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Syntheses and ^{1}H- and ^{13}C-Nuclear Magnetic Resonance Spectra of All Positional Isomers of Methyl Mono-*O*-tetradecanoyl-α- and β-D-Glucopyranosides[1,2]

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All the isomers of the mono-*O*-myristoyl derivative of methyl α- and β-D-glucopyranosides were unambiguously prepared, and their ^{1}H- and ^{13}C-NMR spectra are discussed in relation to the stereochemistry of the pyranose ring and ester grouping.

The acylation shifts on introducing a myristoyl group at each carbon atom of the pyranose ring in the acyl derivatives were tabulated and were shown to be additive parameters for diacyl derivatives. A diacyl mixture obtained by direct acylation of methyl β-D-glucopyranoside could be completely analyzed by ^{13}C-NMR. The effects of orientational differences of an anomeric methoxyl group on pyranose carbon shielding were also clarified in every mono-*O*-myristoyl-D-glucopyranoside. An anomalous effect at C^2 of the 2-*O*-acyl derivative is suggested to originate from a conformational change of the ester group in the β-anomer.

Keywords——selective acylation; methyl mono-*O*-acyl-D-glucoside; GC; ^{1}H-NMR; ^{13}C-NMR; acylation shift; additivity of shifts; steric interaction effect

In the preceding paper[4] we reported regioselective syntheses of all isomeric mono-*O*-acyl-D-glucopyranoses possessing caprinoyl to stearoyl moieties as the acyl group and described their physical and spectroscopic properties. The 2-*O*-acyl and 4-*O*-acyl derivatives were found to be anomeric mixtures of α- and β-forms, giving complex spectral patterns in pyridine solution. To make possible detailed analyses of the nuclear magnetic resonance (NMR) spectra of these anomeric mixtures, we intended to prepare mono-O-acyl derivatives of anomerically homogeneous methyl D-glucopyranosides. In addition, the preparation of all the positional and stereochemical isomers of such mono-O-acylglucosides and examination of their physical and spectroscopic properties were expected to provide information useful for the structural elucidation of naturally occurring acylsugar derivatives, since most acylglucose derivatives in nature occur as glucosides (usually in the β-form).

This paper describes regioselective syntheses of all isomers of mono-*O*-tetradecanoyl derivatives of methyl α- and β-D-glucopyranosides (Iα and Iβ) and presents analyses of their ^{1}H–(PMR) and ^{13}C–NMR (CMR) spectra.

Our syntheses of these acyl derivatives essentially followed the method employed in the preceding paper[4] (see Chart 1). After the preparation of suitably protected mono-*O*-acylglucoside derivatives, the protecting group (s) were removed by hydrogenolysis under neutral conditions to avoid acid- or base-catalyzed acyl migration, and the homogeneities of the resulting mono-*O*-acylglucosides were confirmed in every case by gas chromatography (GC) of their trimethylsilyl (TMS) derivatives. The tetradecanoyl (myristoyl) moiety was chosen as

1) Part II of "Utilization of Sugars in Organic Synthesis." Part I: ref. 4)
2) A part of this work was presented at the 99th Annual Meeting of the Pharmaceutical Society of Japan, Sapporo, August, 1979, Abstr., p. 212.
3) Location: *13-1 Takara-machi, Kanazawa 920, Japan.*
4) K. Yoshimoto, K. Tahara, S. Suzuki, K. Sasaki, Y. Nishikawa, and Y. Tsuda, *Chem. Pharm. Bull.*, **27**, 2661 (1979).

an acyl group for comparison of the spectral data with those obtained in previous mono-*O*-acylglucose series.

Regioselective Syntheses of Methyl Mono-*O*-tetradecanoyl-*α*- and *β*-D-glucopyranosides

The syntheses started from the 4,6-*O*-benzylidene derivatives (II*α* and II*β*). Many partial acylation studies[5,6] have suggested differences between the reactivities of the hydroxy groups in the *α*- and *β*-glucosides, although the products vary depending upon the acylating agents and the reaction conditions, and have not always been rigorously established.[6] For example, with toluene-*p*-sulfonyl chloride in pyridine as the acylating agent, the *β*-isomer (II*β*) gave the 3-*O*-sulfonate in greater yield than that substituted at position 2, whereas the *α*-isomer (II*α*) gave a high yield of the 2-*O*-sulfonate under similar reaction conditions.[5d]

Acylation of II*α* and II*β* with 1.5—2 eq. mol of myristoyl chloride in pyridine confirmed the above results. From the *α*-isomer (II*α*) 2-*O*-myristate (IV*α*) was obtained exclusively (60%) together with 2,3-di-*O*-myristate (III*α*) (~20%). Although the formation of 3-*O*-myristate (V*α*) was indicated by thin layer chromatography (TLC), its ratio to 2-*O*-myristate was *ca.* 1:10.[7] In contrast, the *β*-isomer (II*β*) gave a *ca.* 2:3[7] mixture of 2-*O*-myristate (IV*β*) and 3-*O*-myristate (V*β*) in addition to 2,3-di-*O*-myristate (III*β*).

Compd.	R^1	R^2	R^3	R^4
I	H	H	H	H
II	H	H	PhCH<	
III	RCO	RCO	PhCH<	
IV	RCO	H	PhCH<	
V	H	RCO	PhCH<	
VI	RCO	RCO	H	H
VII	RCO	H	H	H
VIII	H	RCO	H	H
IX	Cbz	H	PhCH<	
X	H	Cbz	PhCH<	
XI	Cbz	RCO	PhCH<	
XII	RCO	Cbz	PhCH<	
XIII	Bn	Bn	PhCH<	
XIV	Bn	Bn	H	H
XV	Bn	Bn	H	Cbz
XVI	H	H	RCO	H
XVII	Bn	Bn	RCO	RCO
XVIII	Bn	Bn	RCO	Cbz
XIX	H	H	RCO	RCO
XX	H	H	H	RCO
XXI	RCO	H	H	RCO
XXII	H	RCO	H	RCO

Bn: $PhCH_2$– Cbz: $PhCH_2OCO$–

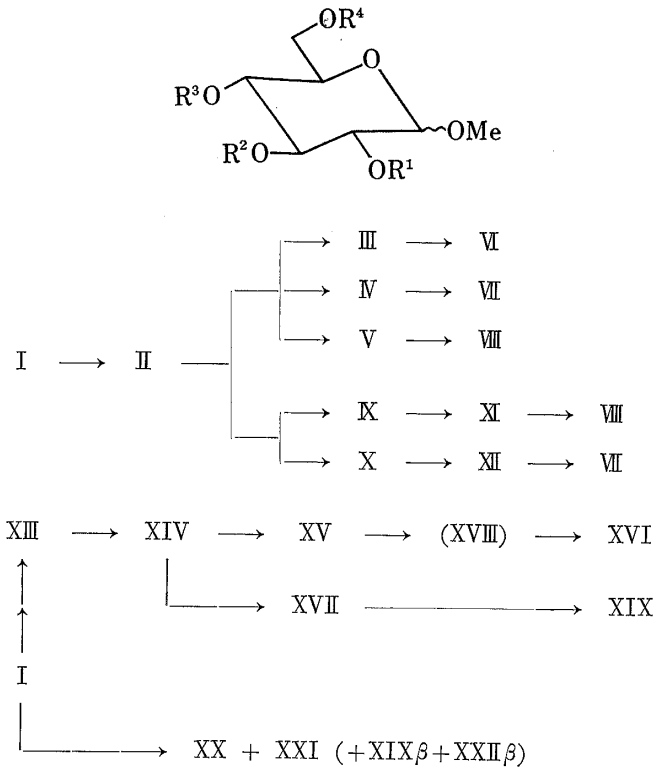


Chart 1

5) *a*) R.W. Jeanloz and D.A. Jeanloz, *J. Am. Chem. Soc.*, **79**, 2579 (1957); *b*) J.J. Willard, J.S. Brimacombe, and R.P. Brueton, *Canad. J. Chem.*, **42**, 2560 (1964); *c*) G.N. Bollenback and F.W. Parrish, *Carbohyd. Res.*, **17**, 431 (1971); *d*) R.D. Guthrie, Anne M. Prior, and S.E. Creasey, *J. Chem. Soc.* (*C*), **1970**, 1961; *e*) S.A. Abbas and A.H. Haines, *Carbohyd. Res.*, **39**, 358 (1975); *f*) H. Hönig and H. Weidmann, *Carbohyd. Res.*, **39**, 374 (1975); *g*) R.M. Munavu and H.H. Szmant, *J. Org. Chem.*, **41**, 1832 (1976) and references cited therein.

