Carbohydrate Research, 119 (1983) 263–268
Elsevier Science Publishers B.V., Amsterdam – Printed in The Netherlands

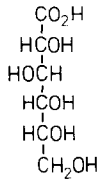
Note

Conformations of D-gluconic, D-mannonic, and D-galactonic acids in solution, as determined by n.m.r. spectroscopy*

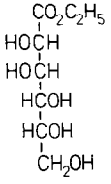
DEREK HORTON†, ZBIGNIEW WAŁASZEK‡, AND IRENA EKIEL**
Department of Chemistry, The Ohio State University, Columbus, OH 43210 (U.S.A.)
(Received February 19th, 1983; accepted for publication, March 14th, 1983)

During the course of broader studies on conformational analysis of lactones of sugar acids in solution[2–5], we became interested in the conformations of sugar acids. Whereas the conformations of D-pentononitriles[6,7], and some D-hexononitriles[7,8] in solution have been rather extensively studied, conformational analysis of aldonic acids has as yet been little explored[2].

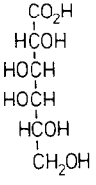
The present work is a ^1H- and ^{13}C-n.m.r.-spectral study on the conformations of three isomeric D-hexonic acids, namely, D-gluconic acid (**1**), D-mannonic acid [because of its extreme tendency to lactonize, the acid was investigated in the form of its ethyl ester (**2**)], and D-galactonic acid (**3**) in solution.



1



2



3

EXPERIMENTAL

Literature procedures were used to prepare D-gluconic acid[9], 2,3,4,5,6-penta-*O*-acetyl-D-gluconic acid[10], ethyl D-mannonate[11], and D-galactonic acid[9]. Sodium D-gluconate was obtained from Pfanstiehl Labs., Waukegan, Illinois. All compounds had physical constant in good agreement with published values and

*For a preliminary report, see ref. 1.
†To whom inquiries should be addressed.
‡Permanent address: Department of Tumor Biology, Institute of Oncology, Gliwice, 44-100 Poland.
**Permanent address: Department of Biophysics, Institute of Experimental Physics, University of Warsaw, Warsaw, 02-089 Poland.

0008-6215/83/$ 03.00

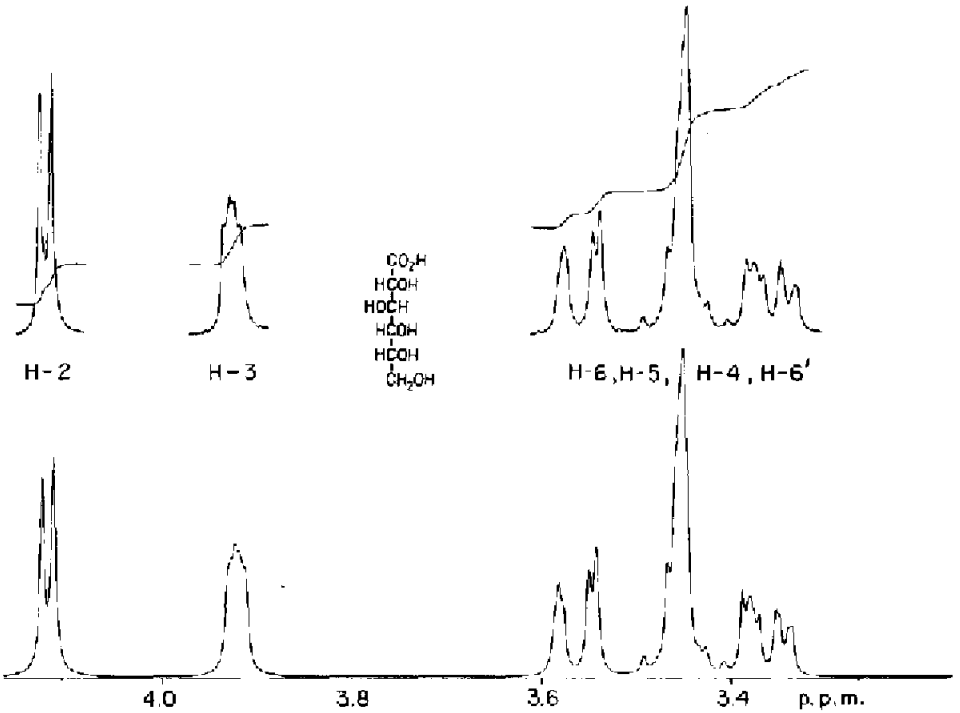


Fig. 1. The 300-MHz, ^{1}H-n.m.r. spectrum of D-gluconic acid (**1**) in dimethyl sulfoxide-d_6 (upper trace) and the simulated spectrum (lower trace).

