DFT Study on O-H Bond Dissociation Enthalpies and Ionization Potentials of Ortho, Para and Meta Substituted Phenols: A Computational Study

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Abstract: *The O-H bond dissociation energies [BDE(O-H)] and ionization potentials of o, p, and m-substituted phenols X-PhOH [X = F, Cl, Br, OH, CN, CH_3, OCH_3, CF_3, NH_2, and NO_2) have been computed using the density functional theory at B3LYP/6-311G** level. The effects of substituents on the BDE(OH) and ionization potential (IP) are analyzed. The DFT computed parameters are used to ascertain their antioxidant potentials. Then, o, p, m-substituted PhOH based new compounds are theoretically proposed as novel antioxidants.*

Keywords - *Phenols; DFT; ionization potentials; bond dissociation energy; antioxidants;*

I.   Introduction

Phenol is a central molecule in organic chemistry. Phenols are present in important amounts in a great variety of plant matrices, such as fruits and leaves [1]. Phenols are widely used as antioxidants in living organisms. Phenoxyl radicals represent important intermediate in many biological applications [2,3]. Antioxidants are well-known for their beneficial effects on human health. An antioxidant is defined as a compound able to decrease oxidation stress, e.g., metal chelator, inhibitor of enzymes involved in oxidative stress, lipid peroxidation inhibitor and free radical scavenger. Nowadays the use of natural antioxidants in areas of great impact to the health of consumers such as food, pharmaceutical and medical is gaining importance. Natural antioxidants can avoid or at least significantly reduce the peroxidation of lipids by free radicals, which are related to variety of disorders and diseases [4]. Antioxidants have attracted more and more attention owing to their potency in the pharmaceutical industry and their applications in food preservation and chemical engineering [5,6].

Recent studies on antioxidant mechanisms indicated that the chain reaction was controlled mainly through free radical scavenging by phenolic hydroxyls of antioxidants [7,8]. The majority of chain-breaking antioxidants, both in nature and in man-made materials are phenolic [9,10]. The biological and chemical activities of phenolic compounds are attributed to the radical scavenging function of their phenolic hydroxyl groups (O-H). The free radical scavenging capacity is the primary antioxidant feature and the structure activity relationship obtained is often correlated to the other antioxidant activities. Free radicals are unstable and highly reactive with adjacent molecules such as lipids, proteins and carbohydrates leading to cellular damage[11]. With the growing evidence showing the connection between the free radicals induced oxidative stress and the development of a range of illnesses such as cardiovascular, congestive heart failure, diabetes, arterial hypertension and cerebrovascular accidents [12] , the role of radical-scavenging antioxidants has received increasing attention [13,14] .

The aim of this work is to computationally determine possible mechanisms for radical scavenging activity via an H-atom vs. an electron-transfer. In this work DFT method is applied to calculate physical descriptors for characterizing their inhibiting ability. Hence, the homolytic bond dissociation enthalpy (BDE) of O-H bonds, reaction ionization potential (IP_r), adiabatic ionization potential(AIP), distribution of HOMO orbital and spin density in the free radicals were particularly calculated. Following quantities were determined from the calculated total enthalpies at 298.15K

$$BDE(O-H) = H(ArO^\cdot) + H(H^\cdot) - H(ArOH) \tag{1}$$

where $H(ArO^\cdot)$ is the enthalpy of the radical generated by H abstraction, $H(H^\cdot)$ is the enthalpy of the hydrogen atom (-0.4997959 Hartrees) and $H(ArOH)$ is the enthalpy of the parent molecule

$$IP_r = H(ArOH^{+\cdot}) + H(e^-) - H(ArOH) \tag{2}$$

where H ($AroH^{+\cdot}$) is the enthalpy of the cation, $H(e^-)$ is the enthalpy of electron (0.00119787Hartree) and $H(ArOH)$ is the enthalpy of the parent molecule.

Understanding substituent effects on molecular properties has long been an important goal in chemistry. The present study deals with the effect of donor and acceptor groups on the radical scavenging activity and antioxidant nature. The aim of this study is to elucidate and compare their potentials of antiradical agents, in order to provide new clues for antioxidant development. In this work, the structural, electronic and molecular properties were investigated at the density functional level. DFT has been found to give accurate evaluation about BDE and IP parameters.

O-H BDE is an important descriptor for characterizing the radical scavenging activities of phenols, several experimental studies have been performed to measure O-H BDE [15,16-19]. Also a number of   DFT calculations of O-H BDE of substituted phenols have been reported. The calculated O-H BDE value of phenol in vacuum reproduces the corresponding experimental ones with considerable accuracy.

II.   Computational methods

The geometries of the molecules and respective radicals, radical cations and anions were optimized employing DFT method with B3LYP functional [20] and the 6-311G** basis set. DFT was chosen because of the excellent compromise between the computational time and the description of the electronic correlation. Throughout our calculations the B3LYP hybrid functional, which consists of the Becke's three parameters exact exchange functional (B3) [21] combined with the non local gradient corrected correlation functional of the Lee-Yang-Parr (LYP) [22] were used. B3LYP/6-311G(d,p) level of theory was employed to perform the reliable optimization of the geometrical parameters of the studied compounds and to calculate physicochemical descriptors characterizing antioxidant ability.

Harmonic vibrational frequencies are analyzed for parent molecules, radicals, cations and anions at the same level of optimization to characterize the nature of stationary points as true minima with no imaginary frequencies of transition states with only one imaginary frequency and to provide thermodynamic quantities such as zero point energy (ZPE) corrections. Spin contaminations have been checked for radicals and radical cations with calculated $<S^2>$ values very close to the expectation value 0.75. Therefore, spin contamination should not bias obtained values. All enthalpies were calculated for 298.15 K and 1.0 atmosphere pressure.

All computational studies were performed with the Gaussian 03 [23] series of programs with density functional methods implemented in the computational package. Graphical representations of the highest occupied molecular orbital (HOMO) and lowest unoccupied molecular orbital (LUMO) data in checkpoint files were created using the Gaussian 03 [23] program package. Molecules with low BDE and IP values are expected to have high activity. Thus in the present study BDE and IP values were used as molecular descriptors in an effort to explain the radical scavenging of compounds. The total enthalpy at 298K consisted of the thermal correction to the enthalpy and the B3LYP calculated single point energy (SPE) values. All values of molecular descriptors were expressed in KJ/mol.

