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On the Possibility of Direct *O*-1β→ -6 Acyl Migration in 1-*O*-Acyl-β-D-glucose Derivatives[1)]

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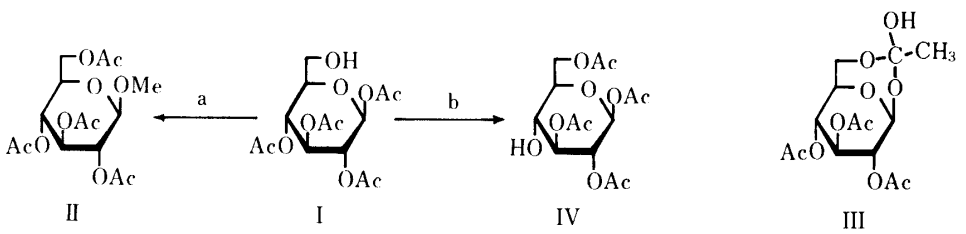
In order to clarify whether or not direct *O*-1β→ -6 acyl migration in *O*-acyl-D-glucose derivatives really occurs, 3-*O*-methyl-1-*O*-myristoyl-β-D-glucopyranose and 3-deoxy-1-*O*-myristoyl-β-D-glucopyranose were synthesized and their acyl migration was examined under thermal, solvolytic, and base- and acid-catalyzed conditions. Neither compound showed any tendency for acyl migration under these conditions (only partial solvolysis was observed under solvolytic conditions). Consequently, it was concluded that *O*-1β→ -6 acyl migration does not occur directly, but proceeds through the path *O*-1β→ -3→ -6.

Keywords——acyl migration; 3-*O*-methyl-1-*O*-myristoyl-β-D-glucopyranose; 3-deoxy-1-*O*-myristoyl-β-D-glucopyranose; *O*-1β→ -6 acyl migration; tuliposide

In 1930, Haworth *et al.*[2)] observed that 1,2,3,4-tetra-*O*-acetyl-β-D-glucose (I) gave, on methylation, methyl 2,3,4,6-tetra-*O*-acetyl-β-D-glucoside (II), and for this process they assumed direct *O*-1β→ -6 acyl migration. They also thought that an isomeric acetate obtained by alkali-catalyzed isomerization of I[3)] was the intermediate 1,6-orthoacetate (III) of the above methylation, but it was later established to be 1,2,3,6-tetra-*O*-acetyl-β-D-glucose (IV) by Bonner,[4)] thus casting doubt on Haworth's initial assumption. Since that time no evidence



II I IV III

a: CH_3I, Ag_2O; b: trace of alkali

Chart 1

of direct *O*-1β→ -6 acyl migration in D-glucose derivatives has appeared in the literature.

In a previous paper,[5)] we clarified the general path of *O*-acyl migration for mono-*O*-myristoyl-D-glucose and -D-glucosides, the result for the former being schematically shown in Chart 2. One of the most important conclusions was that among the conceivable *trans*-migrations those of *O*-1β→ -2 and *O*-3→ -4 do not occur, although *O*-2→ -3 and the reverse migration take place readily. Another important conclusion is that migrations through a $^1C_4$(D) conformation such as *O*-1β→ -3 and *O*-3→ -6 do take place, thus suggesting that the migration of 1β-*O*-acyl- to 6-*O*-acyl-D-glucose proceeds through the path of *O*-1β→ -3→ -6. Our results, however, could not reveal the presence or absence of direct *O*-1β→ -6 migration, which might occur in addition to *O*-3→ -6 migration.

