Carbohydrate Research, 28 (1973) 365–370

Note

Conformational analysis of di-D-fructose dianhydrides by p.m.r. spectroscopy*

R. W. BINKLEY,
Department of Chemistry, The Cleveland State University, Cleveland, Ohio 44115 (U. S. A.)
W. W. BINKLEY,
New York Sugar Trade Laboratory, 300 Terminal Avenue West,
Clark, New Jersey 07066 (U. S. A.)
AND A. A. GREY
Canadian 200-MHz NMR Centre, Ontario Research Foundation,
Sheridan Park, Ontario (Canada)

(Received November 24th, 1972; accepted with revisions, March 1st, 1973)

Four crystalline di-D-fructose dianhydrides (**1**–**4**), previously designated diheterolevulosans I–IV, have been obtained by the action of concentrated hydrochloric acid on D-fructose[1]. Each of these sugars was found to possess three rings, two D-fructose and one substituted 1,4-dioxane. The D-fructose rings in **1** and **4** were found by periodate oxidation to be pyranoid moieties only[1b,1e]; **2** and **3** each possessed one furanoid and one pyranoid residue[1b,1d].

The recent advances in high-resolution ^{1}H nuclear magnetic resonance (p.m.r.) spectroscopy have made it possible to determine the conformations of the ring systems in D-fructose-containing oligosaccharides[2]. We have determined the spectra of the di-D-fructose dianhydride hexaacetates (**1a**–**4a**) at 220 MHz and report herein the results of these determinations, together with conformational assignments to the ring systems in each of the four di-D-fructose dianhydrides (**1**–**4**).

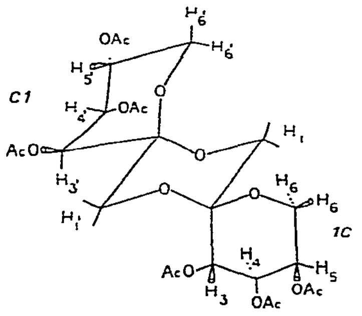
RESULTS AND DISCUSSION

General analysis of the p.m.r. spectra. — The proton signals in the 220-MHz p.m.r. spectra of the peracetylated di-D-fructose dianhydrides* in benzene-d_6 were resolved sufficiently to permit first-order analysis of all spectra except a portion of the spectrum of **1a** (see Fig. 1). The downfield signals of six protons (5.0–6.0 p.p.m.) arise from H-3, H-4, H-5, H-3′, H-4′, and H-5′ of the constituent D-fructose rings; the conformations of these rings were deduced from the first-order coupling constants: $J_{3,4}$, $J_{4,5}$, $J_{3',4'}$, and $J_{4',5'}$ (see Table I). Whenever possible, all assignments were checked by decoupling experiments. The central 1,4-dioxane rings of the dianhydrides

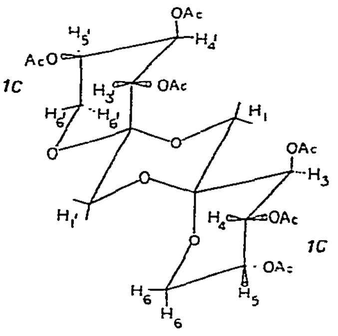
---

*Dedicated to Dr. Louis Long, Jr., in honor of his 70th birthday.

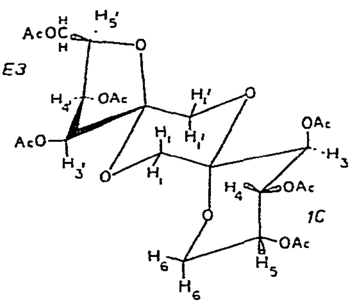
*It is assumed here that acetylation does not alter the basic conformation of the ring systems; see Ref. 1 for acylation conditions.



