(c) A mixture of isatoic anhydride (3) (295 mg) and 1,2,3,4-tetrahydro-1-keto-β-carboline (13)[9] (280 mg) was heated at 190—200° for 2 hr and extracted with chloroform. The extract was washed successively with aqueous 10% sodium hydroxide solution and water, dried over Na_2SO_4 and evaporated. Recrystallization of the residue from ethyl acetate afforded rutecarpine (6) (183 mg, 42.3%) as colorless needles, mp 256—257° (lit.,[5] mp 258°), IR and NMR spectra of which were superimposable on those of the above sample prepared by the method (a).

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Studies on Catalytic Hydrogenation of the Exocyclic Double Bond in Reducing Disaccharides

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Effects of solvents and catalysts in catalytic hydrogenation of the exocyclic double bond in disaccharide-5-ene heptaacetates, synthesized from maltose, lactose, and cellobiose, were investigated. A stereospecific hydrogenation proceeded in such a way that the corresponding 6-deoxy-L-ido isomer was predominant over the 6-deoxy-D-gluco isomer.

Preparations of 6-deoxy-maltose, 6-deoxy-α-cellobiose, 4-O-α-D-glucopyranosyl-6-deoxy-L-idopyranose, and 4-O-β-D-glucopyranosyl-6-deoxy-L-idopyranose were also described.

Keywords——catalytic hydrogenation; maltose-5-ene heptaacetate; lactose-5-ene heptaacetate; cellobiose-5-ene heptaacetate; 6-deoxy-maltose; 6-deoxy-α-cellobiose; disaccharides having 6-deoxy-L-idopyranose

We reported previously[2] that the exocyclic double bond in lactose-5-ene heptaacetate (8) was reduced as formation of the 6-deoxy-L-ido isomer (11) was predominant over the 6-deoxy-D-gluco isomer (5). Khan and Jenner[3] showed subsequently that catalytic hydrogenation of sucrose-5-ene heptaacetate gave the L-ido and the D-gluco isomers in the yields of 45 and 10%, respectively. Except for the two papers, no paper has been reported on catalytic hydrogenation of the exocyclic double bond in disaccharides. Therefore, to clarify the mode of hydrogenation in disaccharide-5-ene heptaacetate, we reduced this compound under different conditions. In this paper, we report the results in full detail.

Authentic heptaacetyl-6-deoxy-β-maltose (4)[4] or -lactose (5)[2] was synthesized from the corresponding 6-deoxy-6-iodo compound (1 or 2), respectively. Heptaacetyl-6-deoxy-β-cellobiose (6) was prepared from heptaacetyl-6-deoxy-6-iodo-β-cellobiose (3).[5] Disaccharide-5-ene heptaacetate (7, 8, or 9) was synthesized by stirring 1, 2, or 3 in dry pyridine with dry silver fluoride, respectively. In the preparation of 8,[2] silver fluoride was added in twice and time of stirring was reduced to almost 1/3, which improved the yield.

1) Location: *Tanabe-dori, Mizuho-ku, Nagoya, 467, Japan.*
2) T. Chiba, M. Haga, and S. Tejima, *Chem. Pharm. Bull.* (Tokyo), **22**, 398 (1974).
3) R. Khan and M.R. Jenner, *Carbohyd. Res.*, **48**, 306 (1976).
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Hydrogenation of **7**, **8**, or **9** afforded two products. They were separated from each other by column chromatography on silica gel. Elution of the mixture from the column with a definite solvent gave the D-gluco isomer (**4**, **5**, or **6**), and the structure was identified by comparison with an authentic sample. After elution of the D-gluco isomer was completed, the second crystal (**10**, **11**, or **12**) was eluted from the column with the same solvent. The product had the same elemental composition as the D-gluco isomer and, in the nuclear magnetic resonance (NMR) spectrum, the methyl protons at C-5 appeared at 1.40, 1.27, or 1.24 ppm as a doublet having $J_{5,6}$=6,7, or 5 Hz, respectively. Therefore, **10**, **11**, or **12** was assigned to the corresponding L-ido isomer. In Table I the ratios of the L-ido isomer to the D-gluco isomer under different conditions were summarized.

