ν^{as} (CH_3)	2937
6.	3024	64.4	100ν^{as} (CH_3)	
7.	2969	82.2	100ν^{s} (CH_3)	
8.	2968	101.5	100ν^{s} (CH_3)	2904
9.	2858	233.4	100ν(C–H)	2784[c]
10.	1626	374.2	67ν(C=O)	1644
11.	1586	373.6	59ν^{Ph} (CC),10 δ^{Ph}(CCH), 10 δ(CHO)	1581
12.	1536	96.2	51δ^{Ph}(CCH), 37ν^{Ph} (CC)	
13.	1503	905.2	69ν^{Ph}(CO^-), 15δ^{Ph}(CHO)	1512
14.	1480	21.7	88$\delta(CH_3)$	
15.	1479	13.8	90$\delta(CH_3)$	
16.	1464	136.6	56$\delta(CH_3)$, 15 δ^{Ph}(CCH),10 ν^{Ph} (CC)	1469
17.	1458	10.0	93$\delta(CH_3)$	
18.	1455	609.8	92$\delta(CH_3)$	
19.	1451	89.4	71$\delta(CH_3)$	
20.	1433	626.5	39 δ^{Ph}(CCH), 19 ν^{Ph} (CC)	
21.	1405	66.2	31 δ(HCO), 16 ν(C–CHO), 10 ν(C=O)	
22.	1372	422.8	48 δ(HCO),13 δ^{Ph}(CCH)	1373
23.	1303	198.1	35 δ^{Ph}(CCH), 20ν^{Ph} (CC)	
24.	1261	859.3	30ν(C–OCH_3), 15 ν^{Ph} (CC)	1278
25.	1206	194.2	30δ^{Ph}(CCH),17δ(CH_3)	1214
26.	1194	45.2	74$\delta(CH_3)$	
27.	1191	16.8	44δ^{Ph}(CCH), 23ν^{Ph} (CC)	
28.	1153	3.4	84$\delta(CH_3)$	
29.	1126	170.2	61$\delta(CH_3)$	1150
30.	1124	36.5	23ν(C–CHO),18 δ^{Ph}(CCH)	1119
31.	1062	503.4	53ν(O–CH_3),17ν(C–CHO)	1080
32.	1010	80.0	43 ν(C–CHO), 13 ν(C–OCH_3)	
33.	972	3.2	21ν^{Ph} (CC), 13 ν(C–OCH_3	

[a] Scaled by 0.9686 [35].
[b] Vibrational modes: ν, stretching; δ, bending. The numbers before the mode symbols indicate % contribution (10 or more) of a given mode to the corresponding normal vibration, according to the potential energy distribution matrix.
[c] Unperturbed frequency.

intense bands in the 1600-1500 cm^{-1} frequency region.

The calculations reproduce very well the frequency of the C=O stretching mode; the difference between measured and scaled calculated values is only 2 cm^{-1} (No.11, Table 2). The ν(C=O) bands are highly intensive in both the experimental and theoretical spectra, but unlike the spectra of vanillin, they are not the highest intensity ones. In a qualitative agreement between theory and experiment, the strongest band in the IR spectrum is attributed to the ν(C–OCH_3) vibrational mode (No.24, Table 2).

The Ph-O coordinate dominates in vibration 26 with predicted frequency of 1236 cm^{-1}. We found the corresponding band at 1256 cm^{-1} in DMSO-d_6 (experimental spectrum). This frequency is not away from the value of 1249 cm^{-1}, measured by Pinchas [58] for the unsubstituted phenol and assigned as ν(Ph-O) on the basis of the $^{16}O/^{18}O$ isotopic shifts.

The theoretical and experimental IR data for the anion are compared in Table 3.

