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Note

Mode of interaction of Cu(II) and Mn(II) with D-ribose and D-arabinose as studied by ^{13}C-n.m.r. spectrometry

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The ability of saccharides to sequester metals has been of continuing interest from the physiological, clinical, and chemical viewpoints, and interactions of saccharides with metal cations have been widely studied by various methods[1–5]. Angyal and his coworkers have conducted extensive ^{1}H-n.m.r. studies on the interactions of various saccharides with alkali-metal, alkaline-earth, and lanthanide cations[2,3]. However, the mode of interactions of saccharides with Cu(II), Mn(II), and other transition metals is not yet clear. It is well recognized that traces of these ions often play vital roles in biological systems[6]; furthermore, Cu(II) has been reported to show, in general, the highest complexing ability toward various saccharides as compared with other metal cations[7]. Here, we report the results of ^{13}C-n.m.r. spectrometric studies of the mode of interaction of Cu(II) and Mn(II) with two aldopentoses, D-ribose and D-arabinose. Interactions of paramagnetic metal cations with various biologically important molecules have been studied by ^{13}C-n.m.r. spectrometry[8–12], and the specific line-broadening technique has been demonstrated by Dill *et al.* to be a useful method for this purpose[11,12].

EXPERIMENTAL

Samples and spectra. — A D_2O solution containing 1 mol · dm^{-3} of saccharide and 0–2.5 × 10^{-2} mol · dm^{-3} of metal chloride was prepared at least one day before measurement. Proton-noise-decoupled ^{13}C-n.m.r. spectra of the sample solutions in 5-mm (i.d.) tubes were recorded by a JEOL JMN-GX-270 (67.8 MHz) spectrometer over a 13.5-kHz range defined by 32K data-points. Pulses (45°, 4 μs) were applied to the sample at 2.0-s intervals 400 times. The probe temperature was kept at 27° by a built-in variable-temperature control-unit, and the decoupling power of 9 W was decreased to 4 W during the pulse-delay time in order to prevent the heating of the sample. Observed signals in the recorded spectra were assigned according to the report of Bock and Pedersen[13].

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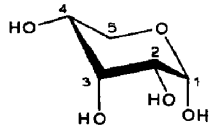
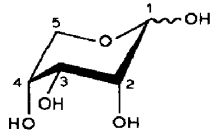
RESULTS AND DISCUSSION

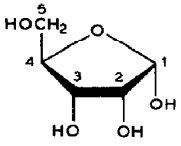
Saccharides having three consecutive hydroxyl groups *a–e–a* disposed in the pyranose form or *cis-cis* in the furanose form are known to interact well with Ca(II), La(III), and other metal ions[2,7]. These sequences are found at C-1–C-3 of the α-pyranose $^4C_1$, C-2–C-4 of the α- and β-pyranose ($^1C_4$), and C-1–C-3 of the α-furanose forms of D-ribose, but not in any of the tautomers of D-arabinose (Fig. 1). Proton-noise-decoupled ^{13}C-n.m.r. spectra of D-ribose and D-arabinose showed well-resolved signals for most of the carbon atoms of their tautomers in the solution (Figs. 2 and 3). The chemical shifts of the signals were in good accord with reported values[13], and the addition of Cu(II) or Mn(II) did not affect the signal shifts. However, the addition of $CuCl_2$ markedly decreased the intensity of the C-1 signal of α-ribofuranose (αF1), and further addition of $CuCl_2$ caused essential disappearance of the αF1 signal. As the relative intensities of the C-4 signals of the tautomers were not much affected by the addition of $CuCl_2$, it is unlikely that the tautomeric composition in solution was altered by the addition of $CuCl_2$ (Fig. 4). Although the C-3 signal (αF3) of α-ribofuranose could not be resolved from that of C-2 (αP2) of α-ribopyranose, the C-2 signal (αF2) of α-ribofuranose also decreased as the $CuCl_2$ concentration increased. Therefore, the specific broadening of the αF1 signal suggests that Cu(II) interacts primarily with the *cis*-diol at C-1–C-2 or possibly with the *cis-cis*-triol at C-1–C-3 of α-ribofuranose. Although it is not readily evident in the spectra, Fig. 4 shows that the signal intensity of C-1 (αP1) of α-ribopyranose also decreased as the $CuCl_2$ concentration increased. This may be an indication that Cu(II) can also interact with α-ribopyranose. However, the signal intensity of C-3 (αP3) of the α-pyranose was not much affected by the addition of $CuCl_2$. As broadening of the αP1 signal was not so marked, it is difficult to conclude from these results whether Cu(II) interacts only with the gauche diol at C-1 and C-2 or with three consecutive hydroxyl groups at C-1–C-3 of α-ribopyranose.



