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CONFORMATIONS OF SOME PER-*O*-ACETYLALDONONITRILES AND 5-(POLYACETOXYALKYL)TETRAZOLES

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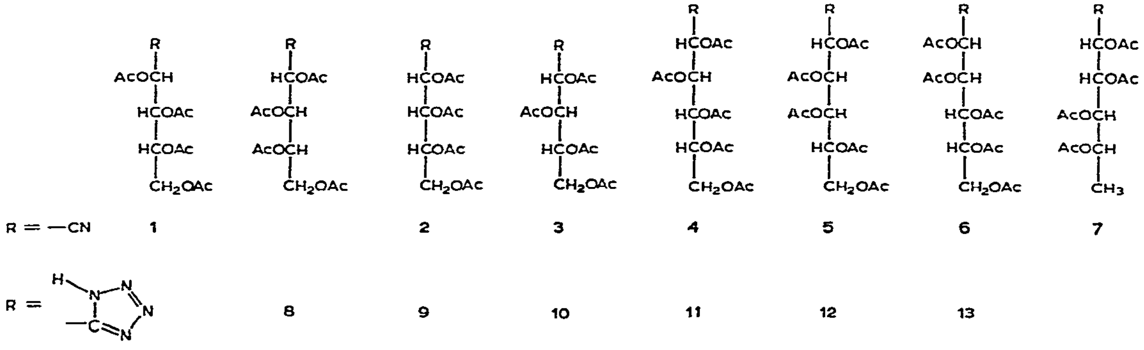
ABSTRACT

The conformations of several per-*O*-acetylaldononitriles and 5-(polyacetoxyalkyl)tetrazoles in pyridine-d_5 solution have been studied by p.m.r. spectroscopy. For compounds of both types, those having the *arabino*, *galacto*, and *manno* configurations take an extended, planar, zigzag arrangement for the carbon chain, whereas, for those having the *xylo*, *ribo*, and *gluco* configurations, the values of the coupling constants indicate that a bent conformation is favored.

INTRODUCTION

Proton magnetic resonance (p.m.r.) spectroscopy has been extensively used for the investigation of the conformation of acyclic sugar derivatives. The procedure has been applied to a great number of derivatives of most of the acyclic monosaccharides[1–17] and, in almost all instances, it has been found that they exist in solution in their extended, planar, zigzag conformation, unless in such a conformation a parallel, 1,3-dipolar interaction would appear; in this case, the carbon chain adopts a bent conformation by rotation about one or more C–C bonds.

In connection with our work on the synthesis of heterocyclic derivatives of monosaccharides[18,19], we now report the results of p.m.r. spectroscopic studies on several per-*O*-acetylaldononitriles and 5-(polyacetoxyalkyl)tetrazoles. From the



R = —CN: 1, 2, 3, 4, 5, 6, 7

R = tetrazolyl: 8, 9, 10, 11, 12, 13

TABLE I

VALUES OF CHEMICAL SHIFTS (δ) AND COUPLING CONSTANTS (J) OF ACETYLATED ALDONONITRILES

Configuration	*Number*	*Chemical shift (p.p.m.)*							*Coupling constant (Hz)*							
		H-2	*H-3*	*H-4*	*H-5*	*H-5'*	*H-6*	*H-6'*	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{4,5'}$	$J_{5,5'}$	$J_{5,6}$	$J_{5,6'}$	$J_{6,6'}$
D-*arabino*	**1**	6.36	6.13	5.66	4.56	4.53	—	—	3.0	8.0	3.0	4.0	12.0	—	—	—
D-*ribo*	**2**	6.36	5.93	5.81	4.61	4.56	—	—	3.0	6.0	3.0	4.5	12.5	—	—	—
D-*xylo*	**3**	6.28	6.03	6.08	4.53	4.43	—	—	5.0	2.5	5.0	6.0	12.0	—	—	—
D-*gluco*	**4**	6.25	5.98	6.06	5.53	—	4.48	4.43	5.5	2.5	8.0	—	—	3.5	5.0	12.0
D-*galacto*	**5**	6.28	6.16	5.96	5.73	—	4.43	4.33	2.5	9.0	2.0	—	—	5.0	7.0	12.0
D-*manno*	**6**	6.13	6.11	5.95	5.51	—	4.41	4.38	10.0	2.0	9.0	—	—	3.5	4.5	12.0
L-*rhamno*	**7**	6.10	6.06	5.61	5.21	—		1.21	10.0	2.0	9.0	—	—		6.0	—