A good agreement between experimental and theoretical IR data can be seen there. The mean absolute deviation between observed and calculated frequencies is 11.0 cm^{-1}. The conversion of syringaldehyde molecule into the oxyanion results in very essential changes in its IR spectrum (Tables 2 and 3 and Fig. 2), e.g.:

- A strong decrease in the ν(C=O) frequency: predicted 53 cm^{-1}, measured 37 cm^{-1}. This value is larger than that measured in the case of *m*-hydroxybenzaldehyde (13 cm^{-1} [57]), due to the strong polar resonance through the *para* phenylene ring, and corresponds to the large σ^+ value of *para*-O^- substituent [59]. The conversion causes slight decrease in the integrated intensity of the carbonyl stretching band.
- Essential intensity increases (more than 8-fold) of the aromatic skeletal bands 8a,b and 19a,b (Wilson's notation), typical for phenolates [60–62].
- A strong intensity increase (2-fold) of the formyl ν(CH) band.
- Shift of the ν(Ph-O) coordinate to higher frequency: predicted 1503 cm^{-1}, measured 1512 cm^{-1} (No. 13, Table 3) that is obviously due to the significant shortening of the Ph–O bond, accompanying the conversion of the syringaldehyde molecule into the oxyanion (see below).

3.3. Structure of syringaldehyde anion

Structure of the anion as present in the DMSO solution, cannot be directly observed, but could be characterized by theoretical calculations. Having in mind the excellent agreement between the experimental and theoretical vibrational data, obtained in this work by B3LYP/6-311++G**, we consider that the predictions of the structural variations caused by the conversion of syringaldehyde in phenoxy anion are reliable. In the literature it is reported [63] that finding good theoretical descriptions of spectroscopic features guarantees obtaining of so good or better structural predictions

within the same theoretical methods and basis set.

The optimized geometry parameters, i.e. bond lengths and bond angles, computed at the B3LYP/6-311++G** level are compared with those found [64] by X-ray for neutral syringaldehyde in Table 3. As we can see in Table 3, the method used gives a good description of steric structure of the molecule. The m.d. are 0.009 Å for bond lengths and 0.81 for bond angle.

The most stable conformer of syringaldehyde is planar (1M in Scheme 1) according to our calculation and corresponds to the one found by monocrystal X-ray diffraction [64]. The 4-hydroxy H atom participates in an intramolecular O–H … O interaction with a neighboring methoxy O atom.

Unlike the molecule, the most stable conformer of the anion is not planar (1A in Scheme 1), with a dihedral angle $C_1C_2O_{12}C_8 = 60.1^\circ$. The conversion of syringaldehyde into the oxyanion leads to changes in all the bond lengths, but the strongest ones are the shortening of the $C_1–O_{10}$ bond with ca. 0.098 Å and lengthening of the adjacent CC ones with ca. 0.05 Å (Table 4). The geometry variations discussed are qualitatively similar to those in the cases of vanillin [55]. This result is not surprising because of the strong O–/acceptor polar resonance through the para phenylene ring. These changes are connected with the formation of a quasi-quinonoidal structure of the *para*-phenylene ring in the oxyanion.

4. Conclusions

DFT B3LYP/6-311++G** calculations in benzene, methanol and water were used to study the ability of syringaldehyde to scavenge free radicals according different antioxidant mechanisms. It is found that in nonlopar environment the preferred mechanism of the antioxidant action of syringaldehyde is direct hydrogen atom transfer. The radical of syringaldehyde is characterized by higher stability than vanillin radical due to more effective delocalization of the odd electron through the conjugated system which is in accordance with its reported superior radical scavenging capacity in crocin bleaching assay. In polar environment the preferred mechanism of antioxidant action of syringaldehyde is sequential proton loss electron transfer which is essentially related to the formation of a phenoxy anoin. Therefore the phenoxy anion of syringaldehyde was generated in DMSO solution and the changes in the force field, steric and electronic structure, resulting from the conversion, were described in detail based on the IR spectral data and DFT computations. The IR spectral analysis shows that the conversion into oxyanion causes a strong decrease in the ν(C=O) frequency and a shift of the ν(Ph-O) coordinate to higher frequency, accompanied by intensity increase of the formyl ν(CH) band and aromatic skeletal bands in the region 1600-1400 cm^{-1}. Based on these spectral data and the calculated structural parameters, it was established that the structure of the oxyanion shows quasi-quinonoidal geometry of the *para*-phenylene ring.

