

The Degradation of Carbohydrates by Alkali. Part X. Acetal Derivatives.*

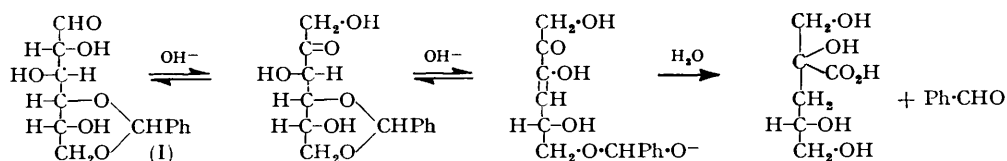
By W. M. CORBETT, J. KENNER, and G. N. RICHARDS.

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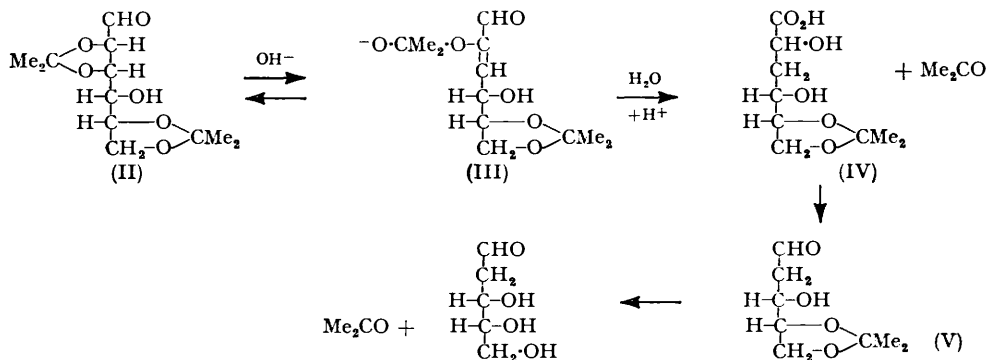
4:6-*O*-Benzylidene-D-glucose and 2:3:5:6-di-*O*-isopropylidene-D-mannose furnish D-glucoisaccharinic and a mixture of 5:6-isopropylidene-D-meta-saccharinic acids respectively on treatment with lime-water.

It has hitherto been accepted that groupings of the acetal type are stable towards alkali, but their relation to alkoxy-groupings suggests that lability should be conferred by the presence of a carbonyl group in the β -position relative to one of the acetal oxygen atoms. The two compounds we have now studied in this respect are representative of the two types in this category which must be distinguished, according as the second acetal oxygen atom is closer to, or more remote from, the carbonyl group than the first.

Thus 4:6-*O*-benzylidene-D-glucose (I) is smoothly converted by lime-water at 25° into a mixture of α - and β -D-glucoisaccharinic acids and benzaldehyde:



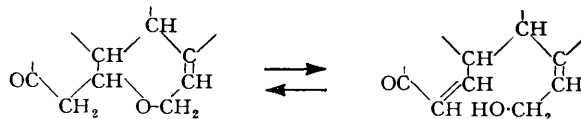
2:3:5:6-Di-*O*-isopropylidene-D-mannose (II) does not exhibit the same facility of decomposition because the anion (III) initially formed cannot at once pass into an α -diketone and thence into a saccharinic acid so that the reversibility of the initial reaction operates. However, dissociation occurs at 100°, yielding 3-deoxy-5:6-isopropylidene-D-gluconic and -mannonic acid (IV) and acetone.



The limited formation of *isostrychnine* from *strychnine* in water at 170° or methyl alcoholic ammonia at 140° (Bacovescue and Pictet, *Ber.*, 1905, **38**, 2787; Leuchs and

* Part IX, *J.*, 1955, 1431.

Nitschke, *ibid.*, 1922, 55, 3171) by opening of the latter's F-ring appears to be a reaction closely analogous to the present:



In this instance separation of the alcoholic from the $\alpha\beta$ -unsaturated carbonyl grouping is impossible and an equilibrium must ensue which is however affected by the energy content of the system.

The nature of the mixed 3-deoxyisopropylidene-D-mannonic and -D-gluconic acids is demonstrated by hydrolysis in presence of sulphuric acid or an acidic resin to acetone and 3-deoxy-D-mannonic and -gluconic acid. Accordingly, when the calcium salts of the mixed isopropylidene-acids are subjected to the Ruff procedure (*Ber.*, 1901, 34, 1362) they yield 2-deoxy-4 : 5-isopropylidene-D-ribose, the identity of which is demonstrated by hydrolysis in presence of an acidic resin. Acetone and 2-deoxy-D-ribose were thus produced, the latter being identified by paper chromatography, but the reaction is not to be regarded as a satisfactory means of preparing it. The 2-deoxyisopropylidene-D-ribose is also accessible by periodate oxidation of the 3-deoxyisopropylidene-D-mannonic-D-gluconic acid mixture, but the product is less satisfactory than that just described.

