# textbook forum

# NMR and the Structure of D-Glucose

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Virtually all major textbooks of organic chemistry begin their discussion of carbohydrate chemistry by presenting evidence that glucose ($C_6H_{12}O_6$) is one of the stereoisomers of 2,3,4,5,6-pentahydroxyhexanal **1**. Later in the chapter, the student is informed that glucose is much more likely to exist in its hemiacetal form, as shown by the Haworth projection **2**.
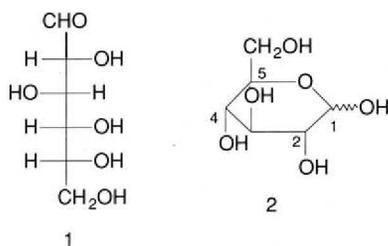
Generally, the only experimental evidence cited for this is the phenomenon of mutarotation—the change in optical activity observed for aqueous solutions of glucose over a period of time. These data are explained by showing the two anomers of glucose, the α- and β-D-glucopyranoses, in equilibrium with a small amount of the "open-chain" structure. The reader is told that, by definition, the α form has the structure shown as **3** below, and the β form has the structure shown as **4**. However, as a rule, no experimental evidence for these assignments is cited.
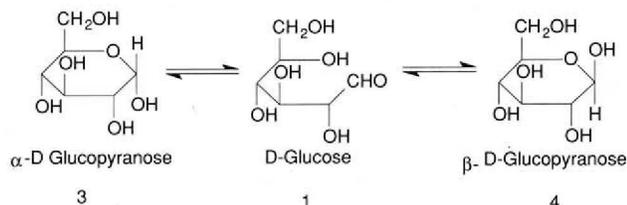
Nuclear magnetic resonance spectrometry, both proton (¹H NMR) and carbon (¹³C NMR), is the ideal technique for obtaining and presenting clear-cut evidence that will help students understand this chemistry. NMR spectra of glucose have been published (1, 2), but probably are not readily available. First, Figure 1 presents clear evidence that a

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[1]Textbooks cite $[\alpha]_D = +112.2°$ for α-D-glucopyranose. The chemical shift of the anomeric C is reported at 93 δ. Molecular-mechanics programs (4) predict a dihedral angle of 53° and $J = 3.49$ Hz. Data acquistion for the ¹³C NMR spectrum took about 30 minutes, and signals from the β anomer can be seen already.

[2]For this solution at equilibrium, most textbooks cite $[\alpha]_D = +52.7°$. For the β anomer, computer programs (4) predict $J = 7.62$ Hz based on a dihedral angle of 174°. The ¹³C NMR resonance position for the anomeric carbon is reported (1) to be 96.8 δ. The $[\alpha]_D$ for pure β-glucopyranose is reported to be +18.7°.
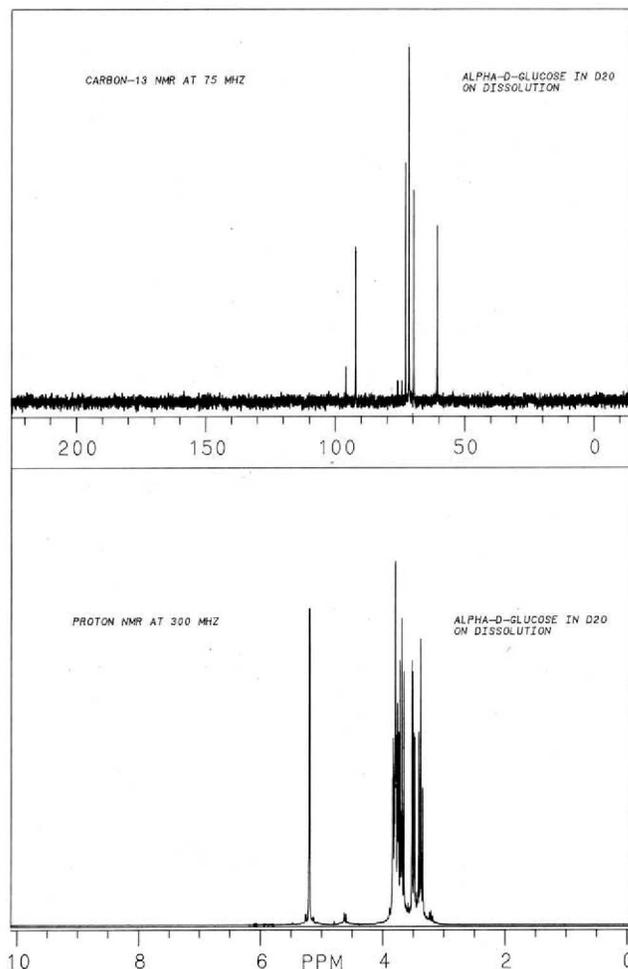