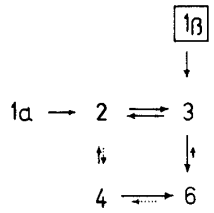
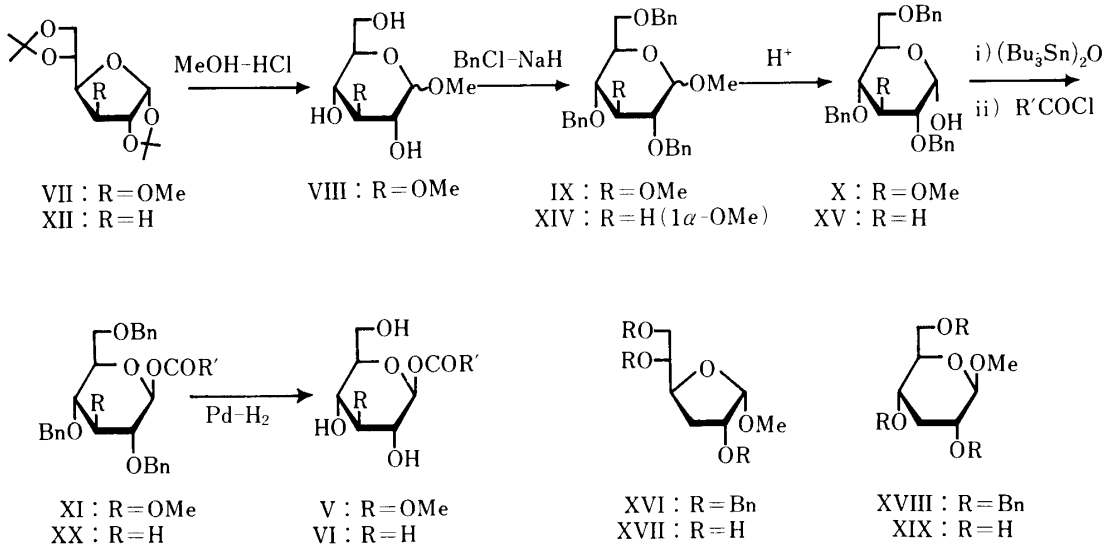


Chart 2. General Paths of *O*-Acyl Migration in D-Glucose Derivatives

Solid arrow: migration observed.
Broken arrow: migration possible but not observed.
Horizontal arrow: migration through $^4C_1$(D) conformation.
Vertical arrow: migration through $^1C_4$(D) conformation.
□, solvolysis in methanol.

The present investigation was undertaken to clarify whether or not direct *O*-1β→ -6 acyl migration really occurs. For this purpose, we have prepared 3-*O*-methyl-1-*O*-myristoyl-β-D-glucopyranose (V) and 3-deoxy-1-*O*-myristoyl-β-D-glucopyranose (VI) and examined their acyl migrations. Both compounds lack OH-3, which would be necessary for *O*-1β→ -3 migration. Therefore, formation of the 6-*O*-acyl derivative from these compounds, if it occurred, would suggest direct *O*-1β→ -6 acyl migration.

3-*O*-Methyl-1-*O*-myristoyl-β-D-glucopyranose (V) was prepared from the known 3-*O*-methyl-1,2;5,6-di-*O*-isopropylidene-α-D-glucofuranose (VII).[6] Acid hydrolysis of VII with MeOH–HCl gave a methyl pyranoside (VIII), which on benzylation by Hakomori's method followed by acid hydrolysis gave crystalline 2,4,6-tri-*O*-benzyl-3-*O*-methyl-α-D-glucopyranose (X). The appearance of only one anomeric proton signal at δ 5.18 (d, J=3.5 Hz) indicated that the compound is the α-anomer with pyranose form. This was converted to the stannic ester on treatment with $(Bu_3Sn)_2O$[7] and acylated with myristoyl chloride to give the 1-*O*-myristoyl derivative (XI). The anomeric proton signals of XI indicated that it is a 17:83 mixture of α- and β-anomer. Benzyl groups were then removed by hydrogenolysis over Pd-black. Chromatography and crystallizations of the product gave the 1β-*O*-myristoyl derivative (V) in a pure crystalline form, mp 163—165 °C. The structure of V was confirmed by the proton nuclear magnetic resonance (^{1}H-NMR) anomeric proton signal at δ 6.29 (d, J=8 Hz) and carbon-13 nuclear magnetic resonance (^{13}C-NMR) C_1 signal at δ 95.7.



Bn : $PhCH_2$- R' : $CH_3(CH_2)_{12}$-

Chart 3

3-Deoxy-1-*O*-myristoyl-β-D-glucopyranose (VI) was synthesized in a manner similar to that used for V from the known 3-deoxy-1,2;5,6-di-*O*-isopropylidene-α-D-glucofuranose (XII).[8] Methanolysis of XII with hot HCl–MeOH gave a somewhat different result from that of the 3-*O*-methyl derivative (VII). Although the gummy product showed only one spot on thin-layer chromatography (TLC), its ^{1}H-NMR showed three OMe peaks (δ 3.34, 3.40, and 3.55), indicating that the product is a mixture of at least three compounds. Eventually benzylation of this mixture gave a product which could be separated to three components by chromatography. The major product (the least mobile one) (40%) was assigned as methyl 2,4,6-tri-*O*-benzyl-3-deoxy-α-D-glucopyranoside (XIV) from the anomeric proton and carbon signals at δ 4.97 (d, J = 3.2 Hz) and δ 97.4, respectively, and was hydrolyzed to the expected 3-deoxy-D-glucose derivative (XV) (this hydrolysis is more rapid than that of the corresponding 3-*O*-methyl derivative (IX)), which crystallized from *n*-hexane–ether as an α-anomer.