III.   Results and discussion

3.1 MOLECULAR GEOMETRIES AND ENERGY PROPERTIES

Obtained total energies of phenol, 30 mono substituted phenols and their respective radicals, radical cations and anions are summarized in **Table (1)**. Analysis of the total energies of mono substituted phenols in ortho, para and meta position reveals that they are almost isoenergetic in the gas phase. The results obtained reveal also that bromine substituted phenol is more energetically stable than rest of the substituted phenols. In the set of compounds including electron donating groups (F, Cl, Br, OH) and electron withdrawing groups (CN, NO$_2$), the OH group was coplanar with the phenyl ring in the equilibrium geometry. A planar structure was evidenced for all compounds except for CH$_3$, OCH$_3$, CF$_3$ and NH$_2$ substituted phenols. The planarity of compounds is an indication of possible extended conjugation and their stronger antioxidant activities. An intramolecular hydrogen bond (IHB) between the 2-hydroxylic hydrogen and the carbonylic oxygen was found in ortho substituted CF$_3$, NH$_2$ and NO$_2$ phenols with bond lengths ranging from 1.715 Å – 2.052 Å. The planar conformation of the above anionic species strongly correlates with the antioxidative activity because it ensures the effective delocalization of the lone pair electron in the phenyl ring. The R(C-O) bond length varied over a much wider range of values (1.335 Å-1.369 Å) for ortho substituted phenols than for meta (1.361Å-1.368Å) and para (1.356 Å-1.374 Å) substituted phenols. The C-O-H bond angle θ increased for para and meta substituted NO$_2$ phenol and decreased at ortho substituent due to IHB. Except for ortho substituted CF$_3$ and NH$_2$ groups there is no significant change in θ for ortho, para and meta substituted phenol. This indicates that introduction of substituent has little effect on these geometrical parameters.

Geometry optimizations on the radicals were performed starting from the optimized structure of the parent molecule after the hydrogen atom was removed from the O-H group. From the obtained bond distances and bond angle data, it can be seen that no significant geometrical change was observed when going from the neutral molecule to the phenoxy (ArO) and cation (AroH) radicals and the anionic forms (ArO) after hydrogen, electron and proton abstraction respectively. Some selected calculated and experimental structural parameters

[24] are reported in Table (2). Taking into account that the experimental data were obtained one can observe quite satisfactory agreement. Bond lengths agree within 0.014 Å and 0.005 Å, while the largest deviation of bond angles appears to be about 2.7°. Thus the selected method was considered accurate and it was applied in the structure optimization of various phenol derivatives. The results revealed that energy minima occurred at **ω** = 0° or ± 180° corresponding to the planar conformations stabilized by resonance structures.

3.2. Electronic properties

The ionization potentials (I), electron affinities (A), total hardness (η), global electronegativity (χ) , softness (S), and global electrophilicity (ω) of the ortho, para and meta substituted phenol molecule calculated with the B3LYP functional and 6-311G(d, p) basis set are presented in Table 3. The two methods of calculating electronic descriptors of the substituted phenols are from energy-vertical and orbital vertical method. The electronic descriptors represented by O and E is obtained by assuming the validity of Koopman's theorem (Orbital vertical) and from total electronic energies when adding and removing electron with the neutral molecule (Energy vertical). The calculated EA's from E_{LUMO} are larger than values by energy-vertical and for IPs values given by negative of HOMO energies are smaller than the calculated energy vertical. Generally electron donor groups are lower IP values and electron acceptor groups higher IP values than phenol. The computed E_{HOMO} values reveals that in the case of electron withdrawing substituents become more negative and while the presence of electron donating substituents results in less negative E_{HOMO} values. The electronic energies and zero point energies were summed to obtain E_0, the total energy at 0K. Ionization potentials were then determined by E_0 (cation) – E_0(parent).

The calculated EA for each species indicate that o-NO_2-PhOH, p-NO_2-PhOH and m-NO_2-PhOH are capable of attracting an electron instead of giving them while p-NH_2-PhOH, o-NH_2-PhOH, m-NH_2-PhOH, o-OCH_3-PhOH, p-OCH_3-PhOH and m-OCH_3-PhOH are proficient of giving electron rather than capturing which is an indication of their antioxidant activity. Analysis of electronegativity value indicates that electron donor group lowers and electron with drawing group increases the χ value. Only for ortho substituted derivatives electron donor group decreases ω and electron withdrawing group increases ω. Ortho, para and meta substituted donor and acceptor groups increases the hardness value and decreases the softness value with respect to phenol. The energy gap of ortho, para and meta substituted hydroxy, bromo, chloro, cyano, methoxy, amino and nitro phenol is less than phenol. There is no difference between the donor and acceptor substituted derivatives based on orbital energy calculation. The E_g of ortho and meta substituted F is higher than the parent molecule. The o-CH_3-PhOH and p-CH_3-PhOH have higher E_g values with respect to phenol. The ortho, para and meta substituted NH_2 derivatives has higher electron donating tendency and NO_2 has lower electron donating tendency among the ten phenol derivatives. The E_g of ortho, and para substituted phenol by energy vertical method is less than the parent molecule with the exception of m-F-PhOH.

The two results obtained by the calculation of electronegativity and electrophilicities agreed very well with the difference in the result. This could be the reason for the low hardness values obtained from the orbital-vertical method than from the energy vertical method. Koopman's theorem neglects the relaxation effect by using the frozen-orbital approximation. This effect is frequently compensated by the oppositely directed error was due to the electron correlation effect, beside neglect in the Hartree-Fock (HF) method. Therefore Koopman's theorem is a crude but useful and fast approach [25].

The molecules dipole moment represents a generalized measure of bond properties and charge densities in a molecule [26]. Molecule with electron acceptor groups due to better charge distribution and increasing distance have higher dipole moment[27], from the obtained data CN substituted phenol has higher dipole moment. The results of the calculated polarizability for substituted phenols showed that all substitution groups leads to increase the average polarizability and cause more reactive than the original molecule except fluorine. The methoxy substituted phenol has average polarizability equal to 81.56 a.u and hence higher reactivity. This is due to the ring delocalizing π electron resonance from the ring groups [27].

3.3 Bond dissociation enthalpies

The homolytic BDE of the hydroxyl bond is an important factor for determination of effectiveness of an antioxidant because the weaker this bond, the higher the antioxidative activity. Moreover, BDE is a thermodynamic parameter, which means that the weaker the bond, the more favourable the reaction with free radicals. Calculated BDE values are often attributed to π electron delocalization, leading to the stabilization of the radicals obtained after H-abstraction. Hence the molecules with the lowest BDE values are more active. The obtained results may be compared with calculations reported previously, either at a lower level of theory or in the study of similar process.

The gas phase BDE value for phenol is computed to be 346.85 KJ/mol at B3LYP/6-311++G** [28], 344.34 KJ/mol at B3LYP/6-311++G**// B3LYP/6-31G** [29], 346.44 KJ/mol at B3LYP/6-31G** [30], 346.44 KJ/mol [31], 351.04 KJ/mol at B3LYP/6-11++G(3df,3pd) [32]. All these values fall in the range of 343.1-

351.5KJ/mol. In this work calculated BDE for the basic structure, phenol in gas phase reached 346.15 KJ/mol. The obtained BDE value is by only 0.7 KJ/mol lower than that of phenol[28] obtained by the same level of theory with an inclusion of diffuse functions.

The substitution of a functional group in the molecule generally causes considerable changes in physio-chemical properties. The substituent effect on O-H bond cleavage as well as on various molecular properties is important. The substituent effects were described in terms of ΔBDES. Calculated O-H BDEs of substituted phenols are compiled in **Table (4)**. The ortho, para and meta-mono substituted phenol among the electron-withdrawing groups NO_2 has the strongest effect to the BDE. The ΔBDE value is 56.14 KJ/mol, 16.83 KJ/mol and 13.4 KJ/mol for ortho, para and meta substituted nitro phenol. The BDE value for ortho, para and meta substituted nitro phenol is 103.03 KJ/mol, 17.04 KJ/mol & 53.2 KJ/mol higher than the amino phenol.

