Electronic Supplementary Information

A Physicochemical Examination of the Free Radical Scavenging Activity of Trolox: Mechanism, Kinetics and Influence of the Environment

Dr. Marta E. Alberto,[1] Prof. Nino Russo,[1] Prof. Andre Grand,[2] Prof. Annia Galano[3*]

[1]*Dipartimento di Chimica - University of Calabria, Arcavacata di Rende, (CS), 87036, Italy.*

[2]*INAC/SCIB UMR E-3 CEA/UJF; CEA-Grenoble 1è Rue des Martyrs, 38054 Grenoble Cedex 9, France.*

[3]*Departamento de Química. Universidad Autónoma Metropolitana-Iztapalapa. San Rafael Atlixco 186, Col. Vicentina. Iztapalapa. C. P. 09340. México D. F. México.*

Contents

* To whom correspondence should be addressed. E-mail: agal@xanum.uam.mx

Table 1S. Gibbs free energies of reaction (ΔG, kcal/mol), at 298.15 K.

path	R1 (I)	R1 (II)	R2 (I)	R2 (II)	R3 (I)	R3 (II)	R4 (I)	R4 (II)
SET	43.24	-7.44	64.38	16.13	56.35	10.65	54.18	11.41
HT-1a	-39.60	-43.51	-5.70	-10.40	-22.52	-26.97	-4.75	-10.22
HT-2a	-28.70	-32.28	5.19	0.83	-11.63	-15.74	6.14	1.01
HT-3a	-29.36	-31.41	4.53	1.69	-12.28	-14.88	5.49	1.88
HT-6a	-29.79	-30.89	4.10	2.21	-12.71	-14.35	5.06	2.40
HT-7	-32.22	-30.89	1.67	2.21	-15.14	-14.35	2.63	2.40
HT-8	-20.28	-22.48	13.61	10.63	-3.20	-5.94	14.57	10.82
HT-9a	-16.82	-19.54	17.07	13.57	0.26	-3.00	18.03	13.75
RAF-1	-17.06	-17.57	14.04	10.75	1.00	-5.06	16.00	11.90
RAF-2	-12.61	-13.34	17.03	15.26	6.16	-0.65	15.35	14.98
RAF-3	-13.44	-14.57	13.33	12.40	-0.47	-3.47	13.74	13.69
RAF-4	-14.34	-12.82	14.80	13.98	3.89	0.30	16.38	13.16
RAF-5	-10.22	-9.36	18.24	15.32	6.14	3.37	16.29	15.82
RAF-6	-15.00	-15.67	16.21	11.05	2.43	-2.26	16.86	11.71

(I) pentyl ethanoate solution, (II) aqueous solution

R1 ≡ $^{\bullet}OH$, R2 ≡ $^{\bullet}OOH$, R3 ≡ $^{\bullet}OCH_3$, R4 ≡ $^{\bullet}OOCH{\equiv}CH_2$

Table 2S. Gibbs free energies of reaction (ΔG, kcal/mol), at 298.15 K, for neutral trolox in aqueous solution.

path	R1	R2	R3	R4
SET	-3.06	20.47	14.99	15.75
HT-1a	-42.05	-8.57	-25.14	-8.39
HT-2a	-31.62	1.85	-14.72	2.04
HT-3a	-31.88	1.59	-14.97	1.78
HT-6a	-31.28	2.20	-14.37	2.39
HT-7	-34.51	-1.03	-17.60	-0.85
HT-8	-21.36	12.11	-4.45	12.30
HT-9a	-18.89	14.58	-1.98	14.77
RAF-1	-17.93	11.89	-0.47	12.09
RAF-2	-13.90	15.37	2.90	11.58
RAF-3	-15.13	10.42	-2.59	11.95
RAF-4	-15.17	14.00	2.70	13.59
RAF-5	-11.86	15.72	5.50	13.32
RAF-6	-15.46	14.33	2.72	15.17

R1 ≡ $^{\bullet}OH$, R2 ≡ $^{\bullet}OOH$, R3 ≡ $^{\bullet}OCH_3$, R4 ≡ $^{\bullet}OOCH{\equiv}CH_2$

Table 3S. Gibbs free energies of SET reactions (ΔG, kcal/mol), at 298.15 K, for the neutral (H_2Tx), mono-anionic (HTx^-), and di-anionic (Tx^{2-}) forms of trolox in aqueous solution; aqueous vertical electron affinities (^{Aq}VEA, eV) and aqueous adiabatic electron affinities (^{Aq}AEA, eV) of the free radicals.

	H_2Tx	HTx^-	Tx^{2-}	^{Aq}VEA	^{Aq}AEA
$^{\bullet}OH$	-3.10	-7.44	-34.37	5.55	5.53
$^{\bullet}OCH_3$	12.03	7.69	-19.25	4.81	4.87
$^{\bullet}OCCl_3$	-42.84	-47.18	-74.11	6.49	7.25
$^{\bullet}OCH_2CHCH_2$	10.66	6.32	-20.62	4.88	4.93
$^{\bullet}OOH$	18.29	13.95	-12.98	4.14	4.60
$^{\bullet}OOCH_3$	20.22	15.88	-11.05	4.04	4.51
$^{\bullet}OOCH_2Cl$	12.25	7.91	-19.03	4.34	4.86
$^{\bullet}OOCHCl_2$	3.41	-0.93	-27.86	4.71	5.24
$^{\bullet}OOCCl_3$	-2.26	-6.60	-33.54	4.95	5.49
$^{\bullet}OOCHCH_2$	15.75	11.41	-15.53	4.22	4.71
$^{\bullet}OOCH_2CHCH_2$	19.42	15.08	-11.85	4.05	4.55
$ArO^{\bullet}$	15.94	11.60	-15.33	4.59	4.70
$DPPH^{\bullet}$	12.35	8.01	-18.93	4.85	4.86
$Br_2^{\bullet-}$	4.98	0.64	-26.30	4.98	5.17
$SO_4^{\bullet}$	-28.40	-32.74	-59.67	6.06	6.62
$NO_2^{\bullet}$	-2.72	-7.06	-33.99	4.45	5.51
$N_3^{\bullet}$	-1.01	-5.35	-32.29	5.51	5.43
$2dG^{\bullet+}$ [(a)]	-10.32	-14.66	-41.59	5.53	5.84

[(a)] 2'-deoxyguanosine radical cation

Table 4S. Gibbs free energies of activation ($\Delta G^{\neq}$, kcal/mol), at 298.15 K for neutral trolox in aqueous solution.

