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CONFORMATIONAL ANALYSIS OF PERACETYLATED HEXONONITRILES

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ABSTRACT

The conformations of six peracetylated hexononitriles in solution have been investigated by Fourier-transform, proton n.m.r. spectroscopy at 90 MHz, with iterative analysis and simulation of many of the spectra. The conformation of tetra-*O*-acetyl-L-arabinononitrile has been re-examined by the same methods. A shift reagent [$Eu(fod)_3$-d_{30}] and spectra at 220 MHz were used to improve spectral dispersion, where necessary. For practically all of the derivatives studied, the vicinal, proton–proton coupling-constants are consistent with a zigzag conformation in which the cyano group lies in the plane of the other carbon atoms of the chain, unless this conformation contains a parallel 1,3-interaction of substituents. Other conformers that are also consistent with the coupling constants observed are discussed, including rotamers about chain-terminal, carbon–carbon bonds.

INTRODUCTION

An interest in the spectroscopic, conformational, and chromatographic properties of cyclic[1] and acyclic[2–4] carbohydrate nitrile derivatives prompted us to examine the conformations of a series of acyclic, acetylated hexononitriles by Fourier-transform, proton n.m.r. spectroscopy. These acyclic nitriles are useful derivatives for the analysis of sugars by gas-chromatographic methods[2–4] that avoid the complexities that are associated with the formation of different ring and anomeric forms in many other methods of derivatization. On the other hand, cyclic carbohydrate nitrile derivatives have proved to be useful intermediates in the synthesis of analogs of the *C*-nucleoside antibiotics[5].

The conformational results from previous n.m.r. studies[6,7] of acetylated pentononitriles, together with the results of many other n.m.r.-spectral[8–16] and X-ray[17–19] investigations of acylated and non-acylated, acyclic carbohydrate derivatives have contributed to development of the generalization that a zigzag

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arrangement of chain carbon atoms is favored unless this results in a 1,3-interaction of substituents. Determination of acyclic conformations by measurement of vicinal, proton–proton coupling-constants is subject to certain interpretative limitations that have been discussed[13]. Almost all previous studies of the conformations of acyclic sugars by proton n.m.r. spectroscopy have been based on spectral analysis by first-order methods[20]. For most of the compounds in this study, at least one set of chemical shifts and coupling constants has been obtained by computerized, iterative analysis of the spectra[21]. Such analysis was less necessary in those instances where the spectra were highly dispersed by the application of high fields or shift reagents.

SCOPE OF THE WORK

The following compounds were studied: tetra-*O*-acetyl-L-arabinononitrile (**1**), penta-*O*-acetyl-D-mannononitrile (**2**), penta-*O*-acetyl-D-gluconononitrile (**3**), penta-*O*-acetyl-D-galactononitrile (**4**), tetra-*O*-acetyl-6-deoxy-L-galactononitrile (**5**), tetra-*O*-acetyl-2-deoxy-D-*arabino*-hexononitrile (**6**), and tetra-*O*-acetyl-2-deoxy-D-*lyxo*-hexononitrile (**7**). Their method of preparation has been described previously[2–4].

RESULTS AND DISCUSSION

In the absence of shift reagents, the proton n.m.r. spectra of compounds **1–7** are comprised of acetyl methyl proton resonances in the range 2.0–2.4 p.p.m. and of methylene and methine proton resonances in the range 2.5–6.4 p.p.m.

Selected, proton chemical-shifts and coupling constants obtained by iterative and first-order spectral analyses are reported in Tables I and II, respectively. However, because of the quantity of data obtained from studies with shift reagents at different concentrations, only data for representative concentrations are reported. No attempt was made either to assign or report the proton resonances of individual, acetyl methyl groups.

For the purpose of interpretation of vicinal coupling-constants in terms of conformations, it was assumed that proton coupling-constants of <4 Hz represent protons having a *gauche* (synclinal) orientation, and that coupling constants of >7 Hz indicate principally a *trans* orientation of the vicinal protons[13]. These limits reflect the broad implications of the Karplus equation[22] and of previous experience in the measurement of proton coupling-constants of carbohydrates[23]. Values of ${}^3J_{gauche}$ as large as 5.8 Hz have been observed for some conformationally homogeneous molecules[23] in which there are few electronegative substituents in close proximity to the vicinal protons (for example, coupling of one of the protons of a ring methylene group with a vicinal proton). Where coupling constants of intermediate magnitude (4–7 Hz) were observed, these were generally assumed to indicate the presence of a conformational equilibrium that contained a significant proportion of the rotamer having the vicinal protons in *trans* orientation. For simplicity, only this rotamer is shown in the conformational diagrams (**1a–7b**), although, in several instances, the

