Molecular Structure and Electronic Spectrum of Ellagic Acid: Semiempirical Molecular Orbital Calculations

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The molecular structure of ellagic acid has been optimized by using PM3 semiempirical MO method. Ellagic acid has been calculated to be planar with the molecular symmetry of C_{2h}. The lactone carbonyl groups are not tilted from the molecular plane. CNDO/S MO method has been used to interpret the experimental uv-vis spectroscopic data. The results of the PM3 and CNDO/S calculations have been in good agreement with the experimental data.

Introduction.

Ellagic acid (Figure 1) is known as the naturally occurring phenolic lactone compound which is a degradation product of hydrolyzable plant tannins. This acid inhibits the carcinogenic properties of a variety of chemical compounds including benzo[a]pyrene-7,8-diol-9,10-epoxide. Wood et al. [1], for example, have shown that ellagic acid has exceptionally high activity in inhibiting mutagenesis by (±)-7β,8α-dihydroxy-9α,10α-epoxy-7,8,9,10-tetrahydrobenzo[a]pyrene (1): this acid is 10 times more potent as an inhibitor of mutagenesis induced by 1 than is riboflavin 5'-phosphate. On the other hand, the spectroscopic properties of ellagic acid have also been studied. Jurd has provided the uv-vis spectrum of ellagic acid [2]. Khac et al. have given the ^{1}H and ^{13}C nmr chemical shifts data [3]. The X-ray structural determination of ellagic acid has been made by two groups. Mathieson and Poppleton [4] have investigated anhydrous ellagic acid, whereas Rossi et al. [5] have investigated ellagic acid dihydrate. In this work, we examine the geometrical structure of ellagic acid by use of PM3 semiempirical molecular orbital calculation method, especially considering whether the -C-O-CO-C part lies in the same plane. Moreover, in order to have a better understanding of the uv-vis spectrum [2], we carried out CNDO/S calculations. The results obtained will be compared with the X-ray and uv-vis spectroscopic data.
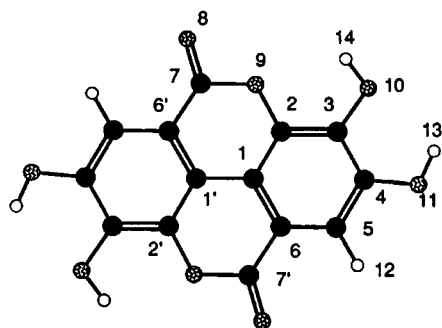

Figure 1. Ellagic acid with the atomic numbering; the carbon atoms are numbered from 1 to 7, the oxygen atoms from 8 to 11, and the hydrogen atoms from 13 to 14.

Computational Method.

Calculations were performed with PM3 method [6,7] in the MOPAC 93 Program [8]. All structural parameters were optimized. The ground-state structure was minimized until a gradient norm of less than 0.05 mdyn/Å was achieved. No symmetry constraints were imposed. To calculate the electronic spectrum, CNDO/S method [9-11] was used. Eighty single excitations were considered. All calculations in this work were carried out with the use of the Silicon graphics (SGI), IRIS INDIGO/ELAN and IBM, RS/6000 model 590.

Results and Discussion.

Calculated Structure.

To gain the structural information on ellagic acid, we carried out the molecular structure calculations by means of the PM3 MO method. PM3 vibrational analysis confirmed that the optimized structure is an energy minimum. The heat of formation is calculated to be -274.457 kcal/mol. Table 1 summarizes the structural parameters obtained. Some parameters are also shown in Figure 2. The results show that ellagic acid has the planar structure, the molecular symmetry group being C_{2h}.

The planar conformation obtained agrees well with the results of the X-ray structural analysis of ellagic acid dihydrate reported by Rossi et al. [5]: their results have revealed that ellagic acid is planar and the lactone carbonyl groups do not deviate from the molecular plane. On the other hand, Mathieson and Poppleton [4] have shown that in anhydrous ellagic acid structure, the lactone carbonyl groups tilt 3.6° from the molecular plane. Our calculation suggests that this tilt is imposed by the crystal packing force.

