Molecular mechanics study on conformation of perylene-quinonoid photosensitizers*

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Abstract Using molecular mechanics method, values of the heat of formation (HF) of different conformations of perylenequinonoid photosensitizer, hypocrellin A (HA) and hypocrellin B (HB) were calculated and the variances of HF after phenolic protons' dissociation were calculated as well. The following was found: (i) The HF values of four conformational isomers of HA and HB are similar to each other, so the four isomers can transform to each other at room temperature. (ii) There exists the difference between the ability of dissociation of phenolic protons of HA and that of HB, the former is higher than the latter. (iii) There exist two intramolecular hydrogen bonds in HA and HB. The bond energy is approximately 8 kJ/mol and the energy of conformation I is lower than that of conformation II. (iv) There exists a low energy spot when phenolic hydroxyl bond twists 180° from the position where hydrogen bond is formed, which suggests that this kind of conformation probably exists. (v) The phenolic hydrogen of HBMC forms hydrogen bond with the neighbouring nitrogen, which is its structure basis of possessing photosensitizing activity.

Keywords: molecular mechanics, perylenequinonoid photosensitizer, conformational isomer, heat of formation, proton dissociation, intramolecular hydrogen bond.

Recently, as people find that perylenequinonoid photosensitizers (PPS) possess the ability of killing cancer cells and inhibiting HIV[1,2], they have paid extensive attention to PPS[3], in which, HA and HB are the most spectacular pigments[4]. Up to date, their photophysical and photochemical properties have been fully studied, but there are many problems remaining to be solved. For example, although the structures of HA and HB are similar to each other (the difference is that HB is formed from HA dehydration, so the seven-membered side ring of HB has one double bond more than the ring of HA), their physical and chemical properties are quite different: the rate of auto-sensitized photooxidation of HA is far higher than that of HB[5], the quantum yield of fluorescence of HB is far lower than that of HA[6], their photosensitizing characteristics are different[7,8], etc. Especially, the intramolecular hydrogen bond of PPS has the utmost importance in stabilizing the structure. But up to now, there exist arguments on whether there are two intramolecular hydrogen bonds in HA and HB, because it has been reported in ref.[9] that the differential Fourier spectra of HB only revealed the existence of one intramolecular hydrogen bond, and the problem whether the other phenolic hydrogen forms hydrogen bond with its neighbouring quinonoid oxygen is unknown. As to the problems on the bond strength of the hydrogen bond and the formation of other kind of intramolecular hydrogen bond, it is difficult to answer them through experiment. So, theoretical study is required urgently. In view of fruitful use of molecular mechanics in studying the conformations of small molecules, in this paper, this

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method is employed to study the above problems. A few results of theoretical significance are obtained, which are contributive to clarifying the structure-effect relationship of PPS.

1 Calculation method

The molecular mechanics program MMX\textsuperscript{[10]} in PCMODEL software was employed to perform the calculations. MMX was revised on the foundation of MM\textsuperscript{2}\textsuperscript{[11]}, a widely used molecular mechanics program. Calculation procedures are as follows: firstly, optimizing part of HA or HB; secondly, adding atomic groups step by step; and finally, completing the whole molecule's optimization. All calculations were carried out on an IBM486 computer.

2 Results and discussion

2.1 HF values of different conformations of HA and HB

As having the unique molecular structure, HA and HB have intramolecular proton transfer in both ground and excited states. So, they show two kinds of isomers (I, II) in solution as shown in scheme 1.

$$\text{Scheme 1}$$

![Scheme 1](image)

Furthermore, as the different twist-directions of perylenequinonoid ring, they give two stereoisomers (the right twisted and the left twisted). So they show four conformations in solution, namely, I (right twisted), II (right twisted), I (left twisted), and II (left twisted). Former experiments indicated that there existed fast equilibrium of isomers I and II of HA and HB in solution at room temperature\textsuperscript{[12]}, which is distinct from another PPS, cercosporin (CP).

The latter two isomers cannot transform to each other unless being heated, and the energy barrier of the process is $20 \times 4.186$ kJ/mol\textsuperscript{[13]}. We calculated the HF values of HA (right twisted) isomers I and II (−792.64 and −798.00 kJ/mol), and left twisted I and II (−791.43 and −777.15 kJ/mol). The corresponding values of HB are −495.72, −503.04, −479.89 and −502.92 kJ/mol, respectively. Evidently, the HF values of the four isomers are similar to each other and unlike CP, which has an energy barrier of $20 \times 4.186$ kJ/mol. This explains in a