Novel Trolox Derivatives as Antioxidant: A DFT Investigation

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Abstract:

In this paper the antioxidant activity of Trolox derivatives investigated by density function theory and polarization continuum model as solvent model in order to propose the novel derivatives with higher antioxidant activity. The effects of various ortho and meta substituents on the reaction enthalpies of antioxidant mechanisms of Trolox investigated. Also the effects of reducing the number of atoms in the heterocyclic ring and replacing the oxygen heteroatom of Trolox with other heteroatoms on the antioxidant activity of Trolox evaluated. Results show that the NH_2, OH and NHMe substituents in meta and ortho positions decrease the BDE and IP values and increase the antioxidant activity. The derivatives *e, c* and *d* with NH, S and Se instead of O have higher antioxidant activity. Obtained results show that reducing the number of atoms in the heterocyclic ring (derivatives *a* and *b*) decrease the BDE and IP values and increase the antioxidant activity of Trolox. The linear dependencies between BDE and IP values of studied Trolox derivatives and corresponding E_{HOMO} and R(O–H) values can be useful to propose novel derivatives with high antioxidant activity.

Keywords:

27   Trolox, Antioxidant, Free Radical, Mechanism, BDE and IP.

28   **Running Title:**

29   Antioxidant activity of Trolox

30

31   **1 Introduction**

32   Natural and synthesized antioxidants can avoid or at least reduce the peroxidation of lipids by free

33   radicals in body.[1] Biological antioxidant defense systems eliminated the excess free radicals,

34   however the weakness of the defense systems in body causes oxidative damage to lipids, proteins,

35   and DNA. Among the antioxidants, Trolox is important lipid soluble peroxyl radical trapping

36   antioxidants that reduce the oxidative degradation of lipids and proteins.[2] The diverse biological

37   activities of Trolox as antioxidant and free radical scavengers are well known. The Trolox (Figure

38   1) acts as an effective inhibitor of lipid peroxidation in membrane systems.[3]

39   The Trolox as phenolic antioxidant (ArOH) inhibit oxidation via two major mechanisms.[4] In

40   hydrogen atom transfer (HAT) mechanism, the phenolic hydrogen atom is transferred. In single

41   electron transfer followed by proton transfer (SET–PT) mechanism, cation radical is formed.[5] The

42   bond dissociation enthalpy (BDE) of the phenolic O–H bond is one of the important parameters in

43   evaluating the HAT antioxidant action; the lower the BDE, the easier the dissociation of the phenolic

44   O–H bond.[5] Ionization potential (IP) represent enthalpy of the first step of SET–PT process.[6] In the

45   SET–PT mechanism, the ionization potential (IP) is the most significant parameter; the lower the IP

46   value, the easier the electron abstraction.[7]

47   The great deals of effort have been devoted to design novel derivatives with high efficiently in order

48   to development of natural antioxidant.[8] Previous studies as compared with phenolic antioxidant

49   show that, the antioxidant activity of Trolox mainly come from its heterocyclic ring, the heteroatom

50   and the substituted methyl groups.[9] The high antioxidant activity of Trolox aroused our interest to

51   investigate the antioxidant activity of Trolox and 30 novel Trolox derivatives. In this article, the

52 possible ways to increase the antioxidant properties of Trolox have been investigated with density

53 function theory (DFT) in gas phase and polarization continuum model (PCM) as solvent method.

54 Generally, there are three ways to propose the novel Trolox derivatives with higher antioxidant

55 activity: (1) The replacement of methyl group by various ortho and meta substituents, (2) Reducing

56 the number of atoms in the heterocyclic ring and (3) The replacement of oxygen heteroatom with

57 other atoms. In this paper, the methyl groups on the aromatic ring of Trolox were replaced with

58 various substituents and the effects of these various substituents on antioxidant activity of Trolox

59 have been investigated. Also the effects of the reducing the size of heterocyclic ring and the

60 replacing oxygen with other heteroatoms on the antioxidant activity of Trolox have been

61 investigated. The antioxidant activity of novel Trolox derivatives were compared with

62 corresponding values of Trolox. These comparisons can be useful for designing novel Trolox

63 derivatives with high antioxidant activity. Also in this paper the dependences between calculated

64 BDE and IP values with O–H bond lengths and E_{HOMO} values have been also investigated. This can

65 be useful in the selection of suitable candidates to propose novel Trolox derivatives with enhanced

66 antioxidant activity.