were chromatographically homogeneous. T.l.c. was performed as described earlier[2]. The ^{1}H-n.m.r. spectra of the aforementioned acids in dimethyl sulfoxide-d_6 and in pyridine-d_5 were recorded either at 100 MHz with a Varian HA-100 instrument or at 300 MHz with a Varian HR-300 spectrometer, as described earlier[2,5]. Computer-simulated spectra were generated with the aid of the program LAOCOON III, in order to extract ^{1}H-n.m.r. chemical-shifts and coupling constants. Proton-decoupled, natural-abundance-carbon-13, pulse Fourier-transform, n.m.r. spectra of the acids and derivatives were recorded with a Bruker HX-90 multinuclear spectrometer, as described earlier[2,3]; the spectra of each compound in D_2O were recorded immediately after dissolution, during mutarotation, and when mutarotation was complete.

DISCUSSION

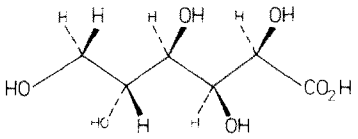
The coupling constants observed for D-gluconic acid (see Fig. 1 and Table I) are interpretable in terms of a conformational equilibrium between the planar, zigzag conformation (**P**) and the $_3G^+$, sickle form (for an explanation of the symbolism, see refs. 12 and 13). Interestingly, both of these conformations have been found for the D-gluconate ion in crystals of potassium D-gluconate[14,15]. We had ear-

TABLE I

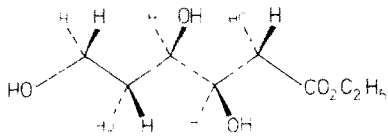
^{1}H-N M R -SPECTRAL DATA FOR D-GLUCONIC ACID (**1**), ETHYL D-MANNONATE (**2**), AND D-GALACTONIC ACID (**3**)

Compound	*Solvent*	*Chemical shifts in δ values*[a]						*Coupling constants in Hz*					
		H-2	*H-3*	*H-4*	*H-5*	*H-6*	*H-6'*	$^3J_{2,3}$	$^3J_{3,4}$	$^3J_{4,5}$	$^3J_{5,6}$	$^3J_{5,6'}$	$^2J_{6,6'}$
1	$(CD_3)_2SO$[b]	4.12d	3.92q	3.45m	3.46m	3.56m	3.36m	3.55	2.55	8.2	3.0	5.3	−10.8
1 pentaacetate	$CDCl_3$[c,d]	5.31d	5.64q	5.50q	5.08o	4.33q	4.12q	3.8	5.0	6.1	4.3	5.7	−12.5
2	$(CD_3)_2SO$[b,e,f]	3.95d	3.78dd	3.45m	3.43m	3.59m	3.38m	9.0	0.5	10.0	2.3	5.0	−10.6
3	C_5D_5N[c]	5.33d	4.95dd	4.59dd	4.75o	4.24m	4.24m	1.5	9.4	1.6	6.0	6.2	−12.6

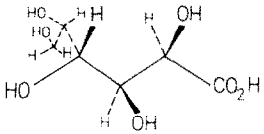
[a]Signal multiplicities: d, doublet; dd, doublet of doublets; m, complex multiplet; o, octet, q, quartet. [b]Spectra recorded at 300 MHz with a Varian HR-300 spectrometer. [c]Recorded at 100 MHz with a Varian HA-100 spectrometer. [d]Chemical shifts of acetyl-group protons: δ 2.16, 2.06, 2.06, 2.06, and 2.02 [e]In the presence of CF_3CO_2H. [f]Chemical shifts of ethyl-group protons: δ 4.07 and 1 20.



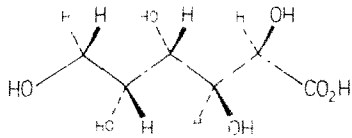
1-P



2-P



$1\text{-}{}_3G^+$



3-P

lier found[2] that the conformational equilibrium of D-glucaric acid appears to involve the ${}_3G^+$ and ${}_2G^-$ sickle forms, together with the planar, zigzag conformation (**P**). Changes in the coupling constants observed after peracetylation of D-gluconic acid indicate a shift of the conformational equilibrium toward the ${}_3G^+$ and, possibly[2], ${}_2G^-$ sickle form(s), whereas the ${}_2G^+$ form has been postulated as the favored conformation of peracetylated D-gluconononitrile in solution[7,8].

The planar, zigzag conformation of D-gluconic acid, which has unfavorable, 1,3-parallel interactions (see ref. 12) of the hydroxyl groups at C-2 and C-4, must apparently be stabilized, as in the crystal[14,15], by a well-defined, intramolecular hydrogen-bond, 4-OH–O-2, and a weaker, intramolecular interaction, 2-OH–O-1. Such intramolecular hydrogen-bonding has been observed in dimethyl sulfoxide solutions of sodium D-glucuronate[16], and sucrose[17], as well as in those of di-, oligo-, and poly-saccharides of D-glucose[18–20]. It now seems clear that the effects of intramolecular hydrogen-bonding on conformational properties of sugars in solution, including aqueous solution[17], need to be studied in detail.

