457. *Deoxy-sugars. Part XXII.* Comparative Rates of Oxidation and Reduction of* D-*Galactose and 2-Deoxy-*D-*galactose.*

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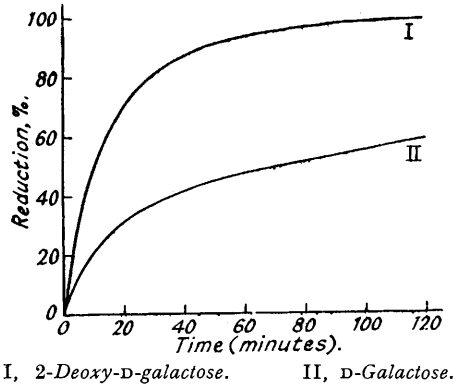
The comparative rates of oxidation and reduction of D-galactose and its 2-deoxy-derivative have been measured. In both cases, reaction is faster with the deoxy-sugar. The results obtained are discussed with reference to other reactions of deoxy-sugars, already reported.

During investigations in progress in this laboratory on the polarographic behaviour of nucleic acids, it became necessary to have information concerning the relative ease of reduction of 2-deoxy-sugars compared with their normal analogues. Apart from the reduction of 2-deoxy-D-glucose with sodium amalgam to yield 2-deoxy-D-sorbitol (-mannitol) (Bergmann *et al.*, *Ber.*, 1923, **56**, 1052) little is known about the reduction of 2-deoxy-hexoses and -pentoses. We now report experiments carried out with D-galactose and 2-deoxy-D-galactose. 2-Deoxy-D-galactose was preferred in these model experiments for reasons already stated (Foster, Overend, and Stacey, *J.*, 1951, 974).



I, 2-*Deoxy*-D-*galactose.* II, D-*Galactose.*

Preliminary experiments showed that 2-deoxy-D-galactose could readily be hydrogenated catalytically to crystalline 2-deoxy-D-dulcitol, in good yield. For the study envisaged Raney nickel proved to be more suitable than platinum oxide as the catalyst. 2-Deoxy-D-dulcitol readily gave a di*iso*propylidene derivative when treated with zinc chloride in dry acetone.

Aqueous solutions of D-galactose and 2-deoxy-D-galactose, which had been allowed to mutarotate to equilibrium, were hydrogenated under identical conditions with a Raney nickel catalyst. It was readily apparent that 2-deoxy-D-galactose absorbed hydrogen faster than did D-galactose. At noted time intervals, aliquots were withdrawn from the solutions without interruption of the experiments. The amount of free reducing sugar remaining in each hydrogenation vessel was estimated from optical rotation measurements and by titration with the Shaffer–Hartmann reagent (*J. Biol. Chem.*, 1921, **45**, 377). Reasonable correlation was obtained between the two methods but the determinations by the latter method are the more accurate, and the figure shows results obtained in this way. It is clear that the deoxy-sugar is more rapidly reduced than the normal sugar.

Attempts to make corresponding measurements on the rates of oxidation of D-galactose and 2-deoxy-D-galactose by bromine are also reported. These measurements were not entirely satisfactory since although 2-deoxy-D-galactose gives the lactone, the results obtained with

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D-galactose indicated that some free galactonic acid was formed in addition to galactonolactone. However, again it appeared that reaction with the deoxy-sugar was faster than with the normal sugar.

The effect of a deoxy-group located at position 2 in pentoses and hexoses on the lability of substituents at position 1 has already been demonstrated (Overend and Stacey, *J. Soc. Food Agr.*, 1950, **1**, 168). Thus the *O*- and *N*-glycosides of 2-deoxy-sugars are more rapidly hydrolysed by acids than are the corresponding normal sugar analogues (Butler, Laland, Overend, and Stacey, *J.*, 1950, 1433). Similarly 2-deoxy-D-ribose-1 phosphate shows very great lability towards various reagents (Friedkin and Kalckar, *J. Biol. Chem.*, 1950, **184**, 449). In addition it has been shown that 2-deoxy-sugars tend to exist in the *aldehydo*-form to a greater extent than the corresponding normal hexoses and pentoses (Overend, *J.*, 1950, 2769). The oxidation and reduction results herein described further demonstrate the greater reactivity of 2-deoxy-sugars.

Experimental.

2-Deoxy-D-dulcitol.—2-Deoxy-D-galactose (1·2 g.) in solution in methanol (40 c.c.) was shaken in an atmosphere of hydrogen at a slight overpressure, at room temperature, with Raney nickel. When the absorption of hydrogen was complete, the solution was filtered and the filtrate evaporated to dryness The syrupy residue crystallised slowly and was recrystallised from methanol. *2-Deoxy-D-dulcitol* (0·7 g.) was obtained as colourless cubes, m. p. 112—113°, $[\alpha]_D^{21}$ +12° (*c*, 1·68 in methanol), +18° (*c*, 1·16 in water) (Found: C, 43·5; H, 8·4. $C_6H_{14}O_5$ requires C, 43·3; H, 8·4%).