The second product (the most mobile one) (20%) was assigned as methyl 2,5,6-tri-*O*-benzyl-3-deoxy-α-D-glucofuranoside (XVI), since the product (XVII) obtained by hydrogenolysis of XVI showed an anomeric proton signal (δ 5.13) with a very small coupling (J = *ca.* 0) and an anomeric carbon signal at δ 110.7, both of which are characteristic of a furanose structure. The third product (the middle one) (20%) was assigned as methyl 2,4,6-tri-*O*-benzyl-3-deoxy-β-D-glucopyranoside (XVIII), since its hydrogenolysis product (XIX) showed an anomeric proton signal (δ 4.59) with a large coupling (d, J = 7.6 Hz) and the anomeric carbon signal at δ 107.7, both of which are characteristic of a pyranose structure.

Compound XV was stannylated as described for X and then converted to the myristate (XX). Interestingly the product was only the β-anomer (as shown by ^{1}H-NMR). Hydrogenolysis of benzyl groups and purification of the product gave the 3-deoxy-1β-*O*-myristoyl derivative (VI), mp 110—112 °C, in a pure form. This showed an anomeric proton signal at δ 6.21 (d, J = 7.8 Hz) and an anomeric carbon signal at δ 97.9, confirming the assigned structure.

Results and Discussion

Acyl migration was carried out under the following four conditions (thermal, solvolytic, and base- and acid-catalyzed): (A) fusion at 170 °C for the 3-*O*-methyl derivative (V) and at 150 °C for the 3-deoxy derivative (VI), (B) standing in MeOH, (C) heating in pyridine, and (D) action of 0.5% *p*-TsOH in dioxane.

First, 3-*O*-methyl-1β-*O*-myristoyl derivative (V) was examined. It was recovered unchanged after exposure to conditions A, C, and D. Under condition B, partial solvolysis of the compound took place, as in the case of 1β-*O*-acyl-D-glucose,[5] giving rise to 3-*O*-methyl-D-glucose and methyl myristate. Fusion at 200 °C produced profound decomposition of the compound, but no 6-*O*-acyl derivative was detected in the product.

There is a possibility that 3-*O*-methyl-1β-*O*-acyl derivatives find it more difficult to adopt a $^1C_4$(D) conformation than 1β-*O*-acyl-D-glucoses for stereochemical reasons; the bulkier 3-OMe group may prevent the compound from adopting a $^1C_4$ conformation. We therefore examined the 3-deoxy-1β-*O*-acyl derivative (VI), which should undergo ring inversion to a $^1C_4$(D) form relatively easily. Again, the compound showed no tendency for acyl migration under the above four conditions. Condition B only resulted in partial solvolysis of the compound to 3-deoxy-D-glucose and methyl myristate.

As shown previously,[5] 1-*O*-myristoyl-β-D-glucose is rather stable to thermal and acid-catalyzed conditions. It was recovered unchanged on fusion at 150 °C (condition A) and after standing in dioxane containing 0.5% *p*-TsOH (condition D), whereas under these conditions the 3-*O*-myristoyl group readily migrated to OH-6. This implies that the 1β-*O*-acyl derivative is less able to take the $^1C_4$(D) conformation than is the 3-*O*-acyl derivative. The stability of the

1β-*O*-acyl group in the 3-*O*-methyl (V) and 3-deoxy (VI) derivatives under the above conditions is therefore not exceptional.

On the other hand, 1-*O*-myristoyl-β-D-glucose migrates under the base-catalyzed condition (condition C). On heating of the compound in pyridine at 120 °C, 60% of the 1β-*O*-acyl group migrates within 1 h to OH-3 and OH-6, indicating that ring inversion of 1β-*O*-acyl-D-glucose to a $^1C_4$ form is actually taking place in pyridine. The 3-*O*-acyl group, of course, migrates under this condition. This ring inversion will be facilitated for the 3-deoxy derivative, since two 1,3-diaxial interactions are eliminated in the $^1C_4$(D) form. Therefore, lack of *O*-1β→ -6 acyl migration in 3-deoxy-1-*O*-myristoyl-β-D-glucose (VI) under the above conditions indicates that direct *O*-1β→ -6 acyl migration in 1-*O*-acyl-β-D-glucopyranose is very difficult. In accordance with our conclusion, Tanaka *et al.*[9] isolated only 3-*O*-acyl-β-D-glucopyranose on hydrolysis of 1-*O*-acyl-4,6-*O*-benzylidene-β-D-glucopyranose with AcOH (95 °C, 2 h).