Table 4
Theoretical (B3LYP/6–311++G**) and experimental bond lengths R (Å) and bond angles A (°) of the syringaldehyde molecule and its anion.

	Molecule			Anion	
	Experimental[a]	Theoretical	Δ[b]	Theoretical	∇[c]
Bond lengths					
R(C^1,C^2)	1.393	1.404	0.011	1.452	−0.057
R(C^1,C^3)	1.403	1.408	0.005	1.467	−0.050
R(C^2,C^4)	1.384	1.395	0.011	1.375	0.020
R(C^3,C^5)	1.375	1.385	0.010	1.373	0.011
R(C^4,C^6)	1.391	1.400	0.009	1.412	−0.021
R(C^5,C^6)	1.391	1.401	0.010	1.421	−0.012
R(C^6,C^7)	1.453	1.472	0.019	1.435	0.036
R(C^2,O^{12})	1.368	1.359	−0.009	1.390	−0.023
R(O^{12},C^8)	1.413	1.422	0.009	1.425	0.017
R(C^1,O^{10})	1.343	1.352	0.009	1.253	0.098
R(C^3,O^{13})	1.360	1.370	0.008	1.378	−0.018
R(O^{13},C^9)	1.434	1.426	−0.008	1.408	0.001
R(C^7,O^{11})	1.212	1.214	0.002	1.435	−0.020
Bond angles					
A(C^2,C^1,C^3)	119.98	120.01	−0.03	116.8	3.17
A(C^1,C^2,C^4)	119.08	119.01	0.07	122.5	−3.46
A(C^2,C^4,C^4)	120.03	120.40	−0.37	121.4	−0.97
A(C^4,C^6,C^5)	121.03	120.81	0.22	118.1	2.72
A(C^6,C^5,C^3)	118.58	118.79	−0.21	121.2	−2.40
A(C^5,C^3,C^1)	120.99	120.98	0.01	123.0	−2.03
A(C^4,C^6,C^7)	118.31	119.11	−0.80	119.5	−0.39
A(C^6,C^7,O^{11})	120.49	125.28	−4.79	128.1	−2.80
A(C^4,C^2,O^{12})	125.38	125.43	−0.05	124.2	1.25
A(C^2,O^{12},C^8)	117.42	118.25	−0.83	117.6	0.68
A(C^2,C^1,O^{10})	117.70	119.57	−1.87	122.8	−3.25
A(C^1,C^3,O^{13})	113.26	113.00	0.26	119.0	−5.97
A(C^3,O^{13},C^9)	117.39	118.38	−0.99	115.4	2.98

[a] See Ref. [64].
[b] Algebraic deviations (Å, degrees) between experimental and theoretical values.
[c] Algebraic deviations (Å, degrees) between theoretical values of the anion and molecule. For atom numbering see Scheme 1.