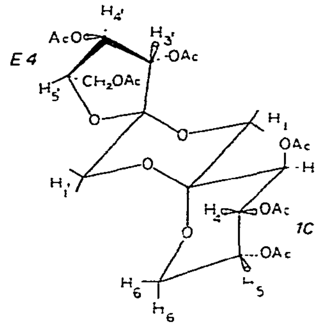
1a



4a



2a



3a

TABLE I

CHEMICAL SHIFTS AND COUPLING CONSTANTS OF THE METHINE AND METHYLENE PROTONS OF THE DI-D-FRUCTOSE DIANHYDRIDE HEXAACETATES (**1a**, **2a**, **3a**, **4a**)

Proton	*Chemical shifts, p.p.m. (coupling constants, Hz)*[a,b]			
	1a	**2a**	**3a**	**4a**
H-3 ($J_{3,4}$)	5.54 (10.5)	5.60 (10.6)	5.57 (11.0)	5.76 (10.9)
H-4 ($J_{4,5}$)	5.74 (3.5)	5.80 (3.5)	5.60 (3.1)	5.60 (3.5)
H-5 ($J_{5e,6a}$)	5.45 (1.5)	5.47	5.34	5.27 (1.5)[c]
H-6 ($J_{5e,6e}$)	3.41 (1.5)	3.40	3.33 (1.5)	3.31 (1.5)[c]
H-6 ($J_{6e,6a}$)	3.50 (−13)	3.51 (−12)	3.41 (−13)	3.31 (−13)
H-3′ ($J_{3',4'}$)		5.43 (1.8)	5.55 (7.5)	5.76 (10.9)
H-4′ ($J_{4',5'}$)		5.21 (5.5)	5.60 (5.1)	5.60 (3.5)
H-5′ ($J_{5',6'}$)	5.41 (9.0)	4.07 (3.5)	4.06 (7.2)	5.27
H-6′ ($J_{5',6'}$)	3.58 (4.5)	4.29 (4.4)	4.29 (3.8)	3.31
H-6′ ($J_{6',6'}$)	3.92 (−11)	4.53 (−12)	4.43 (−12)	3.31 (−13)
H-1	4.00	3.72	3.93	3.49
H-1	3.72	3.72	3.65	3.49
H-1	3.64	3.82	4.08	4.12
H-1	3.53	4.10	3.82	4.12

[a]Data taken from spectra of acetate in benzene-d_6. [b]All geminal coupling-constants are presumed to be negative. [c]$[J_{5e,6a}+J_{5e,6e}]$ = 3.0 Hz.