TABLE II

VALUES OF CHEMICAL SHIFTS (δ) AND COUPLING CONSTANTS (J) OF 5-(POLYACETOXYALKYL)TETRAZOLES

Configuration	*Number*	*Chemical shift (p.p.m.)*							*Coupling constant (Hz)*							
		H-2	*H-3*	*H-4*	*H-5*	*H-5'*	*H-6*	*H-6'*	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{4,5'}$	$J_{5,5'}$	$J_{5,6}$	$J_{5,6'}$	$J_{6,6'}$
L-*arabino*	**8**	7.05	6.23	5.73	4.55	4.50	—	—	3.0	8.0	3.0	5.0	12.0	—	—	—
D-*ribo*	**9**	7.06	6.33	5.88	4.65	4.58	—	—	5.0	7.0	3.0	5.0	12.0	—	—	—
D-*xylo*	**10**	7.10	6.44	5.75	4.58	4.48	—	—	7.0	4.0	4.5	6.5	12.0	—	—	—
D-*gluco*	**11**	6.91	6.46	5.78	5.53	—	4.41	4.35	7.5	3.0	8.0	—	—	3.0	5.0	12.0
D-*galacto*	**12**	6.91	6.10	5.91	5.71	—	4.41	4.28	2.0	10.0	1.5	—	—	5.0	7.0	12.0
D-*manno*	**13**	6.81	6.26	6.10	5.53	—	4.48	4.37	9.0	2.0	9.0	—	—	3.5	5.0	12.0

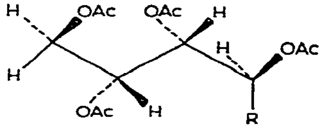
values of the coupling constants measured for the different compounds, it was possible to infer the most probable conformation of each of these compounds in solution.

The data on chemical shifts and coupling constants for per-*O*-acetylaldononitriles are recorded in Table I; those for the 5-(polyacetoxyalkyl)tetrazoles are given in Table II.

DISCUSSION

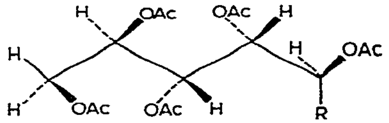
1. *Nitriles*

Binkley *et al.*[11] reported spectral data and conformational assignments for the complete set of acetylated D-pentononitriles. Apart from chemical-shift differences that are accounted for by the change of solvent (dimethyl sulfoxide-d_6 in the work of Binkley *et al.*, and pyridine-d_5 in ours), their results and those presented in Table I (compounds **1**, **2**, and **3**) are in fair agreement, except for those for tetra-*O*-acetyl-D-xylononitrile (**3**). They indicated[11] that compound **3** seems to adopt a sickle arrangement of the carbon skeleton by rotation of the C-3–C-4 bond of the planar, zigzag conformation. We find that, in pyridine, compound **3** is also not in the planar, zigzag form (which presents a 1,3-parallel interaction of *O*-acetyl groups), but that the favored conformer appears to be **3a**, formed by rotation of the C-2–C-3 bond. Such an arrangement does not present a 1,3-interaction and agrees with the coupling-constant values of the spectrum.



