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MYRISTOYL ESTERS OF LACTOSE

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ABSTRACT

Whereas lactose did not undergo a base-catalyzed transesterification with methyl esters of fatty acids, methyl β-lactoside reacted under identical conditions to give mono- and di-myristates. This difference in behavior is explained in terms of the formation of an unreactive, internally chelated potassium–lactose complex. Supporting evidence for this hypothesis is the observed change in the anomeric equilibrium of lactose in the presence of potassium carbonate. The monomyristates of methyl β-lactoside were assigned the structures of 3′ and 6′ derivatives, and it is concluded that the diesters are the 3′,6′, and 6,6′ derivatives.

INTRODUCTION

Osipow *et al.*[1] developed a process for the preparation of fatty acid esters of sucrose[2] by transesterification of methyl esters of fatty acids in *N,N*-dimethylformamide in the presence of potassium carbonate. However, this process failed in the case of lactose[3]. Thus, in order to utilize lactose in base-catalyzed esterification, it had to be converted with sodium borohydride first into lactitol, and then subjected to transesterification[4]. This difference in the behavior of sucrose and lactose was confirmed in this laboratory under experimental conditions that avoid an oxidation of the carbohydrate.

Relevant to the aforementioned behavior of lactose is the observation that, while primary hydroxyl groups of carbohydrates are generally more reactive toward esterification as compared to secondary hydroxyl groups[5], OH-3′of methyl β-lactoside appears[6] to be more reactive towards benzoyl chloride in pyridine than OH-6. The failure of lactose to react in the base-catalyzed transesterification was attributed[3] to the spatial proximity of the primary hydroxyl groups in the molecule. An alternative explanation for the lack of reactivity of lactose towards base-catalyzed transesterification is based on the preferential ionization of OH-1 of lactose, and the exceptional stabilization of the ion pair by internal chelation[7] (**1**).

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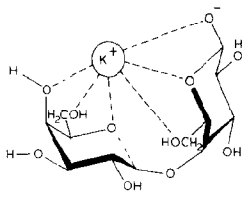
Such a complex would be expected to deactivate the lactose anion as a nucleophile in the reaction with an ester.



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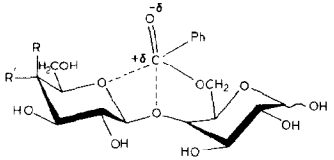
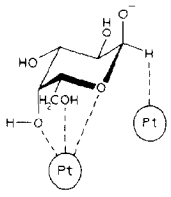


2 R = OH, R′ = H
3 R = H, R′ = OH



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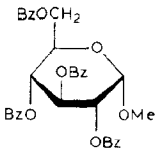
This paper provides evidence in favor of this hypothesis. A similar, multiple coordination has been proposed[8] for 6-*O*-benzoyllactose (**2**) in order to explain the resistance of the benzoate group to hydrolysis. Similarly, the relative resistance of the 6-*O*-benzoylmaltose to a nucleophilic attack by ammonia was attributed[9] to the internal coordination of the carbonyl carbon of the benzoate group with three oxygen atoms of the maltose molecule (**3**). Finally, in a recent study of the catalytic dehydrogenation of a series of monosaccharides on a platinum surface, the exceptionally high absorption capability of D-galactose was explained[10] in terms of a favorable triple coordination of the oxygen atoms of O-4, -5, and -6 on the metallic surface (**4**). The proposed complexation of **2** is similar, except that it also involves the D-glucose residue of lactose.

RESULTS AND DISCUSSION

In order to test the aforementioned hypothesis, the transesterification of methyl β-lactoside, and the effect of varying concentrations of potassium ion on the anomeric equilibrium of *O*-deuterated lactose was studied. The results are summarized in Tables I–IV. For comparison, the chemical shifts and coupling constants of H-1 and -1′ in α-lactose, and methyl 2,3,4,6-tetra-*O*-benzoyl-α-D-glucopyranoside and methyl -α-D-mannopyranoside were also examined (Table V).



