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Structure of 2-C-(hydroxymethyl)-D-ribose (hamamelose) in the solid-state analyzed by CP MAS NMR and X-ray crystallography

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Abstract—D-Hamamelose, a branched-chain ribose (2-C-(hydroxymethyl)-D-ribose), has been synthesized and its solid-state structure analyzed by ^{13}C CP MAS NMR spectra and X-ray data. The presence of the complex pattern of resonances in the anomeric region, as well as in the ring carbon region, in ^{13}C CP MAS NMR spectrum indicated that the mixture of four cyclic forms, α- and β-furanoses, as well as both α- and β-pyranoses were present in the solid-state. X-ray analysis of crystals showed that D-hamamelose belongs to the monoclinic system with unit cell: $a = 4.790$ Å, $b = 8.671$ Å, $c = 8.880$ Å and $\beta = 98.89°$, space group $P2_1$. The furanose ring has the $_2E$ conformation.

Keywords: D-Hamamelose; Plant tannins; Solid-state; NMR; X-ray; Carboxylase/oxygenase regulators

1. Introduction

Branched-chain sugars are components of many natural biologically active compounds and have been subject of interest on their synthesis, structure and biological properties. D-Hamamelose, a branched-chain ribose (2-C-(hydroxymethyl)-D-ribose), is widely distributed among many plant species and found predominantly in their leaves.[1,2] D-Hamamelose, and especially its derivative hamamelitannin, is known as a potent scavenger of reactive oxygen species involved in degenerative diseases.[3,4] This branched-chain saccharide is currently intensively studied also due to its relationship to a regulator of the enzyme ribulose bisphosphate carboxylase/oxygenase.[5,6]

Methodologies for the stereo-controlled construction of the carbon–carbon bond in carbohydrate chemistry are very challenging. Synthesis of many of natural branched-chain sugars have therefore been approached by new synthetic techniques during the past decade.[7–9] These studies were aimed, not only at finding the most efficient way to synthesize these compounds, but to analyze their structure and biological properties. Recently, D-hamamelose was effectively prepared from D-fructose utilizing the catalytic effect of molybdate ions.[10,11] Other biologically active higher saccharides were also obtained by this method and allowed further studies of their structure and biological properties.[12,13] One of the sought after issues in glycobiology is the detailed understanding of the biosynthesis of higher saccharides and their role in intracellular communication that occurs in plants. This knowledge is only possible when the structural details of these saccharides are fully understood. The present report is aimed at detailed examination of structural properties of D-hamamelose by analysis of ^{13}C CP MAS NMR spectra and X-ray data.

2. Results and discussion

The presence of all four cyclic forms in aqueous solution, α,β-furanoses and α,β-pyranoses, were observed in high-resolution 1D and 2D NMR spectra in previous studies.[10,11,14] The integral intensities in ^1H NMR

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Table 1. 75.45 MHz ^{13}C NMR chemical shifts (δ, ppm) of D-hamamelose in aqueous solution and in solid-state

		C-1	C-2	C-3	C-4	C-5	C-2′
Solution[a]	α-Furanose	97.8	78.3	70.6	81.6	62.9	61.3
	β-Furanose	101.5	81.2	71.6	82.5	63.6	62.9
	α-Pyranose	94.8	75.3	66.9	68.9	66.5	61.1
	β-Pyranose	95.3	75.7	66.6	68.6	63.6	63.4
Solid-state	α-Furanose	94.2	[b]	71.0	81.1	65.2	62.7
	β-Furanose	100.6	[b]	72.9	82.6	65.2	65.2
	α-Pyranose	90.7	[b]	70.5	70.5	68.0	60.6
	β-Pyranose	90.7	[b]	68.7	70.5	68.0	62.7

[a] Taken from Refs. 11 and 14.
[b] Not assigned.

spectrum (not shown) indicated that the furanose form is more abundant (~67%) than the pyranose one and the values of chemical shifts based on former analyses are listed in Table 1.