path	R1	R2	R3	R4
SET	0.64			
HT-1a	~0.00	12.62	~0.00	8.49
HT-2a	6.59		14.40	
HT-3a	5.56		12.09	
HT-6a	6.83		13.00	
HT-7	5.01	20.10	12.99	19.15
HT-8	7.23		16.37	
HT-9a	9.05		18.10	
RAF-1	1.70		9.39	
RAF-2	3.04			
RAF-3	3.30		12.15	
RAF-4	1.60			
RAF-5	3.61			
RAF-6	3.44			

R1 ≡ $^{\bullet}OH$, R2 ≡ $^{\bullet}OOH$, R3 ≡ $^{\bullet}OCH_3$, R4 ≡ $^{\bullet}OOCH{\equiv}CH_2$

Table 5S. Gibbs free energies of activation ($\Delta G^{\neq}$, kcal/mol), at 298.15 K, for the SET reactions of neutral (H_2Tx), mono-anionic (HTx^-), and di-anionic (Tx^{2-}) forms of trolox in aqueous solution.

	H_2Tx	HTx^-	Tx^{2-}
$^{\bullet}OH$	0.63	0.02	30.23
$^{\bullet}OCH_3$	12.22	7.72	3.55
$^{\bullet}OCCl_3$	2.96	5.05	25.14
$^{\bullet}OCH_2CHCH_2$	10.72	6.46	4.74
$^{\bullet}OOH$	18.30	14.17	0.30
$^{\bullet}OOCH_3$	20.24	15.96	0.66
$^{\bullet}OOCH_2Cl$	12.99	9.58	~0.00
$^{\bullet}OOCHCl_2$	6.90	4.43	0.97
$^{\bullet}OOCCl_3$	4.04	2.19	2.55
$^{\bullet}OOCHCH_2$	15.91	12.10	0.10
$^{\bullet}OOCH_2CHCH_2$	19.42	15.27	0.60
$ArO^{\bullet}$	16.64	11.68	0.89
$DPPH^{\bullet}$	12.91	8.02	4.92
$Br_2^{\bullet-}$	6.10	3.27	4.80
$SO_4^{\bullet}$	0.65	1.89	19.63
$NO_2^{\bullet}$	6.79	4.79	0.05
$N_3^{\bullet}$	1.07	~0.00	35.93
$2dG^{\bullet+}$ [(a)]	0.37	~0.00	13.58

[(a)] 2'-deoxyguanosine radical cation

Table 6S. Reorganization energies (λ, kcal/mol) and difference (-λ)-ΔG for the SET reactions of neutral (H_2Tx), mono-anionic (HTx^-), and di-anionic (Tx^{2-}) forms of trolox in aqueous solution.

	λ			(-λ)-ΔG		
	H_2Tx	HTx^-	Tx^{2-}	H_2Tx	HTx^-	Tx^{2-}
$^{\bullet}OH$	7.45	6.76	6.45	-4.35	0.68	**27.92**
$^{\bullet}OCH_3$	9.35	8.67	8.36	-21.38	-16.36	10.89
$^{\bullet}OCCl_3$	25.48	24.80	24.49	17.36	**22.38**	**49.63**
$^{\bullet}OCH_2CHCH_2$	9.17	8.48	8.17	-19.83	-14.80	12.45
$^{\bullet}OOH$	18.61	17.93	17.61	-36.90	-31.88	-4.63
$^{\bullet}OOCH_3$	18.91	18.23	17.91	-39.13	-34.11	-6.86
$^{\bullet}OOCH_2Cl$	19.93	19.25	18.94	-32.18	-27.16	0.09
$^{\bullet}OOCHCl_2$	20.22	19.54	19.22	-23.63	-18.61	8.64
$^{\bullet}OOCCl_3$	20.44	19.76	19.44	-18.18	-13.15	14.09
$^{\bullet}OOCHCH_2$	19.23	18.55	18.24	-34.98	-29.96	-2.71
$^{\bullet}OOCH_2CHCH_2$	19.53	18.85	18.53	-38.95	-33.93	-6.68
$ArO^{\bullet}$	10.51	9.82	9.51	-26.45	-21.42	5.82
$DPPH^{\bullet}$	8.10	7.42	7.10	-20.45	-15.42	11.82
$Br_2^{\bullet-}$	12.46	11.78	11.47	-17.44	-12.42	14.83
$SO_4^{\bullet}$	21.02	20.34	20.02	7.38	12.40	**39.65**
$NO_2^{\bullet}$	32.38	31.69	31.38	-29.66	-24.64	2.61
$N_3^{\bullet}$	6.13	5.44	5.13	-5.12	-0.09	**27.16**
$2dG^{\bullet+}$ [(a)]	15.01	14.32	14.01	-4.69	0.33	**27.58**

[(a)] 2'-deoxyguanosine radical cation

Table 7S. Rate constants at 298.15 K, in $M^{-1}s^{-1}$, for neutral trolox in aqueous solution.

path	R1	R2	R3	R4
SET	8.14E+09			
HT-1a	1.91E+09	3.45E+03	1.72E+09	3.70E+06
HT-2a	2.39E+08		4.47E+03	
HT-3a	8.57E+08		1.29E+05	
HT-6a	1.67E+08		3.29E+04	
HT-7	1.11E+09	2.28E-02	1.64E+04	1.14E-01
HT-8	5.98E+07		9.67E+01	
HT-9a	4.31E+06		1.65E+01	
RAF-1	1.90E+09		1.61E+06	
RAF-2	1.86E+09			
RAF-3	1.84E+09		1.54E+04	
RAF-4	1.90E+09			
RAF-5	1.79E+09			
RAF-6	1.82E+09			
Overall	**2.36E+10**	**3.45E+03**	**1.29E+09**	**3.70E+06**

R1 ≡ $^{\bullet}OH$, R2 ≡ $^{\bullet}OOH$, R3 ≡ $^{\bullet}OCH_3$, R4 ≡ $^{\bullet}OOCH{\equiv}CH_2$

Table 8S. Rate constants at 298.15 K, in $M^{-1}s^{-1}$, for the SET reactions of neutral (H_2Tx), mono-anionic (HTx^-), and di-anionic (Tx^{2-}) forms of trolox in aqueous solution.