The BDE of para substituted phenols with strong electron withdrawing groups NO_2, CN and CF_3 groups are higher than strong electron donating group NH_2, differences are in 45.11-53.2KJ/mol range. Results on BDE indicate that the most efficient system acting as hydrogen donors are para substituted with OH, Br, Cl, F, CH_3, CH_3O and NH_2 for which the values of BDE are smaller than that of phenol reference system. The computed gas phase O-H BDE of para substituted phenols bearing electron withdrawing groups such as CF_3, CN and NO_2 are larger than that of electron releasing groups.

When one hydrogen atom at the ortho position in phenol is replaced by a methyl group the O-H bond dissociation enthalpy decreases by 19.28 KJ/mol. The ortho substitution of phenol molecule with CN, CF_3 and NO_2 groups entails the increase of the BDE compared to phenol due to electron withdrawing capabilities of this group. The effect of electron donating substituent decreases the BDE by 4.27 KJ/mol to 46.89 KJ/mol with respect to phenol. The radical-scavenging activity of ArOH is efficiently enhanced by substitution of electron donating groups [33-37]. Donors cause the BDE's to be slightly lower than that in the parent, whereas acceptors cause the BDEs to be slightly higher [38]. The O-H BDE of ortho, para substituted phenols is much lower than meta substituted phenols except for CF_3 and NO_2 substituents. The electronic effect on O-H BDE shows that electron donating groups reduce and electron with drawing groups enhance the parameter. The mean absolute deviation (MAD) of BDE of para substituted phenols is −6.51 KJ/mol.

The phenols bearing OH or OCH_3 groups in the para position are usually characterized by marked antioxidant effects due to the electron releasing properties of these substituents that considerably reduce the O-H BDE value. The stabilization of the phenoxyl radical due to electron releasing power of the para NH_2 group is computed slightly larger than that produced by the OH group as expected because of the greater electron releasing capability of the nitrogen atom. The computed O-H BDE of para substituted phenols bearing electron withdrawing groups such as CN and NO_2 in agreement with experimental data [39]. This trend is opposite to that observed in the presence of electron releasing groups. All values except p-CN group differences in BDE against [40] reach 0.18-18.92 KJ/mol for para and meta substituted phenols. This indicates that larger basis set does not affect BDE values significantly. Differences between BDE values obtained for substituted phenol [41] with B3LYP/6-31G(d,p)//6-311+G(2d,2p) level of theory and those obtained in this work reaches 7.38 − 36 KJ/mol in the gas phase. Previous studies[42] showed that O-H BDE values of mono substituted phenol depend on the various quantum chemical methods.

Theoretical BDEs of mono-substituted phenols with strong electron withdrawing groups CN and CF_3 at ortho, para and meta positions are in 1.78 - 6.08 KJ/mol range. In NO_2 BDEs lie slightly wider by 3.43 - 42.74 KJ/mol range with respect to orho, para and meta substituted ones. The stabilization of the phenoxyl radical due to the electron releasing power of para NH_2 is computed to be slightly larger than that produced by the OH group as expected because of the greater electron releasing power of the NH_2 group. Phenols substituted with electron releasing groups such as Cl, F and CH_3O, are computed to have the same BDE in ortho and para positions. O-H BDE calculations explain that phenols with amino group in ortho and para position can exhibit high free radical scavenging activity. The calculated BDE values are smaller than IP values proving that H-atom transfer ability is more favourable than electron transfer. The obtained result show that the B3LYP/6-311G** approach may provide an accurate and economical method for predicting BDE of substituted phenols.

3.4 Ionization potentials
The value of IP represents the ease of the single electron transfer which is one of the possible mechanisms by which an antioxidant can deactivate free radicals. **Table 4** summarizes ionization potentials computed for ortho, para and meta substituted phenols. In this work, the calculated gas phase IP for non-substituted phenol reached 796.87 KJ/mol. Values that are expressed relative to the phenol molecule are denoted ΔIP = IP (X-phenol) - IP (phenol). The set of substituents contains three representative electron withdrawing groups NO_2, CF_3, CN and seven electron donating groups Br, F, Cl, CH_3, OH, OCH_3 and NH_2. IP values suggested that compounds bearing methoxy groups could act as electron donors given that the computed values were lower than that of phenol.

The halogens in ortho position induce an average of 6 KJ/mol rise in IP respectively. The IP values of phenol with the strongest electron withdrawing group (NO_2) in ortho, para and meta position were higher by 61.82, 72.27 and 65.98 KJ/mol in comparison with non-substituted phenol. Highest IP values were found for strong electron withdrawing substituents (NO_2, CF_3 & CN), while the lowest ones were obtained for strong electron donating substituents (NH_2, OCH_3 & OH). The average deviation of ΔIP values of strong electron donating substituents in ortho, para and meta positions are in 46-96 KJ/ml range. The decrease in IPs in electron donating substituted molecules is a combined result of the radical cations stabilization and the parent molecule destabilization. However, increased IPs of electron withdrawing substituted structures may stem from the combination of both the molecules and the radical cations destabilization.

The stabilization of phenoxyl radical due to the electron releasing power of the NH_2 group is computed to be slightly larger than that produced by the OH group as expected because of the greater electron releasing capability of nitrogen atom. The ortho, para and meta substituted phenol with strong electron donating group NH_2, IP values are 71.15, 125.63 and 90.89 KJ/mol lower in comparison to phenol respectively. The decrease in the IP of the molecules with OH group in the ortho, para and meta position are 48.31, 61.62 and 27.74 KJ/mol respectively. The mean absolute deviation (MAD) between ΔIP values are -4.02, 5.13 and -16.10 KJ/mol for ortho, meta and para substituted derivatives of phenol. The mean absolute deviation of 5.13 KJ/mol for this meta substituted phenol derivatives is somewhat higher than for the para and ortho substituted phenol. Of the 10 substituents p-NH_2-PhOH has ΔIP value that is too low by 125.63 KJ/mol. Klein et al [43] have investigated IP values of para and meta substituted phenols employing the B3LYP approach. Obtained trends in this work are in agreement with results for substituted phenols [43].

3.5 Spin density and frontier orbitals

The spin density is an important parameter to characterize the stability of free radicals, because the energy of a free radical can be efficiently decreased if the unpaired electron is highly delocalized through the conjugated system[44]. One of the most important parameters which can be used to characterize the antioxidant activity is also the spin density distribution in free radicals. The stability of free radicals and the antioxidant potency are mainly determined by this factor.

The spin density of the radicals studied was computed using unrestricted B3LYP/6-311G** level of theory in gas phase. The spin density was considered to be a more realistic parameter which provides a better representation of the reactivity. Table (5) lists the spin density of O atom after the H atom connected being abstracted in each radical. On the basis of obtained results the radicals formed from phenol and ortho substituted phenols, C1, C3 and C5 are centres of negative spin density while C2, C4 and C6 are centres of positive spin density.

