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Note

New approach to the complexation of iron(III) with fructose

Maja Tonković
Ruđer Bošković Institute, 41000 Zagreb (Croatia)

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The complexes of iron(III) with monosaccharides have an important role in the transport of this metal across cell membranes[1,2]. The complexation properties of monosaccharides maintain the iron(III) in solution in a low molecular weight, soluble, and stable configuration over a wide pH range[3]. Iron(III)–sugar complexes can be isolated from aqueous solution by the addition of ethanol to a final concentration of 80% (v/v)[3]. The characterization of the isolated complexes of iron(III) with various kinds of sugars and polyols have been performed by molecular weight determination, Mössbauer and infrared spectroscopy[4,5], EPR spectroscopy[6], and extended X-ray absorption fine structure spectroscopy (EXAFS)[7]. It has been considered for a long time that the chelating ability of sugars is associated with the dihydroxyacetone structure, which is found in the open-chain fructose molecule[8]. It was proposed that, in these complexes, the iron atom is incorporated into a six-membered ring, bound through the hydroxyl oxygen atoms to C-1 and C-3 of the fructose molecule. Nagy et al.[7] also proposed the bonding of the open-chain form of fructose, but through the hydroxyl-oxygen atoms on C-1 and C-2; this kind of bonding was first proposed by Charley et al.[3].

On the other hand, the binding of fructose to other elements, such as Ca, Mg, UO_2^{2+}, Zn, Cd, Hg, and Al, was found to be in a cyclic form either as a pyranose and/or furanose ring[9–12].

In an aqueous solution of D-fructose, an equilibrium is established between α-D-fructopyranose, β-D-fructopyranose, α-D-fructofuranose, β-D-fructofuranose, and the acyclic isomer. The actual composition depends on the pH, temperature, and other factors. A solution of D-fructose in D_2O at 30°C contains 2% α-pyranose, 70% β-pyranose, 5% α-furanose, and 23% β-furanose[13]. The open-chain form was found by ^{13}C NMR spectroscopy at 80°C only in a small amount (3%)[14].

Since ^{13}C NMR spectroscopy is a very useful method for the identification and characterization of carbohydrates and their complexes, in this paper the ^{13}C NMR spectrum of the Fe–D-fructose complex is reported in order to find out whether iron(III) is the only element to bind an open-chain form of fructose. In the ^{13}C NMR spectrum of the free ligand, D-fructose, eighteen signals were present,

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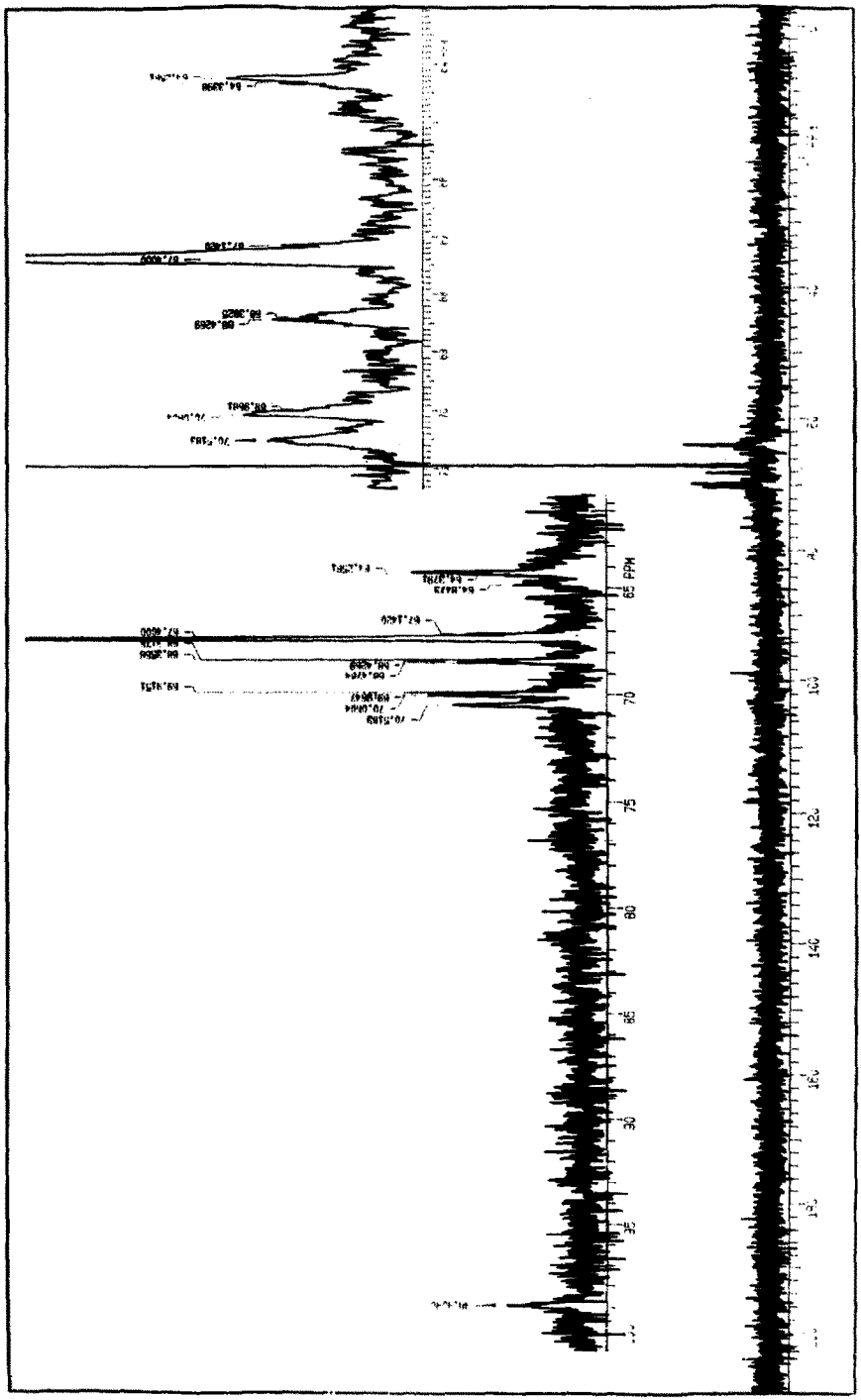