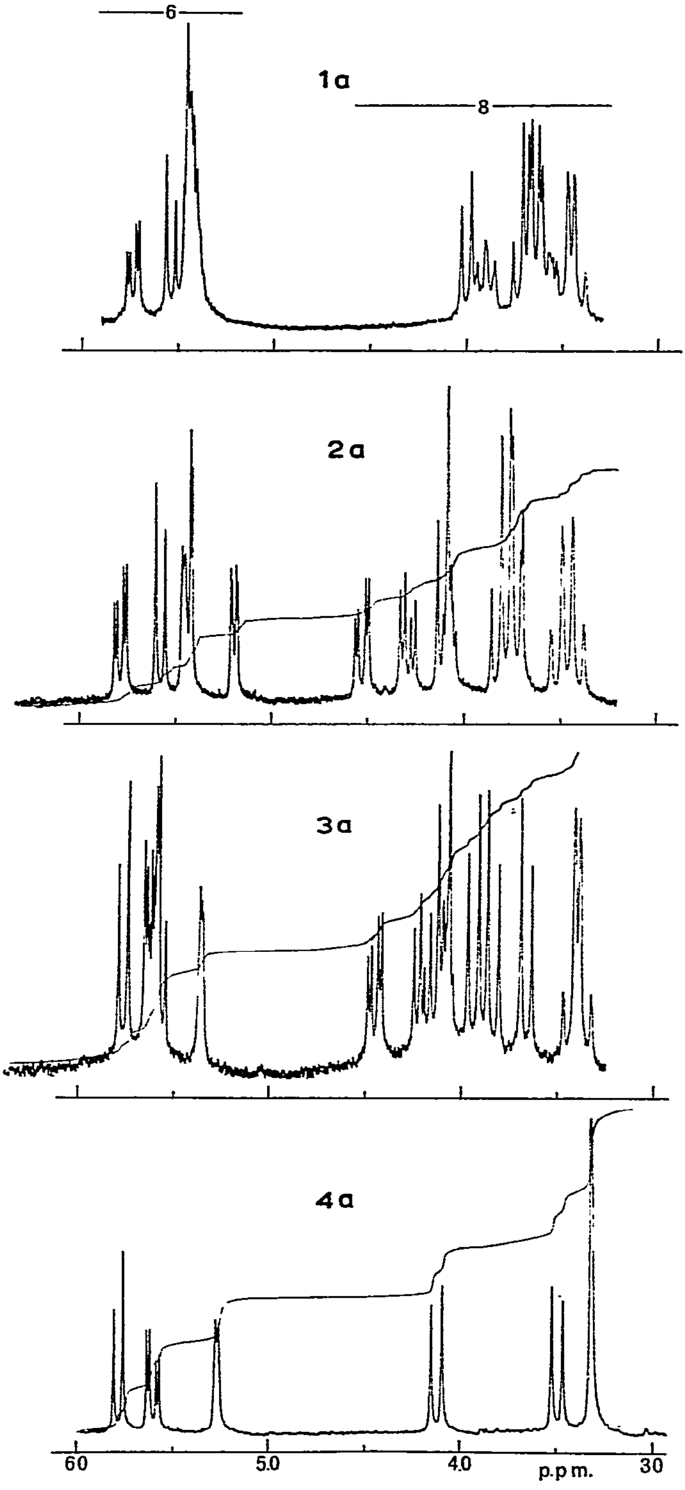


Fig. 1. P.m.r. spectra at 220 MHz in benzene-d_6 of the di-D-fructose dianhydride hexaacetates (**1a**-**4a**); the acetyl resonance portion is omitted. Numbers on the curves denote integrated number of protons.

are assigned conformations resulting from maximum stabilizing anomeric effects and minimum steric interactions.

Hexaacetate (**1a**) *of* **1**. — Chemical data have shown that **1** possesses two D-fructopyranose rings[1b]. The $J_{3,4}$ (10.5 Hz) and $J_{4,5}$ (3.5 Hz) values from the p.m.r. spectrum of **1a** indicated that H-3 and H-4 are oriented antiparallel, and H-4 and H-5 gauche; this disposition of these three protons is compatible with the *1C* conformation for one of the constituent D-fructose residues in **1**. As the signals for H-3′, H-4′, and H-5′ in the second pyranoid ring of **1a** were not resolved, determination of its conformation was achieved by analysis of the H-6′a, H-6′e resonance patterns. The coupling constants extracted from the AB portion of the ABX subsystem (H-6′a, H-6′e, H-5′) gave $J_{5',6'a}$ 9.0 Hz, and $J_{6'a,6'e}$ 11 Hz. Double irradiation in the complex H-5′ region at 5.41 p.p.m., resulted in a simple AB quartet (J 11 Hz) for the geminal H-6′a, H-6′e pair. The magnitude of the coupling constants associated with H-5′ suggest that H-5′ must be axially oriented and related trans and gauche, respectively, to H-6′a and H-6′e. Only a *C1*(D) chair conformation can successfully accommodate this geometry in a D-fructopyranose ring. Additional supporting evidence can be obtained from the chemical shifts of the constituent acetate groups (see Table II). The average chemical shift for the axial and equatorial acetate groups of sugar acetates in chloroform-*d* is 2.14 ±0.04 and 2.04 ±0.05 p.p.m., respectively[3]. Acetate chemical-shift data indicated the presence of three axial and three equatorial acetate groups in **1a**. As the *1C* conformer of D-fructopyranose would require two equatorial and one axial ring-acetate groups, the other ring in **1a** would possess two axial and one equatorial acetate groups, indicating the *C1*(D) conformation. The conformational structure of **1** is thus indicated to be 1′,2-anhydro-1-*O*-D-fructopyranosyl-(*1C*)-D-fructopyranose-(*C1*).

