

948. *The Cross-linking of Cellulose and its Derivatives. Part IV.¹
The Action of Hydrazine on the Toluene-*p*-sulphonates of Di-*O*-isopropylidene-D-galactose and -D-fructose.*

By W. M. CORBETT and D. WINTERS.

With anhydrous hydrazine, di-*O*-isopropylidene-6-*O*-toluene-*p*-sulphonyl-D-galactose gives, in addition to the known 6-deoxy-6-hydrazinodi-*O*-isopropylidene-D-galactose and hydrazone-6,6'-di-(6-deoxydi-*O*-isopropylidene-D-galactose), the corresponding symmetrical derivative and the reduction product di-*O*-isopropylidene-D-fucose. Similarly, di-*O*-isopropylidene-1-*O*-toluene-*p*-sulphonyl-D-fructose gives 1-deoxy-1-hydrazinodi-*O*-isopropylidene-D-fructose and 1-deoxydi-*O*-isopropylidene-D-fructose, but no bis-derivative has been isolated. The hydrazine derivative of fructose undergoes addition to di-*O*-isopropylidene-D-glucose 3-crotonate, giving 1-deoxydi-*O*-isopropylidene-1-(3-methyl-5-oxopyrazolidin-1-yl)-D-fructose.

A CONVENIENT method was required for the introduction of free amino-groups into cellulose for its cross-linking by addition of an aminocellulose to cellulose crotonate as described in Part I.² This has been achieved by 2-cyanoethylation of ethyl cellulose (D.S. *ca.* 2) followed by reduction of the cyano-group,³ but that method leads to long cross-links. Efforts have therefore been made to develop methods for conversion of 6-*O*-toluene-*p*-sulphonyl-D-glucose repeating units in cellulose toluene-*p*-sulphonate into 6-amino-6-deoxy-D-glucose repeating units which will give shorter cross-links. Replacement of the sulphonic ester groups occurs only to a limited extent with ammonia, but more readily with anhydrous hydrazine to give hydrazino-derivatives.⁴ Wolfrom and his co-workers⁵ treated several carbohydrate toluene-*p*-sulphonates with hydrazine and reduced the products, which were not isolated, to the amino-derivatives, but yields were not high, indicating that side reactions occur. Such side reactions with cellulose toluene-*p*-sulphonate would lead to repeating groups other than those of 6-amino-6-deoxyglucose and glucose. The possible structure of such groups has been established by a study of the action of hydrazine on the toluene-*p*-sulphonates of di-*O*-isopropylidene-D-galactose and -D-fructose.

Some decomposition of the carbohydrate occurred when the D-galactose derivative was heated with hydrazine at 150° for 20 hr. The hydrazine also decomposed giving ammonia, and among the other volatile products was a thiol (detected by smell only), indicating some reduction of the sulphonate. In addition to the asymmetrical hydrazine (I) described

¹ Part III, Corbett and McKay, *J.*, 1961, 2930.

² Corbett and McKay, *J. Soc. Dyers and Colourists*, in the press.

³ Corbett, unpublished work; cf. *J.*, 1961, 2926.

⁴ Freudenberg and his co-workers, (*a*) *Ber.*, 1922, 55, 3233; *Ber.*, 1923, 56, (*b*) 1243, (*c*) 2119.

⁵ Wolfrom and his co-workers, *J. Amer. Chem. Soc.*, 1958, 80, 4885; 1959, 81, 3716; Armstrong, Ph.D. Thesis, Ohio State University, 1958.

1-Deoxy-1-hydrazinodi-*O*-isopropylidene-D-fructose with di-*O*-isopropylidene-D-glucose 3-crotonate (XII) gives a complex mixture. Fractional distillation of the product gave di-*O*-isopropylidene-D-glucose and a syrup from which was isolated a further syrup, probably the pyrazolidone (XIII), formed by addition of the primary amine group to the unsaturated group followed by elimination of di-*O*-isopropylidene-D-glucose. The syrup (? XIII) gave a crystalline toluene-*p*-sulphonate which, because it showed infrared carbonyl absorption at *ca.* 1730 cm^{-1} , must be the *N*-derivative and not the *O*-derivative arising from the tautomeric form.