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References

[1] X. Li, W. Cao, Y. Shen, N. Li, X.-P. Dong, K.-J. Wang, Y.-X. Cheng, Antioxidant compounds from Rosa laevigata fruits, Food Chem. 130 (2012) 575–580.
[2] E.S. Yapo, H.T. Kouakou, L.K. Kouakou, J.Y. Kouadio, P. Kouamé, J.-M. Mérillon, Phenolic profiles of pineapple fruits (Ananas comosus L. Merrill) Influence of the origin of suckers, Austr. J. Basic Appl. Sci. 5 (2011) 1372–1378.
[3] D.T. Mai, T.D. Le, T.P. Nguyen, N.M. Phan, H.A. Nguyen, T.T.P. Nguyen, L.Q. Tran, A new aldehyde compound from the fruit of Pandanus tectorius Parkinson ex Du Roi, Nat. Prod. Res. 29 (2015) 1437–1441.
[4] M. Colaric, R. Veberic, A. Solar, M. Hudina, F. Stampar, Phenolic acids, syringaldehyde, and juglone in fruits of different cultivars of *Juglans regia* L. J. Agric. Food Chem. 53 (2005) 6390–6398.
[5] S. Kermasha, M. Goetghebeur, J. Dumont, Determination of Phenolic Compound Profiles in Maple Products by High-Performance Liquid Chromatography, J. Agric. Food Chem. 43 (1995) 708–716.
[6] A.M. Asamarai, P.B. Addis, R.J. Epley, T.P. Krick, Wild Rice Hull Antioxidants, J. Agric. Food Chem. 44 (1996) 126–130.
[7] B. Yi, L. Hu, W. Mei, K. Zhou, H. Wang, Y. Luo, X. Wei, H. Dai, Antioxidant Phenolic Compounds of Cassava (Manihot esculenta) from Hainan, Molecules 16 (2010) 10157–10167.
[8] M.N.M. Ibrahim, R.B. Sriprasanthi, S. Shamsudeen, F. Adam, S.A. Bhawani, A concise review of the natural existence, synthesis, properties, and applications of syringaldehyde, BioRes. 7 (2012) 4377–4399.
[9] C.H. Huang, M.F. Chen, H.H. Chung, J.T. Cheng, Antihyperglycemic effect of syringaldehyde in streptozotocin-induced diabetic rats, J. Nat. Prod. 75 (2012) 1465–1468.
[10] N. Paixao, V. Pereira, J.C. Marques, J.S. Camara, Quantification of polyphenols with potential antioxidant properties in wines using reverse phase HPLC, J. Sep. Sci. 31 (2008) 2189–2198.
[11] F.W.B. Aquino, S. Rodrigues, R.F. Nascimento, A.R.S. Casimiro, Simultaneous determination of aging markers in sugar cane spirits, Food Chem. 98 (2006) 569–574.
[12] M.D. Guillen, M.L. Ibargoitia, Volatile components of aqueous liquid smokes from *Vitis vinifera* L. shoots and *Fagus sylvatica* L. wood, J. Sci. Food Agric. 72 (1996) 104–110.
[13] M.D. Guillen, M.J. Manzanos, Study of the volatile composition of an aqueous oak smoke preparation, Food Chem. 79 (2002) 283–292.
[14] M.D. Guillen, M.L. Ibargoitia, New components with potential antioxidant and organoleptic properties, detected for the first time in liquid smoke flavoring preparations, J. Agric. Food Chem. 46 (1998) 1276–1285.
[15] R. Estrada-Munoz, E.A.E. Boyle, J.L. Marsden, Liquid smoke effects on Escherichia coli O157:H7, and its antioxidant properties in beef products, J. Food Sci. 63 (1998) 150–153.
[16] E. Sunen, C. Aristimuno, B. Fernandez-Galian, Activity of smoke wood condensates against Aeromonas hydrophila and Listeria monocytogenes in vacuum-packaged, cold-smoked rainbow trout stored at 4°C, Food Res. Int. 36 (2003) 111–116.
[17] S.A. Coronado, G.R. Trout, F.R. Dunshea, N.P. Shah, Effect of dietary vitamin E,fishmeal and wood and liquid smoke on the oxidative stability of bacon

