

# Antioxidant activity of fullerene C60 against OH free radicals: A quantum chemistry and computational kinetics study

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## ABSTRACT

In this work, we have studied the antioxidant activity of fullerene C60 towards OH free radicals, using quantum chemistry and computational kinetics methods. Energy profiles are calculated using different basis sets, and reaction rate constants are reported for the first time. The reaction rate constant for the addition of the OH radical to the fullerene C60 is reported for the first time. A value of  $1.37 \times 10^{-10} \text{ cm}^3 \text{ molecules}^{-1} \text{ s}^{-1}$  is obtained, which is close to the diffusion limit. Energetic considerations show that, once a first radical is attached to the fullerene cage, further additions are increasingly feasible, suggesting that fullerene can act as an OH radical sponge. The reaction energies oscillate as a function of the number of OH groups, because for even numbers of OH groups, reactions are barrier-less recombinations, while for odd numbers of OH groups they are radical-molecule reactions. After addition of the fourth OH radical, the energy favored path leads to a broken fullerene structure.

**Keywords:** fullerene C60, antioxidant activity, biological applications, quantum chemistry, computational kinetics.

## 1 INTRODUCTION

Fullerenes are considered to be the world's most efficient radical scavenger, and they represent an attractive tool for biological applications. It has been demonstrated both *in vivo* and *in vitro*, that fullerenes and related structures reduce the toxicity of free radical assault on neuronal tissue, reacting readily with free radicals that are often the cause of cell damage or death. Several studies on the ability of fullerenes<sup>1,2,3</sup> and graphite<sup>4,5</sup> to easily react with free radicals have been reported. In a recent theoretical work<sup>6</sup>, it has been demonstrated that carbon nanotubes can act as free radical scavengers.

Although there is strong evidence that antioxidant activity is an intrinsic property of fullerenes, the mechanism of radical scavenging and neuroprotection are still unclear.

The aim of this work is to study the mechanism and kinetics of the gas phase reaction between fullerene C60 and hydroxyl radicals, using quantum chemistry and computational kinetics methods. Energy profiles will be calculated using the M052X functional, and the reaction rate constants will be reported. Reactions will be modeled for successive addition of one to four OH groups at several relative positions of the trapped radicals.

## 2 COMPUTATIONAL METHODOLOGY

All electronic calculations are performed with Gaussian 09 package of programs.<sup>7</sup> Geometry optimizations and frequency calculations are carried out using the M05-2X functional<sup>8</sup> in conjunction with the 6-31G basis set. The M05-2X functional has been recommended for kinetic calculations by their developers.<sup>8</sup> No symmetry constraints have been imposed in the geometry optimizations. Thermodynamic corrections at 298 K are included in the calculation of relative energies. Spin-unrestricted calculations are used for open shell systems.

Any theoretical model aiming to make predictions concerning practical applications must be analyzed in terms of Gibbs free energies, which implies the necessity of performing frequency calculations that are particularly expensive. Frequency calculations are performed at with XXX, while stationary points energies have been improved by single point calculations with a larger basis set.

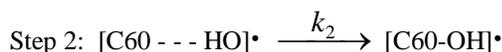
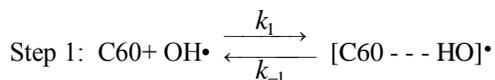
Rate constants are computed with Conventional Transition State Theory (TST)<sup>9-11</sup> as implemented in TheRate program,<sup>12</sup> using energy values, partition functions and thermodynamic data taken from the quantum-mechanical calculations and the equation:

$$k = \sigma \kappa \frac{k_B T}{h} e^{-(\Delta G^\ddagger)/RT} \quad (1)$$

where  $k_B$  and  $h$  are the Boltzman and Planck constants;  $\Delta G^\ddagger$  is the Gibbs free energy of activation;  $\sigma$  represents the reaction path degeneracy, accounting for the number of equivalent reaction paths; and  $\kappa$  accounts for tunneling corrections.