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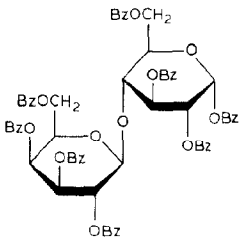

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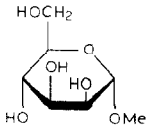

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TABLE I

EQUILIBRATION OF α- INTO β-($^2H_8$)LACTOSE IN DI($^2H_3$)METHYL SULFOXIDE SOLUTION IN THE PRESENCE OF POTASSIUM CARBONATE[a]

Time (h)	*Anomer (%)*	
	α	*β*
0	100	
0.17	60	40
0.50	40	60
1.00	36	64
2.00	33	67
9.00	32	68
30.00	20	80
36.00	20	80

[a]Potassium carbonate (173 g) was added to a solution of α-($^2H_8$)lactose in di($^2H_3$)methyl sulfoxide (0.50 mL) (0.50M lactose) to give an equimolar solution. [b]Average of duplicate experiments.

TABLE II

EQUILIBRATION OF α- INTO β-($^2H_8$)LACTOSE IN *N,N*-($^2H_7$)DIMETHYLFORMAMIDE SOLUTION IN THE PRESENCE OF POTASSIUM CARBONATE[a] AND DEUTERIUM OXIDE[b] AT 40°

Potassium carbonate (g)	*Time (h)*	*Anomer (%)*	
		α	*β*
None[b]	72	~100	
0.0173 g, K_2CO_3/lactose,	0.21	75	25
molar ratio = 1.0:1.0	0.5	75	25
	0.80	62	38
	1.0	41	59
	2.73	36	64
	22	36	64
0.0346 g, K_2CO_3/lactose,	22.60	10	90
molar ratio = 2.0:1.0			

[a]Added to a solution of lactose in *N,N*-($^2H_7$)dimethylformamide (0.5 mL, 0.5M lactose). [b]In the presence of potassium carbonate and absence of deuterium oxide only the signal of H-1e was detected (Fig. 1).

Methyl 2,3,4,6-tetra-*O*-benzoyl-α-D-glucopyranoside (**5**), α-lactose octabenzoate (**6**), and methyl α-D-mannopyranoside (**7**) are not capable of mutarotation and, where solubility permits a comparison, the signal H-1*e* was shifted downfield when ($^2H_1$)chloroform was replaced by di($^2H_3$)methyl sulfoxide. This suggested that the solvation by dimethyl sulfoxide is stronger than by chloroform, even though the latter solvent is expected to form hydrogen bonds with the available oxygen atoms of **5** and **6**. The solvation of **7** by dimethyl sulfoxide produced not

TABLE III

EQUILIBRATION OF α- INTO β-($^2H_8$)LACTOSE[a] IN DEUTERIUM OXIDE SOLUTION AT 40°

Time (h)	*Anomer (%)*	
	α	β
0.5	60, 65[b]	40, 35[b]
1	55, 57[b]	45, 43[b]
12	35, 35[b]	65, 65[b]
18	35[c]	65[c]
30	35	65

[a]0.50M Lactose in deuterium oxide (0.50 mL). [b]Duplicate runs. [c]The equilibrium ratio of β to α anomer of 13:7 corresponds to a $\Delta G° = -1.6$ kJ/mol.

TABLE IV

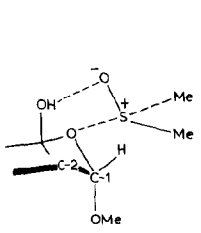
THE EFFECT OF POTASSIUM ION CONCENTRATION ON THE EQUILIBRIUM COMPOSITION OF α- AND β-($^2H_8$)LACTOSE IN DEUTERIUM OXIDE AT 40°

Potassium carbonate (g)[a]	% α	% β	*Molar ratio K_2CO_3/lactose-d_8*
None	35	65	0
0.0173	32	68	1
0.0346	32	68	2
0.0519	33	67	3
0.1038	29	71	6
0.15100	26	74	9
0.1730	29	71	10
0.2000	22	78	12
0.2422	19	81	14
0.3460	18	82	20
0.3506	15[b]	85[b]	20.5