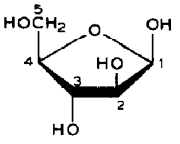
α-D-ribopyranose-$^4C_1$



α- and β-D-ribopyranose-$^1C_4$



α-D-ribofuranose



β-D-arabinofuranose

Fig. 1. Tautomers of D-ribose and D-arabinose.

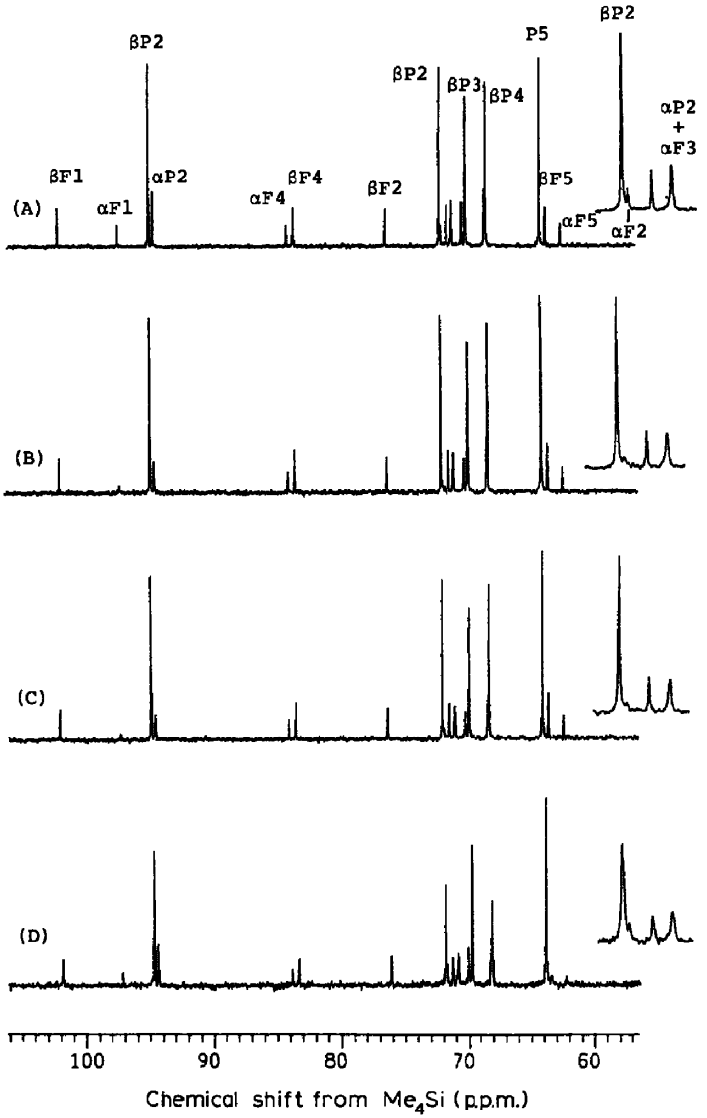


Fig. 2. Typical ^{13}C-n.m.r. spectra of D-ribose (1 mol · dm^{-3}) in D_2O at 27° (A) in the absence of metal salt, and in the presence of (B) $CuCl_2$ (5×10^{-3} mol · dm^{-3}), (C) $CuCl_2$ (1×10^{-2} mol · dm^{-3}) and (D) $MnCl_2$ (5×10^{-3}). The βP2 and αF2 signals are shown on the right (× 4).