67 **< Figure 1>**

68 **2 Computational details**

69 The geometry of studied Trolox derivatives and their respective radicals and cation radicals were

70 optimized using the DFT method with B3LYP functional and the 6–31G (d, p) basis set.[10, 11] Single

71 point calculations were performed using 6–311++G (2d, 2p) basis set.[12, 13] The optimized structures

72 were confirmed to be real minima by frequency calculations. All reported enthalpies were zero point

73 (ZPE) corrected with unscaled frequencies. In present paper we chosen the water as polar solvent

74 and the solvent contribution to the total enthalpies was computed by polarization continuum model

75 (PCM) that presents good accuracy, reliability, adaptability, and a reduced computational effort in

76   describing solvent effects.[8, 9] All calculations were performed using Gaussian 03 program package.[14]

77   All enthalpies were calculated for 298.15 K and 1.0 atmosphere pressure.

78   **3 Results and discussion**

79   **3.1 The BDE and IP values of substituted Troloxs**

80   In previous studies, the substituent effect on reaction enthalpies of substituted phenols have been

81   investigated in gas phase and solvent and results shown that DFT/B3LYP and PCM methods

82   describe the substituent effect in very good agreement with corresponding experimental results.[15,]

83   [16]

84   This work represents the first theoretical systematic study of BDE and IP values of substituted

85   Trolox derivatives. For the whole HAT and SET–PT mechanism energetics knowledge, it is

86   important to investigate the substituent effect on the BDE and IP values for substituted Trolox

87   derivatives. Replacing the Me groups of Trolox with various substituents can be considered as a

88   suitable way to improve the antioxidant activity of Trolox. In this section we investigated the effect

89   of various substituents on the reaction enthalpies of antioxidant mechanisms of Trolox in order to

90   find the suitable substituents that can decrease the BDE and IP values and increase the antioxidant

91   activity of Trolox.

92   The computed BDE and ΔBDE values for ortho and meta substituted Trolox derivatives (Figure 1)

93   are reported in Table I. The calculated BDE of Trolox reached 381.8 and 370.1 kJ/mol in gas phase

94   and water, respectively. For ortho NMe_2, NH_2 and NHMe substituted Trolox derivatives the BDE

95   values are lower ca 34.0–38.2 and 25.5–29.9 kJ/mol in comparison to Trolox, in gas phase and

96   water, respectively.

97   The NMe_2, NH_2 and NHMe groups in meta position decrease the BDE values of Trolox ca 21.8–

98   23.8 and 14.2–17.8 kJ/mol in gas phase and water, respectively. For ortho OH substituted Trolox

99   the BDE values are lower than Trolox ca 27.7 and 20.2 kJ/mol in gas phase and water, respectively.

100   The OH group in meta position decrease the BDE values of Trolox ca 20.3 and 13.1 kJ/mol, in gas

101 phase and water, respectively. For ortho substituted Trolox with alkyl groups, the BDE values are

102 6.9–11.6 and 4.0–6.8 kJ/mol lower than Trolox in gas phase and water, respectively. The alkyl

103 groups in meta position decrease the BDE values of Trolox ca 4.4–6.7 and 2.9–4.1 kJ/mol, in gas

104 phase and water, respectively.

105 The computed IP and ΔIP values for substituent Troloxs in gas phase and water are reported in Table

106 II. The calculated IP for the Trolox reached 689.8 and 432.5 kJ/mol in gas phase and water,

107 respectively. Calculated results reveal that lower IP values were found for strong EDG substituents

108 (NMe_2, NH_2, and NHMe). For ortho substituted Trolox with strong EDGs NMe_2, NHMe and NH_2;

109 IP values are lower ca 74.7–77.3 and 53.6–59.0 kJ/mol in comparison to Trolox in gas phase and

110 water, respectively. The NMe_2, NH_2, and NHMe in the meta position induce 60.1–61.2 and 47.1–

111 48.3 kJ/mol decrease in IP in comparison to Trolox in gas phase and water, respectively.

112 Decreases in IP of the Trolox with OH group are ca 48.1–63.1 and 33.7–44.5 kJ/mol in gas phase

113 and water, respectively. The IP values of Trolox with the alkyl groups are lower ca 19.0–33.3 and

114 12.7–21.4 kJ/mol in comparison to Trolox in gas phase and water, respectively.

115 The decrease in BDE and IP values in EDG–substituted Trolox derivatives is a combined result of

116 the radicals and radical cations stabilization and the parent molecules destabilization.

