Chinese Chemical Letters Vol. 12, No. 2, pp. 117–118, 2001

Synthesis and Properties of An Aminated hypocrellin B

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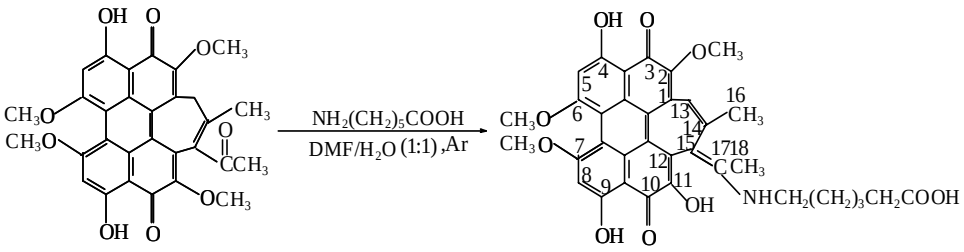
Abstraction: A new aminated-perylenequinone derivative **2** was synthesized by the reaction of **1** (hypocrellin B) with 6-aminohexanoic-acid. The structure of **2** was identified by UV-Vis, MS, IR and ^{1}H-NMR. The amphiphility, spectrum and photochemical properties of **2** were reported.

Keywords: Hypocrellins, amination, amphiphility, photochemical properties.

Photodynamic therapy (PDT), using red light and photosensitizers (Sens), is a promising new treatment for tumor. The naturally occurred hypocrellins,including hypocrellin A (HA) and hypocrellin B (HB,**1**), have been proposed as the potential photosensitizers for PDT. It has been the subject of many investigations to improve the red absorption and water-solubility of natural hypocrellins by the structural modifications[1~3]. In this paper, a new derivative **2** was synthesized from **1** and characterized. Both the red absorption and amphiphility of **2** were improved. The efficiencies of singlet oxygen ($^1O_2$) and semiquione radical anion ($Sens^{-\cdot}$) generated by phototsensitization of **2** were compared with parent **1**.

Hypocrellin A (HA) was isolated from the fungus sacs of hypocrella *bambase*. **1** was prepared from HA by the published method[4]. **2** was synthesized from **1** with the excess of 6-aminohexanoic-acid in an argon-gassed DMF-H_2O solution (1:1,PH$\geqslant$13) (**Scheme**). The residue was purified by 1% citric acid-silica TLC, using 4:2:1 petroleum ether/ethyl acetate/ethanol as eluent to give pure **2** as a blue solid in 45% yield.

Scheme



1: HB **2**

Compound **2**: UV-Vis:($CHCl_3$ λ_{max},nm, lg ε) : 457 (4.17), 550 (sh), 581 (4.22), 630 (sh). MALDI-TOF MS. M+1: m/z 628. IR (KBr, cm^{-1}): 3443 (-OH), 1717 (-C=O of –COOH), 1605 (-C=O of quinone). ^{1}H-NMR ($CDCl_3$, ppm): 16.40 (m, 2H, 4,9-O**H**), 7.20 (s, 1H, 11-O**H**), 6.50 and 6.44 (s, 2H, 5,8-**H**), 5.29 (s, 1H, 13-**H**), 4.21 (s, 3H, 2-OC**H**$_3$), 4.04 (s, 3H, 6-OC**H**$_3$), 3.99 (s, 3H, 7-OC**H**$_3$), 3.80 (m, 2H, -NHC**H**$_2$), 2.20 (m, 2H, -C**H**$_2$COOH), 2.35 (s, 3H, 16-C**H**$_3$), 1.69 (s, 3H, 18-C**H**$_3$), 1.53~2.00 (m,6H,-NHCH$_2$(C**H**$_2$)$_3$-).

The partition coefficients of hypocrellins between *n*-octanol and phosphate-buffered solution (PH=7.4) were spectrophotometrically measured. Nothing could be detected in the buffer phase for **1** due to its poor hydrophility. The partition coefficient of **2** was determined to be 6.5, indicating an improved amphiphility for **2**. Moreover, the absorption peaks of **2** shifted to 583 nm and 630 nm (sh), extending to 800 nm. The efficient red-shift was observed, compared with parent **1** (λ_{max}=464 nm, lg ε =4.33).

The singlet oxygen ($^1O_2$) is generated by the reaction of the excited photosensitizer with oxygen (reaction Ⅰ). The quantum yields (Φ_{1O2}) were determined by the

$$Sens^* + O_2 \longrightarrow Sens + {}^1O_2 \qquad (Ⅰ)$$

9,10-diphenyanthyance-bleaching method[5]. Φ_{1O2} were found to be 0.76 and 0.18 for **1** and **2** in $CHCl_3$ at 470 nm, respectively.

The ESR hyperfine structure of semiquinone radical anion of **2**, generated by the photoinduced electron transfer between **2** and electron doner (**D**), was observed (reaction Ⅱ). The relative efficiency for generation of $\mathbf{2}^{-\cdot}$, in the presence of

$$Sens^* + D \longrightarrow Sens^{-\bullet} + D^{+\bullet} \qquad (Ⅱ)$$

1-benzyl-1,4-dihydronicontiamide (BNAH) as an electron donor, was measured with BNAH-oxidation method[6] at 470 nm in deaerated CH_3CN, using **1** as reference (Φ_{HB} $_{-\cdot}$=1.00). The relative efficiency for generation of $\mathbf{2}^{-\cdot}$ was established to be 1.94.

The studies of the photodynmic properties of **2** are under way.

Acknowledgment

We are grateful to the National Natural Science Foundation of China (Project No.39830090 and No.39970871) for their financial support to this research.

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Received 6 July, 2000