The lack of the above path in 1β-*O*-acyl-D-glucopyranose is probably due to the relative instability of a trioxepine intermediate (*O*-1β→ -6) with respect to an *m*-dioxane intermediate (*O*-1β→ -3). However, the possibility that this path may operate under different conditions is not completely excluded.

In 1968, Tschesche *et al.*[10] isolated from *Tulipa gesneriana* L. a bacterio- and fungi-toxic principle, tuliposide-A, elucidating the structure as 1-*O*-(γ-hydroxy-α-methylenebutyroyl)-β-D-glucopyranose. According to them, tuliposide-A readily rearranges to the biologically inactive 6-*O*-acyl derivative merely on standing at room temperature. The nature of Tschesche's tuliposide is surprisingly different from that of our 1β-*O*-acyl derivatives. We consider that tuliposide-A, if its structure is as proposed, should be stable to acyl migration at room temperature, but should be unstable to solvolysis. Very recently we have synthesized the compound having the structure of Tschesche's tuliposide-A, and confirmed that, on standing at room temperature, it decomposed into D-glucose and α-methylene-γ-butyrolactone by intramolecular solvolysis, but no acyl migration was observed.[11]

Experimental

General——Melting points were determined on a Yanagimoto micro hot stage melting point apparatus and are uncorrected. The infrared (IR) spectra were taken as KBr disks on a Jasco A202 spectrometer and are given in cm^{-1}. Optical rotations were measured in $CHCl_3$ or MeOH with a Jasco DIP-181 digital polarimeter. ^{1}H-NMR (100 MHz) spectra were recorded with a JEOL FX-100 FT NMR spectrometer in chloroform-*d* or in pyridine-d_5 (pyr-d_5) solution with tetramethylsilane as an internal standard. Column chromatography was performed on Wakogel C-200 (silica gel). For TLC, Kieselgel $60F_{254}$ precoated plates were used and spots were visualized by spraying 1% $Ce(SO_4)_2$ in 10% H_2SO_4 and heating the plates at 100 °C until coloration took place.

1,2;5,6-Di-*O*-isopropylidene-3-*O*-methyl-α-D-glucofuranose (VII)——Compound VII was synthesized from 1,2;5,6-di-*O*-isopropylidene-α-D-glucofuranose by methylation according to Hakomori's procedure, as a colorless syrup (yield, 86%), bp 170 °C (4 mmHg), $[\alpha]_D^{18}$ −37° (*c* = 1.0, abs. EtOH) [lit. bp 105 °C (3 mmHg), $[\alpha]_D^{20}$ −34° (*c* = 1.2, abs. EtOH)].[6]

Methyl 3-*O*-Methyl-α- and β-D-Glucopyranoside (VIII)——The 3-*O*-methyl derivative (VII) (3.5 g, 12.7 mmol) was heated under reflux in methanol (38.7 ml) containing conc. HCl (0.75 ml) for 6 h. The cooled reaction mixture was neutralized with Amberlite IRA-400 (HCO_3^- form), filtered, and concentrated *in vacuo* to leave a syrup, which was chromatographed. Elution with $CHCl_3$–MeOH (10 : 1) gave VIII as a colorless syrup (2.0 g, 75%). IR (film): 3370, 2940, 2830, 890. ^{1}H-NMR ($CDCl_3$) δ: 3.44 and 3.68 (each 3H, s, –OMe), 4.23 (0.4H, d, *J* = 7.5 Hz, C_1–H (β-anomer)), 4.74 (0.6H, d, *J* = 3.5 Hz, C_1–H (α-anomer)).