117 The theoretical and experimental BDE and IP values of substituted phenols are compiled in Table

118 III in the gas phase and water.[17–22] Obtained results in present work about the substituent effect

119 trends on the BDE and IP of Trolox derivatives are in agreement with reported results in Table III.

120 These studies on the substituted phenols shows that, the substituents in ortho or para positions exert

121 stronger influence upon BDE and IP when compared with same substituents in meta positions.

122 Computed BDE and IP values of substituted Trolox derivatives show the same trend, namely,

123 substituents in ortho positions exert stronger influence upon BDE and IP than substituents in meta

124 position. Results show that Trolox derivatives with lower BDE and IP values have higher

125 antioxidant activity in compaction to Trolox. Therefore, calculated results show that replacing the

126 Me group in Trolox with higher electron donating group such as the NHMe, NH_2 and OH in ortho

127 position can improve the antioxidant activity of Trolox.

128 <center>**<Table I>, <Table II>, <Table III>**</center>

129 **3.2 The BDE and IP values of Trolox derivatives *a* and *b***

130 The reducing the number of atoms in the heterocyclic ring of Trolox can be considered as a suitable

131 way to improve the antioxidant properties of Trolox. In previous studies Grisar et al. designed the

132 structure analogue based on structure *a*, and also reported that this compound has an inhibition rate

133 1.8 times higher than that of α–tocopherol on free radical.[23, 24] In this section we investigated the

134 effect of heterocyclic ring size on reaction enthalpies of antioxidant mechanisms of Trolox. The

135 main aim of this section is identify of the novel Trolox derivatives with higher antioxidant activity.

136 Figure 1 shows novel structures (*a* and *b*) obtained by reducing the number of atoms in the

137 heterocyclic ring.

138 The computed BDE and IP values for novel derivatives *a* and *b* in gas phase and water are reported

139 in Table IV. The BDE value decreases from 337.8 to 344.6 and 337.1 to 340.3 kJ/mol in the **a** to **b**

140 structure in the gas phase and water, respectively; also the IP value decreases from 630.1 to 640.9

141 and 386.3 to 393.5 kJ/mol in gas phase and water, respectively. An inspection of the ΔBDE values

142 appearing in Table IV shows that reducing the number of atoms in the heterocyclic ring from 6

143 (Trolox) to 5 (structure *b*) and 4 (structure *b*) causes a decrease ca 37.2–44.4 and 29.8–33.0 kJ/mol

144 in gas phase and water, respectively. Also, the IP value of Trolox decreases ca 48.9–59.7 and 39.1–

145 46.2 kJ/mol by reducing the number of atoms in the heterocyclic ring from 6 to 5 and 4 in gas phase

146 and water, respectively. The p–type orbital of the oxygen atom in the heterocyclic ring of Trolox

147 can delocalize the unpaired electrons improving the stability of the phenoxyl radical and phenoxyl

148 cation radical. The computed results indicated that the hydrogen atom and electron donating ability

149 increase with reducing the number of atoms in the heterocyclic ring of Trolox. Therefore the

150 antioxidant activity of derivatives *a* and *b* are higher than Trolox.

<center>6</center>

3.3 The BDE and IP values of Trolox derivatives *c–j*

In this section, the effects of replacing the oxygen heteroatom with other heteroatoms on the antioxidant activity of the Trolox were investigated. Accordingly, S, Se, NH, PH, AsH, CH$_2$, SiH$_2$ and GeH$_2$ groups were replaced with oxygen hetroatom in Trolox. The derivatives obtained by replacing the oxygen heteroatom with other mentioned heteroatoms are shown in Figure 1 (derivatives *c–j*). Finding the effect of each heteroatom on the reaction enthalpies of antioxidant mechanism can be very important and useful to propose novel antioxidant structures with high performance.

In previous studies the novel derivatives of vitamin E that oxygen heteroatom replacing with Sulfur (S) and selenium (Se) heteroatom have been synthesized experimentally and results (EPR equilibration technique) show that the BDE value of vitamin E can be decreased ca 4 kJ/mol by replacing the oxygen heteroatom with selenium (Se) heteroatom approximately.[25] In previous study the obtained experimental results reveal that *e* derivative has higher antioxidant than Trolox because nitrogen has less electronegative than oxygen and high ability via conjugate delocalization of its lone pair of electrons to stabilize a neighboring radical center.[26]

The computed BDE and IP values of novel derivatives *c–j* are reported in Table IV. Results show that BDE and IP values of derivatives *c* and *d* are lower than the corresponding values of Trolox in gas phase and water. The differences between BDE value of derivatives *c* and *d* with Trolox in gas phase are 21.8 and 17 kJ/mol, respectively. Results show that the BDE values of derivatives *c* and *d* in water are lower than Trolox 12.1 and 11.7 kJ/mol, respectively. Results show that these differences between the IP values of derivatives *c* and *d* and corresponding value for Trolox in gas phase are 39.1 and 32.6 kJ/mol, respectively. Also IP values of derivatives *c* and *d* in water are lower than Trolox ca 25.7 and 17.6 kJ/mol, respectively. Therefore, the antioxidant activities of derivatives *c* and *d* are slightly higher than Trolox in gas phase and water.