TABLE II

CHEMICAL SHIFTS OF THE ACETATE RESONANCES OF THE DI-D-FRUCTOSE DIANHYDRIDE HEXAACETATES **1a, 2a, 3a, 4a**)

Chemical shifts of peaks observed, ppm (integral)					
1a		2a	3a	4a	
C_6D_6	$CDCl_3$	C_6D_6	C_6D_6	C_6D_6	$CDCl_3$
1.55 (3)	1.98 (3)	1.58 (6)	1.56 (3)		2.01 (6)
1.66 (3)	2.05 (3)		1.66 (6)	1.68 (6)	
1.695 (3)	2.08 (3)				
1.70 (3)	2.13 (6)	1.70 (6)	1.71 (3)	1.72 (6)	
1.72 (3)					
1.74 (3)	2.16 (3)	1.76 (6)			2.18 (12)
			1.83 (3)		
			1.91 (3)		
				2.14 (6)	

Hexaacetate (**2a**) *of* **2**. — The sugar moieties in **2** were deduced to be D-fructofuranose and D-fructopyranose by chemical analysis[1b]. The $J_{3,4}$ (10.6 Hz) and $J_{4,5}$

(3.5 Hz) values from the p.m.r. spectrum of **2a** showed that the orientations of H-3, H-4, and H-5 are in agreement with those for the *1C*(D) conformation of the pyranoid ring. The $J_{3',4'}$ (1.8 Hz) and $J_{4',5'}$ (5.5 Hz) values are consistent with a D-fructofuranose ring having C-3 out of the plane of the other ring atoms[4]. The coupling constants for H-6′, 6′, and H-5′ were typical for an ABX system of an exocyclic methylene group and provide additional evidence for the presence of a furanoid ring. Compound **2** may be depicted conformationally as 1′,2-anhydro-1-*O*-D-fructopyranosyl-(*1C*)-D-fructofuranose-(*E3*).

Hexaacetate (**3a**) *of* **3**. — Periodate-oxidation studies on **3** revealed the presence of one pyranoid and one furanoid ring in this di-D-fructose dianhydride[1d]. The $J_{3,4}$ (11.0 Hz) and $J_{4,5}$ (3.1 Hz) values from the p.m.r. spectrum of **3a** indicate the *1C* conformation for the pyranoid ring. The $J_{3'4'}$ (7.5 Hz) and $J_{4'5'}$ (5.1 Hz) values from the spectrum of **3a** reflecte a difference in the conformation of the furanoid rings in **2** and **3**; these values strongly suggest that C-4 of the D-fructofuranose ring is out of the plane of the other ring-atoms[4]. The signals for H-6′, 6′, and H-5′ of **3a** appear in the same region of the spectrum (4.06–4.43) as the corresponding signals in the spectrum of **2a**, and the coupling constants for H-6′, 6′ and H-5′ of **3a** are indicative of an exocyclic methylene group, affording additional evidence for the presence of the furanoid ring. The conformations of the sugar residues in **3** were thus deduced to be 1′, 2-anhydro-1-*O*-D-fructopyranosyl (*1C*)-D-fructofuranose (*E4*).

