# 1:1 Adduct Ion Formation of Simple Carbohydrate Derivatives with Cations Using FAB Mass Spectrometry. Comparison of *O*-Acetyl, *N*-Butyl, and *O*-Methyl Modifications

Masami SAWADA,* Motohiro SHIZUMA, Yoshio TAKAI, Hitoshi YAMADA, Takanori TANAKA, Yasuo OKUMURA, Yukio HIDAKA, Terukiyo HANAFUSA, and Shigetoshi TAKAHASHI
Material Analysis Center, The Institute of Scientific and Industrial Research, Osaka University, 8-1 Mihogaoka, Ibaraki, Osaka 567
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The 1:1 adduct ion formation between a series of per-*O*-acetylated aldopyranoses (family **1**) or *N*-butylated glycosylamines (family **2**) and an organic/metallic cation ($n$-$C_8H_{17}NH_3^+$/$K^+$ or $Li^+$) has been examined using quantitative FAB mass spectrometry. The per-*O*-acetyl modifications dramatically lead to negated selectivity of the carbohydrates toward the cation which has been clearly observed in per-*O*-methyl modifications. On the other hand, the mono-*N*-butyl modifications provide a similar selectivity pattern to mono-*O*-methyl ones. These results are understood on the basis of electronic and structural considerations.

Noncovalent interactions are significantly important in all biological systems. Both the understanding and application of noncovalent complexations have been significantly developing in recent years, especially for host-guest type interactions of crown ethers,[1] cyclodextrins,[2] designed organic,[3] organometallic compounds,[4] etc.[5] Although carbohydrates are known to occupy important positions in living systems, there have been surprisingly few works where carbohydrates are realized as organic hosts or, more generally, natural receptors of cationic or neutral species except for cyclodextrin derivatives. Examples are Angyal's works on complexations of simple carbohydrates with a variety of metallic cations[6] and some related works.[7]

Under continuous studies using fast atom bombardment mass spectrometry (FABMS) of simple carbohydrates, we have demonstrated the importance of host-guest type interactions with organic or metallic cations in particular cases.[8-12] These studies were based upon permethyl- or monomethyl-substituted aldopyranoses. Our present interest is expanded to determine, in the next step, the effectiveness of carbohydrates with functional modifications other than methyl substitution, in the view of modified electronic and steric effects on 1:1 adduct ion formation. Especially, multisite interaction is of general importance in interactions of polyfunctional molecules with ions. For this reason, we selected the modifications of simple aldopyranoses by peracetyl substitution (family **1**) and mono-*N*-butyl substitution (family **2**) as the example of glycosylamines, and compared those of the previous per-*O*-methyl (family **3**) and non-*O*-methyl methyl glycosides (family **4**). Acceptor/donor substituent effects (for family **1**/**3**) and nitrogen/oxygen atomic effects (for family **2**/**4**) on complexations will be pointed out. Therefore, the work has shown the effect of structural factors on the carbohydrate selectivities toward cations for the 1:1 adduct ion formation using FABMS. This will reflect some noncovalent interactions responsible for the complexation features detected by FABMS.

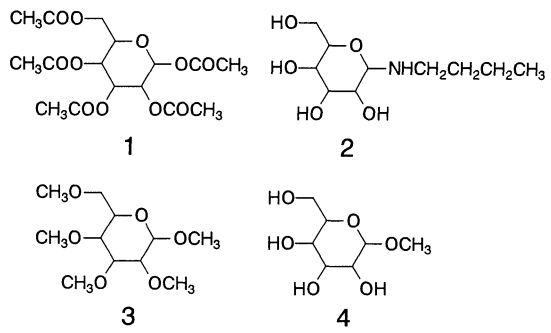


Chart 1.

Host-guest type interactions have been studied using various techniques, for example, NMR spectrometry,[13] solvent extraction,[14] ion transport,[15] UV,[16] HPLC,[17] ion selective electrode,[18] calorimetry,[19] X-ray diffraction,[20] and mass spectrometry.[21] However, very limited applications of FABMS were reported[22,23] except for the crown ether complexations.[24] Consequently, it is noted that weak noncovalent interactions between simple carbohydrate derivatives and organic/metallic cations[6] can be successfully detected by FAB mass spectrometry.