## 3 RESULTS

Reaction between OH radicals and fullerene C60 may take place, in principle, either by electron transfer or by OH addition. In the gas phase, however, only the latter occurs. For the formation of the first C60 + OH adduct, the reaction occurs in two steps: the first one leading to the formation of the prereactive [C60...HO] complex (RC) and the second one yielding the corresponding C60-OH adduct radical and water.



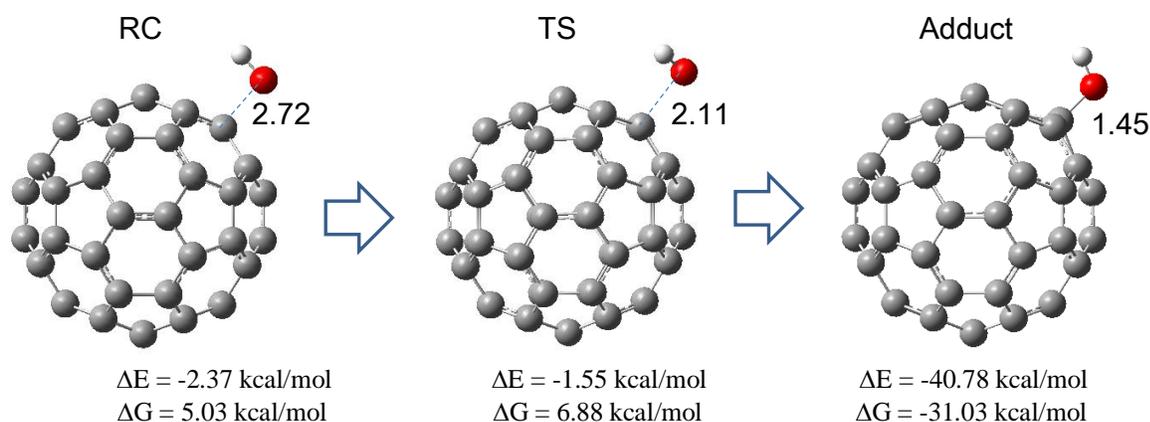


Figure 1: Optimized structure of the stationary points along the first OH addition reaction path.

The fully optimized structures of RC, the transition state (TS) and the C60-OH adduct are shown in Figure 1. In the first one, the OH radical lies approximately over the center of a six-membered ring at a distance of 2.72 Å, while in the transition state, it has approached a carbon atom at a distance of 2.11 Å. In the adduct complex, the OH radical is bound to a carbon atom. Relative energies are calculated with respect to the sum of the separated reactants (fullerene C60 and OH radical) and they are also reported in Figure 1.

For the C60 + OH reaction the tunneling correction is close to 1, because it is an addition reaction; and the reaction path degeneracy  $\sigma$  is equal to 60 because all carbon atoms are equivalent. Thus, the calculated rate constant for the formation of the first C60-OH adduct is equal to  $1.37 \times 10^{-10} \text{ cm}^3 \text{ molecules}^{-1} \text{ s}^{-1}$ , which is very close to the diffusion limit in the gas phase.

Once a free radical is attached to the C60 structure, the latter becomes a free radical itself. Such a C60 radical is expected to be much more reactive than the original C60 structure. Therefore, addition of a second OH radical is a barrierless recombination of two radicals and it should be energetically favored. Subsequent OH-addition reactions were modeled up to four OH groups, at different relative positions of the trapped radicals.

For addition of a second radical, six different reaction sites were considered (Figure 2): the two OH groups bonded to carbon atoms that are next to each other on either a six-membered (structure I) or a five-membered ring (structure II); two OH groups separated by one C atom (structures III and IV); two OH groups separated by two C atoms (structure V); two OH groups on opposite sides of fullerene (structure VI).

As geometries in Figure 1 show, when the second OH is in the vicinity of the first one, the two groups are oriented in such a way that the H atom in one of them is pointing towards the O atom in the other, leading to an intramolecular interaction. The distance between these atoms was found to be 1.779 Å and 1.801 Å for isomers I and II, respectively. For isomers III and IV, on the other hand, the two hydroxyl groups are too far apart to interact

significantly, and the H atoms in the OH groups are pointing towards the center of a ring, probably due to an H- $\pi$  interaction previously described in other aromatic compounds. No interaction between OH groups is possible in isomers V and VI. As a result, the geometrical features suggest that adduct I should have the lowest energy of all of the modeled structures.

