Carbohydrate Research, 83 (1980) 379–382
Elsevier Scientific Publishing Company, Amsterdam – Printed in The Netherlands

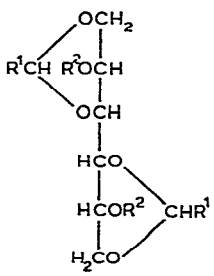
Note

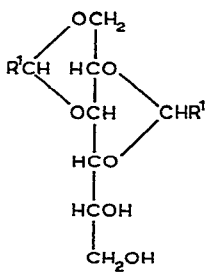
Diethoxyphosphinylethylidene acetals of D-mannitol and D-glucitol*

SHAUL YANAI, MORDEHAI HALMANN, AND DAVID VOFSI
The Weizmann Institute of Science, Rehovot (Israel)
(Received August 23rd, 1979, accepted for publication, October 15th, 1979)

In the reactions[1] of 2,2-dialkoxyethylphosphonates with galactitol, the phosphorus atom exercises an electronic effect that influences the nature of the products, and there is apparent deviation from the Barker and Bourne rules[2] We now report on the reactions of D-mannitol and D-glucitol with diethyl 2,2-diethoxyethylphosphonate[1] With aldehydes, D-mannitol affords 1,3 4,6-diacetals[3] and D-glucitol yields 1,3 2,4-diacetals[4–6]

Diethyl 2,2-diethoxyethylphosphonate reacted with D-mannitol in the presence of conc hydrochloric or hydrobromic acid, or anhydrous hydrogen chloride, to give a single product, namely, the di(phosphonoacetal) **1** The formation of **1** was most rapid in the presence of hydrobromic acid Syrupy **1** consumed practically no periodate, contained 6 8% of hydroxyl groups, and its dibenzoate (**2**) and diacetate (**3**) were syrupy The chemical shifts of the acetal proton (δ 4 9) and the acetal carbon (δ 97 5) in the n m r spectra of **1** were characteristic of a 1,3-dioxane system[7] A dilute solution of **1** in $CHCl_3$ showed i r absorption (3575 cm^{-1}) for hydrogen-





$R^1 = CH_2P(O)(OEt)_2$

1 R^2 = H
2 R^2 = Bz
3 R^2 = Ac

4

*Phosphonated Acetals, Part V For Part IV, see ref 1

0008-6215/80/0000–0000/$ 02 25,

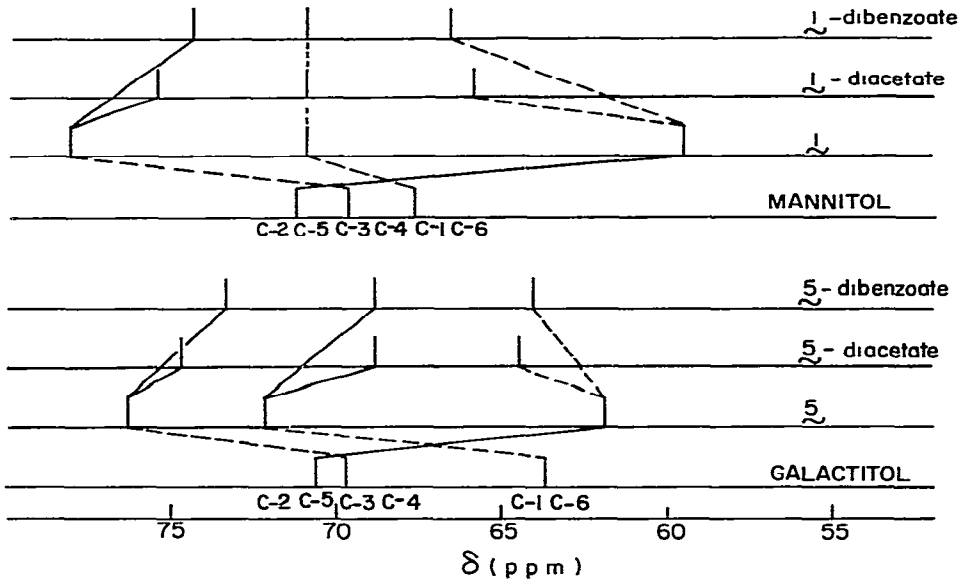


Fig 1 ^{13}C-Chemical shift data for the bis(2-diethoxyphosphinylethylidene) acetals of D-mannitol and -galactitol

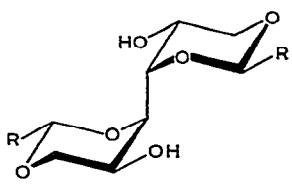
bonded hydroxyl groups Comparative ^{13}C-n m r spectroscopy of **1** with analogous compounds[1] confirmed the 1,3 4,6-diacetal structure Thus, **1** is in accord with the Barker and Bourne rules