Methyl 2,4,6-Tri-*O*-benzyl-3-*O*-methyl-α- and β-D-Glucopyranoside (IX)——Dimsyl anion [prepared from 50% NaH (0.6 g) and dimethylsulfoxide (DMSO) (5 ml)] was added to a solution of VIII (1.70 g, 8.17 mmol) in DMSO (15 ml) and the mixture was stirred for 2 h at room temperature under an argon atmosphere. Benzyl chloride (1.6 g, 1.5 eq mol) was added dropwise to the above solution and the reaction mixture was stirred for 3 h at room temperature under an argon atmosphere. The mixture was poured into ice water and extracted with $CHCl_3$. The extract was washed with water several times, dried over Na_2SO_4, and concentrated to give a pale yellow syrup, which was chromatographed in $CHCl_3$. Concentration of the $CHCl_3$ eluate gave IX as a colorless syrup (3.3 g, 85%). IR (film): 3025, 1500, 1450. ^{1}H-NMR ($CDCl_3$) δ: 3.35 and 3.68 (each 3H, s, –OMe).

2,4,6-Tri-*O*-benzyl-3-*O*-methyl-α-D-glucopyranose (X)——The benzyl derivative (IX) (2.3 g, 4.8 mmol) was dissolved in hot AcOH (20 ml), boiling 2 N H_2SO_4 (6 ml) was added, and the mixture was refluxed for 2 h on an oil bath. Then another 5 ml of boiling 2 N H_2SO_4 was added and heating was continued for a further 3 h. The cooled mixture was extracted with $CHCl_3$ (150 ml). The extract was washed with water, $NaHCO_3$ aq. and water, dried over Na_2SO_4, and concentrated to give a syrup, which was chromatographed over Florisil eluting with benzene, CH_2Cl_2, and $CHCl_3$. The CH_2Cl_2 eluate gave X (1.7 g, 80%), as colorless needles from *n*-hexane–ether, mp 124—125 °C, $[\alpha]_D^{19}$ +48° ($c=1.0$, $CHCl_3$). The optical rotation was unchanged after 24 h. IR: 3400, 3030, 855. ^{1}H-NMR ($CDCl_3$) δ: 7.28—7.43 (15H, Ph × 3), 5.18 (1H, d, $J=3.5$ Hz, C_1–H), 3.68 (6H, s, –OMe × 2). *Anal.* Calcd for $C_{28}H_{32}O_6$: C, 72.39; H, 6.94. Found: C, 72.25; H, 6.81.

2,4,6-Tri-*O*-benzyl-3-*O*-methyl-1-*O*-myristoyl-α- and β-D-Glucopyranoside (XI)——A mixture of X (560 mg, 1.2 mmol) and $(Bu_3Sn)_2O$ (930 mg, 1.3 eq mol) in dry toluene (15 ml) was refluxed for 30 min, then half of the solvent was distilled off to remove moisture as an azeotropic mixture. To this mixture, myristoyl chloride (770 mg, 2.6 eq mol) in dry pyridine (2 ml) was added dropwise at 0 °C, and the whole was stirred overnight at room temperature. The reaction mixture was poured into ice water and extracted with ether. The ethereal extract was washed with water, sat. $NaHCO_3$ aq. and water, dried over Na_2SO_4, and concentrated to give a colorless syrup, which was passed through a short silica gel column eluting with benzene to yield a semi-solid (800 mg). This was dissolved in *n*-hexane and passed through a short column of basic alumina. Concentration of the eluate gave XI as a solid. IR: 1755, 940. ^{1}H-NMR ($CDCl_3$) δ: 7.22—7.34 (15H, Ph × 3), 6.33 (0.17H, d, $J=3.5$ Hz, C_1–H (α-anomer)), 5.37 (0.83H, d, $J=8$ Hz, C_1–H (β-anomer)), 3.64 (3H, s, –OMe).

3-*O*-Methyl-1-*O*-myristoyl-β-D-glucopyranose (V)——The above solid (XI) in EtOH (20 ml)–CH_2Cl_2 (20 ml) was hydrogenolyzed over Pd-black (500 mg) for 4 h at room temperature. Chromatography of the product in $CHCl_3$–MeOH (20 : 1) gave a solid, which was crystallized from acetone to give V (400 mg, 83%) as colorless needles, mp 163—165 °C, $[\alpha]_D^{19}$ −1.9° ($c=1.0$, MeOH). IR: 1732, 947. ^{1}H-NMR (pyr-d_5) δ: 6.29 (1H, d, $J=8$ Hz, C_1–H), 3.92 (3H, s, –OMe). ^{13}C-NMR (pyr-d_5) δ: 95.7 (C_1), 73.6 (C_2), 88.4 (C_3), 70.2 (C_4), 79.1 (C_5), 61.9 (C_6). *Anal.* Calcd for $C_{21}H_{40}O_7$: C, 62.35; H, 9.97. Found: C, 62.60; H, 10.20.