175   Calculated BDE and IP values for derivative *e* are lower than the corresponding values of Trolox in

176   gas phase and water. Obtained results show that differences between BDE values of derivative *e*

177   with Trolox are ca 48.4 and 37.8 kJ/mol in gas phase and water, respectively. Also results show that

178   differences between IP values of derivative *e* with Trolox are ca 67.3 and 54.2 kJ/mol in gas phase

179   and water, respectively. It is due to nitrogen have less electronegative than oxygen and it able to

180   stabilize a radical or radical cation form by conjugative delocalization comfortably and therefore

181   derivative *e* have lower BDE and IP values and higher antioxidant activity in comparison to Trolox

182   in gas phase and water.

183   Calculated results show that the BDE values of derivatives *f* and *g* were lower than the

184   corresponding value of Trolox ca 8.0 and 7.5 kJ/mol in water and ca 16.7 and 13.0 in gas phase,

185   respectively. Also calculated results show that the IP values of derivatives *f* and *g* were lower than

186   the corresponding value of Trolox ca 33.8 and 22.9 kJ/mol in gas phase and ca 16.9 and 9.6 in water,

187   respectively.

188   Computed results show that the BDE and IP values for other studied derivatives (*h*, *i* and *j*) are

189   higher than corresponding values of Trolox in gas phase and water. A fundamental reason can be

190   related to the lack of the lone pair of electrons in the case of CH_2, SiH_2 and GeH_2 groups. Therefore,

191   these groups are not able to stabilize a radical or radical cation formed from the first step of HAT

192   and SET–PT mechanisms. According to obtained results, replacing the oxygen heteroatom with

193   other heteroatoms such as NH, S and Se is a suitable way to propos novel Trolox derivatives with

194   higher antioxidant activity than Trolox in gas phase and water.

195   <div align="center">**<Table IV>**</div>

196   **3.4 The E_{HOMO} and R(O–H) values of studied Trolox derivatives**

197   To accelerate the discovery of novel antioxidants, considerable effort has been devoted to

198   investigating the structure activity relationships for antioxidants. The energy of the highest occupied

199   molecular orbital (E_{HOMO}) represents an alternative parameter to assess the electron donating ability

200 of antioxidants. This is widely used in the antioxidant study because of the simple calculation

201 procedure, where the only calculation for parent molecule is required.[27, 28] The E_{HOMO} represents an

202 applicable parameter for prediction of antioxidant activity and oxidant scavenging ability via SET–

203 PT mechanism.[29] As a general rule, the higher the E_{HOMO}, the more active the compound is as an

204 antioxidant.[30]

205 The computed E_{HOMO} values of ortho and meta substituted Troloxs and derivatives *a–j* are

206 summarized in Table V. The orbital spatial distribution of HOMO and LUMO optimized structure

207 of some Trolox derivatives are drown in figure 2. Obtained E_{HOMO} values for Trolox is –5.1 eV.

208 Results show that EWG–substituents increase the absolute E_{HOMO} values and EDG–substituents

209 decrease the absolute E_{HOMO} values in comparison to corresponding value of Trolox. Therefore,

210 Trolox derivatives with strong EDGs such as NHMe, NH_2 and OH are better electron donors, i.e.

211 they enter SET–PT mechanism more easily and have lower IP values and have higher antioxidant

212 activity.

213 The computed E_{HOMO} values of derivatives *a* and *b* are less negative that Trolox. Therefore,

214 derivatives *a* and *b* are better electron donors and high antioxidant activity than Trolox. An

215 inspection of Table V results reveal that replacing the oxygen heteroatom with S and Se heteroatom,

216 cause the E_{HOMO} become less negative and these derivatives should possess the higher radical

217 trapping potential than Trolox. Replacements of oxygen heteroatom with NH heteroatom cause a

218 sharp decrease in the absolute value of E_{HOMO}. On country other heteroatom increased the absolute

219 value of E_{HOMO} and cause corresponding derivatives have lower radical trapping potential than

220 Trolox. Therefore obtained results show that E_{HOMO} as suitable antioxidant scale can predict the

221 antioxidant activity of studied Trolox derivatives.

