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Proton Magnetic Resonance Studies on Specifically Deuterated Sucrose Acetates[1]

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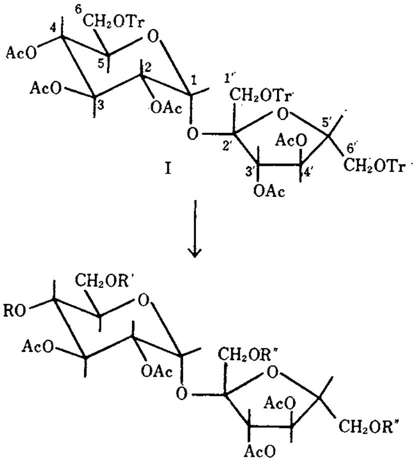
In the proton magnetic resonance spectrum of octa-*O*-acetylsucrose, an individual acetoxy group signal was assigned by direct comparisons of the spectra of specifically deuterated octa-*O*-acetylsucroses and that of nondeuterated one. The structures of 2,3,6,3′,4′-penta-*O*-acetylsucrose and 2,3,4,3′,4′-penta-*O*-acetylsucrose were further confirmed definitively by the present studies.

Penta-*O*-acetylsucrose of mp 156°C (II) was first prepared in a crystalline form by McKeown and his co-workers[2] by detritylation of penta-*O*-acetyl-tri-*O*-tritylsucrose (I) in boiling aqueous acetic acid. The structure of I was assigned to be 2,3,4,3′,4′-penta-*O*-acetyl-6,1′,6′-tri-*O*-tritylsucrose[3] by the relatively higher reactivity of the primary hydroxyl groups, compared with the secondary ones, towards trityl chloride,[2,4] and soon after this structure was confirmed by methylation of tri-*O*-tritylsucrose.[5]



II R=H, R′=Ac, R″=H
III R=Ac, R′=R″=H
IV R=COCD$_3$, R′=Ac, R″=COCD$_3$
V R=Ac, R′=R″=COCD$_3$
Ac=COCH$_3$, Tr=$(C_6H_5)C$

Accordingly the structure of II was first supposed to be 2,3,4,3′,4′-penta-*O*-acetylsucrose,[2] but on the way to establish the structure by methylation of its free hydroxyl groups, it was suspected that an acetyl migration from C-4 to C-6 might occur in a glucose moiety during the reaction leading to 2,3,6,3′,4′-penta-*O*-acetyl-4,1′,6′-tri-*O*-methylsucrose from II.[2,3]

Later Lemieux and Barrette[6] reexamined the structure of II and described that II seemed to be 2,3,6,3′,4′-penta-*O*-acetylsucrose, judging from the results of careful treatments of tritosylate of II with sodium iodide and sodium ethoxide.

While Bredereck and his co-workers[7] prepared another penta-*O*-acetylsucrose of mp 122°C (III) by detritylation of I with hydrobromic acid in glacial acetic acid under ice cooling and described that III was 2,3,4,3′,4′-panta-*O*-acetylsucrose on the bases of its chemical behaviors.

The present authors wish to establish the structural differences between II and III by a definitive method and to open a new field for further synthetic works in sucrose chemistry.

Proton magnetic resonance (PMR) spectroscopy had been proved to be a powerful tool for structural studies of sugar derivatives,[8,9] and so if it could be possible to distinguish an individual PMR signal arisen from each acetoxy group in octa-*O*-acetylsucrose, the structures of the two different penta-

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[1] Supported in part by a grant of the Japanese Ministry of Education.

[2] G. E. McKeown, R. S. E. Serenius and L. D. Hayward, *Can. J. Chem.*, **35**, 28 (1957).

[3] This numbering system for the position of sucrose molecule was proposed by Hockett and Zief: R. C. Hockett and M. Zief, *J. Amer. Chem. Soc.*, **72**, 1839 (1950).

[4] B. Helferich, *Advan. Carbohydrate Chem.*, **3**, 79 (1948).