6) E.J. Bourne, M. Stacey, C.E.M. Tatlow, and J.C. Tatlow, *J. Chem. Soc.*, **1951**, 826.

7) The ratio was determined as follows. The 4,6-*O*-benzylidene mono-*O*-myristate mixture was hydrogenolyzed over Pd-black and the resulting mono-*O*-myristate was converted to the TMS derivative, then analyzed by GC.

Acylation of IIα and IIβ with carbobenzoxy chloride (CbzCl) gave similar results, though the reaction was less regioselective, as suggested previously[4]; IIα gave the 2-*O*-Cbz derivative (IXα) exclusively and IIβ gave both the 2-*O*-Cbz and 3-*O*-Cbz isomers (IXβ and Xβ) with a preponderance of the latter. Further acylation of IXα, IXβ, and Xβ with myristoyl chloride gave the corresponding *O*-myristates (XIα, XIβ, and XIIβ).

Hydrogenolysis of the Cbz derivatives (XIα and XIIβ) over Pd-black gave interesting results; the Cbz group was removed first, giving rise to methyl 4,6-*O*-benzylidene-3-*O*-myristoyl-α-D-glucopyranoside (Vα) and methyl 4,6-*O*-benzylidene-2-*O*-myristoyl-β-D-glucopyranoside (IVβ), the minor products in the acylation of IIα and IIβ, respectively.

Hydrogenolysis of these protected acylglucosides in ethanol over Pd-black yielded the desired 2- and 3-mono-*O*-myristoyl-D-glucopyranosides (VIIα, VIIβ, VIIIα, and VIIIβ) and the 2,3-di-*O*-myristoyl derivatives (VIα and VIβ).

For the preparation of the 4-*O*-myristates (XVIα and XVIβ), the 4,6-*O*-benzylidene derivatives (IIα and IIβ) were converted to the known 2,3-di-*O*-benzyl derivatives (XIIIα and XIIIβ),[8] which were hydrolyzed with acetic acid to the 4,6-dihydroxy derivatives (XIVα and XIVβ, respectively). Partial acylation of XIVα and XIVβ with CbzCl gave the 6-*O*-Cbz derivatives (XVα and XVβ) in good yield: these were then acylated with myristoyl chloride to give 6-*O*-Cbz-4-*O*-myristates (XVIIIα and XVIIIβ) and hydrogenolyzed as above to yield the desired methyl 4-*O*-myristoyl-α- and β-D-glucopyranosides (XVIα and XVIβ, respectively). Previously, Yoshimoto *et al.*[4] reported partial 4→6 acyl migration during hydrogenolysis of benzyl 2,3-di-*O*-benzyl-6-*O*-Cbz-4-*O*-myristoyl-α-D-glucopyranoside to 4-*O*-myristoyl-D-glucopyranose. However, such an acyl migration was not observed during the present transformations.

Complete acylation of XIVα and XIVβ with myristoyl chloride and hydrogenolysis of the resulting dimyristates (XVIIα and XVIIβ) afforded the corresponding 4,6-di-*O*-myristates (XIXα and XIXβ).

The 6-*O*-myristates (XXα and XXβ) might be conveniently prepared by direct acylations of Iα and Iβ, since the primary hydroxy groups of carbohydrates are considered to be more reactive to acylation than the secondary hydroxy groups.[9] Acylations of Iα and Iβ with a limited amount of myristoyl chloride in pyridine at 100° gave, as expected, the 6-*O*-myristoyl derivatives (XXα and XXβ) as major products together with some di- and tri-*O*-acyl derivatives.

Interestingly, remarkable differences in composition were observed between the dimyristate fraction obtained from α-D-glucoside and that from β-D-glucoside. The α-isomer (Iα) gave 2,6-di-*O*-myristate (XXIα) exclusively, which became the major product when the acylation was carried out with an excess (1.5 eq. mol) of acyl chloride, in agreement with the suggestion that 2-OH is the most reactive when acylation of α-D-glucopyranoside is carried beyond the stage of the primary hydroxy group.[5c,9,10] In contrast, the β-isomer (Iβ) gave a mixture of three dimyristates, which was separated into two fractions in almost equal amounts by chromatography on silica gel. GC and CMR analyses of these fractions revealed that the more mobile one (Fr. 7) was the 3,6-di-*O*-myristate (XXIIβ) and the less mobile fraction (Fr. 8) was a mixture of the 2,6-di-*O*-myristate (XXIβ) and 4,6-di-*O*-myristate (XIXβ) with a slight excess of the former (see below). These results indicate that the reactivities of the hydroxy groups in methyl β-D-glucopyranoside (Iβ) are, in contrast to those suggested for the α-D-glucopyranoside (Iα) (6-OH>2-OH>3-OH>4-OH),[10] in the following order: 6-OH⋙3-OH>2-OH>4-OH. This is in accord with the results obtained in selective benzoylation

8) *a*) D.J. Bell and J. Lorber, *J. Chem. Soc.* (*C*), **1940**, 453; *b*) J.C. Dennison and D.I. McGilrray, *J. Chem. Soc.*, **1951**, 1616; *c*) Y. Kondo, *Agr. Biol. Chem.*, **39**, 1879 (1975).
9) J.M. Sugihara, *Adv. Carbohydr. Chem.*, **8**, 1 (1953).
10) J.M. Williams and A.C. Richardson, *Tetrahedron*, **23**, 1369 (1967).

of methyl 6-deoxy-α- and β-D-glucopyranosides.[11]

TLC and GC of Methyl *O*-Myristoyl-D-glucopyranosides

All the mono-*O*-myristoyl-D-glucopyranosides had *Rf* values between 0.4 and 0.6 with $CHCl_3$–MeOH (10: 1) as a solvent system (Table I), indicating that they are scarcely distinguishable by TLC.

GC as the TMS derivatives (Table I) gave well separated peaks in most cases for each anomeric series, suggesting that this method may be suitable for analyzing acylglucoside mixtures of each anomeric series. However, peak separations between 3-*O*-myristate and 4-*O*-myristate of both the α- and β-anomers were poor. The dimyristates also gave well separated peaks, though peak broadening due to poorer volatility was noted.

Table I. TLC and GC Analysis of Methyl *O*-Myristoyl-D-glucopyranosides

Isomers	α-D-Glucosides		β-D-Glucosides	
	TLC[a] *Rf*	GC[b] r.r.t.	TLC[a] *Rf*	GC[b] r.r.t.
Monomyristate				
2-*O*-(VII)	0.50	0.80	0.43	0.79
3-*O*-(VIII)	0.56	0.70	0.54	0.70
4-*O*-(XVI)	0.48	0.69	0.50	0.72
6-*O*-(XX)	0.41	0.90	0.43	0.84
Dimyristate				
2,3-di-*O*-(VI)	0.31	7.11	0.34	7.16
2,6-di-*O*-(XXI)	0.43	10.40	0.31	(9.02)[c]
4,6-di-*O*-(XIX)	0.40	8.13	0.31	7.96
Fr. 7 (3,6-di-*O*-)			0.48	7.98
Fr. 8 (2,6-+4,6-di-*O*-)			0.31	7.96 9.02

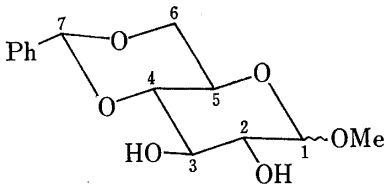
a) Merck plates precoated with Silica Gel 60 F_{254}. Solvent system: for monomyristate, $CHCl_3$: MeOH=10: 1; for dimyristate, $CHCl_3$: MeOH=20: 1.
b) As the TMS derivative. Column temp.: for monomyristate, 250°; for dimyristate, 280°. Internal standard: cholesterol, 1.00 (6.80 min at 250° and 2.25 min at 280°).
c) Data obtained from Fr. 8.