## Results and Discussion

Table 1 shows the relative peak-intensity (RPI) values. [$I(M+A)^+/I(R+A)^+$], of the per-*O*-acetylaldopyranoses (family **1**) with octylammonium ion using quantitative FAB mass spectrometry. Here, $I(M+A)^+$ denotes peak-intensity of the 1:1 adduct ion between a selected aldopyranose derivative (M) and a cation, $n$-$C_8H_{17}NH_3^+$ ($A^+$). FABMS measurements are performed using the same internal standard method previously described.[8] As an internal standard (R), another aldopyranose derivative, for example, permethylated α-D-mannopyranose or methyl 2,3,4,6-tetra-*O*-acetyl-β-D-glucoside is chosen and added (see Experimental). The molar concentration ratio of M to R is 1:1. From Table 1, no

Table 1. Relative FABMS Peak-Intensity Values, $[I(M+A)^+/I(R+A)^+]$, of Family **1** with Octylammonium Ion[a)]

| M | $[I(M+A)^+/I(R+A)^+]$ | | | |
|---|---|---|---|---|
| | Matrix=NBA[b)] | | Matrix=Glycerol[c)] | |
| α-Glc-$(OAc)_5$ | 0.86 | (1.2) | 0.52 | (1.1) |
| β-Glc-$(OAc)_5$ | 0.72 | (1.0) | 0.46 | (1.0) |
| α-Gal-$(OAc)_5$ | 0.68 | (0.9) | | |
| β-Gal-$(OAc)_5$ | 0.66 | (0.9) | | |
| α-Man-$(OAc)_5$ | 0.85 | (1.2) | 0.64 | (1.4) |
| β-Man-$(OAc)_5$ | 0.76 | (1.1) | | |
| α-Tal-$(OAc)_5$ | 0.57 | (0.8) | 0.44 | (1.0) |

a) $A^+X^-=n\text{-}C_8H_{17}NH_3^+Cl^-$. b) R=α-Man-$(OMe)_5$; Methyl tetra-*O*-methyl-α-D-mannopyranoside. Standard errors are within ±0.05 ($n$=3). Normalization values for a set of M are shown in parentheses; $[I(M+A)^+/I(R+A)^+]$=1.0 for β-Glc-$(OAc)_5$. c) R=methyl 2,3,4,6-tetra-*O*-acetyl-β-D-glucoside. Standard errors are within ±0.04.

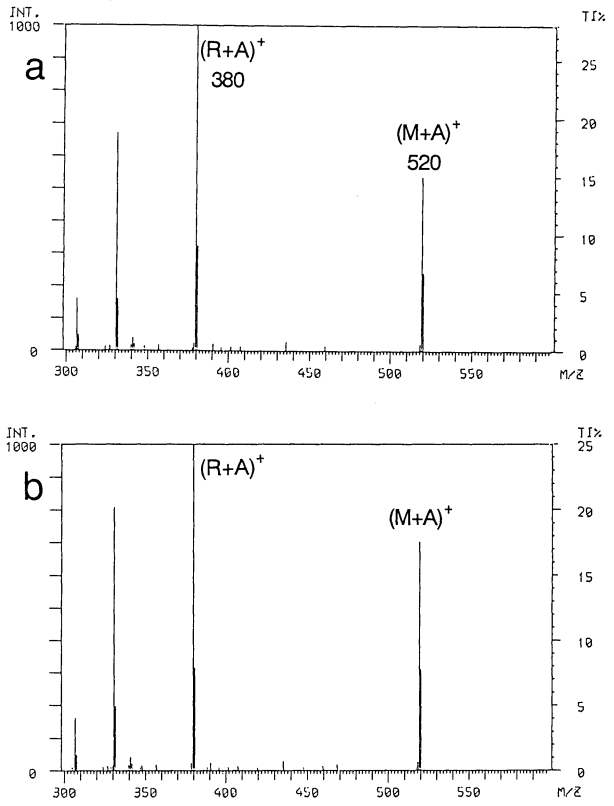


Fig. 1. Quantitative FAB mass spectra for a mixture of per-*O*-acetylaldopyranoses (M), octylammonium ion, and α-Man-$(OMe)_5$ as an internal standard (R) with NBA matrix (10 times accumulation). (a) M=α-Tal-$(OAc)_5$. (b) M=β-Man-$(OAc)_5$.

appreciable matrix effects can be observed for this type of 1 : 1 adduct ion formation: Normalized RPI values are almost equal for the matrices of NBA and glycerol. Typical FAB mass spectra are shown in Fig. 1.