[5] G. E. McKeown and L. D. Hayward, *Can. J. Chem.*, **35**, 992 (1957).

[6] R. U. Lemieux and J. P. Barrette, *J. Amer. Chem. Soc.*, **80**, 2243 (1958).

[7] H. Bredereck, H. Zinner, A. Wagner, G. Faber, W. Greider and W. Huber, *Chem. Ber.*, **91**, 2824 (1958).

[8] R. U. Lemieux, R. K. Kullnig and R. Y. Moir, *J. Amer. Chem. Soc.*, **80**, 2237 (1958).

[9] R. U. Lemieux, R. K. Kullnig, H. J. Bernstein and W. G. Schneider, *ibid.*, **80**, 6098 (1958).

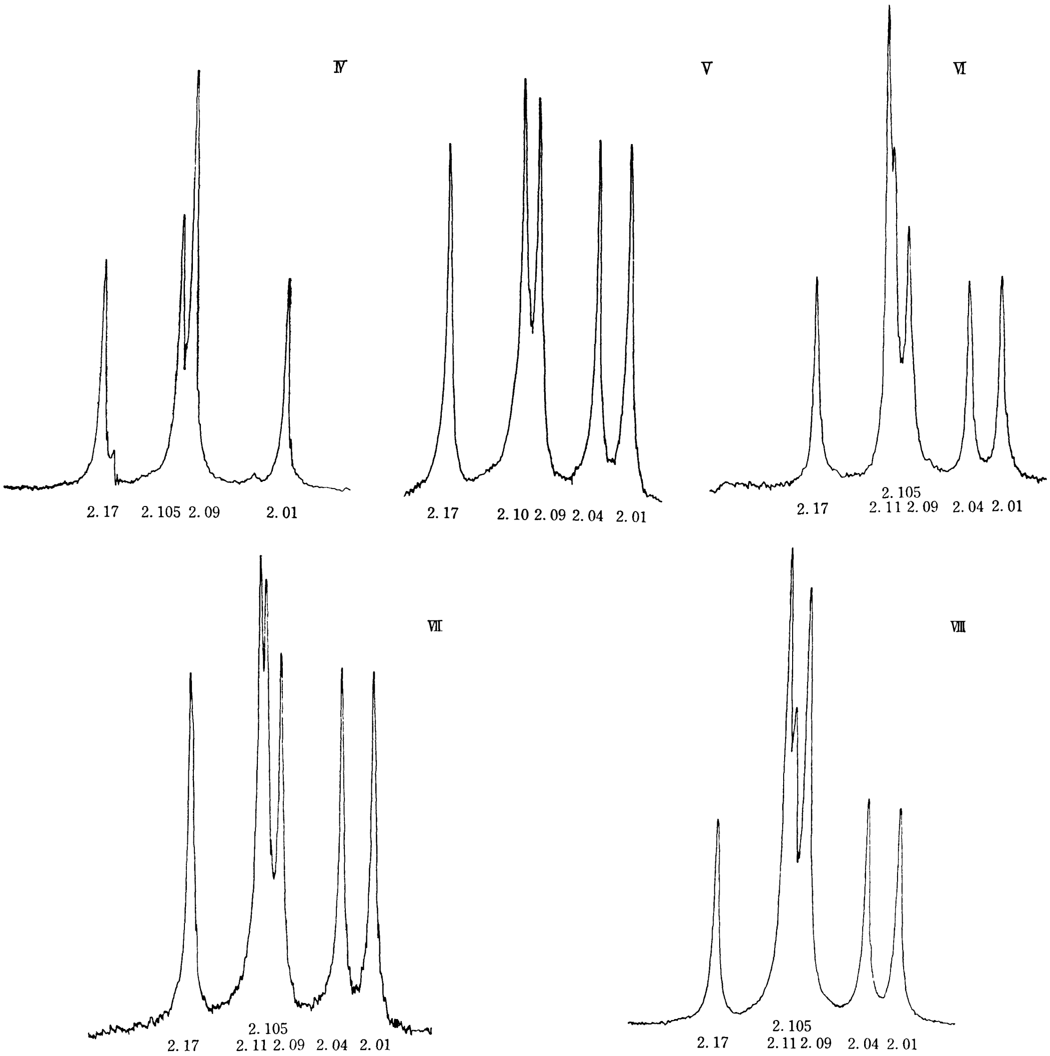

Fig. 1. The acetoxy group signals in the PMR spectra of specifically deuterated derivatives.

