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Inactivation of free radical species with selected triazoles

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Introduction

Many diseases such as cancer, inflammation, hypertension, and cardiovascular disorders can occur as a consequence of free radicals' action in the human body, due to the environmental and modern lifestyle factors. Most of the natural and artificial antioxidants cannot pass the blood-brain barrier, so the molecules locally produced are gaining more attention these days. More than 20% of oxygen is used in the brain, and it is clear that the species present there are constantly exposed to the reactive oxygen species (ROS).

Aim

Various quantum-mechanical methods are used to quantify the antioxidant activity in numerous studies. The reactions between the molecules with antioxidative properties and free radicals can follow two different pathways: H-atom abstraction and radical adduct formation. In this study, the evaluation of possible inactivation of the three free radicals (hydroxyl, hydroperoxyl, and chloromethylperoxyl radical) with chosen 1,2,4-triazole-3-thiones is performed. The reactions of antioxidant mechanism between the triazoles and mentioned radicals are investigated thermodynamically. The thermodynamic parameters that describe H-atom abstraction mechanisms are calculated and analysed.

Methodology

The equilibrium geometries of all studied compounds, radical cations, radicals and anions, as well as all other species that participate in the reactions of investigated mechanisms, were calculated using B3LYP-D3 functional in conjunction with 6-311++G(d,p) basis set. All calculations are performed in methanol, as a polar solvent.

Conclusion

Analyzing the results obtained for hydroxyl radical, it is notable that it can be scavenged via HAT and SPLET mechanisms. The lower values are obtained for ΔH_{BDE}, indicating HAT as preferred mechanism of antioxidant action. In the case of hydroperoxyl radical, achieved ΔH_{PA} values are lower than the corresponding values obtained for HAT mechanism. This fact makes SPLET mechanistic pathway the most favorable for antioxidant action. Regarding chloromethylperoxyl radical, there is present competition between HAT and SPLET mechanisms. As far as SET-PT mechanism is concerned, it is not a possible reaction pathway for inactivation of neither of the investigated radicals.

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Results

The obtained results show that all of the three investigated radicals can be neutralized with the examined triazoles, the only question is which mechanistic pathway to follow.

	HAT	SET-PT		SPLET	
	ΔH_{BDE}	ΔH_{IP}	ΔH_{PDE}	ΔH_{PA}	ΔH_{ETE}
4a-N10 + ·OH	-146	24	-170	-72	-74
4a – N8 + ·OH	-136		-161	-81	-56
4a –O6 + ·OH	-132		-157	-55	-77
4a-N10 + ·OOH	-6	126	-132	-33	27
4a – N8 + ·OOH	4		-122	-42	46
4a –O6 + ·OOH	8		-118	-16	24
4a-N10 + CH_2ClOO·	-9	102	-111	-13	4
4a – N8 + CH_2ClOO·	1		-101	-21	22
4a –O6 + CH_2ClOO·	5		-97	5	0
4d-N10 + ·OH	-148	-5	-142	-56	-91
4d – N8 + ·OH	-146		-140	-71	-75
4d –O4 + ·OH	-168		-163	-67	-101
4d-N10 + ·OOH	-8	96	-104	-18	10
4d – N8 + ·OOH	-6		-102	-33	27
4d –O4 + ·OOH	-28		-124	-29	0
4d-N10 + CH_2ClOO·	-11	72	-83	3	-14
4d – N8 + CH_2ClOO·	-9		-81	-12	3
4d –O4 + CH_2ClOO·	-31		-103	-8	-23
4f-N10 + ·OH	-146	24	-170	-73	-72
4f - N8 + ·OH	-136		-160	-82	-54
4f –O6 + ·OH	-158		-182	-73	-85
4f –O5 + ·OH	-156		-180	-59	-97
4f-N10 + ·OOH	-6	125	-131	-35	29
4f - N8 + ·OOH	4		-122	-43	47
4f –O6 + ·OOH	-19		-144	-35	16
4f –O5 + ·OOH	-17		-142	-21	4
4f-N10 + CH_2ClOO·	-9	102	-110	-14	5
4f - N8 + CH_2ClOO·	1		-101	-23	23
4f –O6 + CH_2ClOO·	-21		-123	-14	-7
4f –O5 + CH_2ClOO·	-19		-121	0	-20
4h-N10 + ·OH	-147	-1	-145	-57	-90
4h - N8 + ·OH	-144		-143	-71	-73
4h –O4 + ·OH	-177		-176	-84	-93
4h –O3 + ·OH	-159		-158	-63	-96
4h-N10 + ·OOH	-7	100	-107	-19	12
4h - N8 + ·OOH	-4		-104	-32	28
4h –O4 + ·OOH	-37		-138	-46	8
4h –O3 + ·OOH	-19		-119	-24	5
4h-N10 + CH_2ClOO·	-10	77	-86	2	-12
4h - N8 + CH_2ClOO·	-7		-83	-11	5
4h –O4 + CH_2ClOO·	-40		-117	-25	-15
4h –O3 + CH_2ClOO·	-22		-99	-4	-19