TABLE I

PROTON CHEMICAL-SHIFTS[a] OF ACETYLATED ALDONONITRILES

Compound	*Configuration*	*Solvent*	*H-2*	*H-2'*[b]	*H-3*	*H-4*	*H-5*	*H-5'*	*H-6*	*H-6'*[b]	*R.m.s. error (Hz)*[c]
1	*arabino*	C_5D_5N	6.406	—	6.141	5.660	4.593	4.472	—	—	0.10
2	*manno*	C_5D_5N	6.221	—	6.123	5.962	5.537	—	4.546	4.420	0.15
3	*gluco*	C_5D_5N	6.364	—	6.107	6.122	5.590	—	4.623	4.446	0.24
		$CDCl_3$	5.52	—	5.38	5.59	5.15	—	4.30	4.09	—
		$CDCl_3$–0.09M Eu(fod)$_3$-d_{30}[d]	7.73	—	8.69	8.96	9.51	—	8.05	8.24	—
4	*galacto*	C_5D_5N	6.353	—	6.163	5.890	5.741	—	4.607	4.267	0.17
5	6-deoxy-*galacto*	C_5D_5N	6.337	—	6.120	5.588	5.359	—	1.232	1.232	0.11
6	2-deoxy-*arabino*-hexonic	C_5D_5N	3.14	3.17	5.82	5.74	5.53	—	4.50	4.42	—
		$CDCl_3$	2.55	2.80	5.36	5.36	5.19	—	4.23	4.18	—
		$CDCl_3$–0.04M Eu(fod)$_3$-d_{30}[d]	3.47	3.24	6.75	7.21	6.95	—	5.89	5.89	—
		$CDCl_3$–0.08M Eu(fod)$_3$-d_{30}[d]	5.09	5.09	10.46	12.14	11.72	—	9.86	10.34	—
7	2-deoxy-*lyxo*-hexonic	C_5D_5N	3.24	3.13	5.63	5.83	5.77	—	4.58	4.31	—

[a]P.p.m. from internal tetramethylsilane. The values tabulated to three decimal places were obtained by iterative analysis, whereas values given to two decimal places were determined by first-order analyses based on the shifts computed for individual peak-maxima. [b]Geminal protons are distinguished by means of a prime for the proton having the larger coupling-constant to the adjacent, vicinal proton. [c]Computed root-mean-square error of the frequencies of the theoretical lines assigned in the iterative analysis. [d]Europium(III) (6,6,7,7,8,8,8-heptafluoro-2,2-dimethyl-3,5-octanedionate)$_3$-d_{30}.

TABLE II

PROTON–PROTON COUPLING-CONSTANTS (Hz) OF ACETYLATED ALDONONITRILES

Compound	*Configuration*	*Solvent*	$J_{2,2'}$[a]	$J_{2,3}$	$J_{2',3}$	$J_{3,4}$	$J_{4,5}$	$J_{4,5'}$	$J_{5,5'}$	$J_{5,6}$	$J_{5,6'}$	$J_{6,6'}$[a]
1	*arabino*	C_5D_5N[b]	—	3.4	—	8.4	3.1	4.9	−12.5	—	—	—
2	*manno*	C_5D_5N[b]	—	5.8	—	1.9	9.2	—	—	2.6	4.8	−12.7
3	*gluco*	C_5D_5N[b]	—	6.0	—	2.5	8.2	—	—	3.0	5.2	−12.4
		$CDCl_3$[c]	—	6.5	—	2.1	8.4	—	—	3.2	4.9	−12.4
		$CDCl_3$–0.09M Eu(fod)$_3$-d_{30}[d]	—	6.5	—	2.3	8.4	—	—	3.2	4.9	−12.7
4	*galacto*	C_5D_5N[b]	—	2.6	—	9.5	2.0	—	—	4.9	7.1	−11.6
5	6-deoxy-*galacto*	C_5D_5N[b]	—	2.5	—	9.8	2.1	—	—	6.5	6.5	—
6	2-deoxy-*arabino*-hexonic	C_5D_5N[c]	−17.2	5.4	6.1	2.6	10.1	—	—	2.4	5.0	−12.6
		C_5D_5N[c,e]	−17.1	5.1	6.6	2.5	9.4	—	—	2.4	4.8	−12.3
		$CDCl_3$[c]	−17.1	5.5	5.8	—	—	—	—	—	—	—
		$CDCl_3$–0.04M Eu(fod)$_3$-d_{30}[c,d]	−17.4	5.3	5.8	2.0	9.9	—	—	—[f]	—[f]	—
		$CDCl_3$: 0.08M Eu(fod)$_3$-d_{30}[c,d]	—	—[g]	—[g]	1.5	8.3	—	—	2.1	3.4	−12.8
7	2-deoxy-*lyxo*-hexonic	C_5D_5N[c,e]	−17.3	4.9	6.1	7.9	3.1	—	—	5.0	6.7	−11.7

[a]Geminal protons are distinguished by the use of a prime for the proton having the larger coupling-constant with the adjacent, vicinal proton. [b]Coupling constants obtained by iterative analysis. [c]Coupling constants measured by first-order analysis. [d]Europium(III)(6,6,7,7,8,8,8-heptafluoro-2,2-dimethyl-3,5-octanedionate)$_3$-d_{30}. [e]At 220 MHz. [f]$J_{5,6} + J_{5,6'} = 7.2$ Hz. [g]$J_{2,3} + J_{2',3} = 11.7$ Hz.

coupling constants observed are obviously derived from averaging of the values of protons in *gauche* and *trans* orientations[24].

