PROTON AND C-13 NUCLEAR MAGNETIC RESONANCE SPECTRA OF SOME BENZOYLATED ALDOHEXOSES

NORMA B. D'ACCORSO, INGE M. E. THIEL*,

Departamento de Química Orgánica, Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires, Ciudad Universitaria, 1428 Buenos Aires (Argentina)

AND MATTHIAS SCHÜLLER Institut für Organische Chemie und Biochemie, Universität Hamburg, Martin-Luther-King-Platz 6, 2000 Hamburg 13 (West Germany) (Received July 8th, 1983; accepted for publication, July 29th, 1983)

ABSTRACT

Chemical shifts and coupling constants of ¹H-n.m.r. spectra of the perbenzoates of α -D-glucopyranose (1), β -D-glucopyranose (2), α -D-galactopyranose (3), α -D-mannopyranose (4), β -D-mannopyranose (5), and α -D-galactofuranose (6) are reported. The ¹³C-n.m.r. chemical shifts of compounds 1–3 and 6, and of penta-Obenzoyl- β -D-galactofuranose (7) are given. Mass spectra were used to differentiate the furanoses 6 and 7 from the pyranose 3.

INTRODUCTION

The ¹H-n.m.r. spectra of the tetrabenzoates of the aldopentopyranoses and some tri-*O*-benzoylaldopentopyranose derivatives were reported by Durette and Horton^{1,2}. They were recorded at 100 MHz, and allowed determination of the conformational equilibrium of these compounds in solution.

RESULTS AND DISCUSSION

Discussion of ¹H-n.m.r. spectra

The ¹H-n.m.r. spectra of some penta-O-benzoylaldohexopyranoses at 60 MHz gave very limited information³, and we have now repeated their recording at 400 MHz, where a complete, first-order analysis was possible. The assignments were confirmed by double-resonance experiments. The chemical shifts and coupling constants of the carbohydrate esters are respectively listed in Tables I and II.

^{*}To whom correspondence should be addressed.

TABLE I

Compound	Chemical shift (δ) ^a								
	Sugar protons							Aromatic protons	
	H-1	H-2	H-3	H-4	H-5	Н-ба	H-6b		
1	6.86d	5.69 d d	6.33t	5.91t	4.63ddd	4.63dd	4.49dd	7.25-8.18	
2	6.31d	5.86dd	6.05t	5.83t	4.41ddd	4.67 dd	4.52dd	7.22-8.04	
3	6.98d	6.05dd	6.15dd	6.21dd	4.86t	4.65dd	4.44dd	7.25-8.22	
6	6.86d	5.96dd	6.30t	4.82dd	5.98ddd	4.84dd	4.78dd	7.09-8.00	
4	6.65d	5.93dd	6.09dd	6.31t	4.60ddd	4.71 dd	4.51dd	7.26-8.26	
5	6.47d	6.14dd	5.84dd	6.20t	4.40ddd	4.77dd	4.57dd	7.25-8.18	

 $^1\text{H-n.m.r}$ chemical shifts (d) and multiplicities in CDCl_3 solution of some penta-O-benzoylaldohexoses recorded at 400 MHz

^aMeasured from an internal reference of Me₄Si. Key: d, doublet; dd, double doublet; ddd, double double doublet; and t, triplet.

TABLE II

VICINAL PROTON-PROTON COUPLING-CONSTANTS (Hz) OF COMPOUNDS 1-6

Compound	Coupling constants (Hz)								
	J _{1,2}	J _{2,3}	J _{3,4}	J _{4,5}	J _{5,6a}	J _{5,6b}	J _{6a,6b}		
1	3.8	10.2	9.9	9.9	3.0	5.4	12.9		
2	8.3	9.7	9.8	9.9	3.0	4.9	12.4		
3	3.6	10.6	3.2	1.0	6.5	6.9	11.4		
6	4.8	7.4	7.2	4.8	4.4	6.7	12.1		
4	2.0	3.2	10.2	10.1	2.6	3.4	12 1		
5	1.0	3.2	10.0	9.9	2.8	4.2	12.3		

From these results, the ${}^{4}C_{1}$ conformation was confirmed for compounds 1–5. Compound 3 showed a slight deformation of the ring, but the compound has essentially the ${}^{4}C_{1}$ conformation.

It was intended to prepare penta-O-benzoyl- β -D-galactopyranose as reported in the literature⁴. Neither the ¹H- nor the ¹³C-n.m.r. spectrum of our compound **6** agreed with the pyranose structure. During the preparation, the free sugar is heated for 1 h in pyridine. Acree *et al.* ⁵ had described the complex mutarotation of D-galactose in pyridine, and the increased formation of furanose structures with increasing temperature. Complex mutarotation for D-galactose in water⁶ had also been reported. The formation of two pairs of peracetylated anomers was described in 1916 by Hudson and Johnson⁷. Shallenberger and Acree^{5,8} described the formation of two pairs of per(trimethylsilyl)-D-galactoses.