The coupling constants found for D-mannonic acid and D-galactonic acid (see Table I) demonstrate that the conformations in solution strongly favor the planar, zigzag (**P**) conformation, which has no 1,3-parallel interactions of hydroxyl groups in either instance. Similar behavior has been observed for peracetylated D-mannono- and D-galactono-nitriles in solution[7,8].

Additional support for the aforementioned conformations as the favored conformations of **1**, **2**, and **3** in solution was afforded by ^{13}C-n.m.r.-spectral analysis (see Tables II and III). It is clear, for example, that C-2, C-3, C-4, C-5, and C-6 in D-mannonic acid and its ethyl ester resonate at almost exactly the same positions. The results indicate the same conformational preference for both compounds. As to D-gluconic acid and its sodium salt, the relatively large shift of the C-2 signal to lower field in sodium D-gluconate might reflect a shift of the confor-

TABLE II

CARBON-13 CHEMICAL SHIFTS FOR SOME D-HEXONIC ACIDS IN D_2O AT ~30°

Compound	*Chemical shifts in p.p.m. downfield from Me_4Si*[a]					
	C-1	*C-2*	*C-3*	*C-4*	*C-5*	*C-6*
D-Gluconic acid	176.7	73.2[b]	72.5[b]	71.7[b]	71.6[b]	63.6
Sodium D-gluconate	179.6	75.0[b]	73.5[b]	72.2[b]	71.9[b]	63.6
D-Mannonic acid[c]	177.4	72.3[b]	71.6[b]	71.3[b]	70.4[b]	64.0
Ethyl D-mannonate[d]	175.7	72.4[b]	71.7[b]	71.5[b]	70.4[b]	64 1
D-Gulonic acid[c]	176.9	73.4[b]	73.2[b]	72.4[b]	71.1[b]	63.6
D-Galactonic acid	177.8	72.05[b]	71.3[b]	70.8[b]	70.1[b]	64.2

[a]For freshly prepared solutions. The original data, referenced to the highest-field signal of sodium 4,4-dimethyl-4-silapentane-1-sulfonate (DSS), were converted according to the equation[21]: δ Me_4Si = δ DSS − 1.6. [b]These assignments may have to be interchanged. [c]As observed[4] in spectra of its fully mutarotated lactone(s). [d]Chemical shifts of the ethyl-group carbon atoms, in p.p.m. downfield from Me_4Si: 63.4; 13.5.

TABLE III

CARBON-13 CHEMICAL SHIFTS OF D-GLUCONIC AND D-GALACTONIC ACID IN Me_2SO-d_6

Compound	*Chemical shifts in p.p.m. downfield from internal Me_4Si, and solvent-induced shifts $\Delta\delta$[a] (in parentheses)*					
	C-1	*C-2*	*C-3*	*C-4*	*C-5*	*C-6*
D-Gluconic acid	174 1 (2.6)	72.5[b] (0.7)	71.9[b] (0.6)	71.2[b] (0.5)	70.3[b] (1.3)	63.0 (0.6)
D-Galactonic acid	175.6 (2.2)	71.4[b] (0.65)	70.1[b] (1.2)	69.6[b] (1.2)	69.0[b] (1.1)	63.1 (1.1)

[a]$\Delta\delta$ = δ in D_2O − δ in Me_2SO-d_6. [b]These assignments may have to be interchanged.

mational equilibrium in favor of the planar, zigzag conformation (**P**). All resonances are shifted to higher field (see Table III) in dueterated dimethyl sulfoxide in comparison with aqueous solution (D_2O). Differences in chemical shifts measured for solutions in D_2O and Me_2SO-d_6 seem to arise from differences in modes of solvation, and they may give some information on hydrogen-bonding systems in solution[2−5]. Solvent-induced shifts ($\Delta\delta$) depend not only on the basicity of a hydroxyl group that is to be protonated by a protic sovent (H_2O, D_2O), but also on the accessibility of the hydroxyl group for such protonation. Hydroxyl groups involved in an intramolecular, hydrogen-bonding system, such as HO-2 and HO-4 in D-gluconic acid, and HO-2 in D-galactonic acid, are less accessible for protonation, and, because of this, the solvent-induced shifts observed for the aforementioned carbon atoms are somewhat smaller. As no dimer solute–solute association has been observed[18,20] for solutions of carbohydrates in dimethyl sulfoxide up to the concentration ~0.7 mol.dm^{-3}, such association has not been considered, either in the present work or in our earlier studies on conformations of lactones of sugar acids[2−5].

