Carbohydrcte Research, 101 (1982) 348–349
Elsevier Scientific Publishing Company, Amsterdam – Printed in The Netherlands

Note

The preparation of decagram quantities of D-psicose by the isomerization of D-fructose, and separation of the products on a calcium-ion cation-exchange resin

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(Received September 17th, 1981; accepted for publication, October 9th, 1981)

It has long been known that the base-catalyzed isomerization of D-fructose affords a mixture from which D-psicose may be isolated. Doner[1] investigated the optimum conditions for the isomerization, and gave, as the best practical procedure for the isolation of D-psicose, a method involving fermentation, to remove sugars other than D-psicose, and subsequent chromatography. Gram quantities of D-psicose were obtained after about three days' work.

We required larger quantities of D-psicose for the synthesis of unnatural nucleosides, and we now report that the isomerization products can be efficiently separated on a cation-exchange resin in the calcium form[2], without the need for a fermentation step. This appears to be a significant improvement on Doner's method; we can prepare about ten grams of pure D-psicose in about 2–3 days.

EXPERIMENTAL

D-Fructose (125 g) in ethanol (750 mL) and triethylamine (25 mL) was boiled for 15 h under reflux, a modification of one method given by Doner[1]. The solution was evaporated to a syrup, and this was dissolved in water (500 mL), and the solution successively washed with chloroform (500 mL) and diethyl ether (400 mL), stirred with charcoal for 1 h, the suspension filtered, and the filtrate de-ionized by stirring with Dowex-50 (H^+) resin (100 mL) for 1 h; the suspension was filtered, and the filtrate was evaporated to a syrup. This was dissolved in 3:7 methanol–water (150 mL), and the solution was chromatographed in three portions (50 mL each) in a column (4.5 × 40 cm) of Dowex AG-50W X-2 (Ca^{2+}) resin (200–400 mesh) with 3:7

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0008-6215/82/0000–0000/S 02.75,

methanol–water as the eluant, 50-mL fractions being collected[2]. The fractionation was monitored by t.l.c. on plastic sheets precoated with PEI-Cellulose F, the eluant being 8:6:3:3 *tert*-butanol–butanone–88% formic acid–water, and the plates were sprayed with 1% *p*-anisidine hydrochloride in ethanol, and developed in an oven for 10 min at 95°. Standards of D-psicose[3], D-fructose, and D-glucose were available.

Fractions containing mainly D-psicose were pooled, and evaporated to a syrup; this was dissolved in water (35 mL), and the solution chromatographed on the aforementioned column, using water as the eluant, the column having been well eluted with water (7 L) prior to the fractionation. The appropriate fractions were pooled, evaporated *in vacuo*, and freeze-dried for 24 h, to give D-psicose (10.0 g, 8%). The ^{13}C-n.m.r. spectrum was the same as that of D-psicose synthesized by the procedure of Tipson *et al.*[3], and was essentially identical to that published by Que and Gray[4]. The positions of the resonances were the same, but the intensities of the peaks differed slightly. The equilibrium composition of D-psicose in solution contains four cyclic forms (anomers of the pyranose and the furanose) in substantial proportions, and these vary with the temperature: $[\alpha]_D^{22}$ +2.9° (*c* 1, water); lit.[5] $[\alpha]_D$ +3.1°. Paper chromatography for 70 h on Whatman No. 1 paper in 3:1:1 (v/v) 1-butanol–ethanol–water, or in the eluant mentioned earlier, showed a single spot, identical with that given by standard D-psicose.

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