	H_2Tx	HTx^-	Tx^{2-}
$^{\bullet}OH$	**8.14E+09**	**8.16E+09**	4.32E-10
$^{\bullet}OCH_3$	6.85E+03	**1.37E+07**	**5.21E+09**
$^{\bullet}OCCl_3$	**6.42E+09**	**1.06E+09**	2.30E-06
$^{\bullet}OCH_2CHCH_2$	8.61E+04	**1.13E+08**	**1.63E+09**
$^{\bullet}OOH$	2.40E-01	2.52E+02	**7.94E+09**
$^{\bullet}OOCH_3$	8.98E-03	1.25E+01	**7.70E+09**
$^{\bullet}OOCH_2Cl$	1.87E+03	5.91E+05	**7.63E+09**
$^{\bullet}OOCHCl_2$	**5.35E+07**	**2.40E+09**	**7.53E+09**
$^{\bullet}OOCCl_3$	**3.57E+09**	**7.19E+09**	**6.91E+09**
$^{\bullet}OOCHCH_2$	1.36E+01	8.42E+03	**7.65E+09**
$^{\bullet}OOCH_2CHCH_2$	3.60E-02	3.98E+01	**7.55E+09**
$ArO^{\bullet}$	3.91E+00	1.70E+04	**7.48E+09**
$DPPH^{\bullet}$	2.15E+03	**8.18E+06**	**1.27E+09**
$Br_2^{\bullet-}$	**2.04E+08**	**5.85E+09**	**1.52E+09**
$SO_4^{\bullet}$	**7.62E+09**	**7.43E+09**	2.54E-02
$NO_2^{\bullet}$	**6.45E+07**	**1.54E+09**	**7.87E+09**
$N_3^{\bullet}$	**7.81E+09**	**7.86E+09**	2.83E-14
$2dG^{\bullet+}$ [(a)]	**7.39E+09**	**7.40E+09**	6.93E+02

[(a)] 2'-deoxyguanosine radical cation

Table 9S. Branching ratios (Γ, %)*, at 298.15 K, for neutral trolox in aqueous solution.

path	R1	R2	R3	R4
SET	34.50			
HT-1a	8.09	~100.00	99.89	~100.00
HT-2a	1.01		~0.00	
HT-3a	3.63		0.01	
HT-6a	0.71		~0.00	
HT-7	4.69	~0.00	~0.00	~0.00
HT-8	0.25		~0.00	
HT-9a	0.02		~0.00	
RAF-1	8.07		0.09	
RAF-2	7.89			
RAF-3	7.78		~0.00	
RAF-4	8.07			
RAF-5	7.57			
RAF-6	7.70			

R1 ≡ $^{\bullet}OH$, R2 ≡ $^{\bullet}OOH$, R3 ≡ $^{\bullet}OCH_3$, R4 ≡ $^{\bullet}OOCH{\equiv}CH_2$
calculated as $\Gamma_i=(k_i/k_{overall})\times100$

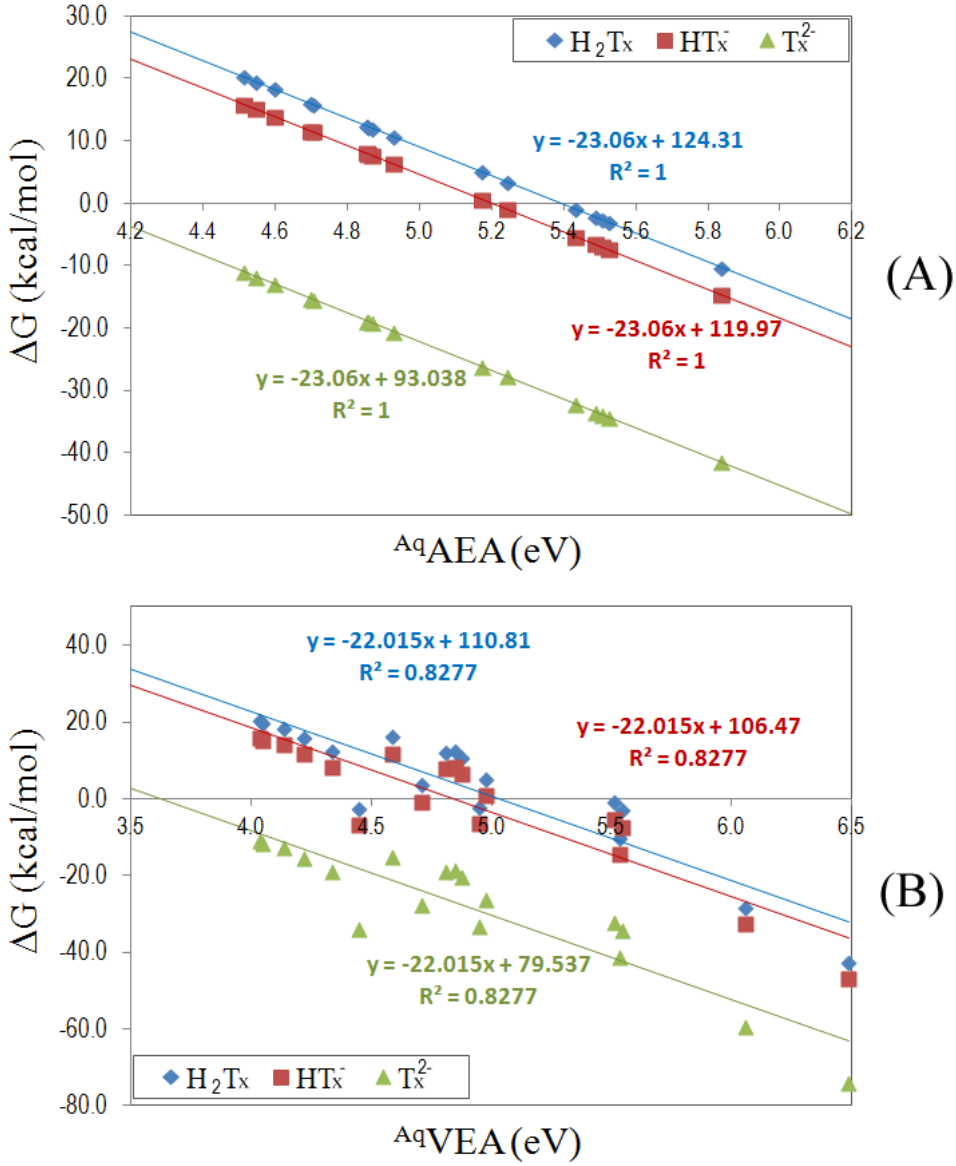

Figure 1S. Linear correlation between the Gibbs energies of the SET reactions (ΔG, kcal/mol) and the aqueous electron affinities, in eV, of the free radicals. (A)≡adiabatic (^{Aq}AEA), B≡vertical (^{Aq}VEA).