TABLE IV

EQUILIBRIUM COMPOSITION[a] OF SOME HEXONIC ACIDS AND THEIR LACTONES IN D_2O[b] AT ~30°

Configuration	*Content of acid and lactones in percent*[c]		
	Acid	*1,5-Lactone*	*1,4-Lactone*
D-*gluco*	66	18	17
D-*manno*	11	5	84
D-*gulo*	13	—	87
D-*galacto*	22.5	—	77.5

[a]Calculated from peak areas of protonated carbon atoms in ^{13}C-n.m.r. spectra, as described earlier[21]. [b]27% (w/v) solutions. [c]±5%.

The equilibrium compositions of the three D-hexonic acids and their lactones in D_2O were estimated from total peak-areas of the all-protonated carbon atoms in proton-decoupled, natural-abundance-carbon-13, pulse Fourier-transform, n.m.r. spectra for equilibrated solutions (see Table IV). Generally, our data are consistent with earlier data obtained by different methods[22]. 1,5-Lactones were observed as the first products of lactonization, as indicated by both ^1H- and ^{13}C-n.m.r. spectra, as well as by t.l.c.[23], but the 1,4-lactones, being thermodynamically more stable than 1,5-lactones[24], prevail in equilibrated solutions. Similar observations had been made for D-pentonic acids and their lactones[5].

REFERENCES

1 D. HORTON, Z. WAŁASZEK, AND I. EKIEL, *Abstr. Pap. Am. Chem. Soc. Meet.*, 184 (1982) CARB-35.
2 D. HORTON AND Z. WAŁASZEK, *Carbohydr. Res.*, 105 (1982) 95–109.
3 D. HORTON AND Z. WAŁASZEK, *Carbohydr. Res.*, 105 (1982) 111–129.
4 Z. WAŁASZEK AND D. HORTON, *Carbohydr. Res.*, 105 (1982) 131–143.
5 Z. WAŁASZEK, D. HORTON AND I. EKIEL, *Carbohydr. Res.*, 106 (1982) 193–201.
6 W. W. BINKLEY, D. R. DILHI AND R. W. BINKLEY, *Carbohydr. Res.*, 18 (1971) 459–465.
7 A. M. SELDES, E. G. GROS, I. M. F. THIEL AND I. O. DEFERRARI, *Carbohydr. Res.*, 39 (1975) 11–17.
8 L. M. SWEETING, B. COXON AND R. VARMA, *Carbohydr. Res.*, 72 (1979) 43–55.
9 J. M. BRACKENBURY AND F. W. UPSON, *J. Am. Chem. Soc.*, 55 (1933) 2512–2514.
10 M. L. WOLFROM, M. KONIGSBERG AND D. I. WEISBLAT, *J. Am. Chem. Soc.*, 61 (1939) 574–575.
11 K. J. GOLDNER AND C. H. ROGERS, *J. Am. Pharm. Assoc.*, 28 (1939) 364–369.
12 D. HORTON AND J. D. WANDER, *J. Org. Chem.*, 39 (1974) 1859–1863, and references cited therein.
13 M. BLANC-MUESSER, J. DEFAYE AND D. HORTON, *Carbohydr. Res.*, 87 (1980) 71–86.
14 G. A. JEFFREY AND E. J. FASISKA, *Carbohydr. Res.*, 21 (1972) 187–199.
15 N. C. PANAGIOTOPOULOS, G. A. JEFFREY, S. J. LA PLACA AND W. C. HAMILTON, *Acta Crystallogr., Sect. B*, 30 (1974) 1421–1430.
16 F. HEATLEY, I. E. SCOTT, R. W. JEANLOZ, AND E. L. WALKER-NASIR, *Carbohydr. Res.*, 99 (1982) 1–11.
17 K. BOCK AND R. U. LEMIEUX, *Carbohydr. Res.*, 100 (1982) 63–74, and references cited therein.
18 B. CASU, M. REGGIANI, G. G. GALLO AND A. VIGEVANI, *Tetrahedron*, 22 (1966) 3061–3083.
19 M. ST.-JACQUES, P. R. SUNDARARAJAN, K. L. TAYLOR AND R. H. MARCHESSAULT, *J. Am. Chem. Soc.*, 98 (1976) 4383–4391.
20 B. GILLET, D. J. NICOLE AND L.-J. DEPUECH, *Tetrahedron Lett.*, (1982) 65–68.
21 D. HORTON AND Z. WAŁASZEK, *Carbohydr. Res.*, 105 (1982) 145–153.
22 S. R. CARTER, W. N. HAWORTH AND R. A. ROBINSON, *J. Chem. Soc.*, (1930) 2125–2133.
23 Z. WAŁASZEK, unpublished results.
24 H. C. BROWN, J. H. BREWSTER AND H. SHECHTER, *J. Am. Chem. Soc.*, 76 (1954) 467–474.