^{1}H-NMR Spectra of Methyl *O*-Myristoyl-D-glucopyranosides

Signal assignments in the PMR spectra of the synthesized *O*-acyl-4,6-*O*-benzylidene derivatives and the methyl *O*-acyl-D-glucopyranosides are shown in Table II and III, respectively.

Anomeric Proton Signals——As suggested previously,[4] throughout all positional isomers of acylglucoside the anomeric proton of α-glucosides resonated downfield by 0.3—0.5 ppm compared with that of the corresponding β-glucosides, with a characteristic doublet coupling pattern: J=3.5—4 Hz in α- and J=7—8 Hz in β-anomers. Some regular relationships between the position of an acyl group and the shift caused by acylation were observed, as follows. A 6-*O*-acyl group caused an upfield shift ($\Delta\delta\sim$0.1 ppm) of the anomeric proton signal in both the α- and β-anomers, while a 4-*O*-acyl group left this proton signal almost unaffected. A 3-*O*-acyl group in both the α- and β-glucosides affected this proton only slightly, producing a variable shift, either upfield or downfield. Introduction of a 2-*O*-acyl group into both the α- and β-anomers caused a downfield shift of the anomeric proton signal, as expected from the increased inductive effect, but the shift values of the α- and β-isomers were remarkably different, $\Delta\delta\sim$0.15 ppm in α- and 0.05 ppm in β-glucosides, suggesting that the ester group of 2-*O*-acyl-α-D-glucopyranosides occupies a conformation where H^1 and carbonyl oxygen are in close proximity (*e.g.*, **A** in Chart 2).

TABLE II. PMR Assignments of 4,6-*O*-Benzylidene Derivatives in Pyridine-d_5 (at 100 MHz)



II

	Chemical shifts (δ)[a]					First-order coupling constants (Hz)		
	H^1(d)[b]	H^2(q)	H^3(t)	H^7(s)	OMe(s)	$J_{1,2}$	$J_{2,3}$	$J_{3,4}$
α-D-glucoside								
IIα	5.09	4.11	4.54	5.81	3.40	3.7	9.5	9.5
2-*O*-Myr. (IVα)	5.26	5.36	4.67	5.78	3.40	3.9	9.3	9.3
3-*O*-Myr. (Vα)	5.08	4.16	6.00	5.76	3.34	3.9	9.5	9.5
2,3-di-*O*-Myr. (IIIα)	5.24	5.36	6.10	5.77	3.35	3.7	9.5	9.5
β-D-glucoside								
IIβ	4.73	4.06	4.33	5.77	3.61	7.6	9.3	9.3
2-*O*-Myr. (IVβ)	4.78	5.59	4.35	5.74	3.56	8.0	9.0	9.0
3-*O*-Myr. (Vβ)	4.74		5.90	5.77	3.59	7.8	9.5	9.3
2,3-di-*O*-Myr. (IIIβ)	4.85	5.53	5.88	5.78	3.55	7.8	9.5	9.3
2-*O*-Cbz (IXβ)	4.82	5.41	4.43	5.77	3.51	8.0	9.0	9.0
3-*O*-Cbz (Xβ)	4.76	4.10	5.71	5.72	3.58	7.6	9.3	9.3

a) Other protons assigned are not indicated.
b) s, singlet; d, doublet; t, triplet; q, quartet.

TABLE III. PMR Assignments of Methyl Mono- and Di-*O*-tetradecanoyl-D-glucopyranoside in Pyridine-d_5 (at 100 MHz)

	Chemical shift (δ)[a]					First-order coupling constants (Hz)		
	H^1(d)	H^2(q)	H^3(t)	H^4(t)	OMe	$J_{1,2}$	$J_{2,3}$	$J_{3,4}$
α-D-glucoside								
Iα	5.14				3.45	3.5		
2-*O*-(VIIα)	5.27	5.33			3.41	3.5	9.5	
3-*O*-(VIIIα)	5.21		6.06		3.36	3.9	9.5	9.5
4-*O*-(XVIα)	5.13		(4.59)[a]	5.61	3.47	3.5	9.5	9.5
6-*O*-(XXα)[b]	5.04				3.42	3.5		
2,3-di-(VIα)	5.29	5.34	6.13		3.38	3.5	9.5	9.5
2,6-di-(XXIα)	5.27	5.32			3.45	3.5	9.5	9.5
4,6-di-(XIXα)	5.08			5.49	3.47	3.5		9.5
β-D-glucoside								
Iβ	4.71				3.60	7.3		
2-*O*-(VIIβ)	4.77	5.55			3.53	8.0	9.5	
3-*O*-(VIIIβ)	4.69		5.83		3.55	7.5	9.5	9.5
4-*O*-(XVIβ)	4.70		(4.27)	5.60	3.56	7.5	9.5	9.5
6-*O*-(XXβ)[b]	4.63				3.57	7.5		
2,3-di-(VIβ)	4.72	5.39	5.76		3.53	7.8	9.5	9.5
3,6-di-(XXIIβ)	4.65		5.78		3.58	7.8	9.3	9.3
4,6-di-(XIXβ)	4.67			5.57	3.60	7.5		9.5

a) Protons at anomeric and carbinylic positions are listed, and the data in parentheses are those for other protons which were eventually assigned.
b) Data at 60 MHz.

Carbinyl Proton Signals——Carbinyl protons (protons geminal to an acyloxy group) were usually readily distinguishable because they appeared in the lowest region in the spectra with characteristic coupling patterns, except in 6-*O*-acyl derivatives in which the protons overlapped with other protons of the sugar moiety.

In 4-*O*-acyl derivatives, H^4 appeared at δ 5.5—5.6 in both the α- and β-anomers as a triplet or sometimes a diffused triplet when $J_{3,4}$ and $J_{4,5}$ were slightly different. The carbinyl protons of 3-*O*-acyl-α-glucosides (δ 6.0—6.1) resonated downfield by 0.2—0.3 ppm compared to those of the corresponding β-glucosides (δ 5.7—5.8). However, their shift values from the original alcohols were approximately equal ($\Delta\delta\sim$1.5 ppm) in both the α- and β-anomers as indicated by the spectra of the corresponding 4,6-*O*-benzylidene derivatives, showing that H^3 in an α-anomer was originally deshielded by 0.2—0.3 ppm relative to that of a β-anomer by *syn*-axial 1α-OMe group. In contrast to 3-*O*-acyl derivatives, H^2 of 2-*O*-acyl-α-glucosides (δ 5.3—5.4) appeared upfield by 0.2 ppm compared with that of the corresponding β-glucosides (δ 5.5—5.6). The corresponding 4,6-*O*-benzylidene derivatives indicated that the shifts ($\Delta\delta$) from the original positions are 1.25 ppm in α- and 1.5 ppm in β-anomers.

As shown in Tables II and III, the coupling constants ($J_{1,2}$, $J_{2,3}$, and $J_{3,4}$) were almost constant in each anomeric series, showing that the conformation of the pyranose ring was altered only slightly, if any, by the introduction of an acyl group (at any position). In some instances H^3 and H^4 appeared as diffused triplets, so that accurate measurements of each coupling constant from the spectra were difficult (in this case, mean values are indicated in Table III as $J_{2,3}$ and $J_{3,4}$).