In the case of phenol radical, the spin density is very high on O1 atom (0.429) and hence the delocalization is weak. The presence of high spin density localized on the phenol radical oxygen atom implies a high reactivity for that site. The spin density is 0.417, 0.396 and 0.393 for ortho substituted fluorine, chlorine and bromine phenols respectively. The spin population appears to be slightly more delocalized for ortho substituted bromine –phenol radical than for radicals from phenol, o-substituted chlorine, fluorine radicals respectively. As observed in **Table (5),** the spin density of O-atom after H-removed in NH_2 ortho substituted phenol radical is lower than other substituted phenol at meta and para positions. Hence the more delocalized the spin density in the radical, the easier is the radical formed and thus lower is the bond dissociation enthalpy [45,46].

The frontier molecular orbitals determine the way the molecule interacts with other species. The frontier orbital gap helps to characterize the chemical reactivity and kinetic stability of the molecule. A molecule with a small frontier orbital gap is more polarizable and is generally associated with a high chemical reactivity, low kinetic stability is also termed as soft molecule [47].

The electron density plots of the HOMO and LUMO are presented in **Figure [1]**. HOMO and LUMO are the major orbitals implicated in chemical reactions. The HOMO is delocalized on entire molecules and lone pair of electron on the oxygen atoms while the LUMO is of antibonding character with π^* distributed on core of the systems in parent molecule. The HOMO of studied substituted phenols is π-orbital while the LUMO is π^* orbital The HOMO energy describing the ability of electron-giving is an adequate parameter for representing the free radical scavenging potential of phenols. The atomic sites characterized by high density of the HOMO distribution are very susceptible to the attack of various reactive agents. In order to understand the relationship between electron delocalization and the reactivity of the radicals, one can examine the electron distribution in the highest occupied molecular orbital. In the case of meta substituted phenols HOMO is mainly localized over the entire molecule except for the CN, CF_3 and NO_2 substituted phenols. The LUMO is localized in phenyl ring and electron donating groups. Ortho substituted studied compounds have a similar distribution pattern of the frontier molecular orbitals. In para substituted molecules the HOMOs are delocalized on benzene ring and oxygen atoms are taking part in the formation of HOMOs, while LUMOs are distributed on the entire systems.

The Fukui function or frontier function is a function that describes the electron density in a frontier orbital, as a result of a small change in the total number of electrons. The condensed Fukui function or condensed reactivity indicator is the same idea, but applied to an atom within a molecule, rather than a point in three dimensional space[48]. Fukui indices indicate the reactive regions as well as nucleophilic (the site for nucleophilic attack would depend on the values of f_k^+ on the atoms with a positive charge density), electrophilic (the site for electrophilic attack will be those atoms bearing a negative charge and where the Fukui function f_k^- is a maximum and radical attack f_k^0 in the molecule[49].

Table (6) present the Fukui indices of substituted phenols evaluated with B3LYP/6-311G** level of theory. High f_k^+ , f_k^- and f_k^0 values are associated with the carbon atom of methoxy group in ortho, para and meta substituted phenols. The carbon atoms in CF_3, CH_3 and CH_3O substituents have equal value of electrophilic attack on para and meta substituted derivatives of phenols. The electrophilic attack value (f_k^-) is higher for electron donating substituents compared to electron withdrawing substituents. The f_k^- of ortho substituted NH_2 group has higher value compared to para and meta position and hence higher activity is observed. This result is consisted with BDE values of substituted phenols. The DFT based reactivity index that has found increasing applications is the dual descriptor [50,51] defined as the partial derivative at constant potential, of the electronic density ρ of an atom with respect to the number (N) of electrons of the system. The index incorporates both the electrophilicity and nucleophilicity of an atom center in a chemical reaction, from its calculation as the difference between Fukui functions for nucleophilic and electrophilic attack. The positive value indicates a site where a nucleophilic attack should be favored, a negative value indicates a site where an electrophilic attack should take place [52].

Atomic Fukui indices or reactivity indices provide information about which atoms in a molecule have a larger tendency to either loose or accept an electron. Shortly, reactivity indices specify which atoms in a molecule are more likely to undergo a nucleophilic or an electrophilic attack. Fukui indices contain two subscripts N(f_NN) or S(f_SS) corresponding to the electron density or the spin density respectively. A high positive value of f_NN for HOMO indicates the atom that is the most reactive towards electronphilic attacks (nucleophilic agent) and a high positive value of f_NN for LUMO indicates the atom that is the most reactive towards nucleophilic attacks (electrophilic agent) [53,54].

IV.   Figures and Tables

TABLE 1. ELECTRONIC ENERGIES OF ORTHO, META AND PARA SUBSTITUTED PHENOLS (ALL VALUES ARE IN HARTREE)

Substituted Species	Neutral molecule			Radical Species			Radical Cation			Anionic Species		
	Ortho	Meta	Para	Ortho	Meta	Para	Ortho	Meta	Para	Ortho	Meta	Para
Br	−2881.09	−2881.09	−2881.09	−2880.44	−2880.44	−2880.44	−2880.78	−2880.78	−2880.79	−2881.12	−2881.05	−2881.05
Cl	−767.17	−767.17	−767.17	−766.52	−766.52	−766.52	−766.86	−766.86	−766.87	−767.16	−767.13	−767.13
F	−406.81	−406.81	−406.81	−406.16	−406.16	−406.17	−406.50	−406.50	−406.51	−406.76	−406.76	−406.77
OH	−382.78	−382.79	−382.79	−382.15	−382.14	−382.15	−382.50	−382.50	−382.51	−382.72	−382.73	−382.73
CN	−399.81	−399.81	−399.81	−399.16	−399.16	−399.16	−399.49	−399.49	−399.49	−399.80	−399.81	−399.80
CH₃	−346.87	−346.87	−346.87	−346.23	−346.23	−346.23	−346.58	−346.58	−346.58	−346.82	−346.82	−346.82
CH₃O	−422.09	−422.10	−422.11	−421.46	−421.45	−421.46	−421.82	−421.82	−421.82	−422.04	−422.04	−422.06
CF₃	−644.69	−644.69	−644.69	−644.04	−644.04	−644.04	−644.37	−644.37	−644.37	−644.67	−644.67	−644.66
NH₂	−362.92	−362.92	−362.92	−362.29	−362.28	−362.29	−362.65	−362.65	−362.66	−362.87	−362.86	−362.86
NO₂	−512.11	−512.10	−512.11	−511.44	−511.45	−511.45	−511.78	−511.78	−511.77	−512.15	−512.14	−512.13

Table 2. B3LYP/6-311G** calculated bond lengths & bond angles for o, m & p substituted phenols[24]