The enthalpies of reaction and the Gibbs free energies of reaction for addition of the second OH radical are reported in Table 2 with respect to PC1. All of the second OH additions are exothermic and exergonic. It seems that there are two factors governing the relative stability of the isomers with two hydroxyl groups on fullerene C60: the ortho/para directing character of the OH group already attached to a six-membered ring, and the H-bond interactions between neighboring OH groups. The first factor favors formation of isomers I and V, whereas H bonding is not possible in isomer III and IV and V. In isomer V, the H-bond intramolecular interaction is possible. According to the results presented in Table 2, adduct I is expected to be the most abundant structure in the gas phase.

Addition of a third OH to adduct I were considered next. This is again a radical-molecule reaction. Three different products were modeled in this case (Figure 3), our choice of isomers being guided by the results obtained in the first addition, which indicate the importance of both the ortho/para effect and the H-bond interactions between neighboring OH groups.

Energies of the third OH addition were computed taking the isomer I and the OH radical as the reactants and they are reported in Table 3. All of these OH additions were found to be exothermic and exergonic. The most probable second OH (isomer I) additions were found to be significantly more exergonic than the first OH additions (that were also radical-molecule reactions), supporting an increase in the reactivity from C60 to C60-OH. Isomer VII is predicted to be the lowest in energy and, therefore, the most abundant. The lower energy of isomer VII compared to isomers VIII and IX seems to be caused by H-bond interactions involving neighboring hydroxyl groups.