Thus, methyl 2,3-di-*O*-myristoyl-α-D-glucopyranoside (VIα) exhibited a triplet at δ 6.13 and a quartet at δ 5.34 together with an anomeric proton doublet at δ 5.29, and methyl 4,6-di-*O*-myristoyl-β-D-glucopyranoside (XIXβ) showed a quartet at δ 5.57 and a doublet at δ 4.67 in addition to 5 proton signals in the δ 3.8—4.6 region. However, analysis of a diester mixture by PMR was found to be difficult because of overlap of the signals.

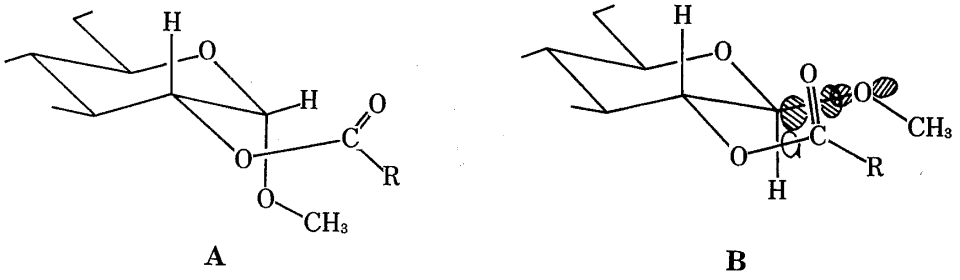


Chart 2

^{13}C-NMR Spectra of Methyl *O*-Myristoyl-D-glucopyranosides

The usefulness of CMR, particularly in carbohydrate chemistry, has been suggested in many cases,[12] and regularities in the changes of chemical shift related to structural and stereochemical alterations have been codified in terms of several factors such as acylation

11) Y. Kondo, K. Miyahara, and N. Kashimura, *Canad. J. Chem.*, **51**, 3272 (1973).

12) *a*) J.B. Stothers, "Carbon-13 NMR Spectroscopy," Academic Press, New York, 1972; *b*) K. Yamasaki, H. Kohda, T. Kobayashi, R. Kasai, and O. Tanaka, *Tetrahedron Lett.*, **1976**, 1005; *c*) K. Tori, S. Seo, Y. Yoshimura, M. Nakamura, Y. Tomita, and H. Ishii, *Tetrahedron Lett.*, **1976**, 4167; *c*) K. Yamasaki, H. Kohda, T. Kobayashi, N. Kaneda, R. Kasai, O. Tanaka and K. Nishi, *Chem. Pharm. Bull.*, **25**, 2895 (1977); *d*) H. Ishii, K. Tori, T. Tozyo, and Y. Yoshimura, *Chem. Lett.*, **1978**, 719; and references therein.

shifts,[13] glycosidation shifts,[14] steric interaction effects,[12a] *etc.* Among those, the acylation shift rule states that on acylation a carbinyl carbon (Cα) is somewhat (+1—+2) deshielded while a β-carbon (C$_\beta$) resonance is displaced markedly upfield (−2——4); the rule was successfully applied to locate the acyl (acetyl or oxalloyl) group in naturally occurring acylglycosides,[15] although the examples were limited to 3-*O*-acyl and 6-*O*-acyl hexopyranosides. The present synthesized mono-*O*-myristoyl-D-glucosides provide a useful opportunity to check the general applicability of this rule not only to glucosides with an acyl group at positions 3 and 6 but also at positions 2 and 4.

The ^{13}C chemical shifts (δ_C) of the methyl *O*-acyl-D-glucopyranosides (Table IV) were compared with those of methyl D-glucopyranosides to derive the acylation shift values as follows: $\Delta\delta_{C_n}=\delta_{C_n}$ (methyl *O*-acyl-D-glucoside)$-\delta_{C_n}$ (methyl D-glucoside). Parenthetical data in Table IV indicate the shift values in pyridine-d_5 caused by an acyl group at different positions in each α- and β-D-glucopyranoside.

TABLE IV. ^{13}C Chemical Shifts (δ_C) of Methyl Mono-*O*-myristoyl-D-glucopyranosides and Acylation Shifts (in Parentheses) in Pyridine-d_5

Isomers	Carbon number							
	C=O	C-1	C-2	C-3	C-4	C-5	C-6	OCH_3
α-D-glucoside								
Methyl(Iα)		101.3 [101.2][a]	73.7 [73.7]	75.3 [75.3]	72.0 [72.0]	74.0 [73.9]	62.8 [62.7]	55.0 [55.0]
2-*O*-(VIIα)	173.6	98.0 (−3.3)[b]	74.8[c] (+1.1)	72.2[c] (−3.1)	72.0 (0)	74.1 (+0.1)	62.5 (−0.3)	54.8 (−0.2)
3-*O*-(VIIIα)	173.7	101.2 (−0.1)	71.9 (−1.8)	77.2[c] (+1.9)	69.6 (−2.4)	74.0 (0)	62.2 (−0.6)	55.0 (0)
4-*O*-(XVIα)	173.2	101.2 (−0.1)	73.9 (+0.2)	72.7[c] (−2.6)	72.9[c] (+0.9)	71.9 (−2.1)	62.3 (−0.5)	55.1 (+0.1)
6-*O*-(XXα)	173.5	101.4 (+0.1)	73.7 (0)	75.3 (0)	71.9 (−0.1)	71.1 (−2.9)	64.6 (+1.8)	55.1 (+0.1)
β-D-glucoside								
Methyl(Iβ)		105.5 [105.4][a]	75.0 [74.8]	78.4 [78.1]	71.5 [71.4]	78.3 [78.1]	62.6 [62.5]	56.7 [56.7]
2-*O*-(VIIβ)	172.8	102.7 (−2.8)[b]	74.7[c] (−0.3)	76.1 (−2.3)	71.7 (+0.2)	78.6 (+0.3)	62.4 (−0.2)	56.4 (−0.3)
3-*O*-(VIIIβ)	173.5	105.4 (−0.1)	73.0 (−2.0)	79.0[c] (+0.6)	69.4[c] (−2.1)	78.2 (−0.1)	62.1 (−0.5)	56.8 (+0.1)
4-*O*-(XVIβ)	173.1	105.5 (0)	75.2 (+0.2)	75.7[c] (−2.7)	72.4[c] (+0.9)	76.1 (−2.2)	62.3 (−0.3)	56.8 (+0.1)
6-*O*-(XX$\delta\beta$)	173.5	105.6 (+0.1)	74.9 (−0.1)	78.3 (−0.1)	71.4 (−0.1)	75.2 (−3.1)	64.5 (+1.9)	56.7 (0)

a) Data in brackets are those of K. Tori. see ref. 14c).
b) +, downfield shift; −, upfield shift.
c) Assignment was confirmed by selective decoupling.

Overall, the results broadly support the validity of the rule, although the shift values in β-D-glucosides were found to differ from those in the corresponding α-anomers, and were variable, depending on the position of the acyl group in the glucosides. In some instances,

13) *a*) D.E. Dorman, D. Bauer, and J.D. Roberts, *J. Org. Chem.*, **40**, 3729 (1975); *b*) M.R. Vignon and J.A. Vottero *Tetrahedron Lett.*, **1976**, 2445; *c*) S.W. Pelletier, Z. Djarmati, and C. Pape, *Tetrahedron*, **32**, 995 (1976); *d*) Y. Terui, K. Tori, and N. Tsuji, *Tetrahedron Lett.*, **1976**, 621.
14) *a*) R. Kasai, M. Suzuo, J. Asakawa, and O. Tanaka, *Tetrahedron Lett.*, **1977**, 175; *b*) K. Tori, S. Seo, Y. Yoshimura, H. Arita, and Y. Tomita, *ibid.*, **1977**, 179; *c*) S. Seo, Y. Tomita, K. Tori, and Y. Yoshimura, *J. Am. Chem. Soc.*, **100**, 3331 (1978).
15) For example, *a*) H. Ishii, S. Seo, K. Tori, T. Tozyo, and Y. Yoshimura, *Tetrahedron Lett.*, **1977**, 1227; *b*) K. Yamasaki, R. Kasai, Y. Masaki, M. Okihara and O. Tanaka, *ibid.*, **1977**, 1231.