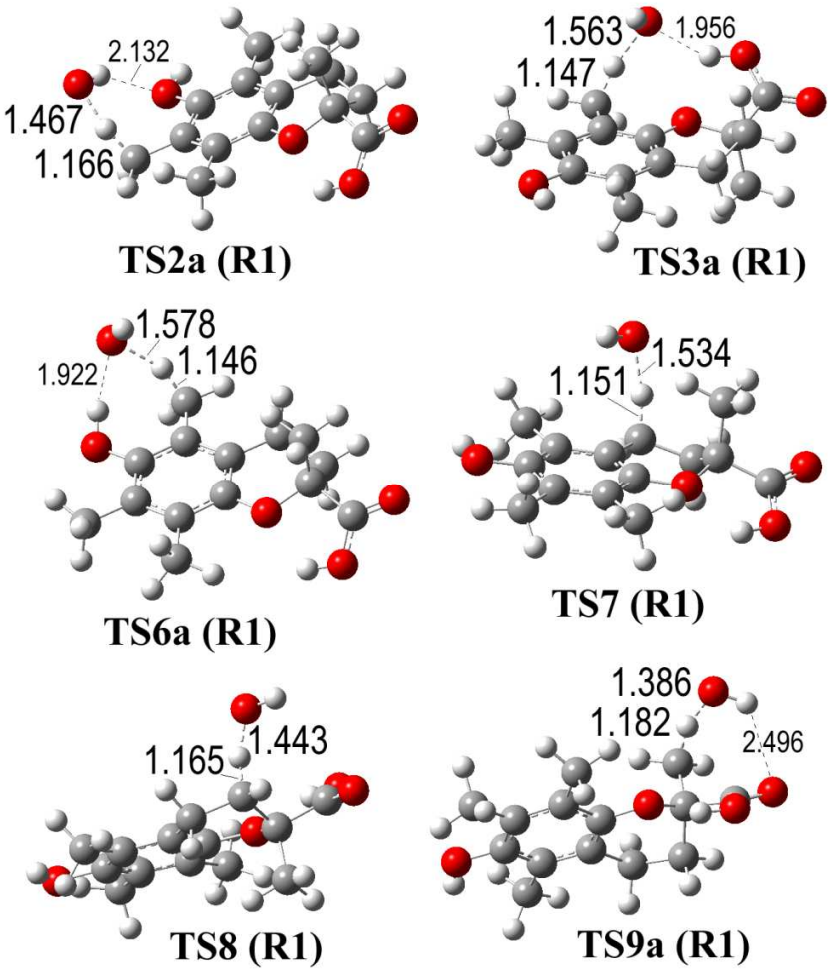

Figure 2S. Fully optimized transition states for the HT reactions between trolox and •OH in pentyl ethanoate solution. Distances are reported in Å.

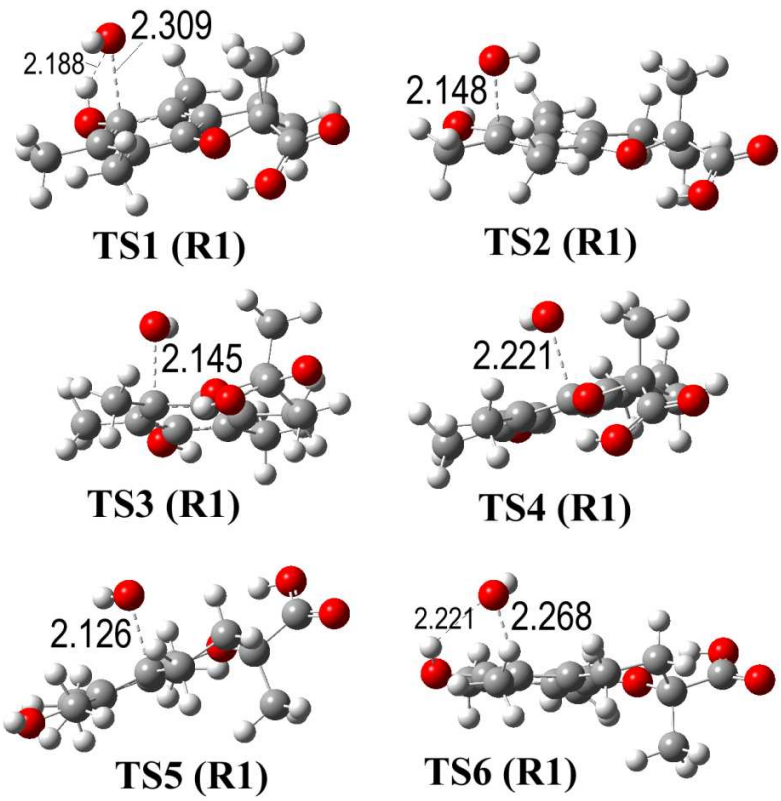

Figure 3S. Fully optimized transition states for the RAF reactions between trolox and •OH in pentyl ethanoate solution. Distances are reported in Å.