We found that, under the conditions given in the literature⁴, a mixture is obtained that consists mainly of the two penta-O-benzoylfuranoses, as may be seen from the ¹³C-n.m.r. spectrum of the crude product. The purified compound **6** had



physical constants that agreed well with those given by Lederkremer and Deferrari⁴ for "penta-O-benzoyl- β -D-galactopyranose". However, this product had a ¹Hn.m.r. spectrum which did not agree in any way with that expected for penta-Obenzoyl- β -D-galactopyranose. We had, as a reference, the nonreducing moiety of 1,2,6,2',3',4',6'-hepta-O-benzoyl- β -lactose⁹ with its β -D-galactopyranosyl ring size and configuration. We observed different chemical shifts and coupling constants for the sterically more-hindered structure of the disaccharide than those observed in the spectrum of compound **6**, and we assigned to **6** the α -D-galactofuranose configuration. The coupling constants agree with the E_1 conformation for this compound. Matsuhiro *et al.*¹⁰ observed similar coupling constants for methyl (methyl α -D-galactofuranosid)uronate and methyl (methyl 2,3,5-tri-O-acetyl- α -D-galactofuranosid)uronate. The ¹³C-n.m.r. spectrum of **6** confirmed our assumption that it had a furanose ring structure, and so did the mass spectrum.

Discussion of some ${}^{13}C$ -n.m.r. spectra

In the literature, there are a few examples of ¹³C-n.m.r. spectra of fully benzoylated carbohydrate derivatives¹¹.

Here, we present the ¹³C-n.m.r. chemical shifts of some benzoylated aldohexoses, recorded at 100.63 MHz with wide-band proton-decoupling. The resonance signals of the primary carbon atom (-CH₂O-) for the pyranose derivatives 1– 3 were readily assigned, as well as those for C-1. For the assignments of the secondary carbon atoms of the pyranose ring, a comparison with the chemical shifts of the corresponding acetates was employed.

Gagnaire et al.¹² made assignments for acetylated D-glucopyranose deriva-

tives, with selective proton-decoupling of the ¹³C-n.m.r. spectra. Lee *et al.*¹³ reported the ¹³C-n.m.r. data for some acetylated derivatives of β -D-galactopyranosides and β -D-glucopyranosides, with selective ¹H-decoupling and Eu(fod)₃-induced shifts to ascertain the correct assignments.

The ¹³C-n.m.r. spectrum of penta-O-benzoyl- α -D-glucopyranose (1) showed five resonance signals for the carbohydrate chain, in addition to those of the carbonyl groups (164.34–165.89 p.p.m.) and the aromatic carbon atoms (128.34–133.83 p.p.m.), and the CDCl₃ signals. One of the five signals had nearly double the intensity of the others, and so we considered that it was due to the overlap of two signals^{*}.

The resonance signal at 90.14 p.p.m. was readily assigned to C-1. The signal for the primary C-6 atom was also well differentiated from those of the secondary carbon atoms and was at 62.60 p.p.m. (highest field).

The signal at 69.07 p.p.m. was assigned to C-4; it is the highest resonance signal for the secondary carbon atoms, and next to the signal of the primary C-6 atom. This agrees with the results reported for all the acetylated and free aldohexopyranoses described in the literature¹²⁻¹⁵.

For the other secondary carbon atoms of the pyranose ring, a sequence similar to that given in the literature^{12,15} for the acetylated compounds was assigned. The resonance signal of double intensity at 70.57 p.p.m. was assigned to C-3 and C-5, as in the literature for penta-O-acetyl- α -D-glucopyranose, due to symmetry considerations¹⁵ and the results of selective irradiation¹². The assignments for the resonance signals of compound 1 are shown in Table III, and all of the signals show a shift to lower field relative to the corresponding acetates.

The ¹³C-n.m.r. spectrum of penta-O-benzoyl- β -D-glucopyranose (2) shows the resonance signals of the carbohydrate chain, the carbonyl groups (164.55–166.04 p.p.m.) and the aromatic carbon atoms (128.29–133.73 p.p.m.), and the

Compound	C-1	C-2	С-3	C-4	C-5	С-6
1	90.14	70.60	70.57	69.07	70.57	62.60
2	(0.99) ^a 02 78	$(1.25)^a$	$(0.62)^a$ 72.95 ^b	$(1.02)^a$	$(0.62)^a$	$(1.00)^a$
2	$(0.98)^a$	$(0.50)^{a}$	($(1.13)^a$	(($(1.10)^a$
2–1	2.64	0.40	2.38^{b}	0.21	2.71 ^b	0.20

TABLE III

 $^{13}\text{C-N}$ M R. CHEMICAL-SHIFT ASSIGNMENTS (IN p.p.m.) OF THE CARBOHYDRATE MOIETY OF PERBENZOYL-ATED D-GLUCOPYRANOSES 1 AND 2

^aDifferences of chemical-shift values from those of the corresponding acetyl derivatives, as given in the literature¹². ^bInversion of assignments for C-3 and C-5 cannot be excluded. ^c(0.15–0.20 or 0.48–0.53).