EXPERIMENTAL

Treatment of 1,2:3,4-Di-O-isopropylidene-6-O-toluene-p-sulphonyl-D-galactose with Hydrazine.—The toluene-*p*-sulphonate (16 g.) was heated with anhydrous hydrazine (40 ml.) for 20 hr. during which a pressure of 40 atm. developed. Water was added to the mixture, smelling of ammonia and a thiol, and the residue (4.86 g.) crystallised from dibutyl ether to give hydrazono-6,6'-di-(6-deoxydi-*O*-isopropylidene-D-galactose) (I) (1.95 g.), m. p. 130—131.5° (lit.,^{4c} m. p. 129—130°) (Found: C, 55.4; H, 8.1; N, 5.2. Calc. for $\text{C}_{24}\text{H}_{40}\text{N}_2\text{O}_{10}$: C, 55.8; H, 7.8; N, 5.4%). From the mother liquor was obtained *hydrazo-6,6'-di-(6-deoxydi-O-isopropylidene-D-galactose)* (VI) (0.86 g.), m. p. 159.5—160.5° [Found: C, 55.8; H, 7.4; N, 5.5%; *M* (Rast), 500. $\text{C}_{24}\text{H}_{40}\text{N}_2\text{O}_{10}$ requires C, 55.8; H, 7.8; N, 5.4%; *M*, 516]. Concentration of the residual mother liquor gave a basic syrup which was dissolved in ether, washed with dilute sulphuric acid followed by aqueous sodium carbonate, dried, and concentrated to a syrup (0.75 g.). This distilled at 90—95°/0.005 mm. (bath-temp.), to give di-*O*-isopropylidene-D-fucose (0.20 g.), m. p. 31°, $[\alpha]_{\text{D}}^{22} - 50.3^\circ$ (*c* 1.43 in chloroform) (lit.,⁷ m. p. 37°, $[\alpha]_{\text{D}} - 52.4^\circ$) (Found: C, 58.9; H, 8.3; N, 0.2. Calc. for $\text{C}_{12}\text{H}_{20}\text{O}_5$: C, 59.0; H, 8.2%).

The aqueous reaction mixture was exhaustively extracted with ether, giving a syrup (4.6 g.) which distilled to give fractions (*a*) (1.11 g.), b. p. 66—78°/0.01 mm., and (*b*) (2.02 g.), b. p. 100—102°/0.005 mm. Fraction (*a*) gave further di-*O*-isopropylidene-D-fucose (0.36 g.), m. p. 31°; fraction (*b*) was impure 6-deoxy-6-hydrazinodi-*O*-isopropylidene-D-galactose (Found: C, 54.1; H, 8.3; N, 7.0. Calc. for $\text{C}_{12}\text{H}_{22}\text{N}_2\text{O}_5$: C, 52.5; H, 8.0; N, 10.2%). With phenyl isocyanate it gave a bisphenylcarbamate, m. p. 234—235° (lit.,^{4c} m. p. 227°) (Found: C, 60.7; H, 6.3; N, 10.8. Calc. for $\text{C}_{26}\text{H}_{32}\text{N}_4\text{O}_7$: C, 60.9; H, 6.3; N, 10.9%).

Reaction of the toluene-*p*-sulphonate (20 g.) with anhydrous hydrazine (50 ml.) at 145—150° for 5 hr. gave the same products in similar yield.

Concentration of the ether-extracted aqueous phase gave a dark syrup (9.9 g.). Acetylation of this did not produce a crystalline derivative, but with toluene-*p*-sulphonyl chloride a sample (4.32 g.) gave crystals (2.20 g.) (from alcohol), m. p. 170—171°, ν_{max} 1630 cm^{-1} (double bond), that were possibly a *N*-toluene-*p*-sulphonyl derivative of an unsaturated hydrazine derivative [Found: C, 59.0; H, 6.7; N, 10.4; S, 11.9%; *M* (Rast), 280. Calc. for $\text{C}_{13}\text{H}_{18}\text{N}_2\text{O}_2\text{S}$: C, 58.8; H, 6.8; N, 10.5; S, 11.0%; *M*, 266].