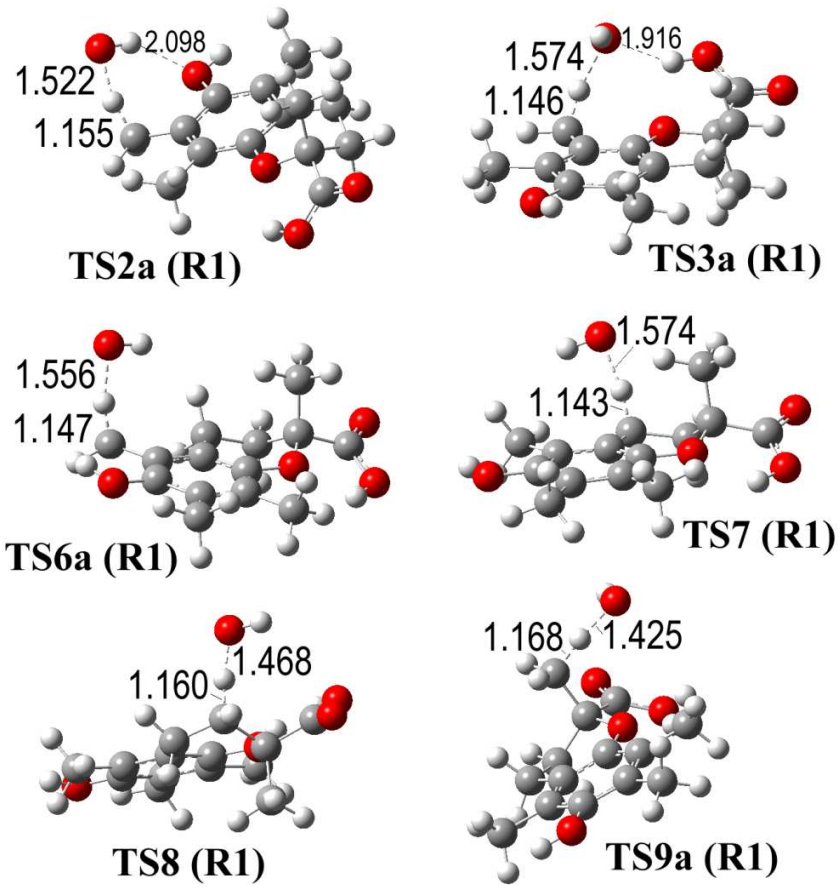

Figure 4S. Fully optimized transition states for the HT reactions between neutral trolox and •OH in aqueous solution. Distances are reported in Å.

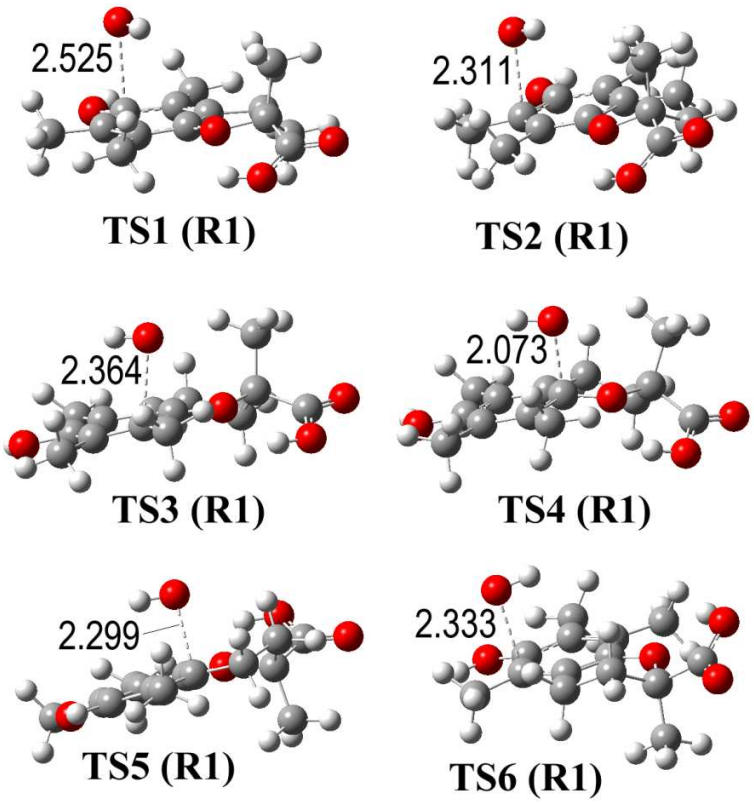

Figure 5S. Fully optimized transition states for the RAF reactions between neutral trolox and •OH in aqueous solution. Distances are reported in Å.

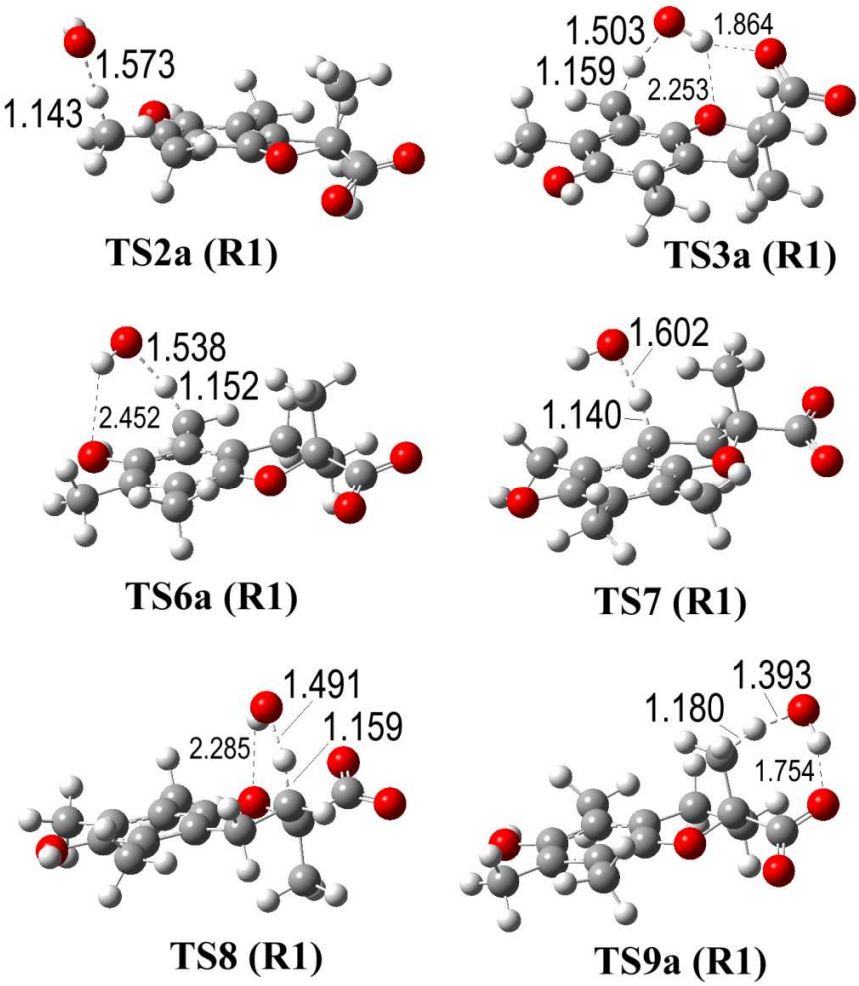

Figure 6S. Fully optimized transition states for the HT reactions between anionic trolox and •OH in aqueous solution. Distances are reported in Å.