In the FAB mass spectra of the *N*-butylglycosylamines (family **2**) with octylammonium ion, the desired 1 : 1 adduct ions were not abundantly observed, but instead, $[M+H-(n\text{-}C_4H_9NH_2)+(n\text{-}C_8H_{17}NH_2)]^+$ ions were observed. These characteristic ions result from transglycosidations.[25)] Therefore, the octylammonium ion is not suitable for our present study. Qualitative FABMS experiments for determining alternative good cations toward the *N*-butylglycosylamines (family **2**) were conducted, as described in a previous report.[8)] After several trials, it was found that metallic cations with one positive charge are suitable for detecting $(M+A)^+$ adduct ions. Table 2 shows the RPI values of family **2** with potassium ion. Here, methyl α-D-mannopyranoside or 15-crown-5 is used as an internal standard (see Experimental). In spite of independent internal standard, the normalized RPI values in parenthesis in Table 2 give good coincidence with each other.

Table 2. Relative FABMS Peak-Intensity Values, $[I(M+A)^+/I(R+A)^+]$, of Family **2** with Potassium Ion

| M | $[I(M+A)^+/I(R+A)^+]$[a)] | | | |
|---|---|---|---|---|
| | R=α-Man-OMe[b)] | | R=15C5[c)] | |
| β-Glc-*N*-Bu | 0.9 | (1.0) | 0.3 | (1.0) |
| β-Gal-*N*-Bu | 1.1 | (1.2) | 0.3 | (1.0) |
| β-Man-*N*-Bu | 2.2 | (2.4) | 0.6 | (2.0) |

a) $A^+X^-=K^+Cl^-$. Matrix=glycerol. Normalization values for a set of M are shown in parentheses. b) Methyl α-D-mannopyranoside. Standard errors are within ±0.03 ($n$=5). c) 15-Crown-5.

Table 3 summarizes the resulting normalized RPI values for families **1** and **2**, together with those for the relevant families **3** and **4**, where the quantity of $[I(M+A)^+/I(R+A)^+]$ is taken as 1.0 for the β-Glc case. These data are visualized in Fig. 2. For the abscissa, a measure of relative gas-phase stabilities, which were previously derived from FABMS/MS(CAD) data,[8)] $\log[a(\mathbf{4}+K)^+/a(DEA+K)^+]$, is utilized ($a$ denotes area-intensity of the corresponding ion in MS/MS spectrum). For the ordinate, logarithmic normalized RPI values are used. Therefore, a degree of selectivity can be evaluated by the slope of this plot: a higher slope in Fig. 2 means higher selectivity of carbohydrate derivatives for the corresponding 1 : 1 adduct ion formations.

For family **1** (per-*O*-acetylaldopyranoses), there is no selectivity (no stereochemical dependency) (slope=0) of aldopyranoses. This is in sharp contrast to a high degree of stereochemical dependency (slope=2.5) for family **3** (per-*O*-methyl glycosides). The order of β-Glc<α-Glc<α-Gal<β-Gal≤α-Man<β-Man<α-Tal<β-Tal in family **3** dramatically changes in the order of β-Glc=α-Glc=α-Gal=β-Gal=α-Man=α-Tal in family **1**. Thus, per-*O*-acetylation strongly masks the stereochemical dependency of carbohydrate derivatives which has been clearly observed in the case of per-*O*-methylation.

These behaviors may be understood on the basis of electronic and structural considerations. (1) Modifica-

Table 3. Comparisons of Relative Peak-Intensity Values, $[I(M+A)^+/I(R+A)^+]$, among Four Families of Modified Carbohydrates[a)]

| Skeleton | Series: | Family 1[b)] | | Family 2[b)] | Family 3 | | | Family 4[c)] | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Matrix: | NBA | G | G | G | G | G | G | G | DEA |
| | $A^+$: | $n$-$C_8H_{17}NH_3^+$ | $n$-$C_8H_{17}NH_3^+$ | $K^+$ | $n$-$C_8H_{17}NH_3^+$[c)] | $K^+$[c)] | $Li^+$[b)] | $n$-$C_8H_{17}NH_3^+$ | $K^+$ | $K^+$ |
| α-Glc | | 1.2 | 1.1 | | 1.3 | 2.5 | | 1.3 | 1.0 | 1.0 |
| β-Glc | | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| α-Gal | | 0.9 | | | 2.0 | 3.5 | | 1.1 | 1.5 | 1.3 |
| β-Gal | | 0.9 | | 1.2 | 3.3 | 5.0 | 4.3 | 1.5 | 2.8 | 2.7 |
| α-Man | | 1.2 | 1.4 | | 3.3 | 5.0 | | 1.9 | 2.5 | 3.3 |
| β-Man | | 1.1 | | 2.4 | 19 | 19 | 7.5 | 2.1 | | |
| α-Tal | | 0.8 | 1.0 | | 30 | 60 | 70 | 2.0 | 1.8 | 4.3 |
| β-Tal | | | | | 120 | 90 | | 2.5 | 2.2 | 5.3 |

a) Normalized as $[I(M+A)^+/I(R+A)^+]=1.0$ for β-Glc. b) Present study. c) Ref. 8.