222 In previous studies[17-22] about antioxidant activity of mono substituted anilines, phenols and

223 thiophenols, it is found that B3LYP/6–311+G (2d,2p) method significantly underestimates vertical

224 the ionization potentials obtained from E_{HOMO} according to the Koopmans' theorem. Therefore, we

225   decided to find expected linear dependence between calculated IPs and corresponding E_{HOMO} values

226   for studied Trolox derivatives. For ortho and meta substituted Troloxs and derivatives **a–j**,

227   correlation coefficients reached 0.94, 0.92 and 0.91, respectively. Obtained equations are as follows:

228   *IP (kJ/mol) = – 435 E_{HOMO} (eV) – 1543*   *(ortho substituted derivatives)*

229   *IP (kJ/mol) = – 227 E_{HOMO} (eV) – 479*   *(meta substituted derivatives)*

230   *IP (kJ/mol) = – 278 E_{HOMO} (eV) – 735*   *(derivatives **a–j**)*

231   The linearity of finding dependences can be considered satisfactory and corresponding equations

232   may be used to rough estimation of IP values from corresponding E_{HOMO} in studied Trolox

233   derivatives or vice versa.

234   In previous studies[17, 20, 22] results show that BDE values of substituted phenols are linearly dependent

235   on the calculated length of the phenolic O–H bond. In this paper the calculated values of R(O–H)

236   bonds corresponding to studied Trolox derivatives tabulated in Table V. The R(O–H) bond length

237   related to Trolox is 0.967 Å. In this work, the dependencies between BDE values of ortho and meta

238   Trolox derivatives and derivatives **a–j** with corresponding R(O–H) values investigated and the

239   correlation coefficients reached 0.96, 0.93 and 0.94, respectively. Obtained equations from the linear

240   regressions are as follows:

241   *BDE (kJ/mol) = 100833 R (O–H, Å) – 97113*   *(ortho substituted derivatives)*

242   *BDE (kJ/mol) = 83944 R (O–H, Å) – 80863*   *(meta substituted derivatives)*

243   *BDE (kJ/mol) = 120676 R (O–H, Å) – 116614*   *(derivatives **a–j**)*

244   Obtained equations enable fast BDE estimations for studied Trolox derivatives from the computed

245   R(O–H) values. The linearity of finding dependences can be considered satisfactory and

246   corresponding equations may be used for rough estimation of BDE values from corresponding R(O–

247   H) in studied Trolox derivatives or vice versa. These linear dependencies between IP and BDE with

248   E_{HOMO} and R(O–H) values of studied Trolox derivatives can be useful in the selection of suitable

249   candidates for the synthesis of novel Trolox derivatives with enhanced antioxidant properties.

250   **<Table V>, <Figure 2>**

251   4 Conclusions

252 In this study, the possible ways for increasing the antioxidant activity of Trolox have been

253 investigated with density function theory in gas phase and polarization continuum model in water.

254 The reaction enthalpies related to the individual steps of antioxidant action mechanisms, HAT and

255 SET–PT for novel antioxidant based on Trolox were calculated. Calculated results show that

256 replacing methyl groups with substituents such as NH_2, OH and NHMe in ortho position can

257 improve the antioxidant activity of Trolox. Results reveal that the derivative *e* with NH hetroatom

258 is better antioxidant than Trolox, due to nitrogen have less electronegative than oxygen and it able

259 to stabilize radical center by conjugative delocalization comfortably and therefore derivative *e* have

260 lower BDE and IP values in comparison to Trolox. Also results show that derivatives *c* and *d* with

261 S and Se heteroatoms, respectively have lower BDE and IP values in comparison to corresponding

262 values of Trolox in gas phase and water. In addition, the results reveal that reducing the number of

263 atoms in the heterocyclic ring is a suitable way to propose novel Trolox derivatives (*a* and *b*) with

264 lower BDE and IP values and higher antioxidant activity. Obtained theoretical results in present

265 paper about antioxidant activity of Trolox derivatives are in agreement with corresponding

266 published experimental values, successfully. The obtained results show that the IP and BDE values

267 of novel Trolox derivatives can be predicted from their corresponding E_{HOMO} and R(O–H) values

268 successfully, respectively. These linear dependencies can be useful for the development of novel

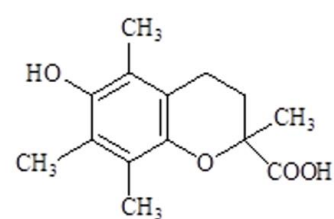269 derivatives with high antioxidant activity based on Trolox.

