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Note

Synthesis of methyl α- and β-maltosides

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Methyl α- and β-maltosides may be prepared by chemical synthesis[1–3], but the procedures are tedious. We have reported[4] good separations of the methyl glycosides of various monosaccharides by use of reverse-phase h.p.l.c. Methyl glycosidation of maltose at elevated temperatures in the presence of Amberlite IR-120 (H^+) resin gave ~10% of a mixture of methyl α- and β-maltosides, a similar proportion being formed in the presence of 0.1% methanolic hydrogen chloride[3].

For maltose at 20–25° in 1% methanolic hydrogen chloride, after 4 days the reaction mixture consisted of methyl maltosides (~35%, α:β ratio ~1:1), maltose (~25%), methyl glucopyranosides (~37%), and methyl glucofuranosides (~3%) (Fig. 1). The methyl maltosides were isolated by preparative h.p.l.c. (see Experimental). The concentration of maltosides was fairly constant at ~35% as long as free maltose remained. After 4 weeks, the methyl glucopyranosides were almost exclusively present (Fig. 1); <1% of glucose was detected at any time during the reaction.

The analytical Dextropak column was packed with a grade of C_{18}-bonded silica specially selected for carbohydrate oligomer separations[4], but it is a versatile column and has other uses in carbohydrate analysis[5]. The preparative cartridge was packed with normal C_{18}-bonded silica of preparative grade.

Resolution of the two methyl maltosides was not apparent in preparative h.p.l.c. (Fig. 2). This is a not uncommon situation when a large amount of material is loaded, but repeated chromatography of the leading and trailing fractions gave the pure glycosides. All of the preparative and analytical h.p.l.c. separations on a 3-g sample of the product mixture obtained after reaction for 4 days were performed in half a day and yielded glycosides of 90% purity. However, these advantages must be weighed against the cost of the h.p.l.c. equipment.

EXPERIMENTAL

A Waters Associates analytical h.p.l.c. system was used, comprising an M6000

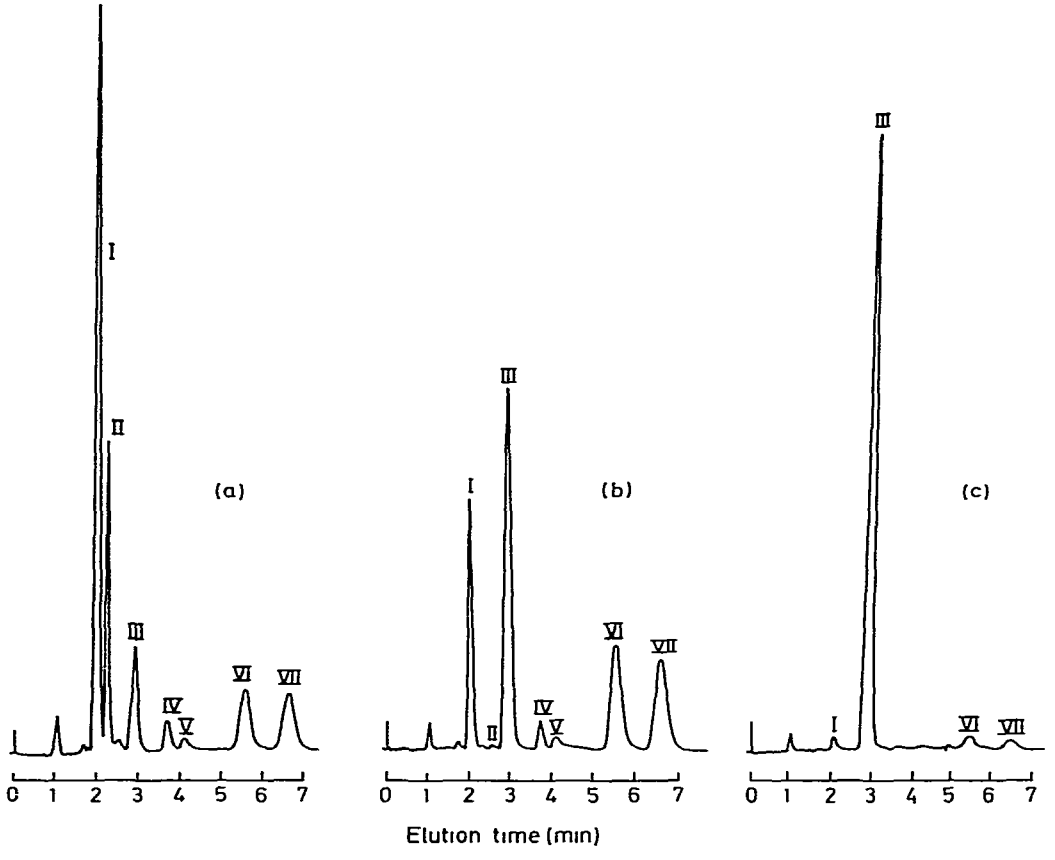

Fig. 1. Analytical h.p.l.c. after glycosidation of maltose in 1% methanolic HCl at 20–25°: (a) after 1 day; (b) after 4 days; and (c) after 30 days. I, Maltose; II, methanol, III, methyl glucopyranosides, IV, methyl α-D-glucofuranoside; V, methyl β-D-glucofuranoside; VI, methyl β-maltoside; and VII, methyl α-maltoside.