The heating problem for solutions of ionic samples caused by the decoupling field is known to be serious when working with a high-frequency n.m.r. spectrometer, and causes a decrease in the signal-to-noise ratio[14]. However, we observed essentially the same specific decreases of the signals for the D-ribose–$CuCl_2$ systems upon using a lower-frequency n.m.r. spectrometer (a JEOL JMN-PFT-100 spectrometer operating at 25 MHz), thus ruling out problems from the possible heating effect with the spectra recorded by a JMN-GX-270 spectrometer.

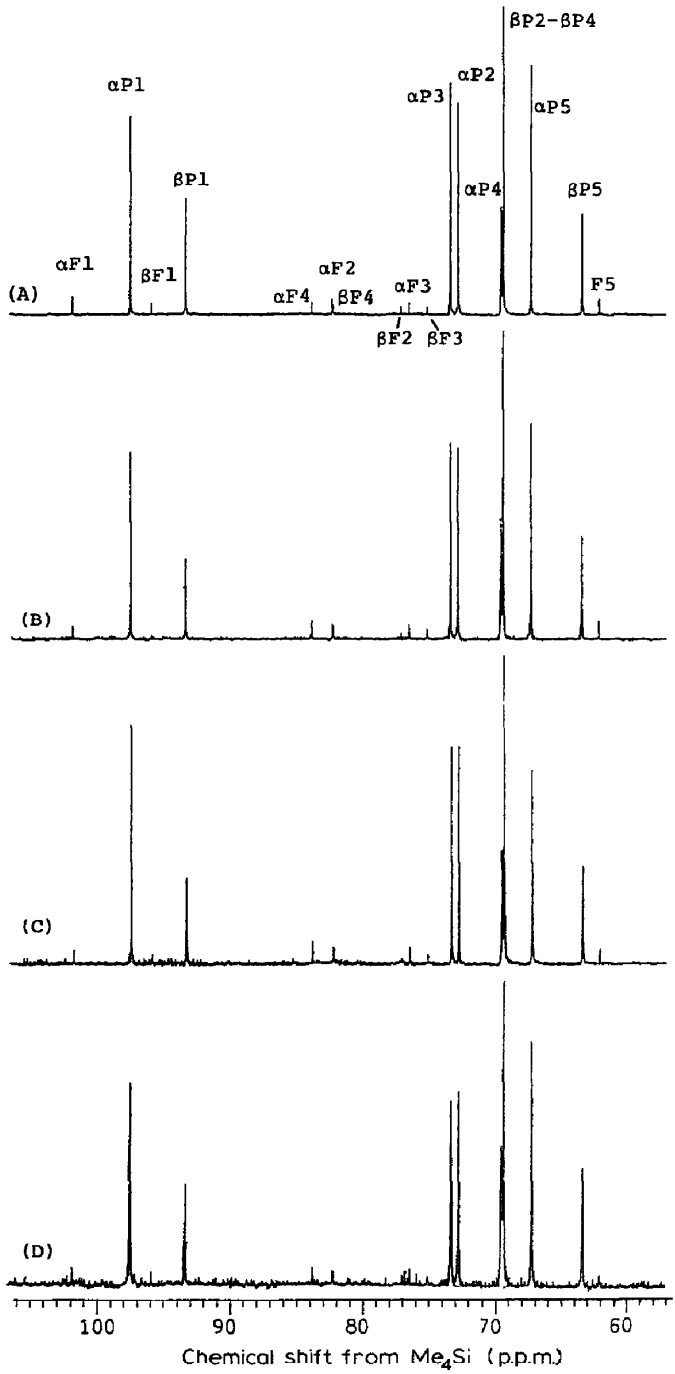


Fig. 3. Typical ^{13}C-n.m.r. spectra of D-arabinose (1 mol · dm^{-3}) in D_2O at 27° (A) in the absence of metal salt, and in the presence of (B) $CuCl_2$ (5×10^{-3} mol · dm^{-3}), (C) $CuCl_2$ (1×10^{-2} mol · dm^{-3}), and (D) $MnCl_2$ (5×10^{-3} mol · dm^{-3}).