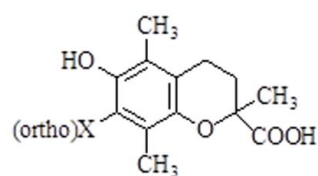## 272   References:

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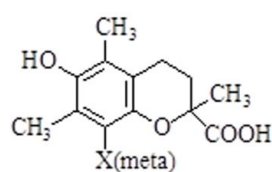314   30. H. Y. Zhang, *J. Am. Oil Chem. Soc.* **75** (1998) 1705

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317   **Figure 1.** Structures of Trolox and Trolox derivatives that studied in this work (X= NMe_2, NH_2,
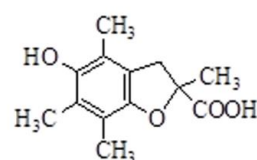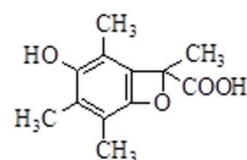318   NHMe, OMe, OH, Ethyl, CH=CH$_2$, Me, t–Bu).

Trolox

ortho substituted Troloxs   **meta substituted Troloxs**   < a >   < b >

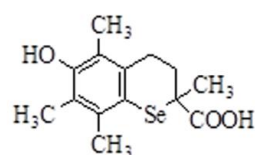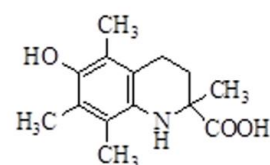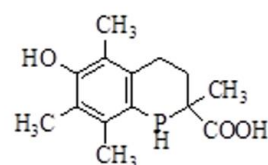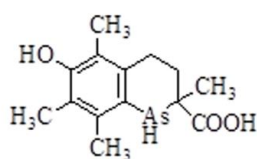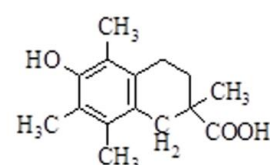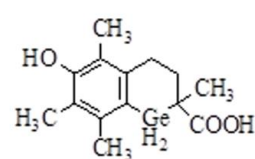< c >   < d >   < e >   < f >