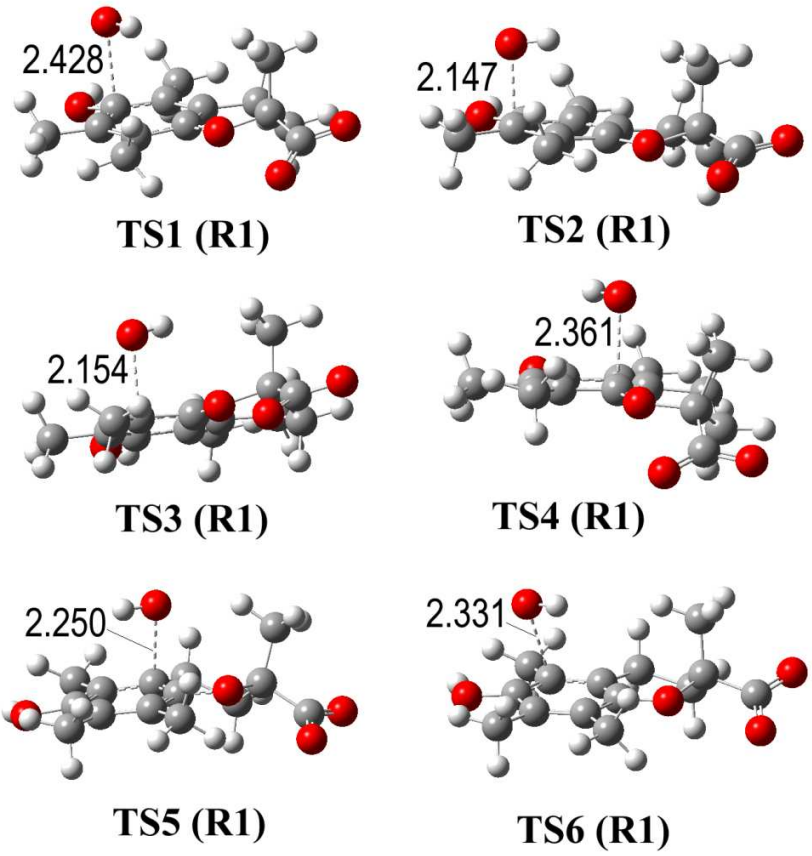

Figure 7S. Fully optimized transition states for the RAF reactions between anionic trolox and •OH in aqueous solution. Distances are reported in Å.

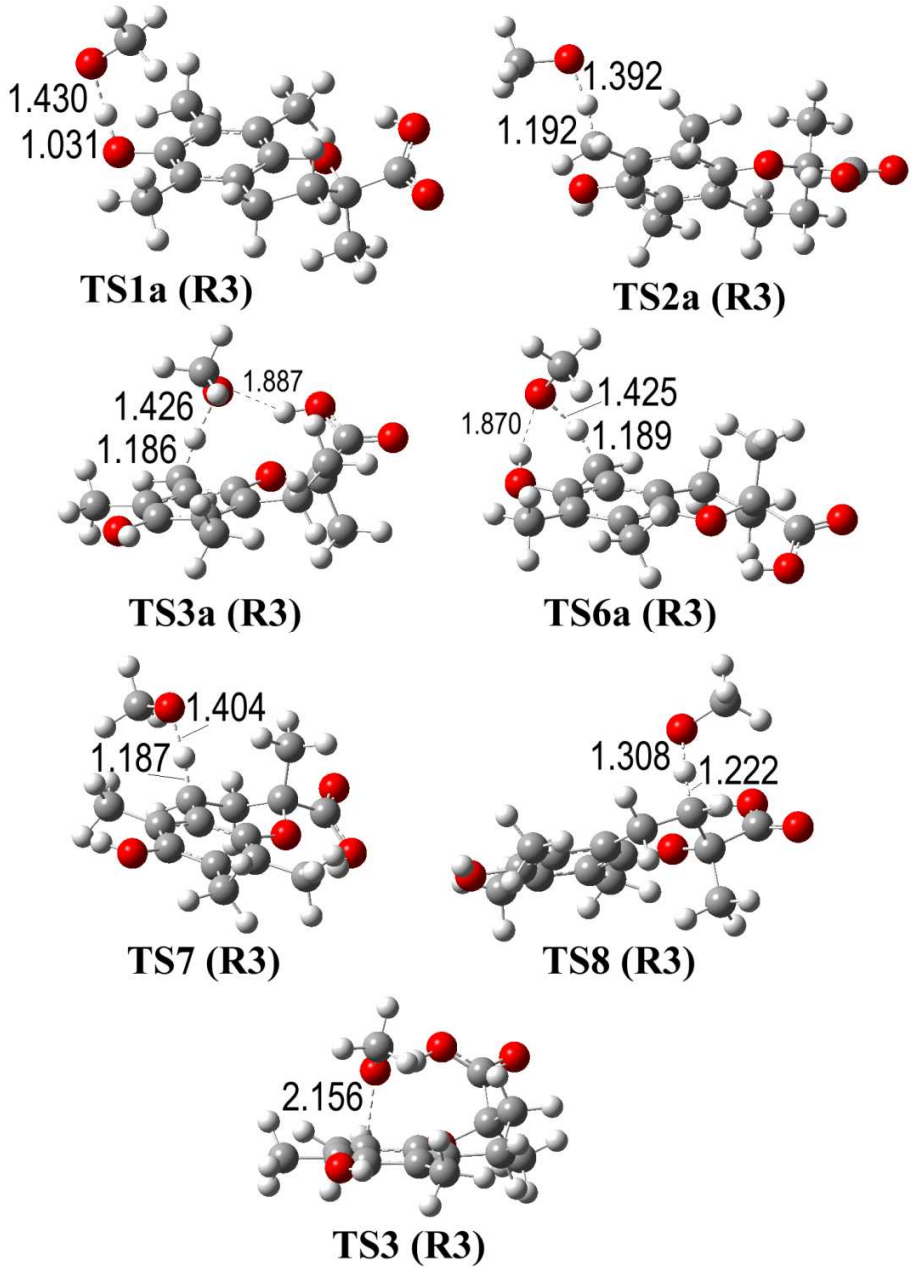

Figure 8S. Fully optimized transition states for the reactions between trolox and $^{\bullet}OCH_3$ in pentyl ethanoate solution. Distances are reported in Å.

