246. *Thermal Mutarotation of Some Methylated* D-*Fructoses.*

By D. J. Bell.

The equilibrium $[\alpha]_D$ in water of methylated fructoses is noticeably affected by temperature. Use of this optical measurement to characterise these sugars therefore demands careful temperature control. A structural factor common to the sugars known to show this thermal mutarotation is noted. The symbol $[^{t_1}\Delta^{t_2}]_D$ is proposed to denote the change in equilibrium $[\alpha]_D$ for a *rise* of 1° C measured between the two temperatures $t_1°$ and $t_2°$.

More than one hundred years ago it was observed that the optical rotation of sugars is affected by temperature; towards the end of the nineteenth century it was found that certain monosaccharides show much greater variations of equilibrium $[\alpha]_D$ with change of temperature than do others (cf. Browne and Zerban, "Sugar Analysis," John Wiley & Sons, New York, 1941, 3rd Edn., pp. 270 *et seq.*). This phenomenon, termed "thermal mutarotation" by Isbell and Pigman (*J. Res. Nat. Bur. Stand.*, 1938, **20**, 773), does not appear to have attracted much attention among academic carbohydrate chemists.

During examination of several specimens of analytically and chromatographically pure crystalline 1 : 3 : 4-trimethyl D-fructose apparent variations in $[\alpha]_D$ were traced to thermal mutarotation which in this substance is more marked than in any other sugar. Other chromatographically pure methylated D-fructoses available in this laboratory likewise show thermal mutarotation (Table 1). It is proposed that the change in equilibrium $[\alpha]_D$ (in water) produced by a *rise* in temperature of 1° C and observed between temperatures $t_1°$ and $t_2°$ shall be denoted by $[^{t_1}\Delta^{t_2}]_D$.

Table 1.

D-Fructose derivative :	1-Me	3-Me	1 : 3 : 4-Me_3	1 : 3 : 4 : 5-Me_4	3 : 4 : 6-Me_3	1 : 3 : 4 : 6-Me_4
$[\alpha]_D^{20\cdot0}$	−63·3°	−61·3°	−55·7°	−122°	+29·5°	+30·3°
$[^5\Delta^{30}]_D$	+0·450	+0·700	+0·820	+0·112	−0·130 *	−0·169

* Isbell and Pigman (*loc. cit.*) found −0·132.

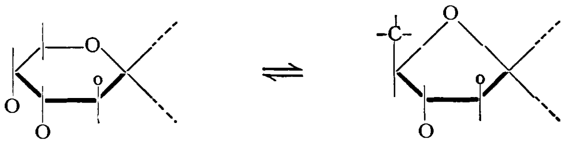
Sugars which can undergo the pyranose $\rightleftharpoons$ furanose change show markedly greater $[\Delta]_D$ when compared with the "fixed" derivatives able to exist in only one ring-form. If keto-sugars and their hydrates are assumed to be absent, the thermal mutarotation of the "fixed" sugars must be almost entirely due to a change in the anomeric equilibria. (A small proportion of the numerical change must be ascribed to such physical effects as alteration of indices of refraction, etc.) It therefore seems probable that the sugars able to assume different ring-forms will owe part of their thermal mutarotation to anomeric interchanges (cf. Isbell and Pigman, *loc. cit.*).

The monosaccharides, and their derivatives, which show thermal mutarotation have a property in common. Table 2 records the known data for dilute (2—8%) solutions. Each of these sugars possesses the *arabo*-configuration with respect to the ring carrying the

TABLE 2.

Sugar	$[\Delta]_D$	References
L-Arabinose	$-0{\cdot}394$	Tanret, *Bull. Soc. chim.*, 1896, **15**, 195.
D-Galactose	$-0{\cdot}209$	Meissl, *J. pr. Chem.*, 1880, **22**, 97.
D-Fructose	$+0{\cdot}580$	Vosburgh, *J. Amer. Chem. Soc.*, 1920, **42**, 1696.
	$+0{\cdot}552$	Tsuzuki *et al.*, *ibid.*, 1950, **72**, 1071.
	$+0{\cdot}549$	Isbell and Pigman, *loc. cit.*
3 (α-D-Glucopyranosyl)-D-fructose (turanose)	$+0{\cdot}549$	*Idem, ibid.*
4-(β-D-Galactopyranosyl)-D-fructose (lactulose)	$+0{\cdot}296$	*Idem, ibid.*

reducing group and undergoes an identical stereoisometric change with the pyranose $\rightleftharpoons$ furanose interconversion (disregarding D- and L-enantiomorphism). The furanose ring has a more symmetrical configuration with respect to the distribution of radicals above and below its plane :



Sugars which possess a symmetrical arrangement of radicals about the *pyranose* ring, *e.g.*, glucose, xylose, and sorbose, do not show thermal mutarotation. It is suggested that other monosaccharides derived from the *arabo*-configuration may also be found to mutarotate thermally, *e.g.*, fucose and altrose.