O-acetylsucroses would be established by PMR spectroscopy. For this aim, deuteration of an individual acetyl group seemed to be feasible, which had been used successfully by Horton and his co-workers for glucosamine derivatives[10,11] and by the present authors for diazabicyclo[3.2.1.]octanetetrol derivatives.[12]

In the present article, it will be described that some of the individual acetoxy group signals are assigned by the PMR (100 MHz) spectroscopic studies of specifically deuterated octa-*O*-acetylsucrose and it enables us to establish the structures of II and III unambiguously.

The compound II was prepared by the method of McKeown and his co-workers[2] and subsequently acylated with acetic anhydride-d_6 in pyridine, giving penta-*O*-acetyl-tri-*O*-trideuterioacetylsucrose (IV). The PMR spectrum of IV in deuteriochloroform revealed four sharp signals at δ 2.01 (3H), 2.09(6H), 2.105(3H) and 2.17(3H), which were attributed to the five acetoxy groups. When this spectrum was compared with the spectrum of nondeuterated octa-*O*-acetylsucrose (VIII)[13-15] which showed six sharp signals at δ 2.01(3H), 2.04(3H), 2.09(6H), 2.105(3H), 2.11(6H) and

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[10] D. Horton, J. B. Hughes, J. S. Jewell, K. D. Philips and W. N. Turner, *J. Org. Chem.*, **32**, 1073 (1967).

[11] D. Horton, W. E. Mast and K. D. Philips, *ibid.*, **32**, 1471 (1967).

[12] T. Suami, S. Ogawa, Y. Naito and H. Sano, *ibid.*, **33**, 2831 (1968).

[13] W. W. Binkley, D. Horton and N. S. Bhacca, *Carbohyd. Res.*, **10**, 245 (1969).

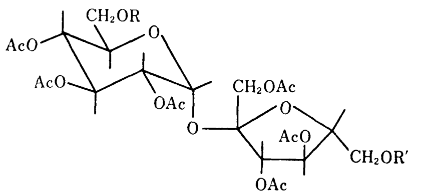
[14] A. Herzfeld, *Ber.*, **13**, 265 (1880).

[15] C. S. Hudson and J. M. Johnson, *J. Amer. Chem. Soc.*, **37**, 2748 (1915).

2.17(3H), it was obvious to see that the two signals at δ 2.04(3H) and 2.11(6H) were missing in the former spectrum (Fig. 1).

Then the compound III was obtained by the method of Bredereck and his co-workers[7] and was acetylated analogously with acetic anhydride-d_6 in pyridine to give another penta-*O*-acetyl-tri-*O*-trideuterioacetylsucrose (V). In the spectrum of V in deuteriochloroform, the two signals at δ 2.09 (3H) and 2.11(6H) were missing, compared with the spectrum of VIII (Fig. 1).