Tetra-O-acetyl-L-arabinononitrile (**1**). — This derivative has been investigated previously[6,7] by first-order analysis of its proton n.m.r. spectra at 60 MHz. We have re-examined the proton n.m.r. spectrum of **1** at 90 MHz by iterative analysis, in order to effect at least one comparison of the results of previous work[6,7] with those of the present study, which are based largely upon iterative analysis. The coupling constants of **1** obtained by iteration (see Table II) are consistent with the zigzag conformation **1a** and also with conformation **1b**, in which the cyano group has been rotated out of the plane of the other carbon atoms of the chain. Presumably, conformation **1a** is of lower energy than **1b**, because of the 1,3-interaction of acetoxyl groups and the higher dipole moment of **1b**. Comparison of the coupling constants (see Table II) of **1** in pyridine-d_5 solution with those measured previously[6,7] for other solvents indicates a solvent dependence of $J_{4,5}$, which suggests variation of the proportions of rotamers about the C-4–C-5 bond with solvent.

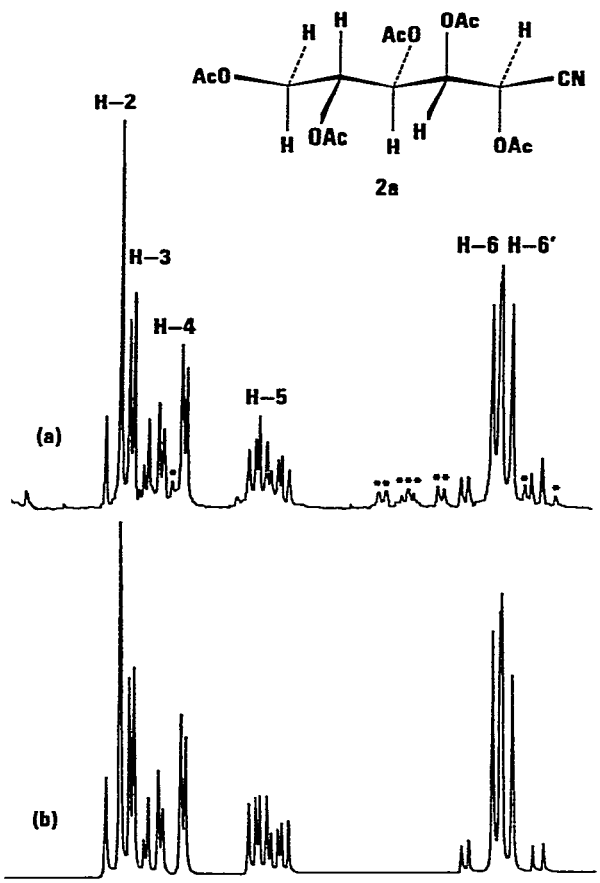


Fig. 1. Proton n.m.r. spectra of penta-*O*-acetyl-D-mannononitrile (**2**): (*a*) Fourier-transform spectrum of a solution in pyridine-d_5 at 90 MHz, (*b*) computed, theoretical spectrum from iterative analysis. (Resonances of impurities are indicated by asterisks.)

