Carbohydrate Research, 95 (1981) 304–307
Elsevier Scientific Publishing Company, Amsterdam – Printed in The Netherlands

Note

The identification of the two crystalline *N*-phenyl-D-ribosylamines ("ribose anilides") by n.m.r. spectroscopy

GWYNN P. ELLIS
Chemistry Department, University of Wales Institute of Science and Technology, Cardiff CF1 3NU (Great Britain)

AND J. MICHAEL WILLIAMS
Chemistry Department, University College of Swansea, Swansea SA2 8PP (Great Britain)

(Received March 10th, 1981; accepted for publication, March 27th, 1981)

Two crystalline *N*-phenyl-D-ribosylamines ("ribose anilides") have been known for many years. Several attempts have been made to ascertain their structure by chemical[1–5] and spectroscopic[6] methods, but these have met with little success, except to exclude the possibility that either isomer contains an acyclic sugar residue. A solution of the related *N*-(4-chlorophenyl)-D-ribosylamine in pyridine was reported[7] to contain a mixture of two isomers, which were identified as the α- and β-pyranosylamines from p.m.r. measurements at 300 MHz.

The ribosylamine having the higher optical rotation ($[\alpha]_D$ +178°, in pyridine) and higher melting point* (~135°), referred to as isomer A by Ellis and Honeyman[3], has been assigned α-furanosylamine[2] and α-pyranosylamine[8] (**1**) structures. The ribosylamine having the lower optical rotation {$[\alpha]_D$ +60°, in pyridine} and lower melting point* (~115°) is a hemihydrate, and has been recommended for the purification of D-ribose[10]. This ribosylamine, referred to as isomer B[5], has been assigned β-pyranosylamine[9], α-pyranosylamine[2], and furanosylamine[11]** structures. A non-crystalline derivative, prepared under conditions which would be expected to give the lower melting form, was assigned the imine structure without any evidence[12]. However, imine structures were excluded for both forms by infrared spectroscopy, which also suggested pyranosylamine structures, although furanosylamine structures could not be excluded[6].

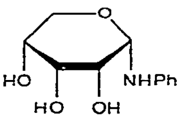
N.m.r. measurements (^{1}H and ^{13}C) on freshly prepared solutions of the higher melting isomer A in such solvents as pyridine and dimethyl sulphoxide, in which

---

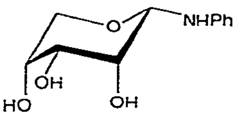
*Many glycosylamines melt with decomposition[8]; the specific rotations are more characteristic and reproducible.

**This isomer B is listed in the Chemical Compounds Index of *Chem. Abstr.* as a ribofuranosylamine.

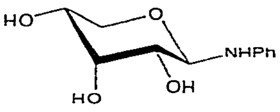
isomerisation is slow, have shown that this solid is the α-pyranosylamine **1**, which exists mainly in the $^1C_4$ conformation (**2**). The pyranoid structure was established by the ^{13}C-n.m.r. spectrum, in which the anomeric carbon resonated at 82.7 p.p.m. and C-5 at 64.2 p.p.m. The latter signal could not be used to determine the ring size, because the chemical shifts of C-5 in the pyranose and furanose tautomers of pentoses are similar[13]. However, the furanose structures are characterised by the chemical shift of C-4, which is more deshielded (by ~10 p.p.m.) than C-4 in the pyranose tautomer[14]. Thus, C-1 and C-4 of the *N*-phenyl-D-ribofuranosylamines would be expected to be the most deshielded of the D-ribose carbons, with chemical shifts greater than 80 p.p.m., and the absence of two such signals established the pyranosylamine structure. A furanoid structure could also be excluded for isomer A by analysis of the hydroxyl-proton region of the p.m.r. spectrum of a solution in CD_3SOCD_3. Three doublets were present, corresponding to three secondary alcohol groups.



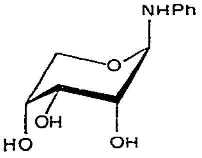
1



2



3



4

The p.m.r. spectrum established the α configuration for isomer A. The small value (<3 Hz) of $J_{1,2}$ excluded the β-pyranosylamine in the $^4C_1$ conformation (**3**). The most-shielded proton (axial H-5, τ 6.31) is consistent with conformation **2**, as are the coupling constants: $J_{4,5a}$ 2 Hz and $J_{4,5e}$ <1 Hz.* Such small coupling constants are characteristic of equatorial protons at C-4 of pyranoid derivatives[15]. The axial H-5 in conformation **4** of the β anomer would be expected to be less shielded, due to the syn-axial phenylamino group. A freshly prepared solution of isomer A in C_5D_5N gave a ^{13}C-n.m.r. spectrum containing five signals for pyranoid carbon atoms; on storage, a slow isomerisation occurred to give a second pyranoid form, with the anomeric carbon signal at 83.3 p.p.m.

