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An Ordering of Complexation Ability for a Series of Permethylated Aldopyranoses with Metal Cations in Solution. ^{1}H-NMR Relaxation Probes

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By using ^{1}H-NMR relaxation technique, an ordering of complexation ability for a series of permethylated aldopyranoses with metal cations in solution has been determined, which is identical with that of the peak-intensity for the 1:1 adduct ions by FAB mass spectrometry.

Despite the intensive studies on complexation ability of metal cations (A^+) with underivatized carbohydrates in solution,[1,2] those with permethylated aldopyranoses (M) remain relatively unexplored. An example has been reported for the complexation of 2,3-O-isopropylidene-4-O-methyl-L-rhamnopyranoside with Na^+ in acetone.[3] However, the studies do not seem to be systematic for a series of aldopyranoses. We recently demonstrated a practical method by using fast atom bombardment mass spectrometry (FABMS) to observe the corresponding 1:1 adduct ions $(M+A)^+$ and described its unique applicability.[4] For this FAB method to be well understood,[5,6] it is required for complexation ability of permethylated aldopyranoses with metallic (or organic) cations in solution to be explored, especially at the weaker side of the complexation ability.[4] We now report for the first time a ranking of the complexation ability with cations in solution (a ranking of stability constant (K_s)[7]) mainly determined by using a ^{1}H-NMR relaxation method.

$$M + A^+ \underset{K_s}{\rightleftharpoons} (M+A)^+ \qquad (1)$$

The utilization of paramagnetic metal cation such as Eu^{3+} has become quite common in probing molecular structures and complexations of organic compounds.[1,2,8] Such paramagnetic cations can generally cause large changes in NMR spectral patterns and in relaxation phenomena due to its

coordinations to the organic molecule. Therefore, complexation ability of a pair of permethylated aldopyranoses with $Eu(FOD)_3$ can be qualitatively differentiated by competitive experiments (Eq. 2); that is, the permethylated aldopyranose which can be bound more strongly by $Eu(FOD)_3$ selectively gives rise to larger chemical shifts and much more line broadenings.

$$(M_1\text{---}Eu(FOD)_3) + M_2 \rightleftharpoons M_1 + (M_2\text{---}Eu(FOD)_3) \qquad (2)$$

Figure 1 shows a typical example (paramagnetic (A) method in Table 1). A small amount of $Eu(FOD)_3$ (much less than 1 equiv.) is added to a $CDCl_3$ solution of β-Gal-5(MeO)[9] (2 μL/0.5 mL). ^{1}H-NMR spectrum changes from (a) to (b), providing chemical shifts and line broadenings. To this solution, β-Man-5(MeO) (2 μL) is added. The spectrum changes to (c), reproducing all the peaks of β-Gal-5(MeO). The observation indicates that β-Gal-5(MeO) is replaced by β-Man-5(MeO) for the complexation with $Eu(FOD)_3$; that is, an ordering of complexation ability is β-Gal-5(MeO) < β-Man-5(MeO). All competitive experiments we have done are summarized in Table 1.

On the other hand, the utilization of diamagnetic cation such as K^+ or NH_4^+ has also become widely spread.[1] The example has been presented in our previous report by using the addition of β-$PhCH_2CH_2NH_3^+PF_6^-$ (PEA) salt in a CD_3CN solution of β-Tal-5(OMe) etc.[4] In general, the induced shifts

Table 1. Data of the competitive experiments for permethylated aldopyranoses at 30 °C

Method	Cation	Solvent	Ordering[a]
paramagnetic (A)[b]	Eu^{3+}	$CDCl_3$	β-Glc < α-Glc, β-Gal < β-Man, α-Glc < α-Gal, β-Gal < α-Man, α-Gal ≤ β-Gal
paramagnetic (B)[c]	Eu^{3+}	$CDCl_3$	α-Man < β-Man
diamagnetic	PEA^+ [d]	CD_3CN	α-Glc << β-Man < α-Tal < β-Tal
A total ranking in solution: β-Glc < α-Glc < α-Gal ≤ β-Gal < α-Man < β-Man < α-Tal < β-Tal			

a) All the compounds are permethylated. b) $[(M_1\text{---}Eu(FOD)_3) + M_2]$ method. c) $[(M_1 + M_2) + Eu(FOD)_3]$ method. d) β-$PhCH_2CH_2NH_3^+$.

caused by adding such a salt depend upon (1) ammount of added salt, (2) stability constant (K_s), and (3) limiting shift (structure of the complex). When the concentration of the PEA salt is kept constant (1.4×10^{-2} M), the magnitude of the induced shift, for example, of the hydrogen attached to the C-2 ring carbon may reflect the ordering of K_s, as far as these complexation sites are almost the same.[4] These data are also listed in Table 1 (diamagnetic method).