In the two spectra of IV and V, the same acetoxy group signals at δ 2.11 with the same intensity of six protons were missing, and accordingly these signals should be arisen from the two acetoxy groups in the common positions. To find out these two acetoxy group, 2,3,4,1′,3′,4′,6′,-hepta-*O*-acetylsucrose[16] was acetylated with acetic anhydride-d_6 giving 2,3,4,1′,3′,4′,6′-hepta-*O*-acetyl-6-*O*-trideuterioacetylsucrose (VI). The PMR spectrum of VI showed a remarkable decrease of the intensity (1/2) of the signal at δ 2.09, compared with the spectrum of the nondeuterated octaacetate. Hence, the signal at δ 2.09 with an intensity of three protons was attributed to the acetoxy group at C-6 in the glucose moiety of sucrose. This assignment of the signal was agreeable with the fact that an acetoxy group at C-6 in methyl α-D-glucopyranoside tetraacetate revealed the signal at δ 2.09.[17]



VI R=$COCD_3$, R′=Ac
VII R=R′=$COCD_3$
VIII R=R′=Ac

To substantiate the above mentioned assignment 2,3,4,1′,3′,4′-hexa-*O*-acetylsucrose[18] was analogously trideuterioacetylated to give 2,3,4,1′,3′,4′,-hexa-*O*-acetyl-6,6′-di-*O*-trideuterioacetylsucrose (VII). The spectrum of VII revealed the marked decreases of intensities of the signals at δ 2.09 (3H) and 2.11(3H), compared with the spectrum of VIII. Thus the signal of an intensity of three protons at δ 2.09 was ascribed to the acetoxy group at C-6 in the glucose moiety and the signal of an intensity of three protons at δ 2.11 was due to the acetoxy group at C-6′ in the fructose moiety.

Also, the signal patterns in a lower field in the spectrum of McKeown's penta-*O*-acetylsucrose II which were attributed to the ring protons gave a valuable information on its structure. The signal at δ 5.07 which was arisen from the ring proton at C-4[13] in octa-*O*-acetylsucrose was markedly shifted to a higher field (δ 3.5—4.2) in the spectrum of II (Fig. 2). This fact provided a strong evidence that an acetoxy group at C-4 was absent in the compound II.

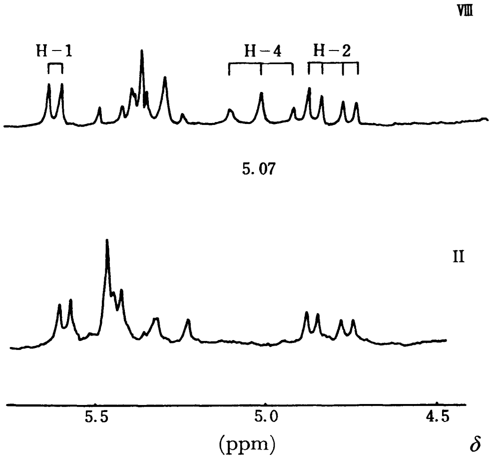


Fig. 2. Partial PMR spectra of II and VIII.

Accordingly the remaining half of the signal at δ 2.11 was due to the acetoxy group at C-4 or C-1′. So if it were arisen from C-4, the diminished signals in the spectrum of V were attributed to three acetoxy groups at C-4, C-6 and C-6′. This caused a big contradiction with the structure of I.

Therefore, the diminished signals at δ 2.11(6H) in the spectra of IV and V should be attributed to the two acetoxy groups at C-1′ and C-6′. Now the structure of V was established to be 2,3,4,3′,4′-penta-*O*-acetyl-6,1′,6′-tri-*O*-trideuterioacetylsucrose and consequently, III was assigned to be 2,3,4,3′4′-penta-*O*-acetylsucrose.

On the other hand, the signal at δ 2.04(3H) disappeared in the spectrum of IV from that of VIII, instead of the diminished signal at δ 2.09(3H) in the spectrum of V. Since Horton and his co-workers[17] described that the signal at δ 2.03 was attributed to the acetoxy group at C-4 of acetylated methyl glucoside, the signal at δ 2.04 in the spectrum of IV was reasonably attributed to the acetoxy group at C-4 of the glucose residue of sucrose. Thus, the structure of IV was assigned to be 2,3,6,3′,4′-penta-*O*-acetyl-4,1′,6′-tri-*O*-trideuterioacetylsucrose and accordingly the structure of II was established to be 2,3,6,3′,4′-penta-*O*-acetylsucrose.