[a]Potassium carbonate added to a solution of lactose in deuterium oxide (0.50 mL) (0.50M lactose) to give an equimolar solution. [b]The equilibrium ratio of β to α anomer of 17:3 corresponds to a $\Delta G° = -4.5$ kJ/mol.

only a downfield shift of the signal of H-1, but also a significantly lower coupling constant, indicative of a change in the dihedral angle between H-1 and H-2, and a flattened pyranose ring at the C-1 terminal due to hydrogen bonding between OH-2 and dimethyl sulfoxide. A stronger hydrogen bonding by deuterium oxide caused an even greater downfield shift of the signal of H-1 and a relatively small coupling constant. These observations raise the possibility that the solvation of **7** may bridge the axial OH-2 and O-5 as shown in **8** and **9**. Such a solvation would be expected to spread the dihedral bond-angle between C-1–H and C-2–H and cause smaller coupling constants.

The preparation of ($^2H_8$)lactose apparently did not perturb the anomeric equilibrium since, upon dissolution of α-($^2H_8$)lactose in either di($^2H_3$)methyl sulf-



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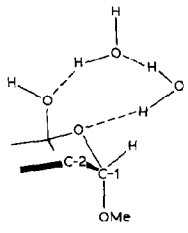

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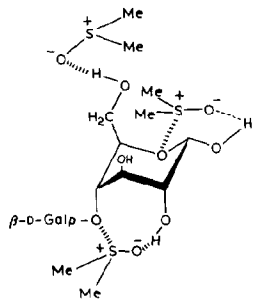

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TABLE V

SOLVENT EFFECTS ON ^{1}H-N.M.R. CHEMICAL SHIFTS OF ANOMERIC PROTONS

Compound	*Solvent*	*Chemical shift (δ) and coupling constant (Hz)*[a]	*Ratio α to β anomer*[b]
Methyl 2,3,4,6-tetra-*O*-benzoyl-α-D-glucopyranoside (**5**)	$CDCl_3$	6.9, $J_{1,2}$ 4, H*e*	~100:0
	$(CD_3)_2SO$	6.98, $J_{1,2}$ 4, H*e*	~100:0
1,2,3,6,2′,3′,4′,6′-Octa-*O*-benzoyl-α-lactose	$CDCl_3$	6.65, $J_{1,2}$ 2.0, H*e*	~100:0
	$(CD_3)_2SO$	6.8, $J_{1,2}$ 2.0, H*e*	~100:0
	$(CD_3)_2SO$[c]	4.90, $J_{1,2}$ 1.5, H*e*	~100:0
	$(CD_3)_2SO$[d]	4.90, $J_{1,2}$ 1.5, H*e*	
		4.77, $J_{1,2}$ 5, H*a*	4:1
		4.50, $J_{1,2}$ 7, H-1′*a*	
α-($^2H_8$)Lactose	$DCON(CD_3)_2$[e]	5.20, $J_{1,2}$ 2, H-1*e*	~100:0
	$DCON(CD_3)_2$[f]	5.20, $J_{1,2}$ 2, H*e*	
		4.70, $J_{1,2}$ 3, H*a*	1:9
		4.50, $J_{1,2}$ 7, H-1*a*	
	D_2O	4.80, *J* 3, H*e*	7:13[g]
		4.40, *J* 7, H*a*	3:17[h]
		4.00, *J* 6.90, H-1′*a*	
Methyl α-D-mannopyranoside (**7**)	$(CD_3)_2SO$	4.90, *J* 1.3, H*e*	~100:1
	D_2O	5.0, *J* 1.6, H*e*	7:3

[a]From Me_4Si signal, at 40°. [b]By integration of the H-1*a* and -1*e* signals. [c]Observation upon preparation of solution (30 min). [d]Observation after 3 days. [e]Observation upon preparation of solution in the presence or absence of potassium carbonate. [f]In the presence of potassium carbonate and deuterium oxide (see Table I). [g]Upon equilibration in pure deuterium oxide (see Table II). [h]Upon equilibration in deuterium oxide in the presence of potassium carbonate (see Table III).