Reactions of the Asymmetrical Hydrazine (I).—(a) *Towards heat.* A dibutyl ether solution (10 ml.) of the hydrazine derivative (0.510 g.) was refluxed for 24 hr. Light petroleum (b. p. 40—60°) was added and the solution filtered and concentrated. The residual syrup (0.495 g.) was digested with hot light petroleum (b. p. 40—60°) and the solid filtered off and recrystallised from aqueous ethanol, to give *tri-(6-deoxydi-O-isopropylidene-D-galactose-6)-hydrazine* (0.125 g.), m. p. 198.5—200° [Found: C, 57.0; H, 7.4; N, 3.7%; *M* (Rast), 690. $\text{C}_{36}\text{H}_{58}\text{N}_2\text{O}_{15}$ requires C, 57.0; H, 7.7; N, 3.7%; *M*, 758].

Concentration of the light petroleum solution gave a syrup (0.278 g.) which in a short-path still at 150°/0.005 mm. afforded a syrup (0.149 g.) absorbing at 1675 cm^{-1} (Found: C, 58.2; H, 8.3; N, 4.1. Calc. for $\text{C}_{16}\text{H}_{29}\text{NO}_6$: C, 58.1; H, 8.8; N, 4.2%). It may be a compound formed by the action of the thermal decomposition products of dibutyl ether with the sugar hydrazine derivative or its decomposition products.

(b) *Towards lithium aluminium hydride.* When the hydrazine derivative was treated with an excess of lithium aluminium hydride in ether at room temperature or under reflux, only the starting material (in high yield) was recovered.

The hydrazine derivative (0.513 g.), dibutyl ether (10 ml.), and lithium aluminium hydride (0.25 g.) were refluxed together for 19 hr. To the cooled solution was added ethyl acetate

⁷ Freudenberg and Raschig, *Ber.*, 1927, **60**, 1633.

followed by water, chloroform, and aqueous sodium potassium tartrate. The aqueous phase was extracted with chloroform and the combined extracts and chloroform phase were dried, treated with charcoal, and concentrated to a syrup (0.368 g.) which partly crystallised from dibutyl ether. The crystals (0.020 g.), after recrystallisation from di-isopropyl ether, had m. p. 122°, undepressed on admixture with the secondary amine (II).

Concentration of the di-isopropyl ether mother liquor gave a syrup which in a short-path still at 100—120°/0.005 mm. afforded a syrup (0.043 g.) which had a complex infrared spectrum and was not identified.

(c) *Towards hydrogen.* The hydrazine derivative (0.983 g.) in absolute methanol (100 ml.) was hydrogenated over Raney nickel (0.5 g.) for 20 hr. at 150°/50 atm. The filtered mixture was concentrated to a syrup (0.885 g.) which crystallised from light petroleum (b. p. 40—60°), giving the secondary amine (0.424 g.), m. p. and mixed m. p. 127—128.5°. The mother liquors were concentrated; in a short-path still at 100—120°/0.005 mm. the residue gave a syrup (0.059 g.) which had a complex infrared spectrum.

Reduction of the Symmetrical Hydrazine (VI).—The derivative, m. p. 153.5—154.5° (0.373 g.), in absolute methanol (50 ml.) was hydrogenated over Raney nickel (0.5 g.) for 20 hr. at 150°/50 atm. The filtered solution was concentrated to a syrup (0.411 g.) which crystallised from dibutyl ether to give tri-(6-deoxydi-*O*-isopropylidene-D-galactose-6)-hydrazine (0.100 g.), m. p. 196.5—198.5°, undepressed upon admixture with the similar product isolated by the action of heat on the asymmetrical hydrazine (I). Concentration of the mother-liquor followed by distillation gave 6-deoxy-6-dimethylaminodi-*O*-isopropylidene-D-galactose (0.307 g.), b. p. 95—100°/0.005 mm. (bath-temp.) (lit.,⁸ b. p. 110—115°/2 mm.) (Found: C, 58.9; H, 8.9; N, 4.8. Calc. for C₁₄H₂₅NO₅: C, 58.7; H, 8.7; N, 4.9%).