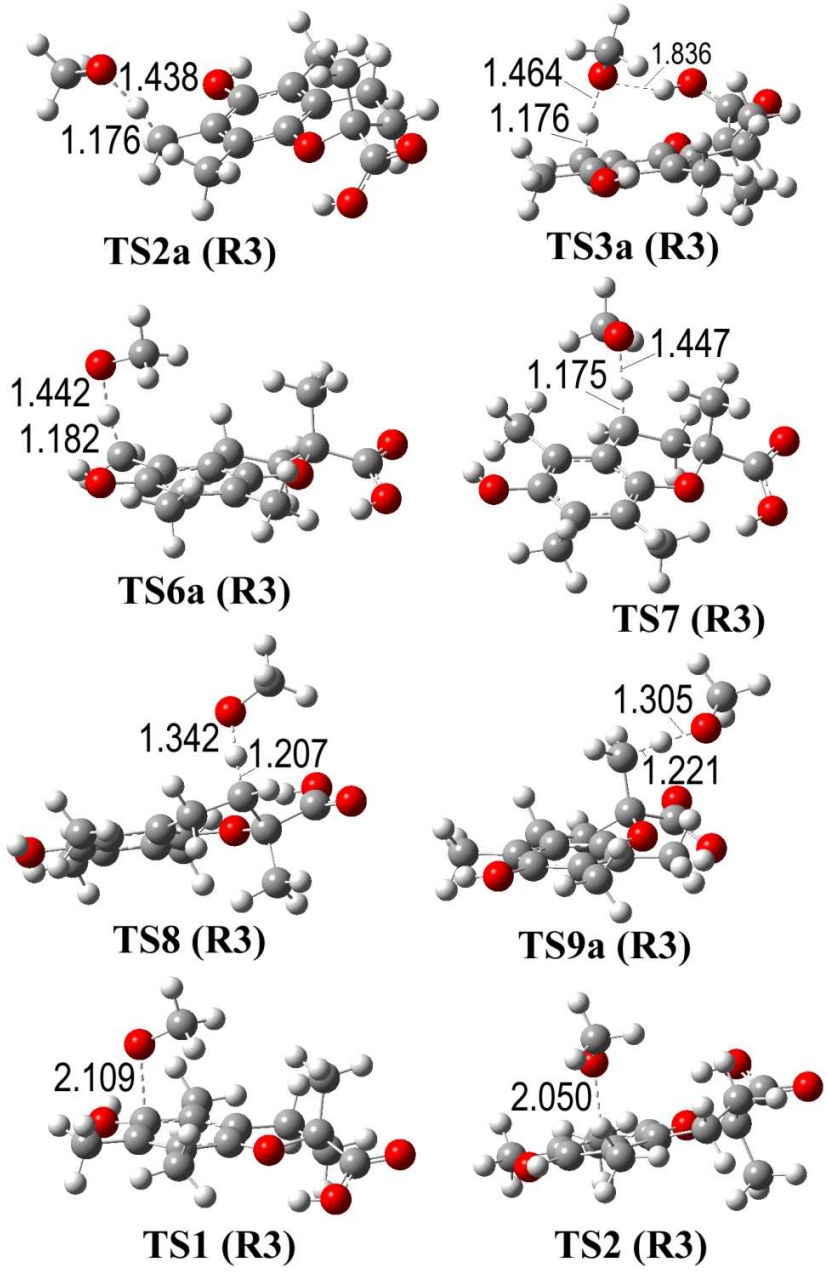

Figure 9S. Fully optimized transition states for the reactions between neutral trolox and $^{\bullet}OCH_3$ in aqueous solution. Distances are reported in Å.

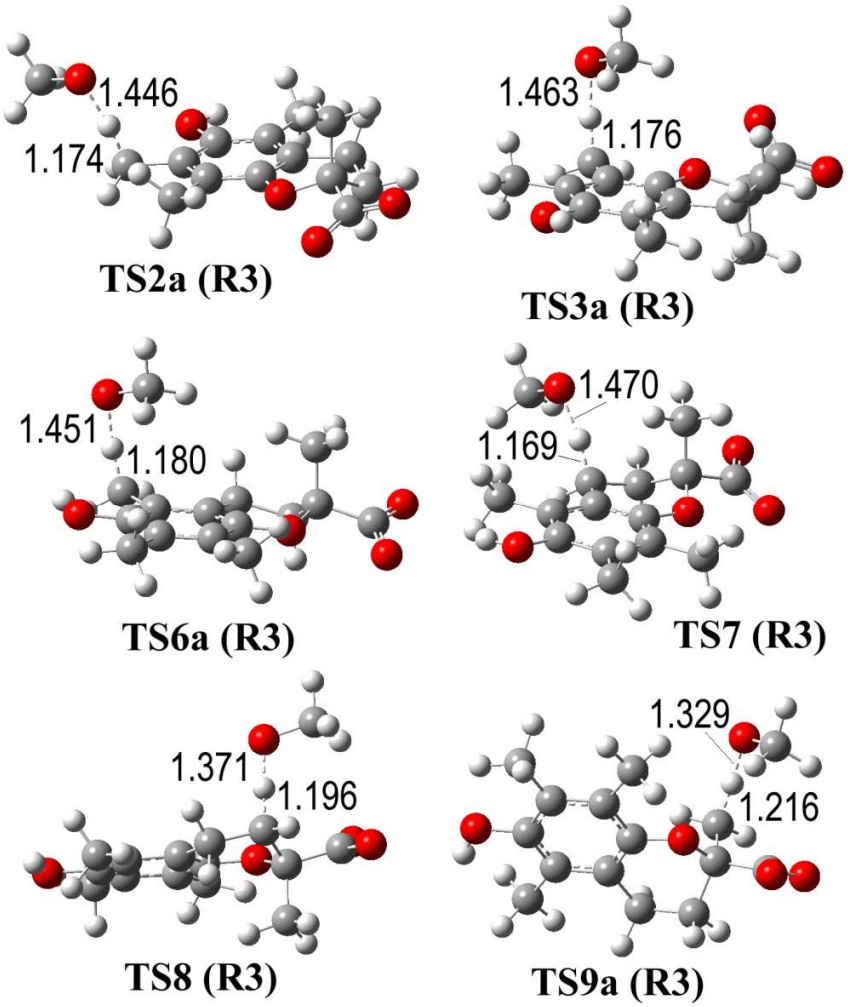

Figure 10S. Fully optimized transition states for the HT reactions between anionic trolox and $^{\bullet}OCH_3$ in aqueous solution. Distances are reported in Å.