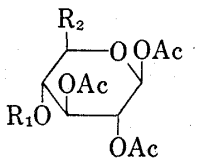
TABLE I. Ratio of 6-Deoxy-L-ido Isomer to 6-Deoxy-D-gluco Isomer

Catalyst	Solvent	Unsaturated disaccharide		
		7[a]	**8**[b]	**9**[c]
PtO_2	AcOEt	7.1	10.4	5.4
PtO_2	MeOH	9.2	5.4	10.7
PtO_2	Toluene	4.2	1.9	2.2
Pd	AcOEt	1.7	11.0	7.2
Pd	MeOH	0.6	4.4	100.0
Pd	Toluene	—[d]	—[d]	—[d]
Raney Ni	AcOEt	3.1	9.8	9.5
Raney Ni	MeOH	4.2	4.1	8.5
Raney Ni	Toluene	1.1	2.9	12.0

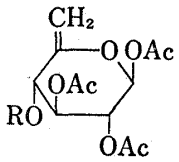
a) Maltose-5-ene heptaacetate. *b*) Lactose-5-ene heptaacetate.
c) Cellobiose-5-ene heptaacetate.
d) Hydrogenation proceeded very slowly and almost all of the starting material was recovered.

The results are briefly summarized as follows. 1) The L-ido isomers are always predominant under all conditions used besides one example: when maltose-5-ene heptaacetate (**7**) is hydrogenated in methanol over palladium, the D-gluco isomer (**4**) is predominant over the L-ido isomer (**10**), and the reason is not yet explicable. 2) Hydrogenation proceeds more stereospecifically in disaccharides having β-D-glycosidic linkage than α-D-glycosidic linkage.

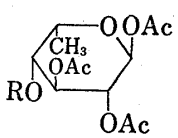
Deacetylation of **4**, **6**, **10**, and **12** afforded 6-deoxy-maltose (**13**), 6-deoxy-α-cellobiose (**14**), 4-O-α-D-glucopyranosyl-6-deoxy-L-idopyranose (**15**), and 4-O-β-D-glucopyranosyl-6-deoxy-L-idopyranose (**16**), respectively, in which only **14** crystallized. The other products were chromatographically homogeneous, amorphous powders.



1: R_1=Ac-α-Glu, R_2=CH_2I
2: R_1=Ac-β-Gal, R_2=CH_2I
3: R_1=Ac-β-Glu, R_2=CH_2I
4: R_1=Ac-α-Glu, R_2=CH_3
5: R_1=Ac-β-Gal, R_2=CH_3
6: R_1=Ac-β-Glu, R_2=CH_3



7: R=Ac-α-Glu
8: R=Ac-β-Gal
9: R=Ac-β-Glu



10: R=Ac-α-Glu
11: R=Ac-β-Gal
12: R=Ac-β-Glu

Ac-α-Glu=2,3,4,6-tetra-O-acetyl-α-D-glucopyranosyl
Ac-β-Gal=2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl
Ac-β-Glu=2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl

Chart 1

Experimental

Melting points were uncorrected. Optical rotations were measured with a Yanagimoto OR-10 automatic polarimeter. Infrared (IR) spectra were recorded with a Jasco Model IR-S spectrometer. NMR spectra were recorded at 100 MHz with a Jeol Model JNM-MH-100 spectrometer for solution in $CDCl_3$ (internal Me_4Si). Chemical shifts were given on the ppm scale. Thin-layer chromatography (TLC) with the multiple (twice) ascending method on pre-coated Silica Gel 60 (E. Merck, Darmstadt, Germany) was performed with solvent combination (v/v): (A), ether–benzene (1: 2), (B), hexane–AcOEt (2: 3), (C), benzene–ether (1: 2). Detection was effected with H_2SO_4. Paper partition chromatography (PPC) was performed by the ascending method with solvent combination (v/v): (D), BuOH–pyridine–H_2O (6: 4: 3), (E), AcOEt–AcOH–H_2O (3: 3: 1), (F), BuOH–EtOH–H_2O (40: 11: 19), and detection was effected with alkaline silver nitrate.[6]

Heptaacetyl-6-deoxy-β-cellobiose (6)——Compound 3[5] (150 mg) was dissolved in AcOEt (10 ml) containing pyridine (10 drops), and the mixture was shaken with H_2 in the presence of freshly prepared Raney Ni catalyst at room temperature under atmospheric pressure: the catalyst was prepared[7] from 2 g of alloy. After removal of the catalyst by filtration, the filtrate was concentrated to dryness. The residue was dissolved in CH_2Cl_2 (20 ml), washed with 10% $Na_2S_2O_3$ and H_2O, dried ($CaCl_2$), and the solvent was evaporated to give a sirup which crystallized from EtOH. Recrystallization from EtOH gave pure **6** (100 mg, 80%), mp 209—212°, $[\alpha]_D^{22}$ −25.3° (c=1, $CHCl_3$). TLC: *Rf* 0.89 (solvent B). NMR δ: 1.33 (3H, d, $J_{5,6}$=5 Hz, C–C$\underline{H}_3$), 2.01, 2.08 (21H, each s, 7×OAc). *Anal.* Calcd. for $C_{26}H_{36}O_{17}$: C, 50.32; H, 5.85. Found: C, 50.35; H, 5.82.