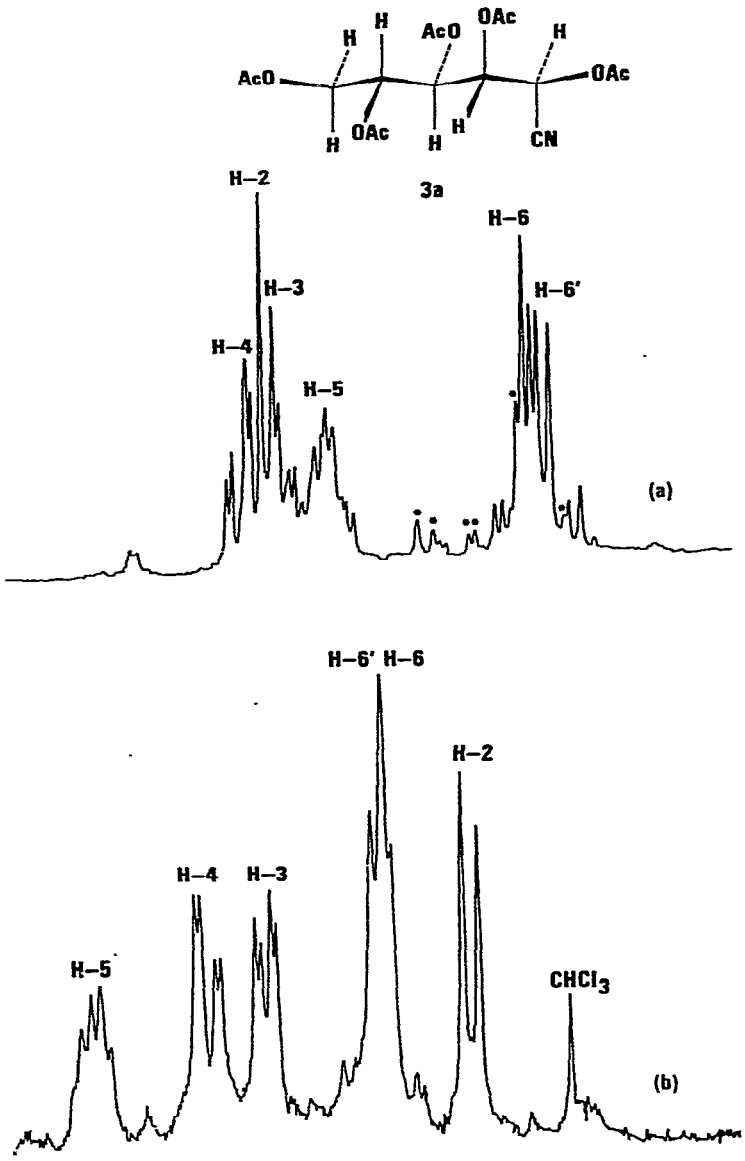


Fig. 2. Fourier-transform, proton n.m.r. spectra of penta-*O*-acetyl-D-glucononitrile (**3**) at 90 MHz: (*a*) in chloroform-*d* solution, (*b*) in chloroform-*d* containing 0.09M europium(III) (6,6,7,7,8,8,8-heptafluoro-2,2-dimethyl-3,5-octanedionate)$_3$-d_{30}. (Resonances of impurities are indicated by asterisks.)

Penta-O-*acetyl*-D-*mannononitrile* (**2**). — Iterative analysis of the proton spectrum (see Fig. 1) of **2** yielded coupling constants (see Table II) that are consistent with either the zigzag conformation (**2a**) or the bent form (**2b**). Conformation **2b** contains two 1,3-interactions of acetoxyl groups and is, presumably, of higher energy than **2a**. As $J_{2,3}$ and $J_{5,6'}$ are of intermediate magnitude (see Table II), other rotameric

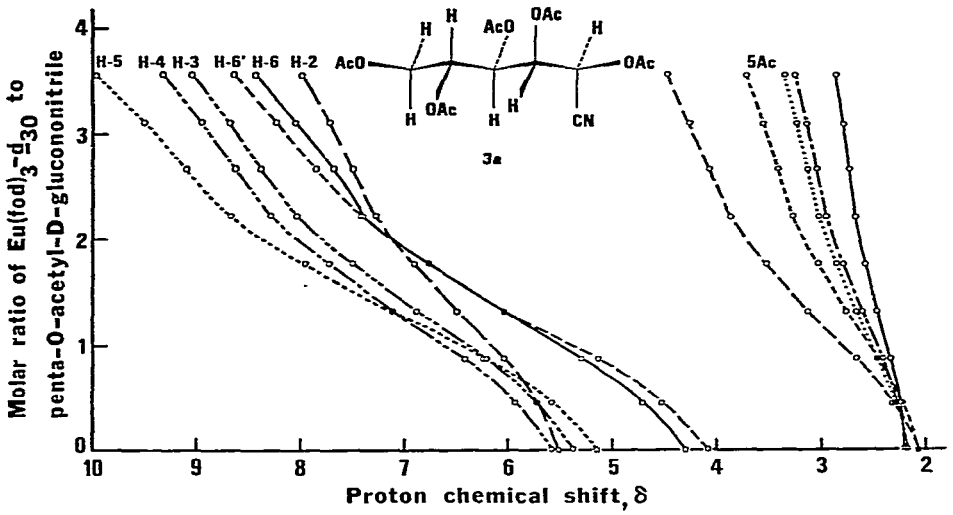


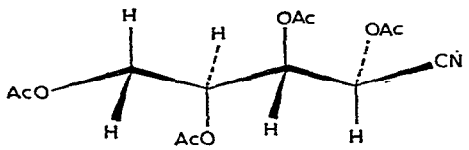
Fig. 3. The proton chemical-shifts of a solution of penta-*O*-acetyl-D-gluconononitrile (3) in chloroform-*d*, plotted *vs.* the molar ratio Eu(fod)$_3$-d_{30}:3.

states about the C-2–C-3 and C-5–C-6 bonds must also be significantly populated, in addition to **2a**.

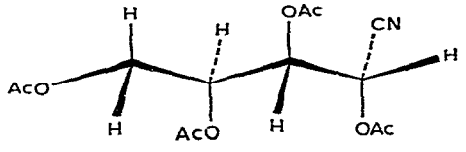
Penta-O-acetyl-D-gluconononitrile (**3**). — The proton spectra of solutions of **3** in pyridine-d_5 and chloroform-*d* (see Fig. 2a) were found to be complex at 90 MHz. However, addition of the shift reagent[25] europium(III) (6,6,7,7,8,8,8-heptafluoro-2,2-dimethyl-3,5-octanedionate)$_3$-d_{30} [Eu(fod)$_3$-d_{30}] to a solution of **3** in chloroform-*d* resulted in substantial dispersion of its spectrum (see Fig. 2b). Plotting of the chemical shifts of **3** that were measured for a range of concentrations of Eu(fod)$_3$-d_{30} revealed the presence of many crossovers of the signals of protons attached to the carbon chain, and also of acetyl methyl proton signals (see Fig. 3). The use of praseodymium chloride for dispersion of the proton signals of D-arabinose diethyl dithioacetal[15], and of Eu(fod)$_3$ for separation of the carbon-13 signals of tetra-*O*-acetyl-β-D-ribopyranose[1], may be compared with the results reported here.

