EFFECT OF DEHYDROGENATION OR DIHYDROGENATION OF C*Α*-C*Β* BOND OF HYDROXYSTILBENES TO THEIR HYDROGEN ATOM DONATING ACTIVITY: A DFT APPROACH

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Abstract– In the present study Density functional theory/Becke's three-parameter hybrid functional combined with the Lee−Yang−Parr correlation functional (DFT/B3LYP) was used to examine the effect of Cα-Cβ bond nature (single, double, triple) in the backbone of hydroxystilbenes to their hydrogen atom transfer (HAT) ability. Tested compounds were *trans*-resveratrol and its derivatives, for which there are some scarce experimental findings, as well as piceatannol and related compounds. For this purpose bond dissociation enthalpy values were computed in the gas phase to study the effect of the structure free from any external influence and in liquid (benzene, water) phase. Benzene was used as a model of a lipid substrate. Simple phenol, which is usually non-reactive, was used as a reference. The double bond, resulting in molecular planarity, was predicted to favor the single hydrogen transfer. The triple bond, resulting in a linear backbone, was predicted to decrease the ease of such transfer. The saturation of the bond, resulting in loss of planarity, was expected to decrease more the activity. The impact of saturation was predicted to be too negative for *trans*-resveratrol. However, for piceatannol, an improvement of HAT efficiency was proposed only under stepwise HAT. Such a finding was related to the ease of allylic hydrogen atom donation after the formation of the o-quinone.

Keywords: *DFT, resveratrol, piceatannol, HAT, radical scavenging*

1. INTRODUCTION

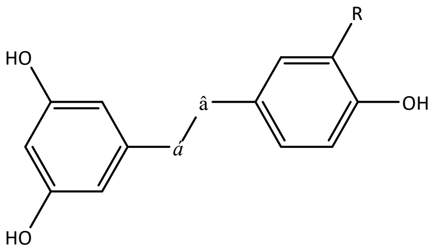
Hydroxystilbenes are bioactive phenolic compounds with extensive conjugation due to the presence of the Cα-Cβ double bond in their backbone. Nevertheless, this bond seems prone to oxidation when the molecules are exposed to UV radiation or to reduction when reaching the intestines due to the microflora [1,2]. As evidenced by the limited number of experimental or theoretical evidence for resveratrol [3-5] both changes seem to affect negatively the antioxidant activity. To shed light on this issue and considering the usefulness of theoretical calculations Density functional theory/Becke's three-parameter hybrid functional combined with the Lee−Yang−Parr correlation functional (DFT/B3LYP) was used to examine the role of this structural features towards the hydrogen atom donating efficiency of hydroxystilbenes, on the basis of Bond Dissociation Enthalpy (BDE) values. The study was carried out without (gas-phase) or with (benzene, water) an environmental influence. Except for resveratrol and related compounds, piceatannol and derivatives were included for comparison (Fig. 1) to inspect whether the presence of a catechol moiety could mask the influence of these changes

2. EXPERIMENTAL

The calculations for the tested compounds and phenol (used as reference) were carried out with Gaussian 09W rev. A.02-SMP program.32 The B3LYP functional was used for geometry optimization and computation of harmonic vibrational frequencies (6-31G basis set) and single-point electronic energy calculations (6-311++G(2d,2p)) [6]. The BDE values were computed as follows:

BDE = Hr + Hh − Hp

Hr is the enthalpy of the radical generated by H atom abstraction, Hh is the enthalpy of the H atom (−0.499897 hartree at this level of theory in the gas phase), and Hp is the enthalpy of the parent molecule. The results were presented in terms of ΔBDE relatively to the BDE value of phenol. Implicit solvent effects (benzene, water) were computed applying the integral equation formalism of the polarized continuum model (IEF-PCM) and the united atom for Hartree−Fock (UAHF) solvation radii.



(1)C*α*-C*β*= single, R=H	Dihydro-resveratrol
(2)C*α*-C*β*= double, R=H	**Resveratrol**
(3)C*α*-C*β*= triple, R=H	Dehydro-resveratrol
(4)C*α*-C*β*= single, R=OH	Dihydro-piceatannol
(5)C*α*-C*β*= double, R=OH	**Piceatannol**
(6)C*α*-C*β*= triple, R=OH	Dehydro-piceatannol

Fig. 1Tested compounds

3. RESULTS AND DISCUSSION

Those of the examined compounds with a double or a triple C*α*-C*β* bond were planar, whereas the dihydro- derivatives deviated from the plane.

As shown in Table 1, the oxidation of the bond (3) in resveratrol resulted in a slight increase of the BDE value relatively to that of phenol, whereas reduction (1) resulted in a significant increase. Thus, (1) was predicted to be a poor hydrogen atom donor and consequently a radical scavenger in line with experimental findings if we accept that the dominant mechanism is the hydrogen atom donation.

Table 1. Lowest ΔBDE values of the tested compounds in the gas and liquid phase at B3LYP/6-31G//6-311++G92d, 2p) level of theory (298 k)

Compound	**ΔBDE (kcal/mol)**		
	Gas phase	Benzene	Water
(1)	-0.5	-0.1	0.6
(2)	-3.9	-7.4	-5.9
(3)	-2.6	-1.5	2.0
(4)	-8.0	-6.7	-3.6
(5)	-12.3	-11.1	-7.8
(6)	-10.6	-8.8	-4.6

The BDE values for phenol in the gas phase, benzene, and water were 84.3, 82.2, and 81.7 kcal/mol

Similar observations were made for (4)-(6) and no masking effect, due to the presence of catechol, was evidenced. The trend was similar when calculations were carried out in the liquid phase, though quantitative differences were found. Despite the presence of a catechol moiety, in the liquid phase, (2) was predicted to donate a single hydrogen atom easier than (4) (benzene, water) and (6) (water). Examination of the compounds towards the ability to donate in a stepwise way more than one hydrogen atoms showed that for (2) no further hydrogen atom is possibly available. A dimmer with a phenoxy radical or adduct with an oxidizing radical could possibly formed instead. Te same is predicted for (3). In the case of (1) strong oxidation conditions can only result in the donation of a second hydrogen atom, even the allylic ones. The catecholic compounds wer predicted to form an o-quinone. Unlike (1), for (6) the allylic hydrogen atom donation seems feasible after quinone formation (ΔBDE=6.4-8.8 kcal/mol) which may continue from the following carbon number (ΔBDE=26.3-34.2 kcal/mol), leading eventually to the formation of (5). Thus, a total of four radicals are predicted to be scavenged through hydrogen atom donation by (6).

4. CONCLUSIONS

Present findings suggest that the nature of C*α*-C*β* bond may affect significantly the hydrogen atom donating efficiency of hydroxystilbenes. The magnitude may depend on the solvent, as well as the substitution pattern.

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