1,2,3-Tri-O-acetyl-4-O-(2,3,4,6-tetra-O-acetyl-α-D-glucopyranosyl)-β-D-*xylo*-hex-5-eno-pyranose (Maltose 5-ene Heptaacetate) (7)——Dry silver fluoride (0.2 g) (completely dried over H_2SO_4 beforehand) was added to a solution of **1** (1 g) in dry pyridine (10 ml) and the suspension was stirred, with exclusion of light, at room temperature. After 6 hr another portion of silver fluoride (0.2 g) was added, and the stirring was continued for further 2 hr. The mixture was diluted with CH_2Cl_2 (50 ml), poured into ice-H_2O (100 ml), filtered, and the filtrate was successively washed with 10% H_2SO_4, satd. $NaHCO_3$, and H_2O. After desiccation ($CaCl_2$), the solvent was removed to afford a sirup which crystallized from EtOH. Recrystallization from EtOH gave pure **7** (613 mg, 74%), mp 128—131.5°, $[\alpha]_D^{26}$ +64.4° (c=0.5, $CHCl_3$). TLC: *Rf* 0.24 (solvent A). IR ν_{max}^{KBr}: 1664 cm^{-1} (C=C). *Anal.* Calcd. for $C_{26}H_{34}O_{17}$: C, 50.49; H, 5.54. Found: C, 50.50; H, 5.69.

1,2,3-Tri-O-acetyl-4-O-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-β-D-*xylo*-hex-5-eno-pyranose (Lactose-5-ene Heptaacetate) (8)——Treatment of **2**[2] (800 mg) as for **7** afforded **8** (504 mg, 76%), mp 166—168°, $[\alpha]_D^{22}$ −59.1° (c=0.99, $CHCl_3$) (lit.[2] mp 168—169°, $[\alpha]_D^{18}$ −57.7° (c=1.04, $CHCl_3$)).

1,2,3-Tri-O-acetyl-4-O-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)-β-D-*xylo*-hex-5-eno-pyranose (Cellobiose-5-ene Heptaacetate) (9)——Treatment of 3[5] (1 g) as for **7** afforded **9** (640 mg, 82%), mp 113—116°, $[\alpha]_D^{24}$ −70° (c=0.98, $CHCl_3$). TLC: *Rf* 0.90 (solvent B). IR ν_{max}^{Nujol}: 1663 cm^{-1} (C=C). *Anal.* Calcd. for $C_{26}H_{34}O_{17}$: C, 50.49; H, 5.54. Found: C, 50.32; H, 5.36.

Catalytic Hydrogenation of Disaccharide-5-ene Heptaacetate——To a solution of compound (each 100 mg of **7**, **8**, or **9**) in solvent (10 ml) was added catalyst: commercial Adams' catalyst having 1—3 mol of H_2O (100 mg), freshly prepared Pd catalyst by reduction[8] of $PdCl_2$ (150 mg) in the same solvent, or Raney Ni catalyst activated[7] from alloy (2 g) was used. The mixture was hydrogenated at room temperature under atmospheric pressure. The catalyst was removed by filtration and the solvent was evaporated to dryness. The residue was chromatographed on a column of silica gel, in which solvent combination (v/v), ether–benzene (1: 2), benzene–ether (1: 2), or hexane–AcOEt (2: 3), was used as eluent of **7**, **8**, or **9**, respectively. The L-ido isomer (**10**, **11**, or **12**) was eluted with the same solvent after elution of the D-gluco isomer (**4**, **5**, or **6**) was completed. The corresponding eluate was evaporated to dryness which crystallized on adding EtOH.

1,2,3-Tri-O-acetyl-4-O-(2,3,4,6-tetra-O-acetyl-α-D-glucopyranosyl)-6-deoxy-α-L-idopyranose (10)——mp 158—159.5°. $[\alpha]_D^{21}$ +28.6° (c=0.64, $CHCl_3$). TLC: *Rf* 0.18 (solvent A). NMR δ: 1.40 (3H, d, $J_{5,6}$=6 Hz, C–C$\underline{H}_3$), 2.00, 2.04, 2.08, 2.10, 2.12 (21H, each s, 7×OAc). *Anal.* Calcd. for $C_{26}H_{36}O_{17}$: C, 50.32; H, 5.85. Found: C, 50.26; H, 5.75.