As a result of the above observations, the values for $[\alpha]_D$ of pure samples of methylated D-fructoses previously published (Bell and Palmer, *J.*, 1949, 2522; *J.*, 1952, 3763) must be considered unreliable since the air temperature of the polarimeter-room had been incorrectly assumed to represent that of the solution in the instrument. Differences of up to 3° have since been found to occur between these two temperatures. The temperature quoted by Albon, Bell, Blanchard, Gross, and Rundell (*J.*, 1953, 24) for the $[\alpha]_D$ of 1 : 3 : 4-trimethyl D-fructose from methylated kestose is, on the other hand, correct.

EXPERIMENTAL

All rotations were observed in water.

Sources of Material.—1 : 3 : 4 : 6-Tetramethyl D-fructose was obtained by chromatography (Bell and Palmer, *J.*, 1949, 2522) from the hydrolysate of methylated irisin and was free from detectable amounts of aldose derivatives or of hexamethyl difructose dianhydrides (cf. Bell and Palmer, *J.*, 1952, 3763). Thrice distilled at 70°/0·01 mm. the liquid had $[\alpha]_D^{20\cdot0}$ $+30{\cdot}3°$ and n_D^{20} 1·4506.

1 : 3 : 4 : 5-Tetramethyl D-fructose was prepared by methylation of β-methyl-D-fructopyranoside followed by hydrolysis of the glycoside. Thrice recrystallised from ether the sugar (prisms) had m. p. 99° and $[\alpha]_D^{20\cdot0}$ at equilibrium, $-122°$.

3 : 4 : 6-Trimethyl D-fructose, isolated chromatographically from hydrolysed trimethyl inulin as a colourless syrup, was thrice distilled in a high vacuum. No trace was found of anhydro-compounds. $[\alpha]_D^{20\cdot0}$ was $+29{\cdot}5°$ and n_D^{20} 1·4651.

1 : 3 : 4-Trimethyl D-fructose was isolated chromatographically from the hydrolysate of methylated grass levan. Thrice crystallised from carbon tetrachloride it had m. p. 73—75°, $[\alpha]_D^{20\cdot0}$ $-55{\cdot}7°$.

3-Methyl D-fructose was kindly provided by Dr. W. B. Glen of Messrs. Ayerst, McKenna and Harrison, Montreal, Canada, and had been prepared through methylation of 1 : 2-4 : 5-di*iso*propylidene D-fructose (Glen, Grant, and Myers, *J.*, 1951, 2568). Thrice recrystallised from ethanol, the substance (needles) had m. p. 129°, $[\alpha]_D^{20}$ $-100°$ (2 minutes), falling to $-62{\cdot}2°$ (const. after 21 hours).

1-Methyl D-fructose was also provided by Dr. Glen, in the form of a brown syrup obtained by hydrolysis of 1-methyl 2 : 3-4 : 5-di*iso*propylidene D-fructose (*idem, loc. cit.*). Evaporation of a solution treated with well-washed charcoal and a mixture of " Deacidite " and " Zeocarb " resins (cf. Wadman, *J.*, 1952, 3051) gave a colourless, stiff syrup having $[\alpha]_D^{20}$ $-63{\cdot}3°$ and n_D^{20} 1·5066 (decrease for *rise* in 1°, 0·00032).

Measurement of Rotations.—Roughly weighed amounts of the appropriate sugars were placed in tared 25-ml. graduated flasks and dried to constant weight in a high vacuum over phosphoric anhydride and potassium hydroxide. [1 : 3 : 4 : 6-Tetramethyl D-fructose is volatile under these conditions (Bell and Palmer, *J.*, 1949, 2522); drying was therefore continued until a loss of ~10% of the original weight was obtained. n_D^{20} was then 1·4507.] Glass-distilled water was used to dissolve the sugars at room temperature and the solutions kept (~24 hours) until temperature-constant $[\alpha]_D$'s were attained. Observations were then made in a 4-dm. jacketed tube, at a minimum of six temperatures between 5·0° and 30·0°. To ensure that equilibria had been attained, polarimetric readings were taken over periods of 20 minutes, the solution being kept at the required temperature. No variations in $[\alpha]_D$'s were noted if the temperature was changed from a lower to a higher, or from a higher to a lower one, even if this was done over the extremes of the range examined. Equilibria were rapidly attained. Solutions of each sugar at three concentrations between 2 and 8% were examined; no "concentration effect" could be detected. In every instance straight-line plots were obtained between $[\alpha]_D$ and temperature.

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