D-Glucitol reacted with diethyl 2,2-diethoxyethylphosphonate to give a mixture of products in the thermodynamically controlled phase, including a non-phosphorus-containing substance (anhydride) The phosphorus-containing derivatives were mainly two diacetals together with a small proportion of a monoacetal Repeated chromatography on silicic acid gave a yellow, syrupy diacetal that contained a terminal, vicinal diol group (periodate consumption, 0 90 and 0 93 mol , formaldehyde liberation, 1 04 and 1 21 mol) The ^{1}H- (δ 5 00) and ^{13}C-n m r data (δ 97 32) for the acetal proton and carbon show the acetal to be of the 1,3-dioxane type Since the acetal rings involve four contiguous hydroxyl groups, this product must be the 1,3 2,4-diacetal **4**

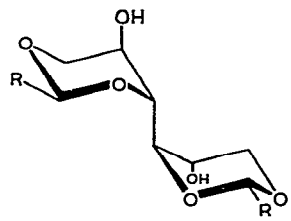
The other di(phosphonoacetal) could not be purified and its structure was not determined. However, we can arrive at some conclusions by comparing conformations of the only diacetal obtained from D-mannitol with the 1,3 4,6-diacetal obtained from galactitol[1] (Fig 1)

Assignment of the chemical shifts of the carbon atoms of the sugar alcohols proved to be specifically linked to the configuration of each carbon atom[8 9], and to their substitutions[10] Fig 1 shows a correlation of the chemical shifts for the ^{13}C-n m r signals of the 1,3 4,6-diacetals of galactitol and mannitol and their dibenzoates and diacetates As expected, acetalation causes positive (downfield) shifts on the substituted carbon atoms, whereas the β and γ effects are negative (upfield shifts)

The α-effect on C-1 for 1,3 4,6-di-*O*-(2-diethoxyphosphinylethylidene)galactitol is ~8 5 p p m , and 6 7 p p m for C-3 due to the β effect of C-4 Similar results are observed for the dibenzoate and diacetate Substitution of an equatorial hydroxyl group causes smaller α-effects (~2 4 p p m) than substitution of an axial group (~6 7 p p m) The results are consistent with the conformations depicted in **5** and **6** For the conformational array $\overset{O}{\diagdown}C\overset{C}{\diagup}\diagdown C^{13}$, upfield shifts were observed for the marked ^{13}C-nucleus when the oxygen atom is antiperiplanar[11] Thus (see Fig 1), $\Delta\delta$ (acetal–parent hexitol) for C-3 of D-mannitol exhibits a greater α-effect compared to C-1, despite the β-effect of C-4, HO-2 is gauche to C-4 for the galactitol diacetal **5**, whereas the arrangement is antiperiplanar in the mannitol diacetal **6**



5



6

The compact 1,3 4,6-conformation **5** was suggested as more favorable, by considering ring oxygen–hydroxyl dipolar interactions and hydrogen-bonding[12] On the other hand, the conformation **6** of acetal **1** is supported by the ^{13}C-n m r data and by the strong hydrogen-bonding that is probably due to a bifurcated hydrogen-bond[13] between HO-2 and O-1 and O-3

EXPERIMENTAL

Instrumentation and analytical methods have been described[1]

*1,3 4,6-Di-*O*-(2-diethoxyphosphinylethylidene)mannitol* (**1**) — D-Mannitol (4 g) and diethyl 2,2-diethoxyethylphosphonate (11 55 g) were allowed to react in the presence of conc hydrochloric acid (10 ml) After 8 days, the mixture was processed in the usual way[1], and chloroform extraction yielded a colourless syrup (11 15 g), n_D^{25} 1 4680, which showed only one component, R_F 0 6, in t l c (Found 12 95 $C_{18}H_{36}O_{12}P_2$ calc P, 12 2) ^{1}H-N m r (60 MHz) δ 1 28 (t, 12 H, J 7 Hz, 4 Me), 2 22 (dd, 4 H, $J_{H,H}$ 5, $J_{P,H}$ 19 Hz, 2 PCH_2), 3 35–4 0 (m, 10 H, protons of sugar skeleton), 4 11 (quin, 8 H, J 7 Hz, 4 $POCH_2$), and 4 9 (2 H, acetal protons), ^{13}C-n m r (22 62 MHz) δ 16 49, 16 23 (Me), 35 14, 28 84 (PCH_2), 62 25, 61 95 ($POCH_2$), 59.51 (C-1,5), 71 06 (C-1,6), 79 22 (C-3,4), and 97 53 (acetal carbon), ^{31}P-n m r (109 3 MHz) δ —26 68 Mass spectrum *m/e* 505 (2 25%), 223 (100), 283 (22 2), 355 (3 1), 253 (4 4), and 447 (5 3) I r data $\nu_{max}^{CHCl_3}$ 3575 (OH), 3540 (OH), 1200