S. No	Species	Bond length R(C-O) Å	Bond length R(O-H) Å	Bond angle θ [°]	Dihedral angle ω [°]
A	Phenol	1.367	0.963	109.1	0°
B	Phenol[a]	1.381	0.958	106.4	0°
1	o- Br-PhoH	1.359	0.963	109.12	180°
2	o -Cl-PhoH	1.358	0.963	109.1	180°
3	o -F-PhoH	1.362	0.963	108.93	180°
4	o -CN-PhoH	1.355	0.963	109.81	180°
5	o -OH-PhoH	1.365	0.962	108.67	180°
6	o -CH₃-PhoH	1.369	0.962	109.61	-60.5°
7	o -OCH₃-PhoH	1.365	0.963	108.52	-61.275°
8	o -CF₃-PhoH	1.358	0.964	110.65	-44.617°
9	o -NH₂-PhoH	1.353	0.976	104.32	-60.340°
10	o -NO₂-PhoH	1.335	0.982	106.89	0°
11	m- Br-PhoH	1.363	0.963	109.38	0°
12	m-Cl-PhoH	1.363	0.963	109.39	0°
13	m-F-PhoH	1.364	0.963	109.52	0°
14	m-CN-PhoH	1.362	0.963	109.65	-180°
15	m-OH-PhoH	1.365	0.963	109.23	-180°
16	m-CH₃-PhoH	1.368	0.963	109.08	89.706°
17	m-OCH₃-PhoH	1.366	0.963	109.16	-61.267°
18	m-CF₃-PhoH	1.363	0.963	109.61	-85.239°
19	m-NH₂-PhoH	1.368	0.962	109.16	26.935°
20	m-NO₂-PhoH	1.361	0.963	109.76	180°
21	p-Br-PhoH	1.365	0.963	109.42	0°
22	p-Cl-PhoH	1.365	0.963	109.45	0°
23	p-F-PhoH	1.368	0.962	109.33	0°
24	p-CN-PhoH	1.358	0.963	109.76	180°
25	p-OH-PhoH	1.372	0.962	109.12	180°
26	p-CH₃-PhoH	1.368	0.963	109.07	-73.685°
27	p-OCH₃-PhoH	1.372	0.962	109.03	-61.272°
28	p-CF₃-PhoH	1.361	0.963	109.58	-97.386°
29	p-NH₂-PhoH	1.374	0.962	108.91	-27.640°
30	p-NO₂-PhoH	1.356	0.963	109.88	0°

Table 3. Electronic properties of ortho, para & meta substituted phenols

Method	Species	IP	EA	η	χ	S	ω	E_g
O	Phenol	6.2206	0.3135	2.9535	3.267	0.1693	1.8069	5.9071
E	Phenol	8.2252	-1.3126	3.4563	4.7689	0.1447	3.29	9.5378
O	o-OH-PhOH	5.804	0.1048	2.8496	2.9544	0.1755	1.5315	5.6992
	p-OH-PhOH	5.6668	0.403	2.6319	3.0349	0.19	1.7498	5.2638
	m-OH-PhOH	6.0287	0.1399	2.9444	3.0843	0.1698	1.6154	5.8889
E	o-OH-PhOH	7.733	-1.4028	4.5679	3.1651	0.1095	1.0965	9.1358
	p-OH-PhOH	7.5977	-1.1773	3.2102	4.3875	0.1558	2.9983	8.775
	m-OH-PhOH	7.7338	-1.1818	4.4578	3.276	0.1122	1.2038	8.9156
O	o-Br-PhOH	6.3991	0.6765	2.8613	3.5378	0.1747	2.1871	5.7226
	p- Br-PhOH	6.2859	0.7399	2.773	3.5129	0.1803	2.2251	5.546
	m-Br-PhOH	6.5256	0.707	2.9093	3.6163	0.1719	2.2475	5.8187
E	o-Br-PhOH	8.232	0.9545	3.6388	4.5933	0.1374	2.8991	7.2775
	p-Br-PhOH	8.102	-0.7605	3.6708	4.4313	0.1803	2.6747	8.8625
	m-Br-PhOH	8.3461	-0.8009	4.5735	3.7726	0.1093	1.556	9.147
O	o-Cl-PhOH	6.4502	0.6699	2.8901	3.5601	0.173	2.1927	5.7803
	p-Cl-PhOH	6.3403	0.7519	2.7942	3.5461	0.1789	2.2501	5.5884
	m-Cl-	6.5632	0.7018	2.9307	3.6325	0.1706	2.2512	5.8614

	PhOH							
	o-Cl-PhOH	8.3032	0.0226	4.1403	4.1629	0.1208	2.0928	8.2806
E	p-Cl-PhOH	8.1808	-0.7758	3.7025	4.4783	0.135	2.7083	8.9566
	m-Cl-PhOH	8.4228	-0.84	4.6314	3.7914	0.108	1.5519	9.2628
	o-F-PhOH	6.3653	0.4248	2.9703	3.3951	0.1683	1.9403	5.9406
O	p-F-PhOH	6.2358	0.6721	2.7818	3.454	0.1797	2.1442	5.5637
	m-F-PhOH	6.4516	0.4542	2.9987	3.4529	0.1667	1.9879	5.9974
	o-F-PhOH	8.3348	-1.0953	4.7151	3.6198	0.106	1.3894	9.4301
E	p-F-PhOH	8.2047	-0.973	3.6159	4.5889	0.1383	2.9119	9.1777
	m-F-PhOH	8.4153	-1.1356	4.7755	3.6399	0.1047	1.3871	9.5509
	o-CN-PhOH	6.887	1.5775	2.6548	4.2322	0.1883	3.3735	5.3095
O	p-CN-PhOH	6.8418	1.3372	2.7523	4.0895	0.1817	3.0382	5.5046
	m-CN-PhOH	6.9264	1.6569	2.6348	4.2917	0.1898	3.4953	5.2695
	o-CN-PhOH	8.7577	-0.0509	4.4043	4.3534	0.1135	2.1515	8.8086
E	p-CN-PhOH	8.6911	-0.2389	4.2261	4.465	0.1183	2.3587	8.93
	m-CN-PhOH	8.8056	0.052	4.3768	4.4288	0.1142	2.2407	8.7536
	o-CH_3-PhOH	6.0919	0.1755	2.9582	3.1337	0.169	1.6598	5.9163
O	p-CH_3-PhOH	5.9838	0.2811	2.8514	3.1325	0.1754	1.7206	5.7027
	m-CH_3-PhOH	6.1164	0.2231	2.9466	3.1697	0.1697	1.7049	5.8932
	o-CH_3-PhOH	8.0065	-1.3297	4.6681	3.3384	0.1071	1.1937	9.3362
E	p-CH_3-PhOH	7.8609	1.2803	3.2903	4.5706	0.152	3.1745	9.1412
	m-CH_3-PhOH	8.0212	-1.2728	4.647	3.3742	0.1076	1.225	9.294
	o-CH_3O-PhOH	5.6973	-0.0057	2.8515	2.8458	0.1753	1.42	5.703
O	p-CH_3O -PhOH	6.1792	0.4359	2.8716	3.3076	0.1741	1.9048	5.7433
	m-CH_3O -PhOH	5.9757	0.1132	2.9312	3.0444	0.1706	1.581	5.8625
	o-CH_3O-PhOH	7.4996	-1.249	4.3743	3.1253	0.1143	1.1165	8.7486
E	p-CH_3O -PhOH	7.3823	-1.1963	3.4151	4.4214	0.1464	2.8621	8.8427
	m-CH_3O -PhOH	7.766	-1.3511	4.5586	3.2075	0.1097	1.1284	9.1171
	o-CF_3-PhOH	6.7436	1.0844	2.8296	3.914	0.1767	2.707	5.6592
O	p-CF_3-PhOH	6.8168	0.8479	2.9844	3.8323	0.1675	2.4606	5.9689
	m-CF_3-PhOH	6.7564	1.1048	2.7523	3.9306	0.1817	2.8066	5.6516
E	o-CF_3-PhOH	8.6316	-0.3448	4.4882	4.1434	0.1114	1.9125	8.9764