during 16 weeks' frozen storage, Meat Sci. 62 (2002) 51–60.
[18] R. Bartolomeazzi, N. Sebastianutto, R. Toniolo, A. Pizzariello, Comparative evaluation of the antioxidant capacity of smoke flavouring phenols by crocin bleaching inhibition, DPPH radical scavenging and oxidation potential, Food Chem. 100 (2007) 1481–1489.
[19] O.G. Bountagkidou, S.A. Ordoudi, M.Z. Tsimidou, Structure–antioxidant activity relationship study of natural hydroxybenzaldehydes using in vitro assays, Food Res. Int. 43 (2010) 2014–2019.
[20] P.G. Pietta, Flavonoids as antioxidants, J. Nat. Prod. 63 (2000) 1035–1042.
[21] E. Worm, C.J. Beukelman, A.J.J. Berg, B.H. Kroes, R.P. Labadie, H. Dijk, Effects of methoxylation of apocynin and analogs on the inhibition of reactive oxygen species production by stimulating human neutrophils, Eur. J. Pharmacol. 433 (2001) 225–230.
[22] R. Stanikunaite, S.I. Khan, J.M. Trappe, S.A. Ross, Cyclooxygenase-2 inhibitory and antioxidant compounds from the truffle Elaphomyces granulates, Phytother. Res. 23 (2009) 575–578.
[23] R.J. Flower, The development of COX-2 inhibitors,, Nat. Rev. Drug Discov. 2 (2003) 179–191.
[24] M. Amir, H.K.Agarwal, Role of COX-2 selective inhibitors for prevention and treatment of cancer, Pharmazie 60 (2005) 563–570.
[25] M.H. Farah, G. Samuelsson, Pharmacologically active phenylpropanoids from Senra incana, Planta Med. 58 (1992) 14–18.
[26] A.A. Bozkurt, G. Mustafa, A. Tarik, O. Adile, S.H. Murat, K. Mesut, K. Yildiray, C. Murat, S. Coskun, Syringaldehyde exerts neuroprotective effect ocerebral ischemia injury in rats through anti-oxidative and anti-apoptotic properties, Neural Regen. Res. 9 (2014) 1884–1890.
[27] C.Y. Lee, A. Sharma, J.E. Cheong, J.L. Nelson, Synthesis and antioxidant properties of dendritic polyphenols, Bioorg. Med. Chem. Lett. 19 (2009) 6326–6330.
[28] M.J. Frisch, G.W. Trucks, H.B. Schlegel, G.E. Scuseria, M.A. Robb, J.R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G.A. Petersson, H. Nakatsuji, M. Caricato, X. Li, H.P. Hratchian, A.F. Izmaylov, J. Bloino, G. Zheng, J.L. Sonnenberg, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, J.A. Montgomery Jr., J.E. Peralta, F. Ogliaro, M. Bearpark, J.J. Heyd, E. Brothers, K.N. Kudin, V.N. Staroverov, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J.C. Burant, S.S. Iyengar, J. Tomasi, M. Cossi, N. Rega, J.M. Millam, M. Klene, J.E. Knox, J.B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R.E. Stratmann, O. Yazyev, A.J. Austin, R. Cammi, C. Pomelli, J.W. Ochterski, R.L. Martin, K. Morokuma, V.G. Zakrzewski, G.A. Voth, P. Salvador, J.J. Dannenberg, S. Dapprich, A.D. Daniels, O. Farkas, J.B. Foresman, J.V. Ortiz, J. Cioslowski, D.J. Fox, Gaussian 09, Revision A.1, Gaussian Inc., Wallingford CT, 2009.
[29] A.D.J. Becke, Density functional thermochemistry. III. The role of exact exchange, J. Chem. Phys. 98 (1993) 5648–5652.
[30] C. Lee, W. Yang, G.R. Parr, Development of the Colle-Salvetti correlation-energy formula into a functional of the electron density, Phys. Rev. 37B (1988) 785–789.
[31] J. Tomasi, B. Mennucci, E. Cances, The IEF version of the PCM solvation method: an overview of a new method addressed to study molecular solutes at the QM ab initio level, J. Mol. Struct. (Theochem) 464 (1999) 211–226.