The results for the anhydrous ellagic acid have also indicated that the lactone carbonyl of the crystal structure is bent toward the oxygen atom, the bond angle O(8)-C(7)-O(9) being 114.9°. The calculated value is 107.4° (Table 1). It turns out therefore that this anomalous bond angle is not due to the crystal packing force but inherent to the molecule.

Table 1

Bond Lengths (Å) and Angles (degree) for Ellagic Acid

Bond Lengths

C(1) - C(2)	1.400
C(1) - C(6)	1.402
C(1) - C(1')	1.443
C(2) - C(3)	1.409
C(2) - O(9)	1.382
C(3) - C(4)	1.416
C(3) - O(10)	1.368
C(4) - C(5)	1.405
C(4) - O(11)	1.365
C(5) - C(6)	1.390
C(5) - H(12)	1.100
C(6) - C(7')	1.475
C(7) - O(8)	1.210
C(7) - O(9)	1.384
O(10) - H(14)	0.949
O(11) - H(13)	0.949

Bond Angles

C(2) - C(1) - C(6)	120.6
C(2) - C(1) - C(1')	119.8
C(6) - C(1) - C(1')	119.6
C(1) - C(2) - C(3)	119.9
C(1) - C(2) - O(9)	122.2
C(3) - C(2) - O(9)	117.9
C(2) - C(3) - C(4)	118.8
C(2) - C(3) - O(10)	124.6
C(4) - C(3) - O(10)	116.7
C(3) - C(4) - C(5)	121.0
C(3) - C(4) - O(11)	124.0
C(5) - C(4) - O(11)	115.0
C(4) - C(5) - C(6)	119.4
C(4) - C(5) - H(12)	120.2
C(6) - C(5) - H(12)	120.4
C(1) - C(6) - C(5)	120.4
C(1) - C(6) - C(7')	117.6
C(5) - C(6) - C(7')	122.1
O(8) - C(7) - O(9)	107.4
O(8) - C(7) - C(6')	130.7
O(9) - C(7) - C(6')	121.9
C(2) - O(9) - C(7)	118.9
C(2) - O(10) - H(14)	108.7
C(4) - O(11) - H(13)	109.2
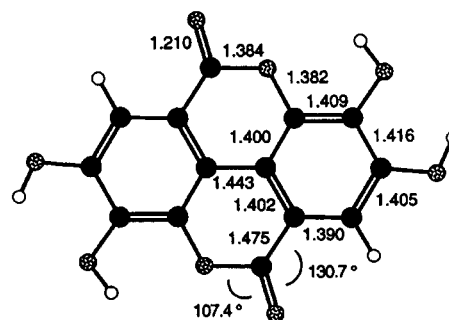
Figure 2. Selected bond lengths (Å) and bond angles (degree).

1	106.8 (s)
2	136.2 (s)
3	140.4 (s)
4	148.2 (s)
5	109.8 (d)
6	112.4 (s)
7	159.1 (s)

a

b
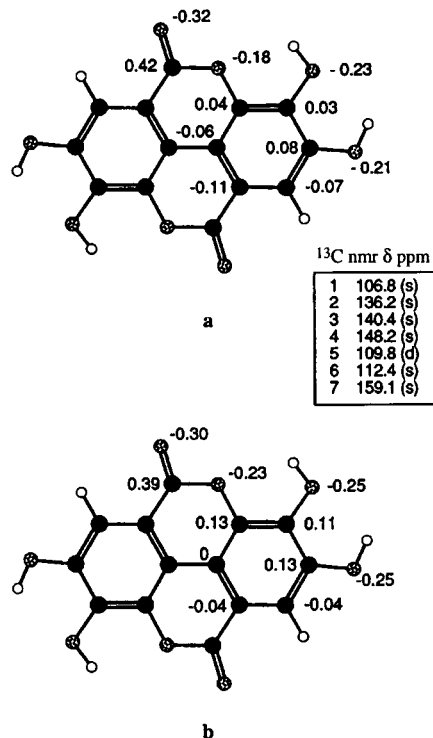
Figure 3. Atomic charges calculated by PM3 (a) and CNDO/2 (b) methods; the results of the CNDO/2 calculation have been reported by Rossi et al. [5]. ^{13}C nmr chemical shifts cited here are given by Khac et al. [3].