Now four individual acetoxy group signals of the

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16) T. Otake, unpublished data. The precursor of this compound: 2,3,4,1′,3′,4′,6′-hepta-*O*-acetyl-6-*O*-triphenylmethylsucrose has been described in the preprint of the 22nd Annual Meeting of the Japan Chemical Society, April (1969), p. 1895.

17) D. Horton and J. H. Lauterback, *J. Org. Chem.*, **34**, 86 (1969).

18) T. Otake and T. Suami, unpublished data.

TABLE 1. CHEMICAL SHIFTS OF ACETYL GROUPS OF SPECIFICALLY DEUTERATED DERIVATIVES

Compound		4-OAc	6-OAc		1′-OAc 6′-OAc	
IV	2.01(1)*	—	2.09(2)	2.105(1)	—	2.17(1)
V	2.01(1)	2.04(1)	2.09(1)	2.10(1)	—	2.17(1)
VI	2.01(1)	2.04(1)	2.09(1)	2.105(1)	2.11(2)	2.17(1)
VII	2.01(1)	2.04(1)	2.09(1)	2.105(1)	2.11(1)	2.17(1)
VIII	2.01(1)	2.04(1)	2.09(2)	2.105(1)	2.11(2)	2.17(1)

* Chemical shifts are expressed in δ-values. Values in parenthesis show number of acetyl groups.

eight ones were assigned in the PMR spectrum of VIII, and the assignments of other four ones are still under way.

But it was readily recognized that the acetoxy group at C-6 in the glucose moiety of sucrose revealed the signal at the same field as was shown by the acetoxy group at C-6 of methyl α-D-glucopyranoside tetraacetate[17] and this was true in the one at C-4. Therefore the two signals at δ 2.01 and 2.09 in the spectrum of VIII might be attributed to the acetoxy groups at C-3 and C-2 respectively in accordance with the Horton's assignment.[17]

The remaining two signals at δ 2.09 and 2.17 could be due to the two acetoxy groups in the fructose residue other than C-1′ and C-6′. The conformations of sucrose and sucrose sodium bromide dihydrate in crystalline states had been described by Brown and Levy,[19] but the conformation of sucrose in a solution is still unfamiliar. But the acetoxy group on C-4′ seemed to widely spread to an outside of the molecule and to be not affected by a deshielding effect of its environments. Therefore this acetoxy group might reveal its signal in a similar position as was shown by an acetyl group on a primary hydroxyl group.

In the low-field regions of the spectra of IV, V, VI, VII and VIII, the same pattern of the signals were observed, which were attributed to the methine and methylene protons[13] and a deuterium isotope effect on the chemical shifts of acetoxy, methine and methylene protons was not distinguished in these 100 MHz spectra.

Thus, Lemieux's[6] and Bredereck's structural assignments[7] of II and III were further confirmed definitively by the present studies.

Experimental

The melting points were determined on a Mitamura Riken micro hot stage. The PMR spectra were determined with a Varian HA-100D (100 MHz) instrument. All the spectra were measured in deuteriochloroform at a concentration of 10% (w/v) at 35°C with tetramethylsilane as an internal standard and the peak positions were expressed in δ-values. Thin layer chromatography (TLC) was run on a glass plate coated with silica gel (Wakogel B-10, Wako pure chemical industries Ltd.) in a solvent system with toluene-methyl ethyl ketone (4 : 1). The spots were detected by spraying a mixture of concd. H_2SO_4 and glacial acetic acid (1 : 1) and heating at 100°C for 30 min. Evaporations were accomplished under reduced pressure with a Tokyo Rikakikai rotary evaporator.