By comparing the results of paramagnetic and diamagnetic methods with each other, we can construct a qualitative ranking of the complexation ability for a series of permethylated aldopyranoses with cations in solution (Table 1). The ordering is completely identical with that of the relative peak-intensity for the corresponding 1:1 adduct ions by FABMS.[4] Interestingly, we further found that logarithms of the relative peak-intensities for the 1:1 adduct ions by FABMS show a good correlation with Angyal's calculated free energies in solution,[10] as shown in Fig. 2. This

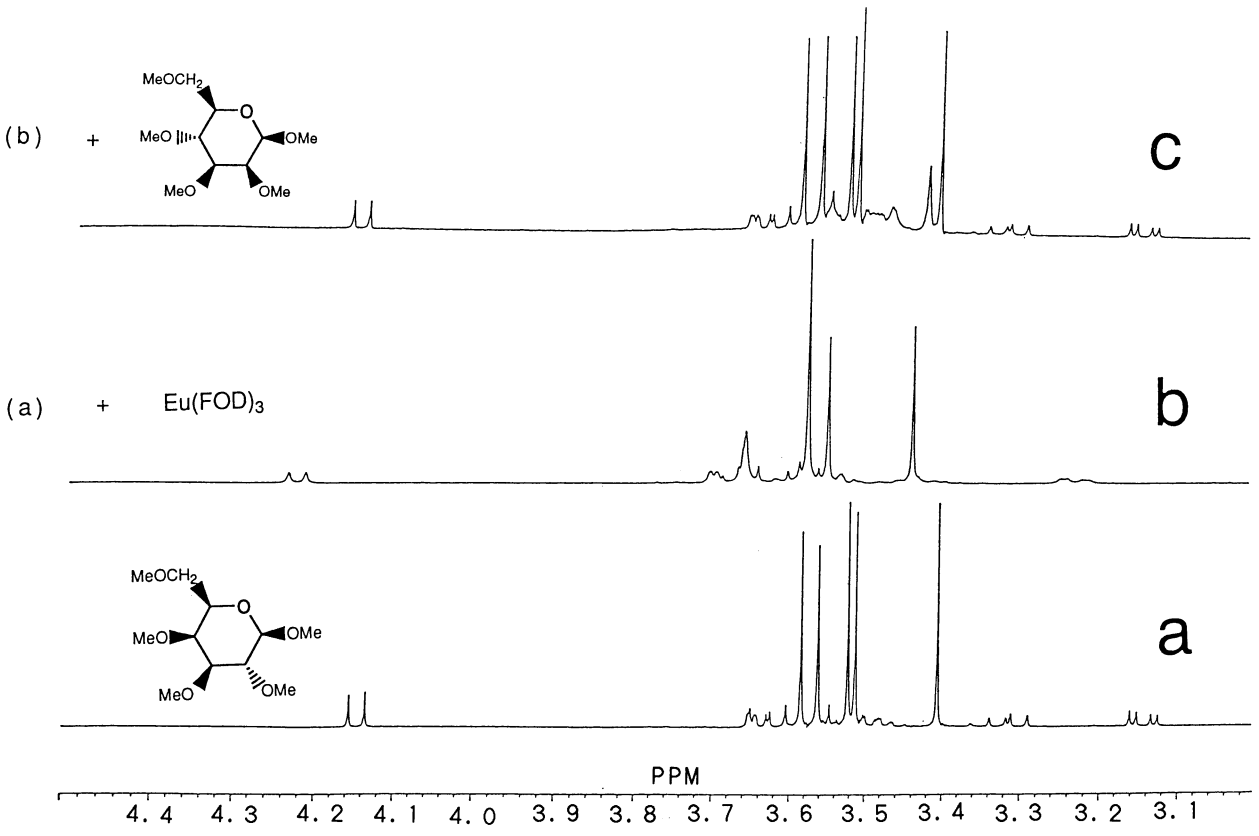

Fig. 1. ^{1}H-NMR spectra (360 MHz) for competitive experiments in $CDCl_3$ at 30 °C. (a); β-Gal-5(MeO).[9] (b); (a) + $Eu(FOD)_3$. (c); (b) + β-Man-5(MeO).

correlation strongly supports our finding that the solution phase ordering is the same as the peak-intensity ordering by FABMS for this series of complexation.

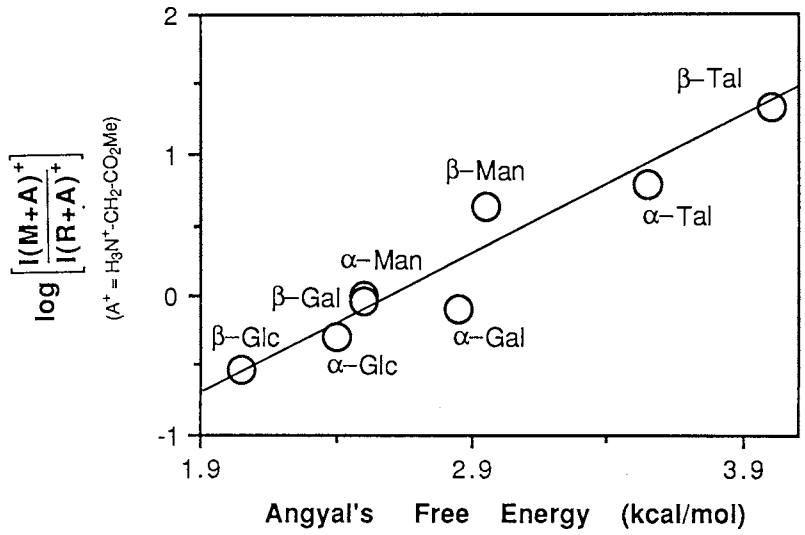

Fig. 2. A correlation of relative peak-intensities by FABMS, $[I(M+A)^+/I(R+A)^+]$,[4] with Angyal's calculated free energies in solution.[10]

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7) We could not determine a set of K_s values because of a very small magnitude of induced shifts.[4]
8) For example, "Nuclear Magnetic Resonance Shift Reagents," ed by R. E. Sievers, Academic Press, New York (1973).
9) Abbreviation; β-Gal-5(MeO) means permethylated β-Galactopyranose.
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