Figure 1. ¹H NMR and ¹³C NMR spectra of α-D-glucose determined quickly after dissolution in D_2O.

sample of D-glucose in D_2O is not an aldehyde. On the ¹H NMR spectrum, there is no signal in the 9- to 10-ppm region where the signal for **H**–C=O should be seen (2, 3). On the ¹³C NMR spectrum, there is no signal in the 200-ppm region where the signal for H–**C**=O would appear.

On ¹H NMR, there is a doublet at 5.2 δ, which is consistent with the existence of a proton that is bonded to a carbon that is bonded to two oxygens (the anomeric carbon, C_1). The coupling constant (J) for this doublet is 3.73 Hz, which is consistent with the smaller axial–equatorial dihedral angle at H–C_1–C_2–H, which is approximately 60°, thus identifying this anomer as the α anomer. This was con-
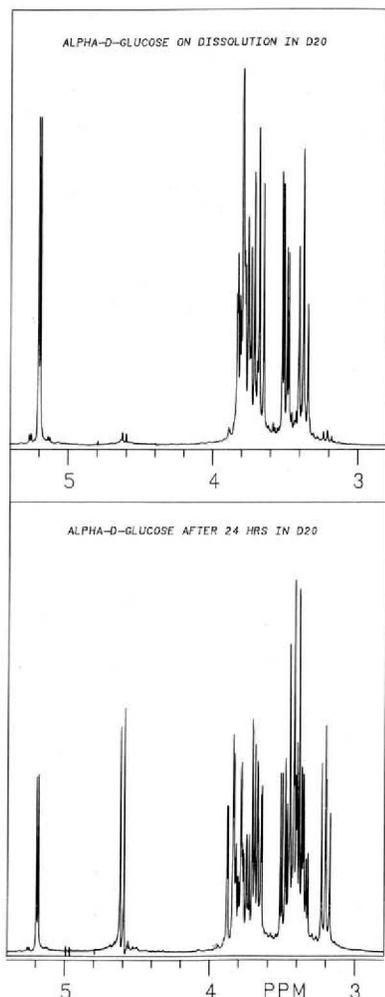
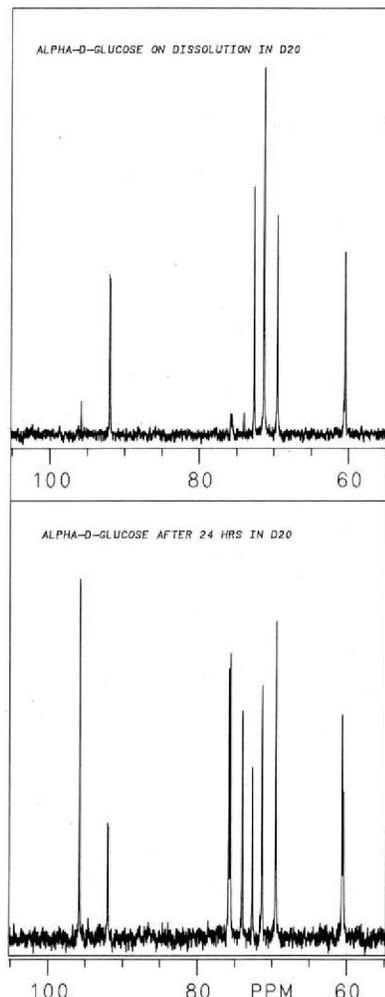Figure 2. ^{1}H NMR spectrum of α-D-glucose. Upon dissolution in D_2O (top). After 24 hours (bottom).