EXPERIMENTAL

Degradation of 4 : 6-O-Benzylidene-D-glucose.—A quantitative study of the course of the reaction with lime-water at 25° was vitiated by separation of a gelatinous precipitate and consequent unsatisfactory sampling, but the odour of benzaldehyde was perceptible after 5 min. and reaction seemed complete after 7 hr. A suspension (5.03 g.) in oxygen-free lime-water (750 ml.; 0.04N) was therefore kept at room temperature for 20 hr. After saturation of the mixture with carbon dioxide brown resinous material (0.95 g.) was removed by filtration. The filtrate on steam-distillation in a stream of nitrogen furnished benzaldehyde [2 : 4-dinitrophenylhydrazone (2.57 g.), m. p. and mixed m. p. 243—244°]. The residue from the distillation, after filtration from calcium carbonate and evaporation, furnished calcium salts (2.52 g.). Fractional crystallisation from aqueous alcohol followed by examination of the acids prepared from the fractions by paper chromatography (butanol-ethanol-acetic acid-water, 45 : 5 : 1 : 49; hydroxylamine-ferric chloride spray; Abdel-Akher and Smith, *J. Amer. Chem. Soc.*, 1951, 73, 5859) showed them to be almost exclusively salts of α -isosaccharinic acid (lactone, R_f 0.48), with a trace of those of the β -acid (lactone, R_f 0.54). Accordingly the less soluble fractions freed from calcium ions by treatment with resin, furnished brucine α -isosaccharinate, m. p. and mixed m. p. 159—161°, $[\alpha]_D^{21} -25^\circ$ (*c*, 1 in H₂O). Nef (*Annalen*, 1910, 376, 89) gives m. p. 164°. The same brucine salt, m. p. and mixed m. p. 158—160°, was also prepared in small yield from the above-mentioned resinous product which also gave a faint odour of benzaldehyde when warmed with dilute acid and so appeared to be in the main a condensation product.

Degradation of 2 : 3-5 : 6-Diisopropylidene-D-mannose.—Dom nuts, kernels of the North African *Hyphaene thebaica*, were found to be a suitable alternative to the usual Central American *Phytalephas macrocarpa* as a source of mannose. The pulverised material was submitted to the procedure of *Org. Synth.*, 22, 86, after preliminary Soxhlet-extraction with trichloroethylene followed by treatment with boiling 1% aqueous sodium hydroxide (cf. Clark, *J. Biol. Chem.*, 1922, 51, 1).

The alkalinity of a solution of 2 : 3-5 : 6-diisopropylidene-D-mannose in saturated oxygen-free lime-water remained unchanged at 25°, but the following data were obtained from a solution (50 ml.) of 0.3453 g. in oxygen-free lime-water (0.042N) at 100° by treating 2-ml. samples with excess of 0.01N-sulphuric acid and titrating the mixture with 0.01N-sodium hydroxide:

Time (hr.)	0.5	1	2.5	4	6	7.5	24
Acid (equiv.)	0.064	0.145	0.312	0.506	0.660	0.682	1.282

The excess of acid finally observed possibly arises from condensation products of the acetone formed.

After a solution (5 l.) of di-*O*-isopropylidene-mannose (39.12 g.) in oxygen-free lime-water