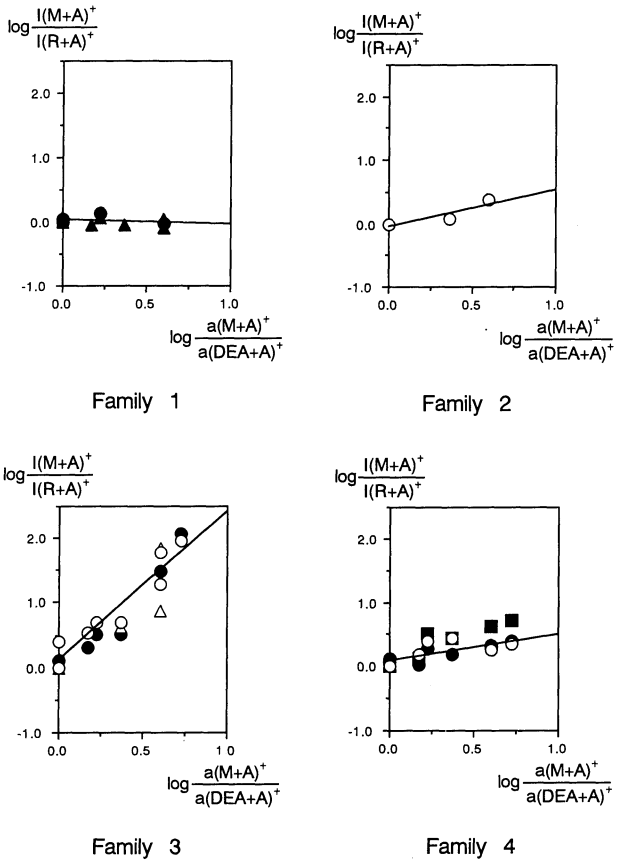


Fig. 2. Selectivities of a series of modified carbohydrates (families **1**, **2**, **3**, and **4**) toward various cations (see data in Table 3). Here, the abscissa is taken from the previous FABMS/MS (CAD) data.[8)] Cation/matrix system (▲; $n$-$C_8H_{17}NH_3^+$/NBA, ○; $K^+$/G (Glycerol), ●; $n$-$C_8H_{17}NH_3^+$/G, △; $Li^+$/G, ■; $K^+$/DEA (diethanolamine)).

tion of the carbohydrate's OH to OAc lowers electron densities on the *O*–Ac oxygens. Since an essential factor of cation binding is electrostatic interaction,[8,26)] this effect directly weakens complexation ability of the carbohydrate's oxygens toward the cation. (2) Congestion of five OAc bulky groups limits the role of the stereochemical dependency of carbohydrate's oxygens for complexation. Because of the conformational flexibility of C–O–Ac functions, other neighboring carbonyl oxygens can also be exerted for the 1 : 1 adduct ion formations. It is well-known that the carbonyl oxygen in an ester linkage takes part in the cation binding. One typical example of this is recognized in the crystal structure of the complex between macrotetrolide nonactin and a $Na^+$ cation.[27)]

On the other hand, as is seen from Fig. 2, the *N*-butylglycosylamines (family **2**) (slope=0.5 in a relatively limited range) shows similar selectivity to the methyl glycoside (family **4**) (slope=0.5): The similarity of functional group effects between *N*-butyl and *O*-methyl for 1 : 1 adduct ion formation is presented. According to the $NH_4^+$ or other cation binding data toward oxygen compounds in the gas-phase equilibria,[28,29)] the contribution of the polarizability effect is important. However, such a polarizability effect is apparently not observed in the present FABMS selectivity. Further, contributions of nitrogen/oxygen atomic effects[29)] can not be apparently differentiated in these two sets in the first-order comparisons. Further comparison between more closely related systems seems to be really important in the high-order analysis.

Accordingly, it should be stressed that per-*O*-acetyl modification markedly negates the selectivity of simple carbohydrates toward cations for 1 : 1 adduct ion formation in FABMS. The effect of *N*-alkyl modification is not significantly different from that of *O*-alkyl modification. However, per-*O*-methyl modification enhances the selectivity toward a cation to a greater extent. Therefore, it is worth mentioning here that the permethylation treatment for carbohydrates provides enhanced sensitivity for the neutral-cation or host-guest interaction detected using this type of FAB mass spectrometry.