The n.m.r. spectra of freshly prepared solutions of the lower melting isomer B showed that two isomers were present in approximately equal amounts; these were the α-pyranosylamine **2** and a second isomer characterised by an anomeric carbon signal at 83.2 p.p.m. and an anomeric proton signal at τ 4.58. That this second isomer was also a pyranosylamine was shown by the presence of only one carbon signal at a chemical shift greater than 80 p.p.m. The value (8 Hz) for $J_{1,2}$ established the β-pyranosylamine structure and the $^4C_1$ conformation (**3**). The second most-deshielded signal (at τ 5.37) was assigned to H-3 of the β anomer by empirical calculation[16], and specific decoupling then enabled C-3 to be assigned in the carbon spectrum.

---

*We believe that the corresponding coupling constant (6.2 Hz) cited[7] for the 4-chlorophenyl analogue is in error.

From a consideration of substituent effects[17], it can be predicted that replacing OH by NHPh at C-1 of D-ribopyranose would cause shielding of C-2. Thus, the most shielded of the methine carbon signals is provisionally assigned to C-2 in both anomers. The ^{13}C-n.m.r. spectrum, after an overnight measurement, revealed the presence of ten weaker signals in the 60–90 p.p.m. region corresponding to the two furanosylamine anomers. The four peaks at 89.8, 85.3, 84.8, and 83.0 p.p.m. were assigned to C-1 and C-4, which are the most deshielded of the furanoid carbon atoms.

The position of the conformational equilibrium for monosaccharide derivatives is influenced by the nature of the anomeric substituent, and the anomeric effect may favour either the axial or equatorial (reverse anomeric effect) orientations for the anomeric substituent. For *N*-substituted pentopyranosylamines, the reverse anomeric effect is strongest for substituents having a positively charged nitrogen atom[18]. The phenylamino group would be expected to have some positive character on the nitrogen atom due to delocalisation of the lone-pair electrons, and this, together with the size of the group, presumably accounts for the preponderance of the conformations **2** and **3**, in each of which the phenylamino group is equatorial.

EXPERIMENTAL

^{1}H-N.m.r. spectra were recorded with Varian HA 100, XL 100, and XL 220 spectrometers. ^{13}C-n.m.r. spectra were recorded with the XL 100 spectrometer, using a 33° pulse, a pulse repetition time of 1.6 s, and a digital resolution in the frequency domain of 1 point per Hz. Me$_4$Si was used as internal standard. Melting points were corrected.

N-*Phenyl-α-*D*-ribopyranosylamine* (*isomer A*). — The crystalline solid with m.p. 126–127° had $[\alpha]_D^{20}$ +178° (c 0.5, pyridine), which was constant during several hours. ^{1}H-N.m.r. data (100 MHz, pyridine-d_5): τ 2.7–3.35 (multiplets, ~5 H, ArH), 3.55 (d superposed on bs, ~4 H, OH + NH), 4.82 (broadened doublet, 1 H, $J_{1,NH}$ 8.5, $J_{1,2}$ ~2.5 Hz, H-1), 5.7–6.0 (m, 4 H), and 6.31 (m, 1 H, H-5*a*). Irradiation at τ 3.55 collapsed the signal at 4.82 to a poorly resolved doublet. After 17 h, the solution gave a spectrum having additional signals at τ 4.58 (broadened t, $J_{1,NH}$ 7 Hz, H-1 of β anomer) and 5.37 (m). D$_2$O Exchange sharpened the signals of the anomeric protons to give τ 4.51 (d, $J_{1,2}$ 8 Hz) and 4.75 (d, $J_{1,2}$ 2.5 Hz). The 220-MHz spectrum was similar to that at 100 MHz, except that a sharp doublet ($J_{5,5'}$ 11 Hz) for H-5*e* could be seen in the 5.7–5.9 multiplet, and the signal for H-5*a* was a double doublet ($J_{5,5'}$ 11, $J_{4,5a}$ 2 Hz).

^{13}C-N.m.r. data (pyridine-d_5): 147.1, 129.4, 118.3, 114.4 (ArC), 82.7 (C-1), 71.7, 71.3, 69.2 (C-2), and 64.2 (C-5) p.p.m. After 17 h, the following additional signals (assigned to the β anomer) were present in the spectrum: 148.3, 129.37, 118.1, 114.3 (ArC), 83.3 (C-1), 72.0 (C-3), 68.9 (C-2), and 64.9 (C-5) p.p.m. Weaker signals were also present, those in the region below 90 p.p.m. being 89.8, 85.3, 84.9, 83.0, 76.0, 72.3, 71.8, 63.3, and 62.7 p.p.m.