Treatment of 2,3,4,5-Di-O-isopropylidene-1-O-toluene-p-sulphonyl-D-fructose with Hydrazine.—The toluene-*p*-sulphonate (40 g.) was heated with anhydrous hydrazine (100 ml.) for 20 hr. at 145° during which a pressure of 50 atm. developed. Water (200 ml.) was added to the mixture which was then exhaustively extracted with ether. Evaporation of the ether gave a colourless syrup (13.73 g.) which was distilled to give fractions (a) (9.75 g.), b. p. 140—142°/0.005 mm. (bath-temp.) (Found: C, 53.0; H, 8.1; N, 5.8%), and (b) (1.34 g.), b. p. 204°/0.005 mm. (bath-temp.) (Found: C, 55.5; H, 7.8; N, 4.5%). Fraction (a) was mainly 1-deoxy-1-hydrazinodi-*O*-isopropylidene-D-fructose, and with phenyl isocyanate gave the *bisphenylcarbamate*, m. p. 195—197° (Found: C, 60.9; H, 6.4; N, 10.2. C₂₆H₃₂N₄O₇ requires C, 60.9; H, 6.3; N, 10.9%). Two fractional distillations of the syrup (3.897 g.) gave 1-deoxydi-*O*-isopropylidene-D-fructose (0.307 g.), b. p. 105—110°/0.005 mm. (Found: C, 58.7; H, 8.3; N, 0.3. C₁₅H₂₀O₅ requires C, 59.0; H, 8.2%).

Addition of 1-Deoxy-1-hydrazinodi-O-isopropylidene-D-fructose to Di-O-isopropylidene-D-glucose 3-Crotonate.—A solution of the hydrazine derivative (4.89 g.) and the crotonate (6.19 g.) in absolute ethanol (75 ml.) was kept at room temperature for 3 days, then concentrated to a syrup containing several components. These could not be isolated in pure form by fractional distillation. Some of the fractions crystallised spontaneously, to give di-*O*-isopropylidene-D-glucose in a yield representing 38% hydrolysis of the crotonate.

The addition product (4.106 g.) was shaken for 24 hr. with water (80 ml.). The residue (1.890 g.) was unchanged starting material. Concentration of the aqueous phase gave a syrup (1.964 g.) which was dissolved in aqueous ammonia (100 ml.; *d* 0.9). The solution was kept at room temperature for 18 hr., then concentrated to a syrup which was extracted with hot light petroleum (b. p. 40—60°). Evaporation of the solvent gave a syrup from which was isolated di-*O*-isopropylidene-D-glucose (0.535 g.), m. p. and mixed m. p. 112.5—113.5°. The residual syrup distilled at 170°/0.005 mm. (bath-temp.) to give 1-deoxydi-*O*-isopropylidene-1-(3-methyl-5-oxopyrazolidin-1-yl)-D-fructose (0.211 g.) (Found: C, 56.2; H, 7.6; N, 6.7. C₁₆H₂₆N₂O₆ requires C, 56.2; H, 7.7; N, 8.2%) which with toluene-*p*-sulphonyl chloride in pyridine gave the 2-*N*-toluene-*p*-sulphonate, m. p. 201.5—203° (Found: C, 56.3; H, 6.7; N, 5.5; S, 6.9. C₂₃H₃₂N₂O₈S requires C, 55.7; H, 6.5; N, 5.7; S, 6.5%).

BRITISH RAYON RESEARCH ASSOCIATION, HEALD GREEN LABORATORIES,
WYTHENSHAW, MANCHESTER, 22.

[Present address (W. M. C.): IMPERIAL CHEMICAL INDUSTRIES LIMITED,
FIBRES DIVISION, HOOKSTONE ROAD,
HARROGATE, YORKS.]

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⁸ Freudenberg and Smeykal, *Ber.*, 1926, **59**, 100.