oxide or *N,N*-($^2H_7$)dimethylformamide, only the signal of H-1*e* was observed. However, with time, the solution in di($^2H_3$)methyl sulfoxide showed an equlibrium composition in the absence of potassium carbonate, whereas, α-($^2H_8$)lactose in *N,N*-($^2H_7$)dimethylformamide did not show any decrease of the H-1*e* signal over 3 days (Table II). In the latter solvent, even the addition of potassium carbonate did not change the results. However, the addition of some deuterium oxide (Table II)

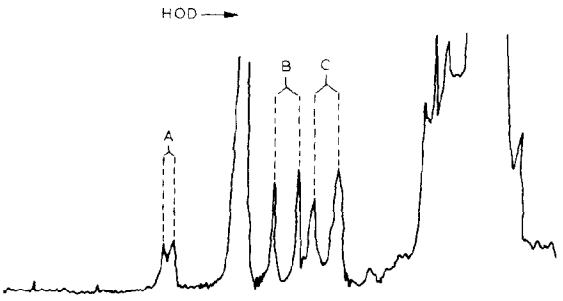


Fig. 1. A portion of the ^{1}H-n.m.r. spectrum of D-($^2H_8$)lactose in deuterium oxide at 40° in the presence of potassium carbonate: (A) H-1*e* ($J_{1,2}$ 3.0 Hz); (B) H-1*a* ($J_{1,2}$ 8.5 Hz); and (C) H-1*a'* ($J_{1,2}$ 7.5 Hz). By integration, A + B = 1 H, and C = 1 H

caused a gradual mutarotation, and the equilibrium was displaced farther in favor of the β anomer upon addition of excess potassium carbonate.

The behavior of α-($^2H_8$)lactose in deuterium oxide is indicative of an equilibration that starts upon dissolution of the sugar (Table III, Fig. 1) even in the absence of potassium carbonate. The equilibrium ratio of β to α anomer 13:7 was reached within 12 h. The results in Table IV show that the equilibrium was displaced further in favor of the β anomer upon gradual addition of potassium carbonate. Thus, the potassium ion is clearly responsible for a stabilization of the β anomer, in support of the internally chelated structure **1**.

The solution of α-($^2H_8$)lactose in di($^2H_3$)methyl sulfoxide showed no immediate appearance of an H-1*a* signal (Table V), but even in the absence of potassium carbonate the signal ratio of H*e* to H*a* changed after three days. Addition of potassium carbonate caused a gradual shift (Table I) in relative intensities of the H-1 signals and the attainment of an equilibrium of anomers that favored the β-D structure. It is noteworthy that, for the same molar ratio of potassium carbonate to lactose, the β anomer was favored to a higher degree in di($^2H_3$)methyl sulfoxide than in *N*,*N*-($^2H_7$)dimethylformamide (4:1, $\Delta G^\circ = -3.6$ kJ/mol *vs.* 16:9, $\Delta G^\circ = -1.5$ kJ/mol, respectively). This indicates that there exists an additional stabilization of the potassium–lactose complex of ΔG° −2.1 kJ/mol for a solution in dimethyl sulfoxide as compared to that in *N*,*N*-dimethylformamide. This difference could be attributed to the stronger hydrogen-bond stabilization by dimethyl sulfoxide of the internally chelated potassium complex **1**.

The appearance of the H-1*a* signal for a solution in di($^2H_3$)methyl sulfoxide after 3 days may be explained either by the unintentional anomerization of the initial α-lactose, or by the induction of a conformational equilibrium in α-lactose due to special solvation effects of dimethyl sulfoxide. Thus, for example, the appearance of an axial-anomeric-proton signal could be due to the presence of a highly solvated D-glucose-$^1C_4$ conformation in the solution of α-D-lactose in di($^2H_3$)methyl sulfoxide (**10**). Complex solvation of carbohydrates in dimethyl