2,3,6,3′,4′-Penta-*O*-acetyl-4,1′,6′-tri-*O*-trideuterioacetylsucrose (IV). 2,3,6,3′,4′-Penta-*O*-acetylsucrose (II), mp 152.5—153.5°C, was prepared by the method of McKeown *et al.*[2] A 170 mg portion of II was acetylated with 0.4 m*l* of acetic anhydride-d_6 in 0.6 m*l* of pyridine and the solution was settled overnight at room temperature. The mixture was evaporated at 60—65°C. Crystallization of the residue from aqueous ethanol gave IV as fine needles, mp 83.5—87°C, yield, 52 mg. The mother liquor was evaporated and the residue was dissolved in chloroform. The chloroform solution was decolorized through a short column of active alumina and then evaporated. The residue was crystallized from aqueous ethanol giving a second crop of IV, mp 83.5—87°C, yield, 127 mg. Total yield was 179 mg (91%). TLC showed the product to be homogeneous with R_f 0.32 (R_f of octa-*O*-acetylsucrose=0.32).

2,3,4,3′,4′-Penta-*O*-acetyl-6,1′,6′-tri-*O*-trideuterioacetylsucrose (V). 2,3,4,3′,4′-Penta-*O*-acetylsucrose (III), mp 128°C, was prepared by the modified method of Bredereck *et al.*[7] A 2.0 g portion of 2,3,4,3′,4′-penta-*O*-acetyl-6,1′,6′-tri-*O*-tritylsucrose[2] was dissolved in a mixture of 7 m*l* of glacial acetic acid and 3 m*l* of chloroform. To the solution, 0.7 m*l* of glacial acetic acid previously saturated with hydrogen bromide was added under ice-cooling with an occasional shaking. After 10 min, the mixture was poured into ice-cold water. The aqueous solution was extracted two times with 10 m*l* of chloroform. The combined chloroform extract was washed with cold water, and evaporated. The residue was dissolved in 10 m*l* of toluene and chromatographed on a column of 10 g of silica gel (Kanto Chemical Co. Ltd. 60—80 mesh). The column was eluted with 150 m*l* of toluene, 200 m*l* of methyl ethyl ketone-toluene (1 : 5), 200 m*l* of methyl ethyl ketone-toluene (3 : 10) and 200 m*l* of methyl ethyl ketone-toluene (1 : 1). The fraction of the last solvent was evaporated to give 470 mg of the residue. The residue was dissolved in 3 m*l* of chloroform and 7 m*l* of ether was added to the solution. The mixture was kept in a refrigerator for 24 hr to give 362 mg of the crystalline product of III, mp 128°C. A 143 mg portion of III was acetylated with 0.2 m*l* of acetic anhydride-d_6 in 1 m*l* of pyridine by the procedure described for the preparation of IV, giving 85 mg of V, mp 83.5—87.5°C. TLC showed practically a single spot of R_f 0.32.

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19) G. M. Brown and H. A. Levy, *Science*, **141**, 921 (1963): G. A. Jeffrey and R. D. Rosenstein, *Advan. Carbohydrate Chem.*, **19**, 11 (1964).

2,3,4,1′,3′,4′,6′-Hepta-*O*-acetyl-6-*O*-trideuterioacetylsucrose (VI). A 135 mg portion of 2,3,4,1′,3′,4′,6′-hepta-*O*-acetylsucrose16) was acetylated with acetic anhydride-f_6 in pyridine by an analogous procedure of the preparation of IV to give 95 mg of crystalline product of VI, mp 84.5—88°C. TLC showed a single spot of R_f 0.32.

2,3,4,1′,3′,4′-Hexa-*O*-acetyl-6,6′-di-*O*-trideuterioacetylsucrose (VII). To a solution of 2,3,4,1′,3′,4′-hexa-*O*-acetylsucrose (169 mg)18) in 1 m*l* of pyridine, 0.12 m*l* of acetic anhydride-d_6 was added and the mixture was treated analogously as described in the preparation of IV to give 11.6 mg of the crystalline product, mp 83—87°C. TLC showed a single spot of R_f 0.32.

Octa-*O*-acetylsucrose (VIII). The product was prepared by the method of Hudson and Johnson15) and recrystallized two times from aqueous ethanol, mp 84—88°C.

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