N-*Phenyl-*D*-ribosylamine* (*"isomer" B*). — The crystalline solid with m.p.

113–115° had $[\alpha]_D^{20}$ +60° (*c* 0.5, pyridine), which was constant during several hours. ^{1}H-N.m.r. data (100 MHz, pyridine-d_5): the spectrum was very similar to that given by a solution of *N*-phenyl-α-D-ribopyranosylamine (isomer A) after standing for 17 h; at 220 MHz: τ 2.7–3.2 (m, ArH), 3.2–3.6 (m, NH + OH), 4.5 (t, *J* 8 Hz, H-1*β*), 4.7 (bs, H-1*α*, obscured by H_2O peak), 5.3 (bs), 5.6–6.0 (m), and 6.2 (dd, *J* 11 and 2 Hz, H-5*a* of α anomer). The same results ($[\alpha]_D$ and spectra) were obtained both after several hours and when the measurements were made as rapidly as possible (within ~2 min) after dissolution of the sample. The ^{1}H-n.m.r. spectrum of a solution $(CD_3)_2SO$ also showed signals for two isomers: τ 3.91 (d, *J* 8 Hz, NH) and 4.05 (d, *J* 9 Hz, NH).

^{13}C-N.m.r. data: (*i*) measured during 1 h after dissolution of sample (pyridine-d_5): 148.2, 147.0, 129.5, 129.4, 118.3, 118.1, 114.39, 114.33 (ArC), 83.2 (C-1), 82.7 (C-1), 72.00, 71.95, 71.6, 71.3, 69.2, 68.8, 64.8 (C-5), and 64.2 (C-5) p.p.m.; (*ii*) an overnight measurement after the solution had stood for 2 h revealed the following, additional, weak signals: 148.1, 147.1, 114.6, 89.8, 85.3, 84.8, 83.0, 75.9, 72.3, 71.8, 71.7, 63.3, and 62.7 p.p.m. These signals were assigned to the two furanosylamine anomers, which were present in equal amounts, the total pyranoid/total furanoid ratio being ~6:1.

ACKNOWLEDGMENTS

We thank the S.R.C. and I.C.I. (Runcorn) for the 220-MHz spectra. Other spectra were measured by Messrs. W. N. Nettle, G. Llewellyn, and J. C. Weeks. The ribose anilides were prepared by Mr. S. R. Szajda.

REFERENCES

1 G. A. Howard, G. W. Kenner, B. Lythgoe, and A. R. Todd, *J. Chem. Soc.*, (1946) 855–861.
2 L. Berger and J. Lee, *J. Org. Chem.*, 11 (1946) 75–83.
3 L. Berger, U. V. Solmssen, F. Leonard, E. Wenis, and J. Lee, *J. Org. Chem.*, 11 (1946) 91–94.
4 K. Butler, S. Laland, W. G. Overend, and M. Stacey, *J. Chem. Soc.*, (1950) 1433–1439.
5 G. P. Ellis and J. Honeyman, *J. Chem. Soc.*, (1952) 1490–1496.
6 G. P. Ellis, *J. Chem. Soc., B*, (1966) 572–576.
7 A. De Bruyn, M. Antenunis, M. Claeyssens, and E. Saman, *Bull. Soc. Chim. Belg.*, 85 (1976) 605–615.
8 G. P. Ellis and J. Honeyman, *Adv. Carbohydr. Chem.*, 10 (1955) 102.
9 S. Tsuiki, *Tohoku J. Exp. Med.*, 61 (1955) 365.
10 R. L. Whistler and J. N. BeMiller, *Methods Carbohydr. Chem.*, 1 (1962) 81–82.
11 M. Taniguchi, K. Koga, and S. Yamada, *Tetrahedron*, 30 (1974) 3547–3552.
12 S. M. Hecht, B. L. Adams, and J. W. Kozarich, *J. Org. Chem.*, 41 (1976) 2303–2311; footnote 27.
13 J. B. Stothers, *Carbon-13 NMR Spectroscopy*, Academic Press, New York, 1972, p. 467.
14 See data in E. Breitmaier and W. Voelter, *^{13}C N.M.R. Spectroscopy*, 2nd edn., Verlag Chemie, Weinheim, 1978, p. 248.
15 P. L. Durette and D. Horton, *Org. Magn. Reson.*, 3 (1971) 420–421.
16 R. U. Lemieux and J. D. Stevens, *Can. J. Chem.*, 44 (1966) 249–262.
17 Ref. 14, p. 208.
18 H. Paulsen, Z. Györgyeak, and M. Friedmann, *Chem. Ber.*, 107 (1974) 1590–1613.