Synthesis of a Novel Mono-(6-N-allylamino-6-deoxy)-β-cyclodextrin Functional Monomer

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Abstract-β-cyclodextrin (β-CD) is a kind of cyclic oligosaccharide with a unit of D-glucopyranose. It shows good molecular recognition ability for its unique physical and chemical properties and suitable cavity structure. It also is an important supermolecule. It is easy to be derived to get a variety of functional monomers which could be used for chromatographic solid phases and molecularly imprinted polymers. A novel mono-(6-N-allylamino-6-deoxy)-β-CD was synthesized by using mono-(6-p-toluenesulfonyl)-β-cyclodextrin (6-OTs-ß-CD) and allylamine as reactants in the solvent of allylamine. The reaction conditions, such as reaction temperature, molar ratio of reactants and reaction time, were optimized. And the yield of 83.9% could be obtained based on the optimized conditions. The product was characterized by FT-IR, MS and 1HNMR. The characterization results further confirmed that the target product of mono-(6-N-allylamino-6-deoxy)-β-CD was successfully synthesized. The product was a novel functional monomer. It could be used for the preparation of polymers for further adsorption study.

Keywords-mono-(6-N-allylamino-6-deoxy)-β-cyclodextrin; mono-(6-p-toluenesulfonyl)-β-cyclodextrin; β-Cyclodextrin; allylamine; functional monomer

I. INTRODUCTION

Cyclodextrins (CDs) are a class of oligosaccharides with a cyclic structure. Both α-CD, β-CD and γ-CD are commonly used, but β-CD is the most widely used for its suitable cavity. β-CD shows good molecular recognition for its special cavity structure, which has hydrophilic exterior and hydrophobic cavity. It can inclusion some special guest compounds [1-2].

The hydroxyl groups in CDs are the reactive groups. But the reactivity of hydroxyl groups on the C-2, C-3 and C-6 are different. Since the alkaline of the hydroxyl group on C-6 is much stronger than the hydroxyl groups on C-2 and C-3, and the nucleophilicity of the hydroxyl group on C-6 also is the strongest. So, the reactivity of hydroxyl group on C-6 is much higher than the hydroxyl groups on C-2 and C-3 [1].

β-CD is an important reactant. It is easy to be derived to get a variety of cyclodextrin derivatives. The hydroxyl groups of C-6, or C-2, or C-3, could be selectively substituted by methyl groups, iodine groups, bromo groups, amine groups or sulfonic acid groups. The hydroxyl groups of C-6 and C-2 and C-3 could also be

simultaneously substituted by methyl groups, iodine groups, bromo groups, amine groups or sulfonic acid groups [3-6]. The derivatives on the hydroxyl groups of C-6 of β-CD were easy to obtain, especially the mono-6-substitued cyclodextrin products, such as mono-(6-*p*-toluenesulfonyl)-β-cyclodextrin (6-OTs-β-CD) [7-9], mono-(6-ethylenediamine-6-deoxy)-β-cyclodextrin [10-11] and other derivative products [12-16].

The ethylenic group also could be introduced to β-CD. The hydroxyl groups could be substituted by acryloyl chloride or methacryloyl chloride [17-18]. The resultant product with ethylenic group was a useful functional monomer. The β-cyclodextrin functional monomers could be used for chromatographic solid phase [19-22] and molecularly imprinted polymers [23-27].

In this study, a novel mono-(6-N-allylamino-6-deoxy)-β-CD was synthesized by using β-CD and allylamine as reactants. Allylamine was used as both reactant and solvent. The reaction conditions of reaction temperature, molar ratio of reactants and reaction time were investigated. Based on the optimized conditions, the yield was up to 83.9% (calculated based on β-CD). It is a useful intermediate product. Its adsorption performance will be further studied.

II. EXPERIMENTAL

2.1 Instruments and reagents

EQUINOX 55 Fourier transform infrared spectrometer (German Bruker Optics Company), Xevo TQ-S mass spectrometer (American Waters company), and Bruker AV-600 MHz nuclear magnetic resonance spectroscopy (Germany Bruker company) were used for structure characterization. PS-20 ultrasonic cleaning machine (Dongguan Jiekang ultrasonic equipment limited company) and FA2004 type electronic balance (Shanghai Hengping Scientific Instrument Ltd.) and XMTD-204 digital thermostat water bath equipment (Jiangsu Jintan Huacheng Kaiyuan experimental instrument factory) were used for the synthesis of mono-(6-N-allylamino-6-deoxy)-β-CD. Allylamine (99%) was purchased from Xiya Reagent Co. Ltd. (Chengdu, China). Other reagents were analytically grand *2.2 Synthesis*