	Species							
	p-CF$_3$-PhOH	8.6929	0.5946	4.0492	4.6438	0.1235	2.6629	9.2875
	m-CF$_3$-PhOH	8.6441	-0.3495	4.4968	4.1473	0.1112	1.9125	8.9936
O	o-NH$_2$-PhOH	6.0023	0.3219	2.8402	3.1621	0.176	1.7603	5.6804
	p-NH$_2$-PhOH	5.2102	0.2158	2.4972	2.713	0.2002	1.4737	4.9944
	m-NH$_2$-PhOH	5.5422	-0.065	2.8036	2.7386	0.1783	1.3375	5.6072
E	o-NH$_2$-PhOH	7.4855	-1.2452	4.3654	3.1202	0.1145	1.1151	8.7307
	p-NH$_2$-PhOH	6.9357	-1.3367	2.7995	4.1362	0.1786	3.0556	8.2724
	m-NH$_2$-PhOH	7.2899	-1.4322	4.3611	2.9289	0.1147	0.9835	8.7221
O	o-NO$_2$-PhOH	7.0258	2.9084	2.0587	4.9671	0.2429	5.9922	4.1174
	p-NO$_2$-PhOH	7.142	2.4207	2.3606	4.7814	0.2118	4.8424	4.7212
	m-NO$_2$-PhOH	7.0244	2.6594	2.1825	4.8419	0.2291	5.3709	4.365
E	o-NO$_2$-PhOH	8.8611	1.2574	3.8019	5.0593	0.1315	3.3663	7.6037
	p-NO$_2$-PhOH	7.142	2.4207	2.3606	4.7814	0.2118	4.8424	4.7212
	m-NO$_2$-PhOH	8.9065	0.9617	3.9724	4.9341	0.1259	3.0643	7.9448

O ─ Orbital-vertical   E ─ Energy-vertical

Table 4. Calculated gas phase BDE & IP for substituted phenols at B3LYP/6-311G level of theory**

S.No	Species	Ortho				Meta				Para			
		O-H BDE (KJ/mol)	ΔBDE	IP (KJ/mol)	ΔIP	O-H BDE (KJ/mol)	ΔBDE	IP (KJ/mol)	ΔIP	O-H BDE (KJ/mol)	ΔBDE	IP (KJ/mol)	ΔIP
1	Br-PhOH	341.9	−4.27	797.3	0.40	349.8	3.67	808.5	11.61	344.5	−1.64	784.6	−12.29
2	Cl-PhOH	340.9	−5.27	804.2	7.28	350.4	4.29	815.9	19.00	342.9	−3.23	792.2	−4.67
3	F-PhOH	338.5	−7.63	807.2	10.37	350.2	4.05	815.1	18.27	338.4	−7.71	794.6	−2.29
4	OH-PhOH	326.9	−19.28	748.6	−48.31	350.4	4.22	769.1	−27.74	323.7	−22.48	735.3	−61.62
5	CN-PhOH	351.3	5.11	848.3	51.47	356.7	10.52	853.0	56.14	354.9	8.74	841.9	45.03
6	CH$_3$-PhOH	335.2	−10.94	775.6	−21.31	344.4	−1.78	799.4	2.48	338.1	−8.04	761.6	−35.30
7	CH$_3$O-PhOH	324.2	−21.96	726.8	−70.05	350.7	4.56	752.9	−44.08	323.6	−22.6	715.1	−81.73
8	CF$_3$-PhOH	359.8	13.69	836.2	39.33	353.8	7.61	837.3	40.46	357.5	11.37	842.1	45.24
9	NH$_2$-PhOH	299.3	−46.89	725.7	−71.15	342.5	−3.64	706.0	−90.89	309.8	−36.37	671.2	−125.6
10	NO$_2$-PhOH	402.3	56.14	858.7	61.82	359.6	13.40	862.9	65.98	363.0	16.83	869.1	72.27

Table 5. Spin density of ortho, meta and para substituted phenols

S. No	Atom	Substituted Species	Spin density		
			Ortho	Meta	Para
1	O1	Bromine	0.393	0.412	0.388
2	O1	Chlorine	0.396	0.425	0.409
3	O1	Fluorine	0.417	0.422	0.420
4	O1	OH	0.389	0.424	0.394
5	O1	CN	0.401	0.444	0.399
6	O1	CH$_3$	−0.306	0.419	0.412
7	O1	CH$_3$O	0.375	0.435	0.415
8	O1	CF$_3$	0.415	0.434	0.431
9	O1	NH$_2$	0.314	0.398	0.365
10	O1	NO$_2$	0.412	0.443	0.419