## Experimental

**Materials.** Per-*O*-acetylaldopyranoses (family **1**) were prepared from acetic anhydride and monosaccharides in pyridine

by the standard method.[30] The products were separated by liquid chromatography on silica gel or recrystallization from appropriate solvents.

**1,2,3,4,6-Penta-*O*-acetyl-α-D-talopyranose;** Recryst. from MeOH–$H_2O$ (14% yield), colorless crystal, mp 101—102°C, $^1$H NMR (360 MHz, $CDCl_3$) δ=6.16 (d, 1H, $J_{1,2}$=1.5 Hz, H-1), 5.36 (m, 1H, H-4), 5.32 (t, 1H, H-3), 5.10 (m, 1H, H-2) 4.32 (m, 1H, H-5), 4.17 (m, 2H, H-6, H-6'), 2.16, 2.15, 2.05, 2.01 (s, 15H, $-COCH_3$). The compound was confirmed by X-ray analysis as the desired one (see later).

**1,2,3,4,6-Penta-*O*-acetyl-β-D-mannopyranose;** Recryst. from EtOH (ca. 4% yield), colorless crystals, mp 116—117°C, $^1$H NMR (360 MHz, $CDCl_3$) δ=5.86 (S, 1H, H-1), 5.49 (d, 1H, $J_{2,3}$=3.2 Hz, H-2), 5.29 (t, 1H, $J_{4,5}$=9.9 Hz, H-4), 5.14 (dd, 1H, $J_{3,4}$=10.0 Hz, $J_{2,3}$=3.2 Hz, H-3), 4.31 (dd, 1H, $J_{5,6}$=5.3 Hz, $J_{6,6'}$=12.3 Hz, H-6), 4.15 (dd, 1H, $J_{5,6'}$=2.3 Hz, $J_{6,6'}$=12.3 Hz, H-6'), 3.81 (m, 1H, H-5), 2.22, 2.11, 2.10, 2.06, 2.01 (S, 15H, $-COCH_3$). Anal. Found: C, 48.97; H, 5.71%. Calcd for $C_{16}H_{22}O_{11}$: C, 49.23; H, 5.68%. The compound was confirmed by X-ray analysis as the desired one (see later).

*N*-butylglycosylamines (family **2**) were synthesized from butylamine and monosaccharides in ethanol by following the literature method[31] with slight modifications.

***N*-Butyl-β-D-glucopyranosylamine:** The corresponding mixture was stirred at room temperature for 4.5 h until it became clear solution; recryst. from MeOH (79% yield), colorless crystals, mp 84—87°C, $[\alpha]_D$=−28.5° (1 h) (*c* 0.5, EtOH), $^1$H NMR (360 MHz, $D_2O$) δ=4.71 (d, 1H, $J_{1,2}$=7.8 Hz, H-1).

***N*-Butyl-β-D-galactopyranosylamine;** Methanol was used as a slovent and the mixture was stirred at 65°C for 3 h (70% yield). Colorless crystals, mp 100—101°C, $[\alpha]_D$=−11.4° (1 h) (*c* 0.5, EtOH), $^1$H NMR (360 MHz, $D_2O$) δ=4.59 (d, 1H, $J_{1,2}$=7.8 Hz, H-1).

***N*-Butyl-β-D-mannopyranosylamine;** Stirring at room temperature for 0.5 h (90% yield), colorless crystals, mp 70—72°C, $[\alpha]_D$=−30.0° (1 h) (*c* 0.5, EtOH), $^1$H NMR (360 MHz, $D_2O$) δ=4.22 (d, 1H, $J_{1,2}$=0.8 Hz, H-1).

**FABMS Measurements.** All positive ion FAB mass spectra were recorded with a JEOL DX300 instrument. Argon was used as the primary atom beam accelerated to 6 keV. The data were collected and processed by using a JMA3100 computer system.[8]

A typical preparation of a sample solution for quantitative FABMS of family **2** was the followings. Methanolic solution of glycosylamine (0.1 M, 5 μL), methanolic solution of internal standard (α-Man-OMe; 0.05 M, 10 μL), aqueous solution of KCl (0.5 M, 5 μL), and (3/1) glycerol/MeOH (20 μL) were mixed. After mixing with a vibrator, 1.5 μL of the resulted solution was deposited on a probe tip for FABMS. The measurement conditions were similar to the previously reported ones.[8] A mass range of *m*/*z* 200—350 was set up and 10 scans between 20 and 30 were averaged. The resulted relative peak-intensity (RPI) was obtained from an average of 3 runs. A plot of $[I(M+A)^+/I(R+A)^+]$ values against scan times is shown in Fig. 3a for an example.