3a
10a

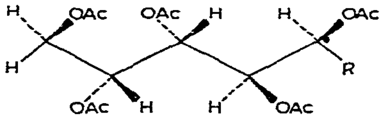
Penta-O-*acetyl*-D-*gluconorritrile* (**4**). — The values of the coupling constants determined for this compound indicate that, in solution in pyridine, the favored conformer is that obtained by rotation of the C-2–C-3 bond from the planar, zigzag arrangement. In this conformation, the 1,3-interaction disappears, and the value of $J_{2,3}$ (5.5 Hz) could be explained by a disposition between H-2 and H-3 not quite, but almost, antiparallel. As $J_{3,4}$ (2.5 Hz) indicates a *gauche* relationship between H-3 and



4a
11a

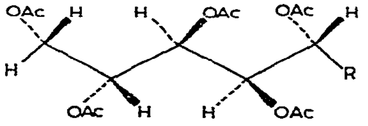
H-4, the latter proton becomes situated inside the deshielding zone of the carbon–nitrogen triple bond, and hence it resonates at a lower field than H-3. The value of 8.0 Hz for $J_{4,5}$ is that expected for an antiparallel disposition of the protons mentioned.

Penta-O-*acetyl*-D-*galactononitrile* (5). — The values of the coupling constants for this compound very clearly indicate a planar, zigzag arrangement of the carbon skeleton. The coupling for antiparallel protons ($J_{3,4}$ 9.0 Hz) and *gauche* protons ($J_{2,3}$ 2.5 Hz, and $J_{4,5}$ 2.0 Hz) are in perfect agreement with the conformer depicted in formula 5a.



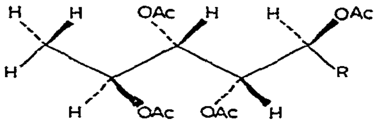
5a
12a

Penta-O-*acetyl*-D-*mannononitrile* (6). — The coupling data for this compound show that the favored conformer must be that having the planar, zigzag disposition of the carbon chain. The coupling for antiparallel protons ($J_{2,3}$ 10.0 Hz, and $J_{4,5}$ 9.0 Hz) are probably extreme values, and the same is true for the *gauche* protons ($J_{3,4}$ 2.0 Hz). All values accord with those expected for the conformer depicted in formula 6a.



6a
13a

Tetra-O-*acetyl*-L-*rhamnononitrile* (7). — This compound gave values similar to those for compound 6, and the favored conformer in solution is that indicated in formula 7a.

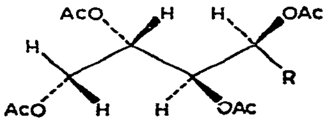


7a

2. *5-(Polyacetoxyalkyl)tetrazoles*

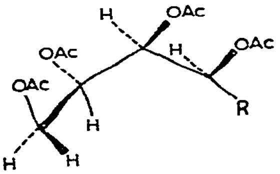
The p.m.r. spectra of all of the 5-(polyacetoxyalkyl)tetrazoles described here show essentially the same pattern of chemical shifts. For the hexose derivatives, there are five signals outside the acetyl zone; for the pentose derivatives, there are four groups of signals outside the acetyl zone. For instance, for the 5-(pentaacetoxypentyl)tetrazoles, the spectra normally display a doublet signal at lowest field, and this is assigned to H-2; then follow two double-doublets, sometimes amenable to first-order analysis, that can be assigned to H-3 and H-4, respectively; farther upfield appears a complex signal (commonly, 7 to 8 lines) assigned to H-5; the methylene group (H-6 and H-6′) resonates farther upfield, as the AB part of an ABX system; then follow the acetyl resonances, which are of no diagnostic value.

*5-(Tetra-O-acetyl-*L-arabino-*tetritol-1-yl)tetrazole* (**8**). — The value of 3.0 Hz for $J_{2,3}$ indicates that those two protons are in a *gauche* arrangement, whereas $J_{3,4}$ (8.0 Hz) shows an antiparallel disposition for H-3 and H-4. These values are in good agreement with those for a planar, zigzag conformation of the carbon skeleton. Therefore, the favored conformer for this compound in solution is as represented in formula **8a**. The values of $J_{4,5}$ (3.0 Hz) and $J_{4,5'}$ (5.0 Hz) indicate a preponderance of that rotamer in which both H-5 and H-5′ are almost *gauche* to H-4, as other arrangements would introduce destabilization by 1,3-interaction of polar groups.