TABLE V. ^{13}C Chemical Shifts (δ) of Methyl *O*-acyl-4,6-*O*-benzylidene-D-glucopyranosides and Acylation Shifts (in parentheses) in Pyridine-d_5

	Carbon number								
	C=O	C-1	C-2	C-3	C-4	C-5	C-6	C-7	OCH_3
α-Glucoside									
2,3-OH(IIα)		102.2	74.1	71.5	83.1	63.3	69.5	102.2	55.3
2-*O*-Myr. (IVα)	173.5	98.6 (−3.6)	74.6 (+0.5)	68.6 (−2.9)	82.8 (−0.3)	63.1 (−0.2)	69.2 (−0.3)	102.2 (0)	55.2 (−0.1)
3-*O*-Myr. (Vα)	173.2	101.8 (−0.2)	71.9 (−2.3)	72.7 (+1.2)	80.1 (−3.0)	63.2 (−0.1)	69.3 (−0.2)	101.8 (−0.4)	55.2 (−0.1)
2,3-di-*O*-Myr. (IIIα)	173.0 172.8	98.3	72.0	69.0	79.4	63.1	69.4	102.0	55.3
β-Glucoside									
2,3-OH(IIβ)		106.1	75.6	74.3	82.3	67.0	69.2	102.0	56.9
2-*O*-Myr. (IVβ)	172.7	103.2 (−2.9)	74.9 (−0.7)	72.2 (−2.1)	82.3 (0)	67.1 (+0.1)	69.0 (−0.2)	102.1 (+0.1)	56.7 (−0.2)
3-*O*-Myr. (Vβ)	172.4	106.0 (−0.1)	73.4 (−2.2)	74.6 (+0.3)	79.6 (−2.7)	66.9 (−0.1)	69.1 (−0.1)	101.7 (−0.3)	57.2 (+0.3)
2-*O*-Cbz(IXβ)		102.8 (−3.3)	79.6 (+4.0)	71.9 (−2.4)	82.0 (−0.3)	67.0 (0)	68.9 (−0.3)	102.0 (0)	56.8 (−0.1)
3-*O*-Cbz(Xβ)		105.8 (−0.3)	69.7 (−5.9)	79.4 (+5.1)	73.2 (−9.1)	66.6 (−0.4)	69.0 (−0.2)	101.7 (−0.3)	57.2 (+0.3)
2,3-di-*O*-Myr,. (IIIβ)	172.9 172.5	102.7	72.3[a]	72.6[a]	79.1	66.8	68.9	101.8	57.0

a) Assignment may be reversed.

TABLE VI. ^{13}C Chemical Shifts (δ) of Methyl Di-*O*-myristoyl-D-glucopyranosides in Pyridine-d_5

	Carbon number						
	C-1	C-2	C-3	C-4	C-5	C-6	OCH_3
α-D-Glucoside							
2,3-di-(VIα)							
Calcd	97.9	73.0	74.1	69.8	74.1	61.9	54.8
Obs.	97.7	72.2	73.6[a]	69.3	74.1	61.8	54.8
2,6-di-(XXIα)							
Calcd	98.1	74.8	72.2	71.9	71.2	64.3	54.9
Obs.	98.0	74.5[a]	72.1[a]	71.9	70.9	64.2	55.0
4,6-di-(XIXα)							
Calcd	101.3	73.9	72.7	72.8	69.0	64.1	55.2
Obs.	101.3	73.6	72.5[a]	72.2[a]	68.6	63.3	55.3
β-D-Glucoside							
2,3-di-(VIβ)							
Calcd	102.6	72.7	76.6	69.6	78.5	61.9	56.5
Obs.	102.3	72.6[a]	76.6[a]	69.0	78.3	61.7	56.6
4,6-di-(XIXβ)							
Calcd	105.6	75.1	75.6	72.3	73.0	64.2	56.8
Obs.	105.6	75.0	75.5[a]	71.7[a]	72.7	63.2	56.8
3,6-di-(XXIIβ)							
Calcd	105.5	72.9	78.9	69.3	75.2	64.0	56.8
Obs. (Fr. 7)	105.6	72.3	78.6[a]	69.5[a]	75.0	63.9	56.8
2,6-di-(XXIβ)							
Calcd	102.8	74.6	76.0	71.9	75.5	64.3	56.4
Obs. (Fr. 8)	102.6	74.5	75.9	71.6	75.3	64.1	56.3
	105.5[b]	75.0	75.4	71.7	72.8	63.2	56.8

a) Assignments were confirmed by selective decoupling.
b) Data in this line are in accord with those for 4,6-dimyristate.

the shifts at C_γ and C_δ are, though small, comparable with those at C_α, and thus should not be ignored, while the shifts at C_β always showed large negative values, in accord with the rule. However, $\Delta\delta_{C\alpha}$ of the 2-*O*-acyl-β-D-glucoside had a sign opposite to that expected. For a rough evaluation of the shifts due to different acyl groups, $\Delta\delta_{C\gamma}$ and $\Delta\delta_{C\delta}$ may be neglected, although both the steric and electronic characteristics of an acyl group must be considered.[13c] Discrepancies of the shift values between those in the glucosides and in the corresponding 4,6-*O*-benzylidene derivatives (Table V) indicate that the shift varies, depending upon the stereochemistry (and rigidity) of the pyranose ring. A Cbz group increased the magnitude of the shift, particularly at C_α, as expected.[13a]

We next investigated whether the acylation shift values are additive for diacyl and polyacyl derivatives. The observed ^{13}C chemical shifts of the various dimyristates were compared with those calculated from the data in Table IV by assuming additivity of the acylation shifts (Table VI). As shown in Table VI, the agreement of these two sets of values is quite satisfactory, indicating that the acylation shift values in Table IV can be adopted as additive parameters for estimating the ^{13}C chemical shifts of diacyl-α- and β-glucopyranosides. This finding was applied for structure elucidation of the dimyristate mixture obtained by direct acylation of methyl β-D-glucopyranoside (Iβ). Of the two fractions of dimyristates (see above), one (Fr. 7) was directly identified as 3,6-di-*O*-myristate (XXIIβ) because of the good agreement between the calculated and the observed δ_C's for each carbon atom of the sugar moiety. The same procedure indicated that the other fraction (Fr. 8) was a mixture of 2,6-(XXIβ) and 4,6-di-*O*-myristates (XIXβ) (see Table VI). No other combinations of the calculated shifts showed such good coincidence with the observed shifts, and this conclusion was supported by GC evidence, one of the two peaks of Fr. 8 being identical with that of the 4,6-di-*O*-myristate (XIXβ) (see Table I).