^{*}Even though it is not possible to integrate ¹³C-n.m.r. spectra, due to the n.O.e., such a big difference could be attributed to overlap of two resonance signals.

Compound	C-1	C-2	C-3	C-4	C-5	C-6
3	90.65	67.72	68.54	68.54	69.48	61.86
6	94.25	76.20	74.06	79.67	70.49	63.07
7	99.77	81.02	77.31	84.17	70.33	63.45
a	94.11(19)	75.82	73.88	79.54		63.06
	99.72(15)	80.98	77.34	84.33	70.35	63.56

¹³C-N M.R. CHEMICAL-SHIFT ASSIGNMENTS (IN p.p.m.) OF THE CARBOHYDRATE MOIETY OF PERBENZOYL-ATED DERIVATIVES OF D-GALACTOSE, **3**, **6**, AND **7**

^aThe reaction mixture of furanoses 6 and 7 obtained. The relative intensities of the C-1 resonance signals are given in parentheses.

 $CDCl_3$ signals. The spectrum was analyzed in a similar way, and the assignments are listed in Table III. The values for C-3 and C-5 might have to be reversed.

Comparison of the spectra of 1 and 2 showed that, again, the chemical shift of the anomeric carbon atom is 2.64 p.p.m. higher for the β than for the α anomer.

The resonance signal assigned to C-4 showed minimum difference. It is farthest from the anomeric center, and C-6 is external to the ring and less influenced by the change at C-1, as also pointed out by Dorman and Roberts¹⁵ for the acetates. The differences are shown in Table III.

The ¹³C-n.m.r. spectra of the α -D-galactopyranose derivatives given in the literature are those of the free sugar¹⁶ and of methyl α -D-galactopyranoside¹⁶, and we used them as references for the assignments for penta-O-benzoyl- α -D-galactopyranose (3). The spectrum showed the resonance signals for carbonyl (164.35–165.73 p.p.m.), the aromatic carbon atoms (128.28–133.77 p.p.m.), the solvent (CDCl₃), and five signals corresponding to the carbohydrate moiety, one of them having a double intensity. We assigned 90.65 p.p.m. to C-1, 61.86 p.p.m. to C-6, and the secondary pyranose carbon atoms by their relation to those of the free sugar. The assignments are given in Table IV.

Structure determination of penta-O-benzoyl-D-galactofuranoses 6 and 7 by means of their ^{13}C -n.m.r. and mass spectra

The ¹³C-n.m.r. spectrum of penta-O-benzoyl- α -D-galactofuranose (6), was recorded at 25.20 and at 100.63 MHz with wide-band proton-decoupling. It showed six resonance signals for the carbohydrate chain, the carbonyl groups (164.87-165.88 p.p.m.), the aromatic carbon atoms (128.18–133.54 p.p.m.), and the CDCl₃. In the spectrum, C-1 appeared at 94.25 p.p.m., C-6 at 63.07 p.p.m., and the rest of the signals were assigned as those of an α -furanose structure by comparison with the spectrum given by Ritchie *et al.*¹⁷ for methyl α -D-galactofuranoside. The chemical-shift assignments are listed in Table IV.

The signals in the spectrum of penta-O-benzoyl- β -D-galactofuranose (7) were similarly assigned. The carbonyl signals appeared at 164.23–165.77 p.p.m.



and those of the aromatic carbon atoms at 128.31–133.43 p.p.m.; those of the carbohydrate part of the molecule are listed in Table IV.

The mass spectra of compound 6, 7, and 3 allowed us to ascertain the furanose structure of compounds 6 and 7. The peaks of diagnostic value in the mass spectrum of penta-O-benzoyl- α -D-galactopyranose (3) gave the fundamental fragments of pyranoses, as postulated for the corresponding acetates in the literature¹⁸.

The mass spectra of penta-O-benzoyl- α -D-galactofuranose (6) and penta-Obenzoyl- β -D-galactofuranose (7) agreed, as regards their peaks of diagnostic value, with the furanose structure proposed, and none of them appear in the mass spectrum of compound 3 (see Scheme 1). These fragmentations were proposed by Biemann *et al.*¹⁸ for similar, acetylated derivatives.