1,2,3-Tri-O-acetyl-4-O-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)-6-deoxy-α-L-idopyranose (12)——mp 142—144°. $[\alpha]_D^{24}$ −60.3° (c=0.82, $CHCl_3$). TLC: *Rf* 0.77 (solvent B). NMR δ: 1.24 (3H, d, $J_{5,6}$=5 Hz, C–C$\underline{H}_3$), 1.98, 2.00, 2.06, 2.08, 2.10 (21H, each s, 7×OAc). *Anal.* Calcd. for $C_{26}H_{36}O_{17}$: C, 50.32; H, 5.85. Found: C, 50.16; H, 5.76.

6-Deoxy-maltose (13)——To a solution of **4** (165 mg) in dry MeOH (3 ml) was added 0.1 N methanolic sodium methoxide (0.14 ml). The mixture was stirred for 3 hr; complete deacetylation was monitored by

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TLC. Dry Amberlite IR-120 (H^+) resin was added and the suspension was stirred for 30 min, filtered, and the filtrate was concentrated to dryness to give an amorphous powder (60 mg, 60%), $[\alpha]_D^{26}$ +126.3° (c=0.66, H_2O). PPC: *Rf* 0.43 (solvent D), 0.25 (solvent E), 0.29 (solvent F). *Anal.* Calcd. for $C_{12}H_{22}O_{10}\cdot 2H_2O$: C, 39.77; H, 7.23. Found: C, 39.64; H, 7.03.

6-Deoxy-α-cellobiose (14)——Deacetylation of **6** (630 mg) as for **13** afforded **14** (300 mg, 91%). After recrystallization from MeOH, **15** showed mp 242—245° (dec.) and $[\alpha]_D^{28}$ +30°→+25.5° (5 hr) (c=1, H_2O). PPC: *Rf* 0.38 (solvent D), 0.27 (solvent E), 0.23 (solvent F). *Anal.* Calcd. for $C_{12}H_{22}O_{10}$: C, 44.17; H, 6.80. Found: C, 43.74; H, 6.96.

4-O-α-D-Glucopyranosyl-6-deoxy-L-idopyranose (15)——Deacetylation of **10** (330 mg) as for **13** afforded **15** (121 mg, 70%), amorphous powder, $[\alpha]_D^{26}$ +91.2° (c=0.62, H_2O). PPC: *Rf* 0.42 (solvent D), 0.28 (solvent E), 0.32 (solvent F). *Anal.* Calcd. for $C_{12}H_{22}O_{10}\cdot 2H_2O$: C, 39.77; H, 7.23. Found: C, 39.48; H, 7.18.

4-O-β-D-Glucopyranosyl-6-deoxy-L-idopyranose (16)——Deacetylation of **12** (128 mg) afforded **16** (67 mg, 99%), amorphous powder, $[\alpha]_D^{16}$ −28.7° (c=0.65, H_2O). PPC: *Rf* 0.39 (solvent D), 0.24 (solvent E), 0.30 (solvent F). *Anal.* Calcd. for $C_{12}H_{22}O_{10}\cdot 2H_2O$: C, 39.77; H, 7.23. Found: C, 39.85; H, 7.13.

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Purines. XX.[1] Synthesis of 1-Substituted 5-Aminoimidazole-4-carboxamidines and Related Compounds[2]

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Several 1-substituted 5-aminoimidazole-4-carboxamidines (**5g—j**) have been prepared from the corresponding N′-alkoxyamidines (**4a—f**) by catalytic hydrogenolysis. In the hydrogenolysis of **4a—f** using Raney Ni catalyst, addition of one molar equivalent of hydrochloric acid accelerated the reaction to give **5g—j** in acceptable yields. The structures of **5g—j** have been confirmed by cyclization to 9-substituted adenines (**6g—j**) and by alkaline hydrolysis to 1-substituted derivatives (**7g—j**) of 5-aminoimidazole-4-carboxamide (AICA).

Keywords——imidazoles; adenines; alkoxyamidine; amidoxime; catalytic hydrogenolysis; Raney nickel catalyst; palladium-on-carbon; cyclization; hydrolysis

In previous papers[4] from this laboratory, we have already shown that the pyrimidine ring of 1-alkoxyadenines (type **1**) is easily opened under mild hydrolytic conditions to produce imidazole derivatives (types **2** and **4**), and that the formamido derivatives (type **2**) cyclize readily to N^6-alkoxyadenines (type **3**). The synthetic utility of this ring opening reaction

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