Table VII. Steric Interaction Effects of the Anomeric Methoxyl Function in Pyridine-d_5

	$\Delta\delta$ (α-anomer$-\beta$-anomer) Carbon number							
	C=O	C-1(α)	C-2(β)	C-3(γ)	C-4(δ)	C-5(γ)	C-6	OCH_3
D-Glucoside								
Methyl		−4.2	−1.3	−3.1	+0.5	−4.3	+0.2	−1.7
		(−3.9)[a]	(−1.5)	(−2.8)	(+0.8)	(−3.7)	(+0.3)	(−1.6)
2-*O*-Acyl	+0.8	−4.7	+0.1	−3.9	+0.3	−4.5	+0.1	−1.6
		(−4.6)	(−0.3)	(−3.6)	(+0.5)	(−4.0)	(+0.2)	(−1.5)
3-*O*-Acyl	+0.2	−4.2	−1.1	−1.8	+0.2	−4.2	+0.1	−1.8
		(−4.2)	(−1.5)	(−1.9)	(+0.5)	(−3.7)	(+0.2)	(−2.0)
4-*O*-Acyl	+0.1	−4.3	−1.3	−3.0	+0.5	−4.2	0	−1.7
6-*O*-Acyl	0	−4.2	−1.2	−3.0	+0.5	−4.1	+0.1	−1.6

a) Parenthetical data indicate the steric interaction effects in the 4,6-*O*-benzylidene derivatives.

Table VII lists the effects of orientational differences of the anomeric methoxyl function on the pyranose carbon shielding. The data agree with the general steric interaction rule,[12a] which was well analyzed for a hydroxyl groups by Dorman *et al.*[16]; an axial methoxyl group increases the shielding of the carbon to which it is bonded as well as those of the β and γ carbons, although the effect at the β-position is expected to be smallest. The shielding effect of a methoxyl group in an (acyl) glucoside differs at the two γ-positions (C^3 and C^5), showing conformational non-equivalence of the two *syn*-diaxial hydrogens, and hence distortion of the geometry of the pyranose ring relative to cyclohexane.[12a] Satisfactory agreements of the shift values in each vertical column (except at C^2 of 2-*O*-acyl and C^3 of 3-*O*-acyl deriva-

16) a) D.E. Dorman, S.J. Angyal, and J.D. Roberts, *J. Am. Chem. Soc.*, **92**, 1351 (1970); b) D.E. Dorman and J.D. Roberts, *ibid.*, **92**, 1355 (1970).

tives), indicate that the conformational change of the ester group caused by orientational change of the methoxyl function was small. 2-*O*-Acylglucoside showed an anomalous shift at C^2 (β to the anomeric position) and slight deviations from expectation at C^1 and C^3, while 3-*O*-acylglucoside gave a rather anomalous shift at C^3 (γ to the anomeric position). In both cases, the most marked deviations were observed at the carbons to which the acyloxy groups were bonded, whereas deviations at the other positions were small or negligible. This anomaly in the case of the 2-*O*-acyl derivative clearly corresponds to the unexpected acylation shift of 2-*O*-acyl-β-glucoside at C_α (see above). The origin of this may be attributed to a conformational difference of the ester group between 2-*O*-acyl-α- and β-glucoside, since PMR data suggested that the conformational change of the pyranose ring is small (see above). Based on the preferred conformations of the β-glucoside linkage[17] and ester[18] group, this phenomenon can reasonably be explained in terms of electrostatic repulsion between non-bonded electrons on C^1-oxygen and π-electrons of the ester carbonyl of 2-*O*-acyl-β-glucoside (**B** in Chart 2), which should produce a slight rotation of the ester group around the O–C(=O) bond, thus decreasing δ_C at C^2. This view is supported by the observation that the ester carbonyl of 2-*O*-acyl-β-glucoside resonance downfield by 0.8 ppm relative to that of the corresponding α-glucoside, while the differences of the carbonyl resonances in the other *O*-acyl isomers were within 0.2 ppm.

Experimental

Unless otherwise stated, mp's were taken on a Yanagimoto micro hot-stage mp apparatus and are uncorrected. Infrared (IR) spectra were taken as KBr discs using a Jasco IR-C spectrometer and are given by cm^{-1}. GC analyses were carried out with a Shimadzu GC4CM-PF gas chromatograph coupled to an FID detector, using a glass column (2 m × 3 mm I.D.) packed with 1.5% OV-1 on Shimalite W (80—100 mesh), with N_2 (70 ml/min, 1.4 kg/cm^2) as a carrier gas. The TMS (trimethylsilyl) derivatives were prepared by the method of Sweeley *et al.*[19] Kieselgel GF_{254} nach Stahl Type 60 was used for TLC, and Wakogel C-200 and Florisil (Wako Chemicals Co. Ltd.) for column chromatography. All organic extracts were washed with water and dried over Na_2SO_4 before concentration by evaporation.

Measurements of NMR Spectra——PMR (at 100 MHz) and natural abundance ^1H noise-decoupled ^{13}C FT NMR (at 25.0 MHz) were recorded on a JEOL FX-100 FT NMR spectrometer using 5-mm spinning tubes at 24°. Samples were dissolved in pyridine-d_5. Tetramethylsilane (Me_4Si) served as an internal reference (δ0). Concentrations were about 0.1—0.3 mmol/ml. FT NMR measurement conditions were as follows: spectral width, 6024 Hz; pulse flipping angle, 45°; acquisition time, 0.6799s; number of data points, 8192. Accuracies of δ values were about ±0.1.

Assignments of ^{13}C-NMR Signals——The ^{13}C signals were assigned using known chemical shift rules,[12a] literature date on methyl α- and β-D-glucopyranosides in pyridine-d_5,[14c] and the ^1H single-frequency off-resonance decoupling technique.[12a] For example, signal assignment of methyl 4-*O*-myristoyl-α-D-glucopyranoside (XVIα) was carried out as follows. Among 6 peaks of the sugar moiety, the peaks at δ 101.2 and 62.3 were readily assignable to C^1 and C^6, respectively. On irradiation of H^4 (δ 5.61) and H^3 (δ 4.59), the signals at δ 72.9 (C^4) and 72.7 (C^3) changed to a singlet, respectively. The remaining two carbon signals were assigned on the basis of their acylation shift and the effect of orientational difference of the methoxyl group.

Myristoylation of Methyl 4,6-*O*-Benzylidene-α-D-glucopyranoside (IIα)——Myristoyl chloride (2 eq. mol) was added dropwise at 0° to a stirred solution of IIα[20] (282 mg) in pyridine (2 ml)-CH_2Cl_2 (4 ml). The mixture was stirred for 3 hr at room temperature, poured into water, and extracted with CH_2Cl_2. Removal of the solvent from the extract gave a solid which was chromatographed in benzene over Florisil (2 × 10 cm). The benzene eluate gave 2,3-di-*O*-myristate (IIIα), mp 77—79° (lit.[5g] mp 80—82°), as needles from *n*-hexane (158 mg). IR: 1740 and 1730.

The $CHCl_3$–MeOH eluate was again chromatographed on SiO_2 (2 × 15 cm) in $CHCl_3$ to yield 2-*O*-myristate (IVα), mp 90—92° (lit.[5g] mp 94—96°), as needles from *n*-hexane (290 mg). IR: 1743.

17) R.U. Lemieux and S. Koto, *Tetrahedron*, **30**, 1933 (1974).
18) Ref. 13*c*) and references therein.
19) C.C. Sweeley, R. Bentley, M. Makita, and W.W. Wells, *J. Am. Chem. Soc.*, **85**, 2497 (1963).
20) *cf.*) M.E. Evans, *Carbohydr. Res.*, **21**, 473 (1972).

Myristoylation of Methyl 4,6-*O*-Benzylidene-*β*-D-glucopyranoside (II*β*)——The *β*-isomer II*β*[20] (282 mg) was acylated with myristoyl chloride (1.5 eq. mol) and worked up as above. Chromatography of the product on Florisil in benzene gave 2,3-di-*O*-myristate (III*β*), mp 79—82°, as needles from *n*-hexane (200 mg). IR: 1743.

Rechromatography of the $CHCl_3$–MeOH eluate on SiO_2 in $CHCl_3$ gave 3-*O*-myristate (V*β*), mp 80—83° (lit.[5g] mp 89—90°), as needles from *n*-hexane (140 mg), and 2-*O*-myristate (IV*β*), mp 114—117° (lit.[5g] mp 113—115°), as needles from *n*-hexane–CH_2Cl_2 (57 mg).