(P=O), 1030–1040 (P-O-Et), and 1400 cm^{-1} (O-C-O) Periodate-ion consumption 0 12 (3 h) and 0 18 mol (24 h)

Catalysis with ~48% hydrobromic acid for 5 days gave 5% (at room temperature) and 10% (at 40°) of 1,4-anhydro-D-mannitol (m p 156–158°)

The dibenzoate **2** of **1** was a yellow syrup (Found P, 8 9 $C_{32}H_{41}O_{14}P_2$ calc P, 8 7) ^{13}C-N m r (22 63 MHz) δ 16 53, 16 27 (Me), 35 04, 29 04 (PCH_2), 62 19, 61 93 ($POCH_2$), 65 88 (C-2,5), 71 02 (C-1,6), 75 60 (C-3,4), 97 45 (acetal C), 128 26–133 66 (Ph), and 149 67 (C=O), ^{31}P-n m r (109 3 MHz) δ −26 7

The diacetate **3** of **1** was a syrup, n_D^{23} 1 4350 ^{13}C-N m r (22 62 MHz) δ 16 49, 16 23 (Me), 20 81 (CH_3CO), 34 84, 28 62 (PCH_2), 62 61, 61 95 ($POCH_2$), 66 61 (C-2,5), 71 06 (C-1,6), 74 51 (C-3,4), 100 5 (acetal C), and 169 75 (C=O)

1,3 2,4-Di-O-(2-diethoxyphosphinylethylidene)-D-glucitol (**4**) — The reaction of D-glucitol with diethyl 2,2-diethoxyethylphosphonate, as described above, gave a syrupy mixture containing mainly di(phosphonoacetals) (97 8%), n_D^{25} 1 4604 (Found· P, 12 8 $C_{18}H_{36}O_{12}P_2$ calc P, 12 25), containing (t l c) components with R_F 0 48 and 0 37 The mixture could not be fractionated by solvent extraction or crystallization Chromatography on Dowex-1 (HO^-) resin, alumina, or diethylaminoethylcellulose (DE52) was unsuccessful Elution of the syrup from silicic acid, with chloroform–methanol (9 1), gave fractions containing the component having R_F 0 52, n_D^{23} 1 4610 ^{1}H-N m r (60 MHz) δ 1 33 (t, 12 H, 4 Me), 2 1, 2 2 (dd, 4 H, PCH_2), 3 35–4 0 (sugar protons), 4 1 (quin, $POCH_2$), and 5 0 (m, 2 H, dioxane acetal proton), ^{13}C-n m r (22 63 MHz) 97 32 (acetal carbon) Mass spectrum *m/e* 505 (M^+ − 1, 1 07%), 476 (M^+ − 30, 2 36), 475 (M^+ − 31, 9 4), 461 (M^+ − 45, 1 33), 445 (M^+ − 61, 1 28), 355 (M^+ − 151, 2 83), 283 (6 56), 223 (15 46), 181 (78), and 153 (23 83) Periodate-ion consumption 0 90 (3 h) and 0 93 mol (24 h), formaldehyde liberation 1 04 and 1 21 mol

REFERENCES

1 S Yanai, M Halmann, and D Vofsi, *Carbohydr Res*, 83 (1980) 243–248
2 S A Barker and E J Bourne, *J Chem Soc*, (1952) 905–909
3 E J Bourne, G T Bruce, and L F Wiggins, *J Chem Soc*, (1951) 2708–2713
4 E J Bourne and L F Wiggins, *J Chem Soc*, (1948) 1933–1936
5 A T Ness, R M Hann, and C S Hudson, *J Am Chem Soc*, 66 (1944) 837–838
6 A T Ness, R M Hann, and C S Hudson, *J Am Chem Soc*, 66 (1944) 665–670
7 T G Bonner, E J Bourne, D Lewis, and L Yuceer, *J Chem Soc, Perkin Trans 1*, (1975) 1323–1325
8 W Voelter, E Breitmaier, G Jung, T Keller, and D Hiss, *Angew Chem Int Ed Engl*, 9 (1970) 803–804
9 W Voelter, E Breitmaier, E B Rathbone and A M Stephen, *Tetrahedron*, 29 (1973) 3845–3848
10 A P G Kieboom, A Sinnema, J M van der Toorn, and H van Bekkum, *J R Neth Chem Soc*, 96 (1977) 35–37
11 E L Eliel, W F Bailey, L D Kopp, R L Willer, D M Grant, R Bertrand, K A Christensen, D K Dalling, M W Duch, E Wenkert, F M Schell, and D W Cochran, *J Am Chem Soc*, 97 (1975) 322–330
12 H B Sinclair and W J Wheadon, *Carbohydr Res*, 4 (1967) 292–297
13 J C Jochims and Y Kobayashi, *Tetrahedron Lett*, (1976) 2065–2068