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Synthesis of Substituted 3*H*-Indole-modified β-Cyclodextrin

Qi CHEN, Xing Hai SHEN*, Hong Cheng GAO*

College of Chemistry and Molecular Engineering, Peking University, Beijing 100871

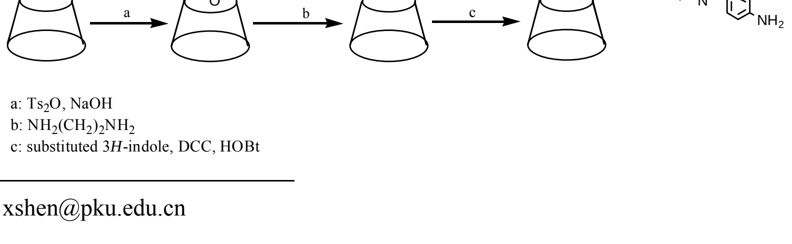
Abstract: Substituted 3*H*-indole modified β-cyclodextrin (β-CD) was prepared by the reaction of 6-deoxy-6-[(2-aminoethyl)amino]-β-CD (CDen) with 2-[(*p*-amino)phenyl]-3, 3-dimethyl-5- carboxyl-3*H*-indole (substituted 3*H*-indole) in the presence of dicyclohexylcarbodiimide (DCC) and 1-hydroxybenzotriazole (HOBt). The product has been characterized by means of elemental analysis, MS and ^{1}H NMR.

Keywords: β-Cyclodextrin, modified, substituted 3*H*-indole.

The hydrophobic cavities of cyclodextrins and the inclusion with various organic molecules in the aqueous solution make them useful in chemical and biological activities[1], one of which is the modified cyclodextrins acting as indicators of molecular recognition. Cyclodextrins, which are spectroscopically inert, can be converted into spectroscopically active compounds by modifing one or two of the hydroxy groups with appropriate chromophores, and used as molecular sensor due to the capability of changing fluorescence and absorption properties upon accommodation of guest molecules[2, 3]. During the last decade, lots of such cyclodextrin derivatives have been synthesized and characterized[4, 5]. Here, we report the synthesis of substituted 3*H*-indole- modified β-CD, a probable guest-responsive fluorescent molecular sensor. In the former studies, it has been observed that substituted 3*H*-indoles have strong fluorescence and their spectroscopy and photophysics are sensitive to environments[6, 7]. We think this molecular sensor might have important applications in molecular recognition.

Experimental

The substituted 3*H*-indole was prepared according to Ref. 8(a,b). 6-Deoxy-6-(*p*-tolyl-



a: Ts_2O, NaOH
b: $NH_2(CH_2)_2NH_2$
c: substituted 3*H*-indole, DCC, HOBt

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* E-mail: xshen@pku.edu.cn

sulfonyl)-β-cyclodextrin (Ts-CD) was prepared according to Ref. 9, while the preparation of CDen was based on Ref. 10.

To a solution of 250 mg CDen in 10 mL of DMF was added 100 mg substituted 3*H*-indole. After the solution was cooled below 0oC, 100 mg DCC and 68 mg HOBt were added. The resulting mixture was stirred for 5 h below 0oC and subsequently for 15 h at room temperature. After insoluble materials were removed by filtration, the filtrate was poured into acetone (300 mL). The resulting precipitate was collected, dissolved in DMSO (5 mL) and reprecipitated by pouring into acetone. This reprecipitation from acetone was repeated until no substituted 3*H*-indole was observed by TLC. The crude product was recrystallized in water to give the desired product as a pale yellow solid (100 mg, 33%).

Anal. calcd for $C_{61}H_{90}N_4O_{35}\cdot 8H_2O$: C, 46.27; H, 6.70; N, 3.54, found: C, 46.26; H, 6.43; N, 3.52. MS (MALDI TOF): *m/z* calcd for $(M + H)^+$ 1439, found: 1439. ^{1}H-NMR (400 MHz, DMSO-d_6, δ ppm): 1.52 (s, 6H, CH_3), 3.20-3.80 (m, overlap with H_2O, $C_{2\text{-}6}H$), 4.49 (s, 6H, O_6H), 4.83 (s, 7H, C_1H), 5.60-5.90 (m, 14H, $O_{2,3}H$), 5.92 (s, 2H, NH_2), 6.60-6.70 (d, 2H, J=8.4 Hz, PhH), 7.45-7.50 (d, 1H, J=7.9 Hz, PhH), 7.80-7.85 (d, 1H, J=7.9 Hz, PhH), 7.90 (s, 1H, PhH), 7.92-8.00 (d, 2H, J=8.4 Hz, PhH).

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