A SYNTHESIS OF D-TAGATOSE FROM D-GALACTURONIC ACID[1]

By P. A. J. Gorin,[2] J. K. N. Jones,[2] and W. W. Reid[3]

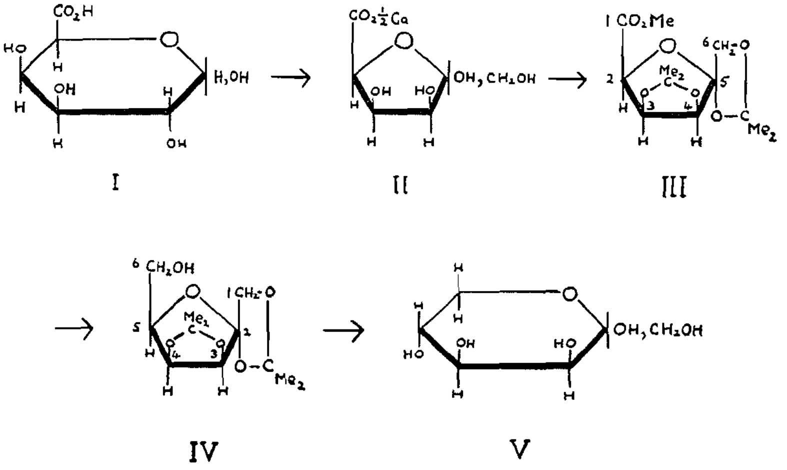
ABSTRACT

D-Tagatose has been synthesized by a series of reactions from D-galacturonic acid.

INTRODUCTION

D-Tagatose is generally prepared by the isomerization of D-galactose with very dilute alkali (1) or hot pyridine (4). However, the yields from these reactions are small and the isolation of the product tedious. D-Tagatose has also been prepared by the biochemical oxidation of the rare sugar derivative D-talitol using *Acetobacter suboxydans* (5).

We now describe a preparation of D-tagatose from D-galacturonic acid. This material is readily prepared by the enzymic hydrolysis of pectic acid (3). Isomerization of D-galacturonic acid (I) with lime water gave the calcium salt of 5-keto-L-galactonic acid (II; 2) which on treatment with an acetone–sulphuric acid mixture followed by esterification with ethereal diazomethane yielded 3,4;5,6-di-*O*-*iso*propylidene-5-keto-L-galactofuronic acid methyl ester (III). An ethereal solution of this material was reduced with lithium aluminum hydride to 1,2;3,4-di-*O*-*iso*propylidene-D-tagatose (IV) which was identical with an authentic specimen prepared from D-tagatose. Acid hydrolysis of (IV) gave a material indistinguishable from D-tagatose (V) in 25% over-all yield from the calcium salt of 5-keto-L-galactonic acid.



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Contribution from the Department of Chemistry, Queen's University, Kingston, Ontario, and the Research Department, H. W. Carter and Company Limited, Coleford, Gloucester, England.
[2] *Department of Chemistry, Queen's University, Kingston, Ontario.*
[3] *Research Department, H. W. Carter and Company Limited, Coleford, Gloucester, England.*

EXPERIMENTAL

Evaporations were carried out under reduced pressure. Optical rotations were measured at 16±2°C. Melting points are uncorrected.

3,4;5,6-*Di-O-isopropylidene*-5-*keto*-L-*galactofuronic Acid Methyl Ester* (III)

The calcium salt of 5-keto-L-galactonic acid (II; 620 mgm.), prepared by the isomerization of D-galacturonic acid (I) by alkali, was shaken in dry acetone (12 ml.) containing sulphuric acid (0.5 ml.) for four hours. The solution, which contained a suspension of calcium sulphate, was neutralized by rapid addition to aqueous lime. The alkaline solution was then neutralized with carbon dioxide, filtered, and the filtrate evaporated to a white solid (the calcium salt of 3,4;5,6-di-*O*-*iso*propylidene-5-keto-L-galactofuronic acid). The free acid was obtained from the salt by the addition of dilute sulphuric acid to an emulsion of ether and a solution of the calcium salt in ice-cold water. The ethereal extract was washed with water (four times), dried (sodium sulphate), filtered, and esterified by addition of an excess of ethereal diazomethane. After 30 min. the solution was evaporated to a sirup which crystallized. Two recrystallizations from ethanol gave white needles (353 mgm.) with m.p. 60°C. and $[\alpha]_D$ +22° (*c*, 1.0 in chloroform). Found: C, 54.4; H, 7.0%. Calc. for $C_{13}H_{20}O_7$: C, 54.2; H, 6.9%.

1,2;3,4-*Di-O-isopropylidene*-D-*tagatose* (*IV*)

3,4;5,6-Di-*O*-*iso*propylidene-5-keto-L-galactofuronic acid methyl ester (III; 848 mgm.) was added with stirring to an excess of lithium aluminum hydride (500 mgm.) in ether (20 ml.). After five hours, excess of reagent was destroyed by addition of ethyl acetate. Water (50 ml.) was added and organic solvents evaporated. The solution was neutralized with acetic acid, filtered, and the filtrate extracted with an equal volume of chloroform. The extract was washed once with water, dried (sodium sulphate), filtered, and evaporated to a sirup (674 mgm.) which crystallized. Two recrystallizations from light petroleum (b.p. 30–60°C.) gave white needles which had m.p. 63–64°C. not depressed on admixture with an authentic specimen of 1,2;3,4-di-*O*-*iso*propylidene-D-tagatose which had been prepared from D-tagatose and $[\alpha]_D$ +64° (*c*, 0.80 in chloroform). Found: C, 55.1; H, 7.5%. Calc. for $C_{12}H_{20}O_6$: C, 55.4; H, 7.6%.

D-*Tagatose* (*V*)

1,2;3,4-Di-*O*-*iso*propylidene-D-tagatose (IV; 173 mgm.) was hydrolyzed by heating in 0.05 *N* sulphuric acid (5 ml.) at 100° for one hour. The reaction mixture was neutralized (aqueous barium hydroxide, then barium carbonate), filtered, and evaporated to a sirup (115 mgm.). The product was crystallized twice from ethanol to give white crystals (71 mgm.) which had m.p. 131–132°C. undepressed on admixture with authentic D-tagatose prepared by isomerization of D-galactose and $[\alpha]_D$ +2° (2 min.) $\rightarrow$ −3° (30 min.; constant value) (*c*, 1.0 in water). Found: C, 40.3; H, 7.0%. Calc. for $C_6H_{12}O_6$: C, 40.0; H, 6.7%.

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REFERENCES

1. De Bruyn, C. A. L. Rec. trav. chim. 14: 150. 1895.
2. Ehrlich, F. and Guttmann, R. Ber. B, 67: 573. 1934.
3. Henglein, F. A. and Hann, M. Makromol. Chem. 2: 289. 1948.
4. Reichstein, T. and Bosshard, W. Helv. Chim. Acta, 17: 753. 1934.
5. Totton, E. L. and Lardy, H. A. J. Am. Chem. Soc. 71: 3076. 1949.