**Table 6. Fukui indices over the atoms of the substituted phenols at B3LYP/6-311G** level of theory.**

Species	Atom	Ortho				Meta				Para			
		f⁺	f⁻	f⁰	Δf	f⁺	f⁻	f⁰	Δf	f⁺	f⁻	f⁰	Δf
Br - PhOH	Br	−0.77	−0.304	−0.537	−0.466	−0.199	−0.264	−0.2315	0.065	−0.198	0.198	0.000	−0.396
Cl- PhOH	Cl	−0.701	−0.247	−0.474	−0.454	−0.175	−0.209	−0.192	0.034	−0.167	−0.266	−0.2165	0.099
F -PhOH	F	−0.084	−0.121	−0.1025	0.037	−0.092	−0.109	−0.1005	0.017	−0.084	−0.137	−0.1105	0.053
OH - PhOH	O	−0.075	−0.123	−0.099	0.0484	−0.067	−0.118	−0.0925	0.051	−0.062	−0.136	−0.099	0.074
	H	−0.034	−0.06	−0.047	0.026	−0.455	−0.051	−0.046	−0.404	−0.035	−0.057	−0.046	0.022
CN-Ph OH	C	−0.097	−0.066	−0.0815	−0.031	−0.11	−0.047	−0.0785	−0.063	−0.115	−0.086	−0.1005	−0.029
	N	−0.132	−0.11	−0.121	−0.022	−0.135	−0.098	−0.1165	−0.037	−0.137	−0.132	−0.1295	−0.005
CF$_3$-Ph OH	C	−0.062	−0.04	−0.051	−0.022	−0.055	−0.044	−0.0495	−0.011	−0.055	−0.039	−0.047	−0.016
	F1	−0.049	−0.048	−0.0485	−0.001	−0.065	−0.036	−0.0505	−0.029	−0.100	−0.045	−0.0725	−0.055
	F2	−0.075	−0.024	−0.0495	−0.051	−0.053	−0.039	−0.046	−0.004	−0.051	−0.047	−0.049	−0.004
	F3	−0.102	−0.36	−0.231	0.258	−0.107	−0.039	−0.073	−0.068	−0.053	−0.044	−0.0485	−0.009
CH$_3$O -Ph OH	C	0.051	0.018	0.069	0.033	0.036	−0.015	−0.0095	0.051	−0.004	−0.015	−0.0095	0.011
	H1	−0.051	−0.055	−0.053	0.004	−0.049	−0.072	−0.0555	0.023	−0.039	−0.072	−0.0555	0.033
	H2	−0.033	−0.055	−0.044	0.022	−0.048	−0.038	−0.056	−0.01	−0.074	−0.038	−0.056	−0.036
	H3	−0.078	−0.057	−0.0675	−0.021	−0.058	−0.053	−0.0365	−0.005	−0.02	−0.053	−0.0365	0.033
	O	−0.056	−0.091	−0.0735	0.035	−0.034	−0.015	−0.0395	−0.019	−0.064	−0.015	−0.0395	−0.049
CH$_3$-Ph OH	C	−0.002	−0.009	−0.0055	0.007	0.004	−0.011	−0.01	0.015	−0.009	−0.011	−0.01	0.002
	H1	−0.072	−0.048	−0.06	−0.024	−0.079	−0.044	−0.0475	−0.035	−0.051	−0.044	−0.0475	−0.007
	H2	−0.072	−0.048	−0.06	−0.024	−0.067	−0.064	−0.054	−0.003	−0.044	−0.064	−0.054	0.02
	H3	−0.044	−0.05	−0.047	0.006	0.058	−0.066	−0.0605	0.124	−0.055	−0.066	−0.0605	0.011
NH$_2$-Ph OH	N1	−0.146	0.000	−0.073	−0.146	−0.016	−0.079	−0.0485	0.063	−0.018	−0.079	−0.0485	0.061
	H1	−0.117	0.000	−0.0585	−0.117	−0.056	−0.08	−0.0635	0.024	−0.047	−0.08	−0.0635	0.033
	H2	−0.14	0.000	−0.07	−0.14	−0.073	−0.08	−0.0615	0.007	−0.043	−0.08	−0.0615	0.037
NO$_2$-PhOH	N1	−0.125	−0.024	−0.0745	−0.101	−0.105	−0.024	−0.0665	−0.081	−0.109	−0.024	−0.0665	−0.015
	O1	−0.185	−0.093	−0.139	−0.092	−0.195	−0.077	−0.136	−0.118	−0.195	−0.077	−0.136	−0.118
	O2	−0.167	−0.057	−0.112	−0.11	−0.192	−0.079	−0.138	−0.113	−0.197	−0.079	−0.138	−0.118

Figure 1. DFT (B3LYP/6-311G level) optimized geometries of o, p, and m-aminophenols with spin density values.**
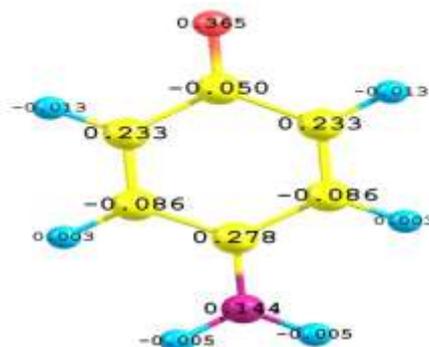
O- NH$_2$- PhOH
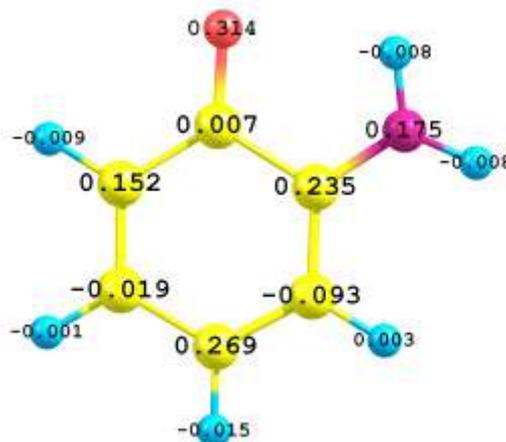
m-NH$_2$ -PhOH
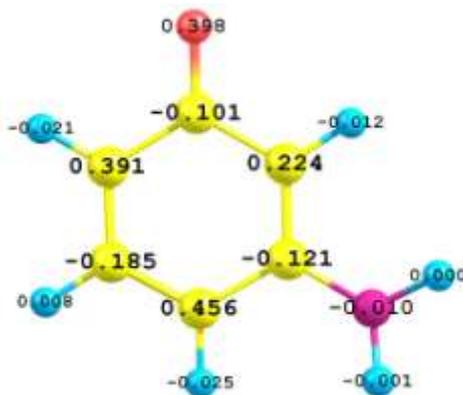
p-NH$_2$ -PhOH

V.   Conclusions

In this article, the bond dissociation enthalpies and ionization potentials of ortho, para and meta substituted phenols in the gas phase were calculated using B3LYP/6-311G** method. The set of substituents include three electron withdrawing groups and seven electron donating groups. The results showed that all substitution groups lead to the increase of average polarizability and cause more reactive than original molecule. The E$_g$ values of ortho, para and meta substituted phenol have lower values with respect to phenol except m-F-PhOH. Meta substituted donor and acceptor groups increase the hardness value with respect to phenol. The largest decrease in BDE results from the strong electron-donating NH$_2$ group. On the contrary the strong electron withdrawing NO$_2$ group results in an increase in BDE. The mean absolute deviation for BDE of ortho and para substituted phenol has reached -4.13 and -6.51 KJ/mol in the gas phase. Substituent in ortho and para positions increases the electron density at the hydroxyl groups and lowers the O-H BDE than substituent in meta position. The calculated results indicate that electron donating ortho and para substituents in the phenolic moiety weaken the O-H bond and thus increase the rate of hydrogen atom transfer. A close inspection of the total molecular energies in influence on IP compared to ortho and meta positions respectively. The present findings are consistent with published results and are excellent primary indicators of free radical scavenging activity. different charge and spin states are in the order of radical > radical cation > anion ≈ neutral. From the obtained results strong electron donating NH$_2$ group in para position found drop in IP value by 125.63 KJ/mol. For OH group in para position decrease in IP reached 61.62 KJ/mol. Halogens in para position have significantly greater.