The deoxydulcitol (0·45 g.) and zinc chloride (1·5 g.) in dry acetone (10 c.c.) were set aside for 3 days. Excess of potassium carbonate solution was then added and the mixture was filtered. Acetone was removed from the filtrate under diminished pressure and the aqueous residue was extracted with ether (4 × 50 c.c.). The solvent was removed from the extract and the syrupy residue was distilled. *Di-isopropylidene 2-deoxy-D-dulcitol* (0·23 g.) was obtained as a colourless oil, b. p. 128—130° (bath-temp.)/ 0·04 mm., n_D^{21} 1·4575 (Found: C, 57·9; H, 9·1. $C_{12}H_{22}O_5$ requires C, 58·5; H, 8·9%).

Measurements of Comparative Rates of Reduction of D-Galactose and 2-Deoxy-D-galactose.—(*a*) In a preliminary experiment equimolecular amounts (0·002 mol.) of D-galactose (0·36 g.) and 2-deoxy-D-galactose (0·328 g.) were separately dissolved in water (10 c.c.), and Raney nickel (0·08 g.) was added to each. The solutions were shaken under identical conditions in an atmosphere of hydrogen and at intervals the volumes of hydrogen consumed were noted. Results obtained were:

2-Deoxy-D-galactose.

Time (minutes)	10	21	30	42	59	79	128	148
Hydrogen consumed (c.c.) ...	8	17	24	31	38	43	49	50

D-Galactose.

Times (minutes)	11	20	41	68	80	100	115	131
Hydrogen consumed (c.c.) ...	5	9	12	15	18	20	22	23

(*b*) Equimolecular aqueous solutions (0·003 mol.) of D-galactose (0·54 g.) and 2-deoxy-D-galactose (0·492 g.), which had been allowed to mutarotate to equilibrium, were separately placed in flasks with a side-arm attached, through which samples could be conveniently withdrawn without interrupting the course of the experiment. Equal quantities of Raney nickel were added to each flask and the solutions were shaken under identical conditions in an atmosphere of hydrogen, which was led from a common reservoir to the hydrogenation vessels *via* a T-tube. At noted intervals of time, aliquots (1 c.c.) were withdrawn from both flasks. Each sample was diluted with water (to 6 c.c.) and filtered. The optical rotation of the sample was measured and then the amount of reducing groups present was estimated by use of the Shaffer–Hartmann reagent (*J. Biol. Chem.*, 1921, **45**, 377). Results obtained were as follows:

2-Deoxy-D-galactose.

Time of hydrogenation (minutes) ...	0	5	15	30	47	85	190
$[\alpha]_D^{17}$ of solution	+57°	+50°	+30°	+25°	+20°	+15°	+15°
Calc. from			Deoxyhexose, %.				
Change in $[\alpha]_D$	100	83	36	24	12	0	0
Shaffer–Hartmann estimation	100	78	36	20	10	0	0

D-Galactose.

Time of hydrogenation (minutes) ...	0	5	15	30	47	85	190
$[\alpha]_D^{17}$ of the solution	+81°	+71°	+62°	+57°	+53°	+40°	+18°
Calc. from			Hexose, %.				
Change in $[\alpha]_D$	100	88	76	70	64	48	22
Shaffer–Hartmann estimation	100	83	74	64	60	47	16

2-Deoxy-D-galactonolactone.—2-Deoxy-D-galactose (2·59 g.) was dissolved in water (25 c.c.), and bromine (5 c.c.) was added. The mixture was kept at 37° for 1 day or at room temperature for 1 week. After these periods the solution no longer reduced Fehling's solution. The excess of bromine was removed by aeration and the hydrogen bromide by precipitation with silver carbonate. Silver in solution was removed by treatment with hydrogen sulphide. After filtration through a charcoal pad

the filtrate was evaporated to dryness and the residue triturated with absolute methanol. Crystallisation from dry acetone gave crystals of 2-deoxy-D-galactonolactone (1·8 g.), m. p. 97—98°, $[\alpha]_D$ —33° (*c*, 1·16 in water) (Found: C, 44·4; H, 6·3. Calc. for $C_6H_{10}O_5$: C, 44·4; H, 6·2%) (cf. Overend, Shafizadeh, and Stacey, *loc. cit.*). It was shown that 2-deoxy-D-galactonolactone induced no change in the methyl-orange indicator used in the subsequent experiment.

Comparative Rates of Oxidation of D-*Galactose and* 2-*Deoxy*-D-*galactose.*—Bromine (1 c.c.) was added separately to equimolecular solutions (15 c.c.) of D-galactose (0·003 mol.) and 2-deoxy-D-galactose (0·003 mol.). The mixtures were kept at 15° and at intervals aliquots (1 c.c.) were withdrawn and added to distilled water (5 c.c.). Excess of bromine was removed by aeration and then the optical rotation of the sample was measured. A portion was titrated with 0·02N-potassium carbonate, with methyl-orange as indicator. Results were as follows:

2-*Deoxy*-D-*galactose.*

Time (hours)	0	4·75	6·5	9	24
Calc. from			Deoxyhexose, %.		
$[\alpha]_D$ measurements	100	24	7	3	3
Titration	100	24	6	0	0

D-*Galactose.*

Time (hours)	0	4·75	6·5	9	24
Calc. from			Hexose, %.		
$[\alpha]_D$ measurements	100	63	40	27	3
Titration	100	42	28	18	<2

(Cf. Kiliani, *Ber.*, 1922, **55**, 75; Pryde, *J.*, 1923, 1808.)

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