Figure 3. The ^{13}C NMR spectrum of α-D-glucose. Upon dissolution in D_2O (top). After 24 hours (bottom).

larger J value (7.93 Hz), which is consistent with the larger axial–axial coupling expected for the β anomer, in which the angle at $H–C_1–C_2–H$ is approximately 180°. This axial hydrogen is upfield from the equatorial hydrogen of the α anomer.[2]

The most obvious of the other new signals is the doublet of doublets near 3.2 δ for the hydrogen on C_2 in the β anomer (1). The ^{13}C NMR spectrum most clearly shows the equilibration by the new signal at 96 ppm and by the doubling of the number of peaks that appear from 6 to 12.

Most textbooks give values, which are determined from optical activity data, for the percent of each anomer of D-glucopyranose present in the equilibrium concentration. These are generally cited as 64% for the β anomer and 36% for the α anomer. While these NMR experiments were not designed to yield quantitative analytical data, the results certainly show that the β-D-glucopyranose is the more stable anomer.

Interestingly, the readily available molecular-mechanics program, *PCModel* (4), yields $\Delta H_f =$ −274.83 kcal/mol for the β anomer and $\Delta H_f =$ −271.60 kcal/mol for the α anomer. Although this difference in values for ΔH_f (3.2 kcal/mol) predicts an equilibrium mixture that would be far too rich in the β anomer ($K_{eq} \approx 293$, ratio ≈ 99.6:0.4), the correct order is obtained.[3]

Students can be helped to understand the chemistry of this important class of compounds by including and discussing spectra such as these in textbook chapters on carbohydrates.

Generation of the Spectra

NMR spectra were measured using approximately 40 mg of sample[4] dissolved in 0.75 mL of solvent on a General Electric QE–Plus NMR spectrometer, which was operated at 300 MHz for ^{1}H NMR and at 75 MHz for ^{13}C NMR. A presaturation pulse sequence, which removed the large signal for the HDO formed by the exchange between the OH groups and the D_2O solvent, was used to determine ^{1}H NMR spectra.

firmed by obtaining $[\alpha]_D = +103.9° \pm 2.1°$ (*c*, 0.1267 g/mL). The ^{13}C NMR spectrum shows a signal near 92 ppm for this C_1 carbon.[1]

After being left to stand in D_2O for 24 h, the D-glucose solution showed a change in specific rotation, as expected ($[\alpha]_D = +55.9° \pm 2°$), and new peaks appeared in both the ^{1}H NMR and ^{13}C NMR spectra. (See Figures 2 and 3). On the ^{1}H NMR spectrum, a new doublet appears that is centered at 4.6 δ. This proton signal exhibits a significantly

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[3] *PCModel* calculations are done "in the gas phase" with the dielectric constant set at 1.5. The optical rotation data are measured in a solvent with the high dielectric constant of 80—water.

[4] Samples labelled "D-Glucose" or "Dextrose" from Mallinkrodt were used.

Literature Cited

1. Curatolo, W.; Neuringer, L. J.; Ruben, D.; Haberkorn, R. *Carbohydrate Research*, **112**, *1983*, 297–300.
2. Pretsch, E.; Clerc, T.; Seibl, J.; Simon, W. *Tables of Spectral Data for Structure Determination of Organic Compounds*, 2nd ed. (translated by Biemann, K.); Springer–Verlag: Berlin, 1989.
3. Kemp, W. *Organic Spectroscopy*, 3rd ed.; Freeman: New York, 1991; Chapter 3.
4. PCModel is published by Serena Software, P. O. Box 3076, Bloomington, IN 47402.