3-Deoxy-1,2;5,6-di-*O*-isopropylidene-α-D-glucofuranose (XII)——The title compound (XII) was synthesized from 1,2;5,6-di-*O*-isopropylidene-α-D-glucofuranose according to the method of Barton and McCombie,[8] as an oil, $[\alpha]_D^{18}$ −7.2° ($c=5$, EtOH) [lit. $[\alpha]_D^{20}$ −7.5° ($c=10$)].[8]

Methyl 3-Deoxy-D-glucosides (XIII)——A solution of XII (4.0 g, 16.4 mmol) in methanol (20 ml) containing 1 N HCl–MeOH (10 ml) was heated under reflux for 8 h. The cooled mixture was neutralized with Amberlite IRA-400 (HCO_3^- form), filtered, and concentrated to give a syrup, which was chromatographed. Concentration of the acetone eluate gave a colorless syrup (XIII) (2.3 g, 79%), which showed a single spot ($Rf=0.53$) on TLC (solvent, $CHCl_3$: MeOH = 3 : 1) but the ^{1}H-NMR spectrum (in pyr-d_5) exhibited three OMe peaks (δ 3.34, 3.40, and 3.55).

Benzylation of Methyl 3-Deoxy-D-glucosides (XIII)——A solution of methyl 3-deoxy-D-glucosides (XIII) (2.2 g) in DMSO (20 ml) was added dropwise to a solution of sodium hydride (2.0 g) in DMSO (30 ml) and the mixture was stirred for 1 h at room temperature under an argon atmosphere. Benzyl chloride (13 g) in DMSO (10 ml) was then added to the above mixture, and the whole was stirred for a further 3 h at room temperature. Work-up of the product in the usual manner gave a pale yellow syrup (4.2 g, 76%), which showed one major spot A ($Rf=0.45$) and two minor spots, B and C ($Rf=0.54$ and 0.60), on TLC (solvent, AcOEt : *n*-hexane = 1 : 3). The ^{1}H-NMR spectrum (in $CDCl_3$) exhibited three OMe peaks (δ 3.36, 3.48, and 3.59). Chromatography of this syrup on a silica gel column eluting with *n*-hexane–AcOEt (10 : 1) separated the components to yield C ($Rf=0.60$; OMe, 3.36), B ($Rf=0.54$; OMe, 3.59), and A ($Rf=0.45$; OMe, 3.48) each as a syrup. A (XIV, 40%): ^{1}H-NMR (pyr-d_5) δ: 7.2—7.5 (15H, Ph × 3), 4.97 (1H, d, $J=3.2$ Hz, C_1–H), 4.4—4.9 (7H), 3.5—4.1 (4H), 3.40 (3H, s, –OMe), 2.4—2.7 (1H, C_3–H), 2.0—2.4 (1H, C_3–H). ^{13}C-NMR (pyr-d_5) δ: 97.4 (C_1), 75.0, 73.4, 72.7, 71.5, 70.9, 70.7, 70.0, 54.7 (OMe), 30.9 (C_3). MS: *m/z* 417 (M^+ −OMe), 325, 253, 219, 181, 161, 91. B (XVIII, 20%): ^{1}H-NMR (pyr-d_5) δ: 7.2—7.5 (15H, Ph × 3), 4.50 (1H, d, $J=7.5$ Hz, C_1–H), 4.3—5.2 (8H), 3.55 (3H, s, –OMe), 3.3—4.0 (3H), 2.6—2.9 (1H, C_3–H), 1.5—1.9 (1H, C_3–H). MS *m/z*: 417 (M^+ −OMe), 357, 325, 253, 181, 163, 148, 91. C (XVI, 20%): ^{1}H-NMR (pyr-d_5) δ: 7.2—7.5 (15H, Ph × 3), 5.20 (1H, s, C_1–H), 4.5—5.0 (7H), 3.7—4.2 (4H), 3.34 (3H, s, –OMe), 2.2—2.4 (2H, C_3–H_2). MS *m/z*: 416, 325, 281, 219, 181, 91.

Compound B (XVIII) was hydrogenolyzed in CH_2Cl_2–MeOH over Pd-black to give a syrup (XIX). ^{1}H-NMR (pyr-d_5) δ: 4.59 (1H, d, $J=7.6$ Hz, C_1–H), 3.7—4.5 (5H), 3.59 (3H, s, –OMe), 2.7—3.0 (1H, C_3–H), 1.98—2.36 (1H, C_3–H). ^{13}C-NMR (pyr-d_5) δ: 107.7 (C_1), 68.9 (C_2), 41.3 (C_3), 65.9 (C_4), 82.0 (C_5), 62.8 (C_6), 56.7 (OMe).