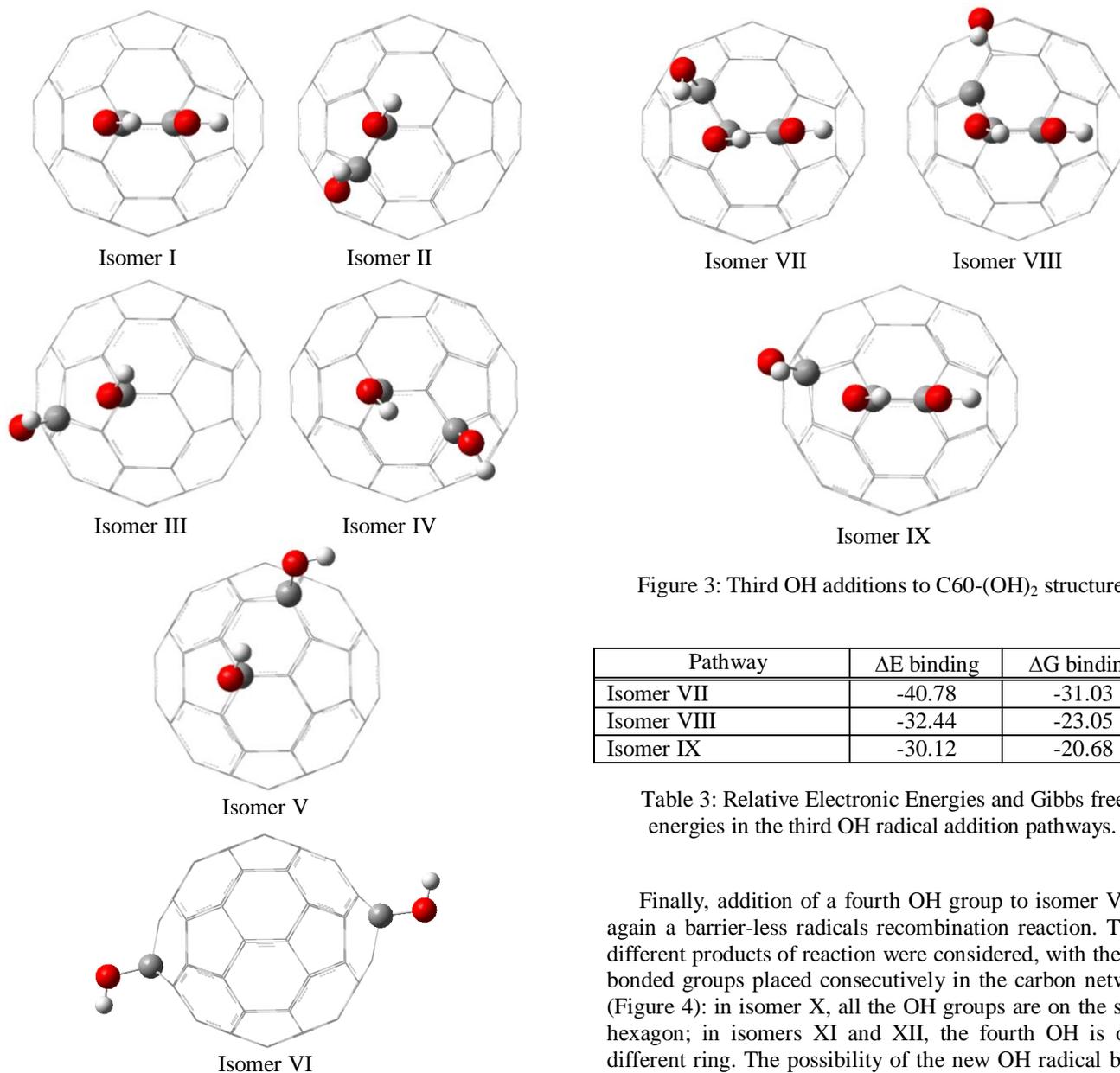


Figure 2: OH addition to the C60-OH adduct radical.

Pathway	$\Delta E$ binding	$\Delta G$ binding
Isomer I	-70.97	-60.47
Isomer II	-50.34	-40.03
Isomer III	-23.51	-13.20
Isomer IV	-13.49	-3.39
Isomer V	-58.62	-48.28
Isomer VI	-10.74	-0.52

Table 2: Relative Electronic Energies and Gibbs free energies in the second OH radical addition pathways.

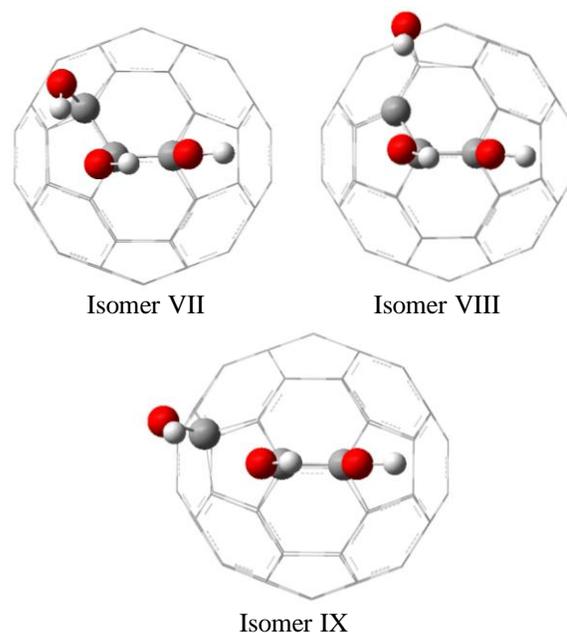


Figure 3: Third OH additions to C60-(OH)<sub>2</sub> structure.

Pathway	$\Delta E$ binding	$\Delta G$ binding
Isomer VII	-40.78	-31.03
Isomer VIII	-32.44	-23.05
Isomer IX	-30.12	-20.68

Table 3: Relative Electronic Energies and Gibbs free energies in the third OH radical addition pathways.

Finally, addition of a fourth OH group to isomer VII is again a barrier-less radicals recombination reaction. Three different products of reaction were considered, with the OH bonded groups placed consecutively in the carbon network (Figure 4): in isomer X, all the OH groups are on the same hexagon; in isomers XI and XII, the fourth OH is on a different ring. The possibility of the new OH radical being added to a C atom at the opposite side of C60 was not considered because, for all of the previously discussed cases, such a possibility was not energetically favored. As the values in Table 4 show, the fourth OH additions are exothermic and exergonic to a larger extent than the third OH additions, as expected for a radical-recombination. Moreover, adduct X  $\Delta H$  and  $\Delta G$  formation values are even larger than the ones for the recombination of radical RC1 with OH.