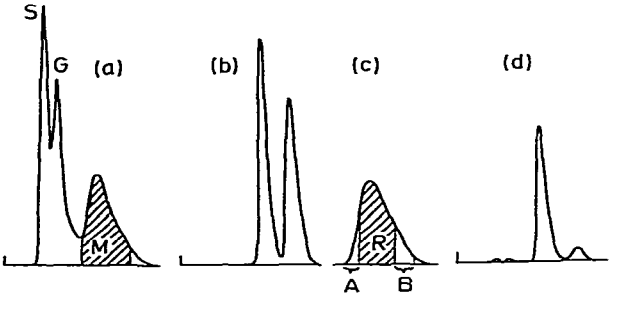

Fig. 2. H.p.l.c. after glycosidation of maltose in 1% methanolic HCl for 4 days at 20–25°. (a) Preparative profile of the reaction mixture; S, maltose + methanol; G, methyl glucosides; M, methyl maltoside. (b) Analytical profile of M from (*a*), which consists of the two methyl maltosides. (c) Preparative profile of M from (a): A, leading-edge fraction (mainly methyl β-maltoside); R, fraction subjected to re-chromatography; B, trailing-edge fraction (mainly methyl α-maltoside). (d) Analytical profile of A from (c), comprising ~90% of methyl β-maltoside and 10% of the α anomer.

pump, a U6K injector, a-R401 refractive-index detector, a radial-compression module (RCM100), and a Dextropak plastic cartridge[4] (10 × 0.8 cm). For preparative h.p.l.c., a Waters Prep LC/System 500A was used with a Prep Pak C_{18} cartridge (30 × 5.7 cm). The eluent was distilled water.

Optical rotations were determined with a Bendix NPL Automatic Polarimeter (143C).

P.m.r. spectra (internal Me_4Si) were obtained for solutions in Me_2SO-d_6 at 25° with a JEOL JNM-FX100 spectrometer. Coupling constants for anomeric protons were determined after D_2O exchange. 1% Methanolic hydrogen chloride solution was made by adding acetyl chloride to dry methanol. Glycoside formation was performed by shaking dry maltose (100 mg) with methanolic hydrogen chloride (20 ml). Samples (1 ml) were withdrawn at intervals (12 h), neutralised with Amberlite IRA-400 (HCO_3^-) resin, and concentrated at 40°, and a solution of the residue in water was filtered and subjected to analytical h.p l.c. On the preparative scale, the reaction of maltose (8 g) with methanolic hydrogen chloride (800 ml) was monitored by analytical h.p.l.c. After 4 days at room temperature, the mixture was neutralised and concentrated, and a portion (3 g) of the syrupy residue was dissolved in water (10 ml) and subjected to preparative h.p.l.c. (flow-rate, 300 ml/min). The fraction (900 mg) containing the methyl maltosides was not resolved, on the preparative column, into the α and β anomers (see Fig. 2a). This fraction was decreased in volume to ~3 ml and re-chromatographed. The leading and trailing edges of the peak were collected and the middle of the peak was recycled (Fig. 2c). This procedure was repeated until the recycled peak became too small and diffuse to handle.

The combined leading and combined trailing fractions [A (375 mg) and B (320 mg), respectively] were >90% pure by analytical h.p.l.c. (Fig. 2d).

Further purification of small samples of fractions A and B on the Dextropak column gave chromatographically pure methyl β-maltoside, m.p. 104–106° (from ethanol), $[\alpha]_D^{20}$ +71° (*c* 0.39, water); {lit.[3] $[\alpha]_D$ +80° (water)}; ^{1}H-n.m.r. data: δ 4.0 (d, 1 H, $J_{1,2}$ 7.9 Hz, H-1); and methyl α-maltoside, $[\alpha]_D^{20}$ +169° (*c* 0.35, water); {lit.[3] $[\alpha]_D$ +179.6° (water)}; ^{1}H-n.m.r. data: δ 4.5 (d, 1 H, $J_{1,2}$ 3.4 Hz, H-1).

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