Hexaacetate (**4a**) *of* **4**. — Methylation and periodate-oxidation studies have indicated that the D-fructose residues both have pyranoid rings[1e]. The p.m.r. spectrum of **4a** is simple showing only six signals (H-3, H-3′, doublet; H-4, H-4′, doublet of doublets; H-5, H-5′, multiplet; H-6,6 and H-6′,6′, singlet; H-1, H-1, H-1′, H-1′, pair of doublets); these data indicate that the paired-off pyranose ring-protons are in identical environments, accounting for the identical superimposed spectra for the pyranoid ring-protons and the four protons in the central 1,4-dioxane ring as well. The $J_{3,4}$ and $J_{3',4'}$ (10.9 Hz) values and $J_{4,5}$ and $J_{4',5'}$ (3.4 Hz) values from the p.m.r. spectrum of **4a** are compatible with the *1C* conformation for both D-fructopyranose residues [$J_{3,4}$ (10.9 Hz) and $J_{4,5}$ (3.4 Hz) values were observed for β-D-fructopyranose-(*1C*) pentaacetate]. The sugar ring conformers in **4** are thus shown to be 1′,2-anhydro-1-*O*-D-fructopyranosyl-(*1C*)-D-fructopyranose-(*1C*).

The only question remaining to be resolved in the elucidation of the total structure of these di-D-fructose dianhydrides is concerned with the configuration of the two anomeric centers in each compound. Utilizing Hudson's[5] rules of isorotation, Wickberg[1e] has established with some certainly that the anomeric configurations of **1** and **4** are α,α′ and β,β′ respectively; application of these rules to the optical-rotatory data for **2** and **3** strongly suggested that the pyranose moieties in these sugars are probably α and β respectively; no assignments were made for the anomeric configurations of the D-fructofuranose rings in **2** and **3***.

---

*Noteworthy is the similarity of the chemical shifts in the fructopyranose ring-system of **1** and **2**, **3**, and **4**. Structures **1** and **2**, which may be predicted from optical-rotatory data to possess an α

A paper in preparation describes the application of ^{13}C nuclear magnetic resonance spectroscopy to the determination of the anomeric configurations in these di-D-fructose dianhydrides.

EXPERIMENTAL

The 220-MHz spectra of compounds **1a**–**4a** in benzene-d_6 or chloroform-d containing tetramethylsilane as the internal standard were measured at about 23° with a Varian HR-220 spectrometer. Homonuclear double-irradiation experiments were carried out under pseudo-frequency decoupling conditions with a Wavetek, Model 101, voltage-controlled generator calibrated to the sweep widths of the spectrometer recorder.

The di-D-fructose dianhydrides and their hexaacetates were prepared by published procedures[1].

ACKNOWLEDGMENTS

We thank Mrs. Valerie Robinson (Ontario Research Foundation) for recording the spectra.

REFERENCES

1 (*a*) A. Pictet and J. Chavan, *Helv. Chim. Acta*, 9 (1926) 809; (*b*) M. L. Wolfrom and M. Grace Blair, *J. Amer. Chem. Soc.*, 70 (1948) 2406; (*c*) M. L. Wolfrom, W. W. Binkley, W. L. Shilling, and H. W. Hilton, *ibid.*, 73 (1951) 3553; (*d*) M. L. Wolfrom, H. W. Hilton, and W. W. Binkley, *ibid.*, 74 (1952) 2867; (*e*) B. Wickberg, *Acta Chem. Scand.*, 8 (1954) 436.

2 W. W. Binkley, D. Horton, and N. S. Bhacca, *Carbohyd. Res.*, 10 (1969) 245.

3 L. Jackmann and S. Sternhell, *Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry*, Pergamon Press, Elmsford, New York, 1960, p. 240.

4 R. U. Lemieux and R. Nagarajan, *Can. J. Chem.*, 42 (1964) 1270.

5 C. S. Hudson, *J. Amer. Chem. Soc.*, 31 (1909) 66.

---

anomeric center that may be associated with their *1C*(D) conformations, have similar chemical shifts for H-3, H-4, H-5, H-6a, and H-6e, whereas **3** and **4** (which may possess β anomeric centers, also in the *1C* conformation) show similar chemical shifts for the same set of protons. In addition, the chemical shifts for H-3 and H-4 of **1** and **2** are interchanged for H-4 and H-3 in **3** and **4**, that is, H-3 resonates at lower fields than H-4 in the predicted β-*1C* conformers whereas H-3 resonates at higher fields than H-4 in the predicted α-*1C* structures.