< g >   < h >   < i >   < j >

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Figure 2. Orbital spatial distribution of HOMO and LUMO optimized structure of the Trolox, Trolox derivatives *a–e* and ortho NMe$_2$ (2), NH$_2$ (3), NHMe (4) and OH (5) substituted Trolox derivatives.
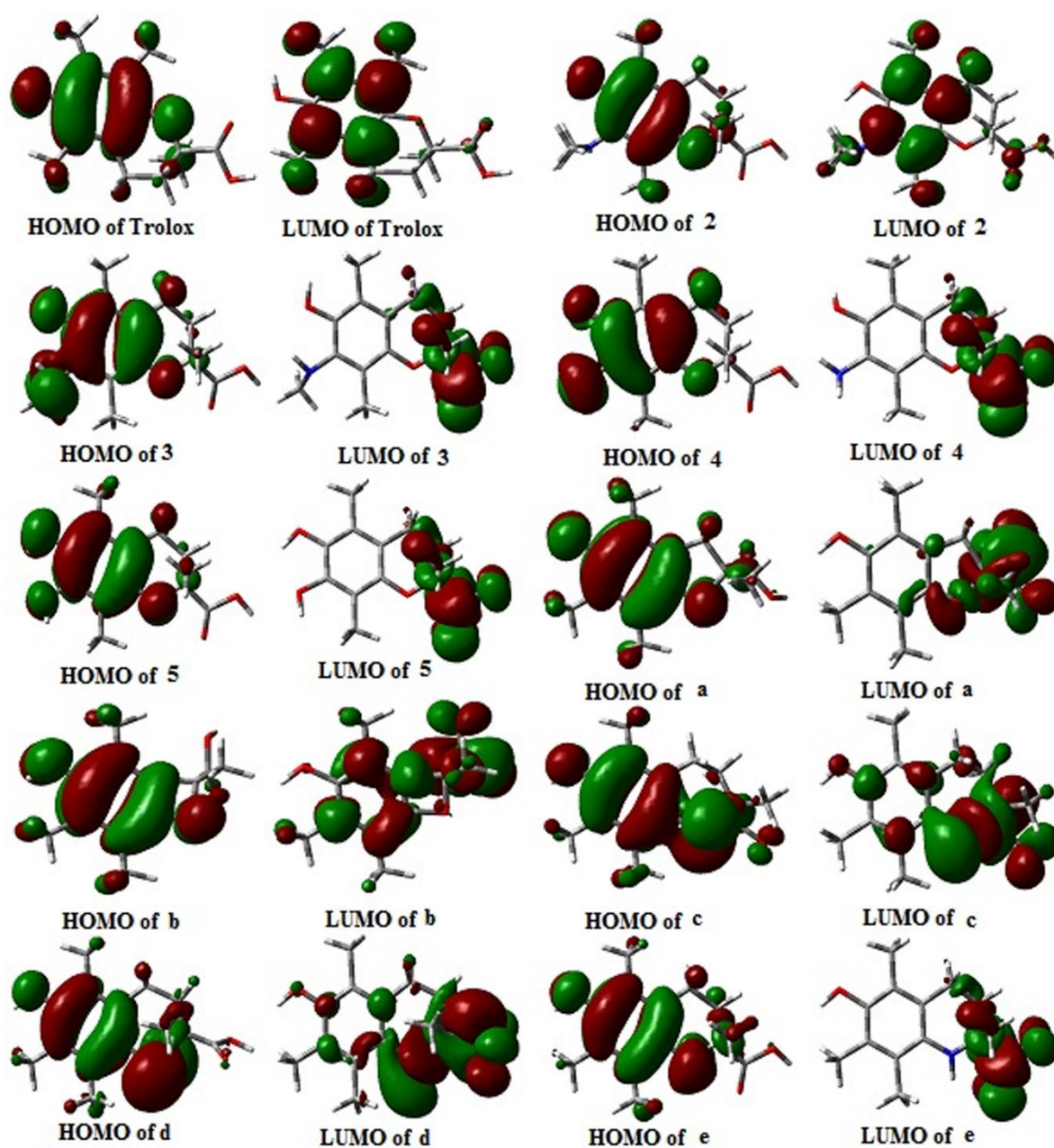

HOMO of Trolox LUMO of Trolox HOMO of 2 LUMO of 2

HOMO of 3 LUMO of 3 HOMO of 4 LUMO of 4

HOMO of 5 LUMO of 5 HOMO of a LUMO of a

HOMO of b LUMO of b HOMO of c LUMO of c

HOMO of d LUMO of d HOMO of e LUMO of e

328   **Table I.** Calculated BDE and ΔBDE (kJ/mol) values of substituted Trolox derivatives.

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Gas					Water			
ortho			meta		ortho		meta	
Derivatives	BDE	ΔBDE	BDE	ΔBDE	BDE	ΔBDE	BDE	ΔBDE
Trolox	381.8	0.0	381.8	0.0	370.1	0.0	370.1	0.0
NMe$_2$	347.9	-34.0	360.0	-21.8	344.6	-25.5	355.9	-14.2
NHMe	345.3	-36.6	358.0	-23.8	342.0	-28.1	354.1	-16.0
NH$_2$	343.6	-38.2	358.4	-23.4	340.2	-29.9	352.3	-17.8
OH	354.1	-27.7	361.5	-20.3	349.9	-20.2	357.0	-13.1
OMe	361.6	-20.3	368.9	-12.9	354.5	-15.6	361.6	-8.5
t–Bu	370.2	-11.6	375.1	-6.7	363.3	-6.8	366.0	-4.1
Me	371.7	-10.1	374.6	-7.2	363.8	-6.2	365.2	-4.8
Ethyl	372.1	-9.7	373.6	-8.2	363.8	-6.3	365.5	-4.6
CH=CH$_2$	375.0	-6.9	377.4	-4.4	366.1	-4.0	367.1	-2.9

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332 **Table II.** Calculated IP and ΔIP (kJ/mol) values of substituted Trolox derivatives.

