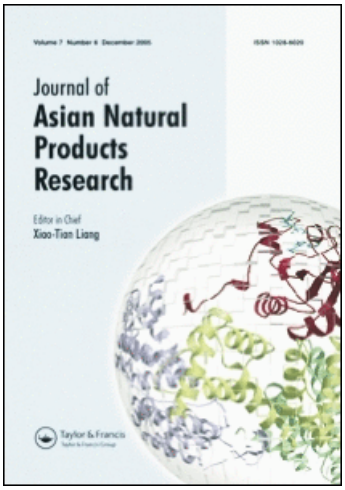

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Synthesis and allylation at the *all* O-6 positions of cyclomaltohexaose

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Synthesis and allylation at the *all* O-6 positions of cyclomaltohexaose

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A method for preparation of per-6-O-substituted cyclodextrin derivatives was developed. The thermostable cyclomaltodextrin glucanotransferase (CGTase) formed mainly cyclomaltohexaose **2** from amylose **1**. The compound **2** was selectively converted to **3** without protection of the other hydroxyl groups by allylation at the *all* O-6 positions in excess base.

Keywords: Cyclomaltodextrin glucanotransferase; Hexakis (6-*O*-allyl)cyclomaltohexaose; Synthesis; Allylation

1. Introduction

Cyclomaltodextrin glucanotransferases (CGTase; EC 2.4.1.19) are able to convert starch into cyclodextrins (CDs), closed-ring structures in which six or more glucose units are joined by means of α-1,4 glucosidic bonds [1]. Depending on the type of CD (with six, seven, or eight glucopyranose residues: α-, β-, or γ-CD, respectively) initially formed, the CD-forming enzymes are classified as α-, β-, or γ-CGTases [2]. They are able to form inclusion complexes with many organic and inorganic molecules, thereby changing the physical and chemical properties of the included compounds. Therefore, CGTase is an important enzyme for the food, cosmetic, and pharmaceutical industries. CGTases are known to catalyse four different transferase reactions: cyclisation, coupling, disproportionation, and hydrolysis [3]. In addition, thermostable CGTase is very useful for industrial utilisation. Liquefaction, which is the first step in the production of CDs from starch, is performed by jetcooking, where a starch slurry is treated with thermostable α-amylase at 105 to 110°C. Thermostable CGTase can be used in liquefaction and then in CD formation without being replaced [4].

CDs and their synthetic derivatives [5] attract much attention due to their complexation abilities. In this study, we will show that CDs' derivatives can be synthesised by the thermostable CGTase catalysing starch and modified chemically.

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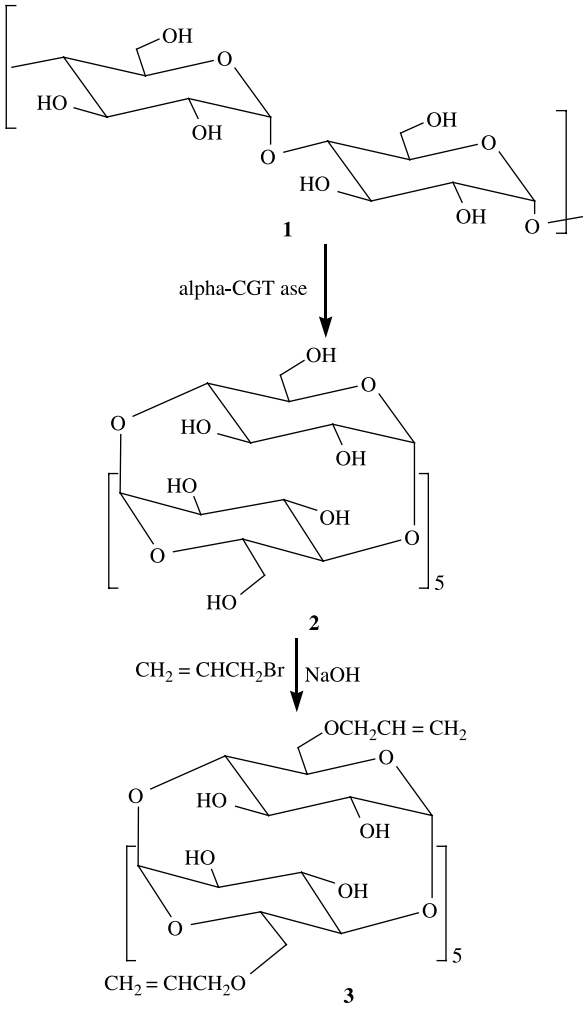

Scheme 1. Synthesis of hexakis (6-*O*-allyl)cyclomaltohexaose **3**.