Methyl 2-*O*-Myristoyl-*α*-D-glucopyranoside (VII*α*)——2-*O*-Myristate IV*α* (90 mg) and Pd-black (100 mg) in EtOH (15 ml) were shaken under H_2 at atmospheric pressure for 6 hr. The catalyst was removed by filtration, washed several times with EtOH, and the combined filtrate and washings were concentrated *in vacuo* to give a solid, which yielded VII*α*, mp 102—104° (lit.[5g] mp 95—96°), as needles on crystallization from *n*-hexane–acetone (yield, 72%).

Methyl 3-*O*-Myristoyl-*β*-D-glucopyranoside (VIII*β*)——Hydrogenolysis of 3-*O*-myristate V*β* (110 mg) as described above gave VIII*β*, mp 85—89°, as needles from *n*-hexane–acetone (yield, 80%). IR: 1701. *Anal.* Calcd for $C_{21}H_{40}O_7$: C, 62.35; H, 9.97. Found: C, 62.44; H, 10.15.

Methyl 2,3-di-*O*-Myristoyl-*α*-(VI*α*) and *β*-D-Glucopyranoside (VI*β*)——The 2,3-dimyristates (III*α* and III*β*) were hydrogenolyzed as described above to give VI*α*, mp 90—90.5°, and VI*β*, mp 75°, respectively. VI*α*; IR: 1731. *Anal.* Calcd for $C_{35}H_{66}O_8$: C, 68.36; H, 10.82. Found: C, 68.04; H, 11.07. VI*β*; IR: 1748 (shoulder) and 1741. *Anal.* Calcd for $C_{35}H_{66}O_8$: C, 68.36; H, 10.82. Found: C, 67.92; H, 11.01.

Carbobenzoxylation of Methyl 4,6-*O*-benzylidene-*α*-D-glucopyranoside (II*α*)——A 30—35% toluene solution of CbzCl (4 eq. mol) was added dropwise to a stirred solution of II*α* (844 mg) in pyridine (10 ml)–CH_2Cl_2 (20 ml) at 0°. The mixture was stirred for 3 days at room temperature, poured into ice-water, and extracted with CH_2Cl_2. Chromatography of the products on Florisil (3×10 cm) in benzene gave methyl 4,6-*O*-benzylidene-2-*O*-Cbz-*α*-D-glucopyranisode (IX*α*) as a colorless gum (yield, 67%). IR: 1747. PMR (in $CDCl_3$ at 60 MHz): 7.25—7.5 (10H, Ph×2), 5.47 (1H, s, PhCH<), 5.13 (2H, s, $PhCH_2OCO$–), 4.95 (1H, d, J=3.8 Hz, C^1–H), 4.61 (1H, q, J=3.8 and 9.5 Hz, C^2–H).

Subsequent elution with benzene–CH_2Cl_2 (1 : 1) gave methyl 4,6-*O*-benzylidene-3-*O*-Cbz-*α*-D-glucopyranoside (X*α*), mp 156—159°, as needles from *n*-hexane–CH_2Cl_2 (yield, 5%). IR: 1743. *Anal.* Calcd for $C_{22}H_{24}O_8$: C, 63.45; H, 5.81. Found: C, 63.05; H, 5.74.

Carbobenzoxylation of Methyl 4,6-*O*-Benzylidene-*β*-D-glucopyranoside (II*β*)——The *β*-isomer II*β* (840 mg) was treated with CbzCl as described above. Chromatographies of the product on Florisil and SiO_2 gave the 3-*O*-Cbz derivative (X*β*), mp 129—131°, as needles from *n*-hexane–CH_2Cl_2 (yield, 54%), and the 2-*O*-Cbz derivative (IX*β*), mp 110—112°, as needles from *n*-hexane–CH_2Cl_2 (yield, 10%). Some starting material (200 mg) was also recovered. X*β*; IR: 1749. *Anal.* Calcd for $C_{22}H_{24}O_8$: C, 63.45; H, 5.81. Found: C, 63.04; H, 5.81. IX*β*; IR: 1740. *Anal.* Calcd for $C_{22}H_{24}O_8$: C, 63.45; H, 5.81. Found: C, 63.34; H, 5.59.

Methyl 4,6-*O*-Benzylidene-3-*O*-myristoyl-*α*-D-glucopyranoside (V*α*)——Myristoyl chloride (3 eq. mol) was added dropwise to a stirred solution of the 2-*O*-Cbz derivative IX*α* (320 mg) in pyridine (2 ml)–CH_2Cl_2 (4 ml) at 0°. The mixture was stirred overnight at room temperature, poured into ice-water, and extracted with CH_2Cl_2. Removal of the solvent and chromatography of the residue on Florisil in *n*-hexane gave the 2-*O*-Cbz-3-*O*-myristoyl derivative (XI*α*) as a colorless gum (yield, quantitative). IR: 1750 and 1740.

This was dissolved in EtOH (20 ml) and hydrogenated over Pd-black (100 mg) for 6 hr. Removal of the catalyst and solvent gave V*α*, mp 120—123° (lit.[5g] mp 121—123°), as needles from *n*-hexane (yield, 91%). IR: 1724.

Methyl 3-*O*-Myristoyl-*α*-D-glucopyranoside (VIII*α*)——Further hydrogenolysis of V*α* in EtOH over Pd-black for 5 hr gave VIII*α*, mp 78—82°, as needles from *n*-hexane–acetone (yield, 78%). IR: 1702. *Anal.* Calcd for $C_{21}H_{40}O_7$: C, 62.35; H, 9.97. Found: C, 62.24; H, 10.26.

Methyl 4,6-*O*-Benzylidene-2-*O*-myristoyl-*β*-D-glucopyranoside (IV*β*)——The Cbz derivative X*β* (260 mg) in pyridine (2 ml)–CH_2Cl_2 (4 ml) was acylated with myristoyl chloride (3 eq. mol) and worked up as above to yield the 3-*O*-Cbz-2-*O*-myristoyl derivative (XII*β*) as a colorless gum. IR: 1767 and 1752. PMR (in $CDCl_3$ at 60 MHz): 5.45 (1H, s, PhCH<), 5.23 (1H, t, J=9.5 Hz, C^3–H), 5.08 (2H, s, $PhCH_2$–), 4.36 (1H, d, J=7.5 Hz, C^1–H). Hydrogenolysis of this as described for V*α* afforded IV*β* (see above), mp and mixed mp 114—117° (yield, 89%).

Methyl 2-*O*-Myristoyl-*β*-D-glucopyranoside (VII*β*)——Further hydrogenolysis of IV*β* in EtOH for 4 hr gave VII*β*, mp 105—110°, as needles from *n*-hexane–acetone (yield, 75%). IR: 1725. *Anal.* Calcd for $C_{21}H_{40}O_7$: C, 62.35; H, 9.97. Found: C, 62.42; H, 10.09.

Methyl 2,3-di-*O*-Benzyl-4,6-*O*-benzylidene-*α*-(XIII*α*) and *β*-D-Glucopyranoside (XIII*β*)——Benzylation of II*α* and II*β* according to Hakomori's method[4] yielded the 2,3-di-*O*-benzyl derivative (XIII*α*), mp 97—99° (lit.[8c] mp 96—99°) as needles (yield, 78%), and XIII*β*, mp 123—126° (lit.[8c] mp 120—122°) as needles (yield, 82%), respectively.

Methyl 2,3-Di-*O*-Benzyl-*α*-(XVI*α*) and *β*-D-Glucopyranoside (XIV*β*)——Compound XIII*α* and XIII*β* were hydrolyzed with 80% AcOH under reflux for 30 min. Crystallization of the products from *n*-hexane–ether gave XIV*α*, mp 76—78°, as needles (yield, 86%), and XIV*β*, mp 126—129°, as needles (yield, 80%), respectively.