For family **1**, (i) 5 μL of DMSO solution of per-*O*-acetylaldopyranose (0.1 M), (ii) 5 μL of DMSO solution which contains internal standard, α-Man-$(OMe)_5$ (0.1 M) and *n*-$C_8H_{17}NH_3Cl^-$ (0.25 M), and (iii) 20 μL of matrix NBA were mixed and used for FABMS measurements. Ten scans between 25 and 35 were averaged. A typical plot of the relative peak-intensities against scan times is shown in Fig. 3b.

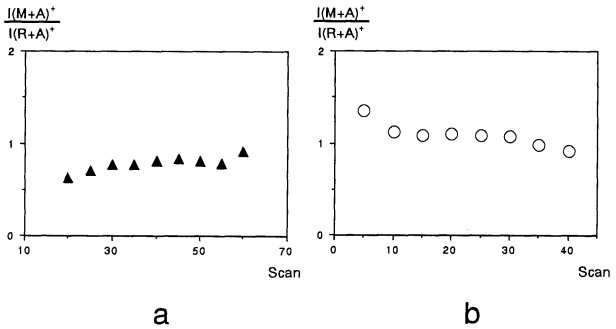


Fig. 3. Plots of $[I(M+A)^+/I(R+A)^+]$ values against scan times. (a) M=α-Gal-$(OAc)_5$; R=α-Man-$(OMe)_5$; $A^+$=*n*-$C_8H_{17}NH_3^+$; matrix=NBA. (b) M=β-Gal-*N*-Bu; R=α-Man-OMe; $A^+$=$K^+$; matrix=glycerol.

**X-Ray Structure Analysis.** Crystals for X-ray analysis of 1,2,3,4,6-penta-*O*-acetyl-α-D-talopyranose were obtained by slow evaporation from an aqueous methanolic solution. X-Ray structure determination was performed with the same direct (MULTAN) method[32] in the TASMAC[33] as our reported ones.[34] The crystal data of this α-Tal-$(OAc)_5$, $C_{16}H_{22}O_6$, are the followings, which are the similar to the literature data:[35] Triclinic, space group *P*1, *a*=8.007 (1), *b*=9.056 (1), *c*=7.449 (1) Å, α=110.13 (1), β=112.92 (1), γ=85.98 (1) °, *V*=465.8 Å$^3$, $D_c$=1.392 g cm$^{-3}$, *R*=0.089 for 910 reflections (Mo *Kα*, λ=0.7107 Å).

On the other hand, crystals of 1,2,3,4,6-penta-*O*-acetyl-β-D-mannopyranose were obtained by recrystallization from ethanol. The crystal data of this β-Man-$(OAc)_5$, $C_{16}H_{22}O_6$, are the follows: Monoclinic, space group $P2_1$, *a*=10.825 (2), *b*=9.640 (1), *c*=9.653 (2) Å, β=107.20° (1), *V*=962.3 Å$^3$, *Z*=2, $D_c$=1.348 g cm$^{-1}$, *R*=0.051 for 2334 reflections (Fig. 4). Atomic coordinates, bond lengths and angles, thermal parameters, and $F_o$–$F_c$ tables of this compound have been deposited as Document No. 8991 at the Office of the Editor of Bull. Chem. Soc. Jpn.

**MNDO Calculations.** Calculations of geometries and energies for the 1 : 1 adduct ion composed of α-Tal-$(OAc)_5$ and $Li^+$ were carried out on a FACOM S3500 superminicomputer (ANCHOR in the TASMAC)[34] by using MNDO methods.[8,36] For obtaining the initial geometry of the complex, the present

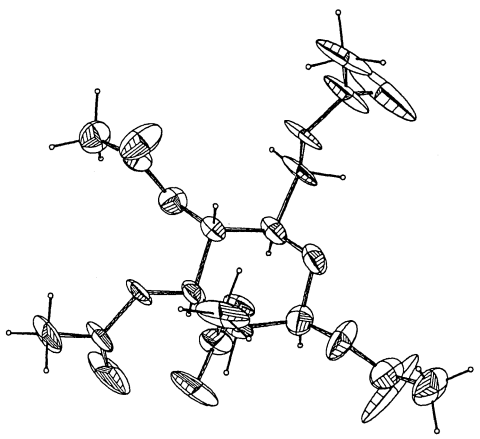

Fig. 4. ORTEP drawing of β-Man-$(OAc)_5$ by X-ray analysis.

crystal structure data were employed.