The coupling constants of **3** in chloroform-*d* solution were found to be unaffected by the presence of the shift reagent (see Table II), and their first-order values and refined values for solutions of **3** in pyridine-d_5 (see Table II) are consistent with conformations **3a** and **3b**. The conformation **3a** (in which the cyano group is exoplanar to C-2–C-6) is expected to be favored, as the alternative (namely, **3b**) contains a 1,3-interaction. An extended zigzag arrangement of the carbon atoms of the chain is not favored in this case, as this would result in a 1,3-interaction of the acetoxyl groups at C-2 and C-4. Because of the small size of the cyano group[26], its exoplanar orientation is not expected to be energetically unfavorable. Again, the observation of less than maximal values for $J_{2,3}$ and $J_{5,6'}$ indicates contributions from other rotamers about C-2–C-3 and C-5–C-6.

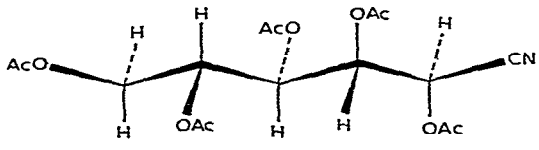
Penta-O-acetyl-D-galactononitrile (**4**). — Iterative analysis of the proton n.m.r.



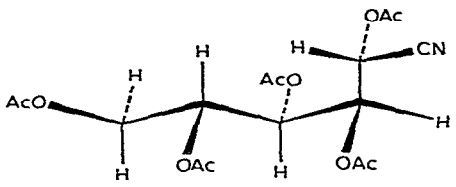
1a



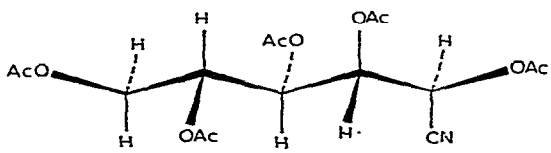
1b



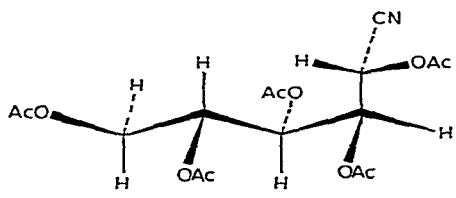
2a



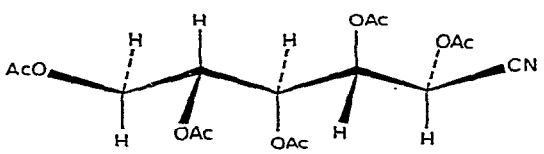
2b



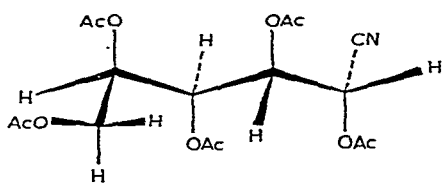
3a



3b



4a



4b

spectrum of **4** (see Fig. 4) gave coupling constants (see Table II) that are consistent with the zigzag form (**4a**), the sickle form (**4b**), and rotamers of these forms (about the C-2–C-3 bond) in which the cyano group is *trans*-coplanar to H-3 (that is, the cyano group is exoplanar to C-2–C-5). As before, conformation **4b** and its C-2–C-3 rotamer may be discounted on the basis of their 1,3-interactions of acetoxyl groups. The extreme values of the coupling constants of **4** imply conformational homogeneity.

Tetra-O-*acetyl-6-deoxy*-L-*galactononitrile* (**5**). — The refined coupling-constants for **5** (see Table II) were found to be similar to those for compound **4** and indicated conformations **5a** and **5b** as possibilities. Because of its 1,3-interactions of acetoxyl groups, conformation **5b** may be discounted in favor of the zigzag form **5a**.

Tetra-O-*acetyl-2-deoxy*-D-arabino-*hexononitrile* (**6**). — The proton spectra of