TABLE VI

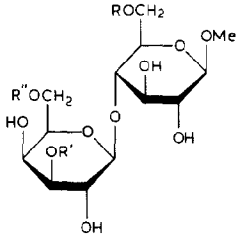
METHYL MONO- AND DI-*O*-MYRISTOYL-β-LACTOSIDE

Compound	*M.p. (degrees)*	*Yield (%)*	R_F[a]	*Analytical data*				
				Calc. for			*Found*	
				Formula	*C*	*H*	*C*	*H*
11	140–150	10	0.70	$C_{41}H_{76}O_{13}$	63.40	9.80	63.34	9.86
12	124–125	15	0.55	$C_{41}H_{76}O_{13}$	63.40	9.80	63.36	10.04
13	105–110	35	0.33	$C_{27}H_{50}O_{12}$	57.24	8.83	56.65	8.79
14	195–200	40	0.30	$C_{27}H_{50}O_{12} \cdot H_2O$	55.47	8.90	55.29	8.57

[a]Silica gel G eluted with 2:2:1 (v/v) benzene–ethyl acetate–ethanol.

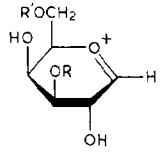
sulfoxide solution has been suggested by previous investigators[11], and the existence of nonbonded, attractive interactions between the sulfur atom of dimethyl sulfoxide and oxygen-containing groups has been proposed on the basis of studies of the self-association of dimethyl sulfoxide[12], its association with phenols[13], and its effect on the anomeric equilibrium of 5-hydroxypentanal[14].

Myristates of methyl β-lactoside. — Methyl β-lactoside[15] was converted into a mixture of two mono- and two di-myristates (**10**–**13**) upon treatment with ethyl myristate in the presence of potassium carbonate. The presence of 18-Crown-6 accelerated the reaction, but otherwise did not affect the distribution of products. The four myristates were separated by column chromatography and their relative yields, melting points, R_F values, and analyses are summarized in Table VI. The assignment of the structures of these products is discussed later. Unlike lactose itself, methyl β-lactoside does not contain a relatively acidic anomeric hydroxyl group, and steric interference of the methoxyl group may also contribute to inhibit the formation of a highly, internally chelated complex with a potassium ion.



11 R = H, R' = R'' = $C_{13}H_{27}CO$
12 R = R'' = $C_{13}H_{27}CO$, R' = H
13 R = R'' = H, R' = $C_{13}H_{27}CO$
14 R = R' = H, R'' = $C_{13}H_{27}CO$

$C_{13}H_{27}CO$ = myristoyl



15 R = $C_{13}H_{27}CO$, R' = H
16 R = H, R' = $C_{13}H_{27}CO$
17 R = R' = $C_{13}H_{27}CO$

A similar mixture of products (15% of **11**, 26% of **12**, 18% of **13**, and 41% of **14**) was obtained in the esterification that employed 1.25 equiv. of myristoyl chloride in a pyridine solution[6]. The similarity of the products obtained in the course of both esterification procedures was established by means of identical t.l.c. behavior and melting points.

The monoesters **13** and **14** were examined for possible intramolecular migration of the ester group. A solution of **12** in *N*,*N*-dimethylformamide and in the presence of a catalytic amount of potassium carbonate showed the presence of both **13** and **14**, the parent lactoside, and a trace of diester after 2 h at 80°. On the other hand, a similar treatment of **14** did not show any evidence of migration of the ester group, and a treatment for 20 h led simply to deacylation. On this basis, and in view of the results of Bhatt *et al.*[6], it is concluded that **13** and **14** are the 3′- and 6′-esters of methyl β-lactoside, respectively. This conclusion is supported by the observation that both monoesters **13** and **14** gave a fragment *m/z* 373 with nearly the same abundance (52.3 and 63.6%, respectively) in m.s. analysis. These fragments presumably correspond to the molecular ions **15** and **16**, expected to be formed in the degradation of the esters of methyl β-lactoside. Thus, the monoesters **13** and **14** are believed to be derived from the D-galactosyl group of the lactose molecule. The mass spectrum of the diester **11** revealed a fragment *m/z* 583 that corresponds to **17**. On this basis, we concluded that the structure of this diester is that of the 3′,6′-dimyristate. The diester **12** then appears to be the 6,6′-derivative of methyl β-lactoside.