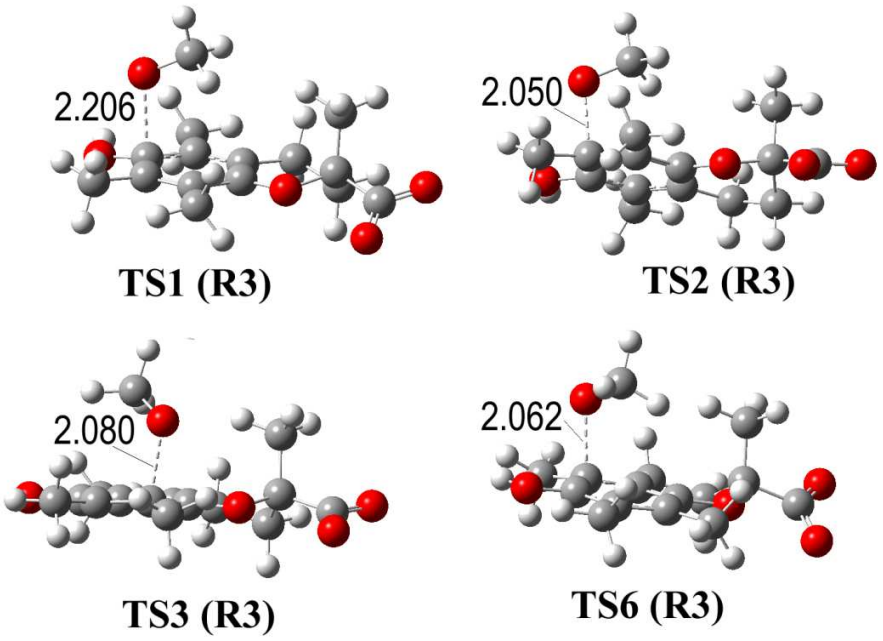

Figure 11S. Fully optimized transition states for the RAF reactions between anionic trolox and $^{\bullet}OCH_3$ in aqueous solution. Distances are reported in Å.

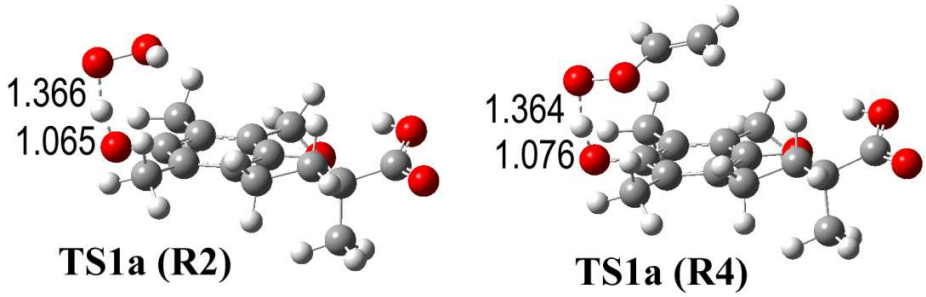

Figure 12S. Fully optimized transition states for the reactions of trolox with $^{\bullet}OOH$ (R2) and $^{\bullet}OOCHCH_2$ (R4) in pentyl ethanoate solution. Distances are reported in Å.

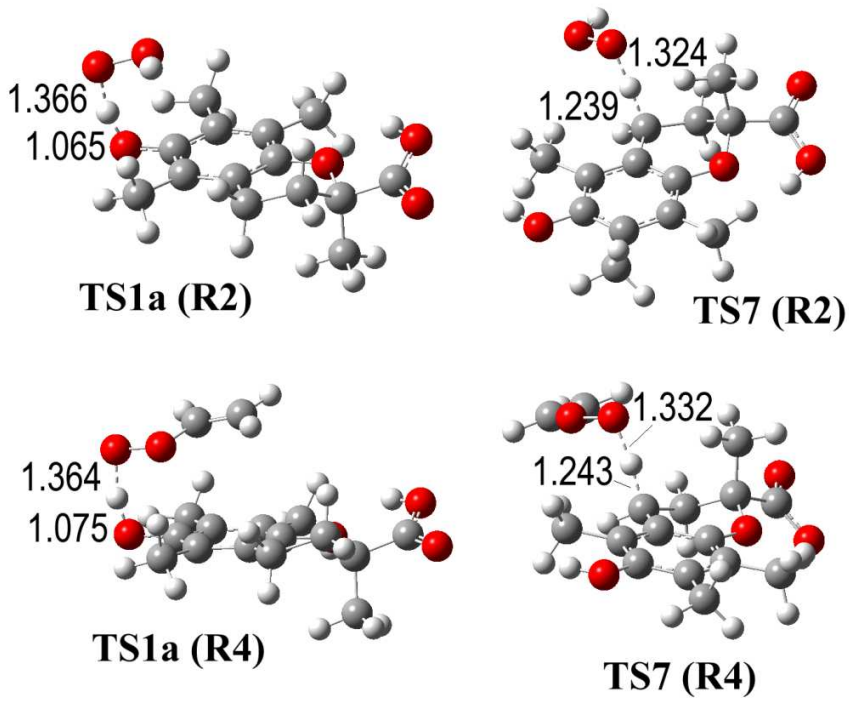

Figure 13S. Fully optimized transition states for the reactions of neutral trolox with •OOH (R2) and •$OOCHCH_2$ (R4) in aqueous solution. Distances are reported in Å.

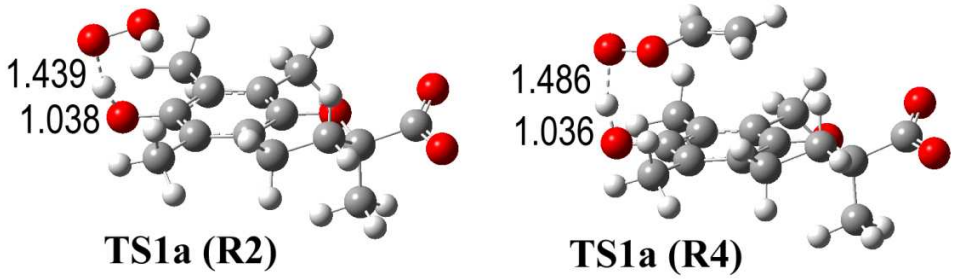

Figure 14S. Fully optimized transition states for the reactions of anionic trolox with •OOH (R2) and •$OOCHCH_2$ (R4) in aqueous solution. Distances are reported in Å.