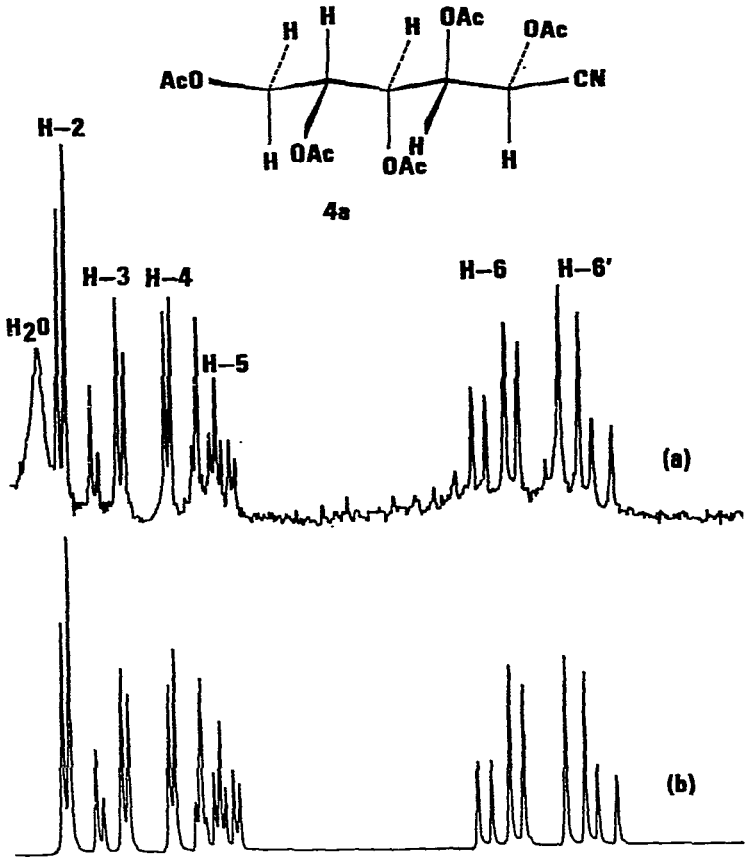
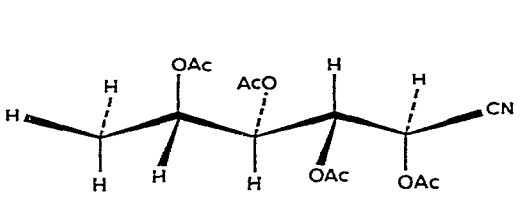
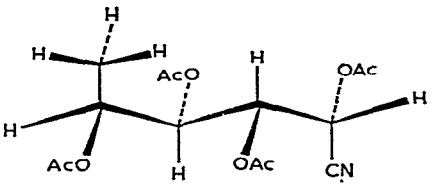


Fig. 4. Proton n.m.r. spectra of penta-*O*-acetyl-D-galactononitrile (**4**): (*a*) Fourier-transform spectrum of a solution in pyridine-d_5 at 90 MHz, (*b*) computed, theoretical spectrum from iterative analysis.

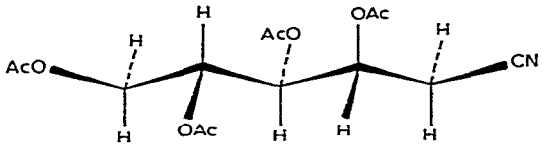
solutions of **6** in pyridine-d_5 and chloroform-*d* showed extensive overlapping of the H-3 and H-4 signals at 90 MHz, and were analyzed after shift-reagent studies [$Eu(fod)_3$-d_{30} in chloroform-*d*] had indicated the assignments. At higher concentrations (0.05–0.08M) of the shift reagent, H-2 and H-2′ were chemically equivalent (see Table I), and only the sum of their couplings with H-3 could be extracted from the H-3 multiplet. A slight decrease in the magnitudes of those coupling constants that could be measured (see Table II) was observed as the concentration of shift reagent was increased to 0.08M, but this decrease was attributed to greater overlapping of lines caused by the slight, line-broadening effects of the reagent, rather than to a change in conformational populations. The coupling constants (see Table II) of the 2-deoxy-*arabino*-hexonic derivative **6** are consistent with both the zigzag form (**6a**) and the sickle form (**6b**), which is similar to **3a**. Although the zigzag conformation is not favored for the *gluco* analog (**3**), because this conformation contains a 1,3-interaction of acetoxyl groups, the replacement of one of these acetoxyl groups (at C-2 of **3**) by a hydrogen atom (to give compound **6**) removes this interaction,



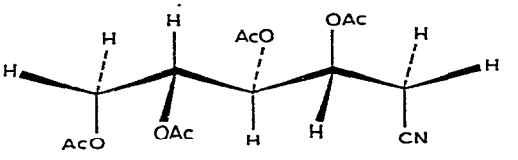
5a



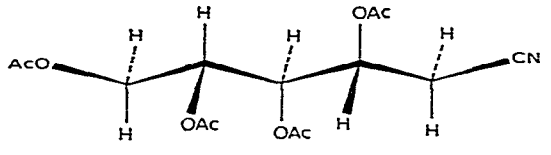
5b



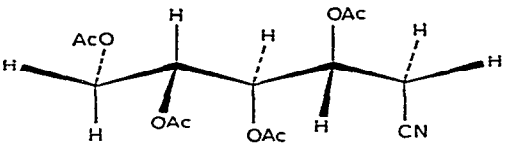
6a



6b



7a



7b

and evidently allows **6** to adopt the zigzag form (**6a**) to a larger extent than does **3**. The less than maximal values of $J_{2',3}$ and $J_{5,6'}$ and the more extreme values of $J_{3,4}$ and $J_{4,5}$ (see Table II) indicate the existence of greater conformational freedom at the ends of the carbon chain of **6** than at its center. Two of the possible rotamers derived by rotations about the C-2–C-3 and C-5–C-6 bonds are depicted in **6a** and **6b**.