Isomer X is predicted to lie 24 kcal/mol lower than isomer XI, in terms of both enthalpy and Gibbs free energy, respectively, probably due to the OH-OH hydrogen bond interactions. Most important, it can be observed that OH addition to isomer X destroys the fullerene C60 structure.

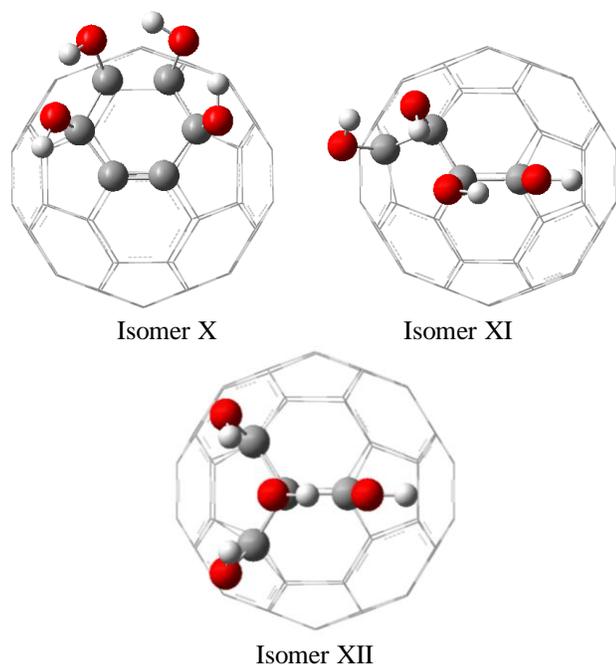


Figure 4: Fourth OH additions to C60-(OH)<sub>2</sub> structure.

Pathway	$\Delta E$ binding	$\Delta G$ binding
Isomer X	-74.21	-63.70
Isomer XI	-50.21	-39.70
Isomer XII	-27.54	-17.23

Table 4: Relative Electronic Energies and Gibbs free energies in the fourth OH radical addition pathways.

On the basis of the previously discussed results, some preliminary generalizations can be made. Once a first radical is attached to a C60, further additions are increasingly feasible. Subsequent additions lead preferentially to products in which the OH groups are able to interact with each other. Comparing the results from this work with those previously reported for the graphite + OH reaction<sup>4,5</sup> it seems that the C60 spherical shape increases the feasibility of the OH-addition process. Finally, for the most stable isomers, relative electronic energies of the reaction are obtained performing single point calculations at higher basis sets, and results are reported in Table 5.

Pathway	6-31G	Sp 6-31G*	Sp 6-311G*
RC	-2.37	-2.18	-2.75
TS	-1.55	-1.42	-2.07
Adduct	-40.78	-34.83	-35.70
Isomer I	-70.97	-73.35	-74.02
Isomer VII	-40.78	-46.22	-46.92
Isomer X	-74.21	-76.72	-77.04

Table 5: Relative Electronic Energies (in kcal/mol) calculated with several basis sets.

## 4 CONCLUSIONS

In this work, we have studied the reaction between fullerene C60 and one to four hydroxyl radicals, using quantum chemistry and computational kinetics methods. On the basis of energetic considerations, we show that, once a first radical is attached to the fullerene cage, further additions are increasingly feasible, suggesting that fullerene can act as an OH radical sponge. Actually, the reaction energies oscillate as a function of the number of OH groups, because for even numbers of OH groups, reactions are barrier-less recombinations, while for odd numbers of OH groups they are radical-molecule reactions. After addition of the fourth OH radical, the energy favored path leads to a broken fullerene structure.

The reaction rate constant for addition of the first OH radical is reported for the first time. A value of  $1.37 \times 10^{-10} \text{ cm}^3 \text{ molecules}^{-1} \text{ s}^{-1}$  is obtained, which is close to the diffusion limit.

Work is in progress to calculate energy profiles and rate constants in different solvents, in order to study possible biological and pharmaceutical applications.

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