2 g 6-OTs-β-CD (1.55 mmol) and 26 mL allylamine (351 mmol) were put into a 250 mL round bottom flask. The flask with a reflux device then was placed in 60 °C water bath. The mixture was stirred for 4 h. After the completion of the reaction, the mixture was cooled to room temperature. 20 mL methanol was added into the mixture. The solution was mixed. Then 80 mL acetonitrile was added. A lot of white precipitate appeared. It was filtered and the white solid was collected. The white solid was purified by methanol and acetonitrile twice. The obtained product was dried under reduced pressure at 40°C for 2 h. The synthetic reaction was shown as Fig .l.

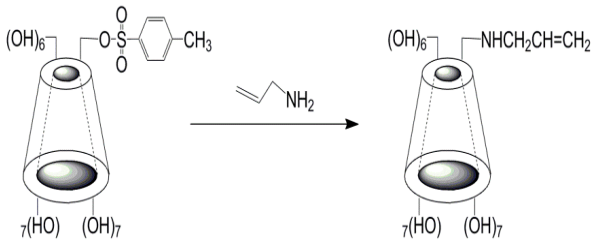

Figure 1. Synthetic reaction of mono-(6-N-allylamino-6-deoxy)-β-cyclodextrin.

III. RESULTS AND DISSCUSSION

3.1 Effect of reaction temperature on the yield

The reaction of 6-OTs-β-CD and allylamine produced the target product. The reaction temperature was set from 50 to 70 °C. The reaction time was set as 4 h. The molar ratio of 6-OTs-β-CD and allylamine was 1:225. The result was list in Table 1. The yield of product increased with the improving temperature. When the temperature was higher than 60 °C, the yield basically maintained at 83%. Therefore, the optimal reaction temperature was selected as 60 °C.

TABLE I Effect of reaction temperature on the yield

Temperature / °C	Yield / %
50	79.9
55	81.2
60	83.1
65	83.3
70	82.7

3.2 Effect of molar ratio of reactants on the yield

On the basis of optimal the temperature, the molar ratio of 6-OTs-β-CD and allylamine was then optimized (Table 2). Since the allylamine was used as both solvent and reactant. The amount of allylamine was much more than 6-OTs-β-CD. The reaction time was set as 4 h. The result showed that a high yield could be obtained when the molar ratio was 1:225. Increasing the amount of allylamine, the yield basically maintained at 83%. Therefore, the optimal molar ratio was selected as 1:225.

TABLE II Effect of molar ratio of reactants on the yield

$n_{(6\text{-OTs-}\beta\text{-CD})}$: $n_{(allylamine)}$	Yield / %
1：175	73.5
1：200	78.4
1：225	83.1
1：250	83.4
1：275	82.3

3.3 Effect of time on the reaction yield

The reaction time was optimized at last. It was varied from 3.0 h to 5.0 h. The result was shown in Table 3. It could be found that the highest yield could be obtained at the time of 4.5 h. So, the reaction time was selected as 4.5 h.

TABLE III Effect of reaction time on the yield

Reaction time / h	Yield / %
3.0	75.4
3.5	79.4
4.0	83.1
4.5	83.9
5.0	82.5

3.4 Product characterization

Both the mono-(6-N-allylamino-6-deoxy)-*β*-cyclodextrin and 6-OTs-*β*-CD were characterized by IR (Fig .2). It could be found from the spectrum of product that the three characteristic absorption peaks of 1601, 1192 and 1178 cm^{-1}, which was in the IR spectrum of 6-OTs-*β*-CD (Fig .2 (a)), had disappeared in the IR spectrum of mono-(6-N-allylamino-6-deoxy)-*β*-cyclodextrin (Fig .2 (b)). The three characteristic absorption peaks were corresponded to sulfonic acid group. On the other hand, four characteristic absorption peaks of 1645, 1557, 1417 and 1298 cm^{-1} had appeared in the spectrum of product. The absorption peaks of 1645 cm^{-1} was corresponded to N-H stretching vibration in the group of allylamine. The absorption peaks of 1557 cm^{-1} was corresponded to C=C stretching vibration in the group of allylamine. The absorption peaks of 1417 cm^{-1} was corresponded to -CH_2- stretching vibration. And the absorption peaks of 1298 cm^{-1} was corresponded to =C-H stretching vibration in the group of allylamine. The results showed that the *p*-toluenesulfonyl group had been substituted by allylamine group. The product of mono-(6-N-allylamino-6-deoxy)-*β*-CD had been successfully synthesized.