CONCLUSIONS

The ¹³C-n.m.r. and mass spectra allowed definitive assignment of the furanose structure to compound 6 (penta-O-benzoyl- α -D-galactofuranose), and assured the validity of our ¹H-n.m.r. assignments.

In the spectra of all these perbenzoylated compounds, we observed a higherfield resonance for all the chain carbon atoms with regard to those of the corresponding free sugars, and lower-field resonances than those of the corresponding acetylated derivatives.

These ¹³C-n.m.r. spectra were needed by us for interpretation of those of benzoylated disaccharide derivatives.

EXPERIMENTAL

General. — Optical rotations were determined with a Perkin–Elmer 141 polarimeter. The compounds were prepared as described in the literature: penta-O-benzoyl- α -D-glucopyranose¹⁹ (1), penta-O-benzoyl- β -D-glucopyranose²⁰ (2), penta-O-benzoyl- α -D-mannopyranose²¹ (4), penta-O-benzoyl- β -D-mannopyranose²² (5), and penta-O-benzoyl- α -D-galactopyranose²³ (3). The ¹H-n.m.r. spectra of compounds 1–6 were recorded with a Bruker WM400 instrument for solutions in CDCl₃, with Me₄Si as the internal standard, and the assignments were confirmed by partial decoupling experiments. The ¹H-n.m.r. spectrum of 7 was recorded at 100 MHz.

The ¹³C-n.m.r. spectra of compounds 1, 2, and 6 were recorded with a Bruker WM400 NMR spectrometer at 100.63 MHz; the ¹³C-n.m.r. spectra of compound 3, of the mixture of furanoses (6 and 7) and of compound 7 were recorded with a Varian XL-100-15 NMR spectrometer, with wide-band proton-decoupling and Me₄Si as the internal standard.

The mass spectra were recorded with a Varian-MAT-112-S mass spectrometer operated at 70 eV in the e.i. mode. The peak intensities are expressed as percentage of total ionization. The most significant m.s. peaks (of diagnostic value) are shown in Scheme 1. For ¹H-n.m.r., see Tables I and II; for ¹³C-n.m.r., see Tables III and IV.

Synthesis of penta-O-benzoyl- α -D-galactofuranose (6) and of penta-O-benzoyl- β -D-galactofuranose (7). — D-Galactose (10 g) was heated with pyridine (150 mL) for 1 h at 100°. The temperature was lowered to 60°, and benzoyl chloride (40 mL) was added portionwise. The mixture was kept for 1.5 h at 60°, and, after 24 h at room temperature, it was stirred into ice-water. The syrup was washed until it solidified. Recrystallized from methanol, it gave 30.3 g (77.3%) of needles formed by two components, as shown by t.l.c. with Kieselgel G plates developed with benzene and exposed to iodine vapor ($R_{\rm F}$ 0.37 and 0.50); m.p. 134–145°, [α]_D +18.1° (c 1, chloroform).

The composition of this mixture was 56% of 6 and 44% of 7 as may be seen from the relation of the optical rotation of the products and the percentage of the intensity of the C-1 peaks in the ¹³C-n.m.r. spectrum of the mixture (see Table IV).

Compound 6 crystallized from 5:1 methanol-acetone as needles. Recrystallized several times, it had m.p. 168–169°, $[\alpha]_D$ +56° (*c* 1, chloroform); R_F 0.37. (These physical constants agree with those given⁴ for "penta-*O*-benzoyl- β -D-galactopyranose": m.p. 168–169°, $[\alpha]_D$ +54.3°; but this structure was not supported by other physical properties.) For ¹H-n.m.r.: see Tables I and II; for ¹³C-n.m.r., see Table IV; and for m.s., see Scheme 1.

Anal. Calc. for C₄₁H₃₂O₁₁: C, 70.28; H, 4.57. Found: C, 70.43; H, 4.74.

Compound 7 separated as insoluble material from 5:1 methanol-acetone, and was recrystallized from acetone; needles; m.p. 162–164°, $[\alpha]_D = -30^\circ$ (c 1, chloroform); $R_F 0.50$. The 100-MHz, ¹H-n.m.r. spectrum did not allow a complete

analysis, but gave: δ 6.81 (1 H, H-1), 6.16 (1 H, H-3), (J 9.5 and 5.0 Hz), 5.90–5.80 (2 H, H-2 + H-5), and 5.00–4.72 (3 H, H-4 + H-6a + H-6b). For the ¹³C-n.m.r. spectrum, see Table IV. For m.s., see Scheme 1.

Anal. Calc. for C₄₁H₃₂O₁₁: C, 70.28; H, 4.57. Found: C, 70.22; H, 4.80.

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