References

[1].   K. E. Heim, A. R. Tagliaferro and D. J. Bobiliya, J. Nutr. Biochem. 13, 2002, 572.
[2].   B. Hallliwell and J. M. C. Gutteridge, Free radicals in biology and medicine, Oxford University, Oxford, 1989.
[3].   F. Gugumus, Oxidation inhibition in organic materials, (CRC, Boca Raton) 1990.
[4].   W. A. Pryor, Free Radical Biol Med 28 (2000) 141.
[5].   N. P. Das and L. Ramanathan, Biochemistry and Clinical Applications, edited by A.S. H. Ong and L. Packer, Birkhauser Verlag, Basel, 1992.
[6].   V. Cody, E. Middleton J. B. Harborne, and Alan R. Liss, Plant flavonoids in Biology and medicine:Biochemical, pharmacological and structure activity relationship, New York, 1986.
[7].   W. Bors, W. Heller, C. Michel and M. Saran, Enzymol, 186, 1990, 343.
[8].   W. J. Xin, B. L. Zhao, X. J. Li and J. W. Hou, Res. Chem. Intermed, 14, 1990, 171.
[9].   G. W. Burton and K. U. Ingold, Acc. Chem. Res. 19, 1986, 194.
[10].   H. Zweifel , Stabilization of polymeric materials, Springer, Berlin, 1997.
[11].   M. A. Kuhn, Am. J. Nurs., 103, 2003, 58.
[12].   J. Chen, J. He, L. Hamm, V. Vatuman, P. K. Whelton and Serum, Hypertension 40, 2002, 810.

[13]. M. Takashima, M. Horie, M. Shichiri, Y. Yogihara, Y. Yoshida and E. Niki, Free Radical Biol. Med., 52, 2012, 1242.
[14]. G. Aldini, K. J. Yeu, E. Niki, R. M. Russell, Biomarkers for antioxidant defense and oxidative damage: Principles and practical applications, (John Wiley & Sons, Wiley- Blackwell, USA, 2010.
[15]. R. M. B. Santos and J. A. M. Simones, J. Phys. Chem., 27, 1998, 707.
[16]. D. D. M. Wayner, E. Lusztyk, D. Page, K. U. Ingold, P. Mulder, L. J. J. Laarhoven andH. S. Aldrich, J. Am. Chem. Soc., 117, 1995, 8737.
[17]. D. D. M. Wayner, E. Lusztyk, D. Page, K. U. Ingold and P. Mulder, J. Org. Chem., 61, 1996, 6430.
[18]. G. Brigati, M. Lucarini, V. Mugnaini and G. F. Pedulli, J. Org. Chem., 67, 2002, 4828.
[19]. J. J. Warren and J. M. Mayer, Proc. Natl. Acad. Sci., USA, 107, 2010, 5282.
[20]. A. D. Becke, Chem. Phys., 98, 1993, 5648.
[21]. A. D. Becke, Phys. Rev. A, 38, 1998, 3098.
[22]. C. Lee, W. Yang and R. G. Parr, Phys. Rev. B, 37, 1988, 785.
[23]. Gaussian 03, Revision D.01, Gaussian, Inc, Pittsburgh PA, 2005.
[24]. H. Lampert, W. Mikenda and A. Karplen, J. Phys. Chem. A, 101, 1997, 2254.
[25]. U. Salzner, J. B. Lagowski, P. G. Pickup and R. A. Poirier, J. Comput. Chem., 18, 1997, 1934.
[26]. [26] K. Sadasivam and R. Kumaresan, Comput. Theor. Chem., 963, 2011, 227.
[27]. M. Oftadeh, S. Naseh and M. Hamadanian, Comput. Theor. Chem., 966, 2011, 20.
[28]. M. Leopoldini, T. Marino, N. Russo and M. Toscano, J. Phys. Chem. A, 108(22), 2004, 4916.
[29]. F. Himo, L. A. Eriksson, M. R. A. Blomberg and P. E. M. Sieghahn, tnI. J. Quantum. Chem., 76, 2000, 714.
[30]. H. Y. Zhang, Y. M. Sun and X. L. Wang, Chem Eur J, 9 2003, 502.
[31]. M. I. De Heer, H. G. Korth, P. Mulder, J Org Chem, 64, 1999, 6969.
[32]. Thavasi V, Leong L P and Bettens R P, J Phys Chem A, 110, 2006,4918.
[33]. Y. M. Sun, X. L. Wang, H. Y. Zhang and D. Z. Chen, Quant Struct-Act Relat, 20, 2001,139.
[34]. J. S. Wright, E. R. Johnson and G. A. DiLabio, J. Am. Chem. Soc., 123, 2001, 1173.
[35]. D. A. Pratt, G. A. DiLabio, G. Brigati, G. F. Pedulli and L. Valgimigli, J. Am. Chem. Soc., 123, 2001, 4625.
[36]. N. Noguchi and E. Niki, Free Radical Biol. Med., 28, 2000, 1538.
[37]. H. Y. Zhang, Quant. Struct –Act. Relat., 19, 2000, 50.
[38]. F. G. Bordwell, J. P. Cheng, M. J. Bausch and J. E. Bares, J. Phys. Org. Chem., 1, 1988, 209.
[39]. G. Maurizio, A. Riccardo and F. P. Gian, J. Org. Chem., 69, 2004, 5460.
[40]. Erik Klein and Vladimir Lukes, J. Mol. Struct. (Theochem),767, 2006,43.
[41]. Carolina A, Iriux A and Marcos C R J Mol Model. 21, 2015, 12.
[42]. Nguyen M T, Thi C N, Truc X N P, Duy Q D, Truong V N, Phan T T T and Pham C N, Am J Chem, 5(4), 2015, 91.
[43]. Klein and Lukes, J Phys Chem A, Vol 110, 44, 2006, 12312.
[44]. W. Chen, P. Guo, J. Song, W. Cao and J. Bian, Bioorg. Med. Chem. Lett., 16, 2006, 3582.
[45]. C. J. Parkinson, P. M. Mayer and L. Radom, J. Chem. Soc. Perkin Trans. 2 (11), 1999, 2305.
[46]. M. Leopoldini, I. P. Pitarch, N. Russo and M. Toscano, J. Phys. Chem. A, 108, 2004, 92.
[47]. L. Fleming, Frontier Orbitals and Organic Chemical Reactions, John Wiley and Sons, New York, 1976.
[48]. R. Bhattacharjee and R. K. Roy, Phys. Chem. Chem. Phys., 16, 2014, 22237.
[49]. R. D. Vargas-Sanchez, A. M. Mendoza-Wilson, R. R. Balandran-Quintana, G. R. Torrescano-Urrutia and A. Sanchez-Escalante, Comp. Theor. Chem., 1058, 2015, 21.
[50]. C. Cardenas, N. Rabi, P. W. Ayers, C. Morell, P. Jaramillo and P. Fuentealba, J. Phys. Chem. A, 113, 2009, 8660.
[51]. J. I. Martinez-Araya , J. Math. Chem., 53, 2015, 451.
[52]. J. L. Gazquez, J. Mex. Chem. Soc., 52, 2008, 3.
[53]. J. S. Murray, F. Abu-Awwad and Politzer, J. Mol. Struct. (Theochem), 501, 2000, 241.
[54]. R. R. Contreras, P. Fuentealba, M. Galvan and P. Perez, Chem. Phys. Lett., 304, 1999, 405.