[32] E. Klein, V. Lukes, M. Ilcin, DFT/B3LYP study of tocopherols and chromans antioxidant action energetics, Chem. Phys. 336 (2007) 51–57.
[33] J. Rimarčík, V. Lukeš, E. Klein, M. Ilčin, Study of the solvent effect on the enthalpies of homolytic and heterolytic N–H bond cleavage in *p*-phenylenediamine and tetracyano-*p*-phenylenediamine, J. Mol. Struct. (Theochem.) 952 (2010) 25–30.
[34] M.H. Jamróz, Vibrational energy distribution analysis (VEDA): Scopes and limitations, Spectrochim. Acta A 114 (2013) 220–230.
[35] J. Merrick, D. Moran, L. Radom, An evaluation of harmonic vibrational frequency scale factors, J. Phys. Chem. A 111 (2007) 11683–11700.
[36] E.N. Frankel, in: E.N. Frankel (Ed.), Lipid Oxidation, The Oily Press, Dundee, Scotland, 1998.
[37] G.W. Burton, T. Doba, E.J. Gabe, L. Hughes, F.L. Lee, L. Prasad, K.U. Ingold, Autoxidation of biological molecules. 4. Maximizing the antioxidant activity of phenols, J. Am. Chem. Soc. 107 (1985) 7053–7065.
[38] M.I. De Heer, P. Mulder, H. Korth, K.U. Ingold, J. Lusztyk, Hydrogen Atom Abstraction Kinetics from Intramolecularly Hydrogen Bonded Ubiquinol-0 and Other (Poly)methoxy Phenols, J. Am. Chem. Soc. 122 (2000) 2355–2360.
[39] J.S. Wright, E.R. Johnson, G.A. DiLabio, Predicting the Activity of Phenolic Antioxidants: Theoretical Method, Analysis of Substituent Effects, and Application to Major Families of Antioxidants, J. Am. Chem. Soc. 123 (2001) 1173–1183.
[40] M. Musialik, G. Litwinienko, Scavenging of dpph· Radicals by Vitamin E Is Accelerated by Its Partial Ionization: the Role of Sequential Proton Loss Electron Transfer, Org. Lett. 7 (2005) 4951–4954.
[41] A.P. Vafiadis, E.G. Bakalbassis, A DFT study on the deprotonation antioxidant mechanistic step of *ortho*-substituted phenolic cation radicals,, Chem. Phys. 316 (2005) 195–204.
[42] M. Musialik, R. Kuzmicz, T.S. Pawlowski, G. Litwinienko, Acidity of hydroxyl groups: an overlooked influence on antiradical properties of flavonoids, J. Org. Chem. 74 (2009) 2699–2709.
[43] E. Wilhelm, R. Battino, Thermodynamic functions of the solubilities of gases in liquids at 25.deg, Chem. Rev. 73 (1973) 1–9.
[44] J. Berkowitz, G.B. Ellison, D. Gutman, Three methods to measure RH bond energies, J. Phys. Chem. 98 (1994) 2744–2765.
[45] G. Litwinienko, K.U. Ingold, Abnormal solvent effects on hydrogen atom abstraction. 1. The reactions of phenols with 2,2-diphenyl-1-picrylhydrazyl (DPPH•) in alcohols,, J. Org. Chem. 68 (2003) 3433–3438.
[46] S.S. Kuma, K.I. Priyadarsini, K.B. Sainis, Free radical scavenging activity of vanillin and o-vanillin using 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical, Redox Rep. 7 (2002) 35–40.
[47] W. Brand-Williams, M.E. Cuvelier, C. Berset, Use of a free radical method to evaluate antioxidant activity, Leb. Wiss. Technol. 28 (1995) 25–30.
[48] V. Bondet, W. Brand-Williams, C. Berset, Kinetics and mechanisms of antioxidant activity using the DPPH free radical method, Leb. Wiss. Technol. 30 (1997) 609–615.