2. Results and discussion

The extremely thermophilic anaerobic archaeon strain B1001 producing CGTase was isolated from a hot-spring environment [6]. The temperatures for starch-degrading activity and cyclodextrin synthesis activity were 110 and 90 to 100°C, respectively. The enzyme formed α-cyclodextrin as the major compound from starch. In our experiment, cyclomaltohexaose **2** was obtained in 62% yield (Scheme 1).

We took advantage of the fact that in excess base the preferred outcome of the reaction of amylose with allyl bromide will be substituted in the O-6 position. The crude product was isolated via precipitation with EtOH and subsequent freeze-drying. The hexakis (6-*O*-allyl)cyclomaltohexaose **3** was obtained in 78% yield. The HSQC spectrum shows that the proton at δ 3.66 is attached to the CH_2 carbon at δ 68.7 (assigned by DEPT spectrum). It is clear that the *O*-allyl group is attached in position 6.

3. Experimental procedures

3.1 General methods

Column chromatography was performed on column of silica gel (Baker, 0.063–0.200 nm). Optical rotations were determined at 25°C with a Perkin–Elmer Model 241-Mc automatic polarimeter. ^{13}C NMR and ^{1}H NMR spectra were recorded using a Bruker DPX-300 spectrometer at 75 and 300 MHz, respectively. Mass spectra were recorded with a VG PLATFORM mass spectrometer using the ESI mode.

3.2 Enzymatic synthesis of cyclomaltohexaose (2)

The CGTase was obtained as previously reported [6]. Reaction mixtures (100 ml) containing 2.5% (w/v) soluble amylose **1** and 50 mmol/L sodium acetate buffer (pH 5.0) were incubated with the purified enzyme at 90°C for 24 h. The reaction was terminated at 0°C. Purification by silica gel column chromatography with $CHCl_3$/MeOH (10:1 [v/v]) gave **2** (7.8 mg) in 62% yield.

*3.3 Synthesis of hexakis (6-*O*-allyl)cyclomaltohexaose (3)*

To the stirred solution of **2** (3.72 mmol) and sodium hydroxide (2.00 g, 50 mmol) in water (20 ml) allyl bromide (323 μl, 3.72 mmol) was added and the resulting emulsion was stirred at room temperature for 12 h. The colourless suspension was diluted with 180 ml of distilled water and neutralisation was performed with HCl. Isolation was performed via precipitation with EtOH and subsequent freeze drying. $[\alpha]_D + 75.3$ (*c* 1.1, H_2O). ^{1}H NMR (300 MHz, D_2O): δ 6.07-5.82 (m, 6H, $CH_2CH{=}CH_2$), 5.39–4.81 (m, 12H, $CH_2CH{=}CH_2$), 5.13 (d, 6H, H-1), 3.70 (m, 6H, H-2), 3.95 (m, 6H, H-3), 3.55 (m, 6H, H-4), 3.72-3.90 (m, 6H, H-5), 3.66 (m, 12H, H-6), 3.61 (s, 12H, $CH_2CH{=}CH_2$), 4.72 (s, 12H, OH). ^{13}C NMR (75 MHz, D_2O): δ 135.6 ($CH_2CH{=}CH_2$), 116.1 ($CH_2CH{=}CH_2$), 102.5-102.0 (C-1), 82.1 (C-4), 73.1 (C-2), 72.8-72.5 (C-3), 71.3 ($CH_2CH{=}CH_2$), 70.7-70.6 (C-5), 68.7 (C-6). ESI-MS: *m*/*z* 1235.1 $[M + Na]^+$. Elemental analysis (%): C, 53.70; H, 6.55. Calcd for $C_{54}H_{84}O_{30}$: C, 53.46; H, 6.98.

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