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	Gas				Water			
	ortho		*meta*		*ortho*		*meta*	
Derivatives	*IP*	*ΔIP*	*IP*	*ΔIP*	*IP*	*ΔIP*	*IP*	*ΔIP*
Trolox	689.8	0.0	689.8	0.0	432.5	0.0	432.5	0.0
NMe₂	612.5	-77.3	629.7	-60.1	373.5	-59.0	385.4	-47.1
NHMe	614.8	-74.9	628.5	-61.2	375.8	-56.8	384.6	-47.9
NH₂	615.1	-74.7	629.6	-60.1	379.0	-53.6	384.2	-48.3
OH	626.7	-63.1	641.6	-48.1	388.1	-44.5	398.9	-33.7
OMe	639.4	-50.4	652.1	-37.7	400.4	-32.1	411.3	-21.3
t–Bu	656.4	-33.3	670.8	-19.0	411.2	-21.4	419.8	-12.7
Me	658.2	-31.5	670.3	-19.5	412.6	-20.0	419.4	-13.1
Ethyl	657.7	-32.0	669.8	-20.0	411.8	-20.8	419.9	-12.7
CH=CH₂	663.8	-26.0	672.8	-17.0	415.8	-16.7	423.0	-9.6

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336 **Table III.** Experimental and theoretical ΔBDE and ΔIP (kJ/mol) values of substituted phenols.[17-22]

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	ΔBDE			ΔIP		
		Theoretical				Theoretic
Substituent	Experimenta	Gas	Wate	Experimenta	Gas	Wate
NMe₂	–40	–43	–31	–67	–71	–66
NHMe	–35	–38	–23	–74	–79	–74
NH₂	–35	–38	–22	–68	–72	–63
OH	–20	–24	–21	–45	–48	–40
OMe	–13	–16	–17	–22	–23	–29
t–Bu	–5	–7	–2	–10	–12	–8
Me	–2	–4	–4	–8	–10	–8
Ethyl	–2	–3	–1	–15	–17	–5
CH=CH₂	–2	–3	3	–7	–6	–11

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341 **Table IV.** Calculated BDE, ΔBDE, IP and ΔIP (kJ/mol) values of Trolox and Trolox derivatives *a*–
342 *j*.
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	Gas		Water		Gas		Water	
Derivatives	*BDE*	*ΔBDE*	*BDE*	*ΔBDE*	*IP*	*ΔIP*	*IP*	*ΔIP*
Trolox	381.8	0.0	370.1	0.0	689.8	0.0	432.5	0.0
a	337.8	-44.0	337.1	-33.0	630.1	-59.7	386.3	-46.2
b	344.6	-37.2	340.3	-29.8	640.9	-48.9	393.5	-39.1
c	360.0	-21.8	357.9	-12.1	650.7	-39.1	406.8	-25.7
d	364.8	-17.0	358.4	-11.7	657.2	-32.6	415.0	-17.6
e	333.4	-48.4	332.3	-37.8	622.5	-67.3	378.3	-54.2
f	365.1	-16.7	362.1	-8.0	656.0	-33.8	415.6	-16.9
g	368.8	-13.0	362.5	-7.5	666.9	-22.9	422.9	-9.6
h	393.3	11.5	377.6	7.6	708.7	18.9	441.2	8.7
i	396.0	14.2	379.2	9.1	710.8	21.0	443.7	11.1
j	399.7	17.9	381.2	11.1	714.9	25.2	447.1	14.5

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346 **Table V.** Calculated E_{HOMO} (eV) and R(O–H, Å) of studied Trolox derivatives.

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Derivative	E_{HOM}	R(O–H)	Derivative	E_{HOM}	R(O–H)	Derivative	E_{HOM}	R(O–H)
Trolox	-5.10	0.96679	*Trolox*	-5.10	0.9667	*a*	-4.89	0.9692
o-NMe₂	-4.92	0.96653	*m-NMe₂*	-4.92	0.9676	*b*	-4.92	0.9692
o-NHMe	-4.90	0.96659	*m-NHMe*	-4.89	0.9675	*c*	-5.02	0.9692
o-NH₂	-4.98	0.96654	*m-NH₂*	-4.84	0.9675	*d*	-5.05	0.9692
o-OH	-4.99	0.96660	*m-OH*	-4.98	0.9676	*e*	-4.85	0.9691
o-OMe	-5.04	0.96660	*m-OMe*	-5.05	0.9676	*f*	-5.08	0.9694
o-t–Bu	-5.02	0.96671	*m-t–Bu*	-5.02	0.9677	*g*	-5.10	0.9694
o-Me	-5.04	0.96684	*m-Me*	-5.02	0.9677	*h*	-5.12	0.9695
o-Ethyl	-5.05	0.96682	*m-Ethyl*	-5.06	0.9677	*i*	-5.15	0.9696
o-CH=CH₂	-5.08	0.96679	*m-CH=C*	-5.09	0.9678	*j*	-5.16	0.9696

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