The formation of esters at the 3′-, as well as the 6- and 6′-hydroxyl groups, raises the question whether substitution of the hydrogen atoms of the same three hydroxyl groups would occur also in the tritylation of methyl β-lactoside. The use of triphenylmethyl tetrafluoroborate in pyridine gave three products that were separated by column chromatography. Elementary analyses and the examination of the u.v. spectra ($A_{259\ nm}$) proved the compounds to be two monotrityl and one ditrityl derivatives. Since tritylation of secondary hydroxyl groups of carbohydrates has been observed previously[16], it is believed that tritylation of methyl β-lactoside occurs also at the 6′ and 3′ positions.

EXPERIMENTAL

General. — T.l.c. and column chromatography were performed with Silica gel G and 2:2:1 (v/v) benzene–ethyl acetate–ethanol as the eluting solvent unless specified otherwise. The ^{1}H-n.m.r. spectra were recorded with Varian A-60A and EM-360A spectrometers at 60 MHz, and chemical shifts (δ) are given relative to the signal of Me_4Si. Elemental analyses were performed by MHW Laboratories and the mass spectra recorded at the Michigan Cancer Foundation, Detroit, Michigan.

Materials. — Methyl 2,3,4,6-tetra-*O*-benzoyl-α-D-glucopyranoside (**5**) and 1,2,3,6,2′,3′,4′,6′-octa-*O*-benzoyllactose (**6**) were prepared by treating the corresponding sugar with benzoyl chloride in pyridine. The benzoates were purified until their physical constants agreed with those reported in the literature[17].

Methyl β-lactoside was prepared in 50% yield as described[15], m.p. 210–221° (lit.[15] m.p. 215–218°).

Anal. Calc. for $C_{13}H_{24}O_{11} \cdot H_2O$: C, 41.70; H, 7.00. Found: C, 41.73; H, 7.13.

Transesterification of methyl β-lactoside with ethyl myristate. — Methyl β-lactoside monohydrate (9.35 g, 25 mmol) was dissolved in a mixture of *N,N*-dimethylformamide (75 mL) and benzene (75 mL), and the solution was dehydrated by means of a Dean–Stark trap. After 3 h, the solution was cooled and the solvents were removed under diminished pressure. The anhydrous residue, dimethyl sulfoxide (200 mL), ethyl myristate (6.40 g, 25 mmol), and potassium carbonate (0.5 g) were heated at 80° and ~10 MPa for 120 h to give a mixure of two monoesters and one diester, and a 65% recovery of the initial methyl β-lactoside. Identical conditions, except for the presence of potassium methoxide (0.25 g, 4 mequiv.) and 18-Crown-6 (1.32 g, 5 mequiv.), gave the same distribution of products but the recovery of methyl β-lactoside was decreased to 58% after a reaction period of 60 h. The reaction mixtures were processed by removal of dimethyl sulfoxide under diminished pressure to give residues that were partitioned between 1-butanol (200 mL) and water (150 mL). The aqueous layer was extracted with additional 1-butanol (75 mL), and the combined extracts were washed with water (100 mL). The 1-butanol layer was evaporated to leave a thick residue that was separated into four compounds (**11**–**14**) by column chromatography. The aqueous layer was evaporated to recover methyl β-lactoside. Compounds **11** (R_F 0.70) and **12** (R_F 0.55) were crystallized from ethyl acetate. Compound **13** (R_F 0.33) was a glassy material which did not crystallize, and **14** (R_F 0.30) crystallized from ethyl acetate–methanol. The physical properties, elemental analyses, and distribution of the products are summarized in Table VI. Compounds **11**, **12**, and **13**, **14** correspond to the di- and mono-myristates of lactose, respectively.