Solid-state ^{13}C CP MAS NMR spectra of carbohydrates are mostly similar with high-resolution data where both the number of resonances and the values of chemical shifts are comparable. In some cases, however, the increased number of resonances indicates that either more than one chemically equivalent molecule is present in the crystal unit cell or various types of crystals are formed due to the different content of water (solvent) molecules in crystals.[15] Inspection of the ^{13}C CPMAS spectrum of crystalline D-hamamelose (Fig. 1A) reveals that several significant differences exist between the CP MAS and solution NMR data. Three resonances in the anomeric region were detected with chemical shifts 100.6, 94.2 and 90.7 ppm (Table 1). The values of the most deshielded resonance correspond well with that of the β-furanose anomeric signal in solution. The remaining two signals are shifted to higher fields than those in aqueous solution. The chemical shift of α-furanose is 94.2 ppm (compared to 97.8 ppm) and the signal at 90.7 ppm likely corresponds to the overlapped both α- and β-pyranoses (~95 ppm in solution). The effect of molybdate ions resulted in a more complicated CP MAS spectrum of the D-hamamelose–Mo(VI) complex, as expected. However, the anomeric region of the spectrum was found to be relatively well resolved indicating that all four forms of D-hamamelose are present in solid-state (Fig. 1B). The displacements of carbons (at the anomeric centres) chemical shifts to higher values (109.3, 105.4, 103.3 and 98.0 ppm) are due to the presence of Mo(VI) ions. The 'shoulder' (85–89 ppm) of the large signal corresponds to C-4 of furanose rings. The corresponding C-4 signals of pure D-hamamelose (82.6 and 81.1 ppm) match well with C-4 furanose resonances in solution (Table 1). C-4 resonances of both pyranose forms are more shielded and tentatively assigned to 70.5 ppm. However, strong overlap in the region 68–72 ppm prevented more precise analysis of CP MAS spectrum.

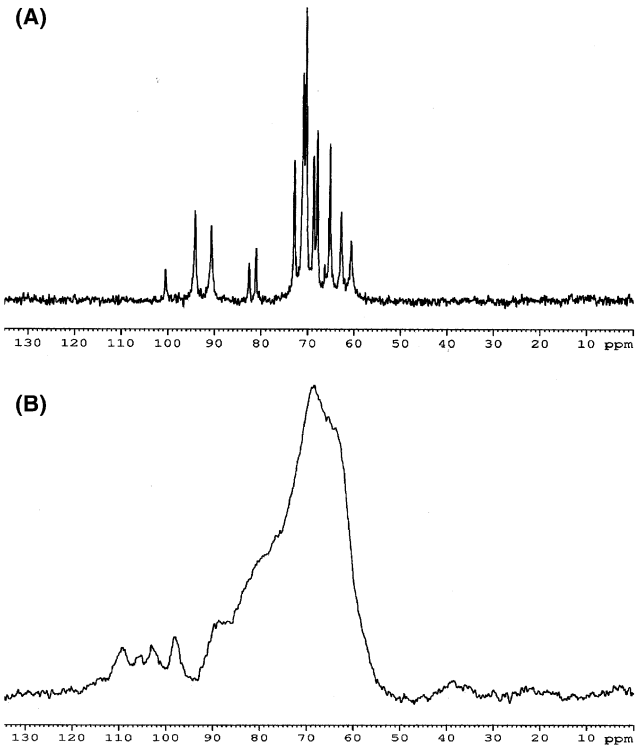

Figure 1. 75.45 MHz ^{13}C CPMAS NMR spectra of crystalline D-hamamelose (A) and the spectrum of the complex of D-hamamelose with molybdic acid (B).

D-Hamamelose has been further re-crystallized to obtain suitable crystals for X-ray study. The crystallographic analysis revealed that the studied molecule existed in the β-furanose form. Figure 2 shows a perspective view and the atom labelling of the X-ray structure of β-D-hamamelose. Examinations of bond lengths and valence angles demonstrate that the values conform to those observed in other furanose analogues.[16] The conformation of D-hamamelose is described by torsion angles reported in Table 2. The endocyclic dihedral angles are in the range of values observed in many structures containing a furanosyl moiety.[17] In particular, the furanose ring of D-hamamelose has a C-2-*exo* pucker. In terms of the conformational descriptors,[18] the pseudorotation phase angle P is of −22.6°, the maximum angle of pseudorotation τ is of 40.2°, and the $_2E$