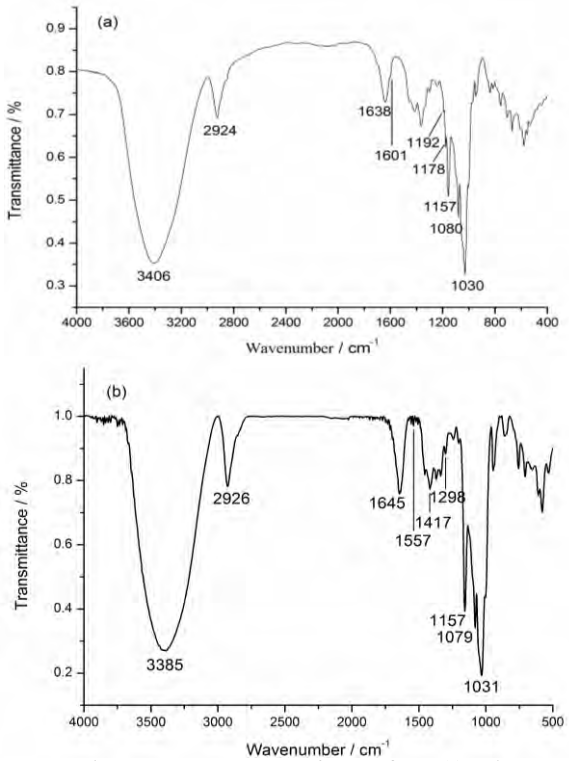

Figure 2. IR spectrum of 6-OTs-ß-CD (a) and mono-(6-N-allylamino-6-deoxy)-β-CD (b)

Mono-(6-N-allylamino-6-deoxy)-*β*-CD also was characterized by MS and ^{1}H NMR (Fig .3). The molecular weight of mono-(6-N-allylamino-6-deoxy)-*β*-CD was 1174. The mass-charge ratio of 1174, 1175, 607 and 599 was corresponded to $[M]^+$, $[M+H]^+$, $[M+H+K]^{2+}$ and $[M+H+Na]^{2+}$, respectively (Fig .3(a)). The ^{1}H NMR spectrum was also characterized. The chemical shift values attributed to each proton were showed as Fig .3(b). The characterization of MS and ^{1}H NMR could further confirm the structure of mono-(6-N-allylamino-6-deoxy)-*β*-CD.

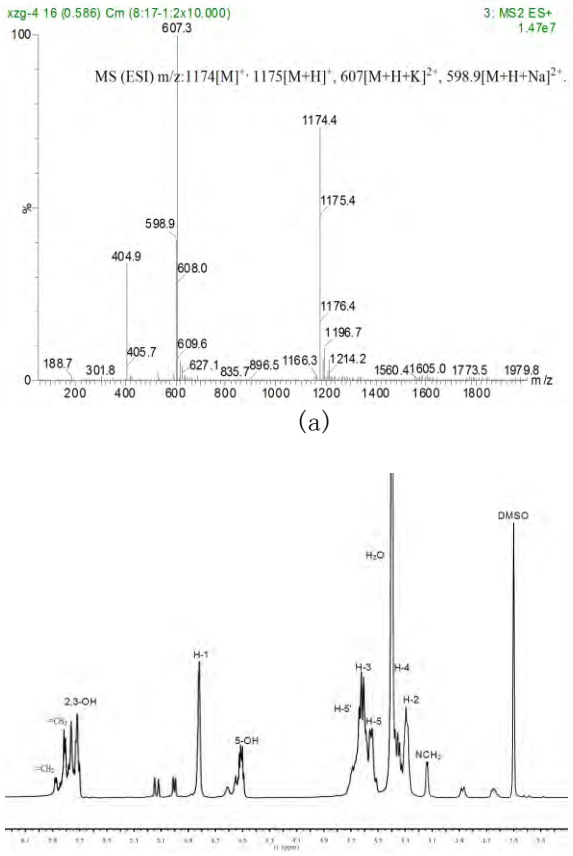

Figure 3. MS (a) and 1H NMR (b) spectrum of mono-(6-N-allylamino-6-deoxy)-β-CD

IV. CONCLUSIONS

Mono-(6-N-allylamino-6-deoxy)-*β*-CD was synthesized by one step reaction. The yield was up to 83.9% (calculated based on *β*-CD) under optimized conditions. The reaction was simple and easy to operate. And the product was easy to purify by solvent treatment. The product had the unsaturated C=C bond. It could be used as a novel useful functional monomer for preparation of polymers. And the adsorption properties of polymers would be further studied in our future work.

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