Monoacylation of methyl β-lactoside with myristoyl chloride. — Methyl β-lactoside monohydrate (7.1 g, 20 mmol) was dissolved in pyridine (200 mL) and the solution distilled at atmospheric pressure until 75 mL of distillate had been collected. The solution was cooled to 0° and myristoyl chloride (6.17 g, 25 mmol) added dropwise to the cooled, stirred solution. T.l.c. examination after 15 h at room temperature indicated the presence of four predominant spots at R_F 0.30, 0.33, 0.55, and 0.70. These spots corresponded to those given by the products of the preceding esterification. Pyridine was removed *in vacuo* and the solid residue partitioned between 1-butanol (300 mL) and 5% aqueous sodium chloride solution (200 mL). The aqueous layer was extracted with additional 1-butanol (50 mL), and the combined 1-butanol layers were washed with salt solution (150 mL) and then evaporated *in vacuo* to leave 11.6 g of a glassy material. A 7-g portion of this material was subjected to column chromatography to give **11** (and traces of higher esters) (1.63 g, 8%); pure **12** (1.05 g, 15%); pure **13** (2.90 g, 41%); and pure **14** (1.35 g, 18%). These products were identical with those obtained *via* transesterification and shown in Table VI.

Attempted equilibration of methyl 3'-O-myristoyl-β-lactoside (**13**) *and methyl 6'-O-myristoyl-β-lactoside* (**14**). — (*a*) Potassium methoxide (10 mg) was added to a solution of **13** (50 mg) in *N,N*-dimethylformamide (5 mL) and the mixture placed in an oil bath set at 80°. The progress of the reaction was followed by t.l.c. at 1, 2, 3, and 20 h. T.l.c. indicated the presence of three major spots corresponding to **13**, **14**, and methyl β-lactoside after 1 h. After 20 h, **13** had been completely de-esterified and only methyl β-lactoside was detected.

(*b*) The monoester **14** was treated as described for **13**. No ester migration was detected after 3 h and only methyl β-lactoside was observed to be present in addition to **14**. After 20 h, complete de-esterification had taken place to give methyl β-lactoside.

Tritylation of methyl β-lactoside. — A solution of methyl β-lactoside monohydrate (3.74 g, 10 mmol) in dry pyridine (150 mL) was heated and distilled at atmospheric pressure until 70 mL of distillate had been collected. The remaining solution was cooled (5°), triphenylmethyl tetrafluoroborate (4.95 g, 15 mmol) was added and the mixture was stirred for 29 h at ambient temperature. Pyridine was removed *in vacuo* and the solid residue equilibrated between 1-butanol (250 mL) and water (150 mL). The water layer was extracted with additional 1-butanol (50 mL) and the combined butanol layers were washed with 10% sodium chloride solution (100 mL) and evaporated *in vacuo* at 40–45° to leave 6.5 g of a solid material. A portion of this material (0.50 g) was separated by column chromatography on Silica gel G (50 g). Elution with benzene (250 mL) gave tritanol (0.10 g) followed by methyl di-*O*-trityl-β-lactoside (0.19 g, R_F 0.35) as a monohydrate, a methyl mono-*O*-trityl-β-lactoside (**A**, 0.12 g, R_F 0.13, m.p. 130–135°) as a dihydrate, and finally another methyl mono-*O*-trityl-β-lactoside (**B**, 0.06 g, R_F 0.06, m.p. 100–105°) as a dihydrate.

Anal. Calc. for $C_{32}H_{38}O_{11} \cdot 2\ H_2O$ (methyl mono-*O*-trityl-β-lactoside): C, 60.57; H, 6.62. Found (**A**): C, 60.40; H, 6.31. Found (**B**): C, 60.22; H, 6.62.

Anal. Calc. for $C_{51}H_{52}O_{11} \cdot H_2O$ (methyl di-*O*-trityl-β-lactoside): C, 71.32; H, 6.30. Found: C, 71.26; H, 6.34.

*Preparation of α-*D*-($^2H_8$)lactose.* — α-Lactose was converted to α-D-($^2H_8$)lactose by repeated precipitation with 2-butanone from a solution in dimethyl sulfoxide and deuterium oxide. The mutarotation of α-($^2H_8$)lactose in the presence of potassium carbonate was followed by ^{1}H-n.m.r.

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