Compound C (XVI) was hydrogenolyzed as above to give a syrup (XVII). ^{1}H-NMR (pyr-d_5) δ: 5.13 (1H, s, C_1–H), 4.4—5.1 (3H), 3.3—3.6 (1H), 3.27 (3H, s, –OMe), 2.3—2.7 (2H, m, C_3–H_2). ^{13}C-NMR (pyr-d_5) δ: 110.7 (C_1), 76.6 (C_2), 36.3 (C_3), 75.9 (C_4), 81.1 (C_5), 65.3 (C_6), 54.4 (OMe).

2,4,6-Tri-*O*-benzyl-3-deoxy-α-D-glucopyranose (XV)——Compound A (XIV) (1.80 g) was dissolved in hot AcOH (20 ml), then boiling 2 N H_2SO_4 (6 ml) was added, and the mixture was gently refluxed for 2 h. Work-up as described for X gave XV (1.40 g, 80%), mp 70—73 °C, as colorless needles from *n*-hexane–ether. $[\alpha]_D^{19}$ +43° ($c=1.0$, $CHCl_3$). This value was unchanged after 24 h. IR: 3430, 3040, 1500, 1460, 835. ^{1}H-NMR (pyr-d_5) δ: 7.20—7.50 (15H, Ph × 3), 5.76 (1H, d, $J=3.2$ Hz, C_1–H). *Anal.* Calcd for $C_{27}H_{30}O_5$: C, 74.63; H, 6.96. Found: C, 74.40; H, 6.97.

2,4,6-Tri-*O*-benzyl-3-deoxy-1-*O*-myristoyl-β-D-glucopyranose (XX)——The deoxy compound (XV) (290 mg,

0.67 mmol) was treated with $(Bu_3Sn)_2O$ followed by myristoyl chloride as described for X. Chromatography of the product in benzene gave the 1β-*O*-myristate (XX), as a semi-solid (432 mg, quantitative yield). IR (film): 3040, 1727, 1700, 1452, 907. ^{1}H-NMR ($CDCl_3$) δ: 7.24—7.32 (15H, Ph × 3), 5.61 (1H, d, J=8 Hz, C_1–H).

3-Deoxy-1-*O*-myristoyl-β-D-glucopyranose (VI)——The 3-deoxy-1β-*O*-myristate (XX) (380 mg) was hydrogenolyzed as described for V to give VI (150 mg, 71%), mp 110—113 °C, as colorless needles from acetone. $[\alpha]_D^{19}$ −7.4° (c=1.0, MeOH). IR: 1730. ^{1}H-NMR (pyr-d_5) δ: 6.21 (1H, d, J=7.8 Hz, C_1–H), 4.04—4.52 (6H, $C_{2,4,5,6}$–H), 3.80—4.04 (1H, m, C_3–H), 2.80—3.04 (1H, m, C_3–H). ^{13}C-NMR (pyr-d_5) δ: 97.9 (C_1), 67.9 (C_2), 41.5 (C_3), 65.2 (C_4), 82.9 (C_5), 62.2 (C_6). *Anal.* Calcd for $C_{20}H_{38}O_6$: C, 64.41; H, 10.23. Found: C, 64.21; H, 10.26. The corresponding 1-*O*-stearate was also prepared. mp 121—122 °C, as colorless leaflets from acetone. $[\alpha]_D^{19}$ −7.9° (c=1.0, MeOH). *Anal.* Calcd for $C_{24}H_{46}O_6$: C, 66.94; H, 10.77. Found: C, 67.01; H, 11.00.

Myristoylation of 3-*O*-Methyl-D-glucopyranose——a) Direct Myristoylation: Myristoyl chloride (2 eq mol) in dry CH_2Cl_2 (1 ml) was added dropwise to a solution of 3-*O*-methyl-D-glucopyranose (60 mg, 0.3 mmol) in dry pyridine (10 ml) at 0 °C, and the mixture was stirred overnight at room temperature. Maximum conversions were checked by TLC. The mixture was poured into ice water and extracted with $CHCl_3$. The extract was washed with water several times, then concentrated *in vacuo* to give a gum, which was chromatographed on Florisil. The benzene eluate gave a di- and tri-myristate mixture, which was not further investigated. The $CHCl_3$ eluate gave mono-myristate (44 mg) which showed two very close spots (triple development) on TLC. This product was a mixture of 6-*O*-myristate (gas chromatography (GC): t_R, 9.6 min (α-anomer) and 10.5 min (β-anomer)) and 1β-*O*-myristate (GC: t_R, 9.6 min) (*ca.* 9 : 1) as determined by ^{13}C-NMR.