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## References

1) For example, a) "Host Guest Complex Chemistry I," ed by F. Vögtle, Springer-Verlag, Berlin (1981). b) F. Vögtle and E. Weber, "The Chemistry of Ethers, Crown Ethers, Hydroxyl Groups, and Their Sulphur Analogues," ed by S. Patai, John Wiley, New York (1980), Part 1, Chap. 2.

2) For example, a) W. Saenger, *Angew. Chem., Int. Ed. Engl.*, **19**, 344 (1980). b) R. J. Clarke, J. H. Coates, and S. F. Lincoln, *Adv. Carbohydr. Chem. Biochem.*, **46**, 205 (1988).

3) For example, a) J. Rebek, Jr., *Angew. Chem., Int. Ed. Engl.*, **29**, 245 (1990). b) Y. Dobashi, A. Dobashi, H. Ochiai, and S. Hara, *J. Am. Chem. Soc.*, **112**, 6121 (1990).

4) For example, K. Maruoka, S. Nagahara, and H. Yamamoto, *J. Am. Chem. Soc.*, **112**, 6115 (1990).

5) For example, J.-M. Lehn, *Angew. Chem., Int. Ed. Engl.*, **27**, 89 (1988).

6) S. J. Angyal, *Adv. Carbohydr. Chem. Biochem.*, **47**, 1 (1989).

7) J. F. Stoddart, *Chem. Soc. Rev.*, **8**, 85 (1979).

8) M. Sawada, L. Ouyang, Y. Takai, H. Yamada, M. Shizuma, T. Kinoshita, T. Mochizuki, and T. Hanafusa, *Bull. Chem. Soc. Jpn.*, **64**, 1243 (1991).

9) Y. Takai, M. Shizuma, Y. Okumura, Y. Hidaka, T. Hanafusa, S. Takahashi, and M. Sawada, *Chem. Lett.*, **1991**, 1451.

10) M. Sawada, L. Ouyang, Y. Takai, H. Yamada, T. Hanafusa, T. Kinoshita, and T. Mochizuki, *Chem. Lett.*, **1990**, 1361.

11) M. Sawada, L. Ouyang, Y. Takai, H. Yamada, and T. Hanafusa, *Chem. Lett.*, **1989**, 1743.

12) M. Sawada, M. shizuma, Y. Takai, H. Yamada, T. Kaneda, and T. Hanafusa, *J. Am. Chem. Soc.*, in press.

13) a) E. P. Kyba, J. M. Timko, L. J. Kaplan, F. Jong, G. W. Gokel, and D. J. Cram, *J. Am. Chem. Soc.*, **100**, 4555 (1978). b) R. B. Davidson, J. S. Bradshaw, B. A. Jones, N. K. Dalley, J. J. Christensen, and R. M. Izatt, *J. Org. Chem.*, **49**, 353 (1984).

14) K. E. Koenig, G. M. Lein, P. Stuckler, T. Kaneda, and D. J. Cram, *J. Am. Chem. Soc.*, **101**, 3553 (1979).

15) M. Newcomb, J. L. Toner, R. C. Helgeson, and D. J. Cram, *J. Am. Chem. Soc.*, **101**, 4941 (1979).

16) T. Kaneda, K. Hirose, and S. Misumi, *J. Am. Chem. Soc.*, **111**, 742 (1989).

17) W. H. Pirkle and T. C. Pochapsky, *Chem. Rev.*, **89**, 347 (1989).

18) H. K. Frensdorff, *J. Am. Chem. Soc.*, **93**, 600 (1971).

19) E. M. Arnett and T. C. Moriatiry, *J. Am. Chem. Soc.*, **93**, 4908 (1971).

20) I. Goldberg, "The Chemistry of Ethers, Crown Ethers, Hydroxyl Groups, and Their Sulphur Analogues," ed by S. Patai, John Wiley, New York (1980), Part 1, Chap. 4.

21) a) A. K. Bose, O. Prakash, G. Y. Hu, and J. Edasery, *J. Org. Chem.*, **48**, 1780 (1983). b) T. Murata, *Bunseki Kagaku*, **34**, 414 (1985). c) N. Malhotra, P. Roepstorff, T. K. Hansen, and J. Becher, *J. Am. Chem. Soc.*, **112**, 3709 (1990). d) B. Ganem, Y.-T. Li, and J. D. Henion, *J. Am. Chem. Soc.*, **113**, 6294 (1991). e) H. Zhang, I.-H. Chu, S. Leming, and D. V. Dearden, *J. Am. Chem. Soc.*, **113**, 7415 (1991).