(0.044N) had been kept for 41 hr. at 100° and cooled, excess of carbon dioxide was added and the mixture boiled and filtered. Acetone 2 : 4-dinitrophenylhydrazone (0.183 g.; m. p. and mixed m. p. 123—125°) was prepared from the first 25 ml. of the distillate from 100 ml. of filtrate. The remainder, when evaporated and extracted with acetone, yielded calcium salts (35.90 g.). By use of this material, (a) an aqueous solution (20 ml.) of 4.696 g., treated with acetone (30 ml.), yielded at room temperature a first fraction (1.706 g.), $[\alpha]_D^{23} - 7.4^\circ$ (c, 1.08 in H₂O) which after recrystallisation from aqueous acetone (2 : 3) had $[\alpha]_D^{24} - 5.2^\circ$ (c, 1.34 in H₂O) and on treatment with Amberlite resin IR-120(H) yielded acetone (2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 123—125°) with 3-deoxy-gluconic and -mannonic acid identified as lactones by paper chromatography (cf. *J.*, 1954, 1784). A second fraction {0.473 g.; $[\alpha]_D^{21} - 18.8^\circ$ (c, 0.854 in H₂O)} separated on further cooling and on recrystallisation from aqueous acetone (2 : 3) had $[\alpha]_D^{24} - 18.2^\circ$ (c, 1.2 in H₂O). Calcium 3-deoxy-5 : 6-O-isopropylidene-mannionate (Found : C, 43.3; H, 6.5; Ca, 8.3. C₁₈H₃₀O₁₂Ca.H₂O requires C, 43.6; H, 6.5; Ca, 8.1%) thus prepared yielded on hydrolysis with acidic resin, acetone, and 3-deoxymannonolactone, m. p. and mixed m. p. 87—89.5°; Nef (*loc. cit.*) gives m. p. 92°. Chromatographic examination did not reveal any 3-deoxygluconolactone. (b) An aqueous solution of 0.323 g., on treatment with Amberlite IR-120(H) resin and concentration, yielded a syrup (0.201 g.) from which a few clusters of crystals, m. p. and mixed m. p. with authentic 3-deoxygluconolactone, 97.5—99.5°. Nef (*loc. cit.*) gives m. p. 104° (c) A solution in dilute sulphuric acid (0.1N; 100 ml.) of 1.575 g., heated 1 hr. at 100°, yielded mixed calcium salts (1.000 g.) after neutralisation with barium carbonate, filtration, and partial distillation [the distillate (50 ml.) yielding acetone 2 : 4-dinitrophenylhydrazone (0.481 g.), m. p. and mixed m. p. 123—125°], treatment with Amberlite IR-120(H) resin, neutralisation with calcium carbonate, filtration, and concentration. From these salts by crystallisation from 33% aqueous ethanol, was obtained calcium 3-deoxymannionate (0.241 g.), $[\alpha]_D^{22} - 22.0^\circ$ (c, 2.41 in H₂O), further characterised by conversion into 3-deoxy- γ -D-mannonolactone (0.156 g.), m. p. and mixed m. p. (Richards, *J.*, 1954, 3638) 83—85°. Nef (*loc. cit.*) gives $[\alpha]_D - 23.3^\circ$ and m. p. 92°. (d) An aqueous solution (100 ml.) of 12.05 g. was treated with barium acetate (1.15 g.) and ferric sulphate (0.60 g.). The mixture was boiled for several minutes, filtered, cooled to 40°, and treated with hydrogen peroxide (30%; 7 ml.). A further equal quantity of peroxide was added when the reaction had subsided. Finally, the cooled mixture was extracted with ether (3 × 50 ml.). The total extract, when dried (Na₂SO₄) and evaporated, furnished a syrup (0.870 g.), $[\alpha]_D^{23} - 4.6^\circ$ (c, 0.86 in H₂O), $[\alpha]_D^{23} + 10.2^\circ$ (c, 0.75 in pyridine), and further material (2.230 g.) resulted from treatment of the aqueous mother-liquors with barium acetate, ferric sulphate, and hydrogen peroxide. Although chromatographic analysis (butanol-pyridine-water; 3 : 2 : 1.5) indicated its essential uniformity (R_F 0.90; trace spots R_F 0.62 and 0.49; silver nitrate, sodium hydroxide spray, Trevelyan, Procter, and Harrison, *Nature*, 1950, 166, 144) analytical data were in poor accord with those required by 2-deoxy-4 : 5-isopropylideneribose, and the usual crystalline derivatives could not be obtained. Traces of formaldehyde (dimedone derivative, m. p. and mixed m. p. 187.5—189.5°) were detected in the product. (e) Calcium ions were removed from a solution (100 ml.) of 5.058 g. by use of the calculated quantity of sodium oxalate, and the filtered solution was then treated with one of sodium metaperiodate (10 g.) and with sodium hydrogen carbonate (0.5M; 30 ml.). The mixture, after 24 hr. in the dark, was filtered, concentrated to a small volume (25 ml.), and extracted with ether (3 × 50 ml.). The extract yielded a pale yellow syrup (1.583 g.) and repetition of the whole operation with the aqueous liquor afforded a further 0.453 g. Chromatographic analysis again furnished a main spot, R_F 0.90 (impurities, R_F 0.75 and 0.66), and treatment of the syrup with Amberlite resin IR-120(H) furnished 2-deoxyribose (R_F 0.61) as main product, but the accompanying impurities (R_F 0.12, 0.23, 0.32, 0.46, 0.69, 0.78) inhibited the isolation of crystalline derivatives from it.

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