Fig. 1. ^{13}C NMR spectrum of Fe–D-fructose complex.

corresponding to the α- and β-furanose and β-pyranose forms of D-fructose assigned according to data reported by Angyal and Bethell[15]. The open-chain form was not detected; there was no signal at 214 ppm, which would correspond to the chemical shift of the carbonyl group. In the ^{13}C NMR spectrum of the Fe–D-fructose complex (Fig. 1), six signals were detected corresponding to the β-pyranose ring form of D-fructose (C-1, 64.85; C-2, 98.91; C-3, 68.43; C-4, 70.52; C-5, 70.06; and C-6, 64.26 ppm). They were almost unchanged in position, but some change in intensity occurred. The chemical shift of the C-1 atom at 64.85 ppm suffered a marked diminution in apparent intensity. The results of ^{13}C NMR spectroscopy indicate that iron(III) binds preferably to fructose in the β-pyranose ring form which is present in an equilibrium solution of D-fructose in the greatest amount.

EXPERIMENTAL

D-(−)-fructose (Merck, Germany) and $FeCl_3 \cdot 6H_2O$ (Merck, Germany) were reagent grade.

The complex was prepared by dissolution of $FeCl_3 \cdot 6H_2O$ (0.02 mol) and D-(−)-fructose (0.2 mol) in H_2O (100 mL). The pH of the solution was adjusted to 11.0 by the addition of 1 M NaOH. A deep-brown solution was obtained. The Fe(III)–D-fructose complex was precipitated by the addition of EtOH and isolated by centrifugation. The precipitate was redissolved in a small volume of water, the pH was adjusted again to 11.0, and the precipitation was repeated. The isolated compound was very soluble in water.

The deduced formula for the Fe–D-fructose complex is $Fe_2(C_6H_{12}O_6)_2(OH)_7Na$. Anal. Calc.: C, 23.46; H, 5.05; Fe, 18.20; Na, 3.74. Found: C, 23.14; H, 4.43; Fe, 16.67; Na, 3.66.

The ^{13}C NMR spectra of the solutions of D-fructose (1 M) and the Fe–D-fructose complex (0.2 M) in D_2O were measured on a Varian Gemini 300 Fourier-transform spectrometer at room temperature in 5-mm o.d. tubes at 75 MHz. The spectral width was 19000 Hz; pulse width, 5.0 μs; pulse width (90°), 15.0 μs; pulse delay, 0.5 s for D-fructose and 2.0 s for Fe–D-fructose. Chemical shifts were measured relative to that of internal 1,4-dioxane, set at 67.4 ppm downfield from that of Me_4Si.

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