Methyl 2,3-Di-*O*-benzyl-6-*O*-Cbz-*α*-(XV*α*) and *β*-D-Glucopyranoside (XV*β*)——The 4,6-dihydroxy compound XIV*α* (1.0 g) in pyridine (1 ml)—CH_2Cl_2 (3 ml) was treated with 30—35% CbzCl in toluene (3 eq. mol) at 0° and the mixture was stirred overnight at room temperature, Work-up as usual and chromatography of the product on Florisil (2×10 cm) gave a small amount of the 4,6-di-*O*-Cbz derivative from the benzene eluate, together with the 6-*O*-Cbz derivative (XV*α*), mp 88—89°, as needles from *n*-hexane–acetone (yield, 73%), from the $CHCl_3$ eluate. IR: 1725. PMR (in $CDCl_3$ at 60 MHz): 7.24 (15H, Ph×3), 5.05 (2H, s, PhC$\underline{H}_2$OCO), 4.57 (1H, d, J=3.5 Hz, C^1–H), 3.28 (3H, s, OC$\underline{H}_3$). *Anal.* Calcd for $C_{29}H_{32}O_8$: C, 68.49; H, 6.34. Found: C, 68.43; H, 6.37.

Similarly XIV*β* gave XV*β*, mp 88—90°, as needles from *n*-hexane–ether (yield, 70%). IR: 1723. PMR (in $CDCl_3$ at 60 MHz): 7.27 and 7.23 (15H, Ph×3), 5.08 (2H, s, PhC$\underline{H}_2$OCO), 3.47 (3H, s, OCH_3). *Anal.* Calcd for $C_{29}H_{32}O_8$: C, 68.49; H, 6.34. Found: C, 68.43; H, 6.37.

Methyl 4-*O*-Myristoyl-*α*-D-glucopyranoside (XVI*α*)——Myristoyl chloride was added to a stirred solution of XV*α* (201 mg) in pyridine (2 ml)–CH_2Cl_2 (4 ml) at 0° and the mixture was stirred for 2 days at room temperature. Work-up as usual and chromatography of the product on Florisil in *n*-hexane gave the 6-*O*-Cbz-4-*O*-myristoyl derivative (as a gum) from the *n*-hexane and benzene eluates. IR: 1750 (broad). PMR (in $CDCl_3$ at 60 MHz): 7.24, 7.22, and 7.18 (15H, Ph×3), 5.07 (2H, s, PhC$\underline{H}_2$OCO), 3.29 (3H, s, OC$\underline{H}_3$), 2.14 (2H, t, J=8 Hz, COC$\underline{H}_2$CH$_2$–), 1.24 (22H, bs, –(C$\underline{H}_2$)$_{11}$CH$_3$), 0.87 (3H, t, J=4 Hz, –(CH$_2$)$_{11}$C$\underline{H}_3$).

This was dissolved in EtOH and hydrogenated over Pd-black as described above. Crystallization of the product from *n*-hexane–acetone gave XVI*α*, mp 97—99°, as needles (yield, 71%). IR: 1741. *Anal.* Calcd for $C_{21}H_{40}O_7$: C, 62.35; H, 9.97. Found: C, 62.07; H, 10.26.

Methyl 4-*O*-Myristoyl-*β*-D-glucopyranoside (XVI*β*)——Compound XV*β* (204 mg) was acylated with myristoyl chloride, then hydrogenolyzed as above to yield XVI*β*, mp 95—98°, as needles from *n*-hexane–acetone (yield, 75%). IR: 1730. *Anal.* Calcd for $C_{21}H_{40}O_7$: C, 62.35; H, 9.97. Found: C, 62.25; H, 10.06.

Methyl 4,6-Di-*O*-myristoyl-*α*- (XIX*α*) and *β*-D-Glucopyranoside (XIX*β*)——The 4,6-dihydroxy compound XIV*α* (164 mg) in pyridine (2 ml)–CH_2Cl_2 (4 ml) was acylated with myristoyl chloride (3 eq. mol) and worked up as usual to give the dimyristoyl derivative (XVII*α*) as a colorless gum. This was dissolved in EtOH and hydrogenated over Pd-black to yield XIX*α*, mp 60—62°, as needles from *n*-hexane (yield, 83%). IR: 1740 (shoulder) and 1731. *Anal.* Calcd for $C_{35}H_{66}O_8$: C, 68.36; H, 10.82. Found: C, 68.17; H, 11.08.

Similarly XIV*β* gave the dimyristoyl derivative (XVII*β*), mp 45—46°, as leaflets (yield, quantitative), and then methyl 4,6-di-*O*-myristoyl-*β*-D-glucopyranoside (XIX*β*), mp 91°, as leaflets from *n*-hexane (yield, 89%). IR: 1748 and 1735. *Anal.* Calcd for $C_{35}H_{66}O_8$: C, 68.36; H, 10.82. Found: C, 68.38; H, 11.10.

Myristoylation of Methyl *α*-D-Glucopyranoside (I*α*)——a) Myristoyl chloride (1.5 eq. mol) was added dropwise with stirring to a cooled solution of I*α* (1.03 g) in pyridine (12 ml). The mixture was stirred for 3 days at room temperature, poured into ice-water, and extracted with $CHCl_3$. Removal of the solvent and chromatographies of the residue on Florisil and SiO_2 in $CHCl_3$ gave 2,6-di-*O*-myristoyl-*α*-D-glucopyranoside (XXI*α*), mp 64—65°, as needles from *n*-hexane (yield, 532 mg). IR: 1740 and 1718. *Anal.* Calcd for $C_{35}H_{66}O_8$: C, 68.36; H, 10.82. Found: C, 68.03; H, 11.08.

b) Acylation of I*α* (1.0 g) with myristoyl chloride (0.8 eq. mol) at 100° for 3 hr and work-up as above gave 2,6-di-*O*-myristate (154 mg) and 6-*O*-myristoyl-*α*-D-glucopyranoside (XX*α*), mp 76—80°, as needles (yield, 190 mg). IR: 1728. *Anal.* Calcd for $C_{21}H_{40}O_7$: C, 62.35; H, 9.97. Found: C, 62.68; H, 10.01.

Myristoylation of Methyl *β*-D-Glucopyranoside (I*β*)——The *β*-isomer I*β* (1.0 g) was acylated with myristoyl chloride (1.0 eq. mol) at 100° for 3 hr and worked up as described above. The product was chromatographed on Florisil in benzene. The benzene and CH_2Cl_2 eluates gave a mixture of di- and tri-myristates. The $CHCl_3$ and $CHCl_3$–MeOH eluates, after concentration and crystallization from *n*-hexane–acetone, gave methyl 6-*O*-myristoyl-*β*-D-glucopyranoside (XX*β*), mp 96—98°, as needles (yield, 378 mg). IR: 1743. *Anal.* Calcd for $C_{21}H_{40}O_7$: C, 62.35; H, 9.97. Found: C, 62.53; H, 10.05.

The above di- and tri-myristate mixture was again chromatographed on SiO_2 in $CHCl_3$. Fr. 1—6 gave a solid which appeared to be a mixture of tri-myristates and was not further investigated. Fr. 7 gave, on crystallization from *n*-hexane, 3,6-di-*O*-myristate (XXII*β*), mp 57—61°, as needles (yield, 55 mg). IR: 1747 (shoulder) and 1739. *Anal.* Calcd for $C_{35}H_{66}O_8$: C, 68.36; H, 10.82. Found: C, 68.49; H, 10.95. Fr. 8 (51 mg) was a solid and was proved to be a mixture of 2,6- (XXI*β*) and 4,6-di-*O*-myristoyl-*β*-D-glucopyranoside (XIX*β*) (see the text). Fr. 9 gave a further crop (30 mg) of 6-*O*-myristate (XX*β*).

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