Tetra-O-*acetyl*-2-*deoxy*-D-lyxo-*hexononitrile* (**7**). — The coupling constants of **7** were measured at 220 MHz (see Table II) and are consistent with both the zigzag (**7a**) and sickle (**7b**) forms. Presumably, form **7b** is not favored, because of the 1,3-interaction between cyano and acetoxyl substituents. The C-5–C-6 rotamers depicted in **7a** and **7b** are not distinguished by the measured values of $J_{5,6}$ and $J_{5,6'}$, although the rotamer (**7b**) in which the acetoxyl group at C-6 is exoplanar to the carbon chain is probably disfavored.

CONCLUSIONS

The vicinal, proton–proton coupling-constants of peracetylated aldononitriles of the *arabino*, *manno*, *galacto*, 6-deoxy-*galacto*, 2-deoxy-*arabino*-hexonic, and 2-deoxy-*lyxo*-hexonic configurations are consistent with zigzag conformations (**1a**, **2a**, **4a**,

5a, **6a**, and **7a**, respectively), in which there are no parallel, 1,3-interactions of acetoxyl groups. A sickle conformation (**3a**) is adopted by the D-gluconononitrile derivative **3**, for which the zigzag conformation would involve a 1,3-interaction. The conformations (**3a** and **6a**, respectively) of the *gluco* and 2-deoxy-*arabino*-hexonic derivatives are not modified by interaction with the Eu(fod)$_3$-d_{30} shift-reagent.

EXPERIMENTAL

General. — Proton n.m.r. spectra of derivatives **1–6** were acquired at 90 MHz and 38° by pulse-Fourier-transform techniques, using a Bruker Scientific* n.m.r. spectrometer, model HFX-11, that was equipped with a pulse amplifier, model B-SV-2P, a Nicolet Instrument Corporation data system, model BNC-12, and internal, time-shared, heteronuclear, field–frequency stabilization on a deuterium signal at 13.8 MHz. The nitrile derivatives (3–5 mg) were examined as their solutions in 0.4 mL of either chloroform-*d* or pyridine-d_5. For shift-reagent studies, one to eight aliquots (0.05 mL) of a solution of europium(III) (6,6,7,7,8,8,8-heptafluoro-2,2-dimethyl-3,5-octanedionate)$_3$-d_{30} (100 mg) in chloroform-*d* (0.5 mL) were added to solutions of the nitriles in chloroform-*d*. For solutions in pyridine-d_5, field-frequency stabilization was established on the deuterium signal at highest field. The free induction decay (f.i.d.) signals were acquired in the single-coil mode by excitation of the samples with an ~70° pulse (90° pulse width, 13 μsec), followed by a delay of 800 μsec prior to data acquisition (1.64 sec) at a rate of 2.5 kHz. The average of at least 100 f.i.d. signals was acquired in 4096 data points, to which were appended a further 4096 zero data-points (zero-filling[13,21]) before Fourier transformation. The real part of the transform then consisted of 4096 points that defined a spectral width of 1.250 kHz and, therefore, a computer-limited resolution of 0.3 Hz. The peak maxima in the spectra were located by software-directed, cursor scanning of the computer memory. The frequency separations of these maxima from tetramethylsilane that were computed and printed by Nicolet software were used for calculation of chemical shifts and coupling constants.

Proton n.m.r. spectra at 220 MHz were recorded at 17°, either in the continuous-wave mode (for **3** and **6**) or pulse-Fourier-transform mode (for **6** and **7**) by using a Varian Associates, model HR-220, superconducting spectrometer. In the latter mode, a 90° pulse (55 μsec, crossed coils) was used with a 5-sec delay between pulses, and 50 f.i.d. signals were averaged within 8192 data points.

Spectral analysis. — The spectra of solutions of compounds **1**, **2**, **4**, and **5** in pyridine-d_5 were analyzed initially by first-order methods, improved values of the chemical shifts being obtained from weighted averages of the peak positions. Coupling constants were determined as the mean spacings of all pairs of lines that were expected

*Mention of commercial equipment in this article does not imply recommendation or endorsement by the National Bureau of Standards.

to exhibit the coupling. The coupling constants and chemical shifts from first-order analysis were refined by iterative adjustment, using the ITRCAL program (a version of LAOCN3, for Nicolet Instrument Corporation 1080 series minicomputers). As, in the ITRCAL program, iteration is restricted to a maximum of six spins, this program could not be used directly for iterative analysis of the spectra of compounds **5–7**. However, iteration for compound **5** was approximated by treatment of the protons on its carbon chain as a five-spin system derived by replacement of the terminal, methyl protons by a single proton. For this five-spin system, it was assumed that the H-5 signal would appear as a quartet with the same line-positions as the four central-lines of the H-5 octet actually observed for compound **5**.