b) $(Bu_3Sn)_2O$ Method: A mixture of 3-*O*-methyl-D-glucopyranose (500 mg, 2.57 mmol) and $(Bu_3Sn)_2O$ (1.5 eq mol) in dry toluene (25 ml) was heated at 140 °C for 2 h under an argon atmosphere. Myristoyl chloride (3 eq mol) in dry toluene (5 ml) was added dropwise to the above solution at 0 °C, and the mixture was stirred overnight at room temperature. The mixture was applied to a column of Florisil which was eluted with *n*-hexane, benzene, $CHCl_3$, and acetone. Concentration of the $CHCl_3$ and acetone eluates gave a solid, which was a mixture of di- and mono-myristate, and the starting material. Chromatography of this solid on silica gel (2 × 10 cm) eluting with $CHCl_3$–MeOH (20 : 1) gave di-myristates (305 mg, 42%) and mono-myristate (542 mg, 52%) which was a mixture of 6-*O*-myristate and 1β-*O*-myristate (*ca.* 8 : 1) as identified by ^{13}C-NMR. ^{13}C-NMR (pyr-d_5) of 3-*O*-methyl-6-*O*-myristoyl-D-glucopyranose: α-anomer, δ 94.1 (C_1), 73.9 (C_2), 85.5 (C_3), 71.3 (C_4), 70.7 (C_5), 64.8 (C_6); β-anomer, δ 98.8 (C_1), 76.4 (C_2), 88.3 (C_3), 70.9 (C_4), 75.0 (C_5), 64.7 (C_6).

Acyl Migration——The following conditions were employed. (A) Thermal condition (fusion): a sample was heated in an open capillary at 170 or 200 (for V) and 150 °C (for VI) for 10 min. (B) Solvolytic condition: a sample in MeOH was kept in a sealed tube at 27 °C for a week. (C) Base-catalyzed condition: a sample in pyridine was heated in a sealed tube at 120 °C for 8 h. (D) Acid-catalyzed condition: a sample in dioxane containing 0.5% *p*-TsOH was kept in a sealed tube at 27 °C for 48 h.

Analysis of the Product——The reaction mixtures from the above reactions were analyzed by ^{13}C-NMR and by GC after conversion to the trimethylsilyl derivatives as described in a previous paper.[5]

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References and Notes

1) Utilization of Sugars in Organic Synthesis. XII. Part XI: ref. 5*b*.
2) W. N. Haworth, E. L. Hirst, and E. G. Teece, *J. Chem. Soc.*, **1930**, 1405.
3) B. Helferich and W. Klein, *Justus Liebigs Ann. Chem.*, **450**, 219 (1926); *idem, ibid.*, **455**, 173 (1927).
4) W. A. Bonner, *J. Am. Chem. Soc.*, **80**, 3697 (1958).
5) *a*) Y. Tsuda and K. Yoshimoto, *Carbohydr. Res.*, **87**, C1 (1981); *b*) K. Yoshimoto and Y. Tsuda, *Chem. Pharm. Bull.*, **31**, 4324 (1983).
6) R. S. Tipson "Methods in Carbohydrate Chemistry," Vol. II, ed. by R. L. Whistler, M. L. Wolfrom, and J. N. BeMiller, Academic Press Inc., New York and London, 1963, p. 154.
7) *a*) T. Ogawa, M. Nozaki, and M. Matsui, *Carbohydr. Res.*, **60**, C7 (1978); *b*) K. Yoshimoto, K. Tahara, S. Suzuki, K. Sasaki, Y. Nishikawa, and Y. Tsuda, *Chem. Pharm. Bull.*, **27**, 2661 (1979).
8) D. H. R. Barton and S. W. McCombie, *J. Chem. Soc., Perkin Trans. 1*, **1975**, 1574.
9) A. K. Tanaka, A. Kobayashi, and K. Yamashita, *Agric. Biol. Chem.*, **43**, 2537 (1979).
10) R. Tschesche, F. J. Kammerer, and G. Wulff, *Chem. Ber.*, **104**, 2057 (1969).
11) K. Yoshimoto, M. Taru, and Y. Tsuda, *Tetrahedron Lett.*, **24**, 2779 (1983).