8a

*5-(Tetra-O-acetyl-*D-ribo-*tetritol-1-yl)tetrazole* (**9**). — The coupling-constant values for this compound are inconsistent with the planar, zigzag conformation. The value of $J_{2,3}$ (5.0 Hz) indicates that the C-2–C-3 bond is rotated to avoid the 1,3-interaction of polar groups. Therefore, H-2 and H-3 presumably adopt the spatial disposition shown in conformer **9a**. The value for $J_{3,4}$ (7.0 Hz) is smaller than that expected for a fully antiparallel disposition; so, the C-3–C-4 bond must undergo slight rotation (to alleviate spatial strain). As discussed for compound **8**, the values of $J_{4,5}$ and $J_{4,5'}$ indicate assumption of a rotamer wherein both H-5 and H-5′ are *gauche* to H-4, as other dispositions would introduce destabilization factors. The conformer **9a** would be favored; it is a distorted, sickle arrangement.



9a

*5-(Tetra-O-acetyl-*D-xylo-*tetritol-1-yl)tetrazole* (**10**). — Although the value of 7.0 Hz for $J_{2,3}$ is somewhat smaller than that expected for a truly antiparallel arrangement, the favored conformer of this compound should have an almost antiparallel disposition of H-2 and H-3, due to rotation of the C-2–C-3 bond of the planar, zigzag conformation. Moreover, the value of 4.0 Hz for $J_{3,4}$ shows an essentially *gauche* relationship between those protons. From the various, possible rotamers that might have values of $J_{4,5}$ and $J_{4,5'}$ of 4.5 and 6.5 Hz, respectively, only the one represented as **10a** would present no destabilization factors. Hence, conformer **10a** is proposed for this compound.

*5-(Penta-O-acetyl-*D-gluco*-pentitol-1-yl)tetrazole* (**11**). — In the favored rotamer of this compound in solution, the C-2–C-3 bond of the planar, zigzag conformation is rotated, thus explaining the value of $J_{2,3}$ (7.5 Hz), which indicates an essentially antiparallel disposition. The value of $J_{3,4}$ (3.0 Hz) shows a *gauche* arrangement between these protons, and $J_{4,5}$ (8.0 Hz) indicates an antiparallel disposition between H-4 and H-5. Hence, the most probable rotamer for this compound is **11a**, in which the relationship represented among H-5, H-6, and H-6′ is the one devoid of any destabilization factors.

*5-(Penta-O-acetyl-*D-galacto*-pentitol-1-yl)tetrazole* (**12**). — The coupling-constant values for this compound indicate a planar, zigzag arrangement for the favored conformer in solution. The values for antiparallel protons ($J_{3,4}$ 10.0 Hz) and for *gauche* protons ($J_{2,3}$ 2.0 Hz, and $J_{4,5}$ 1.5 Hz) are in good agreement with those expected for conformer **12a**.

*5-(Penta-O-acetyl-*D-manno*-pentitol-1-yl)tetrazole* (**13**). — The coupling values indicate that an extended, planar, zigzag conformation does not present any unfavorable nonbonded interactions. The coupling-constant data are almost identical to the values expected for antiparallel ($J_{2,3}$ 9.0 Hz, and $J_{4,5}$ 9.0 Hz) and for *gauche* protons ($J_{3,4}$ 2.0 Hz). All values accord with those expected for conformer **13a**.

EXPERIMENTAL

The peracetylated pentono- and hexono-nitriles used in this work were prepared according to literature data, as follows: D-*ribo*[19], D-*arabino*[20], D-*xylo*[21], D-*gluco*[22], D-*galacto*[23], D-*manno*[24], and L-*rhamno*[25]. The corresponding tetrazole derivatives were prepared as described elsewhere[18,19]. The p.m.r. spectra were recorded with a Varian A-60 spectrometer at ~38°. The concentration of each sample was ~10%, in pyridine-d_5 containing ~1% of tetramethylsilane, used as the internal standard. Chemical shifts are given on the δ scale, and were measured from the chart recording. Coupling constants are reported in Hz, and are apparent coupling-values determined from the chart. These measured spacings do not give the true value of J, although they serve to differentiate between antiparallel and *gauche* orientations.

ACKNOWLEDGMENTS

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