Iterative computations were continued until attempts to reassign transitions led to no further convergence of the program. In all instances, the r.m.s. error of the computed line-frequencies was less than the frequency resolution (303 mHz) defined by the size of the data set.

The first-order assignments of the spectra of solutions of **3** and **6** in pyridine-d_5 or chloroform-*d* were not obvious until a shift reagent had been used to disperse the spectra of the solutions in chloroform-*d*. At the higher concentrations (0.05–0.1M) of Eu(fod)$_3$-d_{30} in this solvent, recognition of the pattern of the spectral multiplets then allowed interpretation of the unshifted, complex spectra of **3** and **6**, and subsequent, iterative analysis of a spectrum of **3**. The spectral assignments of **3** and **6** at 90 MHz were supported by their spectra at 220 MHz.

The spectra of compounds **1–7** were simulated by means of either the NMRCAL or ITRCAL programs (Nicolet Instrument Corporation) which allow computation of theoretical spectra for up to six and seven spins, respectively. Good agreement between theoretical and experimental spectra was obtained in all cases. As the ITRCAL program did not permit iterative analyses of the seven-spin systems of compounds **6** and **7**, their chemical shifts were adjusted manually until satisfactory simulation by the ITRCAL program was achieved.

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REFERENCES

1 For a bibliography of the early work on these derivatives, see B. COXON, *Ann. N.Y. Acad. Sci.*, 222 (1973) 952–970.
2 R. VARMA, R. S. VARMA, AND A. H. WARDI, *J. Chromatogr.*, 77 (1973) 222–227.
3 R. VARMA, R. S. VARMA, W. S. ALLEN, AND A. H. WARDI, *J. Chromatogr.*, 86 (1973) 205–210.
4 R. S. VARMA, R. VARMA, W. S. ALLEN, AND A. H. WARDI, *J. Chromatogr.*, 93 (1974) 221–228.
5 For a recent review of these applications, see S. HANESSIAN AND A. G. PERNET, *Adv. Carbohydr. Chem. Biochem.*, 33 (1976) 111–188.
6 J. B. LEE AND B. F. SCANLON, *Tetrahedron*, 25 (1969) 3413–3428.

7 W. W. BINKLEY, D. R. DIEHL, AND R. W. BINKLEY, *Carbohydr. Res.*, 18 (1971) 459–465.
8 P. L. DURETTE AND D. HORTON, *Adv. Carbohydr. Chem. Biochem.*, 26 (1971) 49–125.
9 S. J. ANGYAL, R. LEFUR, AND D. GAGNAIRE, *Carbohydr. Res.*, 23 (1972) 121–134.
10 S. J. ANGYAL, R. LEFUR, AND D. GAGNAIRE, *Carbohydr. Res.*, 23 (1972) 135–138.
11 P. L. DURETTE, D. HORTON, AND J. D. WANDER, *Adv. Chem. Ser.*, 117 (1973) 147–176.
12 D. HORTON, P. L. DURETTE, AND J. D. WANDER, *Ann. N.Y. Acad. Sci.*, 222 (1973) 884–914.
13 B. COXON, R. S. TIPSON, M. ALEXANDER, AND J. O. DEFERRARI, *Carbohydr. Res.*, 35 (1974) 15–31.
14 D. HORTON, D. C. BAKER, AND S. S. KOKRADY, *Ann. N.Y. Acad. Sci.*, 255 (1975) 131–150.
15 D. HORTON, *Pure Appl. Chem.*, 42 (1975) 301–325.
16 J. D. WANDER AND D. HORTON, *Adv. Carbohydr. Chem. Biochem.*, 32 (1976) 15–123.
17 G. A. JEFFREY AND H. S. KIM, *Carbohydr. Res.*, 14 (1970) 207–216.
18 G. A. JEFFREY, *Adv. Chem. Ser.*, 117 (1973) 177–196.
19 G. A. JEFFREY AND M. SUNDARALINGAM, *Adv. Carbohydr. Chem. Biochem.*, 30 (1974) 445–466; 31 (1975) 347–371; 32 (1976) 353–384; 34 (1977) 345–378.
20 For exceptions to this generalization, see refs. 9 and 10.
21 For a discussion of this method as applied to carbohydrates, see B. COXON, *Adv. Carbohydr. Chem. Biochem.*, 27 (1972) 7–83.
22 M. KARPLUS, *J. Chem. Phys.*, 30 (1959) 11–15; *J. Am. Chem. Soc.*, 85 (1963) 2870–2871.
23 B. COXON, *Methods Carbohydr. Chem.*, 6 (1972) 513–539.
24 Compare A. DE BRUYN AND M. ANTEUNIS, *Carbohydr. Res.*, 47 (1976) 311–314.
25 R. E. RONDEAU AND R. E. SIEVERS, *J. Am. Chem. Soc.*, 93 (1971) 1522–1524.
26 E. L. ELIEL, N. L. ALLINGER, S. J. ANGYAL, AND G. A. MORRISON, *Conformational Analysis*, Interscience, New York, 1965, p. 442.