22) a) C. Fenselau, "Ion Formation from Organic Solids," ed by A. Benninghoven, Springer-Verlag, Berlin (1983), p. 90. b) C. Fenselau and R. J. Cotter, *Chem. Rev.*, **87**, 501 (1987). c) J. R. Pare, K. Jankowski, and J. W. Apsimon, *Adv. Heterocycl. Chem.*, **42**, 335 (1987). d) A. Dell, *Adv. Carbohydr. Chem. Biochem.*, **45**, 19 (1987).

23) a) C. E. Ballou and A. Dell, *Carbohydr. Res.*, **140**, 139 (1985). b) P. R. Ashton, J. F. Stoddart, and R. Zarzycki, *Tetrahedron Lett.*, **29**, 2103 (1988). c) J. A. Leary and S. F. Pedersen, *J. Org. Chem.*, **54**, 5650 (1989).

24) a) R. A. W. Johnstone and M. E. Rose, *J. Chem. Soc., Chem. Commun.*, **1983**, 1268. b) R. A. W. Johnstone, I. A. S. Lewis, and M. E. Rose, *Tetrahedron*, **39**, 1597 (1983). c) R. A. W. Johnstone and I. A. S. Lewis, *J. Mass. Spectrom. Ion Phys.*, **46**, 451 (1983). d) D. Parker, *J. Chem. Soc., Chem. Commun.*, **1985**, 1129. e) P. D. Beer, *J. Chem. Soc., Chem. Commun.*, **1985**, 1115. f) J. M. Miller, S. J. Brown, R. Theberge, and J. H. Clark, *J. Chem. Soc., Dalton Trans.*, **1986**, 2525. g) G. Bonas, C. Bosso, and M. R. Vignon, *Rapid Commun. Mass Spectrom.*, **88**, 2 (1988). h) K. Laali and R. P. Lattimer, *J. Org. Chem.*, **54**, 496 (1989). i) D. P. Michaud, J. N. Kyranos, T. F. Brennan, and P. Vouros, *Anal. Chem.*, **62**, 1069 (1990). j) M. Takayama, T. Fukai, T. Nomura, and T. Yamauchi, *Org. Mass Spectrom.*, **26**, 655 (1991).

25) R. Bognar, P. Nanasi, and E. Memes-Nanasi, *J. Chem. Soc.*, **1955**, 33.

26) MNDO calculation suggests that the $Li^+$ cationic center which is used instead of octylammonium ion as the simplest model[8] is located at 2.2 Å from $O_2$ and $O_4$, and 3.1 Å from ring-O.

27) R. Hilgenfeld and W. Saenger, "Host Guest Complex Chemistry, Macrocycles," ed by F. Vögtle and E. Weber, Springer-Verlag, Berlin (1985), p. 43.

28) M. Meot-Ner, *J. Am. Chem. Soc.*, **105**, 4912 (1983).

29) a) R. W. Taft and R. D. Topsom, *Prog. Phys. Org. Chem.*, **16**, 1 (1987). b) J.-F. Gal and P.-C. Maria, *Prog. Phys. Org. Chem.*, **17**, 159 (1990).

30) a) J. Conchie and G. A. Levvy, *Methods Carbohydr. Chem.*, **2**, 345 (1963). b) J. N. C. Whyte, *Can. J. Chem.*, **47**, 4083 (1969).

31) a) J. A. G. Perez, J. C. P. Albarran, J. L. J. Requejo, M. A. Gonzalez, and J. M. Fernandez-Bolanos, *Carbohydr. Res.*, **131**, 71 (1984). b) W. Pigman, E. A. Cleveland, D. H. Couch, and J. H. Cleveland, *J. Am. Chem. Soc.*, **73**, 1976 (1951).

32) a) P. Main, S. E. Hull, L. Lessinger, G. Germain, J.-P. Declercq, and M. M. Woolfson, MULTAN 78, Univ. of York (England), 1978. b) P. Main, G. Germain, and M. M. Woolfson, MULTAN 84, Univ. of York (England), 1984.

33) M. Sawada, *Chemistry*, **42**, 300 (1987).

34) a) M. Sawada, T. Tanaka, Y. Takai, T. Hanafusa, T. Taniguchi, M. Kawamura, and T. Uchiyama, *Carbohydr. Res.*, **217**, 7 (1991). b) H. Matsubara, T. Tanaka, Y. Takai, M. Sawada, K. Seto, H. Imazaki, and S. Takahashi, *Bull. Chem. Soc. Jpn.*, **64**, 2103 (1991).

35) V. J. Kopf and P. Koll, *Acta Crystallogr., Sect. B*, **37**, 1127 (1981).

36) Original MNDO programs were obtained through QCPE, Indiana University.