[49] J. Kawabata, Y. Okamoto, A. Kodama, T. Makimoto, T. Kasai, Oxidative dimers produced from protocatechuic and gallic esters in the DPPH radical scavenging reaction, J. Sci. Food Agric. 50 (2002) 5468–5471.
[50] E.N. Hristea, I.C. Covaci-Cîmpeanu, G. Ioniţaă, P. Ioniţaă, C. Draghici, M.T. Caăproiu, M. Hillebrand, T. Constantinescu, A.T. Balaban, Reactions of 2,2-Diphenyl-1-picrylhydrazyl (DPPH) with Two Syringylic Phenols or One Aroxide Derivative, Eur. J. Org. Chem. 2009 (2009) 626–634.
[51] M.J.T. Arts, J.S. Dallinga, H.P. Voss, G.R.M.N. Haenen, A. Bast, A critical appraisal of the use of the antioxidant capacity (TEAC) assay in defining optimal antioxidant structures, Food Chem. 80 (2003) 409–414.
[52] A.M. Osman, K.K.Y. Wong, S.J. Hill, A. Fernyhough, Isolation and the characterization of the degradation products of the mediator ABTS-derived radicals formed upon reaction with polyphenols, Biochem. Biophys. Res. Commun. 340 (2006) 597–603.
[53] Y.I. Binev, M.K. Georgieva, S.I. Novkova, The conversion of phenylpropanedinitrile (phenylmalononitrile) into the carbanion, followed by IR spectra, ab initio and DFT force field calculations,, Spectroch. Acta A 59 (2003) 3041–3052.
[54] A.D. Popova, M.K. Georgieva, O.I. Petrov, K.V. Petrova, E.A. Velcheva, IR spectral and structural studies of 4-aminobenzenesulfonamide (sulfanilamide)-d_0, -d4, and -^{15}N, as well as their azanions: Combined DFT B3LYP/experimental approach, Int. J. Quant. Chem. 107 (2007) 1752–1764.
[55] E.A. Velcheva, B.A. Stamboliyska, IR spectral and structural changes caused by the conversion of 3-methoxy-4-hydroxybenzaldehyde (vanillin) into the oxyanion, Spectrochim. Acta A 60 (2004) 2013–2019.
[56] S. Stoyanov, Scaling of Computed Cyano-Stretching Frequencies and IR Intensities of Nitriles, their Anions, and Radicals, J. Phys. Chem. 114 (2010) 5149–5161.
[57] B.A. Stamboliyska, E.A. Velcheva, I.G. Binev, IR spectral and structural changes caused by the conversion of 3-hydroxybenzaldehyde into the oxyanion, Spectrochim. Acta A 59 (2003) 1541–1548.
[58] S. Pinchas, The C-O stretching frequency of hydrated isotopic phenolate ions, Spectrochim. Acta A 28 (1972) 801–802.
[59] E.A. Velcheva, I.G. Binev, I.N. Juchnovski, IR studies in the substituted benzaldehyde series provide a new definition of sigma-plus constants of ionic substituents, Spectrochim. Acta A 59 (2003) 1745–1749.
[60] E.A. Velcheva, B.A. Stamboliyska, P.J. Boyadjieva, Theoretical and IR spectral studies on the conversion of 3-hydroxy-4-methoxybenzaldehyde (isovanillin) into the oxyanion, Asian Chem. Lett. 13 (2009) 135–142.
[61] E.A. Velcheva, B.A. Stamboliyska, P.J. Boyadjieva, DFT and experimental study on the IR spectra and structure of 2-hydroxy-3-methoxybenzaldehyde (o-vanillin) and its oxyanion, J. Mol. Struct. 963 (2010) 57–62.
[62] E.A. Velcheva, B.A. Stamboliyska, Structural changes caused by the conversion of 2-hydroxybenzamide (salicylamide) into the oxyanion, J. Mol. Struct. 875 (2008) 264–271.
[63] N.L. Allinger, Y.J. Fan, Force field calculations on glyoxal, quinones, and related compound, J. Comput. Chem. 15 (1994) 251–268.
[64] T. Kolev, R. Wortmann, M. Spiteller, W.S. Sheldrick, M. Heller, 4-Hydroxy-3,5-dimethoxy-benzaldehyde (syringaldehyde), Acta Cryst. E60 (2004) o1387–o1388.