The optimized structure includes the delocalized six-membered carbon rings. The diamagnetic ring current is therefore expected. This is confirmed by the ^{1}H nmr spectroscopic analysis [3]: δH = 7.50 ppm.

The planar structure also indicates that ellagic acid has sp^2-hybridized carbon atoms; most of ^{13}C nmr chemical shifts are predicted to appear in the aromatic region [12], in agreement with the results of the ^{13}C nmr spectroscopic analysis [3]. Correlation between ^{13}C nmr values and charge densities of the carbon atoms of a molecule has been reported [12,13]. Figure 3a summarizes the distribution of the calculated charge densities and the ^{13}C nmr spectrum of ellagic acid. Roughly speaking, the larger positive charge indicates the larger chemical shift (δ-value). The most deshielded ^{13}C resonance at 159.1 ppm is assigned to C(7) and C(7'), which have the largest positive charge.

For comparison, Figure 3b shows the charge densities obtained using the different method. The original report of the crystal structure determination of ellagic acid [5] also gave the results of a CNDO/2 calculation. The charges so obtained show reasonable agreement with our results. The largest discrepancy arises for C(2) where CNDO/2 gave a charge of 0.13 e and PM3 predicts a value of 0.04 e. As pointed out by Rossi et al. [5], ellagic acid has two negatively charged edges.

Electronic Spectrum.

To discuss the excited states of ellagic acid, we carried out uv-vis spectroscopic calculations of the acid by using the CNDO/S method. When calculating the electronic

spectrum, we use the molecular structure obtained by PM3 method. Table 2 presents the calculated transition energies and intensities for comparison with the available experimental data [2]. Our calculations predict that ellagic acid has a weak absorption band at 350 nm. Thus, the weak absorption peak at 366 nm of the acid is assigned to the allowed transition of B_u symmetry. At a little shorter wavelength (324 nm), one additional transition with similar oscillator strength is predicted. This suggests that the shoulder at 352 nm should be assigned to the second allowed transition of B_u symmetry. Moreover, our calculation predicts that the acid has two strong absorption bands at 256 and 242 nm. In this region, only one peak at 255 nm is observed in ethanol solution. However, Jurd [2] has also reported that addition of sodium acetate to alcoholic solution of this acid results in a significant alternation in the low wave length band of the spectrum: this band (255 nm) is characteristically divided into two bands at 278 and 256 nm. This indicates that these bands should be assigned to the third and the fourth allowed transition of

B_u symmetry. It is therefore most likely that the peak at 255 nm in ethanol solution is composed of the two transitions. It is observed that the absorption peaks can be well accounted for by using the predicted singlet transition of ellagic acid.

Conclusion.

The geometrical structure and electronic spectrum of ellagic acid have been calculated by use of semiempirical PM3 and CNDO/S methods. The results are compared with experimental structural determination and the observed electronic spectrum. The PM3 calculations have shown that ellagic acid has a planar structure, in good agreement with the experimental results for ellagic acid dihydrate. The observed electronic spectrum of ellagic acid has been well interpreted by use of the results of the CNDO/S calculation.

Table 2

Calculated Singlet Transition Energies (ΔE)
and Intensities (f) of Ellagic Acid

transition symmetry	ΔE/nm	theoretical f		experimental [a] ΔE/nm
B_u	350.0	0.2193	$(\pi \rightarrow \pi^*)$	366
B_u	323.5	0.1406	$(\pi \rightarrow \pi^*)$	352 (sh) [b]
A_g	320.1	forb.	$(\pi \rightarrow \pi^*)$	
A_u	320.0	0.0000	$(n \rightarrow \pi^*)$	
B_g	319.4	forb.	$(n \rightarrow \pi^*)$	
A_g	282.3	forb.	$(\pi \rightarrow \pi^*)$	
B_u	256.1	1.6219	$(\pi \rightarrow \pi^*)$	
A_g	254.7	forb.	$(\pi \rightarrow \pi^*)$	255
B_u	241.5	1.0911	$(\pi \rightarrow \pi^*)$	
A_g	230.9	forb.	$(\pi \rightarrow \pi^*)$	

[a] Reference Jurd (1959). [b] sh = shoulder.

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