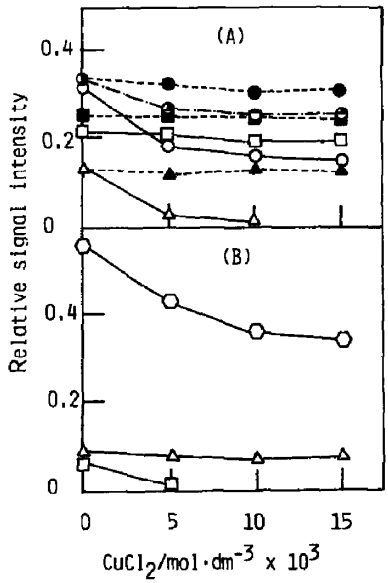


Fig. 4. Effect of $CuCl_2$ on the relative intensities of the ^{13}C-signals of aldopentoses. (A) Signal intensities of D-ribose tautomers relative to those of β-ribopyranose; (—○—) αP1, (—△—) αF1, and (—□—) βF1 relative to that of βP1; (---◑---) αP3 relative to that of βP3; and (---●---) αP4, (---▲---) αF4, and (---■---) βF4 relative to that of βP4. (B) Signal intensities of (—⬡—) βP1, (—△—) αF1, and (—□—) βF1 of D-arabinose relative to that of C-1 of α-arabinopyranose.

With D-arabinose (Fig. 3), the signal intensities for C-1 and C-2 (βF1 and βF2) but not for C-3 and C-4 of β-arabinofuranose decreased as the $CuCl_2$ concentration increased, and the βF1 signal practically disappeared at higher $CuCl_2$ concentration. This result provides direct evidence that Cu(II) preferentially interacts with the *cis*-diol of β-arabinofuranose, even though this tautomer lacks the sequence of three consecutive hydroxyl groups suitably disposed for metal coordination and is a minor component in the solution. It is also observed that the C-1 signal (βP1) of β-arabinopyranose decreased as the $CuCl_2$ concentration in-

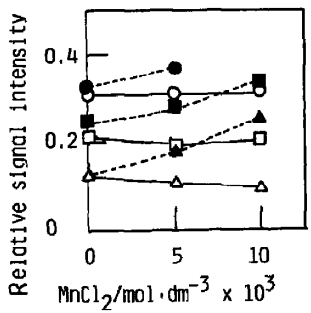


Fig. 5. Effect of $MnCl_2$ on the relative intensities of ^{13}C-signals of D-ribose. Signal intensities of (—○—) αP1, (—△—) αF1, and (—□—) βF1 relative to that of βP1, and those of (---●---) αP4, (---▲---) αF4, and (---■---) βF4 relative to that of βP4.

creased, suggesting that Cu(II) can also interact with the gauche diol at C-1 and C-2 of the β-pyranose.

In contrast, addition of $MnCl_2$ first affects the C-5 signals (F5) of the furanose forms of both D-ribose and D-arabinose (Figs. 2 and 3). As these carbon atoms are located outside of the furanose rings, the disappearance of F5 signals may be attributable to easier accessibility of Mn(II) toward the 5-hydroxyl group of the furanose. Similar broadening was observed (unpublished result) for the C-1 and C-6 signals of D-fructofuranoses in the presence of $MnCl_2$, in concurrence with this observation. Further addition of $MnCl_2$ to a solution of D-ribose decreased the C-2 and C-4 signals (βP2 and βP4) of β-ribopyranose with substantial broadening, indicating that Mn(II) preferentially interacts with the *a–e–a* arrangement of three hydroxyl groups in the pyranose form rather than with those in the furanose form (Fig. 5). Further addition of $MnCl_2$ caused nonspecific broadening of the signals of D-arabinose and the signal-to-noise ratio of the spectrum was greatly decreased, suggesting that Mn(II) does not interact strongly with D-arabinose.

Thus, Cu(II) and Mn(II) are shown to exhibit different modes of interaction with hydroxyl-group sequences in monosaccharides. It is noteworthy that Cu(II) has a smaller ionic radius (0.76 or 0.87 Å) than those of Mn(II) (0.96), Ca(II) (1.14), and La(III) (1.22)[15], and this may be the reason that Cu(II) preferentially interacts with a *cis*-diol group of the furanose form. As the *cis*-diol arrangement can be found in almost all saccharides, it is not surprising that Cu(II) shows high complexing ability toward a variety of saccharides.

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